

STUDIES IN THE DIBENZOBIPHENYLENE SERIES

by

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TO JULIE  
AND MY PARENTS

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## SUMMARY

1. The photodimer bis-cinnamylidenemalonic acid under the catalytic oxidative conditions of Lemieux-Johnson gave 2,4-diphenylcyclobutane-1,3-dialdehyde ( $\alpha$ -truxaldehyde). The Lemieux and Rudloff method however did not give the expected  $\alpha$ -truxillic acid.
2. Intramolecular ring closure of 1,3-diphenylcyclobutane-2,4-diacetic acid gave a diketone which could not be aromatized by oxidation to 5,11-dihydroxydibenzo[a,g]biphenylene. Reduction of the diketone gave 5:6:6a:6b:11:12:12a:12b-octahydro-5,11-dihydroxybenzo[a,g]biphenylene. Naphthalene was obtained as the product of dehydration. Reduction of the diketone to 5:6:6a:6b:11:12:12a:12b-octahydrodibenzo[a,g]biphenylene by the method of Caglioti failed to give the expected product.
3. Solid-state photodimerization of styrylacetic acid did not give a photodimer.
4.  $\beta$ -Phenylacetylnaphthalene gave in the Reformatsky reaction, ethyl 3-hydroxy-3-(2-naphthyl)-4-phenylbutyrate, which in turn gave 3-(2-naphthyl)-4-phenylbutyric acid. Other routes via Wittig intermediates also proved successful. Intramolecular ring closure of the carboxylic acid gave 1-benzyl-4,5-benzindan-3-one. The oximino derivative gave the corresponding diazoketone which, upon irradiation, ring contracted to give 2-benzylneptho[a]cyclobutene carboxylic acid. Ring closure to the dibenzo[a,h]biphenylene structure could not be accomplished by the usual methods.

5. 3-Hydroxy-3-(2-naphthyl)-4-phenylbutyric acid underwent what was shown to be a concerted d hydration-decarboxylation reaction to give a rearranged product,  $\beta$ -methyl- $\beta$ -(2-naphthyl)styrene.
6. The reactivity of some 1- and 2-naphthyl ketones was compared with respect to Grignard and Wittig reagents.
7. Generation of 1-iodobenzocyclobutadiene gave on dimerization 5-iodobenzo[a]biphenylene, the lithio derivative of which gave 4-(5-benzo[a]biphenylenyl)-4-oxobutyric acid. The preparation of dibenzo[a,c]biphenylene was discontinued at this point.

## CONTENTS

	<u>Page</u>	<u>Experimental</u>
ACKNOWLEDGEMENTS		
SUMMARY		
INTRODUCTION	1	
OBJECT OF RESEARCH	43	
<u>DISCUSSION</u>		
<u>SECTION I</u>	44	
Introduction to Section I	45	
1.1 Photodimerization of Cinnamylidenemalonic acid	48	118
1.2 Lemieux reagents	49	119
1.3 Heterogeneous and homogeneous catalysis	53	122
1.4 Dibenz[a,g]biphenylene structure	55	125
1.5 Oxidation and aromatization	55	125
1.6 Reduction and aromatization	56	126
1.7 Dibenz[a,g]biphenylene	58	127
1.8 Photodimerization of Cinnamylideneacetic acid and styrylacetic acid	61	129
1.9 Conclusion to Section I.		
<u>SECTION II</u>	64	
Introduction to Section II	65	
<u>Part I</u>		
2.1 Ring contraction of cyclopentenone derivatives	67	
2.2 Tetralin acylation	68	133
2.3 Friedel-Crafts acylation of naphthalene	70	134
2.4 The Reformatsky reaction	71	135
2.5 The Wittig reaction	74	140
2.6 Catalytic hydrogenation	81	144
2.7 Ring closure	82	146
2.8 Oximino- and diazoketones	87	149
2.9 Ring contraction of the cyclopentenone ring	91	152
2.10 The dibenz[a,h]biphenylene structure	93	153
Conclusion to Part I	96	

	<u>Page</u>	<u>Experimental</u>
<u>Part II</u>		
2.11 Dehydration reaction	98	156
2.12 Fragmentation reactions	99	157
2.13 1- and 2-Naphthyl ketones	103	157
<u>SECTION III</u>		
Introduction to Section III	108	
3.1 1,2-Diiodobenzocyclobutene	110	162
3.2 Dimerization of 1-iodobenzocyclobutadiene	110	162
3.3 Chain extension	111	163
Conclusion to Section III	114	
<u>EXPERIMENTAL</u>		
Introduction to Experimental Section	115	
Section I	117	
Section II	132	
Section III	161	
BIBLIOGRAPHY	168	

## ACKNOWLEDGEMENTS

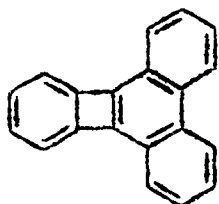
I have pleasure in recording my sincere thanks to Professor Neil Campbell for his guidance and encouragement throughout the period of this work.

My thanks are also due to Professor Sir Edmund L. Hirst and Professor J.I.G. Cadogan for the provision of laboratory and library facilities, and to the Science Research Council for the award of a maintenance grant.

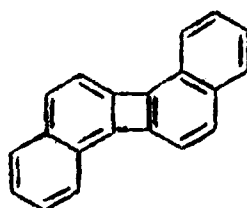


INTRODUCTION

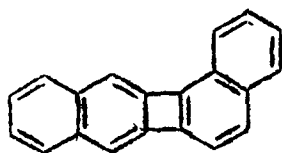
The dibenzobiphenylenes form the greater part of a group of compounds derived from biphenylene by benzene annellation, the benzobiphenylenes. Two monobenzo- and five dibenzobiphenylenes are possible, all of which are known. Similarly two tribenzo- and one tetrabenzobiphenylene may be written, but none of these has yet been prepared.



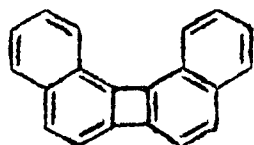
Dibenzo[a,c]biphenylene



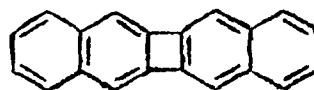
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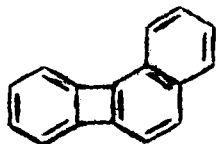
Dibenzo[a,h]biphenylene



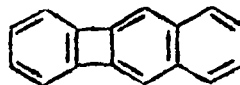
Dibenzo[a,i]biphenylene



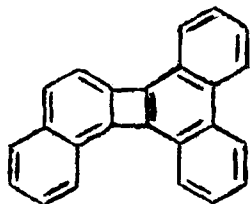
Dibenzo[b,h]biphenylene



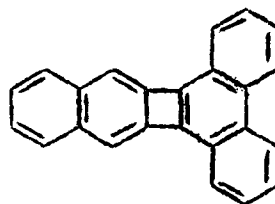
Benzo[a]biphenylene



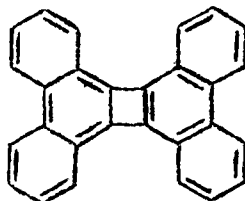
Benzo[b]biphenylene



Tribenzo[a,c,g]biphenylene



Tribenzo[a,c,h]biphenylene

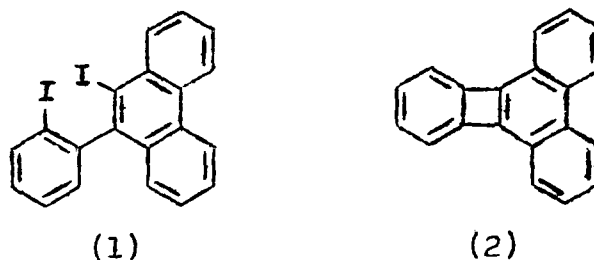


Tetrabenzo[a,c,g,i]biphenylene

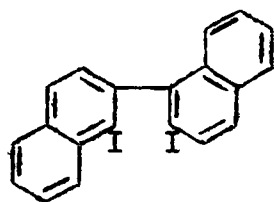
For the most part, the methods used to synthesise the benzo- and the dibenzobiphenylenes are merely extensions of those found to be successful in the preparation of biphenylene itself. With a few notable exceptions, in the dibenzobiphenylene series the two aromatic halves are joined together, the formation of the four-membered ring being the final stage in the synthesis. Two main

types of ring-formation reactions are involved, the dimerization of 1,2- and 2,3-naphthylene intermediates and the formation of the second linking bond from substituted binaphthyls. Lothrop's synthesis of biphenylene,<sup>1</sup> by heating 2,2'-dihalobiphenyls with cuprous oxide ( $\text{Cu}_2\text{O}$ ) has been made use of, and can be regarded as an example of the latter method. A case in point is the synthesis of dibenzo[a,c]biphenylene.

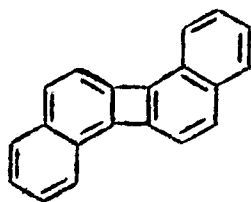
Dibenzo[a,c]biphenylene



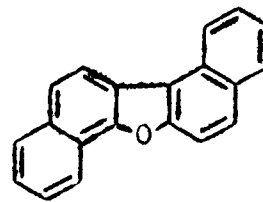
In a reaction directly analogous to the Lothrop synthesis of biphenylene, 9-iodo-10-(2'-iodophenyl)phenanthrene (1) was pyrolysed at  $240\text{-}340^\circ$  with cuprous oxide to give the [a,c]-isomer (2) in approximately 20% yield.<sup>2</sup> Isolated as its purple 2,4,7-trinitrofluorenone complex m.p.  $213\text{-}215^\circ$ , the free hydrocarbon (2) is generated by decomposition of the complex on an alumina column as orange-red needles m.p.  $183\text{-}184^\circ$  (decomp.)

Dibenzo[a,g]biphenylene

(3)



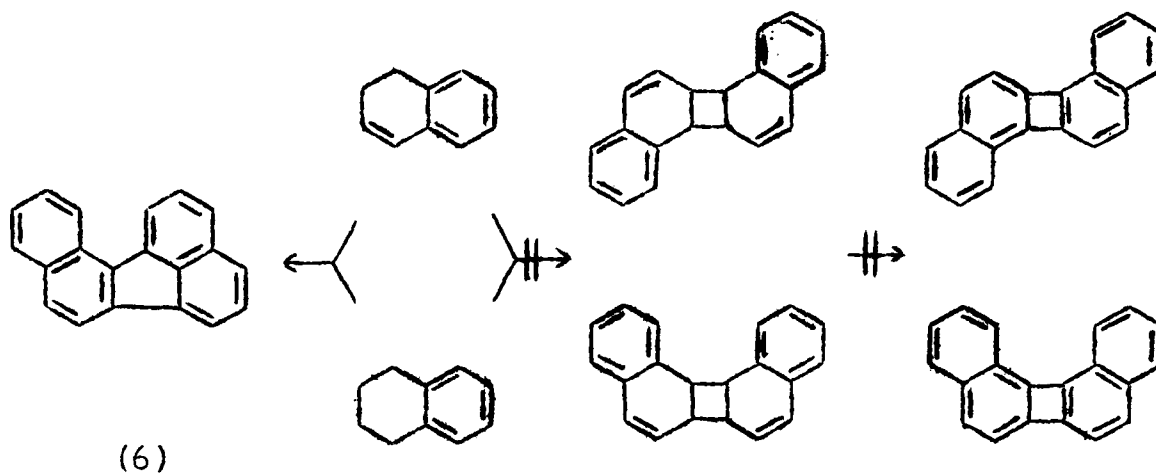
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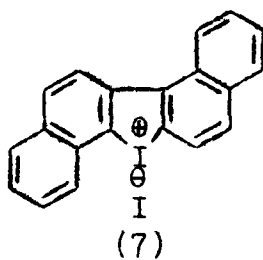
(5)

As with the [a,c]-isomer, dibenzo[a,g]biphenylene (4) was obtained in approximately 10% yield<sup>3</sup> by pyrolysis with cuprous oxide of 1',2-diodo-1,2'-binaphthyl (3) as orange-red plates m.p. 146-147.5° (decomp.). The 2,4,7-trinitrofluorenone derivative of (4) forms dark green needles m.p. 224°-225° and the hydrocarbon (4) is best stored in this form. Varying amounts of dinaphtho[1,2-b:1',2'-d]furan (5) were also obtained.

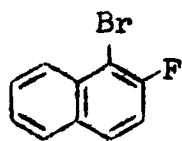
Prior to this, several unsuccessful attempts had been made to synthesise either the [a,g] or the [a,i] isomer, the first claim of the synthesis of any dibenzobiphenylene coming from Braun and Kirschbaum.<sup>4</sup> According to these authors, 1,2-dihydronaphthalene underwent dimerization in the presence of sulphuric acid to give a hydrocarbon which was said to be either dibenzo[a,g]- or dibenzo[a,i]biphenylene. The same compound C<sub>20</sub>H<sub>12</sub>, m.p. 165° was obtained by Dansi and Ferri<sup>5</sup> by treating tetralin with aluminium chloride. These claims were invalidated by Orchin and Reggel<sup>6</sup> who established the structure of the hydrocarbon to be benzo[j]fluorathene (6).



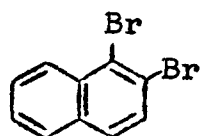
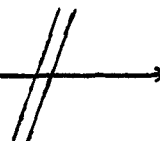
In contrast to Barton's successful synthesis, albeit in low yield, the Lothrop method in the hands of Ward and Pearson<sup>7</sup> using dinaphtho[1,2-b:1',2'-d]iodonium iodide (7) failed to give any of the expected dibenzo[a,g]biphenylene (4) product.



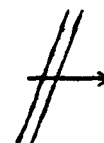
The same lack of success attended the attempted dimerization of 1,2-naphthalynes generated from 1,2-dihalonaphthalenes.<sup>8</sup>



(1) Li amalgam/ether  
 (2) Li amalgam/T.H.F.



(1) copper-double Ullmann  
 (2) naphthalene/ $\text{AlCl}_3$ -Friedel Crafts  
 (3) K or Na in ether or T.H.F.

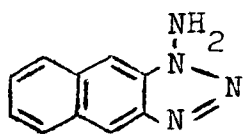


A hydrocarbon product, obtained from the reaction of 1-bromo-2-iodonaphthalene with magnesium in ether, by Ward and Pearson,<sup>9</sup> m.p.  $271^\circ$ , whose ultra-violet spectrum suggested that it might indeed be dibenzo[a,g]biphenylene (4) was proved otherwise as it was not identical with the authentic compound obtained by Barton.<sup>10</sup>

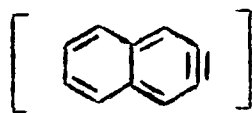
The [a,g]isomer was finally obtained from a 1,2-naphthyne (17) intermediate, again by Barton,<sup>10</sup> in 1967. Oxidation of 1-amino-1H-naphtho[1,2-d]triazole (9) with lead tetra-acetate gave a mixture of [a,g] and [a,i] isomers in 30% and 13% yields respectively.

### Dibenzo[a,h]biphenylene

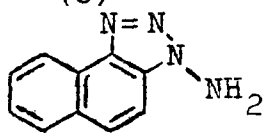
Bright yellow leaflets m.pt.  $164-165^\circ$



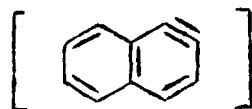
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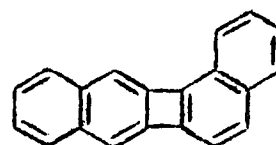
(16)



(9)

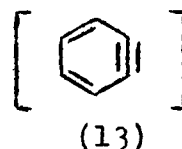
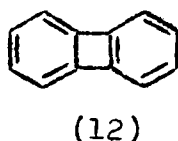
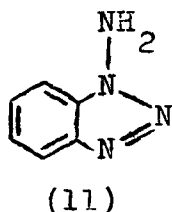


(17)



(10)

The generation of a benzyne intermediate under mild conditions by the action of lead-tetra-acetate on 1-aminobenzotriazole (11) was first exploited by Campbell and Rees.<sup>11</sup>



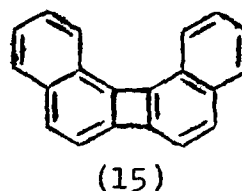
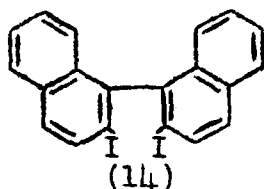
Oxidation of the triazole gave the benzyne intermediate (13) which, in the absence of benzyne "acceptors", dimerized to give high yields of biphenylene (12), approximately 80%.

Applying this method to the naphthalene series, Barton and Jones<sup>10</sup> were able to prepare a number of mono- and dibenzo-biphenylenes in good yields; in the case of dibenzo[b,h]biphenylene the yield was as high as 75%. Making use of "crossed" aryne reactions, these authors successfully synthesized, in satisfactory yields, benzo[a]-, benzo[b]-, dibenzo[a,g]-, dibenzp[a,i]-, dibenzo[b,h]- and dibenzo[a,h]biphenylene.

From oxidation of an equimolar mixture of 1-amino-1H-naphtho[2,3-d]triazole (8) and 1-amino-1H-naphtho[1,2-d]triazole (9), dibenzo[a,h]biphenylene was obtained in 38% yield, the reaction proceeding via a 2,3-naphthyne (16) and a 1,2-naphthyne (17) generated from the respective triazoles.

The [a,h] isomer was the last of the five isomeric dibenzobiphenylenes to be synthesised, the other four having already been prepared.

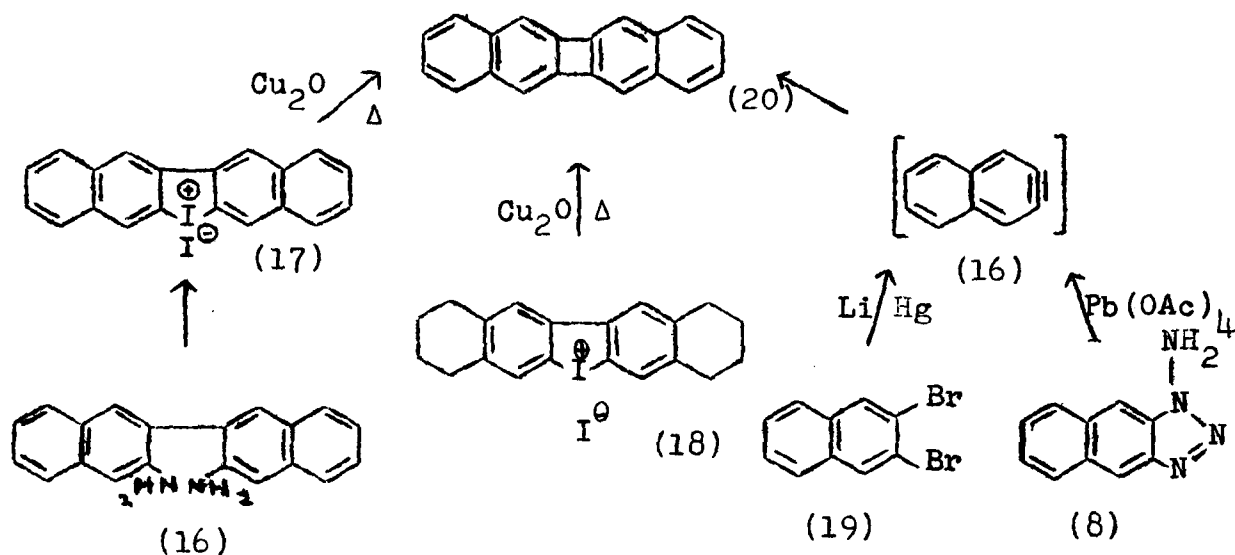


Dibenzo[a,i]biphenylene

Until quite recently, the only successful method in the synthesis of dibenzo[a,i] biphenylene (15) was that of Lothrop. In a series of 70 experiments based on 2,2'-diiodo-1,1'-binaphthyl (14), Cava and Stucker<sup>12</sup> reported an average yield of 5.65%.

This yield has been more than doubled in Barton's<sup>10</sup> 1,2-naphthylene (17) dimerization reaction, where the intermediate was generated from 1-amino-1H-naphtho[1,2-d]triazole (9) and gave as product, a mixture of dibenzo[a,i]- (13%) and dibenzo[a,g]-biphenylene (30%).

Dibenzo[a,i]biphenylene forms deep red needles m.p. 136.8 - 138.9° (decomp.) which are thermally unstable, the compound being best isolated and stored as its dark purple 2,4,7-trinitrofluorenone complex.

Dibenzo[b,h]biphenylene

Pale yellow plates m.pt.  $376 \pm 2^\circ$ , sublimes unchanged  
 $340-345^\circ$ .

The linear isomer (20) is much the most stable of the five dibenzobiphenylenes and resembles the parent compound, biphenylene, more than do the angularly annellated isomers. Not surprisingly, it was the first dibenzobiphenylene to be prepared and the majority of work done in this field has been concerned with compounds having the "linear" carbon skeleton. The methods of synthesis are similar to those used for the angular isomers, the methods often being extended from the linear to the angular case, with varying success. However, there are some routes which are unique to the linear isomer which could not be applied to the angular.

The first successful synthesis of a dibenzobiphenylene was reported by Curtis and Viswanath<sup>13</sup> who obtained the iodonium iodide via the diazotization of 3,3'-diamino-2,2'-binaphthyl (16) and

subsequent treatment of the resulting bis (diazonium) salt with sodium iodide. Pyrolysis of the crude iodonium iodide with cuprous oxide gave dibenzo[b,h]biphenylene in 3% yield. Rather unexpectedly, it was also obtained from 1,2,3,4,8,9,10,11-octahydro-naphth[2,3-b:2',3'-d]iodonium iodide (18) by Ward and Pearson.<sup>9</sup>

Initial attempts at dehalogenation of 2,3-dibromonaphthalene with lithium amalgam in ether,<sup>14</sup> and of 2-bromo-3-iodonaphthalene with copper bronze in dimethyl formamide<sup>8</sup> gave yields of 0.2% and 0.9% respectively. The dimerization of the 2,3-naphthyne intermediate was finally efficiently carried out by Barton<sup>10</sup> who obtained a yield of 75%.

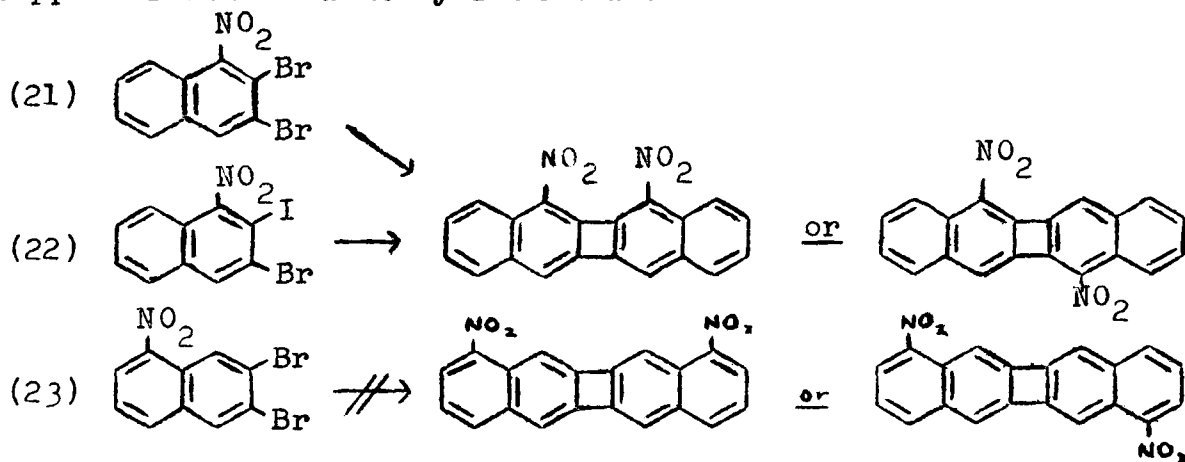
The generation of benzyne and to some extent naphthyne intermediates in the formation of, for the most part, substituted biphenylenes and dibenzobiphenylenes by the pyrolytic fragmentation of a heterocyclic ring has been studied extensively.<sup>15</sup> This work is comparable to the chemical fragmentation of a heterocyclic ring that has already been demonstrated.

#### Substituted Dibenzo[b,h]biphenylenes

The direct introduction of a substituent into a dibenzobiphenylene nucleus has not been reported; the site of maximum reactivity in [b,h] has been predicted to be the 5-position.<sup>16</sup> The only substituted dibenzobiphenylenes known belong to this type of compound. In some cases this is a direct result of unique synthetic methods which cannot be used for the angular isomers. In all cases synthesis, not substitution gives the product.

Ullmann. Although it is seldom the case that o-dihaloaryls will give biphenylenes or benzobiphenylene, under the conditions of the Ullmann reaction, it has been shown that 2-bromo-3-iodonaphthalene does give dibenzo[b,h]biphenylene in very low yield. The reaction probably proceeds via a 2,3-naphthalene intermediate (16).

Similarly Ward and Marriott<sup>14</sup> obtained what they consider to be a dinitrodibenzobiphenylene by refluxing 2,3-dibromo-1-nitronaphthalene (21) or 3-bromo-2-iodo-1-nitronaphthalene (22) with copper bronze in dimethylformamide.

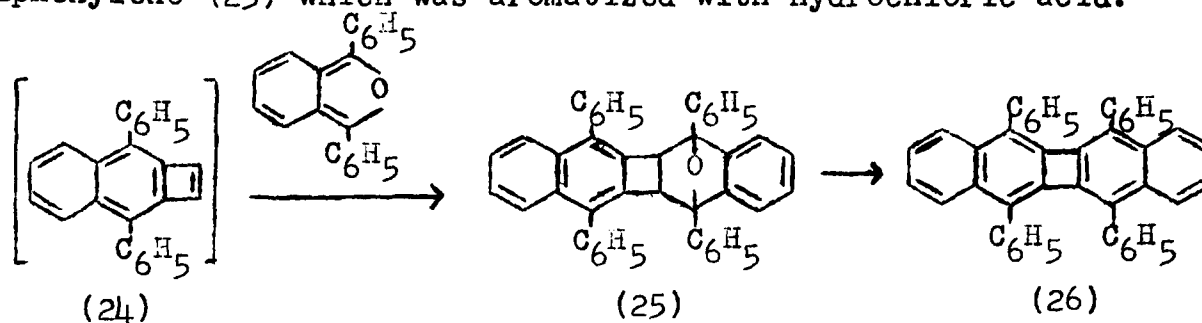


Under the same conditions 2,3-dibromo-5-nitronaphthalene (23) failed to give any dinitrodibenzobiphenylene.

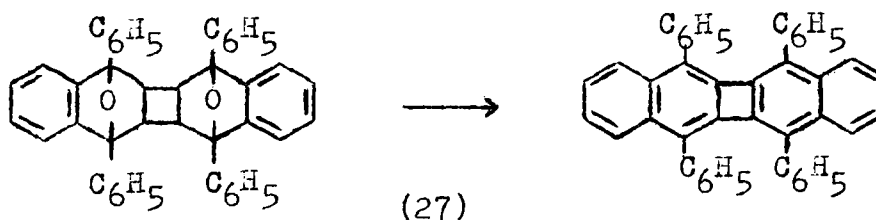
### Naphthocyclobutadiene

Starting from the adduct of cyclooctatetraene and dimethyl acetylenedicarboxylate and following an extensive reaction sequence, which involved 3,8-diphenylnaphtho[b]cyclobutadiene (24) as an intermediate, 5,6,11,12-tetraphenyldibenzo[b,h]biphenylene (26) was obtained in good yield. Generated in the presence of diphenylisobenzofuran the naphthocyclobutadiene was trapped giving

5,6,11,12-tetraphenyl-5,12-oxa-5,5a,11b,12-tetrahydrodibenzo[b,h]-biphenylene (25) which was aromatized with hydrochloric acid.<sup>14</sup>



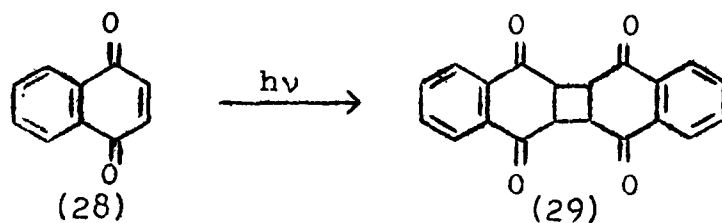
The same tetraphenyldibenzobiphenylene was obtained by Avram *et al.*<sup>17</sup> both from compound (25) and from 5,6,11,12-tetraphenyl-5,12;6,11-dioxa-5,5a,6,11,11a,11b,12-octahydrodibenzo[b,h]-biphenylene (27) by dehydration.



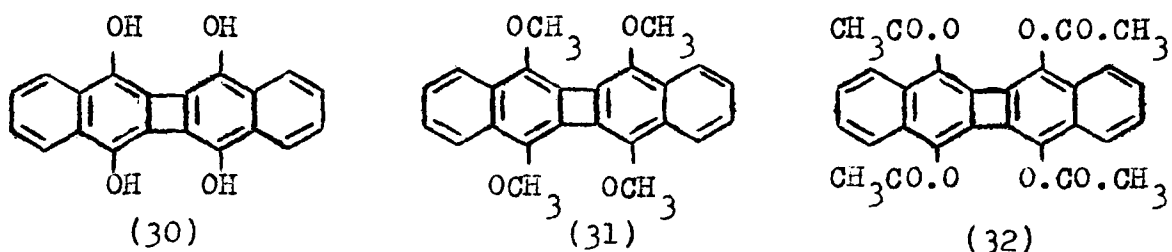
### Dimerization

Although several dibenzobiphenylenes have been prepared by dimerization of naphthalene intermediates, it is only in the case of [b,h] derivatives that dimerization of an olefinic bond, followed by reduction of the cyclobutane ring, has afforded dibenzobiphenylenes.

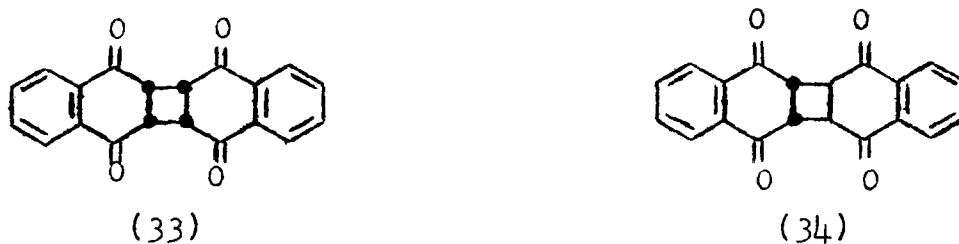
The initial step in all reactions of this type is the photodimerization<sup>18</sup> of 1,4-naphthoquinone (28).



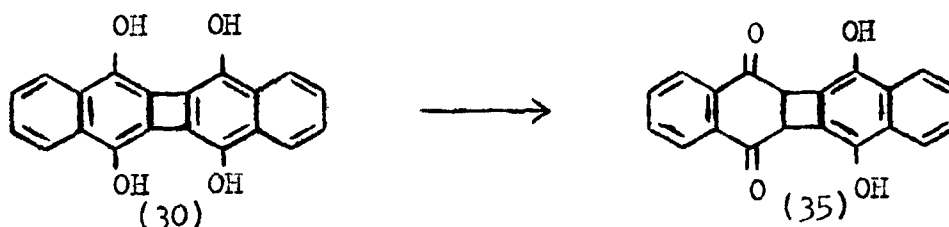
The photodimer underwent base-catalyzed isomerization to give 5,6,11,12-tetrahydroxydibenzo[b,h]biphenylene (30) and also gave the 5,6,11,12-tetramethoxy- (31) and the 5,6,11,12-tetraacetoxy- (32) compounds.



Following the initial work done by Bruce, Dekker *et al.*<sup>19</sup> studied the stereochemistry of the photodimers of some  $\alpha,\beta$ -unsaturated carboxylic compounds. In the case of trans-benzalacetone, they showed the solid-state photodimerization proceeded in a head-to-tail fashion producing photodimers of the  $\alpha$ -truxillic type. In the case of 1,4-naphthoquinone, syn- (33) and anti- (34) dimers were possible, and the latter, the more stable of the two, was shown to be formed.

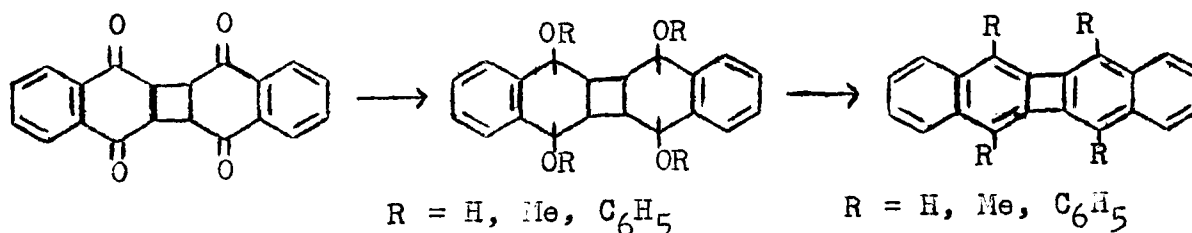


Further work by Dekker<sup>20</sup> showed the aromatized enol-form to undergo spontaneous ketonization to the cyclobutene (35) in neutral media, in direct contrast to what would be expected by analogy with aromatic chemistry in general.



In acidic solution an equilibrium is established between (34) and (35) in the ratio 1:3, a situation that is also obtained from the syn-isomer in the same conditions.

Although the photodimer and the 5,6,11,12-tetrahydroxy-compound had been known for some time, it was some years before the parent was synthesized by this route.<sup>21</sup>



This high yield photodimerization seems an obvious route to dibenzo-[b,h]biphenylenes and several 5,6,11,12-tetrasubstituted compounds have been synthesized, including those above, by this method. The carbon skeleton is built up in one step although full use of this has only recently been exploited.

Both monobenzophenylenes have been prepared and, as they represent the half-way stage between biphenylene and the dibenzobiphenylenes, stepwise comparisons between the three types of compound can be drawn.

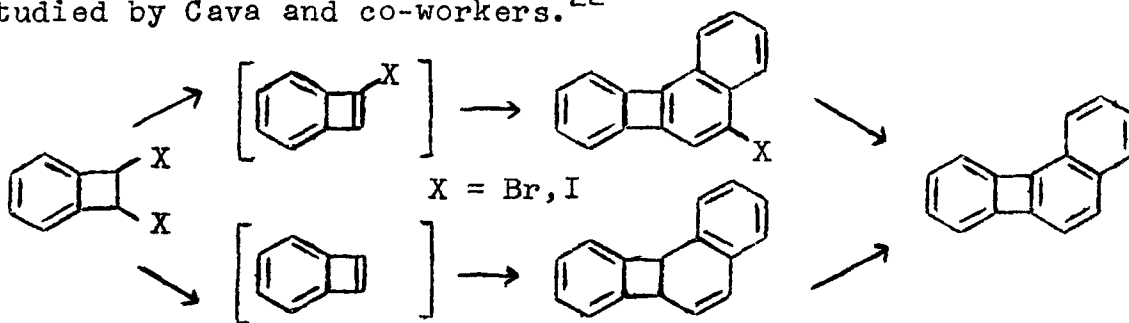
As with the dibenzobiphenylenes, the introduction of a substituent into either of the monobenzobiphenylenes has not been reported and no predictions as to the sites of maximum reactivity have been made. The few derivatives known are substituted in the 5- or 5,6-positions of the [a] isomer and in the 5,10-positions of the [b] isomer, both as a direct result of their mode of formation.

Although Lothrop's method has proven successful in the synthesis of benzo[a]biphenylene,<sup>13</sup> and Barton's triazole, crossed aryne reactions<sup>10</sup> have yielded both benzo[a]- and benzo[b]-biphenylene in 36% and 65% yield respectively, it is again the dimerization of reactive intermediates that has been most successful in their synthesis.

### Benzo[a]biphenylene

First synthesised by Cava and Stucker<sup>12</sup> as bright yellow needles m.p. 72-72.8°, again best isolated and purified as its sparingly soluble, black, 2,4,7-trinitrofluorenone derivative m.p. 201.5°-202.5°.

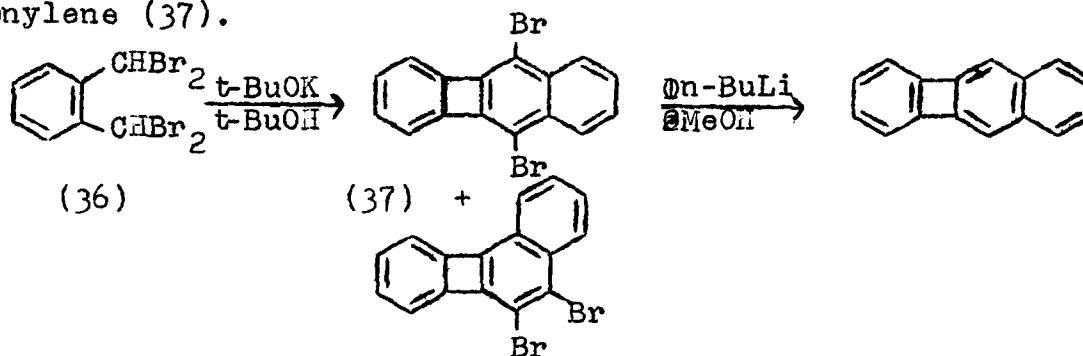
The parent compound, and its 5- or 5,6-substituted derivatives are most readily obtained as the dimerization products of benzocyclobutadienes. These reactions have been fully studied by Cava and co-workers.<sup>22</sup>



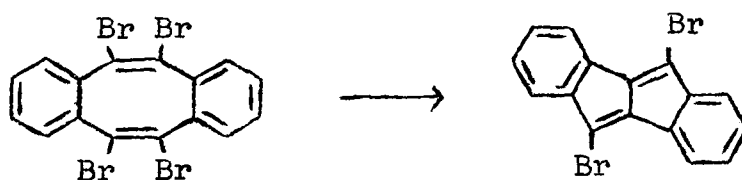


Benzo[b]diphenylene

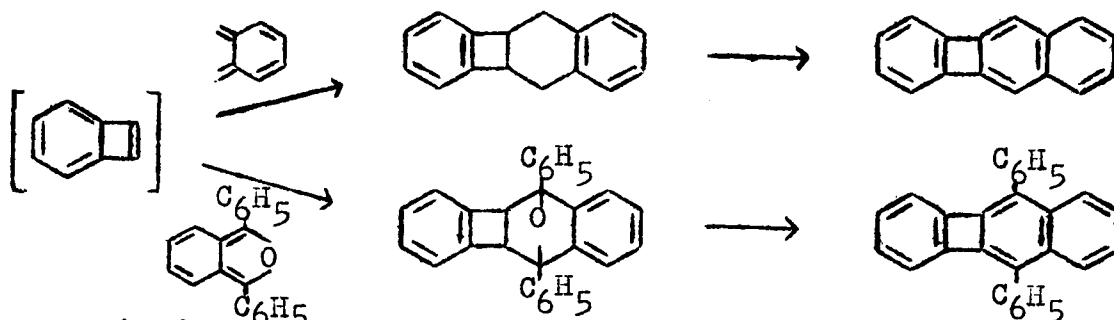
More stable than the angular isomer, benzo[b]biphenylene<sup>23</sup> is a pale yellow crystalline compound m.p. 242.6-243.2°, forming a red 2,4,7-trinitrofluorenone complex m.p. 214-216°. It is prepared in good yield from an unusual transformation of  $\alpha,\alpha,\alpha',\alpha'$ -tetrabromo-o-xylene (36) via 5,10-dibromobenzo[b]-biphenylene (37).



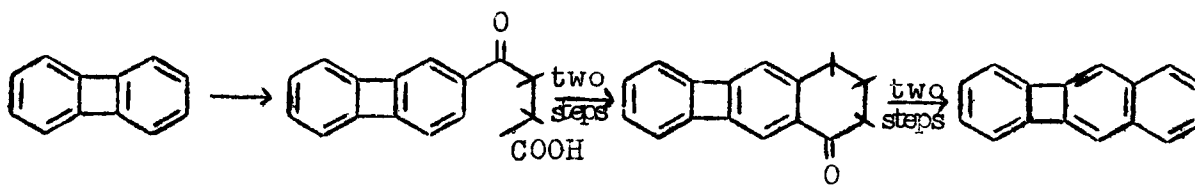
This reaction was originally reported as proceeding via tetrabromodibenzocyclooctatetraene (38) but synthesis of this compound has shown that on heating it gives 5,10-dibromoindeno-[2,1-a]indene.<sup>24</sup>



Two reactions<sup>25,26</sup> involving benzocyclobutadiene has given benzo[b]biphenylenes.

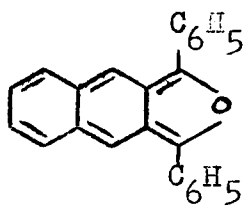


An interesting sequence of reactions built a fourth ring onto the biphenylene nucleus to give benzo[b]biphenylene.<sup>27</sup> This is a direct parallel to the multi-stage preparation of naphthalene from benzene.

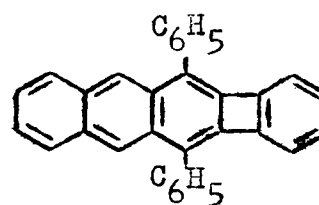


### Other Benzobiphenylenes

Only one higher analogy is known, 5,12-diphenyl-naphtho[2,3-b]biphenylene (38), obtained in the same manner as 5,10-diphenylbenzo[b]biphenylene by trapping benzocyclobutadiene, in this case with 1,3-diphenylnaphtho[2,3-c]furan (39).



(39)



(38)

The interest and importance of biphenylene compounds lie in the fact that they contain a cyclobutadiene-like ring in a stable, and in the case of biphenylene itself, an aromatic environment. Explanation of this stability can only be found in consideration of and reflection on the properties of cyclobutadiene itself and cyclobutadiene chemistry in general. Extrapolation from the monocyclic case to that of the dibenzobiphenylenes can then be seen to predict the observed properties of these compounds. So extensive is the work done recently on cyclobutadiene-related compounds that it can be treated separately, divorced from other four-membered ring, cyclobutane and cyclobutene, chemistry. It shall be seen, on comparison of the five isomeric dibenzobiphenylenes, that their chemical and physical properties stem from, and can be related directly to the central four-membered ring and on its cyclobutadienoid character.

### Historical Background

Cyclobutadiene is the first member of the "annulene" series of monocyclic hydrocarbons formally made up of alternating single and double bonds<sup>28</sup> and having the general formula  $(C_2H_2)_n$ . After Kekulé's suggested benzene formula,<sup>29</sup> put forward in 1865, it was the simplest neutral molecule which could conceivably possess aromaticity. As early as 1894, an attempt to synthesise cyclobutadiene itself was made by Perkin and his lack of success was to be experienced by many workers during more than seventy years.

Although Wilstätter likewise failed in 1905, he at least had the satisfaction of preparing cyclooctatetraene, the third member of the series, in 1911. At this time, before the development of molecular orbital theory, it was quite naturally assumed that cyclobutadiene would be a stable aromatic system with a chemistry paralleling that of benzene.

Hückel's rules,<sup>30</sup> expounded in 1931, predicted that cyclobutadiene and cyclooctatetraene, systems containing  $4n$   $\pi$ -electrons, would not possess the aromatic properties associated with compounds, such as benzene, having  $(4n + 2)$   $\pi$ -electrons. Study of the properties of cyclooctatetraene by Raphael<sup>31</sup> in 1959 showed it to be a non-planar cyclic polyene, confirming Hückel's theory. Unfortunately, cyclobutadiene proved more elusive and although there was evidence of it as a transient intermediate<sup>32</sup> in various reactions, it was not until 1965 that Watts, Fitzpatrick and Pettit<sup>33</sup> obtained the free compound as an extremely reactive diene, dimerizing on formation in the absence of trapping reagents.

Prior to this date, as a consequence of the inability to obtain a cyclobutadiene, extensive research developed around the cyclobutadiene metal complexes and compounds containing cyclobutadiene-like ring systems, such as biphenylene. Interest in this latter field began with the synthesis of biphenylene by Lothrop<sup>1</sup> in 1941 which was then the only "stable derivative" known. A great deal of information has been amassed on this single compound and it has been studied by a variety of physical methods including X-ray

crystallography. Of particular interest was the distribution of electron density in the three rings which could explain the surprising stability and the chemical reactions of biphenylene. (Review by Baker and McOmie<sup>31</sup>, and Cava<sup>34</sup>).

In consideration of the dibenzobiphenylenes, just as there are marked differences between benzene and naphthalene or higher analogues, so, in this series, a distinction can be seen. Unlike the symmetrical "aromatic sextet" of benzene,<sup>35</sup> the electron distribution in other fused-ring aromatic hydrocarbons cannot be represented accurately by the Armit and Robinson "circle" formulae.<sup>36</sup> In the latter case, some bonds are of much higher bond order than others, e.g. the 9,10-bond of phenanthrene, and the chemistry of these compounds can often be based on this unsymmetrical distribution. This effect is much more important in the dibenzobiphenylenes due to the presence of the cyclobutadienoid ring and hence the parent dibenzobiphenylenes differ appreciably from biphenylene itself in physical properties, the chemistry being for the most part unknown at this time.

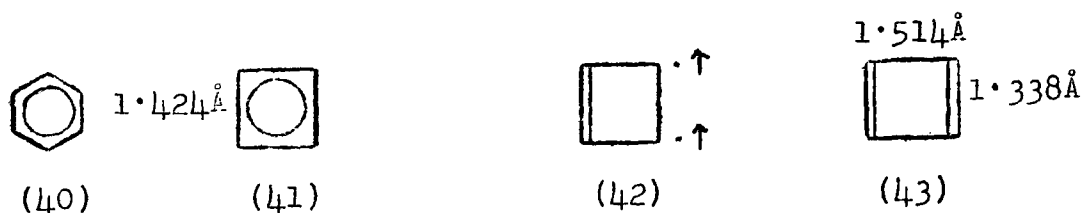
Although recent research stems from Lothrop's synthesis of biphenylene, he was not the first to obtain a compound of this type, and no introduction to this subject would be complete without mention of the work carried out by H. Finkelstein<sup>37</sup> in Strasbourg in 1909. The first preparation of a benzocyclobutene and of a benzobiphenylene was reported in the Doctoral dissertation of Hans Finkelstein, a pupil of J. Thiele. Unheeded until 1957,

credit only came, fifty years after the work had been carried out, with the publication of the first part of the late Dr. Finkelstein's thesis in 1959 by Baker and McOmie in the *Chemische Berichte*<sup>37</sup> for that year. Authenticated by Cava and Stucker,<sup>22</sup> this anticipated by thirty-two years the preparation of biphenylene.

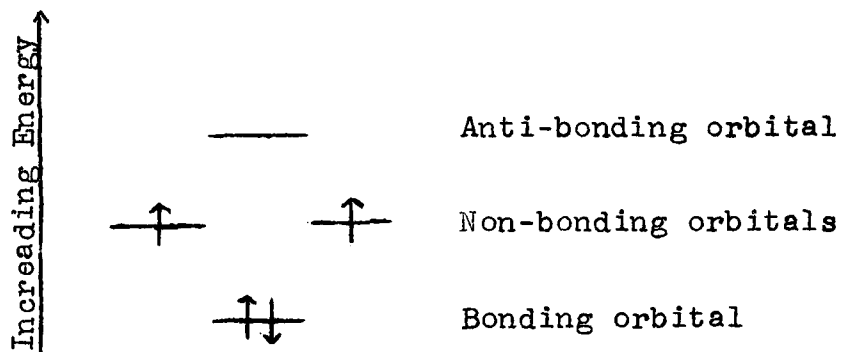
Electronic Factors Influencing the Stability of and the Chemistry  
of Cyclobutadienoid Compounds

Cyclobutadiene

There is a great deal of evidence to suggest that the cyclobutadiene system is kinetically and thermodynamically unstable.<sup>38</sup> Cyclobutadiene<sup>39</sup> and its substituted derivatives such as tetrachloro-, tetramethyl- and even tetraphenylcyclobutadiene,<sup>40</sup> a highly conjugated molecule, dimerize on generation but can be readily trapped as Diels-Alder adducts. Experience of the resonance theory applied to benzene (40) suggests that cyclobutadiene itself should be a square molecule (41) and on this assumption, simple Hückel molecular orbital theory predicts a triplet electronic ground state<sup>41</sup> (42). However, more elaborate calculations lead to the very different conclusion that the molecule consists of a rectangular arrangement of atoms with alternating double and single bonds and having a singlet electronic ground state<sup>42</sup> (43). Self-consistent field molecular orbital calculations give the geometry shown.



Having one bonding, two non-bonding and one anti-bonding orbital, its four electrons would be expected to be distributed as shown.<sup>43</sup>



A report by Watts, Fitzpatrick and Pettit<sup>44</sup> shows that cyclobutadiene acts as a diene and a dienophile in a stereospecific manner, supporting the theory that it possesses a singlet electronic ground state and by implication has the structure (43).

Applying molecular orbital theories to  $C_{2n}H_{2n}$ , Lennard-Jones<sup>45</sup> came to the conclusion that when  $n$  is odd (e.g. benzene), the most stable form is the resonance hybrid (40). In cyclic molecules such as cyclobutadiene, where  $n$  is even, alternate bonds would have different lengths. Similarly in cyclooctatetraene, which does not have a closed shell of  $\pi$ -electrons, there is no overlap between the orbitals of the separate double bonds. It has a polyolefinic character with alternating single and double bonds of  $1.466\text{\AA}$  and  $1.334\text{\AA}$  respectively.

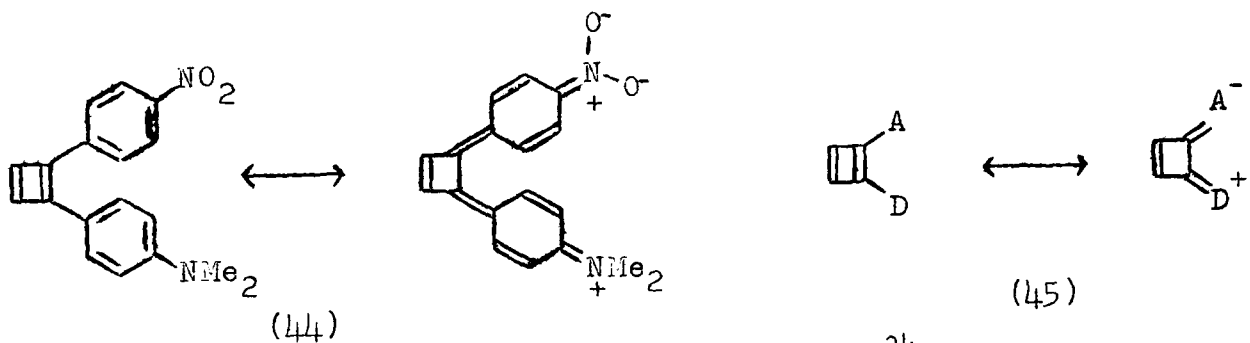
In conclusion, it can be said that the lowest state of cyclobutadiene is a rectangular singlet which possesses essentially isolated double bonds (43) and no resonance energy. The lowest excited state will be a square triplet.

The instability of this four-membered ring system is diminished by electronic or structural features in a variety of compounds all of which are stable and may be viewed as cyclobutadienoid systems.

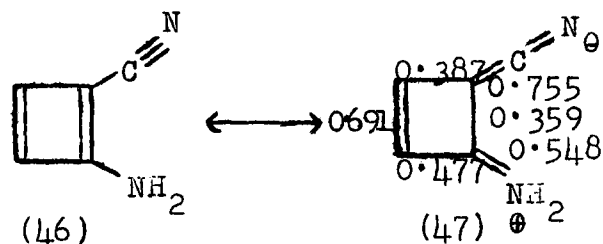


### Stable Cyclobutadienes

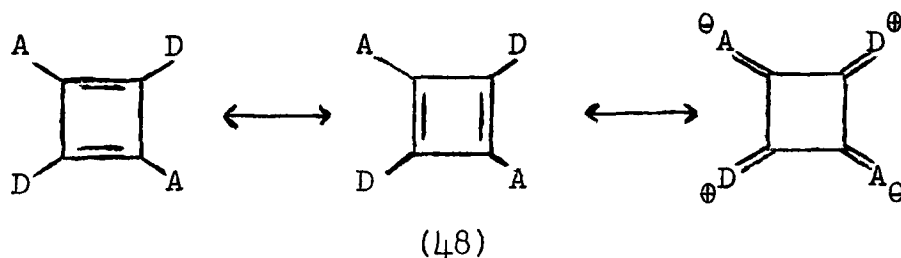
With the dimerization, on its generation, of tetraphenylcyclobutadiene hopes for an isolable cyclobutadiene appeared very slight. The only possibility seemed to come from a prediction made by Roberts<sup>46</sup> who suggested that 1-(*p*-dimethylanilino-2-(*p*-nitrophenyl)cyclobutadiene (44) might have the "best possible type of cyclobutadiene structure for stable existence", although the predominant resonance form would be of a dimethylenecyclobutene structure. The stability of this type of compound (45) would be derived from the "push-pull" effect of the neighbouring substituents D (electron donor) and A (electron acceptor), using the notation of Gompper and Seybold.<sup>47</sup>



Simple molecular orbital calculations<sup>34</sup> show that a cyclobutadiene with conjugated electron-donating and electron-accepting groups should have considerable resonance energy. An HMO calculation<sup>48</sup> on 2-amino-1,3-cyclobutadiene-1-carbonitrile (46) predicts the most important form to be (47), with the  $\pi$ -bond orders shown, a stable electronic arrangement.



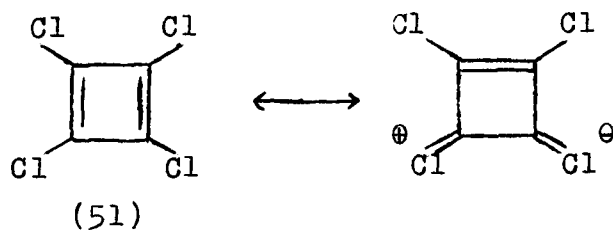
Attempts to obtain a compound of this type failed<sup>38</sup> until, extending this theory Gompper and Seybold suggested that the effect would be greater in a tetrasubstituted molecule (48).



With the synthesis of compound (50), m.p. 50-52°, these authors claim the first preparation of a stable cyclobutadiene obtained from the dimerization of the ynamine (49). The structural evidence is based on the mass, infra-red and ultraviolet spectra.

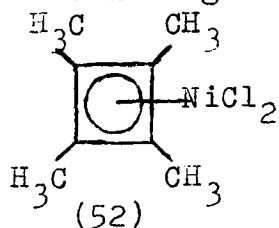


This theory of stabilization is also used to explain the relative ease with which transient tetrachlorocyclobutadiene (51) can be generated. Here the relative stability of the compound is thought to rest on the ability of chlorine both to accept and to donate electron density, analogous to the above.<sup>49</sup>



### Metal Complexes

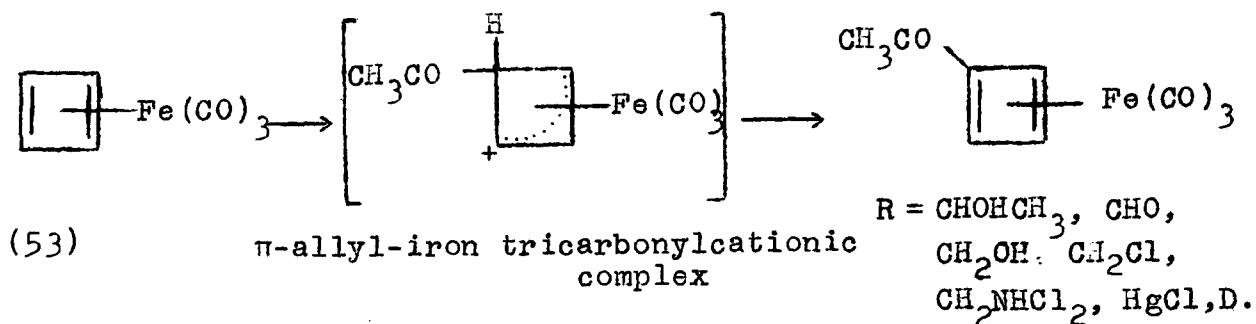
The possible existence of these compounds was predicted in 1956 by Longuet-Higgins and Orgel.<sup>52</sup> Complexes of cyclobutadienes with transition metals, bear little electronic resemblance to cyclobutadiene itself.<sup>50</sup> Nonetheless, work in this field would not have progressed to its present position were it not for these complexes. The first was obtained in 1959 by Criegee and Schröder,<sup>51</sup> tetramethylcyclobutadiene-nickel chloride (52). Not true cyclobutadienes, the stability of the complexes is due to the overlap of favourably oriented metal *d* orbitals with the antibonding  $\pi$ -orbitals of the four-membered ring.



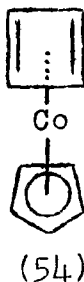
In cyclobutadiene complexes such as cyclobutadieneiron tricarbonyl (53) the nuclear magnetic spectrum shows a single peak, in this case at  $6.09\tau$ , indicating the equivalence of all four protons.

Pettit and co-workers<sup>53</sup> have claimed a "new aromatic system" in obtaining a wide range of substituted cyclobutadienes

by electrophilic substitution on the parent complex, cyclobutadiene-iron tricarbonyl (53).



These reactions can be compared to those of ferrocene and the substitution of the cyclopentadienyl radical. An interesting complex cyclobutadiene-( $\pi$ -cyclopentadienyl) cobalt (54) has been prepared by Amiet and Pettit,<sup>54</sup> and undergoes electrophilic substitution in the four-membered ring.



Free cyclobutadiene is obtained by the action of ceric ions on the complex (53) causing its decomposition.<sup>33</sup>

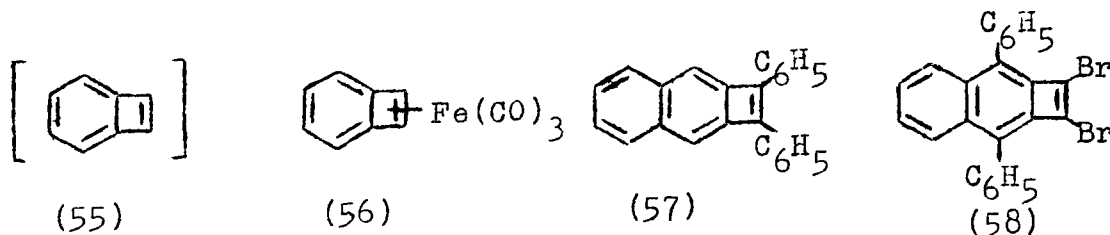
### Benzocyclobutadiene

It might naively be expected that benzocyclobutadiene (55) would have a stability intermediate between that of cyclobutadiene and biphenylene. Molecular orbital calculations<sup>55</sup> however suggest and experimental data confirm<sup>56</sup> that benzocyclobutadiene, wherein the cyclobutadiene ring is stabilized by fusion with a benzene ring

on one side only, differs markedly from biphenylene wherein benzene rings are fused to both sides. The simplest description of the latter<sup>16</sup> is that there are two aromatic regions in the molecule with only a little cross-conjugation in the ground state. The corresponding description of the former is that there is one aromatic region and one olefinic double bond with only a little mutual conjugation. In neither case does it seem chemically appropriate to speak of a genuine cyclobutadiene-like structure.

There is ample evidence of benzocyclobutadienes as unstable, reactive intermediates, readily trapped as Diels-Alder adducts<sup>26</sup> and, in their absence, dimerizing.<sup>22</sup> In both cases, these compounds can give benzobiphenylene structures and have been exploited as precursors.

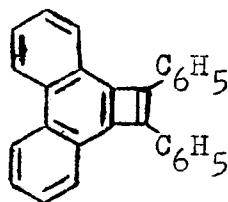
The system has been stabilised by metal complexing (56).<sup>57</sup> The only examples of stable free compounds are 1,2-diphenylnaphtho[b]cyclobutadiene (57),<sup>58</sup> and 1,2-dibromo-3,8-diphenylnaphtho[6]-cyclobutadiene (58).<sup>59</sup>



The stability of (57) has been attributed to the fact that the 2,3-bond in naphthalene has less double bond character than the 1,2-bond (or the ring bonds in benzene) and that in consequence the four-membered ring is fused to a bond which has a very low bond order.

The four-membered ring thus has more cyclobutene than cyclobutadiene character. The nuclear magnetic spectrum<sup>58</sup> indicates a remarkably fixed double bond structure in the adjacent 1,2-bonds for, in addition to showing 14 protons in the normal aromatic region, there are two protons giving a sharp peak very near to the position of the peak given by the vinyl hydrogens in cis-stilbene.

If the stability of this compound is connected with the low bond order of the bond common to the four- and six-membered rings, then it follows that a molecule wherein the four-membered ring is fused to a bond of high bond order, should not be stable. So it is that 1,2-diphenylphenanthro[1]cyclobutadiene (59)<sup>60</sup> is a highly unstable molecule reacting spontaneously with oxygen



(59)

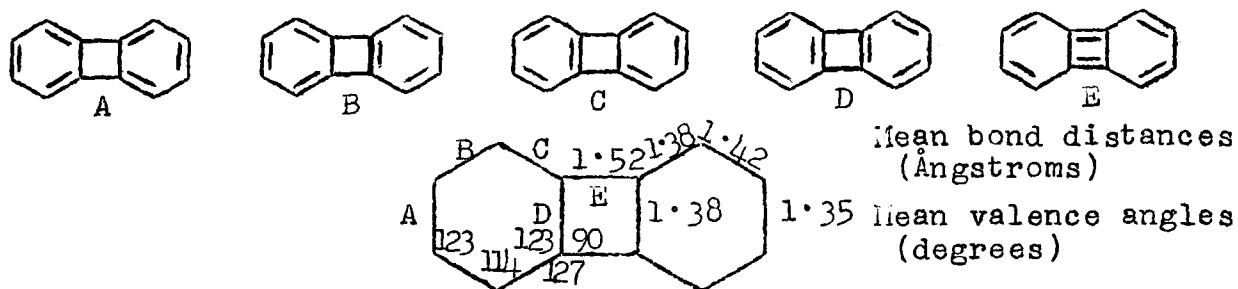
### Biphenylene and the Benzobiphenylenes

Having considered the other "cyclobutadiene" compounds, the case of biphenylene can now be seen in perspective. It now becomes clear that the electronic configuration in the four-membered ring must be appreciably different in biphenylene, which is not simply a progressive step in the cyclobutadiene-benzocyclobutadiene-biphenylene series, but a compound of unexpected stability. Thermally stable, m.p. 110-111°, it undergoes nucleophilic, electrophilic and free-radical substitution and shows itself to be

an aromatic compound. It can readily be seen why Lothrop's claim of synthesis, amongst a host of false claims, was greeted with some scepticism. Parent of a unique series of polynuclear aromatic hydrocarbons, its properties and those of the whole series are related to the four-membered ring structure. (Reviews - Baker and McOmie,<sup>31</sup> and Cava<sup>34</sup>). As reviews on this compound and its derivatives are available, its properties will only be mentioned where they bear relevance to the dibenzobiphenylenes.

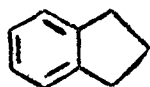
It should perhaps be stated at this point that, although formally derivatives of cyclobutadiene, no biphenylene-type compound contains a cyclobutadiene structure as such. To a greater or lesser extent, the four-membered rings in this unusual group of compounds, does its utmost to avoid cyclobutadienoid character. The more the ring is forced towards this unstable structure by the prevailing electronic influences in the molecule, the further the compound moves away from stability.

Of the five Kekulé structures that can be written for biphenylene, D and E (cyclobutadiene) can be considered to be high-energy forms contributing very little to the resonance hybrid. B and C are cyclobutene forms and A, a cyclobutane, was suggested by Baker<sup>61</sup> to be the most satisfactory single structure.

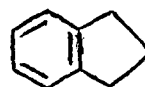


This has been confirmed by Mak and Trotter,<sup>62</sup> by X-ray analysis of crystalline biphenylene; the calculated mean bond distances and valence angles are summarized here (59). When the experimentally determined bond lengths are compared with the hybrid bond of benzene ( $1.39 \pm 0.02 \text{ \AA}$ ) and with the saturated C-C bond ( $1.54 \text{ \AA}$ ), it is apparent the bond A has slightly more and bond B slightly less, double-bond character than the aromatic linkage in benzene. In the completely planar molecule, the central bonds joining the two six-membered rings are significantly longer than the bonds making up the rings, almost as long as C-C single bonds. This had been predicted from molecular orbital calculations.<sup>63</sup>

Indeed the same conclusion could be reached if biphenylene is viewed as an extreme case of the Mills-Nixon effect<sup>64</sup> where in A there would be less strain, due to distortion, of the valency angles. When applied to indane structure (60) is preferred to structure (61) and so in this case.



(60)



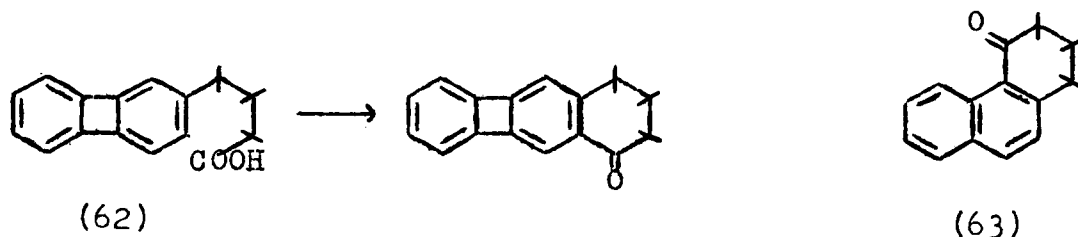
(61)

It can be seen that far from being a cyclobutadiene derivative, a compound of this type will approximate to a tetramethylenecyclobutane or a dimethylenecyclobutene structure, biphenylene existing as a hybrid of these forms.

Chemical evidence for bond A having a higher bond order than bond B comes from the ring closure of compound (62), a step in



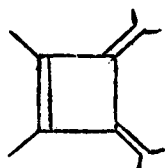
the preparation of benzo[b]biphenylene.<sup>27</sup> Just as ring closure in the naphthalene series occurs exclusively at the 1-position (63), so here the ring is formed across the bond of highest order.



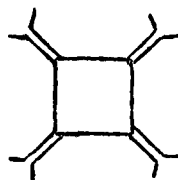
The nuclear magnetic resonance spectrum of biphenylene has been interpreted as showing ring currents only in the six-membered rings<sup>65</sup> and as indicating electronic interaction between these rings. There is ample evidence to show that the two six-membered rings are not entirely independent. Thus there is ultra-violet absorption at much longer wavelengths than in the case of biphenyl, suggesting quite extreme conjugation between the two benzenoid rings.<sup>66</sup>

It is therefore relatively certain that a degree of bond fixation in the central ring of biphenylene approximates the four-membered ring to a tetramethylene cyclobutane structure, with some influence coming from the two possible dimethylene cyclobutene structures. Examination of the parent compounds lends weight to this concept. Both dimethylenecyclobutene (64) and tetramethylene-cyclobutane (65) have four-membered rings in which the carbon atoms are all  $sp^2$ -trigonally hybridized, just as they are in cyclobutadiene, and both compounds have a stability far in excess of that of cyclobutadiene. Samples of (64) have been stored under

nitrogen in a refrigerator for several days without appreciable



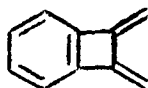
(64)



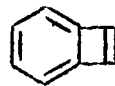
(65)

polymerization, and dilute hexane solutions of (65) are indefinitely stable at  $-78^{\circ}$ . The most characteristic chemical property of both these compounds is their marked sensitivity to oxygen; on brief exposure to air, they polymerize rapidly to give intractable products. Initially synthesized by Blomquist and Maithis,<sup>67</sup> (64) was subsequently obtained in 85% yield by Huntsman and Wristers<sup>68</sup> as a stable liquid b.p.  $72^{\circ}/759$  mm Hg. Tetramethylene-cyclobutane however is non-isolable at room temperatures as it dimerizes on heating the hexane solution. Nonetheless, both compounds are many times more stable than cyclobutadiene, and it is obvious that the instability of this compound arises from some factor other than simple ring strain.

A step nearer gives the compound 1,2-dimethylenebenzocyclobutene (66); synthesized and studied by Cava et al.,<sup>69</sup> it is a colourless low-melting solid m.p.  $15-16^{\circ}$  polymerizing to a thick gum at room temperature. In contrast to benzocyclobutadiene, (67) the ease of polymerization is similar to that of 3,4-dimethylene-cyclobutene (64).



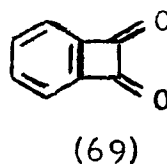
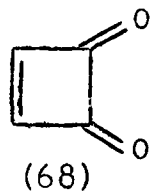
(66)



(67)

Just as in the monocyclic case, the deviation away from the cyclobutadiene structure towards the dimethylenecyclobutene structure increases the stability of the compound.

Although not exactly comparable, it is this structure which exists in the exceptionally stable cyclobutadienequinone (68), and 1,2-benzocyclobutadienequinone (69).



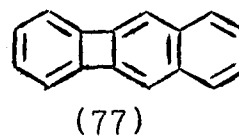
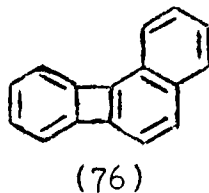
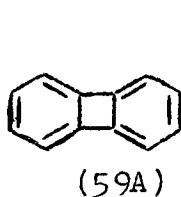
The crucial factor affecting the stability of the four-membered ring systems discussed must be the distribution of electron density within the ring. It can be seen from X-ray studies of biphenylene that the ring is not symmetrical and the system approximates to a diallyl structure.



It is this distribution of electron density away from the central ring which gives biphenylene its stability and disruption of this symmetrical arrangement by benzenoid annellation and subsequently greater bond fixation in the dibenzobiphenylenes can explain the observed differences in stability of these compounds.

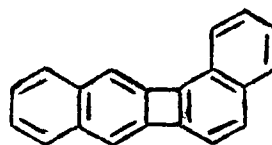
The Dibenzobiphenylenes

Sufficient evidence is available to indicate that structure (59A) is the main contributor to the resonance hybrid of biphenylene.<sup>61</sup> It might be expected that this electronic configuration would be altered to varying extents in the benzo[a]- and benzo[b]biphenylene molecules. However, no great difference in stability between the two monobenzobiphenylenes has been reported,<sup>22,23</sup> presumably because the benzene ring, on the opposite side of the four-membered ring, can adapt to the influences of the naphthalene entity on the other side and hence absorb any bond fixation. This is only possible where the benzene ring exists unhampered by other influences, and can explain the relative stability of the [a,c]isomer which must at least adopt a cyclobutene structure (72). Where there is no release of electron density from the four-membered ring in this way, it ascribes a cyclobutadienoid form and the stability of the compound is lower, as in the [a,i] and [a,g]isomers. To avoid this, the naphthalene rings would have to adopt unfavourable ortho-quinoid structures (75). Accordingly, whereas the linear [b,h] isomer is an exceedingly stable compound,<sup>13</sup> subliming uncharged at 350°, the [a,i]isomer, in which the benzene annellation is angular, is much deeper in colour and behaves as a highly unsaturated compound.<sup>12</sup>

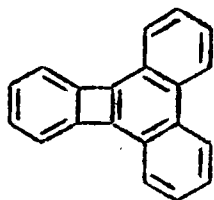




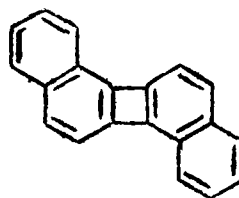
(70)



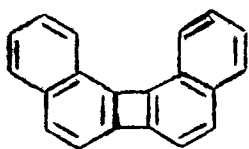
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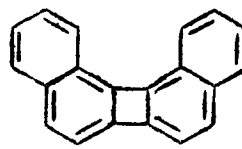
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(74)

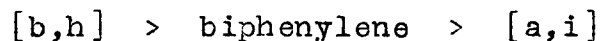


(73)



(75)

The effects of benzene annellation were discussed by Ali and Coulson<sup>16</sup> who calculated that the resonance energy of the [b,h]isomer exceeded that of the [a,i]isomer by about 4.3 kcal/mole. They concluded that the degree of bond fixation increased in the order:

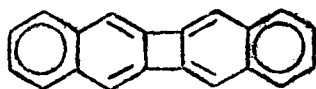


and that the 6a-6b bond in the [a,i]isomer was longer than the 12b-12e bond by some 0.005 Ångstroms. In the more symmetric

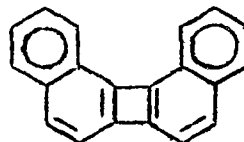
[a,g]isomer these bonds are equal. These predictions of double-bond fixation correspond exactly to the sequence of stability of these molecules, hence the greater the degree of bond fixation, the less the extent of conjugation and the lower the stability. The extra benzenoid annellation of biphenylene lowers the bond orders of the two connecting bonds in [a,i] but increases them in [b,h].

The difference in stability has been rationalized on the basis of Hückel's molecular orbital theory by both Pullman<sup>70</sup> and Coulson.<sup>16</sup> The former author suggested that the difference was due in part to less interaction between the two naphthalene moieties in view of the longer crosslinks in the angular isomer. Steric hindrance between C<sub>1</sub> and C<sub>12</sub> in (73) was considered and also the possibility of a low-lying triplet state in the [a,i] isomer due to the relatively low energy of the  $N \rightarrow V_1$  transition.

The predominance of resonance forms (78) and (79)

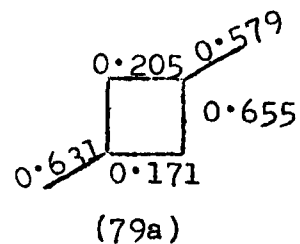
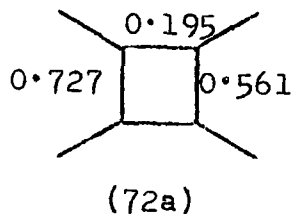
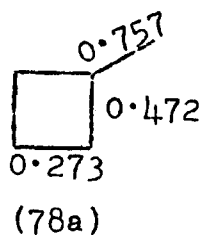


(78)



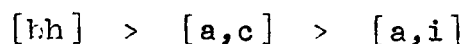
(79)

suggested by the HMO  $\pi$ -bond orders was emphasized by Coulson.<sup>16</sup> The importance of these forms being stressed further by an approximate SCMO calculation involving successive iteration of  $\beta$ , by the Longuet-Higgins and Salem<sup>71</sup> procedure, giving the  $\pi$ -bond orders shown in (78a) and (79a).



The infra-red spectrum of the [b,h]isomer exhibits a characteristic olefinic absorption at  $1612 \text{ cm}^{-1}$  which is attributed to the C=C stretching vibration of the localized double bond adjacent to the 4 mem. ring.<sup>21</sup>

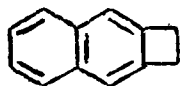
Hückel H.O. calculations in the hands of Barton et al.,<sup>72</sup> similarly gave an order of stability



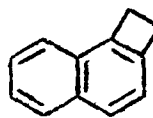
The  $\pi$ -bond orders in the central ring were obtained for the [a,c] isomer (72a) and compared with those obtained by Ali and Coulson.<sup>16</sup> It was noted that, although [a,c] is more stable than [a,i], the total  $\pi$ -bond order in the central ring (72a) is hardly less than in (73a). This is due to the very high bond order of the 8b-12b bond, corresponding to a phenanthrene 9-10 bond, brought about by the angular annellation of two benzene rings on one side of the biphenylene system. The high bond order is confirmed experimentally by the compound's facile reaction to give a dibromide by the addition of bromine at this bond.<sup>2</sup> It appears that the double bond character of the 8b-12b bond is offset by bond fixation in the

benzene ring so that structure (72) represents the main contributor to the resonance hybrid.

Assuming the naphthalene units adopt Kekulé structures (70-74), a simple correlation would give the linear isomers less cyclobutadienoid character than the angular, and hence greater stability. A parallel may be seen in the case of the naphthocyclobutenes,<sup>73</sup> where the linear [b] isomer (81) is a crystalline solid m.p.  $86.5^{\circ}$  while the less stable angular [a] isomers (82) is an oil b.p.  $98^{\circ}$  (1-2 mm.)

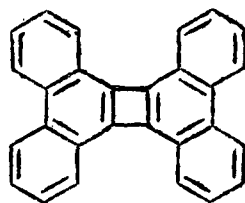


(81)



(82)

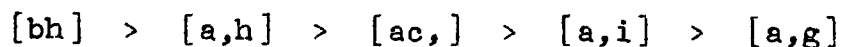
Likewise, attempts to isolate tetrabenzo[a,c,g,i]-biphenylene (83) have proven unsuccessful.<sup>74</sup> No evidence of formation was obtained on reaction of 10,10'-diiodo-9,9'-biphenanthryl with cuprous oxide; similar failure was experienced in an attempted dimerization of 9,10-phenanthryne. This is attributed to the predicted lack of stability of the angularly annellated product.



(83)



This simple theory agrees with the conclusions reached by Dewar and Gleicher<sup>42</sup> who, from SCF MO calculations predicted that the stability of the dibenzobiphenylenes would be of the order:



The synthesis and study of the five isomeric hydrocarbons have since confirmed this prediction.

Decreasing stability is accompanied by a darkening in colour throughout the series, the [a,g] isomer being best kept as the 2,4,7-trinitrofluorenone complex, as it decomposes in methanol or hexane solution at room temperature. Both the [b,h] and the [a,c] isomers sublime unchanged but the [a,i] isomer, although quite stable in the usual organic solvents at room temperature, decomposes to a dark gum when heated at 160° in vacuo. Dilute solutions of the [a,c] isomer slowly decolorise on exposure to light, the two less stable isomers [a,i] and [a,g] being readily bleached, possibly through a photochemical oxidative process.

The more the four-membered ring has to adopt a diene character, the more the reactions of the compound approach those of an olefin. Addition reactions, rather than substitution, are seen in the [a,c] isomer which readily adds bromine across the 8b-12b bond, but this compound does not react as a diene towards tetracyanoethylene in tetrahydrofuran, where no adduct is formed.<sup>2</sup> No analogous reactions have yet been reported for the [a,i] or [a,g] isomers but they will almost certainly undergo addition reactions more readily than the [a,c] isomer. Bromination across

the four-membered ring has however been reported for some 5-substituted benzo[a]biphenylenes.<sup>75</sup>

All the dibenzobiphenylenes are readily hydrogenated by Raney nickel with reductive rupture of the four-membered ring, a normal reaction of biphenylene derivatives. Some anomalies do occur however where more than one product is possible. The [b,h], [a,c] and [a,g] give the expected products, 2,2'-binaphthyl, 9-phenylphenanthrene and 1,2'-binaphthyl respectively, as expected by reductive cleavage of either of the two linking bonds. Here only one product is possible. Unexpectedly the [a,h] and the [a,i] isomers give only 2,2'-binaphthyl. The other possible products are respectively 1,2'-binaphthyl and 1,1'-binaphthyl, but neither of these were detected. To obtain these products exclusively, it would require cleavage of the stronger and more stoically hindered bond, but as the reaction takes place only in the presence of a metal catalyst, this may well be a surface effect.<sup>72</sup>

### Spectra

The ultraviolet spectra of the dibenzobiphenylenes and of the benzobiphenylenes in general, resemble that of biphenylene in that they consists of two distinct groups of absorption bands (three in the case of the [a,c]isomer only) and differ from that of biphenyl which has only one absorption maximum at 245 m $\mu$ . The set of bands at lower wavelengths is the more intense of the two in all cases. They have been ascribed, for biphenylene, to the second and

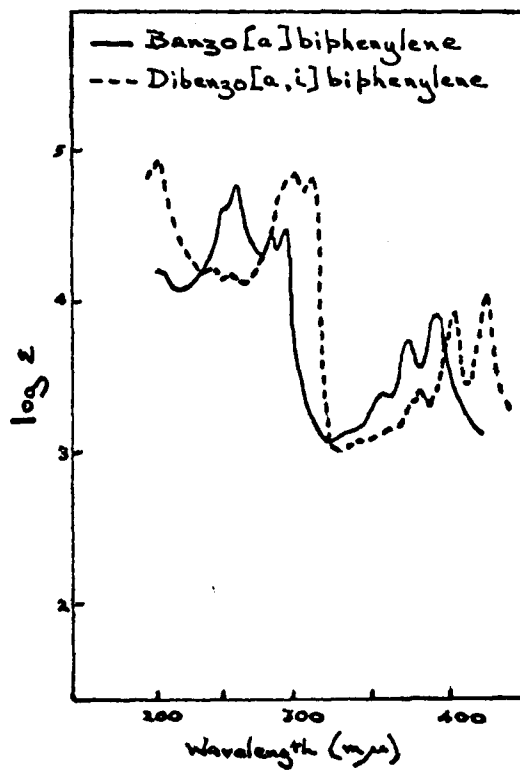
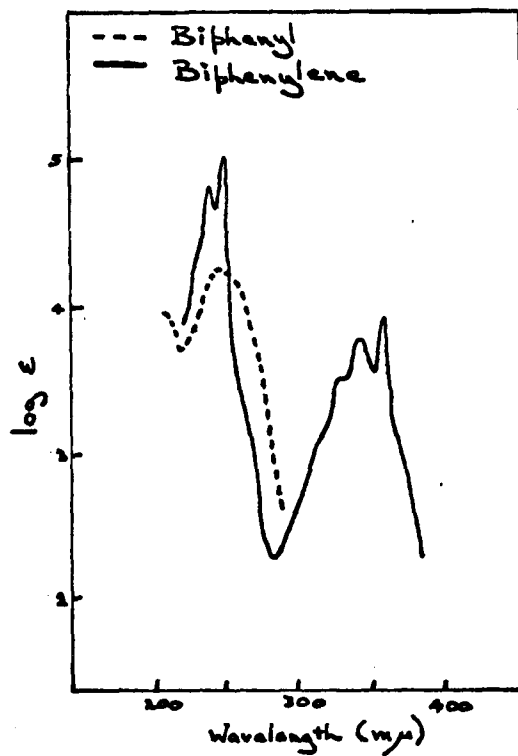
first electronic transitions respectively.<sup>76</sup> The longer wavelength bands are considered to be made up of two overlapping band systems, one of slightly higher and one of slightly lower frequency,<sup>77</sup> and are considered to indicate that there is some degree of resonance interaction ( $\pi$ -orbital overlap) between the two benzene rings, despite the unusual length of the bonds which unite them. The [a,g] isomer has a marked resemblance to benzo[a]biphenylene as, to a lesser extent, have all the angular isomers. With increased annellation, the groups of bands are shifted to longer wavelengths and are centred on

Wavelength ( $\mu$ )		
240	335	biphenylene
270	385	benzo[a]biphenylene
300	400	dibenzo[a,i]biphenylene

The absorption maxima of the [b,h] isomer predicted by Crawford<sup>78</sup> are in fair agreement with the experimental values.

The infra-red spectra of these compounds are typical of aromatic hydrocarbons and, as such, resemble one another to some extent. Differences occur at low frequencies in the hydrogen out-of-plane bending bands due to the different substitution patterns in the molecules e.g. the [b,h] isomer shows a peak at  $880 \text{ cm}^{-1}$  and one at  $745 \text{ cm}^{-1}$  ( $13.45 \mu$  and  $11.40 \mu$ ) characteristic of 1,2-disubstituted and 1,2,4,5-tetrasubstituted benzene rings.

Little data has been collected concerning the nuclear magnetic resonance spectra of these compounds. The parent hydrocarbons show complex multiplets, e.g. the [a,c] isomer shows three multiplets of 4,6 and 2 protons respectively.



OBJECT OF RESEARCH

The object of research is to devise new synthetic routes to the parent dibenzobiphenylenes or to substituted compounds, of which few are known at the present time, and whose chemical properties are of great interest. High yield routes will allow the study of the electron distribution and the bond fixation in the nuclei by methods similar to those used in the elucidation of the structure of simple fused-ring hydrocarbons such as naphthalene and phenanthrene.<sup>79</sup> Due to the inaccessibility of these compounds, their chemistry has only been touched on, although with the success of Barton's<sup>10</sup> aryne and some other methods, this will surely be remedied in the near future. Although the physical properties of the parent hydrocarbons have been studied, and found to agree with theoretical predictions on stability,<sup>42</sup> no chemical evidence from direct substitution into any of the nuclei has been reported.

Synthetic routes attempted can be classified as involving cyclobutane, cyclobutene and cyclobutadiene intermediates.

## DISCUSSION

SECTION I

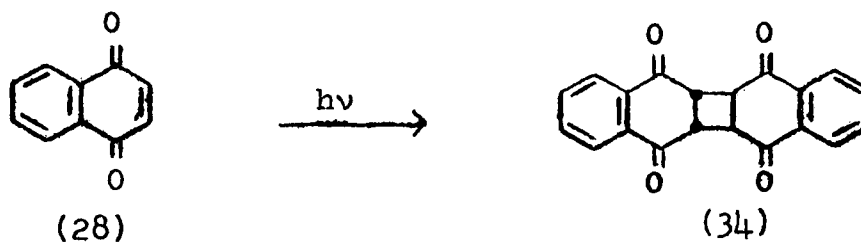
Attempts to synthesize dibenzo[a,g]biphenylene from cyclobutane precursors and the preparation of compounds with this carbon skeleton.

### Introduction to Section I

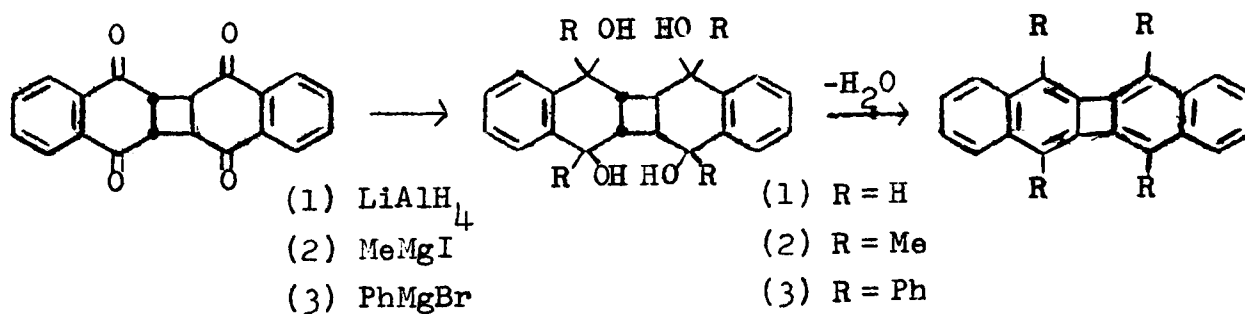
Among the most common photochemical reactions is the dimerization of olefinic compounds, giving a cyclobutane derivative.<sup>19</sup> An unsymmetrically disubstituted olefin  $R_1R_2C=CHR^1$  can theoretically give one or more of twelve isomeric dimers depending on whether head-to-head or head-to-tail dimerization takes place with syn or anti or with cis or trans ring junctions. Although in the liquid phase a mixture of several isomers is often formed, in almost all solid-state dimerizations, only one isomer is produced. The success or failure of solid-state processes is dependent upon the distance, in the crystal, separating the centres involved in bond formation. In this case, this is the distance between the double bonds, which are assumed to be parallel. The situation can be further complicated by the crystallization of some compounds in more than one form. Trans-cinnamic acids, for example, crystallize in three such modifications and therefore yield a complex product upon irradiation. No predictions about the course of such solid-state reactions can therefore be made without consideration of the crystal lattice geometry.

As mentioned in the introduction, a photochemical reaction of this type has been used in dibenzobiphenylene chemistry. The dimerization of 1,4-naphthaquinone (28) has been shown<sup>19</sup> to give exclusively the more stable anti-isomer (34), only two photodimers, syn and anti, being possible in this case.





In a single quantitative step, the dibenzo[b,h]biphenylene structure is obtained, although it was several years before the hydrocarbon itself was synthesized by this route.<sup>21</sup> Base catalysed isomerization gave the tetrahydroxy compound (30) and several other 5,6,11,12-tetrasubstituted compounds have been obtained from this photodimer.

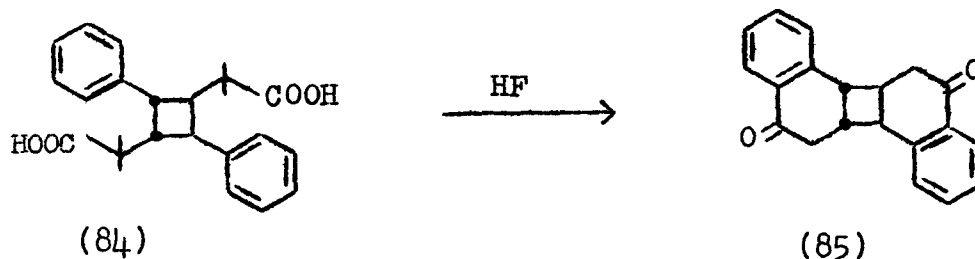


Due to the planarity of the naphthoquinone molecule, only two photodimers are possible, syn- and anti-, either of which could feasibly be transformed to a dibenzobiphenylene. In our case, where ring closure takes place after dimerization, it is essential that the cyclobutane ring takes up one of these two configurations. Only a cis- relationship between the two condensing

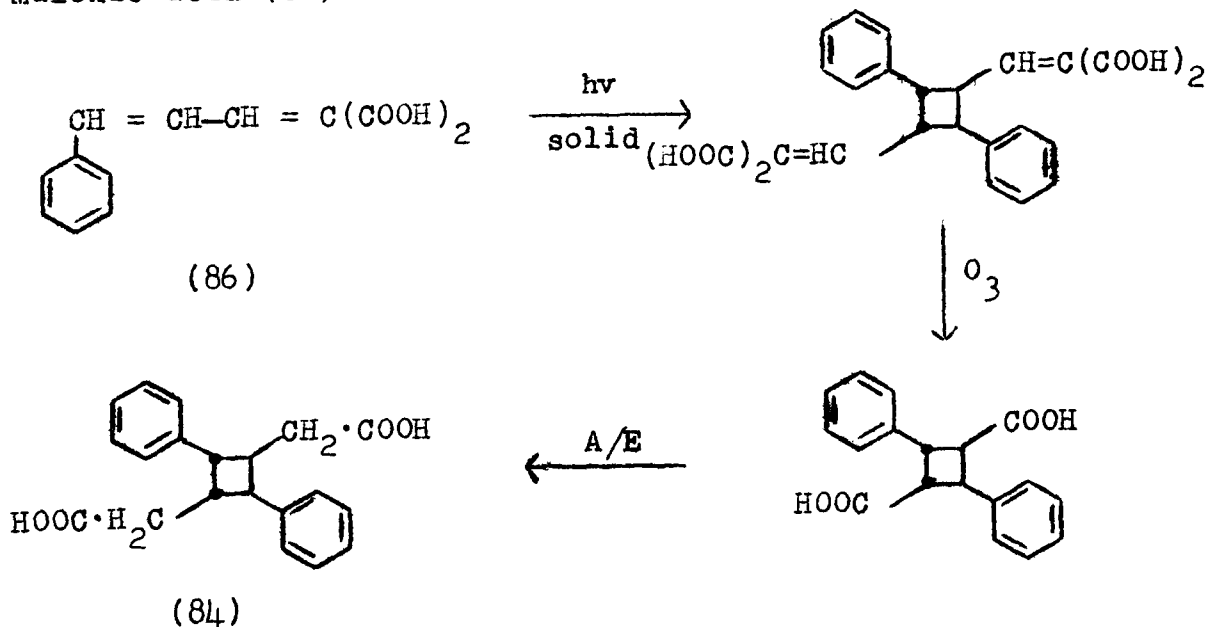
groups could give a stable ring-closure product. The stereospecific photodimerization of cinnemylidene malonic acid, to give a dimer of the  $\alpha$ -truxillic type, fulfills this condition.

### 1.1. Photodimerization of Cinnamylidene Malonic Acid

The diketone (85), somewhat similar to the photodimer obtained by Dekker, was prepared by dehydrative ring-closure of 1,3-diphenylcyclobutane-2,4-diacetic acid (84).<sup>80</sup>



The diacid (84) was derived from  $\alpha$ -truxillic acid (86) by Arndt-Eistert chain extension and would, of necessity, have to have either a cis-anti-cis or a cis-syn-cis structure. As shown, an anti structure is obtained from the stereospecific photodimerization of cinnamylidene malonic acid (86).



It was considered worthwhile to try and extend this route and, if it proved successful in obtaining a dibenzo[a,g]biphenylene, to repeat the process using compounds substituted in the benzene ring.

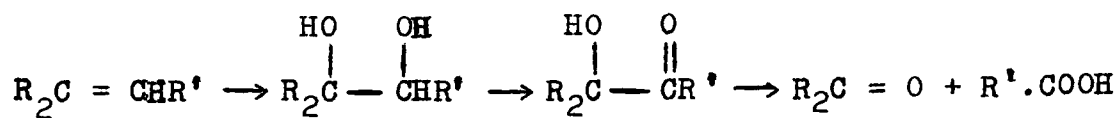
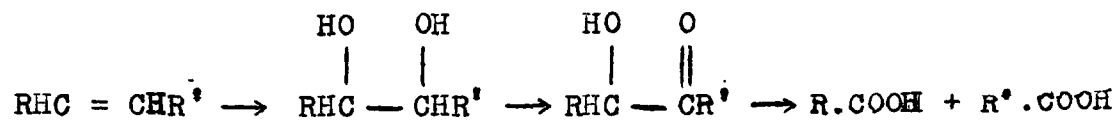
The dimer (84) was originally degraded to  $\alpha$ -truxillic acid by bubbling an oxygen/ozone mixture through a suspension of the dimer in glacial acetic acid containing a little water. In the presence of water, ozonides are cleaved by hydrolysis, decomposing to give aldehydes or ketones and hydrogen peroxide. This is generally destroyed by a mild reducing agent such as zinc dust in order to prevent further oxidation, but in this case more hydrogen peroxide was added in order to obtain a carboxylic acid product. The yield of crude  $\alpha$ -truxillic acid obtained on repeating this method, over several experiments, never exceeded 35% and two modifications of the route were considered at this point.

## 1.2. Lemieux Reagents

### Lemieux-von Rudloff

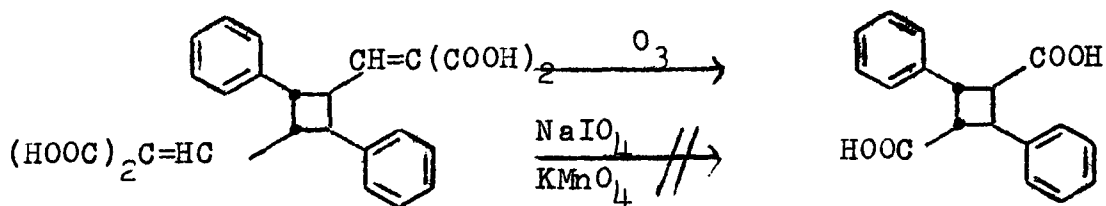
Two methods of cleavage of an olefinic bond have been developed by Lemieux, both of which involve oxidation with sodium periodate and catalysts. In the Lemieux-von Rudloff method,<sup>81</sup> an aqueous solution of sodium periodate (0.019M) and potassium permanganate (0.0034M) rapidly cleaves a double bond at 25°C and at pH 7-8. The intense purple manganese (VII), permanganate  $[\text{MnO}_4]^-$  is reduced only to the deep green manganese (VI), manganate  $[\text{MnO}_4]^{2-}$  state, from which it is regenerated by the periodate which itself does not attack the olefin. The  $\alpha$ -ketol intermediate in some cases can be isolated

confirming the reaction scheme.



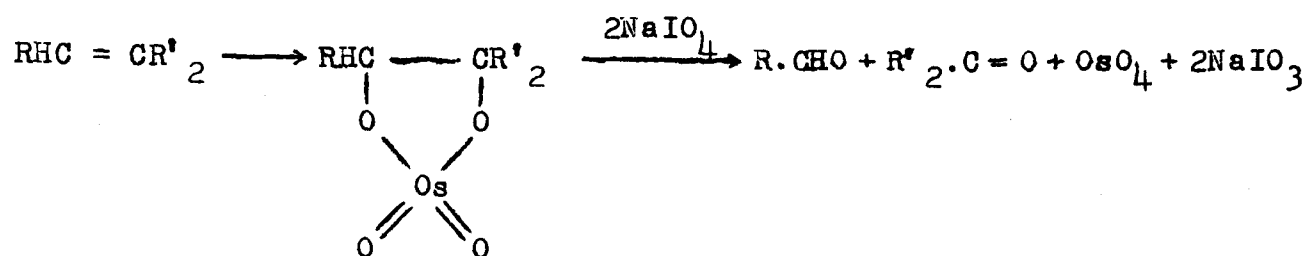
### $\alpha$ -Ketols

In the hope of obtaining  $\alpha$ -truxillic acid in perhaps greater yield, as has been reported for azelaic acid by Cunstone and Morris,<sup>82</sup> the photodimer of cinnamylidene malonic acid was subjected to the above method. An acidic product was extracted into sodium bicarbonate solution but upon isolation a brown oil, which did not solidify and could not be crystallized, was obtained. Spectral data gave little information about the structures of the mixture of carboxylic acids obtained and the method was therefore considered to have failed in its aim and abandoned.

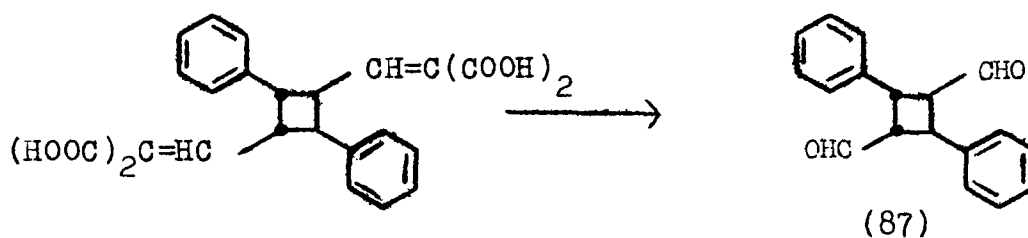


### Lemieux-Johnson

The Lemieux-Johnson method<sup>83</sup> is a catalytic heterogeneous reaction in which osmium tetroxide adds to a double bond to form an osmate ester which is oxidised by periodate with cleavage to carbonyl compounds and regeneration of the osmium tetroxide.

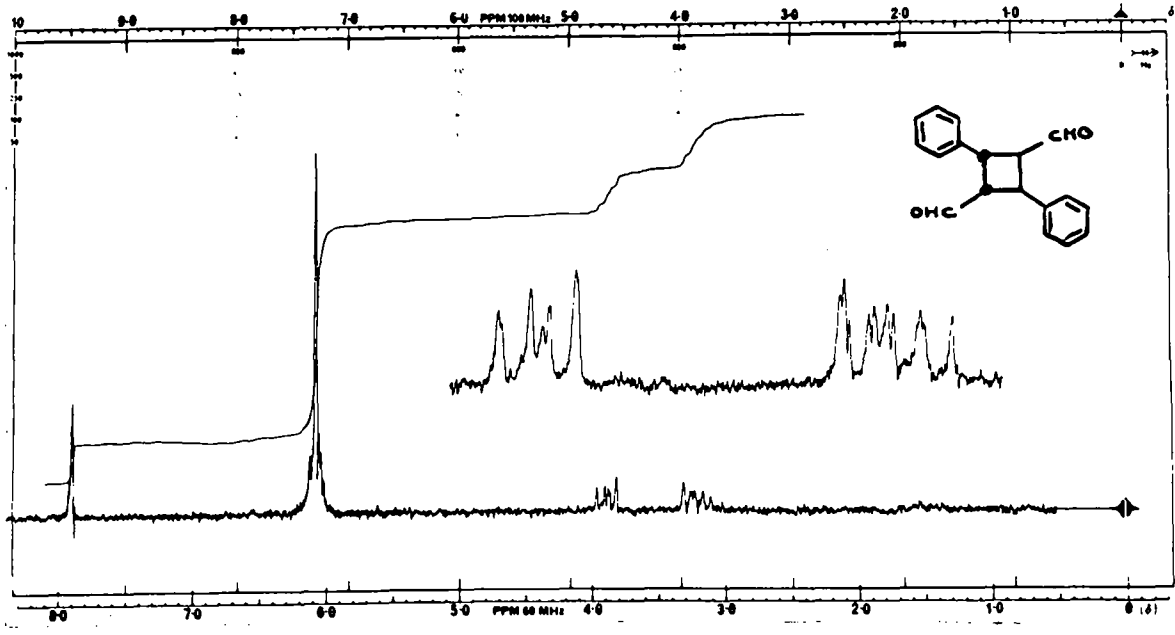
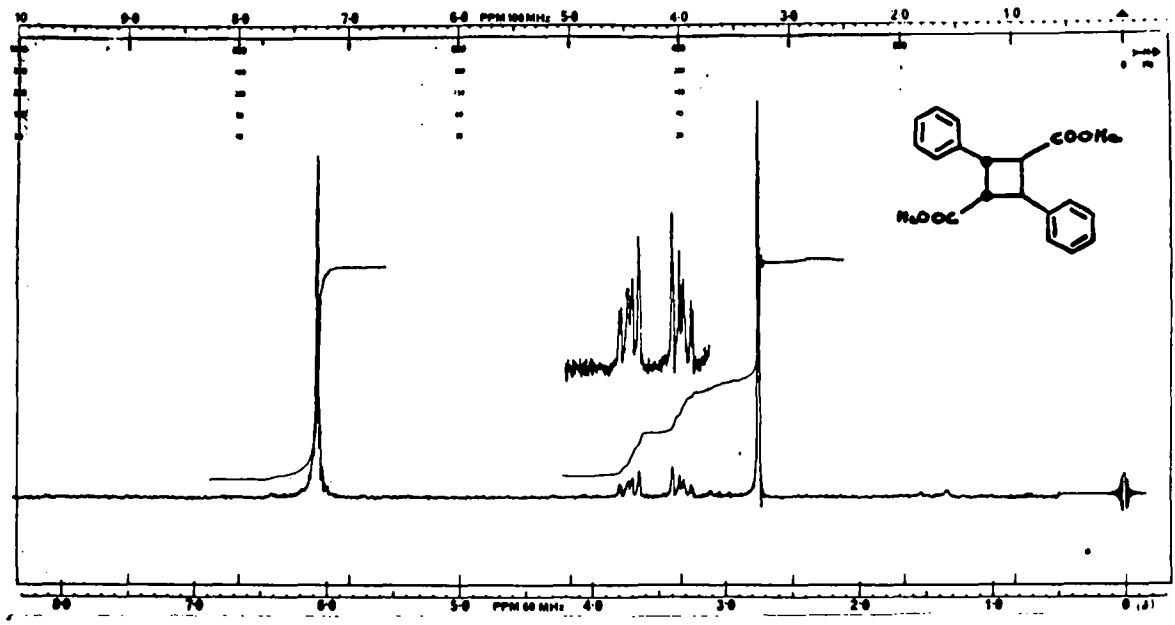


Moderate success was achieved in applying this oxidation, in that the dialdehyde (87) was synthesized, albeit in very low yield.



A feature of this catalytic method is that the rate of formation of the dark osmate ester provides an indication of the relative reactivity of the olefin. Compounds having an unhindered methylene group gives a colouration in 10-30 minutes whereas hindered olefins may require 4-12 hours for visual perception of oxidation, in which case the periodate is added over a period of 1-4 days at  $4^\circ\text{C}$ . The glacial acetic acid solution of the dimer became dark brown in colour after about 15 minutes and darkened to black within an hour. Upon the addition of a very small quantity of sodium iodate, this colour was discharged immediately. With 80% acetic acid as solvent, the catalytic amount of osmium tetroxide could be conveniently removed by distillation at  $40^\circ/20$  m.m.Hg.

The hitherto unreported dialdehyde gave the normal aldehydic chemical reactions with Schiff's, Fehling's and Tollen's reagents



and its structure was verified by mass spectroscopy, analysis, the infra-red ( $\nu_{C=O}$  , 1703  $\text{cm}^{-1}$ ; aldehydic CH, 2700  $\text{cm}^{-1}$  and 2800  $\text{cm}^{-1}$ ; cyclobutane CH, 3000  $\text{cm}^{-1}$  and 2900  $\text{cm}^{-1}$ ) and the nuclear magnetic resonance spectra (doublet 0.52 $\tau$ , two aldehydic protons; multiplet 2.71 $\tau$ , ten aromatic protons; quartet 5.35 $\tau$ , two cyclobutane protons; quartet 6.15 $\tau$ , two cyclobutane protons). There is some coupling of the hydrogens in the four-membered ring and the aldehydic protons which splits the 0.52 $\tau$  peak into a doublet but the coupling constant  $J$  is very small and is barely discernible.

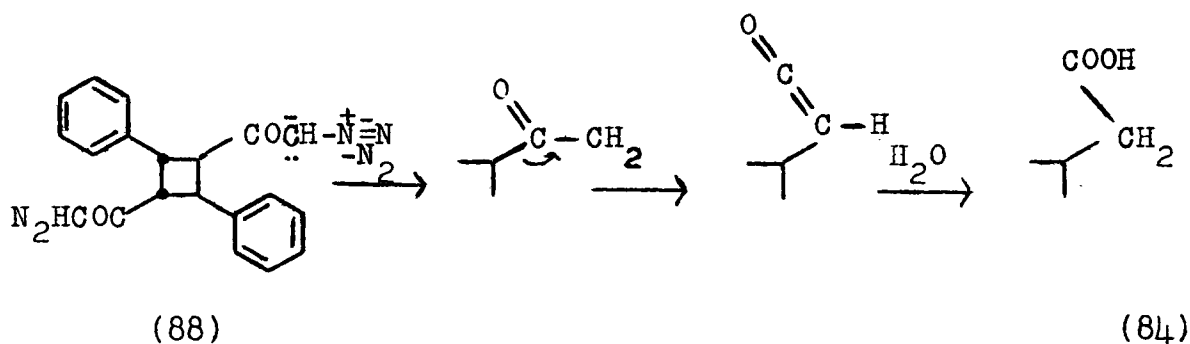
Although opening up a wide range of possibilities, the dialdehyde was not exploited as the yield was less than 20%. It readily formed a di-2,4-dinitrophenylhydrazone and a preliminary examination of its physical properties showed it to be very prone to polymerization and rearrangement.

Although a clear solution was obtained on first isolating the product in ether, if left in the sunlight, this solution quite quickly changed to a dark brown colour. Similarly, if the white solid was dried at  $\sim 50^\circ$  for more than a few hours, the melting point rose from  $110^\circ$  to  $> 210^\circ$  and the colour of the solid became slightly brown due to some form of decomposition. The melting point quoted ( $110^\circ$ ) was obtained after filtering the crude reaction product through a chromatographic column of acid-washed alumina; evaporation of the solvent gave a white solid. This also served to remove any traces of catalyst still present.



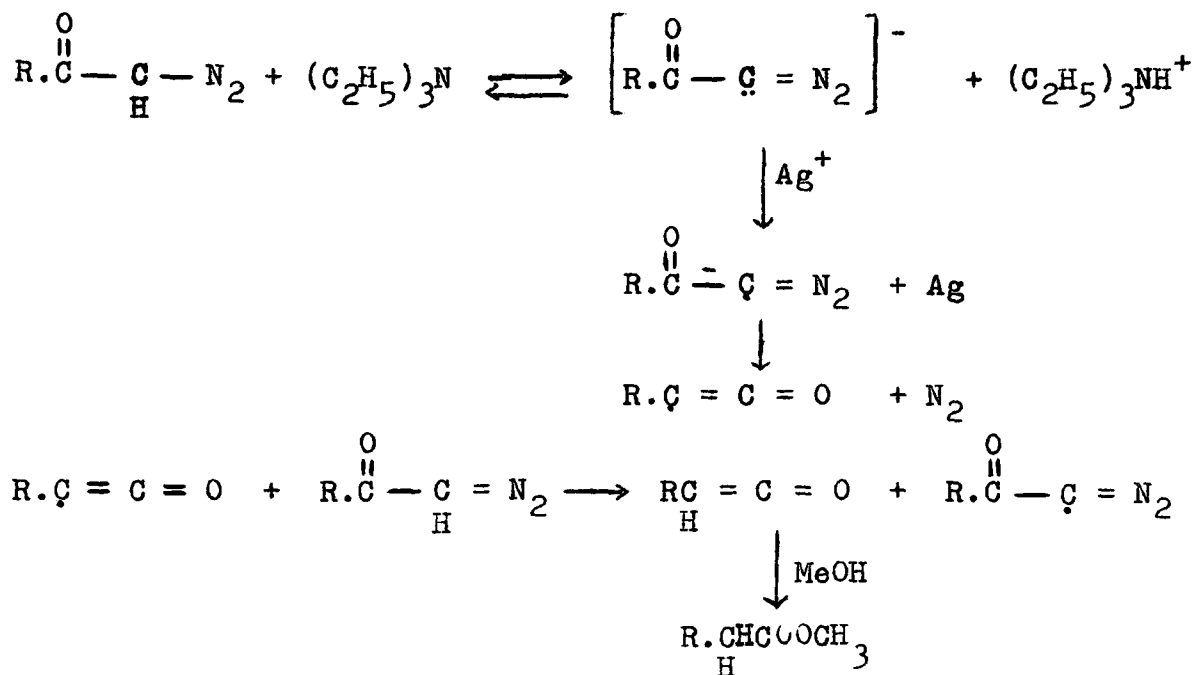
### 1.3 Heterogeneous and Homogeneous Catalysis

The impure  $\alpha$ -truxillic acid obtained from the ozonolysis of the photodimer was recrystallized from methanol as a white crystalline solid. Thionyl chloride gave the acid chloride as a stable solid which could be recrystallized from benzene as colourless prisms. A solution of this compound in sodium-dry ether was added to a cold ( $0 - 5^{\circ}\text{C}$ ) solution of diazomethane in dry ether and from this the relatively stable diazomethyl ketone (88) was isolated as a semi-solid yellow oil (I.R.  $2100\text{ cm}^{-1}$ ).

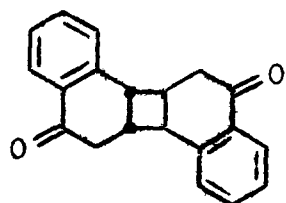


The rearrangement of the diazoketone (88) to the homologous acid (84) using a silver/silver oxide catalyst in methanol is reported as giving a 52% yield.<sup>80</sup> In our experience however, the Wolff rearrangement of the diazoketone proved to be somewhat erratic. Large variations in yield were experienced in virtually identical experiments and in no case was the yield found to exceed 20%. It would appear that the sample of catalyst and the technique employed could not be relied upon to give a satisfactory reproducible result. This very problem was encountered by Newman and Beal<sup>84</sup> who reported

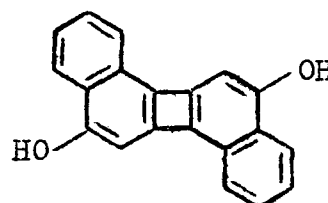
a new procedure by which the rearrangement could be carried out in homogeneous solution under milder conditions than those above, according to the reaction scheme shown.



The necessity of a hydrogen atom alpha to both the carbonyl and the diazo group is demonstrated in this scheme which also explains the function of the silver ion and the base, triethylamine. In this case, using a solution of silver benzoate in triethylamine, nitrogen evolution commenced upon the addition of a few drops of the reagent and the colour of the solution darkened, owing to precipitation of metallic silver. This method gave a higher yield of the methyl diester than that obtained using the Ag/Ag<sub>2</sub>O catalyst (~ 35%) but in no case did it approach the 50% yield reported.



(85)



(89)

#### 1.4 Dibenzo[a,g]Biphenylene Skeleton

The diketone (85) was obtained from the diacid (84) by cyclodehydration with anhydrous hydrofluoric acid. An attempted aromatization,<sup>80</sup> by bromination of the ketone and subsequent dehydrobromination and enolisation, was reported as failing to give the expected dihydroxybiphenylene (89).

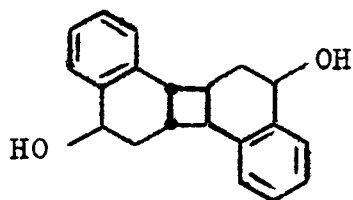
#### 1.5 Oxidation and Aromatization

An attempt was made to aromatize the diketone (85) to 5,11-dihydroxydibenzo[a,g]biphenylene (89) by chemical dehydrogenation followed by rearrangement, using p-chloranil in refluxing xylene. The instability of the [a,g] system might well disallow the isolation of the aromatic compound at the reaction temperature, but an indication of whether dehydrogenation had taken place or not would be provided from the other possible product 1:2:4:5-tetrachloro-3:6-dihydroxybenzene, tetrachlorohydroquinone. A sample of this material was obtained by reduction of 2:3:5:6-tetrachloro-p-benzoquinone, p-chloranil, with sodium dithionite. Upon refluxing, the colour of the solution darkened almost immediately from a clear orange to an opaque dark brown and after 2 hours, the product was chromatographed on silica gel. The crystalline product obtained in this way was identified as tetrachlorohydroquinone (75% theoretical) while the black oily residue gave no other isolable compound, even after further chromatographic separation. The hydroquinone showed the oxidation to have taken place but the total absence of any identifiable solid product showed the thermal instability of the product so formed.

The experiment was repeated in milder conditions, firstly in a 1:1, benzene:toluene mixture and secondly in benzene alone, but in both cases no reaction was observed. The p-chloranil was recovered in > 80% yield in both cases along with a small quantity of decomposition tar. At the higher temperature ( $\sim 140^{\circ}$ ), the dehydrogenation of the ketone occurs with subsequent breakdown of the dibenzobiphenylene skeleton giving intractable tars. At lower temperatures, the ketone does not react and can be recovered to some extent along with some tar, presumably from thermal decomposition of the ketone.

#### 1.6 Reduction and Aromatization

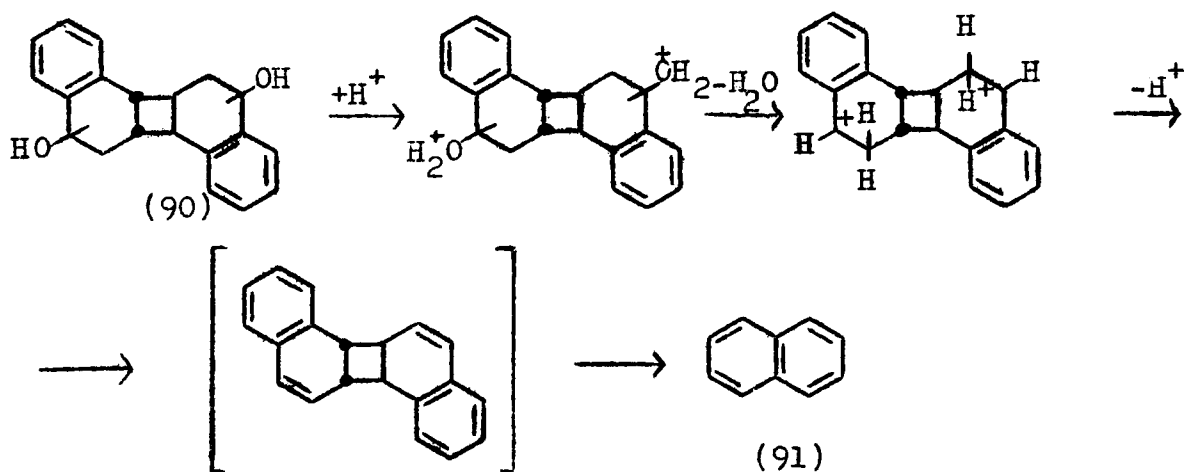
On reduction with potassium borohydride in methanol, the diketone (85) gave two identifiable products, namely the dihydroxy compound (90) and, rather unexpectedly, naphthalene (91). After refluxing for five minutes, the reaction was terminated and any excess borohydride neutralised by the addition of excess dilute hydrochloric acid. The oily reaction product was chromatographed on a silica gel column, elution with benzene giving an oil which solidified to a semi-crystalline mass on standing. Two recrystallizations from methanol afforded a small quantity of clear needles, turning opaque upon loss of solvent of crystallization. They gave a relatively sharp melting point  $165-7^{\circ}$  and a depressed melting point when mixed with the starting diketone. Analysis and spectral evidence confirmed the structure (90).



(90)

Before the crude product was placed on the silica-gel column it was observed that, around the neck of the flask, clear crystal prisms had collected due to sublimation. These were removed and were found to be naphthalene (91) from the mass spectrum parent peak  $m/e$  128 and mixed melting point (m.p.  $80^\circ$ , no depression on mixing with an authentic sample).

It is considered that naphthalene is formed via the dehydration of the diol (90) as shown, perhaps in the acidic conditions of the work up. The unsaturated product of the dehydration is a 1,2-dimer of naphthalene and attains aromatization by cleavage of the cyclobutane ring, the driving force of the rearrangement being this aromatization of the naphthalene nuclei.



The only comparable compound as yet isolated is the phenanthrene dimer (92) which, although stable at room temperature, when heated at  $240^{\circ}$  gives phenanthrene.<sup>85</sup>



Attempted dehydrogenation of the diol (90) met with the same lack of success that accompanied the dehydrogenation of the diketone itself in that, under the same conditions, intractable tars were obtained along with tetrachlorohydroquinone. As with the diketone, the dibenzo[a,g]biphenylene structure is considered to be obtained but decomposes at the high reaction temperature on formation.

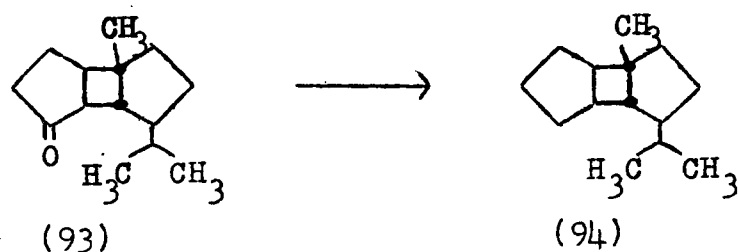
### 1.7 Dibenzo[a,g]biphenylene

It was finally decided to reduce the ketonic groupings completely to methylene groups in order to obtain the octahydro-dibenzo[a,g]biphenylene (96). This was done in the hope that milder dehydrogenation conditions, carried out in the presence of 2,4,7-trinitrofluorenone, might provide the best possible conditions for the isolation of the more stable, deep green complex m.p.  $224-225^{\circ}$ .<sup>10</sup>

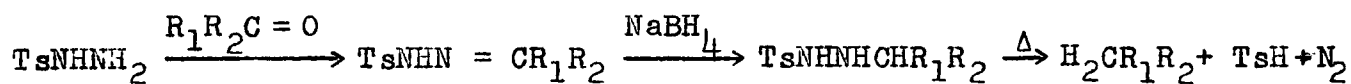
A simple method for the deoxygenation of aliphatic aldehydes

and ketones under mild, neutral conditions was introduced by Caglioti<sup>86</sup> which involves the reaction of the tosylhydrazone derivative with sodium borohydride in methanol.

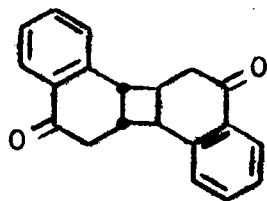
This reaction has been used successfully in the cyclobutane field by White and Gupta<sup>87</sup> who obtained norbourbonane (94) from norbourbonone (93), demonstrating the inertness of the four-membered ring to these reagents.



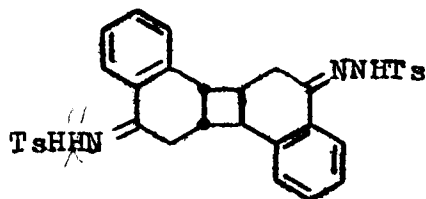
In the case of aromatic carbonyl compounds, Caglioti found that the hydrazone was best reduced by lithium aluminium hydride. Both sodium borohydride and lithium aluminium hydride reduce the C = N - bond of the tosylhydrazone giving intermediate tosylhydrazides CH - NH - which decompose thermally in protic solvents, with or without basic catalysts, to the alkane, p-toluenesulphoric acid and nitrogen.<sup>88</sup>



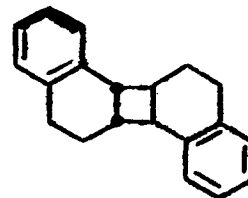
The diketone (85) and tosylhydrazine, refluxed together in methanol for two hours gave the insoluble white ditosylhydrazone (95).



(85)



(95)



(96)

Caglioti et al.<sup>86</sup> obtained tetralin from  $\alpha$ -tetralone, in the analogous reaction to the above, in 30-35% yield by the use of sodium borohydride in methanol. The ditosylhydrazone (95) was found to be almost completely insoluble in methanol, however after refluxing for 4 hours, the reaction mixture appeared as a clear solution. This was extracted with ether and with water, the organic layer giving only a very small quantity of brown oil. On acidification of the aqueous layer a white precipitate was deposited and filtered off. When dry this compound dissolved in chloroform at room temperature and recrystallized without heating. The deposited material was found to be starting material, that is the ditosylhydrazone (> 75%), from its infra-red spectrum and melting point. It would appear that a soluble complex between the ditosylhydrazone and the borohydride in basic solution is decomposed by acid giving a tosylhydrazone hydrochloride. This in turn is decomposed in the chloroform solution to give the free ditosylhydrazone (95).



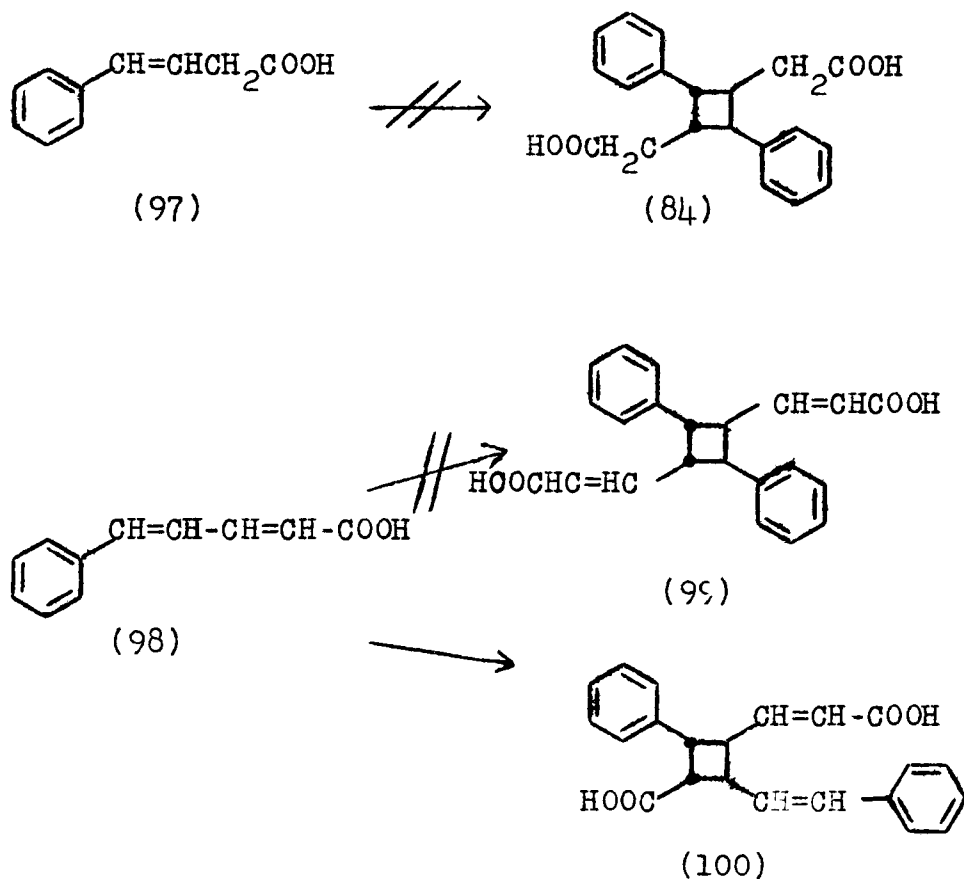
The reduction experiment was repeated with lithium aluminium hydride in tetrahydrofuran to give a residue that was chromatographed on alumina. No product could be isolated from the brown oil obtained which gave no distinct parent peak in the mass spectrum at  $m/e$  260. Two of the most abundant ions at  $m/e$  128 and  $m/e$  130 were considered to be naphthalene and 1,2-dihydronaphthalene fragment ions. The infra-red spectrum exhibited a peak at  $3350\text{ cm}^{-1}$ . These observations were interpreted as showing that the thermal decomposition of the tosylhydrazide could not be considered analogous to that of tetralone.

In this case, a mixture of nitrogen containing compounds and decomposition products, such as naphthalene, of the hydrocarbon (96) are obtained. Thermal decomposition of the tosylhydrazide (95) in this series appears to be accompanied by cleavage of the [a,g] carbon skeleton, as in the case of the dihydroxy compound. This decomposition of a tosylhydrazide to give a nitrogen-containing product rather than the anticipated hydrocarbon has been encountered by N.H. Wilson<sup>89</sup> of this Department in the case of 3-formylfluoranthene.

#### 1.8 Photodimerization of Cinnamylidene Acetic Acid and Styrylacetic Acid

The series of steps required to give the diacid (84) gives a low yield due to the length of the synthetic route and, in particular, the unreliability of the Arndt-Eistert reaction. The dimerization of styrylacetic acid (97), 4-phenyl-3-butenic acid, or cinnamylidene

acetic acid (98), 5-phenyl-2,4-pentadienoic acid, might avoid some of this complexity.



Although cinnamic acids give complex products on solid-state dimerization, as was stated in the introduction it is the crystal structure that determines the feasibility and the stereochemical direction of the reaction. A Stobbe condensation of benzaldehyde and diethyl succinate, following Johnson's<sup>90</sup> method, failed to give the required product. Styrylacetic acid was finally obtained in 40% yield from a Knoevenagel condensation<sup>91</sup> of phenylacetaldehyde

and malonic acid. Attempted dimerization under the same reaction conditions as previously employed, gave only starting material, recovered in almost quantitative yield. A single attempt at dimerization of an ethanol/water solution met with the expected result that an inseparable mixture of truxillic and truxinic isomers was obtained.

Cinnamylidene acetic acid (98) was obtained by the decarboxylation of cinnamylidene malonic acid (86) in pyridine with copper bronze. It was subsequently discovered that dimerization of the monoacid proceeds in a different stereospecific manner to that of the diacid. By degradation Riiber<sup>92</sup> showed that the dimer (100) was formed and although the dimer (99) was finally obtained by decarboxylation of the cinnamylidene malonic acid dimer in vacuo,<sup>93</sup> the compound was not exploited further.

#### 1.9 Conclusion to Section I.

It would appear from the work carried out on cyclobutane compounds that dibenzo[a,g]biphenylenes have been obtained but, under the oxidative conditions employed, these compounds have proven too unstable to be isolated. Several direct precursors have been synthesized requiring only the loss of hydrogen to aromatize and adopt the dibenzobiphenylene structure. Although the instability of the [a,g] system has prevented the isolation of any derivatives, it is considered likely that suitably mild reaction conditions, involving the synthesis of more stable dibenzobiphenylenes, should give the aromatic structures from cyclobutane precursors.

SECTION IIPART I

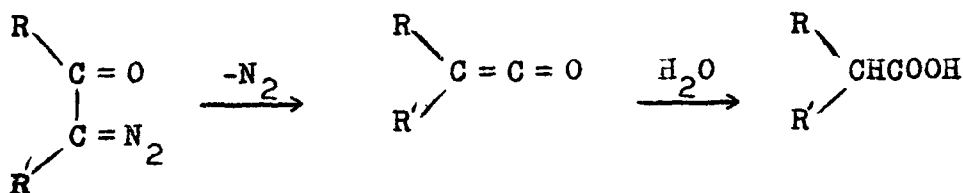
Attempted formation of dibenzo[a,h]biphenylene from a cyclobutene precursor, itself obtained by a photochemical ring contraction of a five-membered ring.

PART II

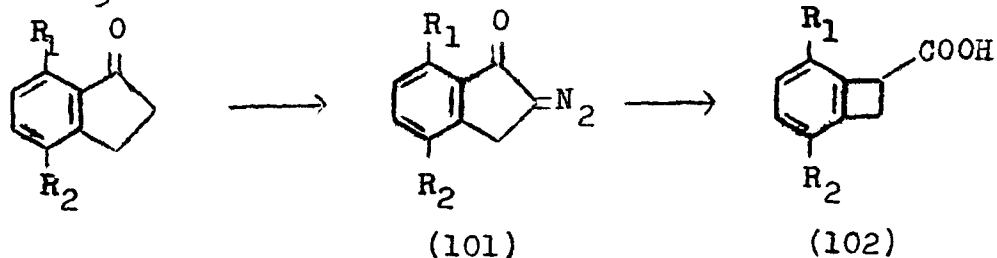
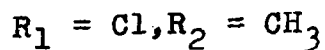
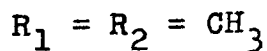
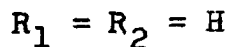
Further research into the chemistry of some 2-substituted naphthalene derivatives prompted by results obtained in the first part of Section II.

Introduction to Section II

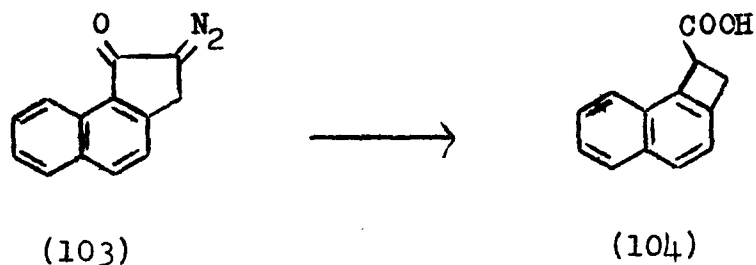
Examples have been quoted in the literature of ring contraction of five-membered rings to four-membered ring structures. The method involves a Wolff rearrangement of an  $\alpha$ -diazoketone to a carboxylic acid by photolysis of the former, giving ring contraction by loss of nitrogen. The rearrangement is by no means limited to the cyclic case described, the general acyclic reaction is thought to involve a ketene intermediate:<sup>93</sup>



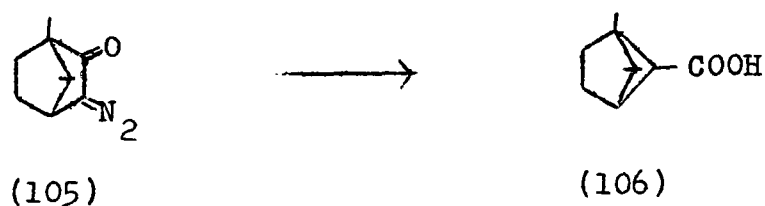
In cyclic systems this gives a route from a cyclopentenone to a cyclobutene carboxylic acid. Thus a 2-diazo-1-indanone (101) gives a benzocyclobutene carboxylic acid (102), as demonstrated by Cava *et al.*<sup>94</sup> who employed the monotosylhydrazones of the diketone as the intermediate from which the diazo compound could be generated by the action of base.



Although not employing the monotosylhydrazone, Horner *et al.*<sup>95</sup> obtained naphtho[a]cyclobutene-1-carboxylic acid (104) in the same way, by photolysis of 2-diazobenz[e]indane-1-one (103).



The method of ring contraction is a general one in that it does not merely apply to the five-membered to four-membered ring structures shown, nor is it limited to homocyclic rings. It is perhaps worth noting that 3-diazocampnor (105) upon ultraviolet irradiation in aqueous dioxan at 0° gave 1,6,6-trimethyl-(1,1,2)-bicyclohexane-2-carboxylic acid (106) in good yield.<sup>96</sup>

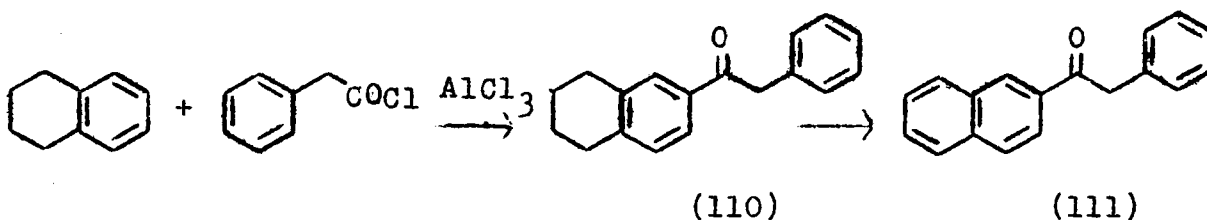




1,2,3,4-Tetrahydronaphthalene, tetralin, was first considered instead of naphthalene as electrophilic substitution, in particular Friedel-Crafts acylation, gives almost exclusive 6-substitution while naphthalene itself normally gives the 1-isomer.

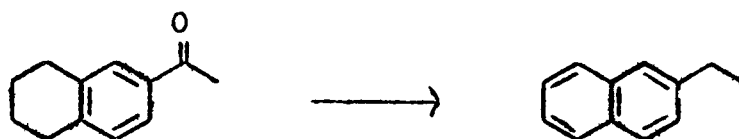
## 2.2 Tetralin Acylation

Electrophilic substitution in 1,2,3,4-tetrahydronaphthalene has been extensively studied, in particular by Fujimura et al. in Japan, and has been shown to occur in the 6-position. For our purpose, Friedel-Crafts acylation of tetralin with phenylacetyl chloride was accomplished by the method of Fujimura et al.,<sup>97</sup> 2-(5,6,7,8-tetrahydronaphthyl) benzyl ketone (110) being obtained in 50% yield. The tetralin used was first washed with concentrated sulphuric acid to remove any sulphur containing compounds, whose presence was demonstrated by the acidic layer turning black. The organic material was washed with sodium carbonate solution, dried over anhydrous magnesium sulphate and distilled giving pure tetralin b.p.  $207.3^{\circ}$ , fraction collected  $206-208^{\circ}$ .





Dehydrogenation of the tetralin ketone (110) to the corresponding naphthalene compound, benzyl 2-naphthyl ketone (111) was effected by *p*-chloranil. Catalytic dehydrogenation, often used as a method of aromatizing hydrogenated compounds such as tetralin, could not be used in this case as this would result in the reduction of the ketonic grouping. This was first experienced by Newman and Zahm<sup>98</sup> using a 20% palladium/charcoal catalyst with several 6-substituted tetralin ketones, and in particular 2-ethyl naphthalene

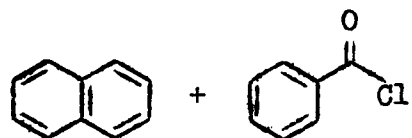


was obtained as product from 2-acetyl-5,6,7,8-tetrahydronaphthalene. An attempt by Orchin<sup>99</sup> et al. to aromatize 2-benzoyltetralin likewise gave 2-benzyl naphthalene.

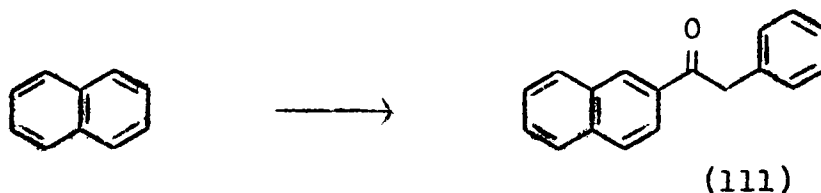
In our case, the oxidation of the tetralin ketone (110) to 2-phenylacetylnaphthalene (111), using *p*-chloranil in refluxing xylene, gave only a 10% yield. It was decided that the aromatic ketone would therefore have to be synthesised by a higher yield route. It is noteworthy that Newman and Zahm<sup>98</sup> attempted catalytic methods of dehydrogenation because of the unreliability of the chemical method and the low yield of ketone obtained.

### 2.3 Friedel-Crafts Acylation of Naphthalene

Although electrophilic substitution in naphthalene has been predicted and found experimentally to occur at the 1-position, it is always accompanied by some attack at the 2-position. In particular it was found that increased 2-substitution could be obtained by suitable choice of solvent and reaction temperature. The yield of 2-ketone in Friedel-Crafts acylation, for example benzoylation, in nitrobenzene as solvent was found to increase with temperature relative to the total yield which fell with increase in temperature.

<u>F/C Acylation</u>	<u>Reaction Temperature</u>	<u>% 1-</u>	<u>% 2-</u>
	35°	68	32
	120°	38	62

Reported as a solvent effect by several authors,<sup>101</sup> Baddeley<sup>100</sup> showed that only one molar equivalent of nitrobenzene or other reagents such as nitromesitylene, or an excess of the acid chloride, was necessary to give increased substitution at the 2-position. The conclusion drawn was that the nitrobenzene added, as did the other reagents, to the acid chloride-aluminium chloride complex to form a larger complex. This bulky extended complex experienced greater steric resistance to attack at the 1-position than at the 2-position.



Almost exclusive acylation of naphthalene at the 2-position was claimed by Buu-Hoi and Cagniant<sup>102</sup> when nitrobenzene was used as solvent. This method,<sup>103</sup> with some slight modifications, gave almost pure 2-phenylacetylnaphthalene (111) in 75% yield that required no further separation of the 1-isomer other than a single recrystallization from ethanol.

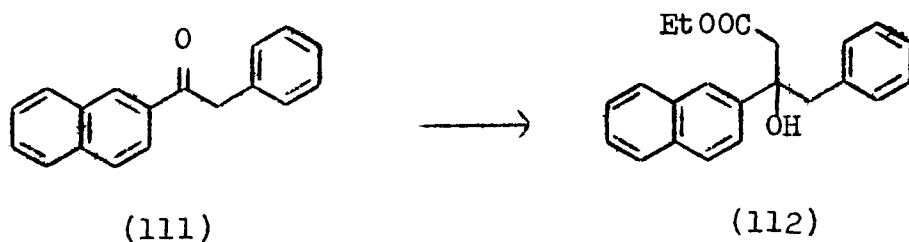
#### 2.4 The Reformatsky Reaction

The Reformatsky reaction of 2-phenylacetylnaphthalene (111), zinc wool and bromoethylacetate proved to be extremely sluggish. Several attempts gave no sign of reaction at all. Even very pure ketone (recrystallized twice from  $\text{CCl}_4$ ) and highly reactive metal<sup>104</sup> could not be relied upon to give reproducible results. A highly active surface was obtained by heating the zinc wool in concentrated sulphuric acid with a few drops of concentrated nitric acid at  $100^\circ$  for 15 mins. The concentrated acid was almost totally decanted and water added, whereupon a vigorous reaction ensued. After washing with water, alcohol, acetone and ether the active metal was used immediately to avoid the possibility of air oxidation and subsequent deactivation of the metal surface. Drying at  $110^\circ$  has been advocated<sup>105</sup> after activation, but the results of several experiments carried out with metal dried in this way showed no advantage over previous experiments.

Zinc is preferable to magnesium as the condensing reagent in the Reformatsky reaction because of the greater tendency of the latter metal to react, in the form of a Grignard reagent, with the

carboxylate group of the halogen ester. This naturally occurs to some extent with zinc also, causing a drop in the yield of hydroxy-ester, but to a much lesser degree than with magnesium. The more reactive metal can however be used where the bromoester is t-butyl,<sup>106</sup> the large group effectively sterically shielding the carboxylate carbonyl from attack.

Rather than use the t-butyl ester and magnesium, the zinc metal was activated as described previously and, based on the results of Miller and Nord,<sup>107</sup> initiators were added to start the reaction. These authors found mercuric chloride most useful, however in our case, iodine was found to be as effective. Once the reaction had started, it was found essential to maintain the reflux temperature while a solution of the bromoester and ketone in sodium-dried benzene was slowly added. If the reaction mixture was once allowed to drop below the reflux temperature, no further reaction took place on reheating, as the metal surface became coated with an insoluble oily zinc complex.



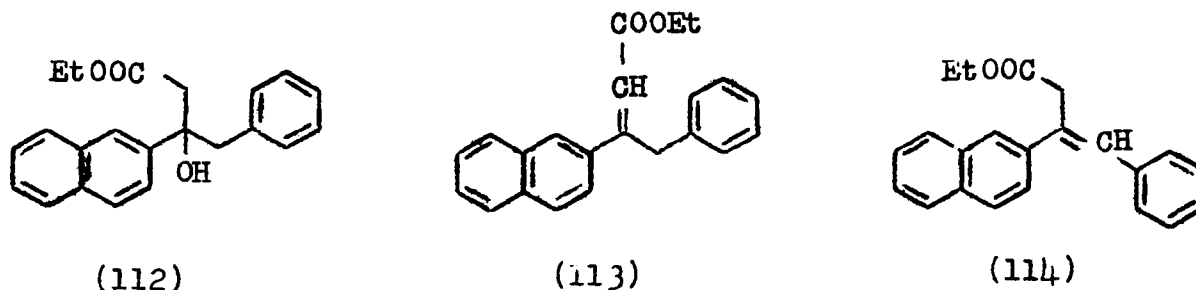
After 2 hrs. of continuous stirring at reflux temperature, the mixture was cooled and the organometallic product decomposed with dilute sulphuric acid, enough to dissolve all the zinc hydroxide

formed. Where all the previously mentioned conditions were strictly adhered to, a high yield of hydroxyester (> 70%) could be obtained but in most cases a lower yield was experienced. Recrystallization of the oily brown product from ethanol gave the hydroxyester (112) as colourless needles, ethyl 3-hydroxy-3-(2-naphthyl)-4-phenylbutyrate.

Similar difficulties have been reported for 1-acetylnaphthalene<sup>108</sup> (25%) and magnesium has been used with limited success in the reaction.<sup>109</sup>

That the hydroxy ester had not undergone dehydration under the reaction conditions employed, was amply demonstrated by the mass spectrum parent peak at  $m/e$  334, and by the infra-red ( $\nu$  OH  $3500\text{cm}^{-1}$  in  $\text{CCl}_4$  solution). The nuclear magnetic resonance spectrum showed a broad singlet at  $5.4\tau$ , which was removed by shaking the deuteriochloroform solution with deuterium oxide ( $\text{D}_2\text{O}$ ), and on this evidence was assigned to the hydroxyl hydrogen atom. The tertiary carbinol was readily dehydrated by formic acid, a relatively mild reagent, in which the ester did not dissolve but remained on the surface of the liquid as an oil. After 1 hour's reflux, an almost quantitative yield of unsaturated ester was obtained.

Dehydration could theoretically proceed by two different routes. Either of the two unsaturated esters (113) or (114) could be formed as the cis- or the trans-isomer.



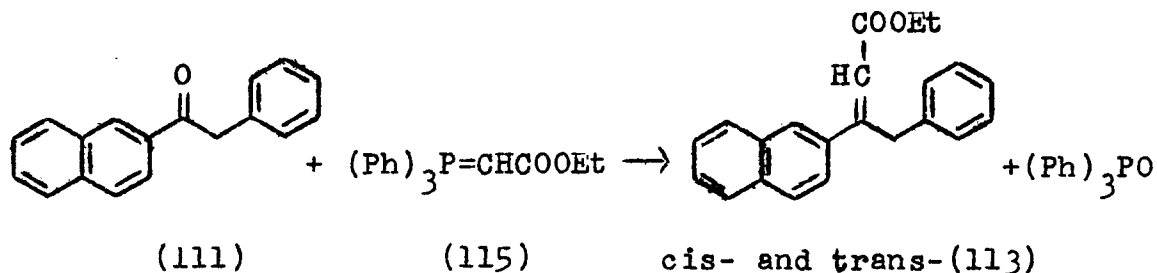
Spectral data gave indications in favour of structure (113). The methylene singlet in the NMR spectrum at  $6.2\tau$  was more characteristic of a benzyl group than a substituted ethyl acetate, although lower than expected for either structure. The carbonyl peak in the IR spectrum at  $1720\text{cm}^{-1}$  indicated some lowering of the stretching frequency due to conjugation. The UV spectrum showed absorption maxima which, when compared with the spectra of 3-(2-naphthyl)acrylic acid<sup>110</sup> and 2-styrylnaphthalene<sup>111</sup> showed similarities with the former.

In order to establish the structure conclusively, and perhaps obtain a more efficient route, an independent synthesis of the ester was attempted. In elucidating the stereochemistry and the mechanism of these reactions, the individual esters will be referred to as *cis*- and *trans*- with respect to the benzyl and ethyl carboxylate groupings in (113), and the phenyl and ethyl acetate groupings in (114). In mechanism diagrams, the 2-naphthyl group appears as  $R_1$  and the benzyl group as  $R_2$ .

## 2.5 The Wittig Reaction

In marked contrast to other olefin syntheses, the Wittig reaction of a carbonyl compound and an alkylidenephosphorane leaves no

doubt as to the position of the resulting double bond.<sup>112</sup> Although the olefin obtained from the dehydration of the hydroxy ester will be the most stable isomer, both this and the other less stable isomers, where the double bond occupies an energetically unfavourable position, could be obtained by this method.



The stable triphenyl ylide (115) was obtained in more than 80% yield<sup>113</sup> by the action of sodium hydroxide on the phosphonium bromide, the latter obtained from triphenylphosphine and ethyl bromoacetate. The olefin synthesis involved the addition of the alkylidenephosphorane (115) to the ketone, followed by elimination of the phosphine oxide  $(\text{Ph})_3\text{PO}$  from the intermediate betaine to give the olefin, ethyl 4-phenyl-3-(2-naphthyl)-but-2-enoate (113). Two reactions were carried out at reflux temperature, one in benzene and one in xylene, the progress of the reaction being monitored by the development of a red coloration, due to the byproduct triphenylphosphine oxide. The red colour took some time to develop (10 mins.) and although darkening with time, indicated that both a high temperature and a long reaction time would be needed for the reaction to go to completion. The stability of the phosphorus ylide was such that after 12 hrs. in refluxing xylene, where a black-red

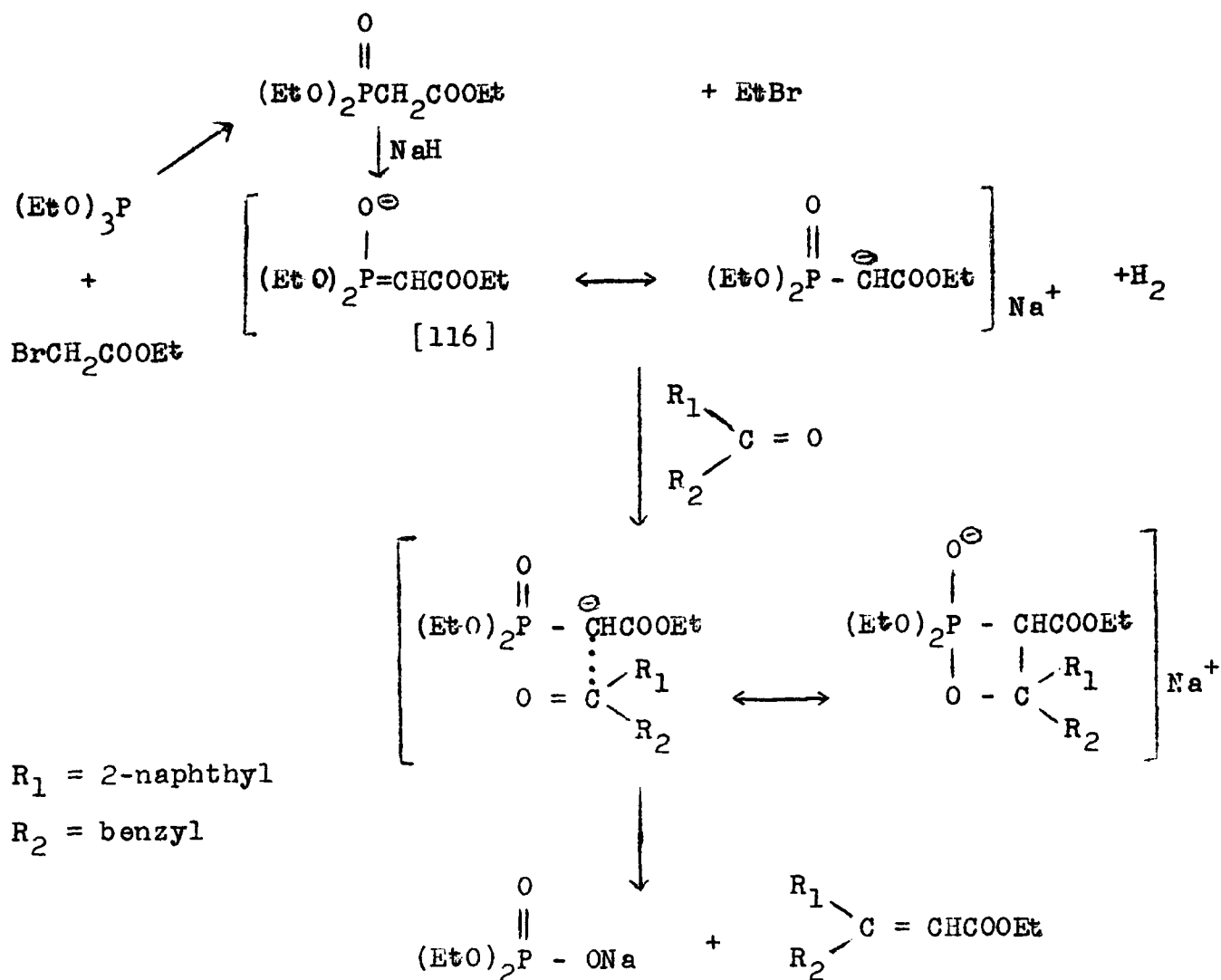
solution was obtained, starting material (20%) could still be isolated on chromatography of the reaction product on an alumina column. The ester product so obtained in low yield (~25%) appeared as a clear oil which could not be crystallized. However, catalytic hydrogenation of this oil gave an almost quantitative yield of the saturated ethyl ester. The stereochemistry of the reaction product was not further studied in this case, but comparison with the results obtained with phosphonate anion leads to the conclusion that a mixture of cis- and trans-olefins were obtained.

The stability and inert character of the triphenyl phosphorane (115) are found to be in agreement with the results obtained by Openshaw and Whittaker<sup>114</sup> who found that olefin formation took place with hindered ketones only under vigorous conditions (boiling xylene, or 150° without solvent).

#### Phosphonate Anions

A more reactive Wittig reagent was prepared by the Michaelis-Arbuzov<sup>115</sup> reaction of triethyl phosphite and ethyl bromoacetate, with elimination of ethyl bromide. Diethyl-(ethylacetate)-phosphonate<sup>116</sup> so formed, on reaction with sodium hydride and evolution of hydrogen generated the phosphonate anion (116) which reacted with the ketone as shown.

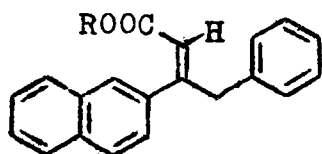




The advantages to be gained in employing this type of compound are that the reaction takes place at low temperatures, room temperature in this case, and that all phosphorus-containing compounds involved are water-soluble. Separation of the olefin from the phosphate ion is thus much easier than from phosphine oxide, obtained as co-product of the previous reaction. Phosphonate anions are stronger nucleophilic reagents than their alkylidenephosphorane counterparts and hence much more reactive.

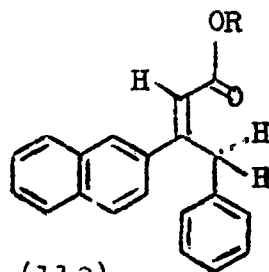
The synthesis was carried out in dimethylformamide and in 1,2-dimethoxyethane, with sodium hydride to generate the phosphonate anion, as advocated by Wadsworth and Emmons.<sup>116</sup> In the former case, a product was isolated on distillation which proved identical to that obtained by dehydration of the Reformatsky hydroxyester. This gave conclusive proof that (113) and not (114) was the true structure of the olefin. The product obtained with the second solvent was not distilled but was taken up in ether and the phosphorus containing compounds removed by washing with water. Chromatography on alumina (30 g. per g.) gave a clear viscous oil. On standing, a small quantity of the already classified unsaturated ester crystallized from the oil, the remainder staying viscous. The nuclear magnetic resonance spectrum of this oil showed the superimposition of two sets of almost identical multiplets only differing in the very slight variance of their chemical shifts. One of these sets matched perfectly the spectrum of the known ester and the other, very slightly offset from the first, was allocated to the other geometrical isomer. The intensities of comparable peaks were roughly the same showing that the oil contained roughly equal quantities of the two isomers, and that the reaction product contained a slight excess (60%) of the more stable ester. Hydrolysis of the ester product gave a similar mixture of cis- and trans-unsaturated carboxylic acids as evidenced by the nuclear magnetic resonance spectrum. Comparing the spectra of the mixtures with those of the unsaturated compounds obtained from the dehydration of the hydroxy ester, it was readily seen that the methylene signals obtained from the Reformatsky compounds

appeared at higher field strengths than the other isomer. This was expected to be the most stable isomer, and can be correlated to structure *trans*- (113) on the basis that the *cis*- (benzyl and ethyl carboxylate) deshielding of the carbonyl on the benzyl methylene group in structure *cis*- (113) will give the lower field resonance seen in the mixtures.



trans-(113) R = Et (113)

trans-(117) R = H (117)



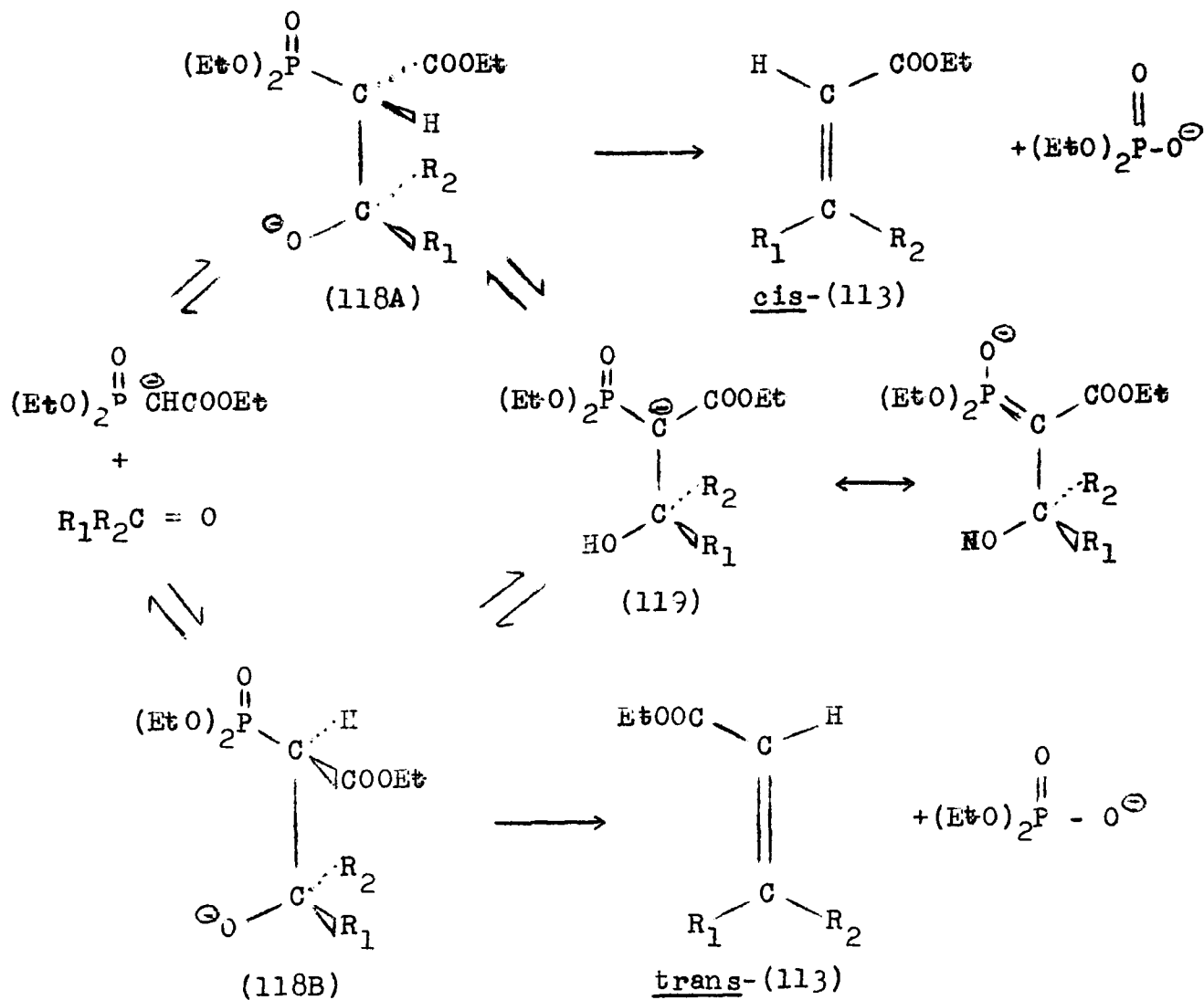
cis-(113)

cis-(117)

<u>Structure</u>	<u>Compound</u>	<u>NMR Spectra (<math>\tau</math> values)</u>		
		$-\text{COOCH}_2\text{CH}_3$ quartet	$-\text{CH}_2\text{Ph}$ singlet	$-\text{COOCH}_2\text{CH}_3$ triplet
<i>trans</i> -(113)	Olefinic ester (dehydration)	5.9	6.2	8.9
<i>cis</i> -& <i>trans</i> -(113)	Mix. olefinic ester (Wittig)	5.8, 5.9	5.4, 6.2	8.75, 8.9
<i>trans</i> -(117)	Olefinic acid (dehydration)	-	6.1	-
<i>cis</i> - & <i>trans</i> - (117)	Mix. olefinic acids (Wittig)	-	5.4, 6.1	-

Comparison of the spectrum of the mixture of esters with that of the phosphorus-containing starting material showed the absence of characteristic peaks belonging to the latter and hence the purity of the ester mixture from phosphorus compounds.

The two geometrical isomers can be considered to be obtained from the following reaction scheme:



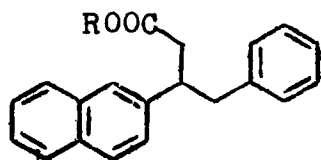
The two isomeric betaine intermediates (118A) and (118B), which lead respectively to the cis- and trans- olefins, are considered to interconvert by either one or both of two processes, reversible betaine formation and betaine interconversion via structure (119). Evidence for the former type of reaction has been reported<sup>117</sup> and loss of the  $\alpha$ -hydrogen as a proton, as indicated by the latter

process, would seem a relatively easy process where, as in this case, there are stabilizing groups present.

It is known that the Wittig reaction is not stereospecific;<sup>118</sup> however, solvents and additives have been shown to have some effect on the proportions of cis- and trans-isomers obtained.<sup>119</sup> The product ratio in 1,2-dimethoxyethane was here shown to be roughly 3:2 in favour of the trans-isomer, while in dimethylformamide only the trans-isomer was identified. This apparent solvent dependence must be considered alongside the possibility that only the more stable isomer survived the distillation of the reaction product. No predictions as to the steric restrictions placed on the intermediates can be made in this case although the predominance of the trans-isomer, neglecting solvating effects, shows that there is more steric hindrance from the benzyl group in (118A) than from the 2-naphthyl group in (118B).

## 2.6 Catalytic hydrogenation

Catalytic hydrogenation of both the trans-(113) ester and the mixture of cis- and trans- esters gave a single saturated ester (120) as product. A quantitative yield of ethyl 3-(2-naphthyl)-4-phenyl butanoate (120) was obtained in both cases, which gave on hydrolysis the saturated acid (121) identical with that obtained from the hydrogenation of the trans-acid (117) and from the mixture of unsaturated acids.



(120) R = Et

(121) R = H

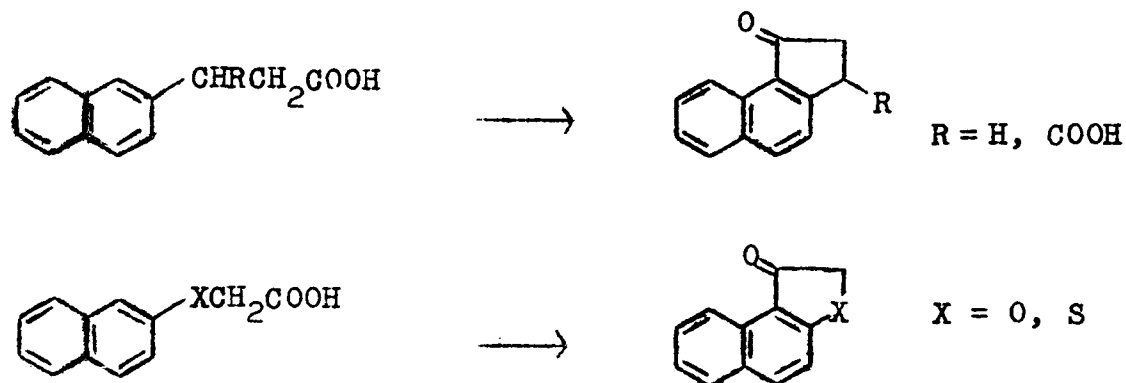
The reactions were carried out in ethanolic solution at room temperature and under atmospheric pressure with a 10% Pd/C catalyst. Previous experiments with 5% Pd/C and PtO<sub>2</sub> proved unsuccessful perhaps due to the age of the catalysts. The ethanolic solution of the olefin was added to 5-10% by weight of catalyst, to avoid the risk of fire, and when the reaction was completed the charcoal was removed by filtration of the solution through a slurry of celite in a sintered-glass funnel.

## 2.7 Ring Closure

### Friedel-Crafts Cycliacylation

Several attempts were made to cyclise 3-(2-naphthyl)-4-phenylbutanoic acid (121) by the reverse Friedel-Crafts reaction.<sup>120</sup> When the reaction was carried out in 1,2-dichloroethane and left overnight at room temperature only an intractable oil was isolated. Similarly, when the acid chloride was added to a suspension of aluminium chloride in benzene at 0° and left overnight, an oil was obtained which did not solidify. Chromatography on an alumina column and recrystallization of the product gave a very low yield of a white solid melting over a wide range of temperature whose NMR spectrum showed a multiplet, integrating for one proton, at 0.85τ.

In view of the experimental results and the difficulty experienced in purifying the ketonic product, it was considered that a mixture of products had been obtained in each case, there being several possible products depending on the reaction route. Several 2-substituted naphthyl acid chlorides are known to ring-close across the 1,2-bond.<sup>121</sup>



Ring closure across the 2,3-bond can be considered as unlikely<sup>122</sup> and therefore the six-membered ring ketone 3-(2-naphthyl)-1-tetralone (122B) is the most probable coproduct.

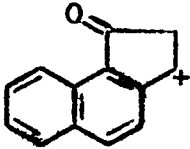

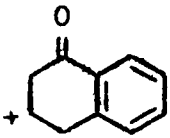
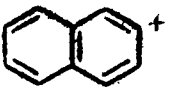


Where the byproduct, as in this case, has appreciable stability a mixture of products might well be expected. The tarry reaction product of ring-closure in the chlorohydrocarbon solvent suggests that the reaction has occurred very quickly and that a shorter reaction time might be effective in obtaining a single isomer. The

Friedel-Crafts reaction is reversible and the impure product can be explained by kinetic and thermodynamic control of the reaction pathways where the longer the reaction time, the greater the amount of the more stable isomer formed. In order to favour the kinetic isomer and obtain as little of the six-membered ketone as possible, the reaction time was cut to 90 minutes at 5-10°. A solution of the acid chloride in benzene was added over 45 minutes to a vigorously agitated suspension of anhydrous aluminium chloride in benzene and, after a further 45 minutes, the reaction was terminated. Distillation of the product under reduced pressure gave a pale brown oil which dissolved in methanol and a minimum of ethanol and crystallized on cooling to give white needles of the ketone already obtained from the former reaction in benzene. The yield in this case rose to a maximum of 20% theoretical.

The structure of the ketone was determined from spectral evidence. The mass spectrum showed a parent peak at  $m/e$  272, identifying the product as arising from intramolecular acylation. The fragmentation pattern then distinguished between the benzindanone (122A) and the naphthyltetralone (122B) structures, by consideration of the most abundant frequent ions, showing structure (122A) to be the ring closure product.

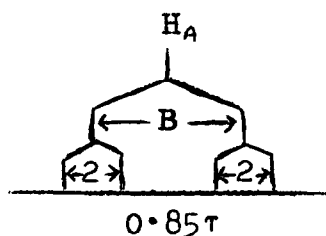
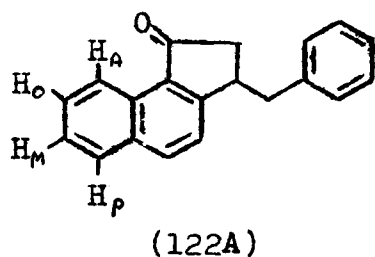


<u>Expected spectrum for</u> <u>(122A)</u>	<u>Product Spectrum</u>	<u>Expected spectrum for</u> <u>(122B)</u>
	272	272 = M <sup>+</sup>
	181	181 = (M-91) <sup>+</sup>
	152	152 = (M-120) <sup>+</sup>
(181-CHO)	91	91 = (M-181) <sup>+</sup>
		
		272
		
		145
		127
		
		116 (145-CHO)

The observed carbonyl stretching frequency of the infra-red spectrum ( $\nu_{C=O}$   $1685\text{cm}^{-1}$  (s)), lower than that expected for a five-membered ring ( $\sim 1740\text{cm}^{-1}$ ) due to conjugation, gives no distinction between the two isomers. However, with a complete spectrum built up from two solution spectra ( $\text{CCl}_4$  and  $\text{CS}_2$ ), the main peaks of the fingerprint region can be distinguished. In particular the peak due to the two adjacent hydrogens out-of-plane bending ( $830\text{cm}^{-1}$ ) at positions 3 and 4 on the naphthalene nucleus is highly characteristic, lending further proof to isomer (122A).

Although having a complex aromatic region ( $1.9\tau - 3.0\tau$ ), the nuclear magnetic resonance spectrum shows one aromatic proton to have been shifted downfield. It is a common feature in 1-substituted naphthalenes that the peri proton is deshielded to some extent relative to the other aromatic protons, depending on the substituent.<sup>123</sup> This effect is found greatest with carbonyl groups where the proton resonates at lower field strengths than the expected aromatic region ( $2 - 3.5\tau$ ), as in 1-acetyl- ( $1.3\tau$ ) and 1-phenylacetylnaphthalene ( $1.25\tau$ ). It is more pronounced in this case due to the lack of

rotation which could move the carbonyl out of the plane of the naphthalene molecule and hence the quartet, integrating for one proton, occurs at  $0.85\tau$ .



$$J_{AO} (\text{ORTHO}) = 8 \text{ c.p.s.}$$

$$J_{AM} (\text{META}) = 2 \text{ c.p.s.}$$

$$J_{AP} (\text{PARA}) = -$$

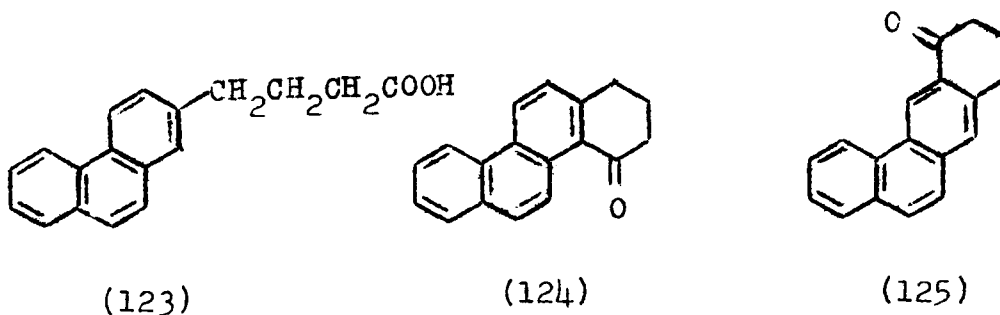
The quartets found in these spectra arise from coupling through the aromatic ring and are due to ortho (6-10 c.p.s.) and meta (1-3 c.p.s.) splitting, the para (0-1 c.p.s.) being too small to be considered. The methylene and methine hydrogens give a second order  $A_2B_2C$  multiplet ( $6.0 - 7.5\tau$ ), integrating in all for five protons.

### Cyclodehydration

Two dehydration experiments on the free acid were carried out in polyphosphoric acid<sup>124</sup> at  $100^\circ$  and  $150^\circ$  respectively. In the former case the acid did not dissolve and was recovered unchanged after 2 hours. In order to obtain a homogeneous reaction medium, the latter experiment was attempted above the melting point of the acid. After 1 hour, the product was chromatographed to give a white solid, the NMR spectrum of which showed it to be a mixture. A quartet at  $0.85\tau$  indicated the presence of a quantity of the expected ketone (122A). This was not isolated and the mixture of

ketones not further studied. The main impurity was probably ketone (122B).

Where, as here, more than one product is possible, the method of cyclisation can determine the direction of ring closure and hence the proportions of isomeric ketones obtained. This was demonstrated by Fieser and Johnson<sup>125</sup> in the cyclisation of 4-(2-phenanthryl)-butyric acid (123) where anhydrous hydrofluoric acid and zinc chloride in acetic acid-anhydride gave ketones (124) and (125) respectively while 85% sulphuric acid and Friedel-Crafts reaction gave mixtures of these isomers.



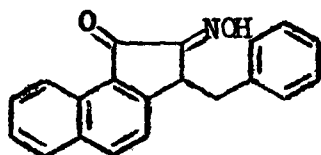
In our case, a single isomer was obtained with anhydrous HF which gave a high yield (77%) of the benzindene (122A), then recrystallized from ether.

## 2.8 Oximino- and Diazoketones

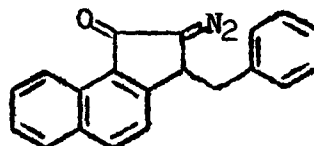
The oximino-derivative of ketone (122A) was prepared by the general reaction of compounds, containing an active methylene group, with nitrous acid. The nitrous acid was here generated in situ. by the addition of n-butyl nitrite to a solution of the ketone in

methyl cellosolve (2-methoxyethanol), acidified with concentrated hydrochloric acid. The n-butyl nitrite was freshly prepared from n-butyl alcohol by the method of Noyes<sup>126</sup> and distilled before use. The resulting dark red product was recrystallized with difficulty to give a low yield (10%) of the yellow diazoketone. A bright red solid was also isolated which was taken to be a nickel complex arising from spatula contamination. Methyl cellosolve has been used as solvent successfully with indanones<sup>94</sup> but in our case, the low solubility of the ketone limited its usefulness. Horner, working on what could be classed as the present compound 4,5-benzindan-3-one,<sup>95</sup> used ethanol as solvent with reasonable success. The ketone (122A) readily recrystallized from ethanol and, to keep the mixture homogeneous, the reaction was carried out at 40°. Once the nitrite had been added, no precipitation occurred on cooling. After an hour, an excess of nitrite was added and the oximinoketone (126) crystallized out.

The second order  $A_2B_2C$  spectrum obtained from the ketone took the form of a series of peaks (6.0 $\tau$  - 7.5 $\tau$ ) in deuteriochloroform. This collapsed to an  $A_2B$  spectrum of a triplet (5.35 $\tau$ ) and a doublet (6.4 $\tau$ ) in deuterioacetone. The oximinoketone was insoluble in  $CDCl_3$  and the TFA spectrum was blurred and indistinct. In  $CD_3COCD_3$ , a clear spectrum was obtained showing the characteristic peak of the peri-hydrogen (1.0 $\tau$ ).

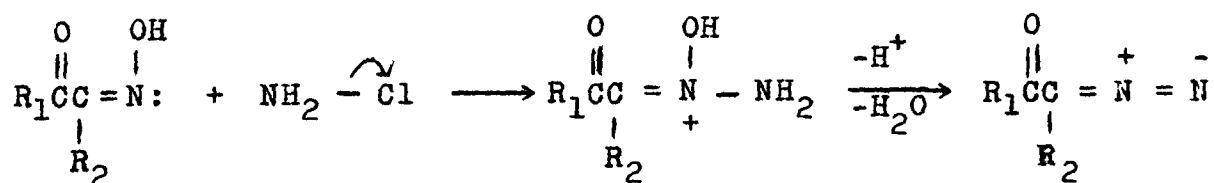


(126)



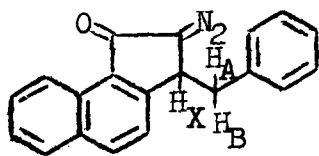
(127)

The diazoketone (127) was prepared in high yield by the reaction of the finely powdered oxime with chloramine in sodium hydroxide solution. Although heterogeneous, this method proved infinitely more successful than a homogeneous reaction, attempted in 1:1 aqueous ethanol, which gave only trace quantities of the required product. The chloramine solution was prepared by mixing ice-cold solutions of sodium hypochlorite and ammonia (sp.g. 0.91, 25%  $\text{NH}_3$ ) at  $0^\circ$  and added dropwise to the suspension. It has been suggested<sup>127</sup> that the reaction involves a sequence of steps initiated by nucleophilic displacement at the chloramine nitrogen. The carbonyl group plays no part in the sequence outlined below and indeed, fluorenone oxime has been converted into diazofluorene by this method.



The NMR spectrum of the oximinoketone (126) gave a methine triplet and a methylene doublet along with a broad hydroxyl peak.

Although an asymmetric centre exists in the molecule, the steric and electronic influences affecting the two diastereoisomers are identical on either side of the benzindenone plane and hence both isomers resonate at the same frequencies giving the simple  $A_2B$  pattern. This equivalence of the spectra of the diastereoisomers also holds for the diazo compound. The NMR spectrum of the diazoketone (127) shows three unsymmetrical quartets. The methine hydrogen quartet centred on  $4.5\tau$  shows two coupling constants 9.2 c.p.s. and 5.4 c.p.s. The other two quartets from each of the two methylene hydrogens shows for  $H_A$ , centred on  $6.5\tau$ , 5.4 c.p.s. and 13.5 c.p.s. and for  $H_B$ , centred on  $7.1\tau$ , 9.3 c.p.s. and 13.5 c.p.s. The methylene hydrogens couple both with the methine hydrogen and with each other due to the non-equivalence of the hydrogen atoms of the methylene group adjacent to the asymmetric centre. The system is therefore ABX where  $J_{AB}$ , the geminal coupling constant, is larger than the vicinal constants,  $J_{AX}$  and  $J_{BX}$ , which are themselves unequal.

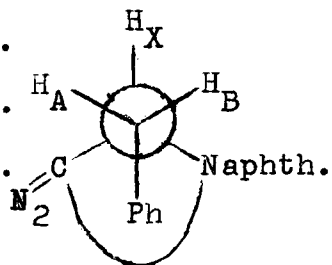


(127)

$$J_{AB} = 13.5 \text{ c.p.s.}$$

$$J_{AX} = 9.2 \text{ c.p.s.}$$

$$J_{BX} = 5.4 \text{ c.p.s.}$$





Rotation about the carbon-carbon bond will favour a staggered conformation, one possibility is shown in the Newman projection above, and an average resonance spectrum of the various conformations will be recorded.

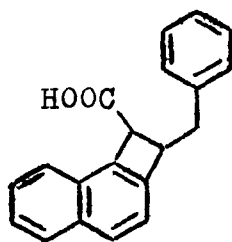
Comparison of the NMR spectra of the oximinoketone (126) and the diazoketone (127) shows the former to exhibit a first order  $A_2B$  spectrum while the latter shows an ABX spectrum for the same three hydrogens. The non-equivalence of the two methylene hydrogens is apparently only observed when one of the two experiences deshielding to a greater extent than the other. The influence of the oxime grouping is insufficient to differentiate between the two, whereas the highly polar diazo group markedly deshields one of the two hydrogen atoms giving the observed spectra.

## 2.9 Ring Contraction of the Cyclopentenone Ring.

Irradiation of the diazoketone was carried out in a Hanovia IL Photochemical Reactor with the lamp immersed in the solution. A tetrahydrofuran:water (5:1) mixture was employed as solvent, any peroxides being removed from the tetrahydrofuran by first passing it through an alumina column. To the solution of the diazoketone, sodium bicarbonate was added (1 g./g. ketone) and the suspension was vigorously agitated throughout the reaction period. After 15 hrs. irradiation, the organic solvent was removed and the residue taken up in chloroform and water. The chloroform layer was extracted with sodium bicarbonate solution to remove any traces of acidic products and the bicarbonate extracts combined. The

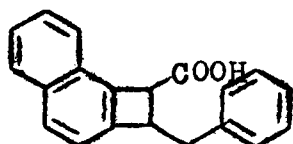


neutral photolysis products were orange-red gums which did not crystallize and were discarded after they were shown to contain no unchanged diazoketone (absence of the  $2100\text{ cm}^{-1}$  infra-red band). Acidification of the bicarbonate extract gave a very low yield of crude carboxylic acid which was isolated and recrystallized from benzene/light petroleum as fine white needles m.p.  $135^{\circ}$ .

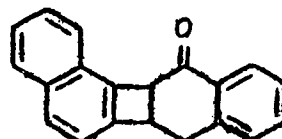
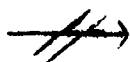


(107)

The NMR spectrum of 2-benzyl-1,2,3,4-tetrahydronaphtho[1,2-b]cyclobutene carboxylic acid (107) showed a broad peak for the carboxylic proton at  $0.4\tau$  and the adjacent methine hydrogen as a doublet ( $5.3\tau$ ), split by the other cyclobutene hydrogen. The latter appeared as a complex multiplet at  $5.8\tau$  and the methylene hydrogens, as with the diazoketone, as quartets at  $6.6\tau$  and  $7.2\tau$ . The acid showed a small peak in the infra-red spectrum at  $1000\text{ cm}^{-1}$  indicative of the cyclobutene ring. The UV spectra between  $220\text{-}290\text{ m}\mu$  of the diazoketone and the carboxylic acid were similar, indicating that the resonance of the benzene ring was essentially unaltered by the ring contraction.

2.10 The dibenzo[a,h]biphenylene structure

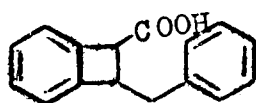
(107)



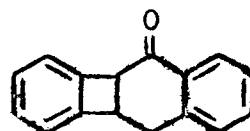
(108)

The finely powdered ring-contracted carboxylic acid (107) was kept in anhydrous hydrofluoric acid for 6 hrs. This gave, on isolation of the neutral product, an oil which did not crystallize and whose IR spectrum indicated a ketonic carbonyl ( $\nu_{C=O}$  (m),  $1710\text{ cm}^{-1}$ ; cf. free acid  $1690\text{ cm}^{-1}$ ). The mass spectrum showed no discernible peak at  $m/e$  270 expected for (108) and in general consisted of a large number of peaks beyond  $m/e$  450 indicating polymerization. The NMR spectrum also showed a large number of peaks which could not be attributed to any single structure and this, along with the other evidence, was taken to show that polymerization, via ring-opening of the four-membered ring in the acidic<sup>129</sup> reaction conditions, giving ketonic products of high molecular weight, has predominated over the anticipated intramolecular cyclodehydration.

Previous work in this Department<sup>80</sup> on the analogous compound (128) failed to give the expected ring closure ketone (129).



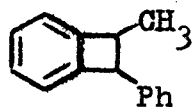
(128)



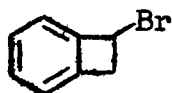
(129)

From the IR spectrum of the product, it was concluded that lactonic products had been obtained ( $\nu$  C=O,  $1770\text{ cm}^{-1}$ ) due to ring opening to olefinic acids which then ring closed to the isomeric lactone cf. Ansell and Gibbs.<sup>128</sup> These authors state that a mixture of lactones and ketones are formed on cyclisation of olefinic acids, the relative proportions of which are dependent both on the cyclising agent and the reaction temperature. Strong acids are reported as favouring lactone formation, as experienced with (128) in anhydrous hydrofluoric acid. Under the same conditions, (107) showed no trace of lactonic products in the IR spectrum, giving what was taken to be a ketonic product.

In both cases, only the isomer in which the benzyl and carboxylic acid groups existed in a cis- configuration about the 1,2-bond could possibly give a stable intramolecular condensation product. The trans-isomer would give rise to a highly strained product in the unlikely event of cyclisation occurring. Few predictions can be made as to the stereochemistry of the two groups although on steric grounds, hydroxyl attack in the hydrolysis of the ketene intermediate of the Wolff rearrangement, might be expected from the side opposite to the benzyl group giving a trans-product. The NMR spectrum however leads to the opposite conclusion. Cava and co-workers have studied the NMR spectra of some benzocyclobutenes<sup>65</sup> and have shown the trans-coupling constant to be much larger than the corresponding cis-coupling constant. This effect is exhibited in the two isomeric 1-methyl-2-phenylbenzocyclobutenes, and in 1-bromobenzocyclobutene the difference is even more pronounced.

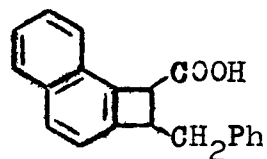


$J_{\text{trans}} = 6.1 \text{ c.p.s.}$   $J_{\text{cis}} = 3.1 \text{ c.p.s.}$



$J_{\text{trans}} = 4.75 \text{ c.p.s.}$   $J_{\text{cis}} = 1.95 \text{ c.p.s.}$

With reference to the carboxylic acid (107), the coupling constant of the machine doublet at  $5.3\tau$  is  $2.3 \text{ c.p.s.}$  indicative, by comparison, of a cis-configuration as shown.



$J_{\text{cis}} = 2.3 \text{ c.p.s.}$

Conclusion to Part I

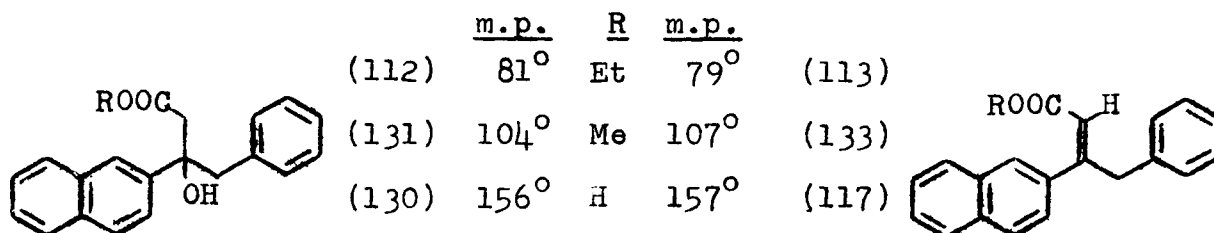
The lack of success reported<sup>80</sup> in the attempted ring closure of the benzocyclobutene carboxylic acid (128) and that experienced here with the corresponding naphthocyclobutene carboxylic acid (107), lead to the conclusion that, due to the instability of the cyclobutene ring in strongly acidic<sup>129</sup> conditions, the simple cyclodehydration reaction cannot be utilised to give the dibenzobiphenylene structure. This does not mean to say that dehydrogenation of a suitable precursor such as (109) will not yield the required aromatic compound, but merely that the route to the former will not be possible via the ring closure of a cyclobutene carboxylic acid.

SECTION II - PART II

In the course of the synthetic work described in Part I a number of problems arose. These disconnected sidelines raised points of interest and were investigated, giving results at variance with earlier work. They are here presented separately, but reference to and comparison with material in Part I is made throughout.

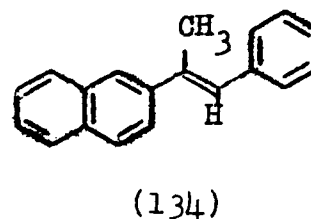
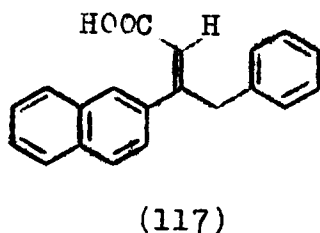
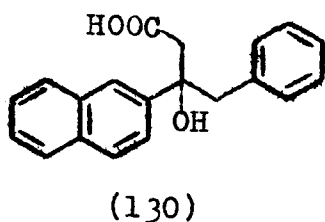
## 2.11 Dehydration Reactions

The hydroxy acid (130) and the methyl ester (131) were obtained from ethyl 3-hydroxy-3-(2-naphthyl)-4-phenylbutanoate (112) by hydrolysis and subsequent esterification. Similarly, the unsaturated acid (117) and methyl ester (133) were obtained from ethyl 3-(2-naphthyl)-4-phenylbut-2-enoate (113).

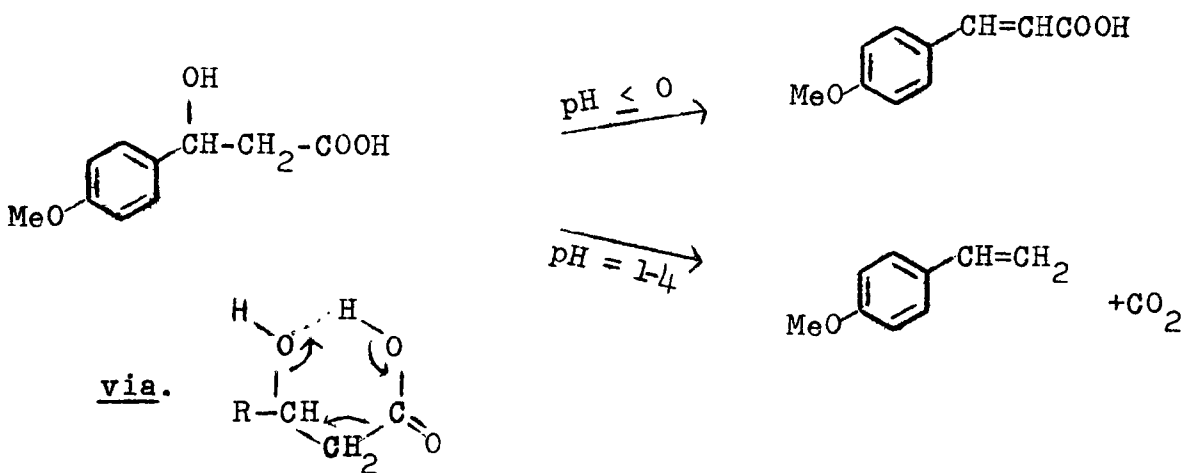


The similarity of the melting-points of the two series will be noted and this led to complications in the identification of the corresponding compounds. That the hydroxy compounds had indeed undergone dehydration, was obvious from the respective analyses, a wide variety of spectral evidence and the depression of the mixed melting points: (112) and (113) etc. Such a phenomenon is unusual, if not unique, and were it not for the physical methods employed, could have proven difficult to resolve.

The methyl ester (131), when dehydrated in the same manner as the ethyl ester (112), gave the unsaturated methyl ester (133). The hydroxy acid (130) however in 50% sulphuric acid gave a low yield of the unsaturated acid (117) along with a high yield of the hydrocarbon (134). In formic acid, the neutral product was obtained entirely, in high yield.



An almost identical situation has been reported for 3-hydroxy-3-(*p*-methoxyphenyl)propionic acid which, in strongly acidic solution, yielded the cinnamic acid derivative, while the main reaction in weakly acidic solution is the decarboxylation to *p*-methoxystyrene presumably via the internally hydrogen bonded intermediate.<sup>130</sup>

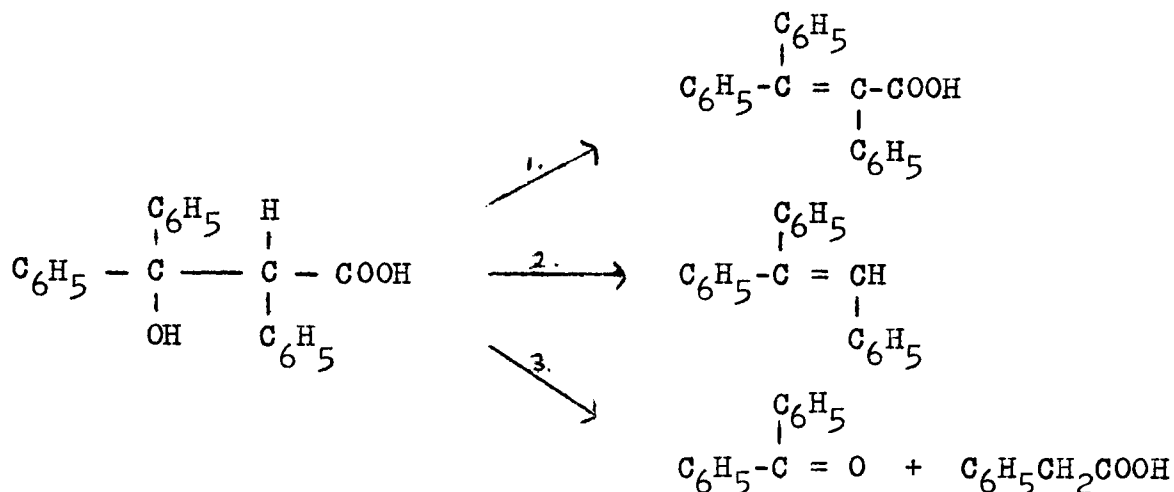


## 2.12 Fragmentation Reactions

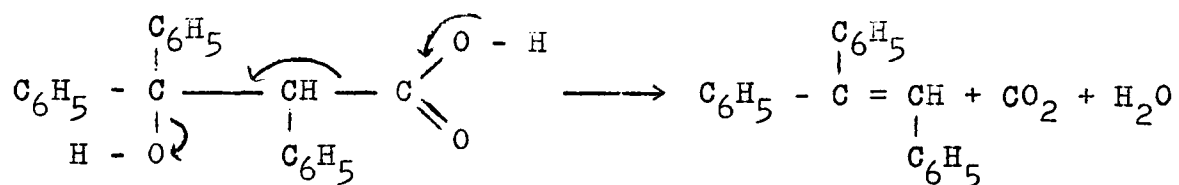
Fragmentation reactions in general, including the decarboxylation of hydroxy acids, have been reviewed as a class of organic reactions by Grob and Schiess.<sup>131</sup> Elucidation of the mechanism comes from work by Ivanoff *et al.*<sup>132</sup> on the action of acetic



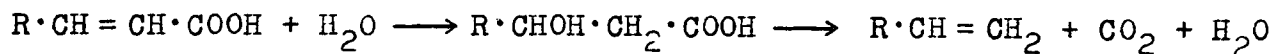
anhydride on certain 2-hydroxy acids. The hydroxy acids were found to decompose by three different routes e.g.



The evidence suggested that the unsaturated acid was not the intermediate in the formation of the unsaturated hydrocarbon and that the driving force of the reaction was the double elimination:

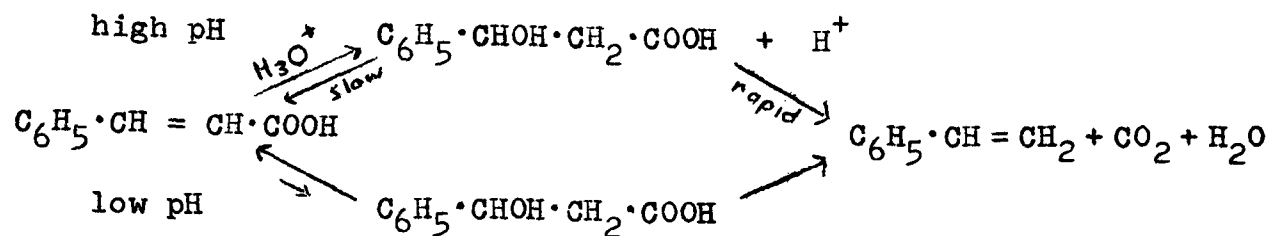


Although the decarboxylation of cinnamic acids in the presence of acids was suggested by Johnson and Heinz<sup>133</sup> to proceed via a carbonium ion intermediate ( $\text{C}_6\text{H}_5 \cdot \overset{+}{\text{C}}\text{H} \cdot \text{CH}_2 \cdot \text{COOH}$ ), Zajac and Nowicke<sup>134</sup> later suggested that the reaction proceeded through the hydroxy acid.



This was confirmed by Noyce and Heller,<sup>135</sup> who studied the behaviour of the acid in varying  $\text{H}^+$  concentrations, and found that at low pH the rate-determining reaction was the hydration of the acid which

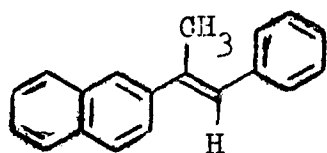
was followed by rapid, synchronous dehydration and decarboxylation.



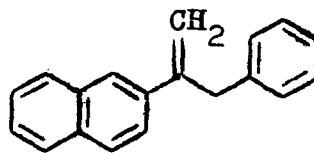
At high pH, only a limited amount of hydroxy acid is formed because of the ease of hydration but this is rapidly removed and the equilibrium re-established.

Both 1,2- and 2,3-unsaturated acids are known to decarboxylate fairly readily, but the ease with which the hydroxy acid (130) gave the unsaturated hydrocarbon suggested that the reaction involved a synchronous fragmentation similar to that described above, rather than a two-step dehydration and subsequent thermal or acid-catalysed decarboxylation. This was confirmed by the failure of an attempted decarboxylation of the unsaturated acid (117), under the same conditions as for the hydroxy acid (130), in which almost 90% starting material was recovered and no neutral product isolated.

The expected hydrocarbon product of the fragmentation reaction involving the hydroxy acid is (135), an isomer of the actual product (134).



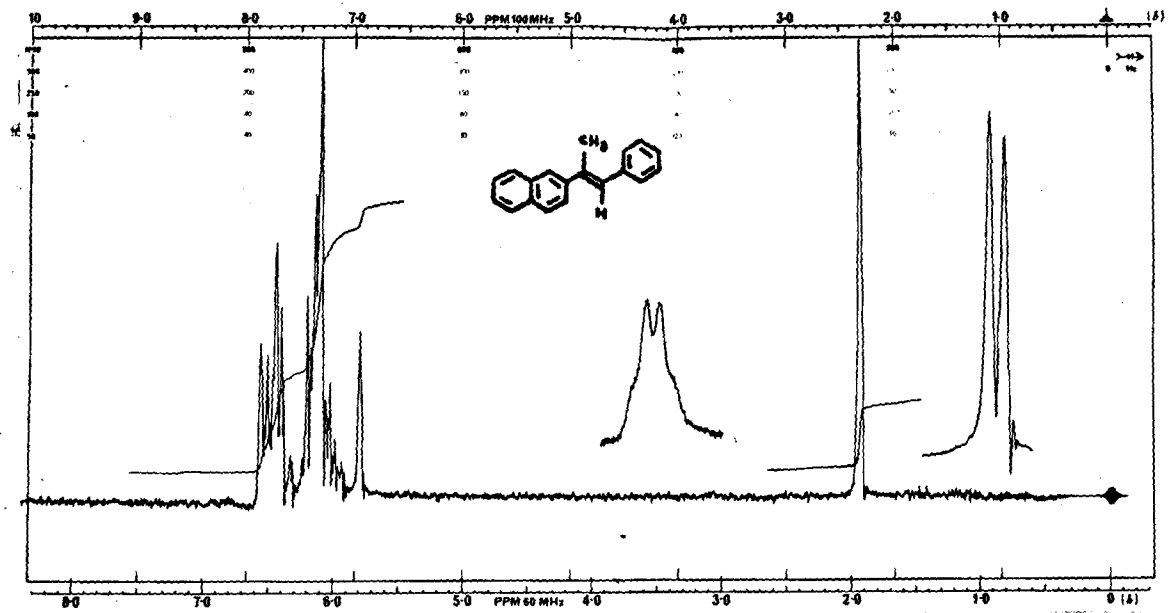
(134)

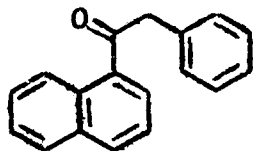


(135)

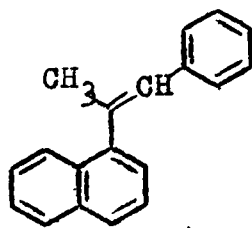
The lack of any trace of the methylene olefin (135) in the NMR spectrum of the product indicates that the fragmentation reaction is accompanied by rearrangement of (135) to (134), giving the compound of maximum conjugation and greatest stability. The other possible route to (134), which would not involve bond migration, would be via the decarboxylation of the 2,3-unsaturated carboxylic acid. This is considered unlikely as it would require the hydroxy acid to dehydrate in a different manner to that experienced with the hydroxy esters. As rearrangement of (135) to (134) either thermally or by acid catalysis is not considered likely in the reaction conditions employed, the conclusion is that fragmentation and rearrangement take place at the same time.

The UV spectrum of (134) was almost identical to that of the unsaturated methyl-(133) and ethyl-(113) esters although the double bond is in a different position. Structure (134) was based on the NMR spectrum which showed a methyl peak at  $7.69\tau$  and an olefinic hydrogen at  $3.06\tau$ ; expansion of the spectrum showed the former to be a doublet and the latter a quartet. The splitting of the peaks is due to allylic coupling, between the hydrogens of the methyl group and the olefinic hydrogen, through the double bond. The coupling constant  $J = 1.4$  c.p.s. is indicative of a trans-relationship across the double bond ( $J$  cis  $\approx 0$ ) as shown in structure (134). Confirmation of structure came from independent syntheses.

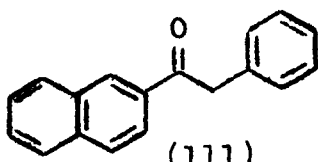


2.13 1- and 2-Naphthyl ketonesPhenylacetylnaphthalene

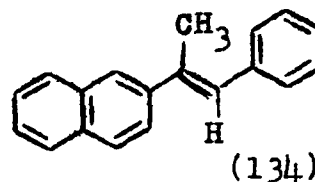
(136)



(137)



(111)



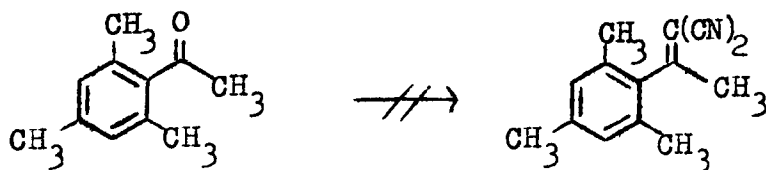
(134)

Cook and Galley<sup>136</sup> reported the Grignard reaction of 1-phenylacetylnaphthalene (136) with methyl magnesium iodide, and subsequent dehydration, to give the hydrocarbon (137). The melting point of this compound, 139°, is that of compound (134), whose structure has already been characterised. These authors also claimed that (136), when boiled gently for 3 hours underwent intramolecular rearrangement to 2-phenylacetylnaphthalene (111).

It was suspected and later proven that the two hydrocarbons were one and the same. In order to establish the structure pure samples of the two ketones were required and to this end a Friedel-Crafts phenylacylation of naphthalene was carried out in 1,2-dichloroethane, giving a mixture of (136) and (111). Separation of the components proved to be difficult, only fractional crystallization of the picrates being effective. Cook and Galley's<sup>136</sup> work was repeated on samples of the pure ketones, whereupon (111) gave the expected hydrocarbon (134) while (136) did not react at all with methyl magnesium iodide. The 1-naphthyl ketone also showed no signs

of reaction in the Reformatsky reaction. It has already been stated that in the acylation of naphthalene an appreciable quantity of 2-substituted compound is obtained along with the 1-naphthyl ketone. Cook's phenylacylation in carbon disulphide and ours in 1,2-dichloroethane gave a mixture of the two isomers (roughly 25% 2-ketone from the NMR spectrum). Both the "thermal rearrangement" reported by Cook and Galley, where the more stable 2-ketone (111), being present in substantial quantity, was recovered from the tarry product, and the isolation of (134) from (136) stem from this impurity of the starting material. In a later paper<sup>137</sup> Cook described the separation of the two phenylacetyl ketones but did not repeat his earlier work on the pure ketones so obtained.

The surprising lack of reactivity of 1-phenylacetylnaphthalene towards even a Grignard reagent can only be related to the steric shielding experienced by the carbonyl function. The 2-isomer is also shielded, but to a lesser extent, as evidenced by the sluggish Reformatsky reaction and the fact that several attempted Knoevenagel reactions with malononitrile yielded only starting ketone. A parallel to the latter can be seen in acetomesitylene<sup>138</sup> where no condensation product was obtained with malononitrile even after refluxing for 2 days, steric factors being responsible in both cases.



It has been shown<sup>139</sup> that the reactivity of ketones of general formula  $\text{PhCOR}$  is greatly reduced in the Grignard addition reaction by branching of R in the 2-position, slightly in the 3- and not at all in the 4-position. This is amply demonstrated in the above cases.

A Wittig reaction of (111) with  $(\text{Ph})_3\text{PCH}_2\text{Br}$ , in which the ylide was generated by potassium *t*-butoxide<sup>140</sup> as a yellow-coloured intermediate, similarly failed in that the hydrocarbon (135) was not obtained.

### Acetylnaphthalene

The structure of (134) was further verified by its synthesis from 2-acetylnaphthalene and benzylmagnesium bromide. Pure 1-acetylnaphthalene, obtained from 1-naphthonitrile,<sup>141</sup> gave no reaction with this Grignard reagent. We also carried out this reaction on commercial 1-acetylnaphthalene and isolated hydrocarbon (134); the NMR spectrum showed the present of approximately 20% 2-ketone and it is this much more reactive isomer which readily reacts to give the observed product. The proportions of the 1- and 2-ketones were easily derived from the relative intensities of the peri-hydrogen (1.25 $\tau$ ) in the former and the hydrogen on  $\text{C}_1$  (1.7 $\tau$ ) in the latter, both of which are shifted downfield from the aromatic multiplets in the NMR spectrum by the proximity of the carbonyl group.

Differences in the steric hinderance experienced by the two isomers are seen in the Grignard reaction above and in the Wittig reaction where 2-acetylnaphthalene reacted with  $(\text{Ph})_3\text{PCH}_2\text{PhBr}$ <sup>142</sup> to

give (134) while 1-acetylnaphthalene did not react at all, dibenzyl being the only product.

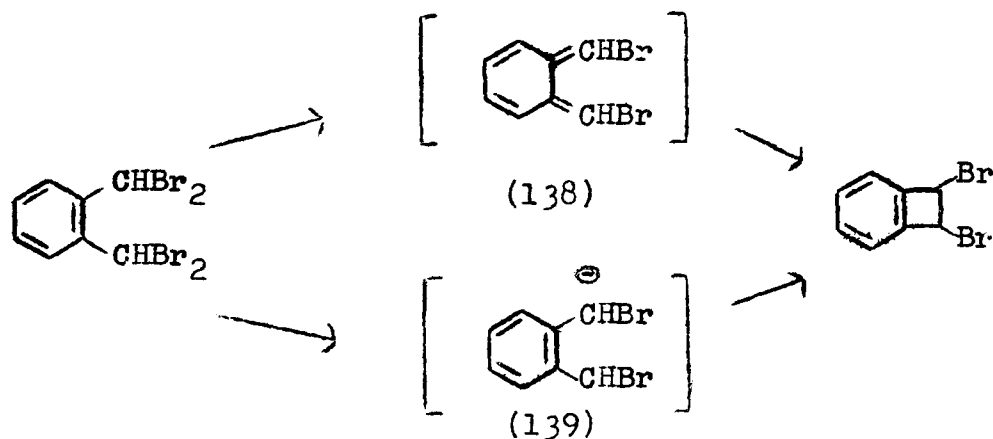


SECTION III

Attempted synthesis of dibenzo[a,c]biphenylene  
by the dimerization of a benzocyclobutadiene intermediate.

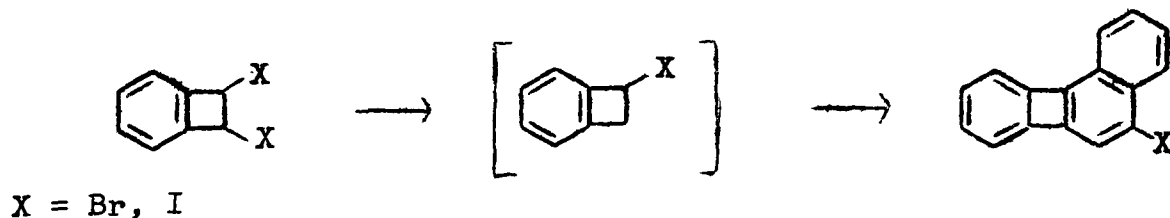
Introduction to Section III

Although not identified as such at the time, the first benzobiphenylene, 1-bromobenzo[*a*]biphenylene, was obtained by Finkelstein<sup>37</sup> via the dimerization of 1-bromobenzocyclobutadiene. This transient intermediate was generated on debromination of 1,2-dibromobenzocyclobutene, the product of reaction of  $\alpha,\alpha,\alpha',\alpha'$ -tetrabromo-*o*-xylene and sodium iodide. This work was later reinvestigated and confirmed by Cava and Napier<sup>22</sup> who characterised the benzobiphenylene and suggested that the initial reaction occurred through a 1,4-elimination of the tetrabromo compound to give the *o*-quinodimethane derivative (138) as intermediate.



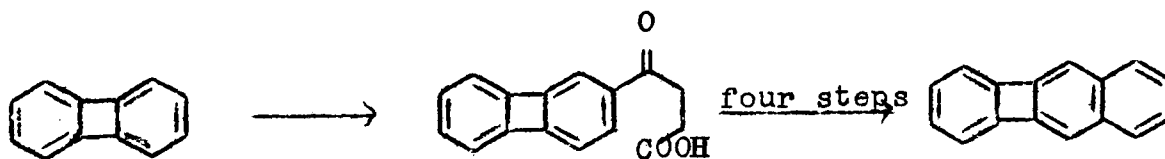
This was considered doubtful by Jensen and Coleman,<sup>143</sup> as only a trans-dibromo product was obtained, and they assumed the generation of an intermediate carbanion (139) to have taken place. Evidence in favour of the former mechanism came from the trapping of the *o*-quinodimethane intermediate as its Diels-Alder adduct with *N*-phenylmaleimide.<sup>144</sup>

When the reaction of the tetrabromoxylene with sodium iodide was carried out over a prolonged period, the dibromo product was converted to 1,2-diodobenzocyclobutene. A more detailed examination<sup>143</sup> of the latter dihalide led to the isolation of the two isomeric diiodides, cis-(8.4%) and trans-(91.6%). As the two diiodides were interconverted by refluxing with sodium iodide in ethanol in the dark, the mixture of products represented the equilibrium ratio. Only the trans-dihalobenzocyclobutenes underwent dehydrohalogenation with potassium t-butoxide in t-butyl alcohol to give the 1-halobenzocyclobutadienes, which dimerized to the respective 5-halobenzobiphenylenes.

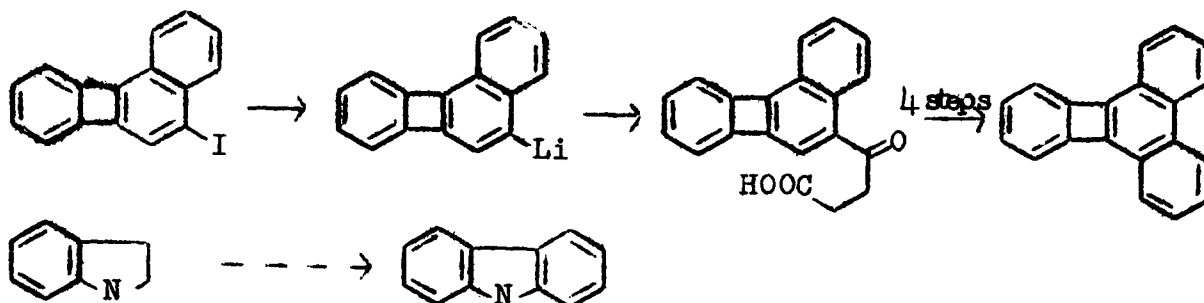


Later Cava et al.,<sup>22</sup> obtained several 5-substituted compounds from 5-iodo-benzo[a]biphenylene.

The possibility of making use of a 5-substituted benzo[a]biphenylene, to give dibenzo[a,c]biphenylene, seemed likely to us, particularly in the light of Barton's<sup>27</sup> multistage synthesis of benzo[b]biphenylene from biphenylene.



On the basis of this previous work, the following reaction scheme was postulated.



The reaction of a Grignard reagent with succinic anhydride as the first step in the formation of six-membered ring has been reported in the indole-carbazole series.<sup>145</sup>

### 3.1 1,2-Diiodobenzocyclobutene

The reaction of  $\alpha,\alpha,\alpha',\alpha'$ -tetrabromo-*o*-xylene with excess sodium iodide in ethanol, over a period of 10 days, gave a high yield (81%) of trans-1,2-diiodobenzocyclobutene, after distillation of the crude reaction product. The cis-isomer (m.p. 150°) is in this way effectively removed from the major, trans-product (m.p. 63°).

### 3.2 Dimerization of 1-iodobenzocyclobutadiene

Trans-1,2-diiodobenzocyclobutene was added dropwise as an oil, obtained by gentle heating of the low melting solid, to a solution of potassium t-butoxide in t-butyl alcohol under an atmosphere of dry nitrogen. Dehydrohalogenation of the diiodide gave the transient intermediate 1-iodobenzocyclobutadiene which immediately dimerized to give 5-iodobenzo[*a*]biphenylene as an orange

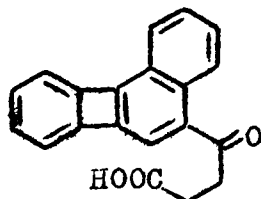
solid which precipitated from the reaction mixture. The crude product was purified by continuous extraction with petroleum ether (40-60°) in a Soxhlet apparatus followed by recrystallization from ethanol.

The NMR spectrum showed a singlet integrating for one hydrogen at 2.6 $\tau$  for the adjacent  $\beta$ -hydrogen, and a quartet at 2.28 $\tau$  due to the peri-hydrogen, deshielded by the steric influence of the large iodine atom.

### 3.3 Chain extension

Several attempts to obtain the Grignard derivative of 5-iodobenz[a]biphenylene failed, in that no sign of reaction was observed between the halide and the magnesium. Similar difficulties have been reported,<sup>22</sup> where the lithium derivative was shown to be more easily obtained. The lithium derivative was prepared in our case under a dry, oxygen-free atmosphere of nitrogen by the addition of a solution of n-butyllithium to a solution of the halide in an ether/benzene mixture. A deep red colouration gave evidence of the halogen-metal interconversion<sup>146</sup> and, after 10 minutes at room temperature, a solution of succinic anhydride in anisole was added, with vigorous stirring. A bright red complex separated out and the suspension was stirred continuously at reflux temperature for 1 hour. Extraction with sodium bicarbonate solution of the acidic product and recrystallization from benzene/light petroleum gave the keto-acid. 4-(5-Benzo[a]biphenylenyl)-4-oxobutyric acid (140) was scarlet in colour while the corresponding anion was lemon

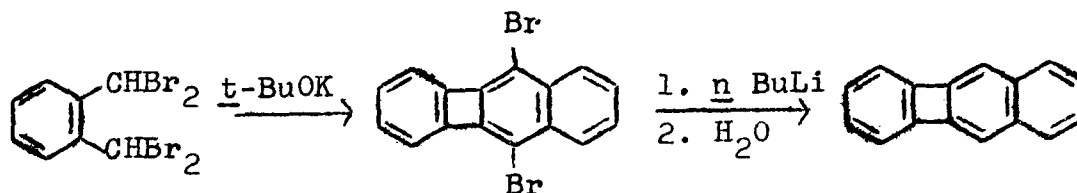
yellow, being very similar to benzo[a]biphenylene-5-carboxylic acid.<sup>22</sup> Indeed, all 5-substituted benzo[a]biphenylenes having a carbonyl group adjacent to the aromatic nucleus are deep red in colour.



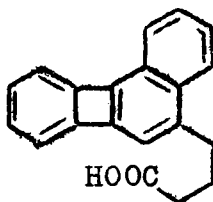
(140)

The NMR spectrum showed two methylenic triplets at 6.76 $\tau$  and 7.2 $\tau$  and the IR spectrum showed two carbonyl peaks at 1670  $\text{cm}^{-1}$  and 1710  $\text{cm}^{-1}$ . The structure (140) was confirmed by mass spectral data and analysis results.

The keto-acid (140) was obtained in low yield (5%) showing side-reactions to be taking place. The only product to be isolated from the neutral fraction however was benzo[b]biphenylene (2% by weight). This is the expected product of the tetrabromoxylene starting material, and its presence shows the Soxhlet extraction and the single recrystallization of 5-iodobenzo[a]biphenylene to be ineffective in removing this impurity completely.



Attempts to reduce the ketonic carbonyl by a modified Clemmensen reduction, in which the keto-acid was dissolved in toluene, failed to give the anticipated substituted butyric acid (141). No single compound could be isolated from the acidic reaction product. The IR spectrum showed a single carbonyl absorption suggesting that the ketonic carbonyl had indeed been reduced, however the NMR spectrum showed a large number of peaks indicative of a mixture of compounds.



(141)

Conclusion to Section III

The parent hydrocarbon, benzo[a]biphenylene, is much less stable than biphenylene itself<sup>75</sup> and the cyclobutadienoid 6a, 10b-bond has been shown to add bromine very easily.<sup>12</sup> It would appear that the conditions of the Clemmensen reduction, although successful in the preparation of 2-biphenylenylbutyric acid, as mentioned in the introduction, are too severe for this particular case. The keto-acid appears to be either thermally or chemically degraded under these conditions. A reduction under milder conditions should prove more successful. There was however insufficient time to allow this to be put to the test. The postulated route seems viable and it is only the lack of experimenting time that prevents its development by us.



EXPERIMENTAL SECTION

Introduction to Experimental Section

1. Melting points were determined on a Kofler melting-point apparatus with a calibrated thermometer, and fitted with a polariser.
2. Infra-red (IR) spectra were recorded on a Unicam S.P.200 Spectrophotometer. The intensities of the absorption maxima are indicated by (s) strong, (m) medium and (w) weak. The group corresponding to the particular absorption maximum is written after the absorption wave number. Spectra were measured for nujol suspensions unless otherwise stated, and calibrated from a polystyrene film.
3. Ultraviolet (UV) spectra were recorded on a Unicam S.P.800 Spectrophotometer. In the UV data given, the wavelengths of absorption maxima are expressed in  $\mu$  ( $\log_{10} \epsilon_{\max}$  in parenthesis). Spectroscopic ethanol was used as solvent unless otherwise stated.
4. Nuclear magnetic resonance (NMR) spectra were recorded on a Perkin-Elmer R10 (60 MHz) instrument or, where more detail was required, on a Varian HA100 (100 MHz). In the NMR data given, the numbers of protons assigned to particular signals were the integral ratios recorded. Spectra were measured in deuteriochloroform with tetramethylsilane as internal standard, unless otherwise stated.
5. Alumina was of Type-H as supplied by Peter Spence and Sons, Widnes. Light petroleum refers to that fraction b.p. 60-80°. Solutions were dried over anhydrous magnesium sulphate.
6. Analyses were carried out by A. Bernhardt, Max-Planck Institut, Mülheim [Ruhr], W. Germany or on a Perkin-Elmer 240 Elemental Analyzer.

7. Mass spectra were recorded using an AEI-GEC MS902 double-focussing instrument.
8. Photochemical reactions were carried out with a Hanovia IL Photochemical Reactor consisting of a mercury vapour arc tube (medium pressure) emitting predominantly 254, 265, 297, 313 and 366 m $\mu$  in the ultraviolet. Arc tubes of synthetic quartz gave 80% transmission down to 185 m $\mu$ , through 1 mm. thickness of quartz.

SECTION I - EXPERIMENTAL RESULTS

1.1 1-Phenylbutadiene 4,4-dicarboxylic acid (86)<sup>149</sup>

(Cinnamylidene malonic acid)

A mixture of equal parts by weight of cinnamaldehyde (200 g., 190.5 ml., 1.52 m.), malonic acid (200 g., 1.9 m.) and glacial acetic acid (200 g., 193.9 ml.) was refluxed on a boiling water bath, in the dark, for 9 hrs. On cooling, the crystalline mass was filtered, washed with a little chloroform, and recrystallized from ethanol to give the diacid as yellow needles.

Yield: 130 g. (68%)

m.p. 206° (Lit.<sup>149</sup> m.p. 208°)

Photodimer of Cinnamylidene Malonic Acid<sup>150</sup>

The finely ground diacid (50 g., 0.11 m.) was suspended in water (1 litre) weakly acidified with hydrochloric acid (10 ml.). A UV lamp was immersed in the mixture and dry nitrogen gas was passed around the arc tube and above the suspension. The constantly stirred mixture was irradiated for 48 hrs. and the dimer recovered by filtration as a white powder.

Yield: quantitative

m.p. 193-4° (Lit.<sup>150</sup> m.p. 195°)

2,4-Diphenylcyclobutane-1,3-dicarboxylic acid<sup>150</sup>

( $\alpha$ -Truxillic acid)

To determine the amount of ozone present in the ozone/oxygen mixture, the ozone generator was first calibrated with potassium iodide solution, by back titration with sodium thiosulphate solution. The output of ozone was calculated in moles per hour with respect

to the set rate of gas flow (bubbles per second). Excess ozone was undesirable as this tended to cause decomposition, and was tested for with moist starch iodide paper where the gas mixture left the reaction vessel.

The dimer, bis-cinnamylidene malonic acid (50 g., 0.11 m.) in glacial acetic acid (325 ml.) and water (50 ml.) was treated at  $-5^{\circ}$  to  $0^{\circ}$  with 14-15 g. ozone. A 10% solution of hydrogen peroxide (375 ml.) was then slowly added, at a temperature below  $30^{\circ}$ . After 5 days, reasonably pure  $\alpha$ -truxillic acid precipitated out and was recrystallized from methyl alcohol.

Yield: 6 g. (20%)

m.p.  $272^{\circ}$  (Lit.<sup>150</sup> m.p.  $274^{\circ}$ )

Esterification of  $\alpha$ -truxillic acid with methyl alcohol gave the methyl ester as fine clear needles which were readily recrystallized from methanol. Hydrolysis of the pure ester gave pure  $\alpha$ -truxillic acid m.p.  $274^{\circ}$ .

m.p.  $174^{\circ}$  (Lit.<sup>150</sup> m.p.  $174^{\circ}$ )

## 1.2 Lemieux Reagents

### Lemieux-van Rudloff<sup>81,82</sup>

The dimer, bis-cinnamylidene malonic acid (2.0 g., 0.0046 m.) was oxidised in aqueous solution (200 ml.) containing t-butyl alcohol (50 ml.), potassium permanganate (0.5g.), sodium periodate (4.12 g., 0.0193 m.) and enough potassium carbonate to give a pH of 8-9. After 12 hrs. at room temperature, dilute hydrochloric acid (5 ml.) was added to the dark brown solution and enough sodium

metabisulphite to convert all the periodate, iodate and iodine into iodide. The decolourised solution was basified and the t-butyl alcohol distilled off under reduced pressure. The residual solution was reacidified and extracted with ether. A small quantity of a brown oil was extracted as the acidic product, which did not solidify and from which no pure product could be isolated.

Lemieux-Johnson<sup>83</sup>

The dimer, bis-cinnamylidene malonic acid (2.0 g., 0.0046 m.) was dissolved in 80% acetic acid (50 ml.) and a suspension of the osmium tetroxide catalyst in water (~10 mg. in 1 ml.) was added. After about fifteen minutes, the solution became dark brown in colour and then black over the first hour due to osmate ester formation. Finely ground sodium periodate (4.12 g.) was added over a period of 4 hrs. Upon the addition of a very small quantity of periodate, the dark colour was immediately discharged. Stirring was continued throughout the addition and for a further 16 hrs. at room temperature when any precipitated sodium salts were filtered off and washed with a little glacial acetic acid. The washings and the acidic solution were combined and evaporated at 40°/20 mm., which also served to remove the catalytic quantity of osmium tetroxide. The residue was taken up in ether and water and the ethereal extract was washed with sodium bicarbonate solution to remove any carboxylic acid present. The organic solution was then dried over anhydrous magnesium sulphate and evaporated, giving an off-white, solid residue. The solid did not recrystallize from normal solvents, the pure dialdehyde being best isolated by filtration through a chromatographic column of acid-

washed alumina, which also removed any last trace of catalyst. Removal of the solvent gave 2,4-diphenylcyclobutane-1,3-dialdehyde,  $\alpha$ -truxaldehyde (87), as a white semi-crystalline solid.

Yield: 0.23g. (19%)

m.p. 110°

Analysis  $C_{18}H_{16}O_2$  required C 81.8% H 6.1%

Mol.Wt. 264.3 found C 82.5% H 6.2%

Mass spectrum Parent peak at 264 m/e units.

<u>IR spectrum</u> (CS <sub>2</sub> )	3000 cm. <sup>-1</sup> (w)	}	(cyclobutane CH)
	2900 cm. <sup>-1</sup> (w)		
	2800 cm. <sup>-1</sup> (w)	}	(aldehydic CH)
	2700 cm. <sup>-1</sup> (w)		
	1703 cm. <sup>-1</sup> (s)		(aldehydic C = O)
700 cm. <sup>-1</sup> (m)		(5 adjacent aromatic protons)	

UV spectrum 218 (4.11), 254 (2.82), 259 (2.90),  
265 (2.82), 270 (2.66).

NMR spectrum

- $\tau$  0.52 (doublet, 2 aldehydic protons)
- $\tau$  2.74 (multiplet, 10 aromatic protons)
- $\tau$  5.35 (multiplet, 2 cyclobutane protons)
- $\tau$  6.15 (multiplet, 2 cyclobutane protons)

The di-2,4-dinitrophenylhydrazone derivative proved difficult to crystallize and a sharp melting point was obtained only after successive recrystallizations from bromobenzene and dioxan. The low analysis result is probably due to the presence of some mono-compound.

m.p. 237° (decomp.)



<u>Analysis</u>	$C_{30}H_{24}N_8O_4$	required	N 17.9%
	Mol. Wt. 624	found	N 15.3%

### 1.3 The Arndt-Eistert Synthesis<sup>151</sup>

Acid chloride Truxillic acid (5.2g. 0.018 m) was refluxed in thionyl chloride containing one drop of dimethylaniline for 90 mins. Excess thionyl chloride was distilled off under reduced pressure, the last traces being removed by distillation with benzene (3 x 50 ml.). A crystalline product was obtained which recrystallized from benzene to give colourless crystals of the relatively stable dichloride.

Yield: quantitative  
m.p. 127° (Lit. m.p. 127°)

Diazomethane A solution of diazomethane (3.4g., 0.08m) in ether (150 ml.) was obtained from the reaction of *p*-tolylsulphonyl-methylnitrosamide and potassium hydroxide.

Diazoketone A solution of the acid dichloride in dry ether (150 ml.), prepared from truxillic acid (5.2g., 0.018m), was added dropwise with constant stirring, to a solution of diazomethane (3.4g., 0.08m) in ether (150 ml.) and the reaction mixture allowed to stand overnight. After removal of the ether under reduced pressure, the di-diazoketone (88) was obtained as a semi-solid pale yellow oil.

IR spectrum

2100 $cm^{-1}$	(s)	(-CHN <sub>2</sub> )
1720 $cm^{-1}$	(s)	} (C = O)
1630 $cm^{-1}$	(s)	

Wolff Rearrangement

A solution of the diazoketone in absolute methanol (80 ml.) was added to a mixture of absolute methanol (60 ml.) and silver oxide (0.75g.) which had previously been boiled until a silver mirror formed. The mixture was refluxed for 30 mins. and a second portion of silver oxide added (0.75g.) and refluxed for a further  $2\frac{1}{2}$  hrs. On cooling the catalyst was removed by filtering the solution through celite and the solvent removed under reduced pressure. The oil obtained in this way was chromatographed on alumina to give the dimethyl ester 2,4-diphenyl-1,3-diacetic acid as an oil which solidified on standing and was recrystallized from methanol.

Yield: 0.85g. (14%)

m.p. 102-104° (Lit. m.p. 100-105°)

Modified Wolff Rearrangement<sup>84</sup>

Silver benzoate was obtained by mixing equivalent solutions of silver nitrate and sodium benzoate. The white precipitate was filtered off, washed with water and dried in a vacuum oven. Extreme dryness of the silver benzoate was desirable as moisture caused precipitation of silver oxide on dissolving the former in triethylamine. Any silver oxide so formed was filtered off before the addition of the solution to the methanolic diazoketone solution. Starting with the same quantity of truxillic acid as before, the experiment was repeated using this catalyst.

A solution of silver benzoate (1.0g., 0.604m.) in triethylamine (10 ml.) was added dropwise, over a period of two hours at room temperature, to a solution of the diazoketone in absolute methanol (150 ml.). The mixture was heated to boiling point for 10 mins., a small quantity of charcoal added and, after a further 10 mins. boiling, it was filtered hot through celite. After removal of the solvents, the residue was dissolved in ether and the solution extracted with sodium bicarbonate solution to remove any benzoic acid or other acidic impurities. Drying and removal of the solvent gave an oil which solidified on standing and was recrystallized from methanol to give the dimethyl ester obtained in the previous experiment. The yield was much better than that obtained in the previous experiment although it was found to diminish with an increase in the amount of catalyst used.

Yield: 1.9g (33%)

m.p. 104° (Lit.<sup>80</sup> m.p. 100-105°)

The dimethyl ester was hydrolysed in 10% sodium hydroxide solution (ethanol:water, 1:1) to give a quantitative yield of the diacetic acid (84) which was recrystallized from benzene/light petroleum.

m.p. 188° (Lit.<sup>80</sup> m.p. 188-190°)

1.4 Hydrofluoric acid cyclisation of 1,3-diphenylcyclobutane-2,4-diacetic acid

The diacid (84) was allowed to stand in anhydrous hydrofluoric acid (20 ml.) for the length of time necessary to evaporate off the excess acid (2-3 hrs.). This gave virtually no ketonic product, the diacid being recovered unchanged.

When the diacid (1.0g., 0.0035m.) was allowed to stand in a covered vessel for 24 hrs., a neutral product was isolated, which on recrystallization from ethyl alcohol gave the diketone (85) as fine white needles.

Yield: 0.6g. (60%)  
 m.p. 184° (Lit.<sup>80</sup> m.p. 184°)

1.5 Attempted preparation of 5,11-dihydroxydibenzo[a,g]biphenylene(89)

A solution of the diketone (0.1g., 0.00035m.) and *p*-chloranil (0.1g., 0.0004m., 15% excess) in xylene (6 ml.) was refluxed for 2½ hrs. The colour of the solution darkened almost immediately from a clear orange to an opaque dark brown. On cooling the solution was chromatographed on a silica gel column. A single crystalline solid was obtained and identified as the tetrachloro-hydroquinone (no depression of m.p. when mixed with an authentic sample obtained by reduction of *p*-chloranil with sodium dithionite). The black residual oil gave no other identifiable compound even after a second silica gel column separation.

The experiment was repeated firstly in refluxing benzene and secondly in a benzene toluene (1:1) mixture but in neither case did

reaction take place. The starting material was recovered in 80% yield along with some decomposition tar.

1.6 5:6:6a:6b:11:12:12a:12b-Octahydro-5,11-dihydroxydibenzo[a,g]-biphenylene (90)

To a solution of the diketone (0.2g., 0.0007m.) in methyl alcohol (25 ml.) was added a solution of potassium borohydride (0.05g., 0.0009m., 25% excess) in a minimum of water. The mixture was refluxed for five mins. and allowed to cool. The reaction was terminated and any excess borohydride neutralised by the addition of an excess of dilute hydrochloric acid. After stirring for 30 mins. the product was extracted into ether, the ethereal solution dried and the solvent evaporated under reduced pressure. At this point, clear crystal prisms were observed to have collected on the neck of the flask, having sublimed from the crude product. These were isolated and found to be of naphthalene from mass spectral evidence (parent peak 128 m/e) and the fact that a mixed m.p. with an authentic sample showed no depression. The residual product was chromatographed on a silica gel column to yield a clear oil which afforded a semi-crystalline mass on standing. Two recrystallizations from methanol gave a small quantity of clear needles which turned opaque on loss of solvent of crystallization. The compound was identified as 5:6:6a:6b:11:12:12a:12b-octahydro-5,11-dihydroxydibenzo[a,g]biphenylene (90).

Yield: 0.064g. (32%)

m.p. 165-7°

Analysis:  $C_{20}H_{20}O_2$  required C 82.2% H 6.9%  
 Mol. Wt. 292.4 found C 82.1% H 6.6%

IR spectrum: 3500  $cm^{-1}$  (s) (-OH)  
 ( $CHCl_3$ )

NMR spectrum:  $\tau$ 2-3 (aromatic multiplet CH)  
 $\tau$ 6-8 (complex methine and methylene multiplets)

Attempts to dehydrogenate and hence aromatize the diol (90) to 5,11-dihydroxydibenzo[a,g]biphenylene (89) using p-chloranil in refluxing xylene gave, as in the previous experiment, black, tarry decomposition residues from which no crystalline product could be isolated.

#### 1.7 p-Toluenesulphonylhydrazone formation

The diketone (0.1g. 0.00035m.) and tosyl hydrazine (0.14g., 0.00076m.) were refluxed together in methanol (10 ml.) for 2 hrs. The insoluble white dihydrazone precipitated out and was collected by filtration.

Yield 0.14g. (66%)

m.p. 241-243°

Analysis:  $C_{34}H_{32}N_4S_2O_4$  required C 65.4% H 5.2% N 9.0%  
 Mol. Wt. 624.7 found C 65.4% H 5.1% N 8.8%

IR spectrum: 3200  $cm^{-1}$  (m) (NH)  
 1330  $cm^{-1}$  (m) }  
 1170  $cm^{-1}$  (s) } ( $SO_2$ )

NMR spectrum:  $\tau$  7.6 (singlet, tolyl -CH<sub>3</sub>)

Attempted preparation of 5:6:6a:6b:11:12:12a:12b-octahydrodibenzo-  
[a,g]biphenylene

Sodium borohydride

Following the general method of Caglioti *et al.*,<sup>86</sup> the insoluble ditosylhydrazone (0.13g., 0.0002m.) and sodium borohydride (0.2g., 0.00025m., 25% excess) were refluxed together in methanol (15 ml.) for 4 hrs. The clear solution obtained was added to water (25 ml.) and extracted with ether (3 x 25 ml.). The organic layer was dried and the solvent evaporated to give a very small quantity of brown oil which did not solidify and was not further characterised. Acidification of the aqueous layer gave a white precipitate which returned from chloroform without heating (the solid dissolved and recrystallized at room temperature). This was shown to be starting material (80%) from its IR spectrum and its melting point (no depression when mixed with a sample of the tosylhydrazone)

Lithium Aluminium Hydride

The ditosylhydrazone (0.95g., 0.00015m.) and lithium aluminium hydride (0.05g., 0.0006m.) were refluxed in tetrahydrofuran (20 ml.) for 4 hrs. Excess lithal was destroyed by the addition of ethyl acetate in ether and then water was cautiously added. The organic product was extracted into ether and the brown oil obtained on drying and removal of solvent was chromatographed on alumina (10g.). No identifiable solid product could be isolated. The IR spectrum of the oil showed a broad peak at  $3350\text{ cm.}^{-1}$  (m) and a smaller peak at  $1165\text{ cm.}^{-1}$  (w). The mass

spectrum showed no distinct parent peak at the expected 260 m/e, but two prominent peaks were observed at 128 m/e and 130 m/e units.

1.8 4-Phenylbut-3-enoic acid  
(Styrylacetic acid)

Stobbe Condensation<sup>90</sup>

Benzaldehyde (5.3g., 0.05m.) and diethyl succinate (13.05g., 0.075m.) were added to a cooled solution of potassium t-butoxide in t-butyl alcohol (5.3g., 0.05m. in 45 ml.). The mixture was refluxed under dry nitrogen for 30 min. and, on cooling, was acidified with dilute hydrochloric acid. The t-butyl alcohol was evaporated under reduced pressure, and the residue extracted with water and ether. The organic phase was washed with 2% sodium hydroxide solution (3 x 20 ml.) and the alkaline washings combined with the aqueous phase. Acidification gave a brown oil which did not solidify nor recrystallize and was taken to be the half-ester product.

A solution of the half-ester (1.5g.) in glacial acetic acid (30 ml.), 48% hydrobromic acid (20 ml.) and water (10 ml.) was refluxed for 5 hrs. Isolation of the acidic product of decarboxylation and recrystallization from methanol gave a white crystalline material m.p. 172°. Styrylacetic acid is reported as having a melting point 87°, and hence this route was not considered practical and discontinued.



Knoevenagel Condensation

A solution of malonic acid (10g., 0.1m.), phenylacetaldehyde (12g., 0.1m.) and two drops of piperidine in magnesium-dried ethanol (30 ml.) was boiled under reflux for 6 hrs. Extraction of the acidic product with sodium bicarbonate solution and subsequent isolation, by acidification of this solution, gave styrylacetic acid which was recrystallized from benzene/light petroleum as white needles.

Yield 6g. (40%)

m.p. 85° (Lit.<sup>91</sup> m.p. 87°)

Attempted dimerization of styrylacetic acid

Under the same reaction conditions as those used in the case of cinnamylidene malonic acid, a finely ground suspension of styrylacetic acid was irradiated for 48 hrs.. Isolation of the white solid product showed it to be starting material (95%), no dimerization having taken place.

Styrylacetic acid (2.5g.) was dissolved in an ethanol-water (1:1) mixture and the experiment repeated. A brownish solution was obtained which gave a brown oil on isolation of the product. If, as expected, a mixture of truxillic- and truxinic- like isomers has been obtained as a result of nonstereospecific dimerization, separation would be expected to be extremely difficult and indeed attempts to crystallize this oil from several solvents failed.

5-Phenylpenta-2:4-dienoic acid  
(Cinnamylideneacetic acid)

Cinnamylidenemalonic acid (5.0g., 0.023m.) was refluxed in pyridine (50 ml.) with a little copper bronze for  $1\frac{1}{2}$  hrs. On cooling, the solution was poured into dilute hydrochloric acid. Extraction with ether and subsequently with sodium bicarbonate solution gave, on acidification and recrystallization of the product from aqueous ethanol, white needles of cinnamylideneacetic acid.

Yield: 2.0g. (50%)

m.p.  $162-3^{\circ}$  Lit.<sup>92</sup> m.p.  $165-166^{\circ}$

Decarboxylation of the photodimer of cinnamylidene malonic acid

The white photodimer of cinnamylidene malonic acid (20g., 0.046m.) was heated in vacuo. At  $180^{\circ}$  the dimer melted and effervescence was observed. After 70 mins. at  $180^{\circ}$  the melt was allowed to cool and a semi-crystalline mass was obtained. A little benzene was added (10 ml.) and, on filtration of the yellowish suspension, a white solid product was isolated. Recrystallization from aqueous ethanol gave very small clear needles of the diacid, the  $\alpha$ -dimer of cinnamylidene acetic acid.

Yield: 1.7g. (95%)

m.p.  $200^{\circ}$  (Lit.<sup>92</sup> m.p.  $204^{\circ}$ ).

SECTION II - EXPERIMENTAL RESULTS

PART I

## 2.2 Friedel-Crafts acylation of 1,2,3,4-tetrahydronaphthalene (tetralin)<sup>97</sup>

The tetralin used was obtained from commercial tetralin by washing with concentrated sulphuric acid to remove any sulphur-containing impurities, whereupon the acid layer went almost black. Washing with sodium carbonate solution, drying over magnesium sulphate and a final distillation gave pure tetralin b.p.  $207.3^{\circ}$  (range taken  $206-208^{\circ}$ ).

Phenylacetic acid (95.0g., 0.699m.) was refluxed in excess thionyl chloride (100 ml.) for 90 mins. Any excess liquid was removed under reduced pressure, the final traces of thionyl chloride being co-distilled with sodium-dried benzene (3 x 50 ml.), leaving the residual acid chloride in almost quantitative yield (~108g., 0.699m.).

A solution of the acid chloride in 1,2-dichloroethane (200 ml.) was added to a solution of tetralin (87.0g., 90 ml., 0.659m.) in the same solvent (200 ml.). The mixture was cooled to  $10^{\circ}$ , and freshly crushed aluminium trichloride (100 g., 0.75m.) was added over a period of 30 mins. Throughout the addition the mixture was stirred vigorously and this was continued for a further 30 mins. at  $10^{\circ}$ . The resulting dark brown solution was poured onto ice acidified with concentrated hydrochloric acid and left overnight at room temperature. The reaction product was extracted into chloroform and the organic layer was washed with sodium carbonate solution and dried over anhydrous magnesium sulphate. Removal of

the solvent under reduced pressure gave a dark brown viscous oil which, on recrystallization from ethanol, gave a crystalline ketonic product. A second recrystallization gave 2-(5,6,7,8-tetrahydronaphthyl)benzyl ketone as yellow needles.

Yield: 83g. (50%)

m.p. 84° (Lit.<sup>97</sup> m.p. 82-84°)

### Chloranil dehydrogenation

Dehydrogenation of the tetralin ketone to the corresponding naphthalene compound, benzyl 2-naphthyl ketone, was carried out with chloranil. A mixture of the ketone (20.0g., 0.08m.) and chloranil (40.0g., 0.17m.) was refluxed in xylene (200 ml.) for 2 hrs. Removal of the solvent under reduced pressure and recrystallization of the crude reaction product from ethanol gave the 2-phenylacetylnaphthalene in low yield.

Yield: 2.0g. (10%)

m.p. 98° (Lit.<sup>137</sup> m.p. 100°)

### 2.3 Friedel-Crafts phenylacylation of naphthalene

The acylation of naphthalene was carried out, with some modifications, according to the method of Bun-Hoi et al.<sup>103</sup> Over a period of 2 hrs. a solution of finely powdered aluminium chloride (134g., 1.0m.) in nitrobenzene (200 ml.) was added slowly to a well-stirred, ice-cold solution of phenylacetyl chloride (155g., 1.0m.) and naphthalene (128g., 1.0m.) in nitrobenzene (300 ml.). The mixture was left at room temperature overnight

and then poured onto iced hydrochloric acid. The nitrobenzene layer was washed with 2N hydrochloric acid until all aluminium salts were thought to have been removed. The solvent was removed by steam distillation until a clear distillate was obtained and the residue taken up in chloroform. Once dried, the solvent was removed and the 2-phenylacetylnaphthalene recrystallized from ethanol and from carbon tetrachloride.

Yield: 188g. (74%)

m.p. 99° (Lit.<sup>137</sup> m.p. 100°)

#### 2.4 Reformatsky reaction

In order to obtain highly active metal,<sup>104</sup> zinc wool was heated in concentrated sulphuric acid, containing a few drops of concentrated nitric acid, at 100° for 15 mins. The concentrated acid was almost totally decanted and water was added whereupon a vigorous reaction ensued. After washing with water, ethanol, acetone and dry ether, the active metal was used immediately. Although drying at 100° has been advocated,<sup>105</sup> in our case no advantage was found to be gained by this procedure. In this way air oxidation and subsequent deactivation of the metal surface was avoided.

2-Phenylacetylnaphthalene (123g., 0.5m.) in sodium-dried benzene (2 litres) was added to a solution of ethyl bromoacetate (83.5g., 56 ml., 0.5m.) in sodium-dried benzene (500 ml.). A quantity of this mixture (100 ml.) in a 5-litre, three-necked flask fitted with a stirrer, dropping funnel and condenser with drying

tube, was heated to reflux temperature. Freshly prepared zinc wool (35.0g., 0.054 gram atoms) was added together with a crystal of iodine and a vigorous reaction set in. The remainder of the mixture was added through the dropping funnel at a rate designed to maintain gentle refluxing. After addition, stirring was continued for 2 hrs. at reflux temperature. On cooling, the product was decomposed with 2N sulphuric acid (sufficient to dissolve all the zinc hydroxide). The benzene layer was dried over magnesium sulphate and the solvent removed under reduced pressure leaving the product as a dark brown oil which gave yellow crystalline material on standing. Recrystallization from ethanol gave ethyl 3-hydroxy-3-(2-naphthyl)-4-phenylbutyrate (112) as colourless needles.

Yield: 131g. (78%)

m.p. 81°

Analysis:  $C_{22}H_{22}O_3$  required C 79.0% H 6.6%  
Mol. Wt. 334.4 found C 79.05% H 6.7%

Mass spectrum: Parent peak at 334 m/e units

IR spectrum: 3500  $cm^{-1}$  (m) (alcohol OH)  
( $CCl_4$ ) 1715  $cm^{-1}$  (s) (ester C = O)  
1040  $cm^{-1}$  (m) (ester C - O)

NMR spectrum:  $\tau$ 2.1-3.2 (complex, 12 aromatic protons)  
 $\tau$ 5.4 (broad hydroxyl proton)  
 $\tau$ 6.1 (quartet, 2 protons -OCH<sub>2</sub>-)  
 $\tau$ 6.5-7.4 (multiplet, 4 methylenic protons)  
 $\tau$ 7.0 (singlet 3 methyl protons)

The ester (112) obtained from the Reformatsky reaction was saponified with a 10% sodium hydroxide solution (1:1, ethanol:water) under reflux for 2 hrs. The aqueous layer was washed with ether and then acidified with dilute hydrochloric acid. The carboxylic acid (130) was precipitated as a white solid which was recrystallized from methylated spirits.

Yield: quantitative

m.p. 156°

Analysis:  $C_{20}H_{18}O_3$  required C 78.4% H 5.9%

Mol. Wt. 306.3 found C 78.5% H 5.9%

Mass spectrum: Parent peak at 306 m/e units

IR spectrum: 3490  $cm^{-1}$  (m) (alcohol OH)  
( $CCl_4$ ) 1710  $cm^{-1}$  (s) (carboxylic acid C = O)

NMR spectrum:  $\tau$ 2.0-3.1 (complex, 12 aromatic protons)  
 $\tau$ 6.5-7.4 (complex, 4 methylenic protons)

Esterification of the carboxylic acid (130) with anhydrous methyl alcohol saturated with gaseous hydrogen chloride gave the methyl ester (131) in almost quantitative yield.

m.p. 104°

Analysis:  $C_{21}H_{18}O_2$  required C 83.4% H 6.0%

Mol. Wt. 302.4 found C 83.5% H 5.9%

Mass spectrum: Parent peak at 302 m/e units

IR spectrum: 3500  $cm^{-1}$  (m) (alcohol OH)  
( $CCl_4$ ) 1705  $cm^{-1}$  (s) (ester C = O)



NMR spectrum:  $\tau$ 2.1-3.1 (complex, 12 aromatic protons)  
 $\tau$ 6.4 (singlet, 3 methyl protons)  
 $\tau$ 6.5-7.4 (multiplet, 4 methylenic protons)

The ester obtained from the Reformatsky reaction (112) was refluxed with formic acid in which it did not dissolve but remained as a pale brown oil on the surface of the liquid. The acid was evaporated under reduced pressure and the solid obtained on cooling the oil was dissolved in chloroform. The organic layer was washed with sodium bicarbonate solution, dried over magnesium sulphate and evaporated to remove the solvent. The resultant oil solidified on standing and the brownish solid was recrystallized from ethanol to give an almost quantitative yield of the unsaturated ethyl ester (113), as fine white needles.

m.p.  $79^{\circ}$

Analysis:  $C_{22}H_{20}O_2$  required C 83.5% H 6.4%  
Mol. Wt. 316.4 found C 83.5% H 6.2%

Mass spectrum: Parent peak at 316 m/e units

IR spectrum:  $1690\text{ cm}^{-1}$  (s) (ester C = O)  
(CCl<sub>4</sub>)

UV spectrum: 210 (4.54), 225 (4.56), 250 (4.57),  
261 (4.64), 298 (4.35).

NMR spectrum:  $\tau$ 2.0-2.9 (complex, 12 aromatic protons and  
1 olefinic proton)  
 $\tau$ 5.9 (quartet, 2 methylenic protons)  
 $\tau$ 6.2 (singlet, 2 methylenic protons)  
 $\tau$ 8.3 (triplet, 3 methyl protons)



methyl ester (133) already classified.

## 2.5 The Wittig Reaction

### Triphenyl Ylide

The triphenyl phosphonium bromide  $(\text{Ph})_3\text{PBrCH}_2\text{COOEt}$  was obtained by the addition of ethyl bromoacetate (16.7g., 0.1m.), with stirring over a period of 30 mins. to a solution of triphenylphosphine (26.2g., 0.1m.) in benzene (150ml.). After a short time, the phosphonium bromide began to crystallize out. Agitation was continued overnight, the precipitate collected by filtration, washed with benzene and 40-60° petroleum ether and dried at a water pump.

Yield: almost quantitative<sup>113</sup>

The product of the previous reaction was dissolved in water (1 litre) and the solution chilled. It was then made alkaline to potassium permanganate by the addition of dilute sodium hydroxide solution dropwise with stirring. Ether (100 ml.) was added to solidify the oily product and the two layer system filtered. The organic layer was dried and the solvent removed. The quantity of solid obtained was added to the filtered material to give the triphenyl ylide,<sup>113</sup>  $(\text{Ph})_3\text{P}=\text{CH}\cdot\text{COOEt}$  (115).

Yield: 29g. (83%)

Two Wittig reactions were attempted, one in benzene and one in xylene, both at reflux temperature. The ketone,  $\beta$ -phenylacetyl-naphthalene (2.46g., 0.01m.) in solvent (50 ml.) was refluxed with the ylide for 3 hrs. In both cases, the solution gradually

assumed a red colouration which deepened with time. Chromatography of the products on alumina gave 30% and 40% starting material from the respective reactions.

The experiment in xylene as solvent was repeated and kept under reflux for 12 hrs. Chromatography as before gave 20% starting ketone. The reaction of the ketone with the triphenyl phosphonium ylide was therefore considered unsuccessful in its aim. The ester product was not isolated nor identified at this stage.

#### Phosphonate anion

Anhydrous, freshly distilled triethyl phosphite (16.6g., 17.2 ml., 0.1m.) was mixed at room temperature with ethyl bromoacetate (16.7g., 11.13 ml., 0.1m.) and the resulting mixture heated to 80°, when some effervescence was observed. After 3 hrs. at 100°, the mixture was heated to 175° and any distilled liquid collected. When no further refluxing occurred it was taken that all the ethyl bromide had been eliminated and removed. The relatively stable diethyl-(ethylacetate)-phosphonate,  $(EtO)_2POCH_2COOEt$  was obtained in almost quantitative yield and not further purified.<sup>116</sup>

The reactive phosphonate anion (116) was generated by sodium hydride firstly in dimethylformamide and secondly in 1,2-dimethoxyethane.

#### Dimethylformamide

Diethyl-(ethylacetate)-phosphonate (22.4g., 0.1m.) was prepared as above. To this was added sodium hydride (4.8g. of a 50% suspension giving 2.4g., 0.1m.) in dimethyl formamide (40 ml.)

over a period of 30 mins. with constant stirring. Effervescence was observed, and the mixture stirred at room temperature for a further 30 mins. before  $\beta$ -phenylacetylnaphthalene (12.3g., 0.05m.) in dimethyl formamide (50 ml.) was added. A deep orange-red suspension was obtained which was left overnight at room temperature. After removal of excess sodium hydride by filtration, water was added, giving a canary yellow precipitate. Extraction of the organic material with chloroform gave a yellow solution which was extracted several times with 10% sodium hydroxide solution, the latter turning deep red, until no further colour was observed in the aqueous phase. The chloroform solution was dried and evaporated to give a yellow brown oil which was distilled under reduced pressure. A clear liquid was first obtained which was thought to be some residual phosphorus containing compound, and then a yellow oil was collected. Chromatography on alumina gave a clear oil as the first fraction and a crystalline yellow solid as the second fraction. The former was recrystallized from carbon tetrachloride and found to be ethyl 3-(2-naphthyl)-4-phenylbut-2-enoate (113), that is the unsaturated ethyl ester m.p.  $79^{\circ}$  obtained from dehydration of the Reformatsky ester (112). The latter was found to be starting material m.p.  $99^{\circ}$  which was recovered in approximately 5% yield.

Yield: 6.2g. (40%)

m.p.  $79^{\circ}$

### 1,2-Dimethoxyethane

The phosphonate (22.4g., 0.1m.) was prepared as before and to this was added sodium hydride (2.4g., 0.1m.) in 1,2-dimethoxyethane

(50 ml.) over a period of 30 mins. After stirring at room temperature for a further 30 mins.,  $\beta$ -phenylacetylnaphthalene (12.3g., 0.05m.) in the same solvent (50 ml.) was added dropwise with stirring. During the addition, and for 1 hr. after addition, the stirred solution was kept at 55°. On cooling the product was extracted in water and ether, the organic layer dried and evaporated. Chromatography of the residue on alumina (300 g.) gave firstly a clear liquid which was discarded. This was followed by a clear viscous oil which, on standing, gave a small quantity of crystalline material, while the bulk of material remained as an oil. This solid was isolated by trituration and identified, after recrystallization, as the unsaturated ethyl ester (113) obtained in the previous reaction. IR and UV spectral evidence indicated that the remaining oil was of a similar structure and elucidation came from the NMR spectrum.

$\tau$ 2.0-3.0	(complex aromatics)
$\tau$ 3.6	(singlet, 1 olefinic proton)
$\tau$ 5.4	(singlet, 2 methylenic protons)
$\tau$ 6.2	(singlet, 2 methylenic protons)
$\tau$ 5.8	(quartet, 2 methylenic protons)
$\tau$ 5.95	(quartet, 2 methylenic protons)
$\tau$ 8.75	(triplet, 3 methyl protons)
$\tau$ 8.85	(triplet, 3 methyl protons)

Two ethyl esters of almost identical structure can be seen to be present, one of which is that isolated from the oil, the unsaturated ethyl ester trans-(113). The other is taken to be the geometrical

isomer cis-(113).

Yield: 7.1g. (45%)

A sample of the oil was hydrolysed to give the carboxylic acid as a white solid.

NMR spectrum:  $\tau$ 2.0-3.0 (complex aromatics)  
 $\tau$ 3.6 (singlet, 1 olefinic proton)  
 $\tau$ 5.35 (singlet, 2 methylenic protons)  
 $\tau$ 6.1 (singlet, 2 methylenic protons)

A mixture of cis- and trans- unsaturated carboxylic acids has been obtained, one of which is the unsaturated acid already classified.

Further proof of the mixtures of cis- and trans- esters and acids came from their respective catalytic hydrogenations. In the former case, a quantitative yield of a single saturated ester (120), and in the latter a single saturated acid (121), were obtained.

## 2.6 Catalytic hydrogenation

The unsaturated ethyl ester (113) and the oily mixture of esters obtained from the Wittig reaction gave the saturated ester, ethyl 3-(2-naphthyl)-4-phenylbutyrate (120). The unsaturated methyl ester (133) gave the corresponding saturated compound. The unsaturated acid (117) and the mixture of acids gave (121). All reactions were carried out under the same conditions and gave almost quantitative yields of the respective products.

A solution of the olefin (0.05m.) in ethyl alcohol (300 ml.) was added to a palladium/charcoal catalyst (10%, 1.5g.). The reaction was carried out at room temperature and under atmospheric

pressure. When no more hydrogen was taken up, the suspension was filtered through a slurry of celite in a sintered-glass funnel to remove the catalyst. The solvent was evaporated under reduced pressure and the solid product recrystallized.

Ethyl ester (120)

m.p.  $38^{\circ}$

Analysis:  $C_{22}H_{22}O_2$  required C 83.0% H 7.0%  
Mol. Wt. 318.4 found C 82.6% H 7.0%

IR spectrum:  $1735\text{ cm}^{-1}$  (s) (ester C = O)

NMR spectrum:  $\tau 2.0-3.0$  (complex, 12 aromatic protons)  
 $\tau 6.0$  (quartet, 2 methylenic protons)  
 $\tau 6.4$  (multiplet, 1 methine proton)  
 $\tau 7.0$  (doublet, 2 methylenic protons)  
 $\tau 7.25$  (doublet, 2 methylenic protons)  
 $\tau 8.95$  (triplet, 3 methyl protons)

Carboxylic acid (121)

m.p.  $143^{\circ}$

Analysis:  $C_{20}H_{18}O_2$  required C 82.7% H 6.25%  
Mol. Wt. 290.4 found C 82.7% H 6.6%

IR spectrum:  $1700\text{ cm}^{-1}$  (s) (acid C = O)

NMR spectrum:  $\tau 0.45$  (broad singlet, 1 acidic proton)  
 $\tau 2.0-3.0$  (complex, 12 aromatic protons)  
 $\tau 6.45$  (multiplet, 1 methine proton)  
 $\tau 7.0$  (doublet, 2 methylenic protons)  
 $\tau 7.25$  (doublet, 2 methylenic protons)

Methyl ester of acid (119)

m.p.  $73^{\circ}$



Analysis:     $C_{21}H_{20}O_2$             required    C 82.9%    H 6.6%  
                  Mol.Wt. 304.4            found      C 82.9%    H 6.6%

IR spectrum: 1740  $cm^{-1}$  (s) (ester C = O)

NMR spectrum:  $\tau$ 6.6 (singlet, 3 methyl protons)

(otherwise almost identical to previous two)

## 2.7 Ring Closure

### Friedel-Crafts cycliacylation

The acid chloride of 3-(2-naphthyl)-4-butyric acid (121) was obtained by the reaction of thionyl chloride and the free acid (2.0g., 0.007m.) in the usual way. The acid chloride in sodium-dried benzene (50 ml.) was added dropwise with constant stirring to a suspension of finely powdered anhydrous aluminium chloride (1.1g., 0.08m.) in anhydrous benzene (50 ml.) at 0-5°C. The resulting dark brown solution was left overnight. The product, once isolated, was chromatographed on alumina (30g. per lg.) giving a pale brown oil which was crystallized from methanol. A second recrystallization from the same solvent gave a white solid.

Yield: 0.2g. (10%)

m.p. 122-126°

The reaction was also attempted, under the same conditions, in 1,2-dichloroethane, where only an intractable oil was isolated which gave no crystalline material on purification.

Better yields were obtained when the acid chloride (3.0g., 0.01m.) in anhydrous benzene (150 ml.) was added, over 45 mins. to a cooled suspension of finely powdered anhydrous aluminium chloride

(3.0g., 0.2m.) in benzene (150 ml.). Stirring was continued for a further 45 mins. at 0-5° and the reaction terminated by pouring the mixture onto iced hydrochloric acid. Extraction, distillation, and recrystallization from methanol and a minimum of ethanol, gave the intramolecular ring-closure ketone (122A).

Yield 0.56g. (19%)

m.p. 126.5° (recrystallized  $\text{CCl}_4$ )

Analysis:  $\text{C}_{20}\text{H}_{16}\text{O}$  required C 88.2% H 5.9%

Mol. Wt. 272.3 found C 87.9% H 5.8%

Mass spectrum: Parent peak at 272 m/e units, other main peaks at 145, 127 and 116 m/e units.

IR spectrum: 1685  $\text{cm}^{-1}$  (s) (ketone  $\text{C}=\text{O}$ ) other peaks at 670, 740, 760, 790, 830 and 875  $\text{cm}^{-1}$  (m).

UV spectrum: 215(4.69), 220(4.65), 226(4.59), 232(4.55), 240(4.50), 247(4.42), 270(3.33), 295(3.85), 307(3.97), 315(3.92), 329(3.74).

NMR spectrum:  $\tau$ 0.85 (quartet, 1 peri proton)  
 $\tau$ 1.9-3.0 (complex, 10 aromatic protons)  
 $\tau$ 6.3 (multiplet, 1 methine proton)  
 $\tau$ 6.6-7.8 (multiplet, 4 methylenic protons)

#### Cyclodehydration

#### Polyphosphoric acid

A mixture of acid (121), (2.0g., 0.007m.), and polyphosphoric acid (30 ml.) was heated for 2 hrs. at 100°. The carboxylic acid did not dissolve but remained as a white solid in the reaction mixture. After work up, 75% starting material was recovered unchanged.

The experiment was repeated at 150° and a homogeneous reaction mixture was obtained. After 1 hr., the reaction was terminated by the addition of water, and the product isolated. Chromatography on alumina of the dark brown oil gave a white solid whose NMR showed a peak at 0.85 $\tau$  and an extremely complex band between 6.0-8.0 $\tau$ . The IR spectrum indicated the presence of more than one compound, showing a broad ketonic C = O at 1670-1705 cm.<sup>-1</sup> Several recrystallizations from methanol and carbon tetrachloride failed to give a pure crystalline product, the melting point being inexact and below 120°.

#### Hydrofluoric acid

Cyclodehydration of acid (121) to the benzindanone (122A) was found to be best carried out using hydrofluoric acid. In a highly efficient fume cupboard, anhydrous hydrofluoric acid (~150 ml.) was added to a finely powdered sample of acid (121), (10g., 0.0345m.) in a polythene beaker. The mixture was stirred to give a uniform paste and covered with a polythene cover. After 4 hrs. the cover was removed and the excess liquid allowed to evaporate overnight in a strong draught. Any traces of residual liquid were neutralised with saturated sodium bicarbonate solution and the ketone was extracted into chloroform. After drying over magnesium sulphate, the solvent was evaporated under reduced pressure to give the ketone which was recrystallized from ether as colourless needles.

Yield 7.2g. (77%)

m.p. 126.5°

2.8 Oximinoketone

n-Butyl nitrite was prepared by the method of Noyes<sup>126</sup> from n-butyl alcohol (37g., 45.7ml., 0.5m.), sodium nitrite (38g., 0.5m.), water (160 ml.) and concentrated sulphuric acid (25g., 13.6ml., Sp.G. 1.88, 0.25m.). The crude product (42g., 81%) was dried over anhydrous magnesium sulphate (2.0g.) and then distilled (75°, 760mm.) to give the pure nitrite (75%), which was used immediately.

The ketone (122A) was dissolved (0.9g., 0.0033m.) in methyl Cellosolve<sup>94</sup> (17.5 ml.) and to the solution was added concentrated hydrochloric acid (1.8 ml.). n-Butyl nitrite (0.4 ml.) was added with stirring and the mixture allowed to stand at room temperature for 90 mins. The resulting orange-red solution was poured into cold water (40 ml.) giving a red oil, which was dissolved in a variety of solvents in attempts to obtain solid material. Two components were isolated, one yellow and the other bright red, both of which gave melting points around 200° with decomposition. Recrystallization of the yellow material finally gave m.p. 210-211°. The red solid was considered to be a complex arising from nickel contamination.

Yield: 0.1g. (10%)

m.p. 210-211° (decomposed)

Analysis: C<sub>20</sub>H<sub>15</sub>N<sub>2</sub>O<sub>2</sub>            required C 79.7% H 5.0% N 4.65%  
Mol. Wt. 301.3            found C 79.3% H 4.8% N 4.3%

The reaction was found to give better yields in ethanol as solvent.<sup>95</sup> The ketone (122A) however readily recrystallized from

ethanol and in order to keep the reaction homogeneous, a warm solution of the ketone in ethanol was used. The ketone (3.0g., 0.01m.) was dissolved in ethanol (50 ml.) and to the warm solution concentrated hydrochloric acid (2 ml.) was added, followed after mixing, by n-butyl nitrite (4.0g., 4 ml., 0.04m.) dropwise, over 5 mins., with constant stirring. After 1 hr., a further quantity of nitrite (4.0g.) was added along with concentrated hydrochloric acid (2 ml.). After a few minutes, crystallization of the product oximinoketone (126) was observed.

Yield: 2.75g. (83%)

m.p. 210-211° (decomp.)

Mass spectrum: Parent peak at 301 m/e units

IR spectrum: 3550  $\text{cm}^{-1}$  (w) (oxime OH)  
 3250  $\text{cm}^{-1}$  (m) (oxime OH)  
 1690  $\text{cm}^{-1}$  (s) (ketone C = O)

NMR spectrum: Oximinoketone insoluble in chloroform and trifluoroacetic acid spectrum indistinct

$\text{D}_3\text{CCOCD}_3$   $\tau$ 1.0 (1 peri proton)  
 $\tau$ 1.8 (doublet, 1 aromatic proton)  
 $\tau$ 2.05 (multiplet, 1 aromatic proton)  
 $\tau$ 2.42 (multiplet, 2 aromatic protons)  
 $\tau$ 3.07 (multiplet, 5 aromatic protons)  
 $\tau$ 5.38 (triplet, 1 methine proton)  
 $\tau$ 6.4 (doublet, 2 methylenic protons)

#### Diazoketone

The finely powdered oxime (1.0g., 0.003m.) was added to a sodium hydroxide solution (100 ml., 2N) at 0°, in which were

dissolved sodium hypochlorite (5.4 ml., 12-14% w/v, 0.01m.) and concentrated ammonia (1.3 ml., 0.905 Sp.G., 0.018m.) solutions. The suspension was stirred at 0° for 4 hrs., a further quantity of sodium hypochlorite (5.4 ml.) and ammonia (1.3 ml.) added, and the suspension left overnight at 0-5°. The solid product was filtered off, washed with water and taken up in ether. After drying and removal of the solvent, a crystalline product was obtained which was recrystallized from benzene/light petroleum to give the diazo-ketone (127) as yellow leaflets.

Yield: 0.78g. (80%)

m.p. 159-160° (decomp.)

The above reaction was first attempted in a homogeneous solution of the oximinoketone in a 1:1 aqueous ethanol sodium hydroxide (2N) solution. A brown oil was obtained which on crystallization from benzene/light petroleum gave only a trace quantity of the diazo compound.

<u>Analysis:</u>	$C_{20}H_{14}N_2O$	required	C 80.5%	H 4.7%	N 9.4%
	Mol.Wt. 298.3	found	C 80.6%	H 4.5%	N 9.0%

Mass spectrum: Parent peak at 270 m/e units due to loss of nitrogen.

IR spectrum: 2100  $cm^{-1}$  (s) (diazo -C = N<sub>2</sub>)

1650  $cm^{-1}$  (s) (broad C = O)

UV spectrum: 213(4.69), 216(4.68), 248(4.47), 255(4.41), 333(4.17),  
342(4.21), 352(4.14).

NMR spectrum:

$\tau$ 0.8	(quartet, 1 peri proton)
$\tau$ 1.95-2.9	(multiplet, 10 aromatic protons)
$\tau$ 4.5	(quartet, 1 methine proton)
$\tau$ 6.5	(quartet, 1 methylene proton)
$\tau$ 7.1	(quartet, 1 methylene proton)

## 2.9 Irradiation of the diazoketone (127)

Irradiation was carried out in tetrahydrofuran:water (5:1) solution in the presence of sodium bicarbonate (2g. per g.). Any peroxides in the former solvent were first removed by passing it down an alumina column.

The yellow diazoketone (127), (1.0g., 0.0034m.) was dissolved in tetrahydrofuran (200 ml.) giving an orange solution. To this was added a solution of sodium bicarbonate (2.0g.) in water (40 ml.) and the mixture irradiated for 15 hrs. After this time, more water (35 ml.) was added and the tetrahydrofuran removed under reduced pressure. The precipitated oily product was taken up in chloroform and shaken with the bicarbonate solution. The organic layer was extracted with sodium bicarbonate solution once more, washed with water, dried and the solvent evaporated. This gave an intractable orange-red tar which did not crystallize. The IR spectrum of this gum showed no peak at  $2100\text{ cm}^{-1}$ , indicating the absence of any starting material, and was therefore discarded.

The aqueous extracts were combined and acidified, the product being extracted into ether. Drying and removal of solvent gave the crude acid which was recrystallized from benzene/light petroleum to give the carboxylic acid as fine white needles.

Yield: 0.1g. (10%)

m.p. 135°

Analysis: C<sub>20</sub>H<sub>16</sub>O<sub>3</sub>      required C 83.3%    H 5.6%  
Mol.Wt. 288.3      found C 83.1%    H 5.4%

Mass spectrum: Parent peak at 288 m/e units

IR spectrum: 3500 cm.<sup>-1</sup> (w) (sharp, free OH)  
3000 cm.<sup>-1</sup> (m) (broad, bonded OH)  
1690 cm.<sup>-1</sup> (s) (acid C = O)

UV spectrum: 210(4.50), 230(4.88), 270(5.13), 275(5.15),  
279(5.17), 290(5.07), 301(4.65), 315(4.60), 323(4.70), 333(4.29).

NMR spectrum: τ0.4 (broad, 1 acidic proton)  
τ2.0-3.0 (complex, 11 aromatic protons)  
τ5.3 (doublet, 1 methine proton)  
τ5.8 (multiplet, 1 methine proton)  
τ6.6 (quartet, 2 methylenic protons)  
τ7.2 (quartet, 2 methylenic protons)

#### 2.10 Attempted formation of the dibenzo[a,h]biphenylene structure

A finely powdered crystalline sample of the cyclobutene carboxylic acid (50 mg., 0.17mm.) was allowed to stand in an excess of anhydrous hydrofluoric acid (10 ml.) for 6 hrs. The excess liquid was allowed to evaporate and any remaining traces of acid were neutralised with saturated sodium bicarbonate solution.

Extraction of the neutral product gave a yellow-brown solid which did not recrystallize from the normal solvents but returned as an oil.



Mass spectrum: large number of peaks beyond and including  
400-500 m/e units

(No parent peak observed at 270 m/e)

IR spectrum:  $1710\text{ cm}^{-1}$  (ketonic C = O )

NMR spectrum:  $\tau 2.0-3.4$  (complex aromatics)

$\tau 5.5-7.5$  (complex multiplets)

In addition to these groups of peaks, there was a large number of  
other unassignable multiplets.

SECTION II - EXPERIMENTAL RESULTS

PART II

## 2.11 Dehydration

The ethyl and methyl esters of 3-hydroxy-3-(2-naphthyl) butyric acid (130) dehydrated in formic acid to give the respective esters of 3-(2-naphthyl)-4-phenylbut-2-enoic acid (117), as previously described. Attempts to dehydrate the former acid itself gave the following results.

### 50% Sulphuric acid

Two products were isolated after refluxing acid (130) in 50% sulphuric acid for 1 hr., one acidic and one neutral. Analysis results showed these to be the unsaturated acid (117) and the hydrocarbon,  $\beta$ -methyl- $\beta$ -(2'-naphthyl)styrene (134), in 10% and 50% yields respectively.

### Formic acid

Under the same conditions employed for dehydration of the two esters, the free acid (130) gave no acidic product after reaction but a high yield (80%) of a neutral product which was identified as the hydrocarbon (134) previously obtained.

m.p. 139°

<u>Analysis:</u>	$C_{19}H_{16}$	required	C	93.4%	H	6.6%
	Mol.Wt. 244.3	found	C	93.5%	H	6.65%

Mass spectrum: Parent peak at 244 m/e units

IR spectrum: 3000  $cm^{-1}$  (m) (aromatic C-H)  
 (CHCl<sub>3</sub>) 1620  $cm^{-1}$  (w) (conjugated C=C)  
 1600  $cm^{-1}$  (m) (aromatic C=C)

UV spectrum: 215(4.40), 224(4.42), 266(4.45), 229(4.27).

NMR spectrum:  $\tau$ 2.1-2.9 (complex, 12 aromatic protons)  
 $\tau$ 3.06 (quartet, 1 olefinic proton)  
 $\tau$ 7.69 (doublet, 3 methyl protons)

### 2.12 Attempted decarboxylation of the unsaturated acid (117)

In an attempt to prove the mechanism of decarboxylation of the hydroxy acid (130), the  $\alpha,\beta$ -unsaturated acid (117) was refluxed in formic acid for 90 mins. (0.5g., 0.0017m.). On heating, the acid dissolved to give a clear solution and on cooling crystallized out. Work up as before gave an acidic product which was shown to be starting material (0.42g., 85%). No neutral product was isolated.

### 2.13 1- and 2-Naphthyl ketones

Friedel-Crafts acylation of naphthalene with phenylacetyl chloride and anhydrous aluminium chloride was effected in 1,2-dichloroethane. Distillation of the product (b.p. 220-221<sup>o</sup>/3-4 mm.) gave a crude mixture of 1- and 2-phenylacetylnaphthalene. The mixture of ketones was dissolved in a minimum of boiling ethanol and to this solution was added a similar solution of an equal weight of picric acid. Fractional recrystallization gave the picrate derivative of 2-phenylacetylnaphthalene as pale lemon-yellow needles;

m.p. 143<sup>o</sup> (Lit.<sup>136</sup> m.p. 143-144<sup>o</sup>)

followed by the picrate derivative of 1-phenylacetylnaphthalene as canary-yellow needles.

m.p. 99<sup>o</sup> (Lit.<sup>136</sup> m.p. 99-100<sup>o</sup>)

The two isomeric ketones were regenerated by shaking a solution of their respective derivatives in ether, with a concentrated aqueous ammonia solution. This gave on isolation and recrystallization from methanol, pure 2-phenylacetylnaphthalene;

m.p.  $100^{\circ}$  (Lit.<sup>136</sup> m.p.  $99-100^{\circ}$ )

and in the same manner, pure 1-phenylacetylnaphthalene as colourless plates.

m.p.  $65^{\circ}$  (Lit.<sup>136</sup> m.p.  $66-67^{\circ}$ )

### 2-Phenylacetylnaphthalene

A Grignard reagent, formed in the usual way from methyl iodide (7.1g., 3.12 ml., 0.05m.) and magnesium turnings (1.22g., 0.05m.), was gradually added to a cooled solution of 2-phenylacetylnaphthalene (12.32g., 0.05m.) in anhydrous ether (50 ml.). After 5 hrs. at room temperature, the product was decomposed with ice and ammonium chloride. Extraction gave the carbinol as an oil which did not crystallize ( $3600\text{ cm.}^{-1}$ , -OH) and was refluxed in formic acid for 1 hr. The product of dehydration was recrystallized from benzene as colourless plates.

Yield 8.0g. (66%)

m.p.  $139^{\circ}$

Analysis and spectral evidence showed this to be the already classified  $\beta$ -naphthyl hydrocarbon (134). There was no depression of melting point when mixed with an authentic sample.

1-Phenylacetylnaphthalene

The Grignard experiment described for the  $\beta$ -ketone was attempted on 1-phenylacetylnaphthalene. No hydrocarbon product was isolated and the NMR spectrum of the reaction product gave no indication of its formation. Starting material was recovered in high yield.

A Reformatsky reaction paralleling that carried out successfully on the  $\beta$ -ketone, likewise failed to give any product other than the recovered starting ketone.

Knoevenagel reaction

Both  $\alpha$ - and  $\beta$ -ketones failed to give any product with malononitrile, either in ethanol with piperidine as catalyst,<sup>147</sup> or in benzene with ammonium acetate as catalyst.<sup>148</sup>

Wittig reaction

An attempt to obtain hydrocarbon (135) by the reaction of 2-phenylacetylnaphthalene and  $(\text{Ph})_3\text{P}=\text{CH}_2$  failed to give any trace of the hydrocarbon. The ylide was formed from  $(\text{Ph})_3\text{PCH}_3\text{Br}$ , by the action of potassium t-butoxide,<sup>141</sup> and appeared in solution as a pale yellow colouration.

The reaction also failed when attempted with 1-phenylacetylnaphthalene.

1- and 2-Acetylnaphthalene

The reaction of 2-acetylnaphthalene with benzyl magnesium bromide gave a high yield of hydrocarbon (134) on dehydration of the

carbinol.

As commercial 1-acetylnaphthalene was shown to contain an appreciable quantity of the  $\alpha$ -isomer, a pure sample of the  $\alpha$ -ketone was obtained from pure 1-naphthonitrile and methyl magnesium iodide.<sup>142</sup> On repeating the above reaction with pure 1-acetylnaphthalene, the Grignard reaction gave no carbinol, only starting ketone being recovered. Dibenzyl was isolated from the reaction mixture in 20% yield.

#### Wittig reaction

To a solution of 2-acetylnaphthalene (1.7g., 0.01m.) in petroleum ether (40-60°, 200 ml.) was added the phosphonium bromide  $(\text{Ph})_3\text{PCH}_2\text{PhBr}$  (4.33g., 0.01m.) and potassium t-butoxide (11.2g., 0.1m.) under a nitrogen atmosphere.<sup>141</sup> The immediately formed ylide was apparent as the bright yellow colouration of the suspension. After continuous shaking for 48 hrs., the suspension had turned deep red. Filtration and elution of the product on an alumina column gave hydrocarbon (134).

Yield: 0.36g. (15%)

The filtered residue was washed with water and extracted into ether to give on isolation, starting material (25%  $\beta$ -ketone).

An identical reaction to that described for the 2-ketone failed to give any sign of reaction with 1-acetylnaphthalene.

SECTION III - EXPERIMENTAL RESULTS



### 3.1 1,2-Diodobenzocyclobutene

A mixture of sodium iodide (510g., 3.4m.) and potassium iodide (22g., 0.13m.) was refluxed with absolute ethanol (1600 ml.) for 30 mins. and 450 ml. ethanol distilled off. To the residual mixture was added  $\alpha,\alpha,\alpha',\alpha'$ -tetrabromo-o-xylene (200 g., 0.48m.) and the resulting mixture was refluxed for 10 days. The reaction vessel was carefully covered to exclude light and the solution was protected from moisture by a drying tube. After cooling, methylene chloride (500 ml.) was added and the resultant slurry poured into cold water (3 litres). Enough sodium thiosulphate was added to reduce all the iodine liberated and, by shaking, all the iodine was removed into the aqueous layer, which was then washed three times with methylene chloride. The organic layer was dried over magnesium sulphate and the solvent removed. The residue was distilled (120-130°/2mm.) and a brown oil was collected (137g.). This solidified on standing to give, as a yellow-brown crystalline solid, trans-1,2-diodobenzocyclobutene.

Yield: 137g. (81%)

m.p. 58-60° (Lit.<sup>143</sup> m.p. 63°)

### 3.2 5-Iodoberzo[a]biphenylene

Potassium (87.7g., 2.24m.) was cut under sodium-dried benzene and quickly added, in small quantities over 1 hr., to t-butyl alcohol (1750 ml.) under a stream of dry, oxygen-free nitrogen. When all the potassium had been added to the now hot solution, the reaction was allowed to proceed at room temperature overnight under

a flow of nitrogen. Refluxing for 1 hr. the following day removed the last traces of potassium metal giving a solution of potassium t-butoxide in t-butyl alcohol.

Trans-1,2-diodobenzocyclobutene (137g., 0.38m.) was added dropwise as an oil (obtained by gentle heating of the low melting solid), with constant stirring, to the butoxide solution under a continuous flow of nitrogen. A yellow solid was immediately precipitated and, after addition, the reaction was completed by refluxing the suspension for 45 mins. Water (1250 ml.) was then cautiously added, followed by sufficient acetic acid to neutralise the excess base. The mixture was cooled and the orange precipitate filtered, washed with water and dried. Recrystallization from ethanol gave orange needles of 5-iodobenzo[a]biphenylene.

Yield: 50g. (40%)

m.p. 131° (Lit.<sup>22</sup> m.p. 131-132°)

UV spectrum: 207(4.55), 227(4.50), 258(4.69), 266(4.88),  
275(4.49), 286(4.64), 297(4.67), 368(3.60), 382(3.92),  
401(4.09), 430(3.55), 460(3.28), 496(2.52).

NMR spectrum:  $\tau$ 2.28 (quartet, 1 peri proton)  
 $\tau$ 2.6 (singlet, 1 aromatic proton)  
 $\tau$ 2.82 (multiplet, 3 aromatic protons)  
 $\tau$ 3.5 (multiplet, 3 aromatic protons)  
 $\tau$ 3.65 (multiplet, 1 aromatic proton)

### 3.3 4-(5-Benzo[a]biphenylenyl)-4-oxobutyric acid

#### n-Butyllithium

Anhydrous ether (100 ml.) was placed in a 250 ml., three-necked flask equipped with a stirrer, condenser with nitrogen

inlet and dropping funnel. The apparatus was swept with dry, oxygen-free nitrogen and lithium wire (4.3g., 0.63 gram atoms), cut into small pieces, was allowed to fall directly into the reaction flask in a stream of nitrogen. With the stirrer started about 30 drops of a solution of n-butyl bromide (34.25g., 27 ml., 0.25m.) in anhydrous ether (50 ml.) was added from the dropping funnel. The reaction mixture was then cooled to  $-10^{\circ}$  by immersing the flask in a Dry Ice-acetone bath kept at about  $-30^{\circ}$  to  $-40^{\circ}$ . The solution became slightly cloudy and bright spots appeared on the lithium when the reaction had started. The remainder of the n-butyl bromide solution was then added at an even rate over a period of 30 mins., while the internal temperature was maintained at  $-10^{\circ}$ . After addition was complete, the reaction mixture was allowed to warm up to  $0^{\circ}$ - $10^{\circ}$  with stirring during 2 hrs. The mixture was then filtered through a plug of glass wool into a dropping funnel already flushed with nitrogen. In this way, an 80% yield of n-butyl lithium was obtained in ether solution.

#### Halogen-metal interconversion

The solution of the organolithium compound prepared above, was added dropwise with vigorous stirring to a solution of 5-iodobenzene [a]biphenylene (23.1g., 0.07m.) in anhydrous ether (400 ml.) and anhydrous benzene (200 ml.), in a three-necked flask already flushed with dry, oxygen-free nitrogen. The clear orange solution of iodide turned a deep opaque red colour which was taken to be associated with the lithio derivative. The reaction was considered

to be complete after 10 mins. at room temperature.

A solution of succinic anhydride (10g., 0.1m.) in anisole (100 ml.) was rapidly added to the red organolithium solution with vigorous stirring. A bright red complex immediately separated out and the suspension was stirred at reflux temperature for 1 hr. On cooling, the suspension was poured into and shaken with glacial acetic acid (80 ml.) in water (250 ml.). The acidic product was extracted into sodium bicarbonate solution, the latter giving on acidification the keto-acid. Recrystallized from benzene/light petroleum, 4-(5-benzo[a]biphenylene)-4-oxobutyric acid was obtained as very small scarlet needles.

Yield: 1.1g. (5%)

m.p. 195.5-196.5°C

<u>Analysis:</u>	$C_{20}H_{14}O_3$	required	C 79.5%	H 4.7%
	Mol. Wt. 302.3	found	C 79.0%	H 4.7%

Mass spectrum: Parent peak at 302 m/e units.

IR spectrum:

3500-2600 $cm^{-1}$	(m)	(broad -OH, acid dimer)
1710 $cm^{-1}$	(s)	(carboxylic acid, C=O)
1670 $cm^{-1}$	(s)	(ketone, C=O)
1100 $cm^{-1}$	(s)	(carboxylic acid, C-O)
930 $cm^{-1}$	(m)	(carboxylic acid dimer, -OH)

UV spectrum: 206(4.42), 220(4.41), 248(4.36), 265(4.71),  
285(4.44), 295(4.45), 360(3.34), 377(3.65), 396(3.86), 433(3.55).

NMR spectrum:  $\tau$ 1.68 (multiplet, 1 peri proton)  
 $\tau$ 2.7 (multiplet, 4 aromatic protons)  
 $\tau$ 2.8 (singlet, 1 aromatic proton)  
 $\tau$ 3.36 (doublet, 2 aromatic protons)  
 $\tau$ 3.48 (multiplet, 1 aromatic proton)  
 $\tau$ 6.76 (triplet, 2 methylenic protons)  
 $\tau$ 7.2 (triplet, 2 methylenic protons)

The neutral product of the preceding reaction was isolated and dissolved in ethanol. A crystalline material separated out which was recrystallized from ethanol and found to be benzo[b]-biphenylene.

Yield: 0.3g. (2%)

m.p.  $243^{\circ}$  (Lit. m.p.  $242.6-243.2^{\circ}$ )

2,4,7-trinitrofluorenone complex m.p.  $215^{\circ}$  (Lit. m.p.  $214-216^{\circ}$ )

The IR and NMR spectra gave evidence of an aromatic hydrocarbon, and the structure was confirmed from mass and UV spectral evidence<sup>27</sup> and analysis results.

#### Attempted Grignard preparation

Several attempts to form the Grignard reagent of 5-iodobenzo[a]biphenylene failed in that no reaction of the halide with the magnesium was observed.

#### Attempted aldehyde formation

A solution of 5-lithiobenzo[a]biphenylene in an ether/benzene mixture (2:1, 60 ml.) was prepared from 5-iodobenzo[a]biphenylene (2.3g., 0.07m.) as previously described. To this solution was added triethyl ortho-formate (9.5g., 10.5 ml., 0.071m) in sodium-

dried benzene (20 ml.) and the mixture refluxed for 10 mins. No product could be isolated from the resultant oil and no characteristic aldehydic proton peak was present in the NMR spectrum.

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