"A STUDY OF THE CONDENSATION REACTIONS
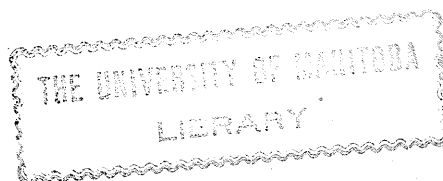
OF UNSATURATED NITROGEN COMPOUNDS."

By

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Being a Thesis

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ACKNOWLEDGMENTS

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PREFACE.

PREFACE.

Of all the discoveries of the past decade in the field of organic chemistry, one of the most fundamental is the "diene synthesis" of Otto Diels and Kurt Alder (also called the Diels-Alder reaction in honor of its discoverers). Not only has this reaction opæened up a new field of synthesis of such naturally occurring compounds as terpenes, camphors, alkaloids and various hydroaromatic and heteroaromatic systems, hitherto rare or inaccessible, but it has further served to interpret or re-interpret mechanisms which have baffled investigators working on various problems, and to elucidate structures, particularly as to whether a conjugated system does or does not exist. A further advantage of this synthesis is that the reaction generally takes place under the mildest conditions, mere mixing at room temperature in a suitable solvent being sufficient. The reaction here is strongly exothermic and the yield nearly quantitative, with negligible formation of undesirable by-products. In other cases, the temperature must be raised to accelerate the addition process, either by fusion or by the use of solvents of varying boiling points, as benzene, toluene or xylene. The use of catalytic reagents has been avoided in nearly all cases investigated to date. The ease with which these reactions take place has prompted Diels to offer the suggestion that the process is going on in nature, perhaps by the polymerization of isoprene units from which the terpenes, sesquiterpenes, and their homologues and derivatives are conveniently considered to be derived.

The "diene synthesis", in its typical course, is a process which must serve as a confirmation of Thiele's Theorem of 1,4-addition. It consists of a "philodiene component" (a substance containing a double or triple bond) adding to a conjugated diene with the formation of an hydroaromatic ring[7]:
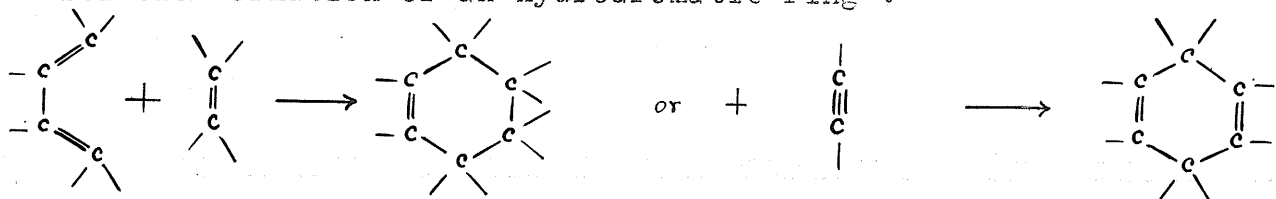
This reaction appears to be a property of carbon compounds. On attempting to apply the method to nitrogenous substances, as pyridine and pyrrole, two other reaction mechanisms were found: (a) reactions of substitution involving displacement of hydrogen; and (b) additions involving the formation of an acetylenic ester chain. These will be dealt with in greater detail in the introductory section of this thesis.

It will be noted that the nitrogen compounds used by Diels and Alder have been so far exclusively cyclic, with but one or two exceptions. The purpose of this investigation, however, is to attempt a "diene synthesis" by the use of acyclic nitrogenous compounds according to the following scheme:

1. 1,4-addition of a conjugated diene to a nitrogen-containing philodiene component:
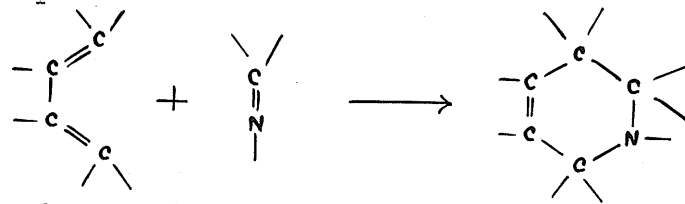
2. 1,4-addition of an anil conjugated with an olefinic linkage to a carbon-containing philodiene component:
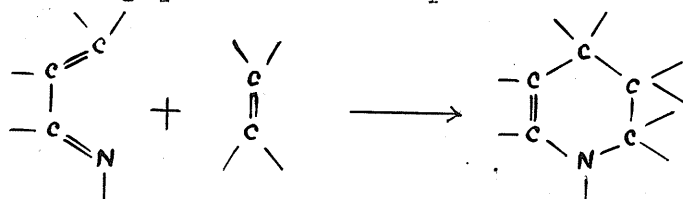
INTRODUCTION.

INTRODUCTION.

A. DIENE SYNTHESES INVOLVING 1,4-ADDITION.

1. HISTORICAL.

In 1906, Albrecht[1] reported the addition of cyclopentadiene to p-quinone with the formation of an equimolecular compound to which he assigned formula (I). This product behaved as a singly-unsaturated diketone and could be catalytically reduced to (II). Further reduction merely converted both ketone groups to secondary alcohols. A dicyclopentadiene-quinone (III) was also isolated, possessing the properties of a diketone.
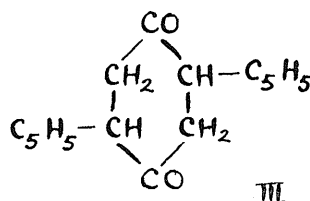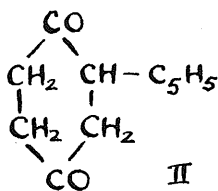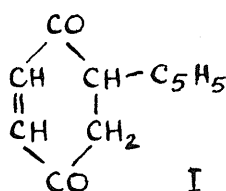
Yet even this explanation for the course of the reaction was unsatisfactory.

Staudinger[2] suggested (IV) in the place of (I), the cyclobutane ring explaining more satisfactorily the easy reformation of the original components under more stringent experimental conditions.
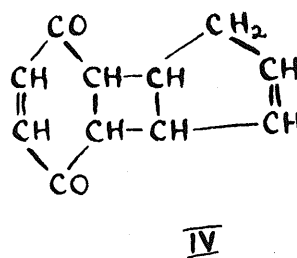
It was not, however, until 1925 that a clue as to the true nature of the addition was proposed. Diels, Blom and Koll[3] pointed out that azo-ester (ROOC-N:N-COOR), which is comparable to a half-quinone, adds smoothly to hydrocarbons containing a system of conjugated double bonds. Both one and two moles of azo-ester can

add to one of cyclopentadiene to yield (V):
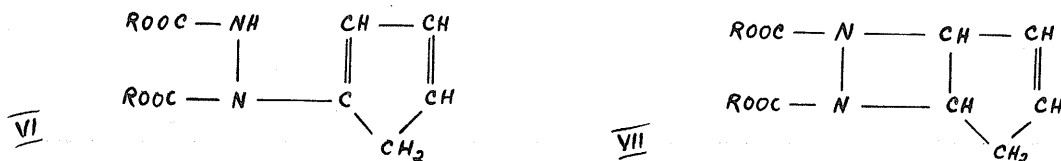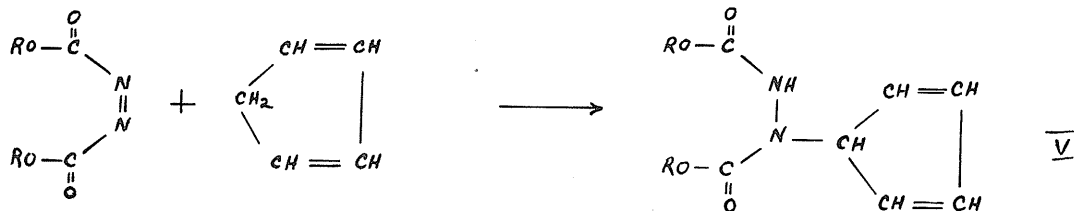
However, because of a lack of agreement with the properties actually observed, conception (V) was excluded, as were also formulae (VI) and (VII).

Euler and Josephson[4] had explained the addition of isoprene to quinone in relation to the system of conjugated double bonds present in the former and on the basis of Thiele's Theorem of 1,4-addition, to yield a partially hydrogenated dimethyl-anthraquinone (VIII):
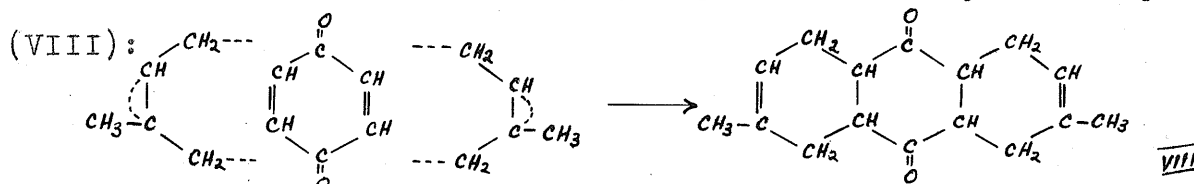
In strict analogy, Diels, Blom and Koll[3] formulated the addition of cyclopentadiene to azo-ester as follows:
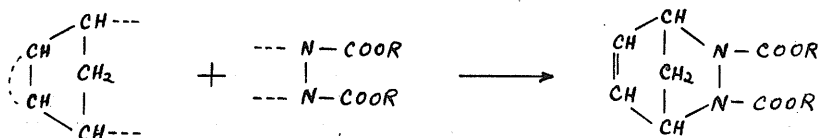
Diels and Alder[5] rightly concluded, therefore, that adducts (I) and (II) obtained by Albrecht must be regarded as endomethylene compounds, and assigned formulae (IX) and (X) to the monocyclo-pentadiene-quinone and the dicyclopentadiene-quinone of Albrecht, respectively.
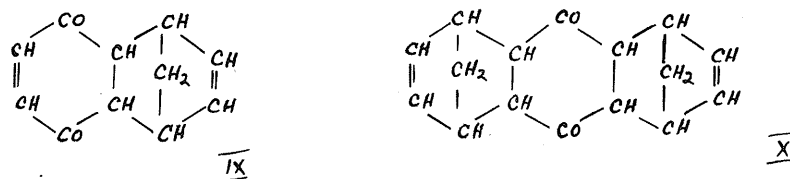
Further proof for the 1,4-course of addition was offered by the fact that one mole of butadiene will take up one mole of α-naphthoquinone with formation of (XI):
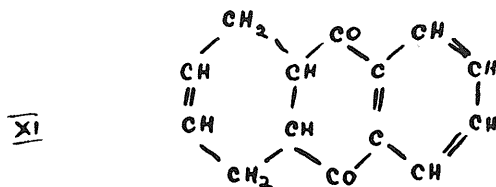
In view of the structural similarity of azo-ester and quinone to maleic, citraconic and itaconic anhydrides, it is not surprising that the last three compounds mentioned add to cyclopentadiene quite readily at ordinary temperatures and "also to complicated hydrocarbons possessing a system of conjugated double bonds, as cyclohexadiene, phellandrene, etc., in the same way as do azo-ester and quinone. The double linkages of the designated unsaturated anhydrides or acids open up, and there results, in every case, a joining up of the free valences in a 1,4-position with the hydrocarbon, as a result of which a new bond is considered to be built between carbon atoms 2 and 3. The numerous products ~~are~~ so obtained are in no way molecular combinations but firmly combined and stable."[5]

A more suitable interpretation of the Diels-Alder reaction has been made in accordance with modern electronic concepts as to the course of organic reactions[40]. Considering the reaction of maleic anhydride on butadiene, we have two electromeric shifts in each molecule, the first being a shift of an electron pair from the carbonyl double bond in the anhydride molecule to the oxygen, giving the latter atom a negative charge so that it may be regarded as a donor center. This electrical transfer is followed by a shift of an electron pair from the carbon-carbon double bond to to the carbon-carbon single bond in order to maintain the quadrivalence of the carbonyl carbon atom. Thus, the β-carbon atom is

imbued with receptor activity. A similar series of electromeric
shifts occurs in the butadiene molecule, creating a donor center
at one of the terminal carbons, a receptor center at the other.

The first step in the reaction is the attachment of the
active donor center of the butadiene to the receptor center of the
anhydride molecule, followed by a shifting back of the electron
pair from the carbonyl oxygen atom, such that the α-carbon atom
of the anhydride becomes a donor center. The latter unites with the
acceptor center of the butadiene chain, forming the final product
(XII), according to the scheme:
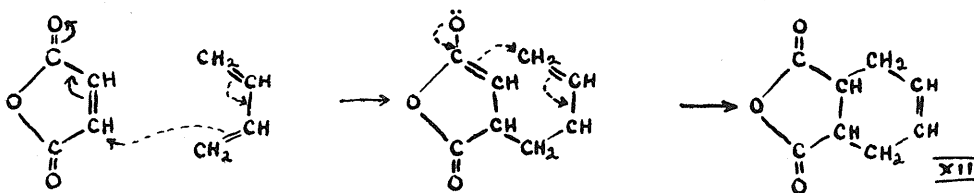
2. OPEN-CHAIN DIENES.

When an open-chain diene such as butadiene or aax isoprene
is brought into reaction with maleic anhydride or acrolein, an
unsaturated cyclohexane derivative is obtained by 1,4-addition[5].
Thus, butadiene and maleic anhydride react to give tetrahydro-Δ^3-o-
phthalic anhydride (I), which can be converted into the corres-
ponding acid by treatment with hot water. Acrolein reacts similarly,
giving Δ^3-tetrahydro-benzaldehyde (II) with butadiene.
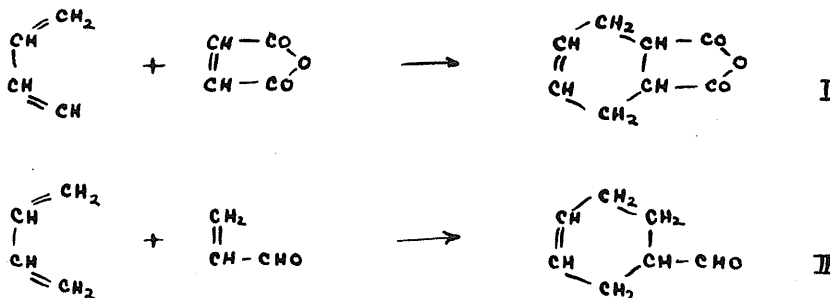
$\beta\gamma$-dimethyl-butadiene, on heating with maleic anhyxdride,

yields (III), while $\alpha\zeta$-dibromo-$\Delta^{\beta\partial}$-hexadiene forms a crystalline derivative possessing the more complex structure (IV).

Farmer and Warren[8] conclude that cyclohexene formation from open-chain dienes is complete and remains unaffected (except as regards the velocity of reaction) by variation of the position of the alkyl substituents.

Even more complicated adducts were obtained with sorbic acid and its derivatives[8,9,10], with muconic acid[8,11], and with myrcene[9]. Thus, maleic anhydride adds to myrcene to form the anhydride (V) of isohexenyl-4-cis-Δ^4-tetrahydrophthalic acid, a reaction which was of importance in demonstrating the presence of a system of conjugated double bonds in myrcene. With crotonaldehyde, (VI) was obtained.

3. ENDOMETHYLENE BRIDGES.

Substances which are characterized by endomethylene bridges can be prepared in a similar manner by using cyclopentadiene and its derivatives. For example, the reaction between maleic anhydride and cyclopentadiene gives a quantitative yield of endomethylene-3,6-tetrahydro-Δ^4-o-phthalic anhydride (I), whereas acrolein and cyclopentadiene produce 2,5-endomethylene-tetrahydro-Δ^4-benzaldehyde (II). This was used by Diels and Alder[9] as a starting material in the preparation of norcamphor (III). Substance (II) could also be converted into norcamphene (IV), the simplest forerunner of

this series.

I   II   III   IV

Further researches along these lines[12] resulted in the preparation of 6-methyl-norcamphor (V) and of 6,6-dimethyl-norcamphor (VI).

V   VI   VII
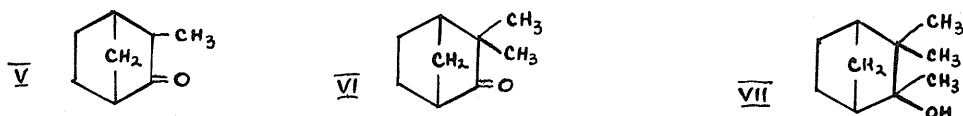
By the action of methyl-magnesium-iodide on (VI), camphenilol (VII) was obtained, and by the splitting off of water, 6,6-dimethyl-camphene (VIII) resulted. By the reversal of the carbon framework according to the method of Bertram and Walbaum[13], (VIII) passed through the acetate of isoborneol into isoborneol (IX) and then by oxidation into camphor (X). In this way, by means of the diene synthesis, a compound was prepared which was an important intermediate in the synthesis of the camphenes and of camphor.

VIII   IX   X
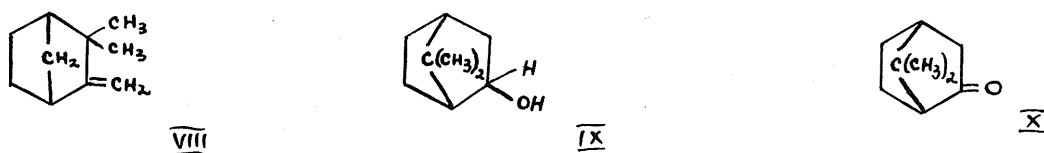
Investigations into the santene series have also been carried out[12].

4. ENDOETHYLENE BRIDGES.

It is also of great interest that cyclohexadiene-1,3 will combine with maleic anhydride in the same manner as cyclopentadiene[14]. The product (I) obtained contains an endoethylene bridge.
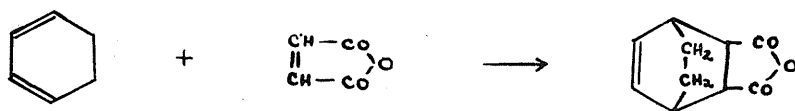
I

According to the investigations of Aschan[15], Mohr[16] and Diels and Alder[17], this seems to be a basic system of rings free of strain.

The complexity of the diene molecule seems to be subordinated in the presence of the characteristic group of double bonds in determining whether a diene synthesis will take place. Thus, maleic anhydride will react[9] with the highly complicated α -phellandrene to give (II). Acrolein and crotonaldehyde react with it in the same manner, proving the consistent course of 1,4-addition as well as verifying the position of the double bonds in α -phellandrene.
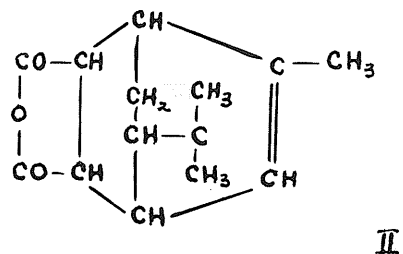
5. QUINONE AND ITS DERIVATIVES.

The ability of various quinone-derivatives to undergo diene syntheses has found important applications in the realm of synthetic organic chemistry.[18] It is possible, choosing the simplest example, to add one mole of a diene, such as butadiene, to p-quinone to give the partially hydrogenated naphthoquinone (I), or two diene molecules to produce the bis-compound (II), the latter being a partially hydrogenated anthraquinone. Both products appear as diketone rather than as quinone in character. With α -naphthoquinone, the adduct obtained by the addition of butadiene is (III), being a partially hydrogenated anthraquinone, but not identical with (II).
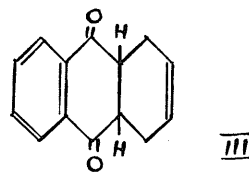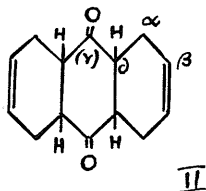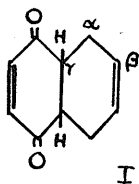
With 1,3-dimethyl-butadiene and α -naphthoquinone, (IV) was obtained by Diels and Alder, while cyclohexadiene-1,3 adds to the

same quinone with formation of (V). The latter readily loses two
H-atoms from the ∂ -position to give 1,4-endoethylene-1,4-
dihydroanthraquinone (VI).
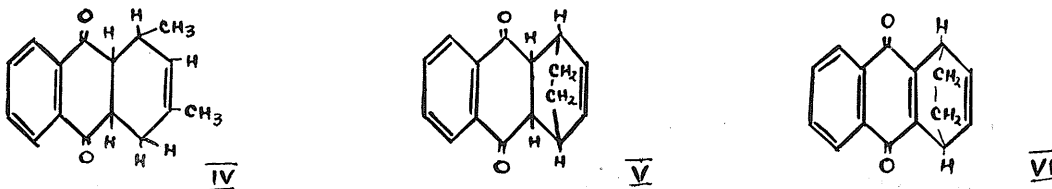
It is impossible, according to Bredt's theorem[19], for the
bridge head and inside bridge, in the camphenes and pinanes at
least, to be loosened. That is, the α -hydrogen atom at the bridge
head in (V) cannot wander to the meso-position, although the ∂ -
hydrogen is qualified to do so. It is, however, possible for the
endoethylene bridge to be thermically split off.

By allowing an excess of isoprene to act on quinone at 100°,
two moles of hydrocarbon will add on with the formation of a
colorless adduct which appears to be a mixture of two bis-isoprene-
quinones:

By the action of air on anx alcoholic-alkaline solution, both forms
lose eight H-atoms and are converted into their basic aromatic
systems, 2,6- and 2,7-dimethyl-anthraquinones, respectively.

In other words, the quinone-diene adduct may be stabilized
by a wandering of hydrogen or by its elimination. In the cases of
the mono-diene-quinones (a) and of the mono-diene- α -naphthoquinones
(b), the wandering of the H-atoms from the γ - and ∂ -positions,
respectively, to the ketone-oxygen, means a stabilization of the
adducts with formation of benzene (c) and naphthalene (d) systems,
respectively. Hence, the ability of these compounds to be acylated
and their tendency to enolize.
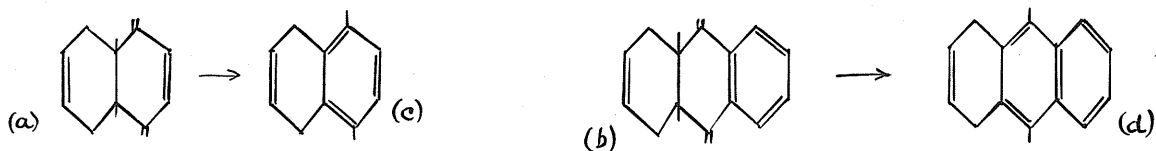
The bis-diene-quinones, however, act differently. Here, by the wandering of two H-atoms from the ∂-position, the stable cyclohexane configuration of the middle ring must go over into a dihydrobenzol:
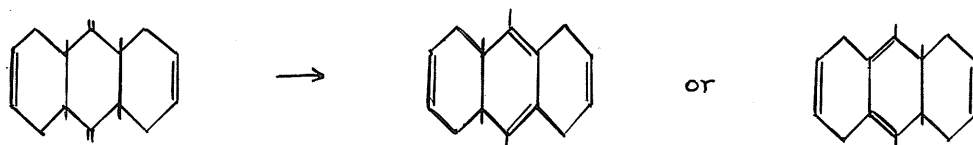
Hence, these compounds are not acetylated by boiling acetic anhydride under similar conditions used for the mono-adducts, while on heating eight H-atoms are lost by oxidation in the air.

Cyclopentadiene, likewise, combines with p-quinone and with α-naphthoquinone with the formation of mono-cyclopentadiene-quinone (VII), of cyclopentadiene-α-naphthoquinone (VIII), and of bis-cyclopentadiene-quinone (IX).
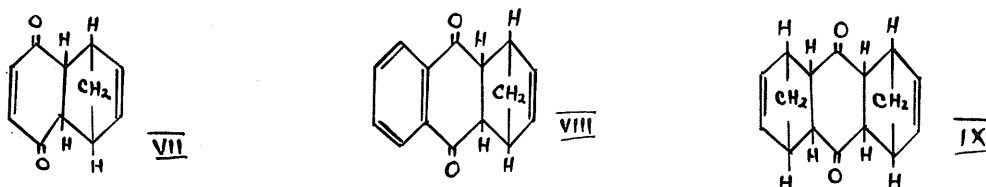
We can therefore regard the diene addition products of the quinones as true 1,4-adducts, formed in the same manner as with other philodienes. There remain, however, two drawbacks to the formulation of the products, especially those with pronounced tautomeric wandering of the γ- or ∂-hydrogen, and those containing endo-bridges which are characterized by marked instability. Diels and Stein assume "that the explanation is to be sought in a spatial structure which must show notable tension, according to the manner of the tension in the camphor systems" (ibid.).

The addition of dienes to di-quinones was attempted by

Fieser and Dunn[20], 2,3-dimethyl-butadiene and naphthacene-di-quinone yielding (X), from which 2,3-dimethyl-anthraquinone and phthalic acid were obtained on alkaline hydrolysis.
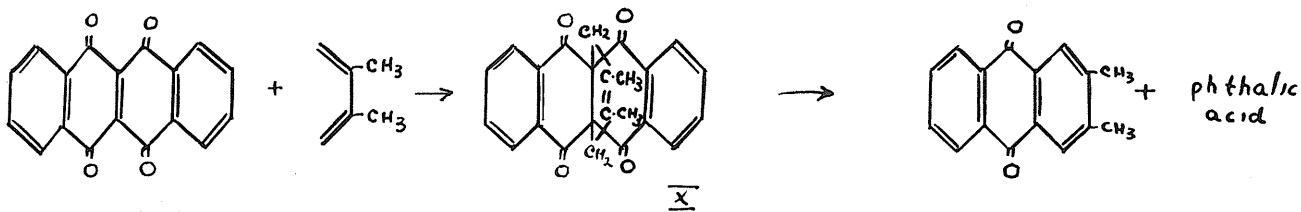
Diene syntheses with substituted quinones have provided interesting results. For example, a mono-addition product (XI) was obtained by the use of butadiene and p-toluoquinone[21], while with p-xyloquinone a liquid mono-butadiene- and a crystalline bis-butadiene adduct, (XII) and (XIII), respectively, were formed.[21,22]
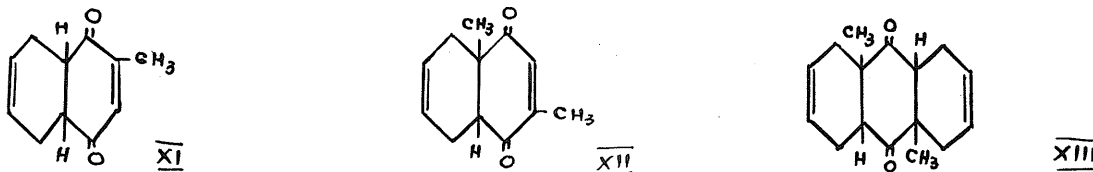
In using alkylated quinones, stress is laid upon the use of the right experimental conditions[22]. Thus, 2,6-dimethyl-naphtho-quinone-3,4 decomposes completely in boiling benzene, an alcoholic solution remaining clear for a longer time. On the other hand, 3-chloro-naphthoquinone-1,2 is more stable in benzene or chloroform than in alcohol.

Whereas some substituents, as the isopropyl group in thymo-quinone, prevent the formation, generally, of the bis-compound, others, such as hydroxyl or halogen, are less firmly attached and may be completely eliminated during or after addition, the new six-atom ring becoming completely aromatic, as in the conversion of α-hydroxy-napthoquinone with 2,3-dimethyl-butadiene to (XIV).
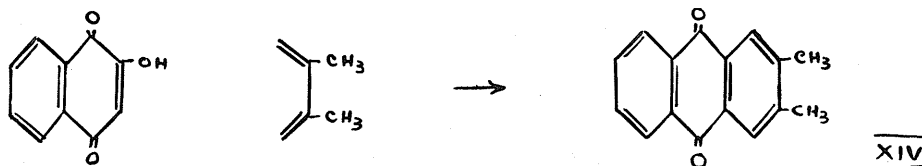
Alkyl-substituted ortho-quinones have been successfully employed in diene reactions[23,24,25], 2,6-dimethyl-3,4-napthoquinone, for example, adding to 2,3-dimethyl-butadiene to give (XV):
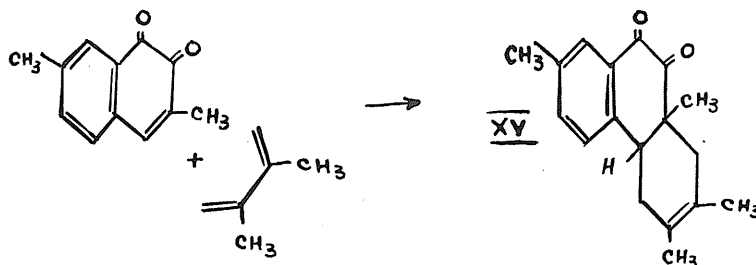
In the hope of making a closer approach to the sterol structure, an attempt was made[25] to condense 7-hydroxy-1,2-naphthoquinone with vinyl-cyclopentene so as to give 7-hydroxy-1,2-cyclopenteno-phenanthrene which exhibits certain features of the oestrone structure, but without success. As a result of this, Fieser and Dunn set out to determine whether an OH-group per se influences the reaction adversely, since they observed that hydroxylated quinones seemed to undergo decomposition before addition occurred.

A decrease in reaction velocity was noted with the progress-ive introduction of OH-groups. Further, nearly all the hydroxylated para-compounds studied condensed satisfactorily with dienes, juglone (XVI) giving a typical adduct with 2,3-dimethyl-butadiene. On the other hand, the reaction product (XIX) from naphthopurpurin (XVII) showed that the addition had actually occurred to give the tautomeric form (XVIII) of naphthopurpurin:
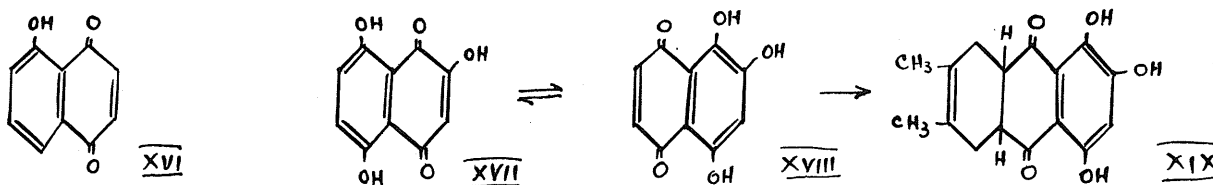
Due to a lack in stability in the hydroxylated 1,2-naphtho-quinones and because of the adverse influence of this type of

substituent group, other substituents were sought which might
stabilize the quinone in the same way as an angular methyl-group,
yet which could be subsequently eliminated. The 3- and 4-halogen
and dihalogen derivatives of 1,2-naphthoquinone were therefore
investigated. 3-Chloro-1,2-naphthoquinone was found to react to
give (XX), the presence of even a trace of alcohol having a delet-
erious effect on the reaction. In the course of a few hours, HCl
would be lost on exposure to the air to give (XXI).
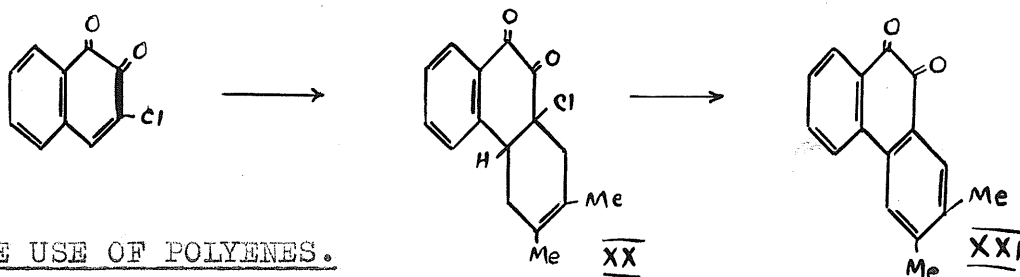
6. THE USE OF POLYENES.

In the addition of maleic anhydride to arylated dienes, to
trienes and to fulvenes, the same course of reaction as with cyclo-
pentadiene was demonstrated[29], 1,6-diphenyl-hexatriene, for
example, giving (I)[8,27].
Had the first anhydride
molecule added in the 1,6-
position, it would have been
possible for a second mole of anhydride to be taken up.

$(R = C_6H_5)$
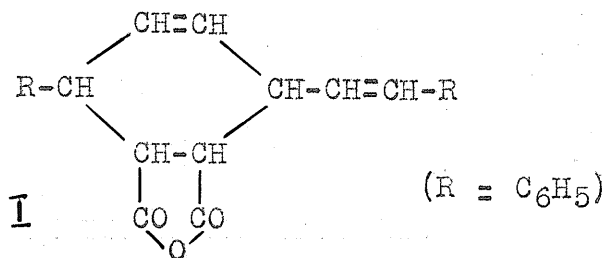
Recognizing the diagnostic value of the addition of maleic
anhydride, should it proceed exclusively in the 1,4-manner, Kuhn
and Wagner-Jauregg[27] investigated a series of polyenes in an
attempt to fix a general rule for the course of the addition process.

1,8-diphenyl-octatetraene takes up two moles of maleic
anhydride to give 6,6'-bis-(3-phenyl-cyclohexene-1,2-dicarboxylic
anhydride). On carrying the reaction out in boiling xylene, in-

stead of by warming to the melting point, a higher-melting isomer
was isolated. The latter had resulted in the first reaction only as
a by-product. This isomerization, also found in the adduct of
1,6-diphenyl-hexatriene, is explained as being due to a probable
displacement of the double bond in the partially hydrogenated
benzene nuclei. A mono-maleic anhydride addition product was
obtained with difficulty since it appeared to be even more reactive
than the original molecule.

With 1,10-diphenyl-decapentaene, two moles of anhydride
add on in the 1,4- and 1,7-positions, the middle bond remaining,
while three moles were taken up in the formation of the chief
addition product of 1,12-diphenyl-dodecahexaene. 1,14-Diphenyl-
tetradecaheptaene behaved similarly to hexaene.

The formation of a ten-membered ring with octatetraene and
of a twelve-membered ring with decapentaene[28] could not be proved.
Only six-membered rings were found to result[27], the reacting diene
group lying at the ends of the chain of the diphenyl-polyene
molecule. This heightened activity at the terminal methine groups
is presented in the following figure:
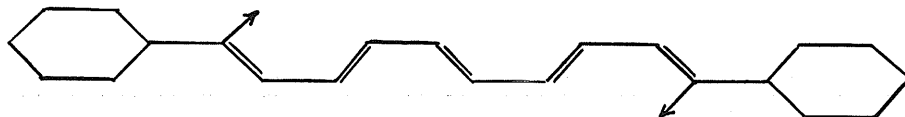
and is a phenomenon which can be related back to the observation of
Thiele[29] that 1,4-carbon atoms in a system of double bonds show
heightened activity in adding hydrogen, and to similar observations
of Kuhn and Winterstein[28] with regard to 1,6-addition of hydrogen
in trienes, 1,8-addition in tetraenes, and 1,10-addition in pentaenes.

That no larger carbon rings, such as by 1,6- or 1,8-addition,
were observed was understandable on spatial grounds, the double bonds
of the diphenyl-polyenes lying in a trans-position (see figure).

7. POLYMERIZATION OF DIENES.

A large number of polymerization reactions of many dienes, such as butadiene, isoprene, cyclopentadiene and cyclohexadiene, have been shown to be true diene syntheses. Thus, in the case of isoprene, Wagner-Jauregg[30] demonstrated three possible courses of dimerization. The formation of dipentene (I) takes place chiefly at 250-290°, while (II) is formed at room temperature or on moderate heating. (III) was produced by warming, with rubber as a by-product[31]. In each case we are dealing with 1,4-addition.
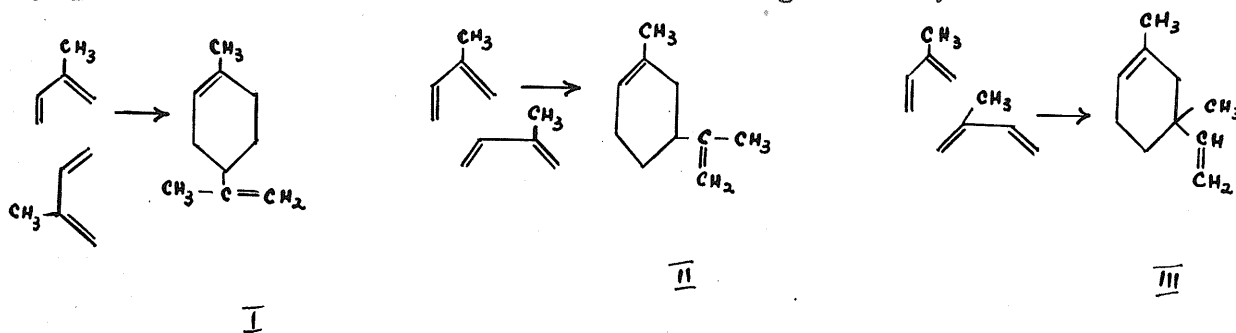
Alder and Rickert[32] concluded that "the polymerization of dienes can proceed in two different directions, of which the first leads to high-molecular rubber-like polymers. This process is effected according to a chain mechanism and is influenced greatly by catalysts, in the positive or negative sense. If carried out in the warmth, then it proceeds to give a concurring reaction which leads to low-molecular terpene-like dimers. This is brought about according to the scheme of the diene synthesis and is characterized by an extraordinary insensitivity to catalytic influences."

Similarly, with cyclopentadiene[32], both di- and tri-cyclopentadiene polymers have been isolated, (IV) and (V), respectively.
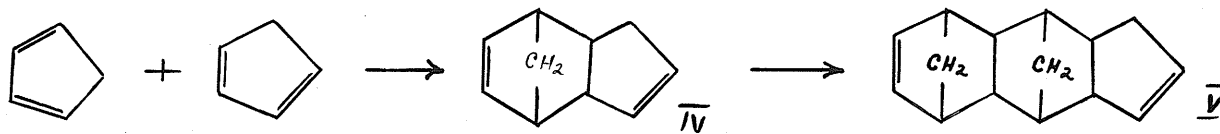
In fact, a seven-membered polymer has been prepared.

Cyclohexadiene[33,34,35] yielded a dimer containing an endo-ethylene bridge.

8. THE USE OF VINYL, STYRYL AND ALLYL COMPOUNDS.

With butadiene, Δ^3-vinyl-cyclohexene (I) is readily obtained[32,36]. By further polymerization, two trimers could conceivably result according to scheme (a) or (b):
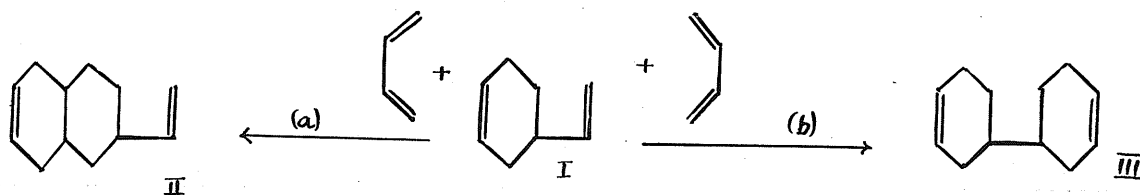
The first scheme (a) is analogous to the formation of tricyclo-pentadiene from dicyclopentadiene and therefore assumes a diene synthesis to the cyclic double bond in (I). According to (b), the vinyl double bond in the dimer is attacked. If (a) is correct, then tributadiene is vinyl-octalin (II), while if the reaction is according to (b), then a (symmetrical) $\Delta^{3,3'}$-octahydro-diphenyl (III) is produced. On investigation, the latter assumption was shown to be correct, although (a) might conceivably take place under other circumstances.

"The characteristic new factor which comes into play in the diene syntheses of Δ^3-vinyl-cyclohexene is the fact that here a single vinyl group takes over the function of the active ethylenic linkage[32]. Till now, this seemed to be a priviledge of such olefinic linkages as are held in adjacence to C:C double bonds and C:C triple bonds, respectively, i.e., an unsaturated group as C:O, C:N, C:C and C_6H_5." Till now the only exceptions from this rule had been the double bond in the bicyclo-(1,2,2)-heptene
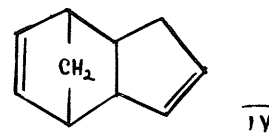
system (IV) and the triple bond in unsubstituted acetylene[37].

The synthesis of the diphenyl system by a diene synthesis with cinnamic aldehyde (V) on the one hand and with Δ^3-vinyl-cyclohexene (I) on the other brings up the question as to whether styrol (VI) and its homologues are also able to undergo the same reaction[36]. Styrol, as an olefinic component for the diene synthesis, must assume a middle position between cinnamic aldehyde and Δ^3-vinyl-cyclohexene insofar "as it lacks the activating influence
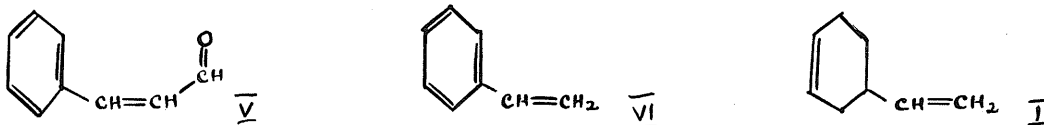
of the carbonyl group of the aldehyde, its double bond, however, lying in adjacence to a phenyl group, a factor which is omitted in Δ^3-vinyl-cyclohexene."

Styrol should therefore be expected to react as readily, if not more so, than Δ^3-vinyl cyclohexene. This it does, yielding (VII) with butadiene. In a like manner, indene (VIII) will react with butadiene to give Δ^2-tetrahydro-fluorene (IX), which can
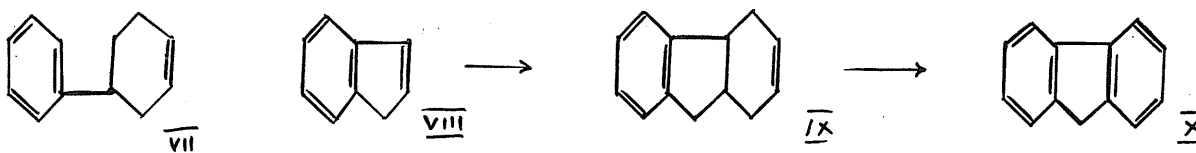
be dehydrogenated with selenium to fluorene (X).

A series of diene syntheses have been carried out[38] with various allyl compounds, the simplest being the addition of cyclopentadiene to allyl alcohol to give (XI), 2,5-endo-methylene-tetrahydro-benzyl alcohol. The reaction with cyclopentadiene took
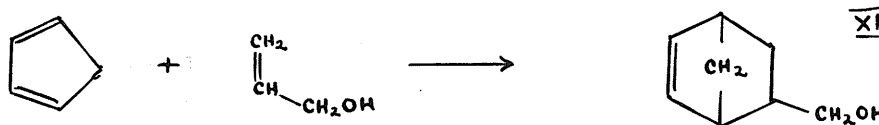
place only on heating to 150°, whereas acrolein, which possesses a carbonyl-group in adjacence to the C:C double bond, reacted at

room temperature. The activating influence of the CO-group can-
not be overlooked in a consideration of reaction velocities.

Other allyl compounds found to react were the ester of allyl
alcohol, and allyl halogenides, amines, cyanide, carboxylic acid,
and iso-thiocyanate.

Where the addition of the double bond in -C:C-R to a con-
jugated diene is being considered, the reaction is independent of
the nature of R, that is, of the functional groups -OH, -Cl, -Br,
-CN, -COOH, -NH$_2$. The inactivity of many such philodienes is
better explained by other factors, as degree of substitution,
spatial arrangement of the substituents at the double bond, ring
closure, etc.

The Diels-Alder reaction has been applied to $\alpha\beta$ -unsatur-
ated nitro-bodies, sulfones and thio-ethers[39]. Thus, cyclopenta-
diene adds smoothly at 100° to nitro-propylene to give the
partially unsaturated adduct (XII) which could be reduced to the
corresponding saturated amine (XIII). 2,3-Dimethyl-butadiene,
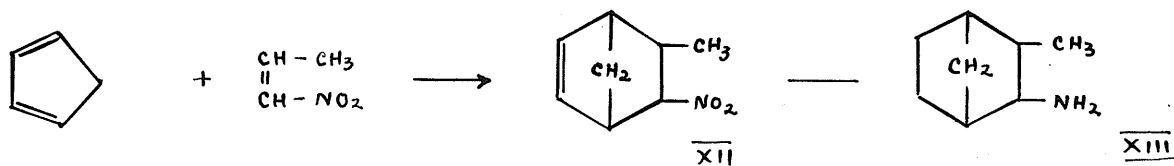
with p-tolyl-vinyl-sulfone, yields p-tolyl-dimethyl-cyclohexenyl-
sulfone (XIV); butadiene adds to Δ^2 -butadiene-sulfone to form (XV);
while with the unsaturated p-tolyl-vinyl-thioether, adduct (XVI)
is produced.
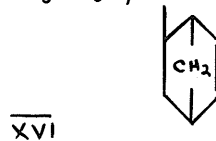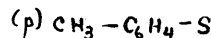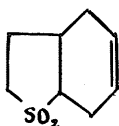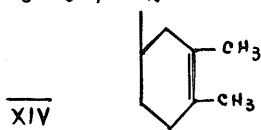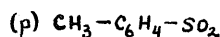
9. ANTHRACENE AND ANTHRACENE DERIVATIVES.

Anthracene and its derivatives were brought into reaction[41]

with various philodiene components, not only producing more
complex adducts as the result of typical Diels-Alder reactions
but also establishing the Armstrong[42]-Hinsberg[43] formula of
anthracene (the orthoquinoid formula of K. H. Meyer[44]) (I). The
adducts obtained possessed structures similar to (II) with maleic
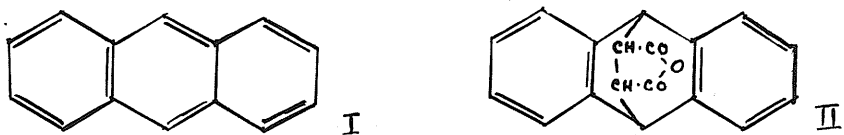
anhydride, in which the addition had taken place at the meso-
carbon atoms 9 and 10. By the linkage relationships of the
anthracenes, it was found that the ethylenic bonds were dis-
tributed on the framework of the fourteen C-atoms in such a way
that a conjugated system was present, with consequent ability to
undergo diene syntheses, although to a smaller extent than in
other conjugated aliphatic or acyclic systems.

With dibromo-maleic anhydride, (III) is obtained. By
treatment with catalytically stimulated hydrogen in glacial
acetic acid, this is converted to (IV) by loss of both Br-atoms
and formation of a double bond in the endoethylene bridge. As
would therefore be expected[45,46], (IV) should react with buta-
diene to give (V). On warming, the latter is decomposed into
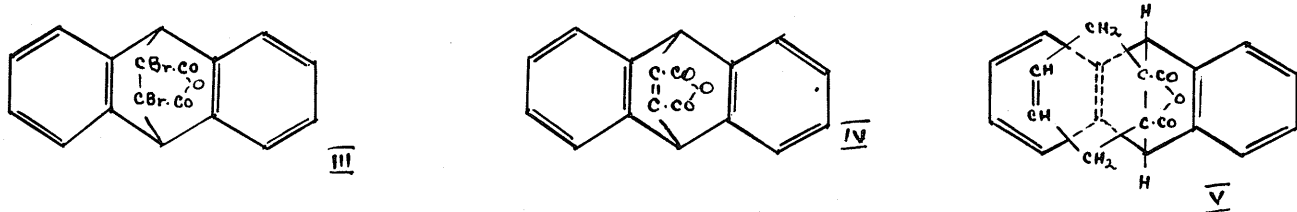
dihydro-anthracene and phthalic anhydride.

The C_4O_3-bridge in (IV) is split off on heating, but whether
it is split off as such
or as a mixture of CO
and CO_2 is not clear,
since heating (IV) in
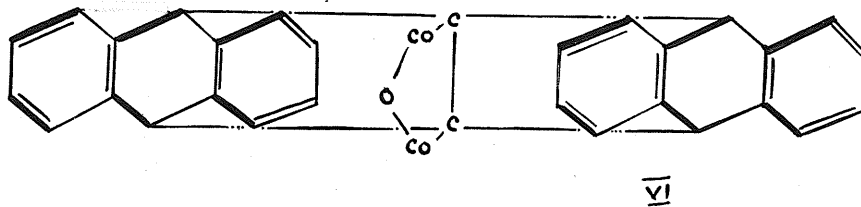
benzene for a long time results in the production of considerable
amounts of CO and CO_2, together with the formation of (VI).

Anthracene undergoes other typical diene syntheses, re-
acting with allyl alcohol[38]
and with quinone[48,49], the
latter giving (VII).
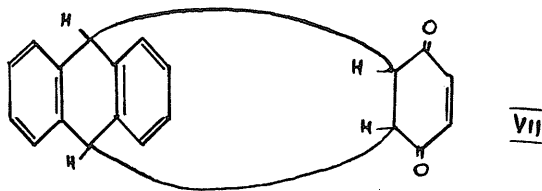
Clar[49] was of the
opinion that the polar character and probably also the spatial
arrangement of substituent groups in the anthracene molecule are
of distinct influence in determining the reaction velocity in
the addition of maleic anhydride.

All anthracene compounds investigated were found to dissec-
iate into their original components on heating, preferably on
fractional sublimation in vacuo in a stream of CO_2, the easily
volatile maleic anhydride being in this way separated from the
less volatile hydrocarbons. This offers a possibility of separ-
ating hydrocarbons of the anthracene type from an hydrocarbon
mixture by their reaction velocities on the one hand and by their
decomposition velocities on the other.

10. SYNTHESES OF PHENANTHRENE DERIVATIVES.

Recent researches in the field of sterol chemistry have
stimulated chemists in attempting to find new methods for synthes-
izing phenanthrene derivatives which show an approach to the sterol
structure or to similar structures showing the desired biological
activity.

Naphthalene derivatives
have been used with success,
Fieser and Hershberg[51,52]
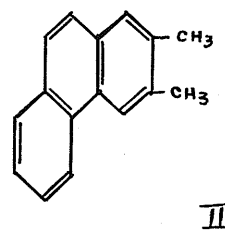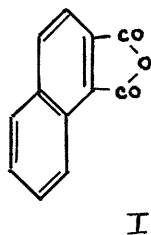
obtaining (II) from (I), 3,4-dihydro-naphthalene-1,2-dicarboxylic anhydride.

Benzphenanthrene derivatives, such as 2,3-dimethyl-chrysene (III) and 6,7-dimethyl-3,4-benzphenanthrene (IV) were prepared by Fieser[52], who also showed that the presence of a dimethylene-bridge in the 5,10-position in such compounds as/3,4-benz-
the
phenanthrene derivative (V), which is approachable by the diene synthesis, adds carcinogenic activity to the molecule.
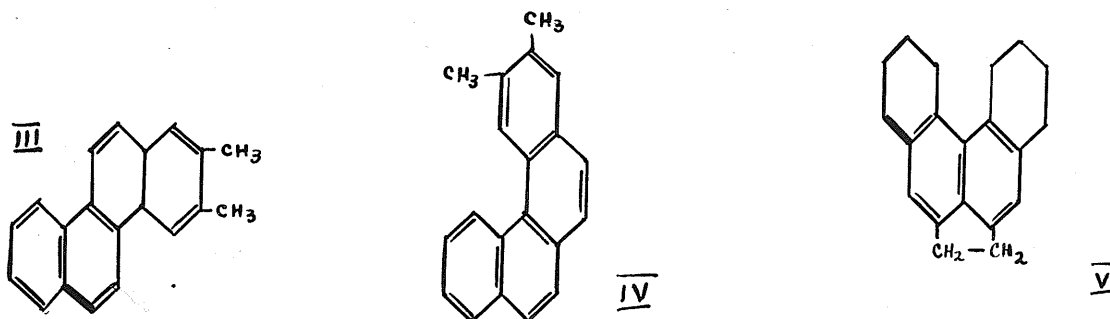
By introducing hydroxyl or methoxyl groups into the phenanthrene dicarboxylic anhydrides, he hoped to achieve derivatives possessing oestrogenic activity[53]. One of the compounds obtained (VI) gave positive results in experiments on mice[54].
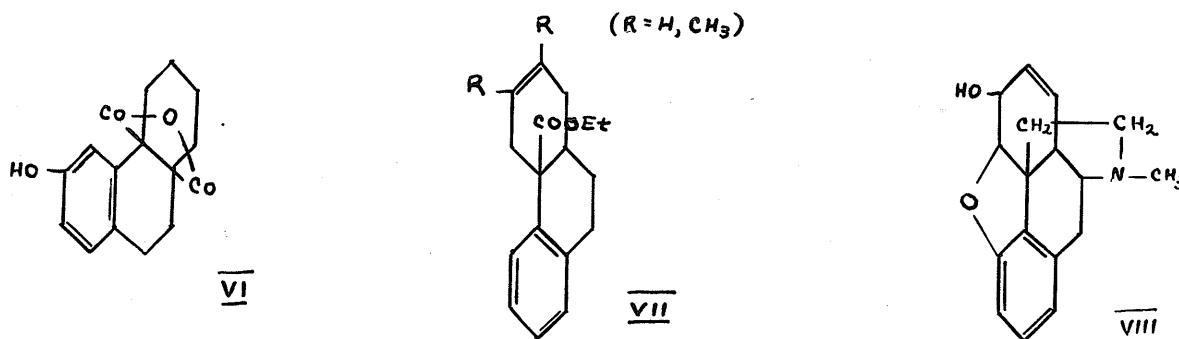
The synthesis[55] of (VII) was of particular interest in connection with the establishment of the actual attachment of the ethanamine chain in the phenanthrene skeleton of morphine (VIII) (Gulland-Robinson formula).

Aryl hexadienes were used in attempts to obtain the phenanthrene structure, but seemed to polymerize due to the action of maleic anhydride[56,57]. Only from ζ-phenyl-Δ^{27}-hexadiene was a

crystalline adduct obtainable in any appreciable yield.

Vinyl derivatives were used with more success[58,59], 2-vinyl-naphthalene, for example, reacting with maleic anhydride to give 2,3,4,12-tetrahydro-phenanthrene-3,4-dicarboxylic anhydride (IX).
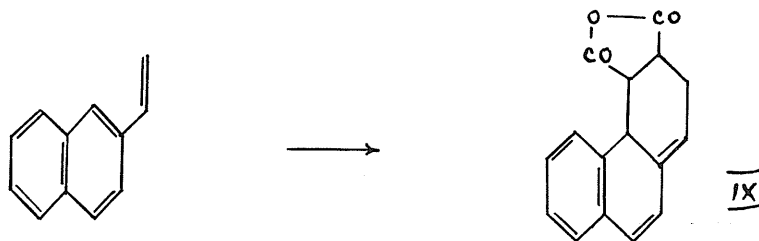
Bachmann and Kloetzel[60,61] were able to approach more closely the sterol structure by the use of cyclopentene derivatives. With 1-(6'-methoxy-2'-naphthyl)-cyclopentene-1 (X) and maleic anhydride the sterol skeleton (XI) resulted, whereas adduct (XIII) was obtained from 1-(β-naphthyl)-2-methyl-cyclopentene-1 (XII).
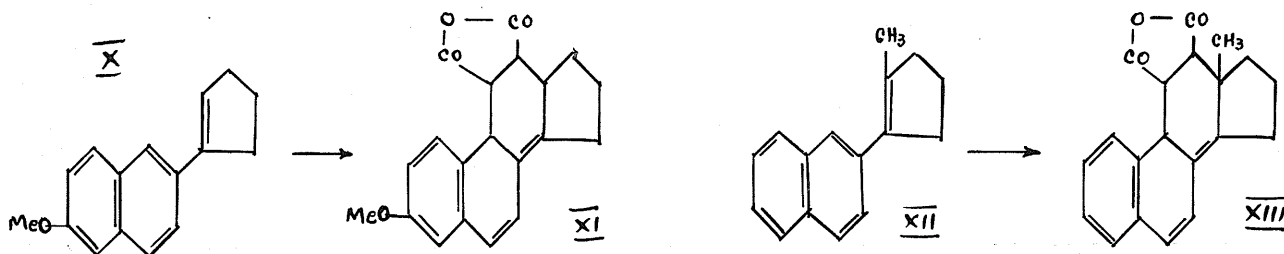
Dr. Elizabeth Dane and her co-workers[67] were able to make a very close approach to the sterol structure by the addition of the methyl-cyclopentene-dione (XIV) to 1-vinyl-6-methoxy-3,4-dihydro-naphthalene (XV) to give a product which may possess one of two alternative structures, (XVIa) or (XVIb).
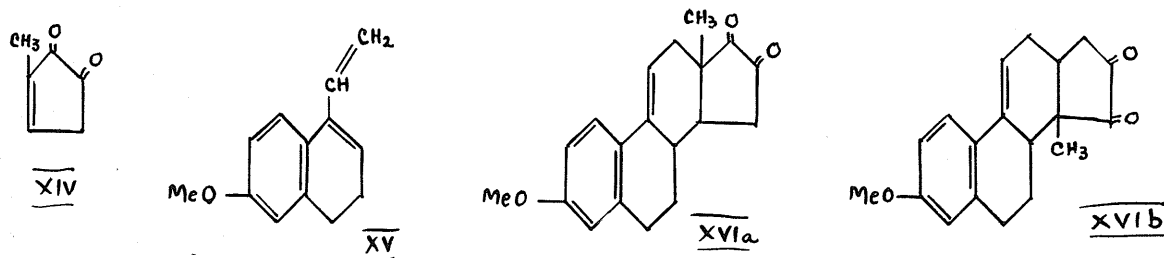
Other types of phenanthrene derivatives have been reported

by Gruber and Adams[63], while the researches of Lehmann[64], though
not successful in obtaining the sterol structures desired, never-
theless produced interesting derivatives.

11. THE DIENE SYNTHESIS AND DETERMINATION OF CONSTITUTION.

One of the more important applications of the Diels-Alder
reaction was in the determination of the presence and in the
location of a system of conjugated double bonds in ergosterol (I)[65,66]
and in certain of its irradiation products, namely, lumisterol,
tachysterol and calciferol, and in the absence of such a system
in the products of super-irradiation, as the suprasterols and
toxisterol. In contrast to ~~chles~~ cholesterol, ergosterol was
found to contain three double bonds of which two are conjugated,
in positions C_5-C_6 and C_7-C_8, the third being in the side chain
at C_{22}-C_{23}. The diene system was first blocked by maleic anhydride,
and the double bond in the side chain hydrogenated under con-
ditions such that the double bond formed by the maleic anhydride
remained unattacked. After careful thermic dissociation of the
anhydride added on, the conjugated system was regenerated, with
the formation of dihydro-ergosterol.
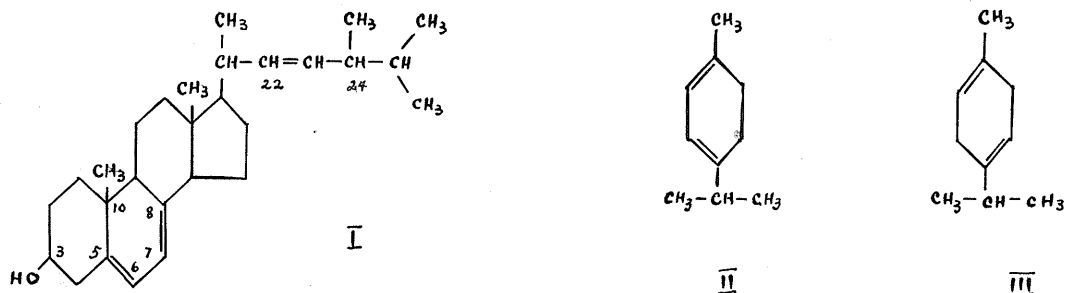
Wallach[67], from observations based on oxidation experiments,
concluded that terpinene (from terpineol) is composed of two
portions, α -terpinene or menthadiene-1,3 (II) and β -terpinene

or menthadiene-1,4 (III). If (II) is correct
for the α-form, a typical adduct should be
obtainable with maleic anhydride, while if
(III) is the correct one, there can be no
diene synthesis. The researches of Diels, Koch and Frost[68] showed
(II) to be the α-isomer due to the formation of (IV).
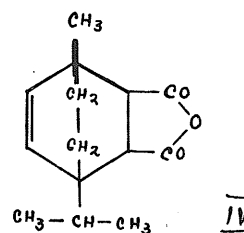
Since the diene synthesis may be applied to the detection
of quinoidation, a typical reaction would result with hydrazo
compounds, provided the latter exist in the tautomeric quinoid
form. Lauer and Miller[69] were able to show that certain p-
hydrazo compounds, but not all, react as if they were quinone
hydrazones. Thus, 2,4-dinitrobenzene-azophenol (V) adds cyclo-
pentadiene with formation of adduct (VI).
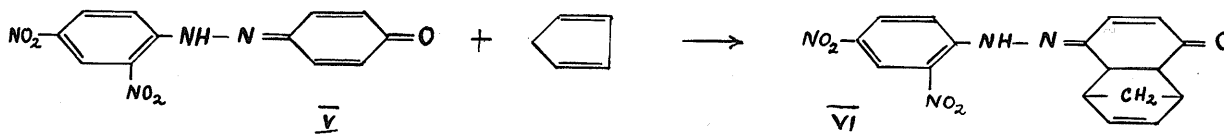
A diene synthesis is not always possible, even when a pair
of conjugated double bonds is present, since comparatively trivial
substitutions often cause this reaction to fail[70]. <u>The diene
synthesis can only be regarded as diagnostic if it leads to
positive results.</u>

For example, the following compounds do not give diene
reactions with naphthoquinone or with maleic anhydride at 100°:
$CH_2Cl-CH:C:CCl-CH:CH_2$; $CH_2:CH-CCl:C:C:CH_2$. This is not due to the
fact that the conjugated system terminates in a series of contig-
uous double bonds, since this arrangement does not preclude 1,4-
addition and since this arrangement is not present in the non-
reactive chloride: $CH_2Cl-CH:CCl-CCl:CH-CH_2Cl$.

12. EFFECTS OF SUBSTITUTION IN THE DIENE COMPONENT.

Chloroprene or 2-chloro-butadiene (CH_2:$CHCl$-CH:CH_2), under ordinary conditions, polymerizes to a rubber-like substance about seven hundred times as rapidly as isoprene or butadiene[71]. The effect of a Br-atom in the 2-position has an even more powerful activating influence[72]. On the other hand, 1-chloro-butadiene polymerizes not much more rapidly than does isoprene and the rubber-like product has very little strength, whereas the corresponding Br-derivative has no rubber-like properties at all. Hence, the activation due to an halogen atom is very closely related to its position[73]. Multiple substitution does not modify this conclusion since tetrachloro-1,2,3,4-butadiene-1,3 does not polymerize at all.

No other type of substitution than a single β-halogen atom has yielded a compound that greatly exceeds butadiene in the speed of its spontaneous polymerization (diene behavior) and at the same time leads to a rubber-like product. Similarly, a β-methyl group increases the activity of the diene, as in isoprene, whereas α-substitution by methyl reduces the tendency to polymerize and unfavorably affects the quality of the product.

The chlorinated 1,3-butadienes may be arranged in the following order as far as the speed of their spontaneous transformation into high polymers is concerned: $\beta\gamma \gg \beta \gg \alpha\beta\gamma > \alpha \gg \alpha\beta\gamma\delta$. and only the second member of this series yields a polymer that is definitely rubber-like.

Both the terminal methylene groups of butadiene must be free; if either is substituted even by an activating group, the speed of polymerization is diminished and / or the properties of

the product are adversely affected. We can therefore arrange the dienes in the following order:

$CH_2:CCl-CH:CH_2$, $CH_2:CCl-CMe:CH_2 \gg CHMe:CCl-CH:CH_2$, $CH_2:CCl-CMe:CHMe$

13. THE ADDITION OF KETENES.

It is of importance in connection with general additive theory to determine with certainty the direction in which addition occurs in the ketenes and to discover whether ketenic addition to conjugated dienes are all of the same type, inevitably leading to four-atom carbon rings instead of to six-atom rings as might be anticipated according to the mechanism of the Diels-Alder reaction[74,75,76,77,78].

For the addition product of diphenyl-ketene to cyclopentadiene, four structures (I), (II), (III) and (IV) are possible:
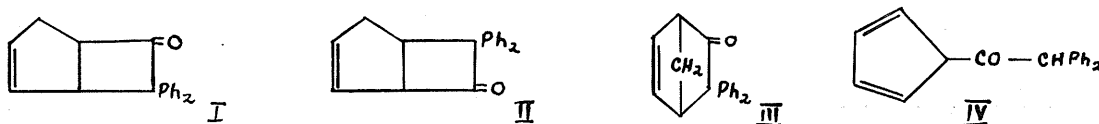
the first two resulting by 1,2-addition, (III) by 1,4-addition and (IV) as the result of the addition of the diene to the ketene as an active hydrogen compound. Actually, however, only (I) was found to result. This compound is able to undergo further addition with cyclopentadiene[78,79] to form a bis-compound, also by 1,2-addition, the resulting product being (V) or (VI).

$(Ph = C_6H_5)$
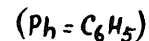
14. THE KINETICS OF THE DIENE SYNTHESIS.

The kinetics of the Diels-Alder reaction have been studied in some of the simpler cases and found to be of the second order,

homogeneous, and only slightly, if at all, complicated by side reactions[81]. The velocity of reaction seems to be about the same in non-polar solvents and in the gaseous state[99,100], although it may be about five times as fast in polar as in non-polar solvents[94]. Fairclough and Hinshelwood (ibid.) conclude that while the stabilization of a polar product by polar solvents may be a factor, some part of the effect may be due to an increase in the collision frequency in such solvents. The heat of reaction in the gaseous state appears to be constant and the same as in non-polar solvents[100].

15. THERMAL DECOMPOSITION OF THE ADDUCTS AND REVERSIBLE ADDITIONS.

On heating 1,4-endoethylene-1,4-dihydro-anthraquinone (I), which resulted by the addition of cyclohexadiene to α -naphthoquinone, a quantitative breakdown into anthraquinone and ethylene took place:
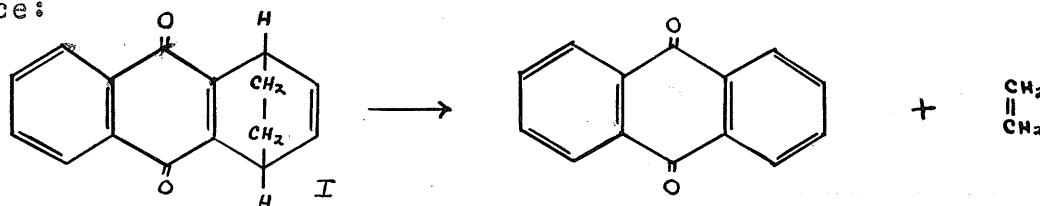
This reaction has been applied[82] to differentiating between five- and six-atom rings on the basis of the difference in stability of their adducts with maleic anhydride. While the adducts of cyclopentadiene, in reversal of the diene synthesis, undergo comparatively easy decomposition into their components on warming, the adducts of the cyclohexadienes are thermostable to quite an extent and decompose only at higher temperatures.
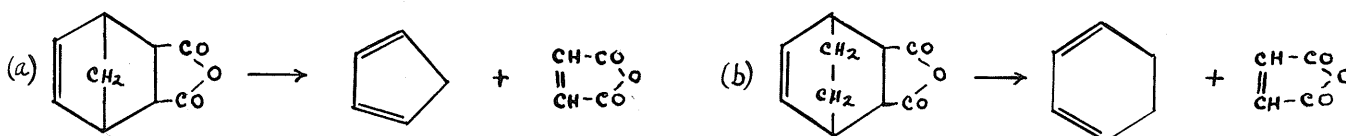
Difficulties of an experimental nature made it necessary
to resort to a simpler and more practical method (than by the use
of maleic anhydride or of p-quinone as philodiene components) for
the differentiation of five- and six-atom cyclic dienes, this being
the decomposition of the adduct of the diene with acetylene-
dicarboxylic ester. With cyclopentadiene, a typical synthesis
occurs, yielding (II). The adduct is doubly unsaturated and poss-

esses an unusual behavior on boiling. It either boils undecomposed,
as in the addition products with cyclopentadiene and its lower
homologues, or in the adducts of the higher-boiling homologues
an intermediate decomposition into its original components sets in,
which combine anew in the receiver by proper distillation.
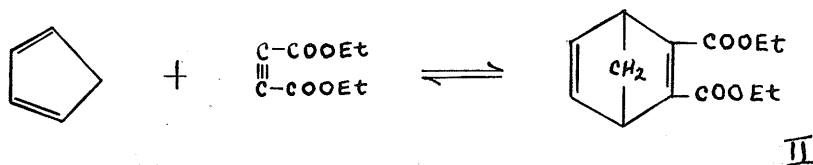
With cyclohexadiene, however, the adduct (III) undergoes a
type of decomposition analogous to that observed with the quinone
or maleic anhydride product:
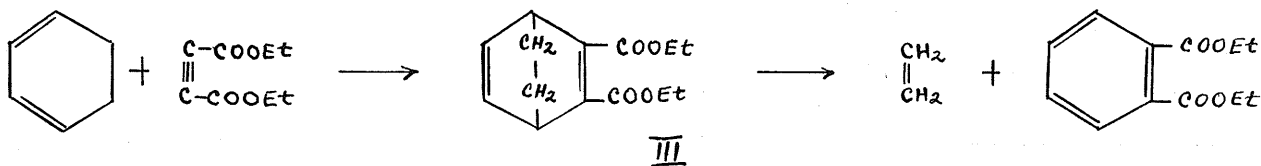
Thus, the adduct of cyclopentadiene with acetylenic ester
is obtained undecomposed in the receiver, whereas the cyclohexa-
diene product distills over to give a derivative poorer in carbon.

The next higher ring homologue of the cyclic dienes is
cycloheptadiene-1,3. This behaves analogously to cyclopentadiene
itself, its acetylenic ester adduct being thermostable, a dissoc-
iation of the endopropylene bridge not being observed[84].

Diels and Thiele[85] made use of this phenomenon in the prep-
aration of the hitherto unknown acid chloride Cl-CO-C:C-CO-Cl of
acetylenic ester and of carbon subnitride N:C-C:C-C:N (cf. [86,87]).
The latter was obtained by conversion of the acid chloride (IV)
into the acid amide (V) and thence into the dinitrile (VI),
followed by thermal decomposition of the latter, while the acid
chloride was obtained by a "displacement procedure" of (IV) with
maleic anhydride:
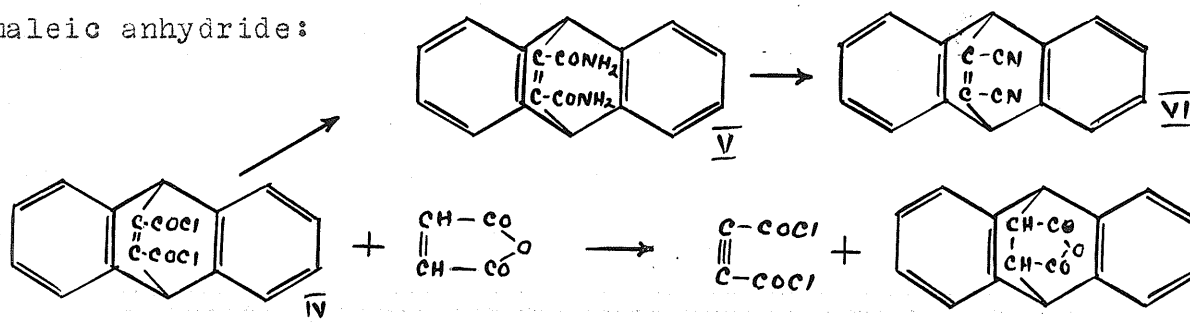
Substances containing endocarbonyl bridges, such as (VII),
have been prepared[37,88,89,90] and shown to lose CO on heating, to
give tetraphenyl-dihydrophthalic anhydride (VIII).

$(R = C_6H_5)$
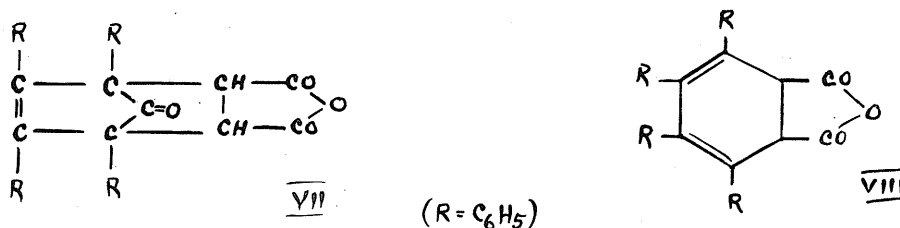
16. SYNTHESIS OF HETERO-RINGS CONTAINING OXYGEN.

The three fundamental
five-membered heterocyclic
rings are furan, pyrrole and

thiophene, containing oxygen, nitrogen and sulfur, respectively.
In view of their structural similarity to cyclopentadiene, they
would appear as suitable for reaction with philodienes. Furan
adds by the 1,4-method[14], pyrrole by substituent addition, whereas
thiophene appears non-reactive with the philodienes studied.

Pyrocinchomic anhydride, for example, adds to furan with the production of a typical diene adduct (I) which can be hydrogenated to give cantharidin (II).
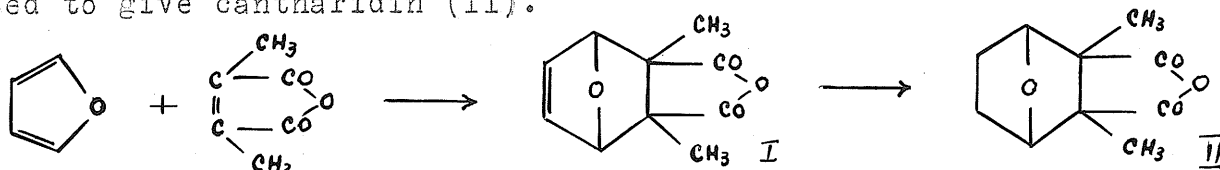
Acetylene dicarboxylic ester has been found to add to furan with formation of both mono- and bis-compounds, containing one and two moles of furan, respectively, to one of the ester. On thermal decomposition, the behavior is exactly the same as with the adducts of cyclopentadiene[84], that is, decomposition with reformation of the original compounds.

Diene adducts with -CO-O- bridges have been prepared and their behavior studied[93]. The product (III) formed by the addition of maleic anhydride to cumalic ester loses
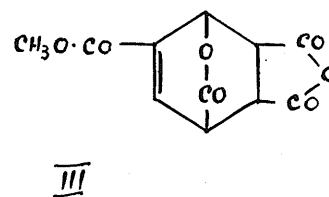
it -CO-O- bridge on heating, with formation of a benzene derivative which can be saponified to trimesic acid.

17. THE STERIC COURSE OF THE DIENE SYNTHESIS.

In the numerous diene syntheses studied, stereochemical questions have presented themselves. In some cases, as in the polymerization of the cyclopentadienes, there has been a general conformity of the stereochemical phenomena observed; in others this regularity has not been confirmed.

Alder and Stein[95,101] recognized the dimerization of cyclopentadiene, structurally, as a diene synthesis, and even from a steric viewpoint were able to clarify the process of addition. They found that at room temperature the endo-dicyclopentadiene (I)

resulted, exclusively, and that only at higher temperatures did
a concurring reaction take place, leading to the exo-isomer (II):
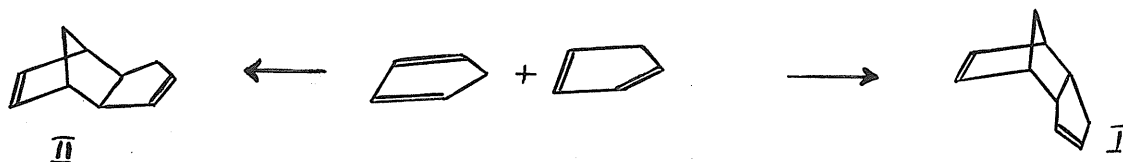
Using maleic anhydride, acrolein, crotonaldehyde and ac-
rylic acid as philodiene components with cyclopentadiene[95,35,96]
as the diene, analogous results were obtained. Furan and sylvan
reacted as did cyclopentadiene to give the endo-isomer[97].

The steric course of the diene synthesis, using both open-
chain and cyclic dienes, with quinone as the philodiene, has
been worked out in an exhaustive paper by Alder and Stein[98].

18. DIENOMETRY.

A quantitative method involving the additive nature of
maleic anhydride for determining the amount of conjugated diene
in a sample of crude fat or oil has been worked out by Kaufmann
and Baltes[102,103,104,105] and applied also to analysing anthracene[106],
petroleum[107], natural resins[108], perfumes[109], ethereal oils[110],
vitamin A, carotene and other oils of vegetable and animal
origins[111]. This method, known as "dienometry" involves the de-
termination of the "diene number" or "maleic anhydride value" (M.A.V.).

The method originally consisted of weighing a 0.1-0.15 gm.
sample of the diene into a 20 cc. Jena glass bomb and, after add-
ing 10 ccs. of a solution of 10 gms. of pure maleic anhydride in
one litre of acetone, kof sealing the bomb and heating for 20
hours at 100°[102]. After cooling and rinsing the contents into a
250 cc. Erlenmeyer flask with 80 ccs. of CO_2-free water, con-
taining a little NaCl, the mixture was left to stand for 6-8 hours,

the residue filtered off and the filtrate titrated with 0.1 N

NaOH, using phenolphthalein as an indicator. Since one mole of

maleic anhydride reacts with one conjugated system, the extent of

the reaction may be expressed in terms of iodine number equivalents.

The diene number is $\dfrac{1.269a}{\text{sample weight}}$ where a is the number of ccs.

0.1 N NaOH required to neutralize the amount of maleic anhydride

that has reacted with the sample.

If x is the diene number of the fatty acid with the conjug-

ated system and D is the diene number of the oil or of the total

fatty acid, then the percentage of fatty acid with the conjugated

system is 100D/x.

More recently, Kaufmann, Baltes and Buter[105] have been able

to determine the excess maleic anhydride and the free acid formed,

respectively, in the presence of the addition product and of the

by-products, immediately after the completion of the reaction, by

means of iodometric titration. Maleic anhydride, on refluxing with

water, is converted to the free acid, which reacts with a mixture

of potassium iodide and iodate, according to the equation:

$$3\ \begin{matrix} CH-COOH \\ \| \\ CH-COOH \end{matrix}\ +\ 5KI\ +\ KIO_3\ =\ 3\ \begin{matrix} CH-COOK \\ \| \\ CH-COOK \end{matrix}\ +\ 3I_2\ +\ 3H_2O$$
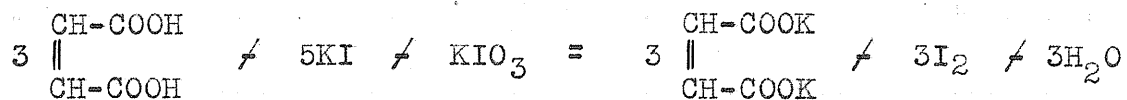
If an excess of thiosulphate is added at the start, the reaction

proceeds quantitatively to a finish. It is seen that one mole of

iodine is equivalent to one of maleic acid or anhydride.

By this method, a weighed amount of diene together with 10 ccs. of 0.1 N maleic anhydride in acetone

are treated in a wide-mouthed bottle with 50 ccs. water, to which

are added 15 ccs. of 4% potassium iodate and 15 ccs. of 24% iodide

solution, followed by 25 ccs. of 0.1 N thiosulphate. After standing

two hours, the mixture is treated with 25 ccs. of 0.1 N iodine and

the excess iodine is determined by titration in the usual manner with standardized sodium thiosulphate solution.

Higher boiling solvents, such as benzene, toluene or xylene, may be used, provided that the mixture is shaken vigorously during the reaction (ibid.).

Correction must be made if amines or hydroxylic compounds, with which maleic anhydride may react, are present[112,113,114].

B. DIENE SYNTHESES OF HETEROCYCLIC NITROGEN COMPOUNDS.

1. SUBSTITUTION WITH DISPLACEMENT OF HYDROGEN.

On the basis of the structural similarity between pyrrole and furan, it might be supposed that a similar diene addition with maleic anhydride would take place. Such, however, is not the case[115].

Diels and Alder found it necessary, in working with pyrrole, to substitute an aqueous solution of maleic acid for the anhydride. During the reaction, a considerable amount of the acid was converted to fumaric acid, but this conversion was not associated with a further reaction between pyrrole and maleic acid.

The action of aqueous maleic acid on pyrrole was as follows, with production of dilevulinic acid (I), together with a small amount of pyrrole-dipropionic acid:

$$
\begin{array}{c}
CH{=}CH \\
\mid \quad {>}NH \\
CH{=}CH
\end{array}
+ 2
\begin{array}{c}
CH{-}COOH \\
\parallel \\
CH{-}COOH
\end{array}
+ 2H_2O = 2CO_2 + NH_3 +
\begin{array}{c}
CH_2{-}CO{-}CH_2CH_2{-}COOH \\
\mid \\
CH_2{-}CO{-}CH_2CH_2{-}COOH
\end{array}
$$

$$\underline{I}$$
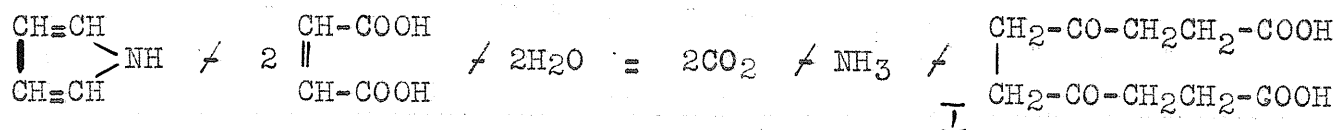
Better results have been obtained using homologues of pyrrole, as α-methyl-pyrrole. To this maleic acid adds nearly quantitatively without formation of fumaric acid, proving that the presence of fumaric acid could only be due to a secondary reaction. The maleic

acid- α -methyl-pyrrole adduct contained both components in a 1:1
ratio whereas pyrrole had reacted with two moles of maleic acid.
In the reaction, the acid had entered the α'-position in α -methyl-
pyrrole by displacement of hydrogen, with formation of α -methyl-
pyrrole- α' -succinic acid (II).

$$
\begin{array}{ccc}
\underset{\substack{||\\ \\ CH_3-C\quad CH}}{CH-CH} & / & \underset{\substack{|\quad\;\;|\\ COOH\;\;COOH}}{CH=CH} \\
\underset{NH}{\diagdown\diagup} & & \\
\end{array}
\quad = \quad
\begin{array}{c}
\underset{\substack{||\quad||\\ CH_3-C\quad C-CH—CH_2}}{CH-CH} \\
\underset{\substack{\diagdown\diagup\;\;\;|\quad\quad|\\ NH\;\;COOH\;\;COOH}}{}\quad \underline{II}
\end{array}
$$
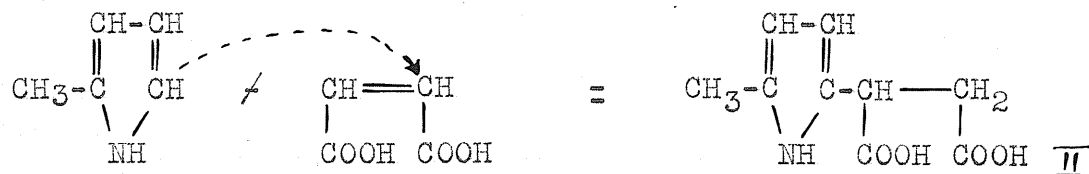
We can now explain the reaction of maleic acid on pyrrole:
In analogy with the above reaction of α -methyl-pyrrole, pyrrole
takes up two moles of maleic acid to form the tetracarboxylic acid
(III) which secondarily splits off CO_2 so as to produce pyrrole-
$\alpha\alpha'$ -dipropionic acid (IV), which then goes over into the corres-
ponding 1,4-diketone, the decane-dione-4,7-diacid-1,10 (I) by
hydrolysis, with simultaneous liberation of ammonia.

$$
\begin{array}{c}
\underset{\substack{||\quad||\\ CH_2-CH—C\quad C-CH—CH_2}}{CH-CH} \\
\underset{\substack{|\quad|\quad\diagdown\diagup\;\;|\quad\quad|\\ COOH\;COOH\;NH\;COOH\;COOH}}{}\;\underline{III}
\end{array}
\xrightarrow{-2CO_2}
\begin{array}{c}
\underset{\substack{||\quad||\\ CH_2-CH_2-C\quad C-CH_2-CH_2}}{CH-CH} \\
\underset{\substack{|\quad\quad\diagdown\diagup\quad\quad|\\ COOH\quad NH\quad COOH}}{}\;\underline{IV}
\end{array}
$$
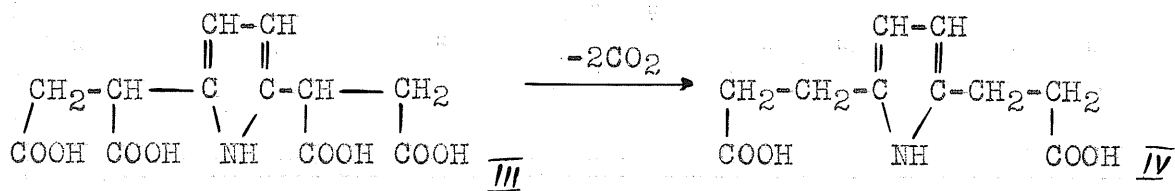
N-methyl-pyrrole behaves like pyrrole, taking up two moles
aqueous maleic acid in the $\alpha\alpha'$-positions. The tetracarboxylic acid
formed (V), by splitting off CO_2, goes smoothly over into N-methyl-
pyrrole-2,5-dipropionic acid, only a small portion of this being
hydrolysed to (I).

$$
\begin{array}{c}
\underset{\substack{||\quad||\\ CH_2—CH—C\quad C—CH—CH_2}}{CH-CH} \\
\underset{\substack{|\quad\;|\quad\diagdown\diagup\;\;|\quad\quad|\\ COOH\;COOH\;N-CH_3\;COOH\;COOH}}{}\;\underline{V}
\end{array}
\qquad
\begin{array}{c}
\underset{\substack{||\quad||\\ CH_3-C\quad C-C=CH_2}}{CH-CH} \\
\underset{\substack{\diagdown\diagup\;\;|\quad\quad|\\ NH\;\;COOH\;COOH}}{}\;\underline{VI}
\end{array}
$$
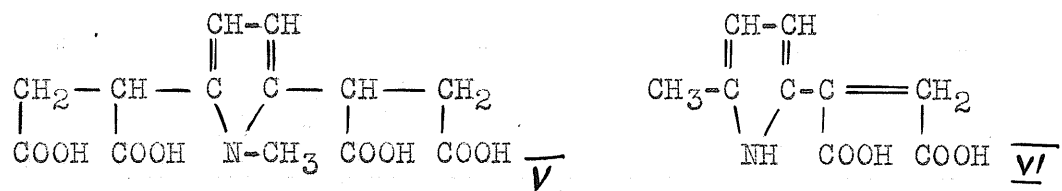
The ability of pyrrole to react with $\alpha\beta$-unsaturated di-
carboxylic acids (in aqueous solution at low temperatures generally)

seems to be general and is therefore a useful method of intro-
ducing side chains containing -COOH groups. It has also been
established that α -methyl-pyrrole will add one mole of acetylene-
dicarboxylic acid to yield (VI).

If instead of acetylene-dicarboxylic acids, its dimethyl
ester were used with N-methyl-pyrrole, two moles of ester are added
to each one of the pyrrole derivative[116]. The first step in the
reaction is seen as a "substitution reaction with displacement of
hydrogen":
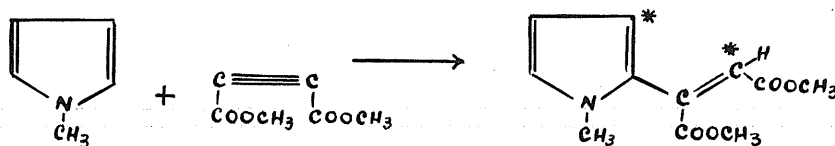
The second step is a true diene synthesis, the second mole
of ester adding in a 1,4-manner at the starred C-atoms, yielding (VII).
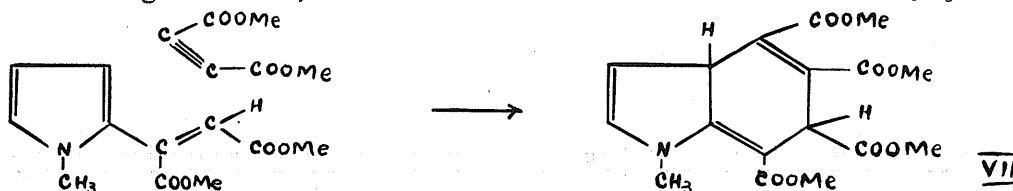
Di-substituted pyrroles in the 2,4-position seem able to add
in the ratio of two moles of pyrrole derivative to one of acetylenic
ester by a twofold "substitution reaction with displacement of
hydrogen, yielding (VIII) with 2,4-dimethyl-pyrrole:
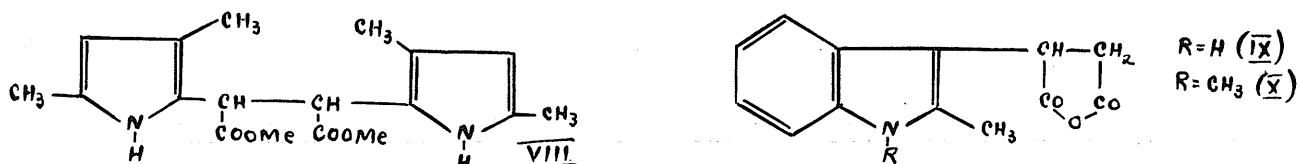
As was noted, maleic acid enters the pyrrole nucleus in the
α -position. In indole derivatives, however, the α -position is
substituted, and so the β -carbon is attacked[117]. Thus, using
maleic anhydride, α -methyl-indole produces (IX) and N, α -
dimethyl-indole gives (X).

Adducts containing two moles of the indole derivatives to
one of maleic anhydride have also been prepared. But in contrast

to the method of single addition, the anhydride group here enters
as a function in the reaction, since the adduct is a monobasic acid.
Of the three O-atoms in this substance, two are contained in a
-COOH group while the third is present in a keto-group connected
with an $\alpha\beta$-double bond. The formula of the α-methyl-indole add-
uct is given by (XI) while that of N,α-dimethyl-indole is (XII).

R=H (XI)
R=CH₃ (XII)
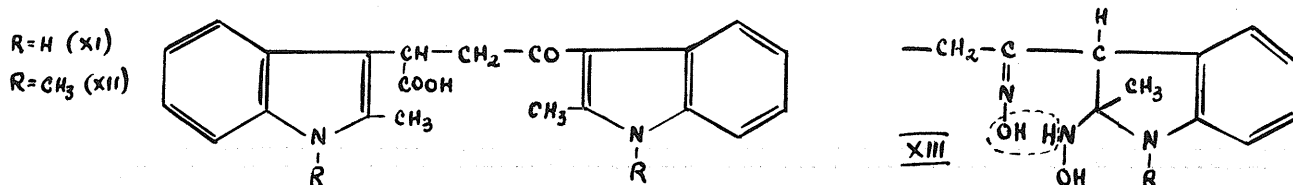
By treatment with hydroxylamine hydrochloride, the complicated
base (XIII) results, which, by splitting off of water, results in
a well-formed oxamino-oxime.

On the other hand[118], N-methyl-indole behaves more like 2,4-
dimethyl-indole, giving adduct (XIV), analogous to (VIII) and con-
taining two moles indole derivative to one of the ester, rather
than adding two moles of ester with the production of an analogue
of (VII). That is, substitution takes place in the α-position
rather than in the β-position.
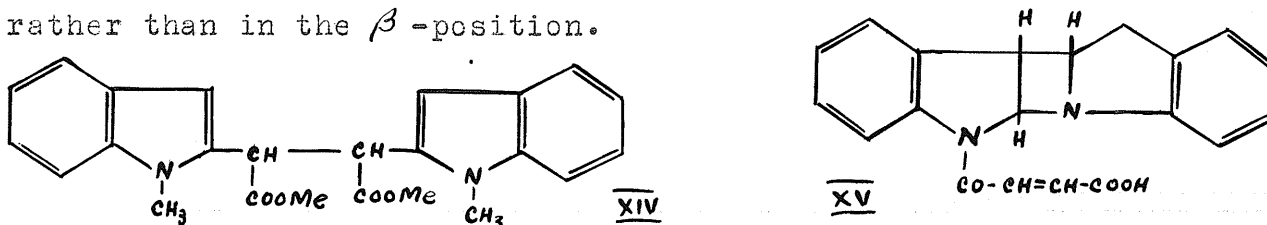
The reaction of maleic anhydride with indole[117] presents yet
another process. Here, a di-indole is formed which then reacts with
maleic anhydride to give the monobasic unsaturated acid (XV).

With skatol, an adduct is obtained containing two moles of
skatol to one of maleic anhydride. It is, however, not the same as
that produced with diskatol, due to steric considerations. Form-
ulae (XVI) and (XVII) represent diskatol and diskatol-maleic
anhydride, respectively. The adduct of two moles of skatol and
maleic anhydride can be regarded as the fumaroid arrangement of

the substituents at the double linkage, while the diskatol adduct
is most probably the malenoid type of arrangement.
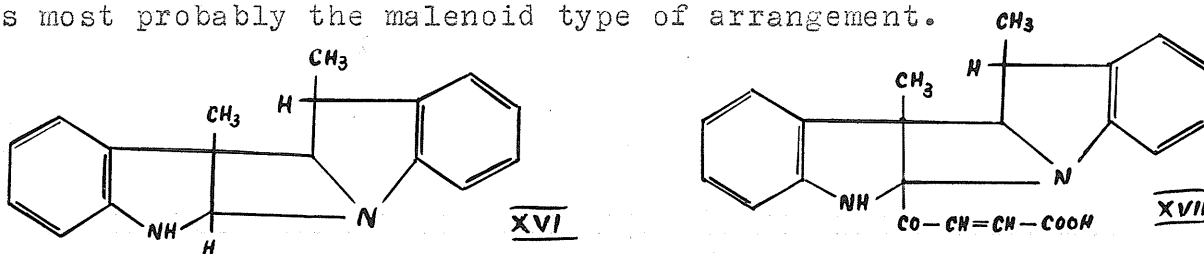
Heterocyclic systems with two N-atoms in the ring were
investigated by Diels and Alder[118]. It was found that substances
such as imidazole and its homologues, as well as pyrazole and its
derivatives, reacted easily, in general, with acetylenic ester, much
as in the pyrrole series, the result of the reaction depending
essentially on the manner of substitution by the methyl-groups.

With 4(5)-methyl-imidazole, for example, acetylenic ester is
added in the ratio of 1:1 with the formation of a colorless adduct
possessing either formula (XVIII) or (XIX):

2. ADDITIONS INVOLVING FORMATION OF AN ACETYLENIC ESTER CHAIN.

(a) Introduction.

With N,α-dimethyl-imidazole, two moles of acetylenic ester
are taken up to give a substance corresponding to the adduct of
N-methyl-pyrrole. But in contrast to the scarcely colored adduct
of N-methyl-pyrrole, this product (I) is bright red, the difference
in color being due to a difference in the method of formation.

In fact, the formation of this substance presents a principle
that is without analogy to any experience in the pyrrole series.
Its importance lies in the fact that all six-membered heterocyclic
substances of the pyridine-type (as pyridine, quinoline, quinaldine,

isoquinoline, stilbazole, etc.) add acetylenic ester according to a similar scheme.

The constitution of adduct (I), formed by the addition of two moles of ester at the group $-N \equiv C(CH_3)-$ of N,α-dimethyl-imidazole, was proved by treatment with bromine. The group $-CH=CH-N-CH_3$ was split off to give (II), and this was subsequently saponified and decarboxylated to α-picoline (III).
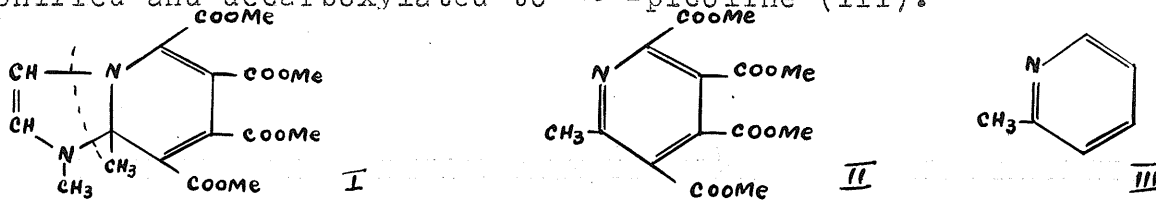
So far we have observed only two types of diene synthesis: (a) 1,4-addition, and (b) substitution with displacement of hydrogen. In the case of N,α-dimethyl-imidazole, however, for the first time, we have the addition of two moles acetylenic ester to a N≡C double bond. This type of reaction, as pointed out above, seems to be general for all nitrogenous heterocyclic rings of the pyridine type. In all these cases, the adduct produced is intensely colored and quite characteristic[119].

The adduct of pyridine with acetylenic ester has been shown to possess structure (IV), being, therefore, quinolizine-1,2,3,4-tetracarboxylic-tetramethyl ester. On oxidative breakdown, indolizin-1,2,3-tricarboxylic ester (V) results by ring contraction. The mechanism is as follows[120]: By the action of nitric acid on (IV) there results an isolatable intermediate product possessing the structure (VI). By careful hydrolysis with warm water, the $-NO_2$ residue is split off to give the nitrate (VII) of an oxide compound. The conversion into the indolizin system takes place by means of a picolinic rearrangement with wandering of the OH-group to give (V). The splitting off of the C-COOMe group seems to be a

stabilization reaction of the hypothetical tricyclic intermediate product (VIII).
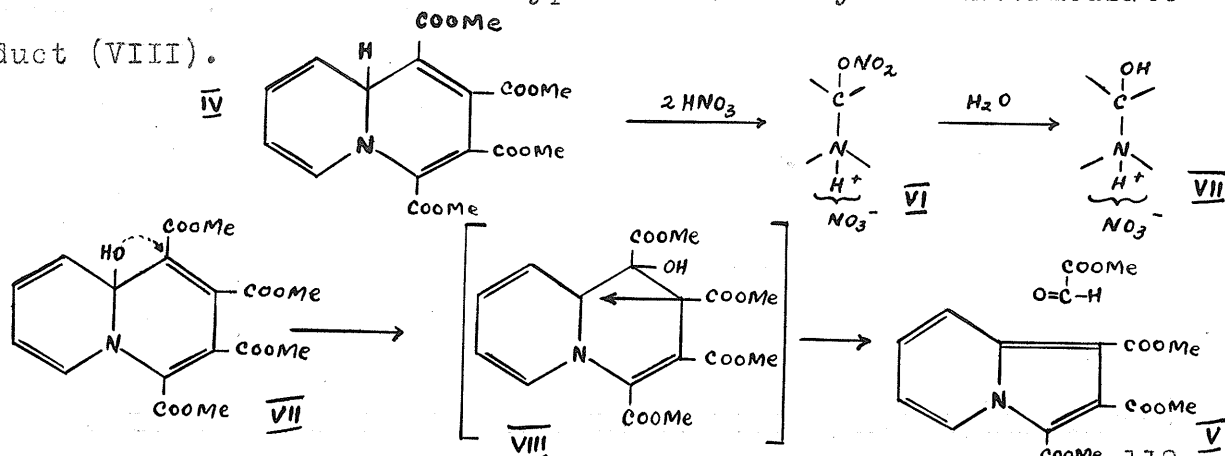
"As in the case of the reaction between N-methyl-pyrrole[119] and acetylenic ester, the process appears as a primary addition with displacement of α -methine-hydrogen and subsequent 1,4-addition of a second ester molecule. Such an interpretation of the process is, however, refuted by the observation that quinaldine, which has no α -methine-hydrogen at its disposal, undergoes the reaction with ease, as do pyridine, quinoline and isoquinoline, with the formation of an adduct to which we must assign formula (IX), on the basis of its properties and reactions.
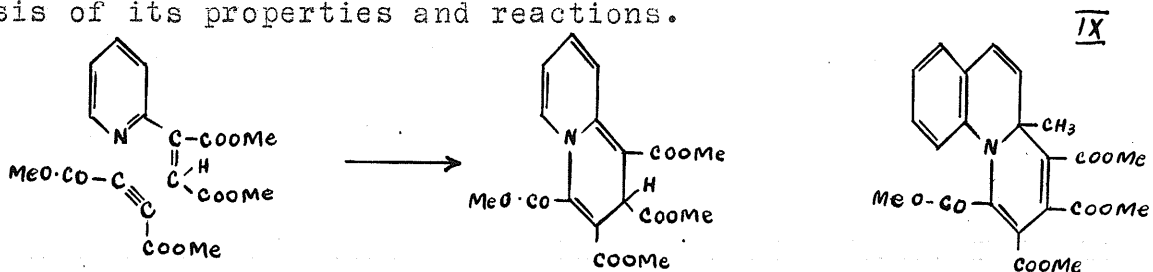
"Under somewhat changed reaction conditions (e.g., if we use acetic acid instead of ether as a solvent), pyridine and acetylenic ester react with the formation of mellitic ester (X). We must assume that this process, which seems to be a variation proceeding at lower temperatures of Berthelot's benzene synthesis:
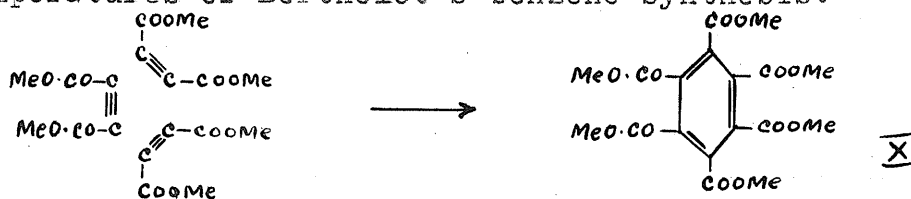
takes place due to the polymerizing action of pyridine. In the same

way it is also necessary to assume that two molecules of acetylenic

ester are first joined to a chain with two free attachment positions:

$$MeO \cdot CO-C \equiv C \quad \quad C \equiv C-COOMe \atop \overset{|}{COOMe} \quad \not\diagup \quad \overset{|}{COOMe} \quad \longrightarrow \quad MeO \cdot CO-\overset{|}{C} = C \underline{\quad\quad} \overset{|}{C} = \overset{|}{C}-COOMe \atop \overset{|}{COOMe \; COOMe}$$
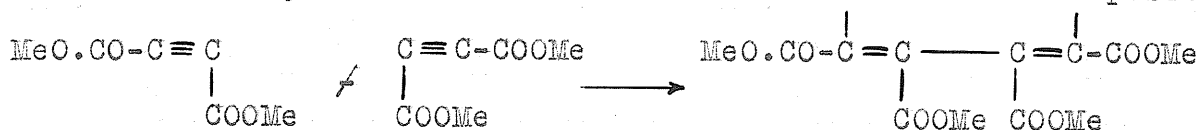
and that this chain then, inasmuch as the conditions for a further

polymerization to mellitic acid are not given, is added on in a

suitable position in the ring system of the heterocyclic compound

named. Such a position is the double bond in the group -C≡N-. This

interpretation of the reaction process is positively explained by

the fact that under all conditions two acetylene molecules are

added. For the other bases, quinoline, isoquinoline and quinaldine,

the structures of their adducts with acetylenic ester are seen by

the strict evidence: they have the same composition, result under

the same conditions and, in reference to color, fluorescence and

other properties, correspond completely to the pyridine adduct (IV),

so that we must then assume that with them, too, the diene syn-

thesis proceeds by taking up an acetylenic ester chain to the -N≡CH-

and -N≡C(CH₃)- groups, respectively."

There is also formed a substance (XII) of composition

$C_{16}H_{13}O_8N$, similar in many respects to (IV) and known as

"Kashimoto's substance" after its discoverer, one of Diels'

students[120]. It differs from (IV) ($C_{17}H_{17}O_8N$) by a lack of CH_4; it

contains all eight O-atoms, but only three methoxy- and no free

carboxyl-groups. It is much stabler with acids than is (IV) and is

only partially saponified on boiling with HCl.

Its formation as a by-product in the reaction of pyridine

on acetylenic ester is important in a study of the complete course

of this type of diene synthesis. The reaction involves the elim-

ination of a methine-hydrogen atom with formation of a double bond

between the nitrogen and the tertiary carbon, and simultaneous

conversion of the trivalent nitrogen into an ammonium ion----in

other words, a dehydrogenation of the yellow substance (IV). It

results from the primary product (VI) by the action of nitric acid

on the yellow substance, passing though the intermediary salt (XI)

into (XII). The Kashimoto body is therefore an inner pyridinium salt.
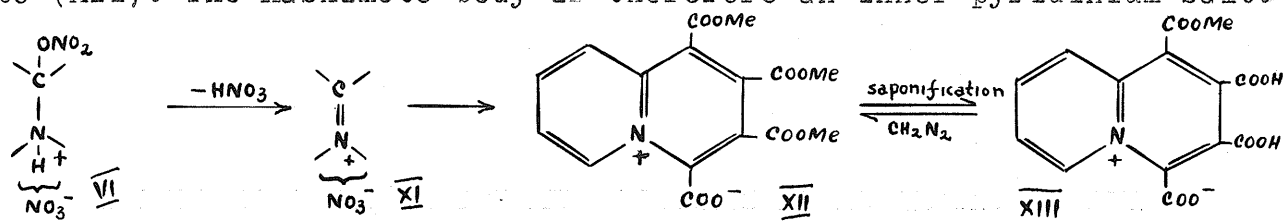
Only two methoxy-groups are hydrolysed, as shown, to give

(XIII). By means of diazomethane, this can be reconverted to the

original Kashimoto substance.

Together with the yellow adduct (IV), there resulted in

considerable amount a red isomer which could be converted into the

yellow under special treatment, such as heating over the melting

point, recrystallization from certain solvents, etc. The reverse

change has not been observed. Diels and Alder[119] suggest that this

red isomer is a "pre-product" of the yellow adduct. This nomen-

clature serves only for the pyridine series and then only for the

solid condition, while for solutions of the pyridine isomers the

reverse serves[121]. Similarly for the isomer pairs in the quinolines

and quinaldines. A more appropriate nomenclature was therfore

proposed, the primary products being termed "labile" so as to

differentiate them from their isomerization products, which are

referred to as "stable."

By employing absolutely acid-free acetylenic ester, conditions

can be so controlled that only the labile red isomer results. The

earlier observed formation of the yellow substance was doubtless a

secondary reaction of the red pre-product.

The isomers may be differentiated in the solid condition by color, the labile form appearing darker than the stable. Measurements of the absorption spectra in methanolic solution showed that the labile isomer absorbed shorter waves than did the yellow form. While the absorption curves of the stable isomer, in the measureable range, shows four maxima, that of the labile product possesses but two. This characteristic curve is found also in the isomer pairs of the quinoline- and quinaldine-series.

The labile-stable isomer relationships were shown to be related to the function of the N-atom. The stable yellow substance acts as a weak, mono-acid base. On warming the hydrochloride, all the methyl-groups are saponified, accompanied by a splitting off of three moles of CO_2 to give the hydrochloride salt of an acid of formula $C_{10}H_9O_2N.HCl$. Oxidation of the latter with permanganate results in the production of α-picolinic acid. With the labile red isomer, however, salt formation has not been observed nor is an -substituted pyridine derivative (such as α-picolinic acid) obtained.

Alkali acts on the stable yellow isomer so as to break its structure down, with production of α-picoline. On the other hand, no α-picoline is obtained with the labile red isomer. Instead, pyridine results, together with aconitic and oxalic acids as further breakdown products.

It is therefore clear that both acetylenic ester molecules in the labile primary form are unquestionably attached to the nitrogen and that, by the conversion to the stable isomer, a return of a C-atom in the α-position to the nitrogen takes place. The reaction scheme is as follows:
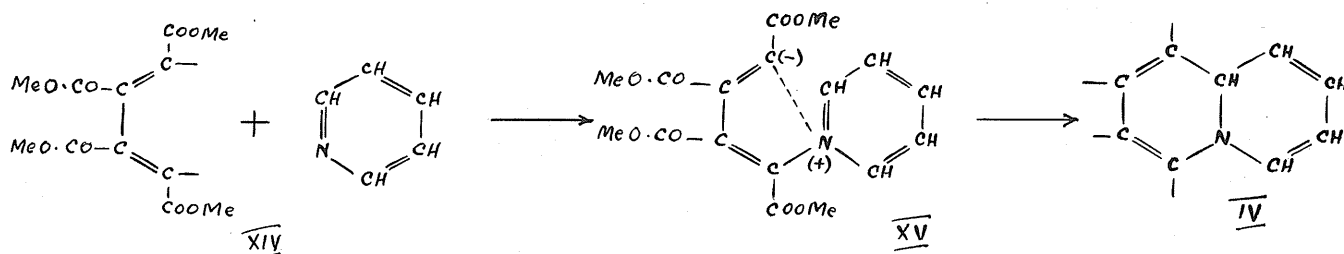
Briefly, the unstable red isomer (XV) results by the attachment of the chain (XIV) to the N-atom in the -CH≡N- bond of the pyridine molecule, followed by the isomerization reaction in the course of which the second attachment position of the chain is fixed to the carbon atom in the -CH≡N- double bond, so as to give (IV), the stable yellow isomer. Structure (XV) is assigned to the labile red isomer, inferring that this compound is an organically-substituted ammonium compound with an ionogenically attached substituent.

Further substantial proof for the structural formulae assigned the stable and labile isomers is offered by the action of diazomethane. While this reagent does not react in benzene solution with the stable adduct, under the same conditions one mole is taken up by the labile isomer. Two isomeric products result, to which formulae (XVIa) and (XVIb) have been assigned. Their structure has been determined by splitting of both to pyrazole-1,2-dicarboxylic acid (XVII), with reformation of unsubstituted pyridine:
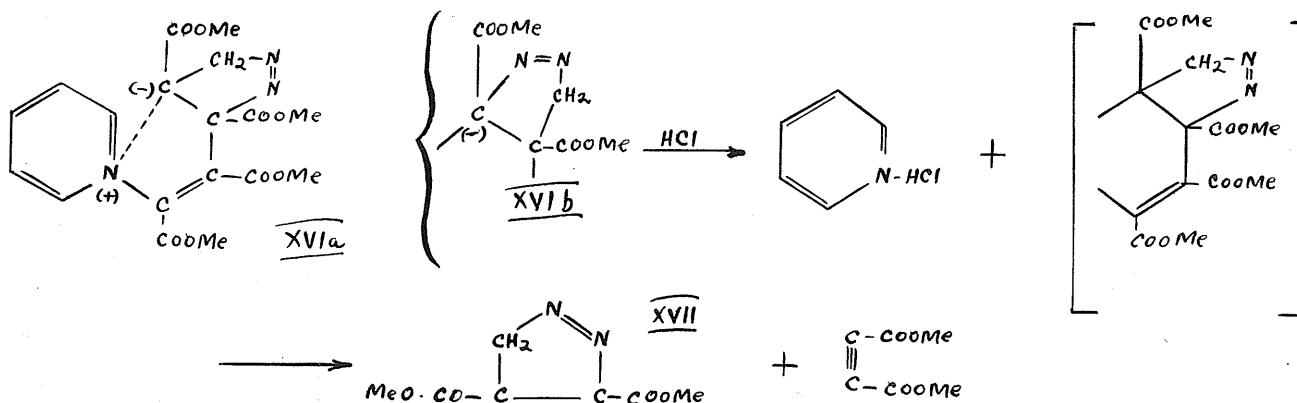
The Kashimoto substance (XII) resulted, as described above, as

a by-product in the reaction of acetylenic ester on pyridine by elimination of the hydrogen atom at the tertiary carbon. It was found that boiling with mercuric acetate in acetic acid for a long time would convert the stable yellow adduct (IV) into the Kashimoto body. If the same oxidizing agent were allowed to act on the labile red isomer, the reaction would take place freely with liberation of heat. This can best be explained by accepting a different mobility of the hydrogen in the labile and in the stable isomer.
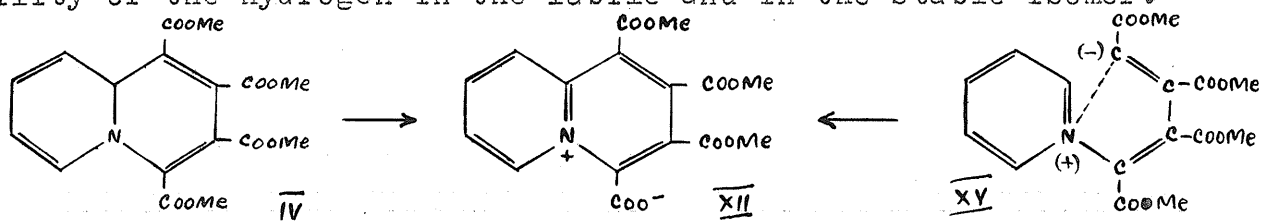
Whereas pyridine reacts with acetylenic ester in ethereal or benzene solution to form the stable yellow adduct (IV), the labile red adduct (XV) and the Kashimoto substance (XII), and in glacial acetic acid to yield mellitic ester, in methanolic solution another reaction process has been observed[122]. A colorless compound, the "white adduct", results, whose composition differs from that of the red or the yellow isomers by a lack of CO, hence being a tetracarboxylic derivative resulting by the addition of one mole of pyridine to two of acetylenic ester.

Diels and Meyer have concluded that its formula is that given by (XVIII).
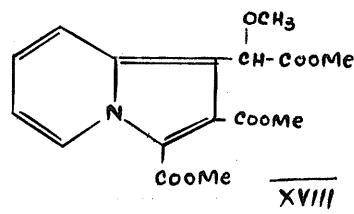
According to Diels and his associates, in the formation of substances (IV), (XII) and (XV), the first action of pyridine on the acetylenic ester molecule is to form a chain of two ester molecules with two free bonds. In ethereal solution, this chain is attached to the N-atom of the pyridine nucleus, whereby the labile isomer results, and this, by stabilization, is converted to the stable.

In methanolic solution, however, an addition of two moles of
methanol to the unsaturated ester chain takes place, giving:

$$\begin{array}{cccc} \text{COOMe} & \text{COOMe} & \text{COOMe} & \text{COOMe} \\ | & | & | & | \\ CH_3O-C —— & CH —— & CH —— & C-OCH_3 \\ | & & & | \end{array} \longrightarrow 2 \quad \begin{array}{c} CH_3O-C-COOCH_3 \\ || \\ MeO.CO-CH \end{array}$$
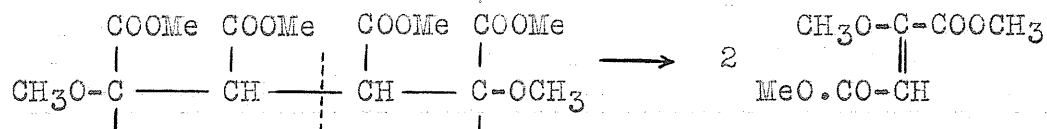
The adduct may break up into two molecules of methoxy-fumaric

ester. This has been isolated in considerable quantity in the

mother liquor. Again, the possibility of only one mole of methanol

adding to the unsaturated chain is offered:

$$\begin{array}{cccc} \text{COOMe} & \text{COOMe} & \text{COOMe} & \text{COOMe} \\ | & | & | & | \\ CH_3O-C —— & CH —— & C === & C \\ | & & & | \end{array}$$
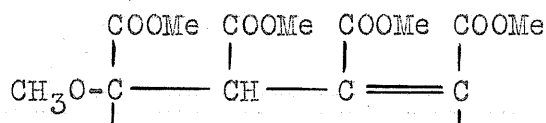
This chain was considered by Diels and Meyer to add to the

N-atom of the pyridine nucleus in the same manner as in the form-

ation of the red isomer, the result being an intermediate product

of structure (XIX). Such a system tends to undergo a stabilization

by formation of a five- or six-atom ring. A displacement of hydrogen

from the starred position in the attachment chain takes place to

yield (XX), and this may stabilize further by elimination of

$CH_3OCH_2-COOCH_3$ to produce indolizine-tricarboxylic ester (V) or

by the elimination of $HCOOCH_3$ with formation of (XVIII), the

"white adduct."
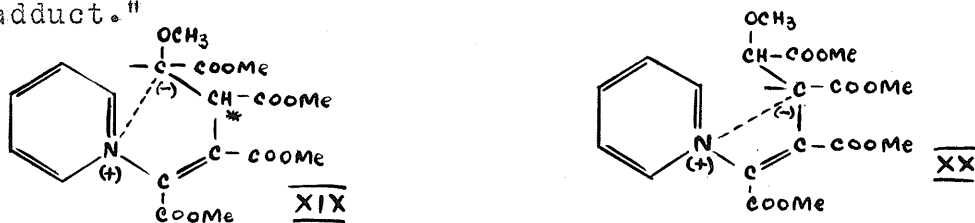
In the quinoline

series[121], two moles of

acetylenic ester were

observed to produce (XXI)

with one mole of quinoline.
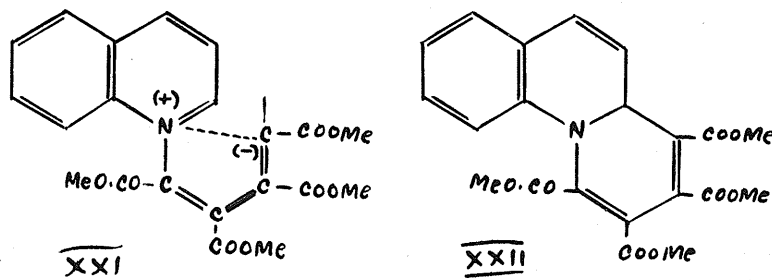
This was found to be the labile isomer since, by heating over the melting point, it could be converted to the stable form (XXII). The two were further differentiated by their absorption spectra, by the addition of the labile adduct in benzene solution to one mole of diazomethane and by alkaline and acid breakdowns which were in complete analogy with the results found in the pyridine series.

(b) Experiments with Quinaldine.

A slight variation from the observations noted above is seen in the case of the quinaldine-adduct. The absorption spectrum of the labile isomer shows a parallel with the labile pyridine type although the curve of the stable form exhibits a deviation. The labile adduct, further, shows similarities with the corresponding form in the pyridine and quinoline series by its action on acids, alkalies and diazomethane. On the other hand, important differences are noted in the case of the stable isomer. Both compounds are formed in approximately equal proportions yet, once formed, cannot be converted into each other, no matter how drastic the conditions. This was first explained by the absence of an H-atom in the α-position to the nitrogen, which results in an important stabilization[121].

The discovery in the quinaldine series of two colored adducts, together with the evidence that one of these possesses the characteristics of the labile type, would suggest that formula (I) be assigned to the labile isomer and (II) to the stable. However, the fact that the labile cannot be converted into the stable form under any conditions led to the conjecture[123] that the resulting stable product does not correspond to the expected formula (II).

Instead, Diels and Kech have advanced the suggestion that the unsaturated chain resulting from two acetylenic ester molecules is attached to three positions in the quinaldine ring, to give (III). This was verified by oxidation experiments.
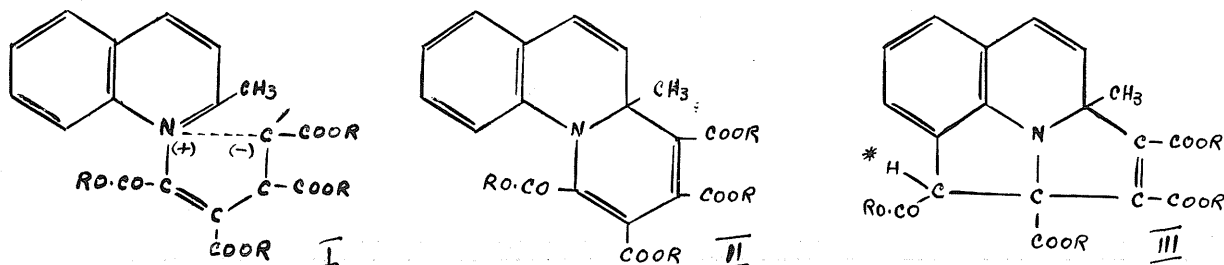
This discovery of a triple attachment of the two additive acetylenic ester molecules is important in determining the formation of a third reaction product which appears in considerable yield on treating quinaldine with acetylenic ester in methanolic solution. In contrast with the labile and stable adducts, both of which are intensely colored, this compound is colorless.

The reaction proceeds as follows: Quinaldine reacts in the tautomeric form (IV) with one mole of acetylenic ester to give the intermediate (V) (not yet isolated), together with one mole of methanol:
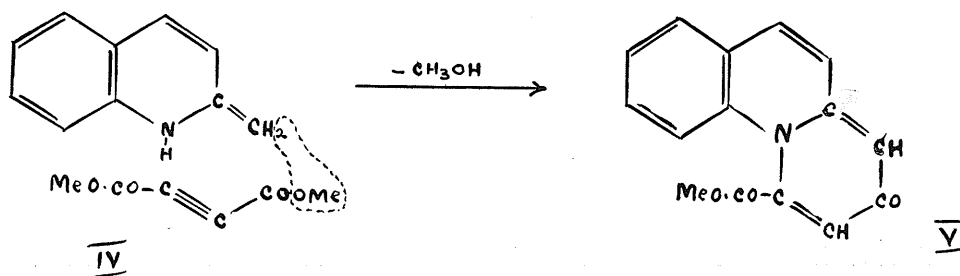
By displacement of the hydrogen atom in the peri-position to the nitrogen, a further acetylenic ester molecule is added on, this time to the benzene nucleus. This intermediate product (VI), however, does not seem to result as such. By further displacement of the starred hydrogen atom, a four-atom ring is closed up instead, yielding the "colorless quinaldine adduct" (VII).

$\overline{VI}$ $\overline{VII}$
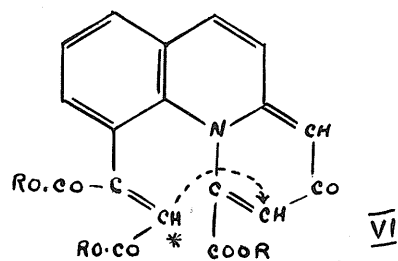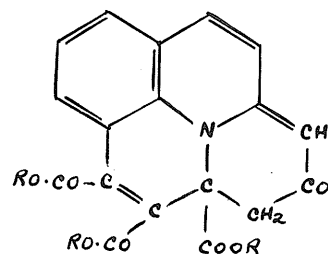
(C) Experiments with α -Picoline.

α -Picoline is analogous to quinaldine in that it is an
α -methylated pyridine derivative, and hence it would be expected
that a similar behavior with acetylenic ester might result. This
has been borne out in only one respect: namely, that the free end
of the unsaturated chain of the labile addition product (I) is pre-
vented from attaching itself at the C-atom of the pyridine nucleus
at which the methyl-group is attached[124]. Rather, the attachment
takes place in the α' -position, resulting in structure (II) for
the stable isomer. This stabilization is made possible since there
is (contrary to quinaldine) an H-atom in the α' -position.

I II
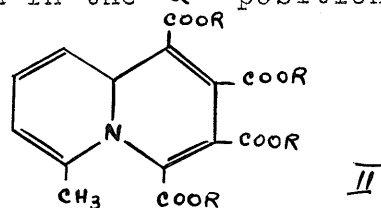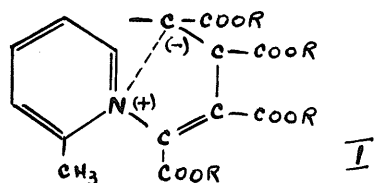
A second adduct (IV), possessing a bichromate-red color, was
isolated in approximately the same yield as (I). Its formation can
be explained in the sense of scheme (III) which hypothesizes a
displacement of one H-atom from the methyl-group to the ester
chain. Adduct (IV) betrays an extraordinary tendency to split off
one mole of methanol with formation of the colorless substance (V).
This is formed by ring closure between the CH_2- and the outer
ester-group and contains three methoxy-groups in addition to dis-
playing phenolic properties.
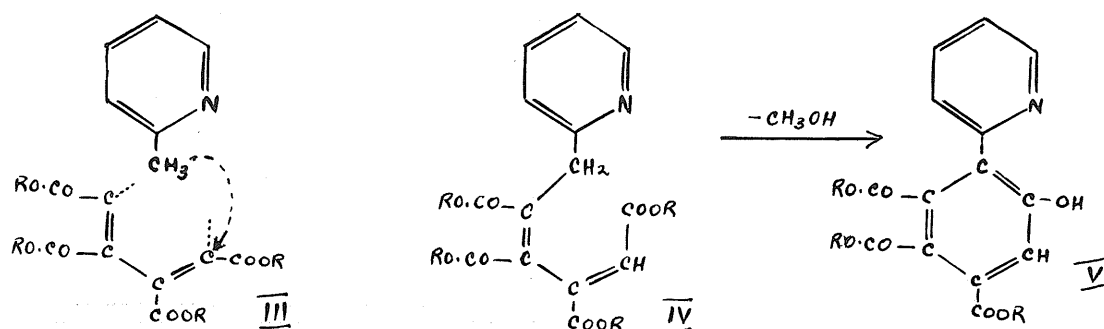
(d) Experiments with Stilbazole.

Stilbazole (I) is a pyridine molecule with
an α -methyl group in which two H-atoms have
been substituted by a "rigid benzal residue."
It will react smoothly[125] with two moles of acetylenic ester to
give products comparable to the stable and labile adducts obtained
in the case of pyridine and quinoline. The labile isomer (II) is
formed by the addition of the ester chain at the N-atom. On boil-
ing with xylene or with phenol it is converted into the "first
stable adduct" (III). A new experience has been reported by Diels
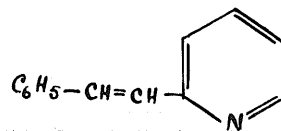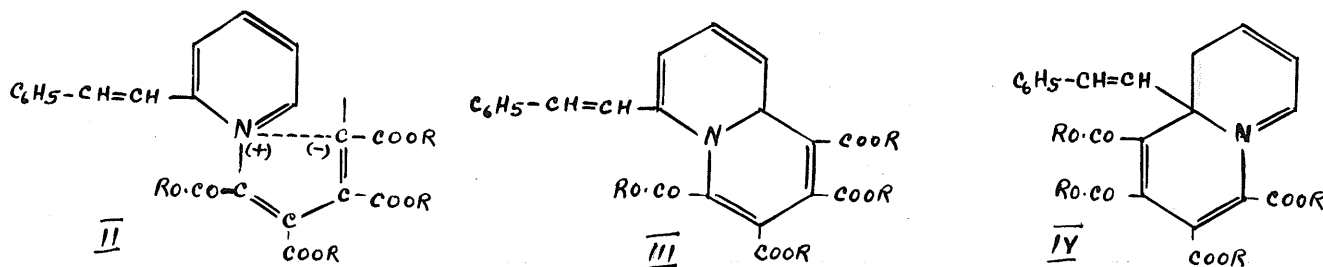
and Moller in that the labile adduct can be changed by boiling
glacial acetic acid into a "second stable isomer" (IV) which also
results from the "first stable isomer" by continued heating with
xylene or by heating for a considerable time over the melting point.
The isomerization relationships are expressed in the table on the
next page. Conversions in the reverse direction, however, have not
been observed.

boiling acetic acid

"labile adduct" ⟶ boiling in xylene ⟶ "second stable
(II)   or melting   isomer" (IV)

boiling phenol   boiling in xylene
                                or fusion

"first stable adduct" (III)
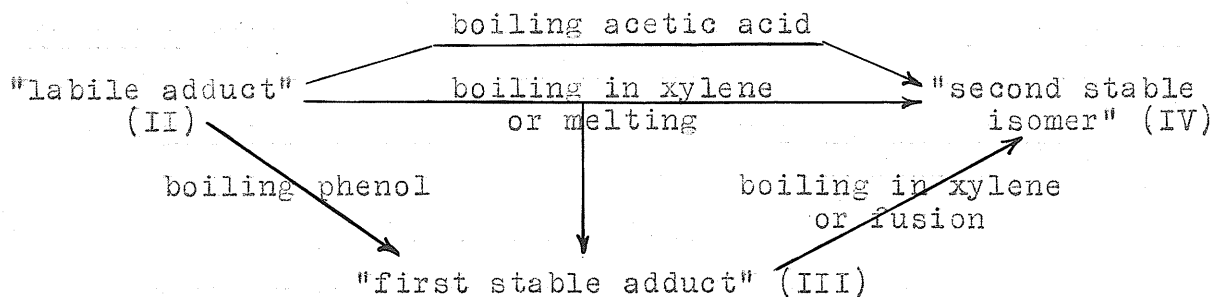
As formulated above, the peculiarity of stilbazole as an
α-substituted pyridine derivative allows two possibilities for
the addition of the acetylenic ester chain to the $>C=N-$ double
bond: the first leads to the "first stable adduct" (III); the
second to the "second stable adduct" (IV) which may be obtained
from (III) by liberation of one end of the acetylenic ester chain
from the α-position and reattachment in the α'-position.

This is, therefore, the first case in which three isomeric
adducts resulted in the addition of acetylenic ester to a compound
of the pyridine type.

(e) Experiments with Isoquinoline.

A somewhat different type of experience has been reported as
the result of investigations carried out with isoquinoline and
acetylenic ester. Instead of obtaining one labile adduct, as was
the case until now, Diels and Harms[126] isolated two "labile isomers"
occurring together although in different proportions, as the
primary reaction products between the components named.
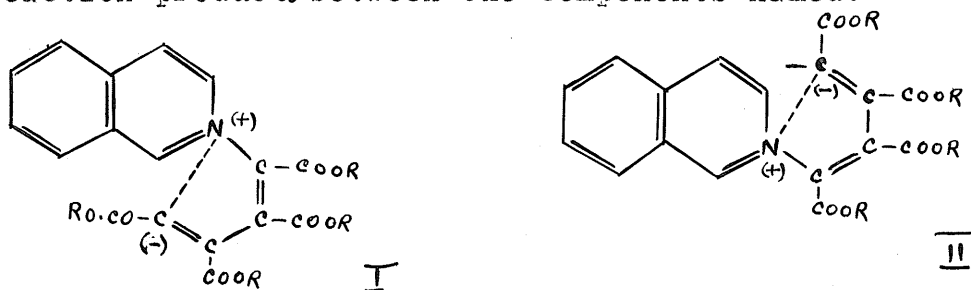
The "first labile adduct" has been assigned formula (I),

while the "second labile adduct" possesses structure (II). The former is identified by its solubility relationships and by its behavior in the light of a quartz lamp as an homologue of the labile pyridine-, quinoline- and stilbazole-adducts and resembles, in its stabilization ability, the stilbazole product.

The action of diazomethane on the "first labile adduct" shows its association to the "labile" series since it may react with this reagent quite readily whereas the stable adduct is not attacked at all. Two isomeric mono-diazomethane-compounds,(III) and (IV), may result, one of which and only one being able to add a second mole of diazomethane with formation of the bis-compound (V). The importance of these reactions is two-fold: firstly, it is demonstrated that both double bonds in the ester chain are not of equal value, and secondly, by the action of HCl on (V), one mole of isoquinoline and two of pyrazole-dicarboxylic acid result.
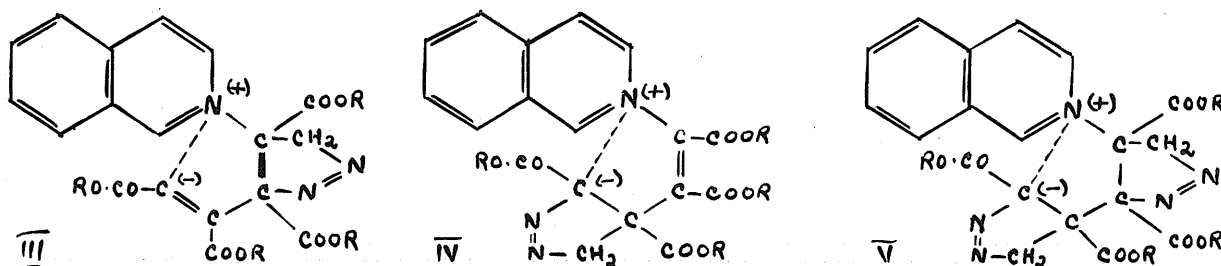
The first labile adduct stabilizes smoothly on heating in xylene, with formation of two stable products. Of these, one (VI)
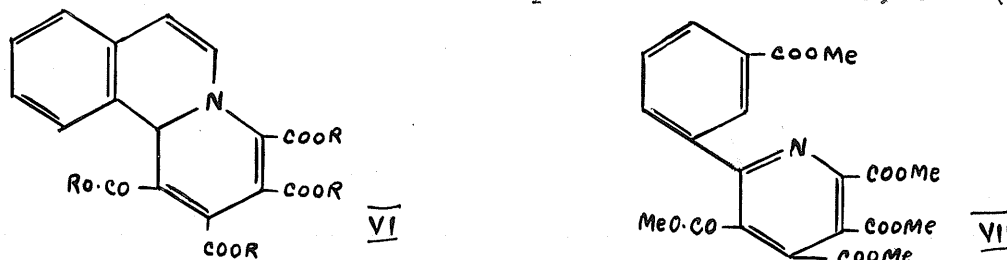
preponderates and shows the reactions characteristic of the stable pyridine adduct. The second stabilization product resulting from the first labile adduct is regarded as a breakdown product possess-

ing structure (VII), as proved by its breakdown to α -phenyl-pyridine. This pentacarboxylic ester was also obtained by the action of bromine or of peroxide on (I).

In contrast to the"first labile adduct," the "second labile adduct" (II) (which results in small quantity only) is quite un-stable and tends to decompose into its components. A different behavior has been noticed on stabilization in that this is not effected by the action of acids. The stabilization of the "first labile isomer" into the "first stable adduct", which took place in nearly quantitative yield by boiling the adduct in xylene, results, in this case, in only a small yield due to a splitting into the original components. The "first labile adduct" is then synthesized from these components and this is finally stabilized to the "first stable isomer."

(f) Reactions of Hydrazo Compounds.

Hydrazo compounds are also able to react with acetylene-dicarboxylic ester with formation of adducts resulting by hydrogen displacement[128]. By the action of acetylenic ester on hydrazo-benzene there is formed a substance whose composition is best ex-pressed by formula (I). The elements of water are added on, as shown in (II). Pyrazolone formation takes place by expulsion of water together with simultaneous splitting off of methanol. The pyrazolone produced is (III).

$$C_6H_5-\overset{(+)}{N}H-C-COOMe$$
$$C_6H_5-NH-\overset{(-)}{C}-COOMe \quad \text{I}$$

$$C_6H_5-N\overset{H}{\underset{OH}{|}}-C-COOMe$$
$$C_6H_5-NH\overset{|}{\underset{MeO\,CO}{|}}\quad \text{II}$$

$$C_6H_5-N\overset{C}{\underset{CH}{\diagdown}}\overset{COOMe}{}$$
$$C_6H_5-N-CO \quad \text{III}$$
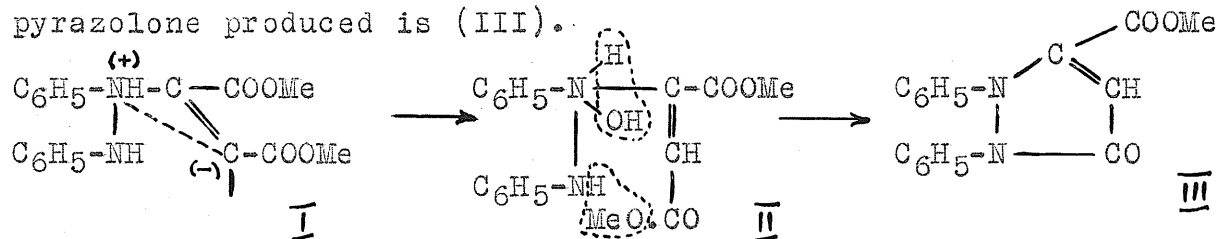
(I), however, may be stabilized in a different way to give

indole-$\alpha\beta$-dicarboxylic ester (V): the unsaturated acetylenic ester chain is attached to a benzene nucleus in an α-position in (IV), whereby, with the accompanying removal of aniline, the above-named indole-derivative is formed.
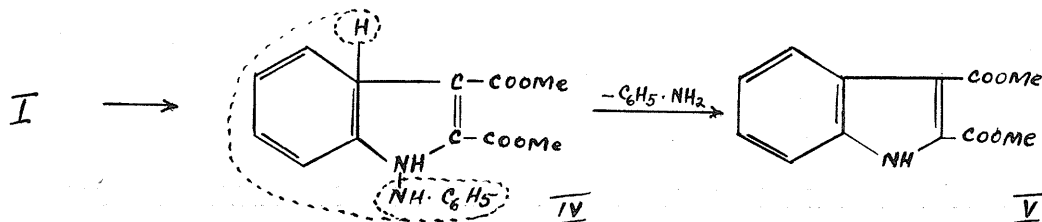
By heating over the melting point or by boiling for a short time with pyridine or with dimethyl-aniline, (I) can be stabilized to give 2-oxy-3-anilido-quinoline-4-carboxylic methyl ester (VIII). The formation of this quinoline derivative can be explained by the fact that the acetylenic ester chain may also become attached to another benzene nucleus, in the α-position! The hypothetical intermediate product (VI) is then formed by splitting off of methanol between the -NH and -COOMe groups, by the breaking off of the -N-N- linkage and attachment of the hydrogen to the nitrogen atom to give the keto-form (VII) of the quinoline derivative (VIII).

The above would suggest that we have, therefore, a method for preparing pyrazolones, indolenes and quinolines from hydrazo-benzene and its derivatives. The smooth formation of such adducts was, in fact, shown to be a general property[129], at least insofar as N,N'-dibenzyl-hydrazine, symmetrical and unsymmetrical phenyl-benzyl-hydrazine, tribenzyl-hydrazine and N-phenyl-N,N'-dibenzyl-hydrazine are concerned.

Thus, unsymmetrical phenyl-benzyl-hydrazine will react with acetylenic ester in methanolic solution to give the labile product (IX), which then splits off a molecule of ammonia with great energy,

forming N-benzyl-indole-dicarboxylic ester (X).
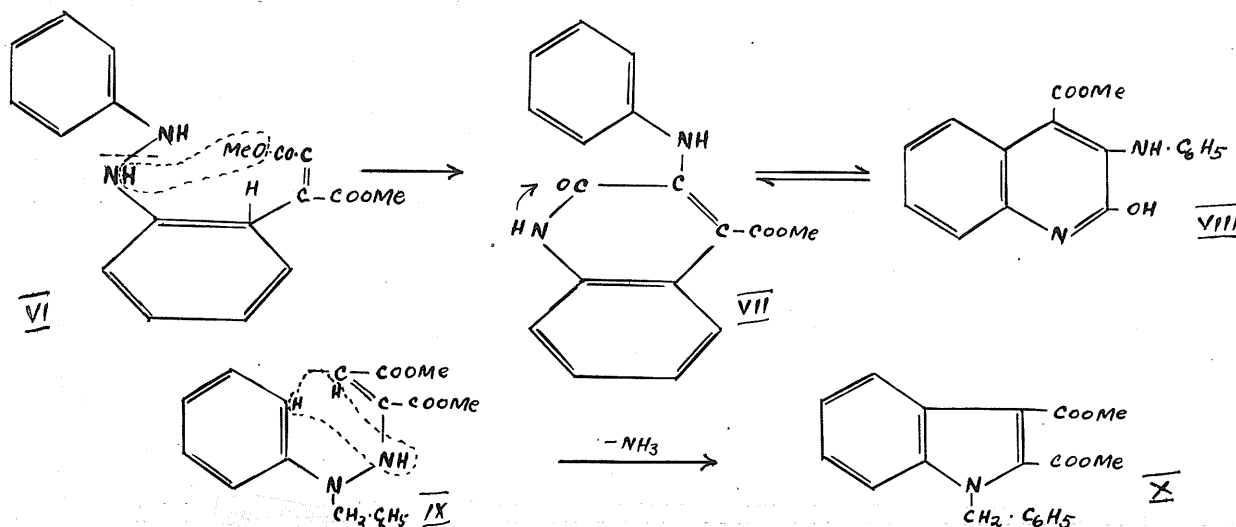
With N-phenyl-N,N'-dibenzyl-hydrazine, two isomeric adducts,
differing in melting point, solubility and color (one being yellow,
the other colorless), have been obtained. By the action of a very
small hydrogen-ion concentration, the yellow substance is converted
to the colorless. The yellow labile form must therefore be repres-
ented by (XI) and the colorless stable isomer by (XII).
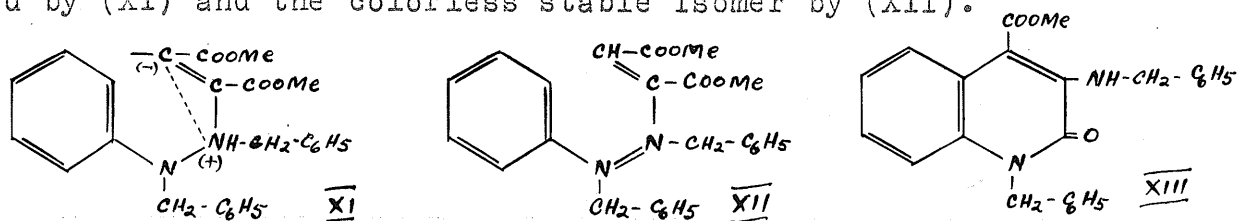
On boiling with xylene both isomers go over into (X), but
in boiling pyridine the quinoline derivative (XIII) results instead.

The explanation is this: The yellow labile isomer (XI) is
first converted to the colorless stable form (XII). By further
hydrogen displacement the diamine (XIVa) is formed, although it
has not been isolated as yet. The basis for accepting the form-

ation of the diamine as an intermediate stage is on the grounds of
its stabilization to the indole derivative (X) and to the quinoline
derivative (XIII). The first of these conversions is understandable
on the assumption that the diamine reacts in the cis-form (XIVa),
the stabilization to the indole derivative resulting on the elim-
ination of benzylamine. The formation of the quinoline derivative,
on the other hand, requires the assumption that the diamine reacts
in the trans-form (XIVb) which, by splitting off of methanol, gives
rise to a ring closure with production of (XIII).
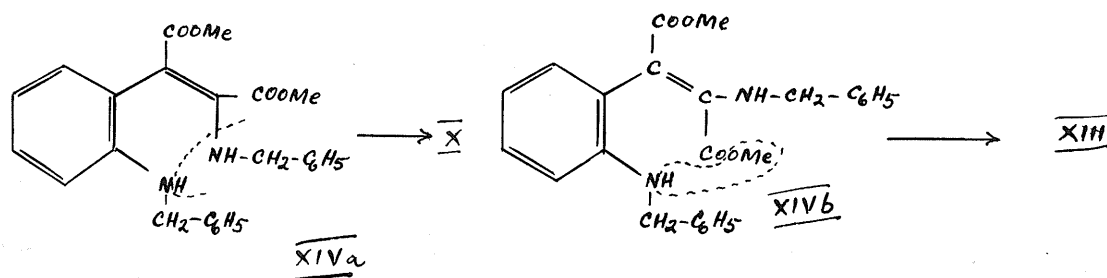
DISCUSSION.

DISCUSSION.

As has been pointed out previously (p. 2), the purpose of this investigation was to attempt a "diene synthesis" by the use of acyclic nitrogenous compounds, according to the following schemes:

1. 1,4-addition of a conjugated diene to a nitrogen-containing philodiene component:
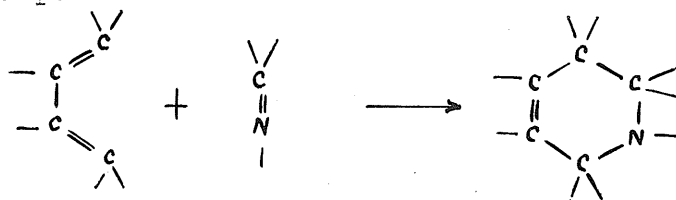
2. 1,4-addition of an anil conjugated with an olefinic linkage to a non-nitrogenous philodiene component:
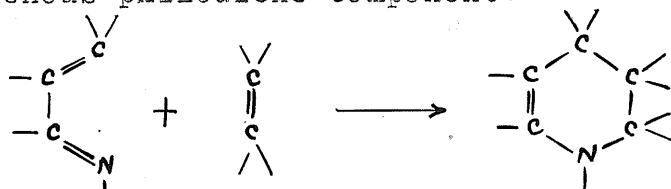
A discussion of the results obtained follows.

From the position of the nitrogen atom, that is, whether located in the philodiene or in the unsaturated anil, it has been deemed advisable to divide this section into two parts.

A. THE NITROGEN ATOM IN THE PHILODIENE COMPONENT.

The materials used were paired as follows: cinnamal acetophenone and benzal aniline; anthracene and benzal aniline; cinnamal acetophenone and phenyl isocyanate; anthracene and benzonitrile; cinnamal acetophenone and benzonitrile; and cinnamal acetophenone and cinnamal aniline.

1. CINNAMAL ACETOPHENONE AND BENZAL ANILINE.

Using cinnamal acetophenone as the diene reagent, a series
of attempts were made to effect a reaction with benzal aniline. The
conditions to which these substances were subjected varied consider-
ably, from mere mixing in solvents such as ether, benzene and glacial
acetic acid, and fusion, to the use of activating agents such as
concentrated sulfuric acid and anhydrous aluminium chloride.

Refluxing equimolecular quantities of cinnamal acetophenone
and benzal aniline for two hours in ether and for two and six hours,
respectively, in benzene, apparently did not present sufficiently
severe conditions for a reaction, both components being recovered
unchanged.

By warming on the water bath at 100°C for one hour in glacial
acetic acid, a slight greenish-red fluorescence was noted. Extract-
ion of the acid solution, after dilution with water, resulted only
in the recovery of some cinnamal acetophenone. After the addition
of sufficient NaOH to make the acid residue alkaline, an ethereal
extraction was carried out, a slight amount of a reddish viscous
mass being obtained. This could not be recrystallized or otherwise
identified. Refluxing in glacial acetic acid for three hours over
an open flame (118°C) gave a more marked fluorescence and a slightly
larger yield of the reddish material.

No reaction was noted by fusing cinnamal acetophenone with
benzal aniline at 100°C for two hours, although the reaction mixture
developed a reddish color. Fusion at 150°C for three hours on the
oil bath, however, resulted in the entire mass becoming quite
viscous and gummy and possessing a red color. Fractional crystall-
ization from ether resulted in the recovery of nearly all the cinn-

amal acetophenone originally used. While no condensation could be observed, the intensity of the coloring was greater than in the fusion mixture obtained by heating the reagents at 100°C, a fact which would suggest that a slight decomposition of one of the initial materials had taken place or that a slight amount of colored product had been formed.

By forcing the reaction by fusion on the oil bath at 180° for ten hours, a red viscous mass was obtained. This was soluble in the common organic solvents, although it could not be re-crystallized from them. The mixture was dissolved in dry ether and dry HCl gas was passed in, resulting in the formation of a buff-colored, flocculent precipitate, amounting to less than 0.1 gms., and melting at 183°.

The experiment was repeated in the hope of obtaining a larger quantity of this substance, the fusion mixture being kept at 180-200° for fifteen hours. After cooling, the red gummy mass resulting was dissolved in dry ether and filtered, yielding a few small whitish crystals, amounting to a few milligrams and melting over 300°, with decomposition. The filtrate was treated as before with dry HCl, giving a reddish brown precipitate, melting at 160°. This was identified as aniline hydrochloride (m.pt. 198°) by the formation of an azo- β -naphthol derivative of m.pt. 130-131°.

A further attempt was made to increase the yield of the substance melting over 300° by carrying out the fusion at 180° for thirty hours. The yield was negligible, as before. Aniline hydro-chloride was again obtained. The high-melting substance was insol-uble in benzene, ether and chloroform, but could be dissolved in acetone. The yield could not be increased by fusion at 180° over

fifteen hours, nor at 220° for twenty hours. Due to the small

yield and to the time factor involved, it seemed inadvisable to

pursue this reaction further, although the possibility remains that

it may be the diene synthesis sought. The small yield may be due to

the fact that the reaction sets in only at temperatures over 150°,

accompanied, however, by a secondary reaction resulting in the

decomposition of most of the reaction product. The substance

melting at 183°, reported above, may be the 300° compound in an

impure condition. Carrying out the reaction under strictly an-

hydrous conditions (a drying-tube at the free end of the air

condenser, sodium-dried ether, and vacuum-dried materials) gave

the high-melting substance as before, although aniline hydrochlor-

ide was no longer formed. The latter results by the action of HCl

on unchanged benzal aniline or on free aniline present in the

reaction mixture.

Activation of a mixture of equimolecular portions of cinn-

amal acetophenone and benzal aniline with concentrated sulfuric

acid, in the cold, was next carried out. Ether extraction of the

acid solution, after dilution with water, resulted in the recovery

of some cinnamal acetophenone, while extraction of the residue,

after making it alkaline, gave a slight amount of a reddish viscous

mass. Heating the reaction mixture for a few minutes in one case and

for half an hour at 100° in the other gave no indication of a

reaction.

An attempt to activate cinnamal acetophenone and benzal aniline

by the use of anhydrous AlCl₃, by refluxing on the water bath in dry

benzene for an hour, was unsuccessful. It was, however, noted that

mere mixing of the cinnamal acetophenone with AlCl₃ produced a red

halochromism. By carrying the reaction out as before, save for an

increase in the time of reaction to three hours, the color changed
to a dark-greenish-black. Extraction with benzene led to an emerald-
green benzene layer, changing slowly to orange-red on standing,
especially in the presence of anhydrous Na_2CO_3 or on warming. On
allowing the solution to evaporate down to dryness, a reddish
viscous mass resulted. This was dissolved in dry ether, with the
exception of a greenish flocculent precipitate which, on filtering
and drying, turned black and tarry. The same flocculent mass could
be precipitated from the ethereal solution by means of ligroin or
of petrol ether.

The ethereal filtrate was divided into two portions. One was
allowed to evaporate to dryness and an attempt made to dissolve it in
alcohol. Only a slight amount did so, the fraction remaining being
of a tarry character, insoluble in benzene and ether and but slightly
in chloroform. The alcohol-soluble fraction must therefore have a
solvent effect on the latter, since a mixture of the two dissolves
readily in the solvents named. The action of dry HCl gas on a sol-
ution of the insoluble fraction in chloroform gave no precipitate,
whereas the gummy mass was precipitated from an ethereal solution
of the alcohol-soluble fraction.

Dry HCl gas was carefully bubbled through the second portion
of the ethereal solution, causing a flocculent material, gummy in
consistency and red, tinged with black, in color, to separate. On
filtering and drying, the mass became tarry and black. The black
blobs were dissolved in 95% ethanol. On the addition of a little
water to this, a yellow crystalline solid was precipitated, melting
at 120°. By the use of ammonia instead of water, the yellow material
was again obtained, melting at 122°. A few crystals of the latter
were dissolved in dry ether and re-precipitated as a green powder by

means of dry HCl, melting at 112°. This would suggest that the 122° substance is a free base and that the 112° compound is its hydro-chloride salt.

A suitable solvent for the salt could not be found, from the point of view of re-crystallization, whereas petrol ether was the only one which could be used for the base. A few reddish crystals of m.pt. 92° were obtained from the latter by filtering an hour after dissolving. No more could be obtained, even after six months, the solution being exposed to the air for this time. After the petrol ether had been evaporated off, a reddish oil was left, but this could not be purified by distillation, even in vacuo, as it went gummy.

In no case was it possible to obtain more than a fraction of a gram of the free base and what was obtained could not be purified. It was therefore necessary to postpone further investigation of this reaction.

2. ANTHRACENE AND BENZAL ANILINE.

The conditions to which anthracene and benzal aniline, in equimolecular proportions, were subjected were: (a) refluxing in benzene for six hours; (b) refluxing in xylol for five hours; and (c) fusion on the oil bath at 180-200° for twelve hours. In each case, the entire amount of anthracene used originally was recovered unchanged.

3. CINNAMAL ACETOPHENONE AND PHENYL ISOCYANATE.

Fusion of cinnamal acetophenone and phenyl isocyanate in the ratio of 1:2 at 100° for two hours and for eight hours, respectively, resulted in the recovery of nearly all the diene component.

By heating on the oil bath at 150° for seven hours, carb-

anilide (m.pt. 238o) was obtained and verified by the preparation
of a bromine derivative subliming at 291°. Considering the possib-
ility that moisture in the atmosphere or in the reagents might be
responsible for the formation of carbanilide, vacuum-dried cinnamal
acetophenone was used, a drying tube being attached to the free end
of the air condenser attached to the reaction flask. The mixture
was fused for eleven hours at 150° and after cooling, the excess of
phenyl-isocyanate was washed out with sodium-dried ether and set
aside in a beaker in the fume cupboard. After a week, a slight amount
of orange-red gummy material was found, still smelling strongly of
isocyanate. No carbanilide could be detected, however, suggesting
that the moisture in the air could not have been responsible for its
formation, at least at room temperature. The residue remaining in
the reaction flask, after removal of the excess isocyanate, was
dissolved in dry benzene and a considerable amount of carbanilide
was immediately filtered off.

Since carbanilide results by the action of water or of aniline
on phenyl isocyanate, one of these reagents must have been present.
Yet how this could have been the case is not clear since the structure
of cinnamal acetophenone precludes the splitting off of water or of
aniline, while the anhydrous conditions and materials employed
eliminated the possibility of free water being present.

By activating the reaction with anhydrous $AlCl_3$, a slight
amount of cinnamal acetophenone was obtained unchanged, together with
a considerable yield of carbanilide. In this case, the fusion was
carried out at 100° for two and a half hours. The carbanilide may
have resulted by the addition of water in decomposing and dissolving
the $AlCl_3$-complex, prior to re-crystallization of the reaction mixture.

4. ANTHRACENE AND BENZONITRILE.

Attempts to condense anthracene and benzonitrile by refluxing in benzene for four hours, in toluene for the same time, and by fusion at 170° for ten hours, resulted, in each case, in the recovery of the anthracene originally used.

A two-phase reaction in the cold with concentrated sulfuric acid was next attempted. On first adding the acid, the mixture turned brownish in color and then, in the course of a few minutes, frothed up, turning greenish black, with liberation of sulfur dioxide. After standing three days, the mixture was diluted with water and extracted with ether, white platelets of benzamide (m.pt. 128°) were being crystallized out. Their formation was due to a partial hydrolysis of the benzonitrile by the acid. A diene synthesis could not be observed.

5. CINNAMAL ACETOPHENONE AND BENZONITRILE.

Refluxing a mixture of cinnamal acetophenone and benzonitrile in benzene for three hours, in chloroform for five hours, and fusion at 100° for four hours and at 150° for five and a half hours proved to be without result. A two-phase reaction, using concentrated sulfuric acid as an activating agent, resulted in an initial fluorescence, but the only product of the reaction was benzamide (m.pt. 128°), due to partial hydrolysis of the nitrile.

6. CINNAMAL ACETOPHENONE AND CINNAMAL ANILINE.

Four reaction possibilities are presented here in that both reagents may act as "diene" or as "philodiene" components. In the event that the cinnamal acetophenone acts as the "diene", it may react with either the carbon-carbon double bond or with the carbon-

nitrogen double bond of the cinnamal aniline. Should the cinnamal aniline, however, act as the "diene", it may condense with either carbon-carbon double linkage of the cinnamal acetophenone molecule.

Refluxing equimolecular amounts of the two compounds, in ether for two hours, in benzene for four hours, in chloroform for the same time, and fusion at 150° for five hours and for ten hours, respectively, were without result, the original materials being recovered unchanged.

B. THE NITROGEN ATOM IN THE UNSATURATED ANIL.

The materials used were paired as follows: cinnamal aniline and anthraquinone-1,4; cinnamal aniline and cinnamic aldehyde; and cinnamal aniline and quinone. A discussion of the results obtained is presented below.

1. CINNAMAL ANILINE AND ANTHRAQUINONE-1,4.

Benzene, chloroform and xylol were used as the reaction media in a series of experiments involving cinnamal aniline, as the unsaturated anil, and anthraquinone-1,4 as the philodiene component. Equimolecular quantities of these substances were refluxed in benzene for five hours, in chloroform for three and five hours, respectively, and in xylol for six hours. No reaction, however, took place, the original materials being recovered unchanged.

An attempt to fuse cinnamal aniline and anthraquinone was rendered difficult due to the tendency of the latter compound to sublimate to the walls of the vessel containing the mixture. After heating for fifteen hours at 180°, 80% of the anthraquinone was recovered unchanged. The remaining mixture was dissolved in dry ether and treated with dry HCl in the hope of precipitating the

the expected product as the hydrochloride. Only a slight amount of a dark reddish-black amorphous tar was obtained. A diene synthesis could not be detected.

2. CINNAMAL ANILINE AND CINNAMIC ALDEHYDE.

Cinnamal aniline was refluxed with cinnamic aldehyde for two hours in ether and for five hours in benzene without any apparent result. By fusion at 100° for two hours, five hours and ten hours, respectively, the reaction mixture turned dark red in color and a benzene solution of it appeared somewhat viscous, but no condensation could be observed in that nearly all the cinnamal aniline was re-covered. Fusion at 150° for five and ten hours, respectively, gave the same result as at 100°, except that the reaction mixture app-eared darker in color and its benzene solution slightly more viscous.

3. CINNAMAL ANILINE AND QUINONE.

Refluxing an ethereal solution containing equimolecular quantities of cinnamal aniline and quinone for two hours on the water bath resulted in the recovery of both components. Substant-ially the same result was obtained by leaving the mixture for a week and by using benzene instead of ether. It was noticed, how-ever, that the longer the mixture was allowed to stand, the darker its color became. Raising the ethereal or benzene solution to the boiling point for a few hours scarcely changed the original pale orange-yellow color, whereas a week's standing at room temperature in a sealed flask caused considerable darkening. On evaporation of the ether, the color of the reaction mixture became almost black. This color did not disappear on re-solution of the solid mass, due to partial oxidation of the quinone or to some complex or by-product formed.

Equimolecular amounts of cinnamal aniline and quinone were fused for two hours at 100-110°, the mixture turning black. After solidification of the melt, the reaction mass was treated with hot ligroin to remove any unchanged cinnamal aniline or quinone present. The residue was then washed out with hot alcohol and filtered. Brown flakes melting at 150° separated out from the alcohol solution, while the black residue, melting at 253°, which was insoluble in alcohol, was refluxed with chloroform, a slight amount only being dissolved. The residue was a black powder melting at 285°. Part of the chloroform solution was evaporated, black crystals of m.pt. 250° being filtered off. To the remainder of the chloroform, petrol ether was added, effecting the separation of black crystals melting at 245°. The 250° substance was identical with the crystals melting at 245° as shown by a mixed melting point.

Recrystallization of the black substances of m.pts. 253°, 285°, and 250°, respectively, from nitrobenzene gave purplish flakes melting at 327°. Further re-crystallization raised the m.pt. to 337°, while re-crystallization following vacuum sublimation gave a melting point reading of 339°. This agrees closely with the value for 2,5-dianilino-quinone (m.pt. 338-342°).

That these substances were 2,5-dianilino-quinone in varying stages of purity was verified by the following tests: carbon and hydrogen determinations; Kjeldahl evaluation of nitrogen; molecular weight by the method of Rast; color reaction with conc. sulfuric acid, and precipitation from the acid by dilution with water; alkaline hydrolysis to 2,5-dioxy-quinone (m.pt. 215-220°); conversion to azophenin (m.pt. 233° found, 236-237° actually).

The formation of 2,5-dianilino-quinone is explained by the

hydrolysis of cinnamal aniline to give cinnamic aldehyde and aniline.
The presence of cinnamic aldehyde in the ligroin solution mentioned
on the previous page was verified by a positive reaction with
Fehling's solution and by the preparation of a semicarbazone (m.pt.
215°). The aniline reacted with the quinone as follows[130]:
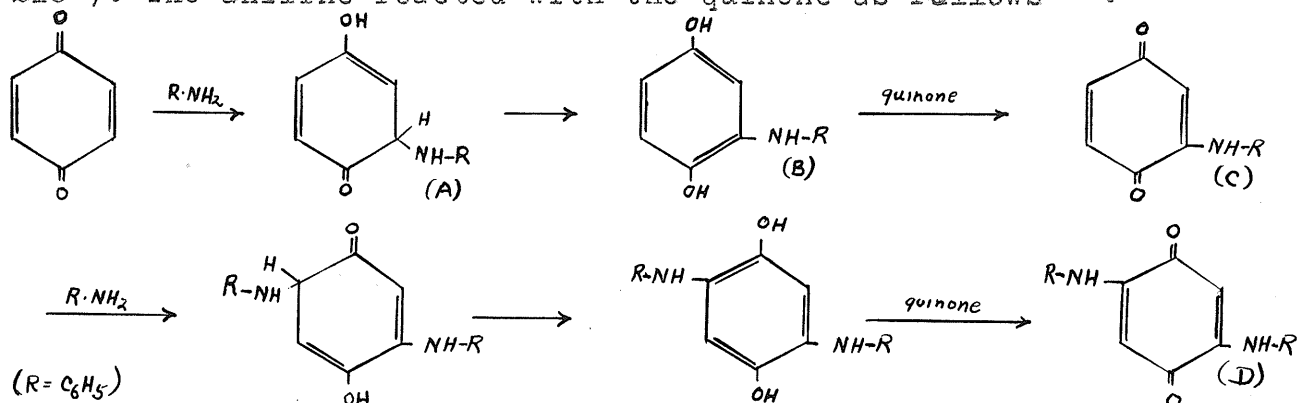
"The reaction is accounted for by assuming that 1,4-addition
first takes place: the intermediate (A) has an active hydrogen atom
which undergoes enolization to give the substituted hydroquinone (B)
which is then oxidized by a mole of the original quinone to furnish
a substituted quinone (C), while the oxidant is reduced to hydro-
quinone. Although a second molecule of aniline could add in several
ways, actually it adds in but one way to furnish (D)."[131]

The brown flakes of m.pt. 150°, obtained from the alcoholic
solution, were re-crystallized from alcohol, melting at 187°. A
mixed melting point with 2,5-dianilino-quinone-monoanil (m.pt. 197°)
gave a lowering to 190°, but this may be due to some impurity in
the 187° sample since the solubility relationships of the latter
substance in the common organic solvents, in acids and alkalies,
and a fairly close agreement in nitrogen content (11.02 and 10.87%
found; 11.54% theoretically) all point to this substance being
2,5-dianilino-quinone-monoanil.

In order to verify the hydrolysis of cinnamal aniline in the

presence of quinone, a similar reaction was carried out with benzal
aniline, both by fusion and in alcoholic solution. 2,5-Dianilino-
quinone was obtained from both but benzaldehyde could not be detected.
In the case of ky cinnamal aniline, hydroquinone was expected as one
of the by-products of the reaction. As such it should have been
present together with the 2,5-dianilino-quinone-monoanil in the
alcoholic solution or with the cinnamic aldehyde in the ligroin
extract. There was not sufficient of it present, however, to detect.
But in the case of benzal aniline, hydroquinone was found in the
alcoholic filtrate after removal of the 2,5-dianilino-quinone, its
presence being verified by a Schotten-Baumen reaction, the benzoyl
derivative melting at 202°.

The reaction of cinnamal aniline on quinone in chloroform also
involved hydrolysis of the unsaturated anil. 2,5-Dianilino-quinone
was removed from the black-colored chloroform solution by filtration.
On evaporation to dryness and extraction of the residue with benzene,
azophenin (m.pt. 233°) instead of 2,5-dianilino-quinone-monoanil was
obtained. Hydroquinone was isolated by extraction with ether of the
crude azophenin.

Just as one set of products had been obtained by fusion of
cinnamal aniline and quinone and another by refluxing a chloroform
solution of these substances, so a different series of compounds were
isolated from a 95% ethanol solution after boiling from thirty
minutes to an hour.

2,5-Dianilino-quinone was filtered off after cooling of the
solution, giving fairly pure crystals, melting at 320-325°. Re-
crystallization from nitrobenzene raised this value 10-15°. Upon
allowing the residual solution to evaporate slowly, a black tar was
obtained, which could not be re-crystallized. It was found necessary,

in order to get the best results to treat the alcoholic filtrate, after removal of the 2,5-dianilino-quinone, with small amounts of water, to precipitate the tar. Considerable difficulty was encountered in the latter operation. The process was continued until the solution was a dark cherry-red color, the tar being collected in a beaker, and the cherry-red solution being allowed to crystallize. Cherry-red crystals were filtered off from the latter, melting at 90-100°, and often brown in color, or appearing to consist of two kinds of crystals, one dark brown, the other fawn-colored. These were later found to be identical. Ether extraction of the filtrate gave a considerable yield of hydroquinone.

The yield of 2,5-dianilino-quinone appeared fairly constant for mixtures of cinnamal aniline and quinone in the ratios of 1:1 to 2:1. Greater yields of the cherry-red substance were obtained, however, by the use of cinnamal aniline and quinone in the ratio of 2:1 and especially 3:2.

In an attempt to determine the nature of the tar, since it formed a considerable amount of the reaction mixture, a portion of it was boiled with water, filtered and the soluble fraction extracted with ether, yielding a ~~plee~~ slight amount of black amorphous powder, melting at 64-69°, with a pleasant fruity odor. It could not be purified sufficiently for purposes of identification due to the small yield and to the degree of impurity.

The portion of the tar insoluble in water could not be steam distilled, while vacuum distillation at 14 mms. pressure gave a slight amount of an oily distillate which was identified as cinnamic aldehyde. Whether the aldehyde was present in the tar as such, due to hydrolysis of the cinnamal aniline, or whether it was obtained by decomposition of the tar cannot be definitely stated.

Several attempts to convert the tar into a crystalline deriv- ative were made, namely: reduction with Zn and HCl and with $SnCl_2$ and HCl; preparation of an acetyl derivative with acetic anhydride; and preparation of an oxime. In each case, however, the tarry res- idue was found unchanged.

The cherry red substance was extracted with benzene in order to eliminate any 2,5-dianilino-quinone present and, after evaporat- ion of the benzene, was re-crystallized from dilute alcohol. The method used is dealt with in detail in the experimental section of this thesis. With care, the cherry-red substance could be obtained in the form of fawn-colored crystals melting at 112°. Various degrees of purity were encountered, depending on the strength of the alcohol used, the crystals being often mixed up with tarry material or with a black amorphous substance. The latter was identical with the fawn-colored crystals since they could be inter-converted by varying the strength of the solvent, the heat of solution, and the method of filtration.

We wish to express our thanks to Dr. G. M. Brownell of the Department of Geology for assisting in the optical examination of these crystals. They were orthorhombic in form and strongly bi- refractive, giving striking colors on rotating the nicol. The crystals were bi-axial and optically positive, the plane of cleav- age being perpendicular to the acute bisectrix.

They gave a violet color with conc. sulfuric acid and yellow with conc. HCl and HNO_3. They dissolved with difficulty in 10% NaOH and were easily soluble in benzene, chloroform, acetone, and slightly soluble in ether and ligroin. They were insoluble in water.

Combustion determinations of carbon and hydrogen gave the following values: carbon 84.44and 84.92%; hydrogen 6.30 and 6.21%.

The amount of nitrogen present, as determined by Kjeldahl analysis, was 5.01 and 5.07%. Molecular weight determinations were carried out by the freezing point method, giving values of 276.7, 241.0 and 258.0. On the basis of these results, the formula of the 112° substance is $C_{19}H_{17}ON$. The theoretical values corresponding to this formula are: molecular weight 275; carbon 82.90%; hydrogen 6.18%; nitrogen 5.09%; and oxygen 5.82%.

The oxygen atom present is ketonic in character since it did not possess reducing properties and since it yielded a well-crystallized semicarbazone, melting at 218°. The nitrogen content was 7.83 and 7.70% as determined by the Kjeldahl method. This surprisingly low value cannot be explained unless a polymerization of the 112° substance had taken place, probably under the influence of the sodium acetate used. Such a result is not surprising, provided that we are dealing with an aniline-substituted quinone or hydroquinone, as several such cases have been reported by Suida and Suida[130]. Hot alcohol, for example, is sufficient to polymerize mono-anilino-quinone.

A bromine derivative melting at 126-128° was obtained by the action of bromine in the cold on an alcoholic solution of the 112° substance, but enough could not be prepared for analysis due to a lack of insufficient of the 112° compound.

Reduction of the latter substance with $SnCl_2$ and HCl gave a lemon-yellow substance which could be re-crystallized from benzene only with difficulty. After four re-crystallizations, the color appeared slightly orange-yellow, the crystals being small and well-formed and melting at 158°. Kjeldahl analyses and combustions for carbon and hydrogen were carried out, but in the course of the latter determinations an inorganic residue was found, amounting to

20-25% of the total weight of the re-crystallized reduction product. This inorganic residue was probably a mixture of $SnCl_2$ and $SnCl_4$. The values obtained for carbon, hydrogen and nitrogen can therefore be assigned no significance. In order to get a more accurate picture of the reduction compound, another method of reduction must be sought for the 112° substance. Due to a lack of materials, however, this had to be postponed.

It is interesting to note, however, that the carbon and hydrogen values found, after correction for the amount of impurity present in the two samples, were 56.50 and 52.40%, and 6.01 and 4.57%, respectively. The uncorrected nitrogen content was 3.48 and 3.55%, which should correspond somewhat to the nitrogen content of the 112° substance.

The reduction product, after four re-crystallizations, was easily soluble in acetone and alcohol, less soluble in hot benzene, chloroform and water, and insoluble in ether, petrol ether and ligroin. It gives an intense yellow color with conc. sulfuric acid; acid permanganate solution is decolorized in the cold, as is bromine water. The action of bromine water is not accompanied by evolution of HBr, but a slight milkiness is produced. The reduction product is soluble in dilute HCl, giving a yellow color, but not in 10% NaOH. The latter test may not, however, be valid, since the particles observed in the alkali solution may be an hydroxide of tin rather than the insoluble reduction substance. On heating with 50% potash solution, ammoniacal vapors are evolved.

A Schotten-Baumen reaction was carried out with the reduction product in the hope of proving the presence of an OH-group and of preparing a benzoyl derivative. It was not expected that the $SnCl_2$ present in the re-crystallized reduction product would affect the

reaction unfavorably. It was noticed, however, that considerable heat
was evolved in the course of the reaction. The benzoyl derivative
resulting gave well-defined white crystalline flakes, upon re-
crystallization from benzene. They melted at 160-161° but were not
identical with the reduction product (m.pt. 158°) due to different
appearance, different solubility relationships, and the proof of a
mixed melting point.

The nitrogen content of the benzoyl derivative, as determined
by Kjeldahl analyses, was 6.47 and 6.30%, while the values for carbon
were 78.89 and 79.22% and for hydrogen 5.67 and 5.52%. Molecular
weight determinations by the method of Rast gave values of 221 and
232. From these results, the formula of the benzoyl derivative should
be $C_{14}H_{12}ON$. This would correspond to a molecular weight of 215 and
would give the following values: carbon 80.00%; hydrogen 5.71%;
nitrogen 6.67%.

The formula of the benzoyl derivative may be written as
$C_8H_7N-CO.C_6H_5$. This differs considerably from the formula of the 112°
substance, $C_{19}H_{17}ON$, which should be structurally identical with the
reduction product, the only difference being a reduction of the
carbonyl group. The reason for this difference is probably due to
alkaline hydrolysis of the 112° substance during the Schotten-Baumen
reaction since an unusually large amount of heat was evolved in the
course of that reaction.

The nature of the 112° substance and its derivatives is being
investigated further. At the present time, however, it is impossible
to suggest a structure for it.

EXPERIMENTAL.

EXPERIMENTAL.

A. THE NITROGEN ATOM IN THE PHILODIENE COMPONENT.

1. CINNAMAL ACETOPHENONE AND BENZAL ANILINE.

The cinnamal acetophenone used was prepared according to the method of Scholtz[132], dissolving 50 g. cinnamic aldehyde, 45 g. acetophenone and 20 g. 10% NaOH in 200 g. alcohol. The golden yellow needles formed were re-crystallized from alcohol, melting at 102-103°. The yield amounted to 85 g.

The benzal aniline used was prepared according to the method of Cohen[133], heating 50 ccs. benzaldehyde and 50 ccs. aniline on the water bath for one hour and re-crystallizing the anil formed from alcohol. The crystals melted at 53°. The yield was 40 g.

The conditions to which these two reaction components were subjected in an attempt to effect a diene synthesis were: re-fluxing in ether, benzene and glacial acetic acid, fusion at various temperatures, and activation with conc. sulfuric acid and with anhydrous $AlCl_3$. The methods used are discussed in detail:

(a) In Ether.

Equimolecular proportions of cinnamal acetophenone (0.6 g.) and of benzal aniline (0.4 g.) were refluxed in ether for two hours. Part of the solvent was evaporated and the product allowed to re-crystallize. Yellow crystals were filtered off, washed with ether and dried. They melted at 102° and were identified as cinnamal acetophenone by means of a mixed melting point. On further evaporation of the ethereal solution, more cinnamal acetophenone separated

until 0.5 g. had been recovered.

That the residue consisted chiefly of benzal aniline was verified by drying, dissolving in dry ether and precipitating aniline hydrochloride, melting at 192° (actually 198°). The formation of this salt can be ascribed to hydrolysis of the anil.

No reaction could be detected under these conditions.

(b) In Benzene.

The experiment was repeated, the components being refluxed in benzene for two hours. The benzene was distilled off and the reaction mixture dissolved in and allowed to crystallize fractionally from ether. 0.4 g. of yellow crystals melting at 101° were separated and identified as cinnamal acetophenone by a mixed melting point. On further standing, more of the diene was obtained, leaving unreacted benzal aniline. As before, a condensation did not take place.

A second attempt was made using benzene, but the reaction was allowed to proceed for six hours. The result here was also negative.

(c) In Glacial Acetic Acid.

Equimolecular proportions of cinnamal acetophenone and benzal aniline were warmed on the water bath with glacial acetic acid for one hour at 100°, a slight greenish-red fluorescence developing. The mixture was then set aside for four days, poured into an excess of water and extracted with ether. The ethereal extract was dried over anhydrous Na_2CO_3, filtered, and most of the ether distilled off. About 0.3 g. of the original 0.6 g. of cinnamal acetophenone were recovered in a very pure condition, melting at 103°.

The aqueous acidic residue was made alkaline with 10% NaOH solution and extracted with ether. After drying, filtering and removal of most of the ether, a rather viscous solution was obtained.

On complete evaporation of the solvent, a slight amount of a red, gummy mass was left. It could not be crystallized, precipitated by means of dry HCl gas from ethereal solution, or otherwise identified.

By repeating the reaction at a higher temperature (refluxing for three hours over an open flame at 118°), the fluorescence became more marked. As before, cinnamal acetophenone was obtained from the ethereal extract of the acid solution, except that only 0.1 g. instead of 0.3 g. resulted, while from the alkaline solution, a larger amount of the red viscous material was obtained. This indicates that the viscous mass was being formed at the expense of the cinnamal acetophenone.

(c) Fusion.

Heating cinnamal acetophenone (0.6 g.) and benzal aniline (0.4 g.) at 100° on the water bath for two hours yielded a reddish fusion mass which crystallized on cooling. By fractional crystallization from ether, three successive portions of cinnamal acetophenone were filtered off, namely: 0.3 g. melting at 101°, 0.1 g. melting at 100°, and 0.1 g. melting at 97°. Their identification was made by a mixed melting point. No reaction was observed.

Fusion on the oil bath at 145-155° for three hours likewise yielded a red, viscous fusion mixture which crystallized on being left to stand overnight. It was then dissolved in ether and fractionally crystallized. The first fraction (0.3 g.) melted at 100° and gave no depression with cinnamal acetophenone; the second fraction of 0.1 g. melted at 96°, a mixed melting point being 98°; a third fraction of 0.1 g. melted at 84°, the mixed melting point being 87-89°. On the basis of these results it was concluded that a diene synthesis had not taken place, although a certain amount of decomposition was noted.

A third attempt to effect a condensation between cinnamal acetophenone and benzal aniline was made by heating on the oil bath at 180° for ten hours. A red viscous mass resulted. On dissolving in benzene and allowing the solvent to evaporate off slowly, no crystals of cinnamal acetophenone separated. Unsuccessful attempts to crystallize the reaction mixture were made with ether, acetone, chloroform, alcohol, carbon tetrachloride, carbon disulfide and ligroin.

It was then dissolved in dry ether and dry HCl gas bubbled through it, causing a buff-colored, flocculent precipitate to separate. This was washed with ether and dried, amounting to 0.1 g. and melting at 183°. Since its melting point was nearly that of aniline hydrochloride (198°), an attempt was made to couple it with β-naphthol after treatment with nitrous acid. It was, however, insoluble in water and its aqueous wash did not yield an azo color.

In order to increase the yield of the 183° substance, the fusion was repeated, using 1.8 g. cinnamal acetophenone and 1.1 g. benzal aniline, heating at 180-200° for fiteen hours. The reaction mixture was left overnight, dissolved in benzene, and set aside to evaporate. The same viscous mass was obtained. On dissolving this in ether and filtering, about a milligram or so of white crystals were obtained, melting over 300° with decomposition. Dry HCl gas was passed through the filtrate, yielding 1.0 grams of a brownish precipitate melting at 124-128°. This was purified by dissolving in ether and re-precipitating with HCl, yielding white crystals melting at 160°. They were soluble in water and on coupling with β-naphthol yielded an azo-β-naphthol derivative melting at 130-131°. By a mixed melting point test with the azo-β-naphthol derivative of

aniline hydrochloride, the 160° substance was identified as aniline hydrochloride.

Due to the small yield of the crystals melting over 300°, a fusion was carried out for thirty hours at 180°, using 3.6 g. of cinnamal acetophenone and 2.4 g. of benzal aniline. Not more than 0.1 g. could be isolated, however. The viscous red mass was again obtained and by the action of HCl on this, aniline hydrochloride was again precipitated. The yield of the high-melting substance could not be increased by heating for twenty hours at 220°. The crystals obtained were insoluble in ether, benzene, chloroform and methanol, but could be dissolved in acetone.

Repeating the fusion under strictly anhydrous conditions (a drying tube at the free end of the condenser attached to the reaction flask, sodium-dried ether and vacuum-dried materials) for fifteen hours at 180°, the quantities of materials used being 1.8 g. of cinnamal acetophenone and 1.1 g. of benzal aniline, the high-melting substance was obtained as before. But on passing HCl gas in, using a CaCl$_2$ drying-tube and a sulfuric acid bubbler in order to dry it thoroughly, aniline hydrochloride was not obtained. We may conclude, therefore, that the presence or absence of water does not affect the yield of the high-melting substance and that water is necessary to catalyse the formation of aniline hydrochloride. Due to the small yield of the high-melting material and to the time factor involved, it seemed inadvisable to pursue this reaction further, although the possibility remains that it may be the diene synthesis sought.

(d) Activation with conc. Sulfuric Acid.

Cinnamal acetophenone (0.6 g.) and benzal aniline (0.4 g.) were thoroughly mixed, covered with conc. sulfuric acid and left

overnight. The color was cherry red due to the action of the acid on the diene. The mixture was poured into water, extracted four times with ether, dried over anhydrous Na_2CO_3 and filtered. On distilling off most of the ether, 0.2 g. of product was obtained. By its appearance, there were two different kinds of crystals, one white in color, the other yellow. Manual separation by means of a hand lens and a pair of tweezers was carried out. The whitish crystals melted at 100°, the yellowish at 101°, both giving no lowering in mixed melting point tests, with cinnamal acetophenone.

The aqueous (acid) residue was neutralized with 10% NaOH, a slight excess of alkali being added to cause it to turn litmus blue. The resulting solution was extracted several times with ether, dried over anhydrous soda ash, filtered and set aside to evaporate. A slight amount of a slightly reddish viscous mass was obtained, amounting to no more than a few milligrams. No condensation could be detected.

The experiment was repeated, using the same quantities of both substances and covering with conc. sulfuric acid, except that the mixture was warmed gently for less than a minute with a bunsen burner in order to dissolve the crystals. The mixture was left over the week-end. A slight fluorescence was noted, the solution being red with transmitted light and green with reflected light. On pouring into water, white colloidal particles appeared throughout the liquid, disappearing by the addition of more water or on heating, and re-appearing again on cooling.

The acid solution was extracted with ether, dried over soda ash, filtered and allowed to evaporate. A minute quantity of yellow crystals were obtained, rendered impure, however, by the presence of an amorphous, black-green residue. Due to the latter, it was

necessary to dissolve the entire product in dilute NaOH, extract with benzene, dry, and allow the solvent to evaporate off. A few yellow crystals melting at 100° were obtained and identified by means of a mixed melting point as cinnamal acetophenone.

The aqueous (acid) residue was made alkaline with 10% NaOH and extracted with ether. The solvent was dried as before, filtered and allowed to evaporate. A few milligrams of a dark colored, viscous material was left. This could not be sufficiently purified for identification.

In carrying out the procedure a third time, the mixture was warmed at 100° on the water bath for thirty minutes. It was left overnight, poured into water and extracted with ether. After drying, a slight yield of greenish-black material was obtained from the solvent, too impure, in view of the small yield, to re-crystallize or identify otherwise. In analogy to the previous experiments, however, this substance may also be taken as cinnamal acetophenone. Repetition of the alkaline extraction yielded no residue, crystalline or amorphous. Hence, as in the other cases, it must be concluded that conc. sulfuric acid does not catalyse a reaction between cinnamal acetophenone and benzal aniline.

(e) Activation with Anhydrous Aluminium Chloride.

To 0.6 g. cinnamal acetophenone and 0.4 g. benzal aniline dissolved in 50 ccs. benzene, 1-2 g. anhydrous AlCl₃ were added, as an activating agent. A red color was produced (halochromism) due to the action of the salt on the diene. The mixture was refluxed on the water bath for an hour, the color deepening. It was then cooled and poured into water to dissolve the aluminium salt. The benzene layer was separated by means of a separatory funnel,

dried over anhydrous Na_2CO_3, filtered and allowed to evaporate. A red viscous mass was obtained.

It was treated with conc. hydrochloric acid for a few minutes and then extracted with benzene, after decanting/the insoluble residue. Most of the viscous mass had dissolved in the acid. On neutralizing and drying the benzene extract, followed by distillation of the solvent, the amorphous mass was obtained unchanged.

The acid solution, after separation of the benzene layer, was made alkaline with NaOH and extracted with benzene. A few crystals of cinnamal acetophenone were isolated from the latter on partial evaporation of the solvent. The diene obtained was, however, impure due to the presence of some of the gummy material.

The aqueous layer containing the aluminium chloride was slightly acidified and extracted with ether. On drying, filtering and partial evaporation of the solvent, a few crystals of cinnamal acetophenone, melting at 100°, were obtained.

The experiment was carried out a second time, using 3.6 g. benzal aniline and 5.4 g. cinnamal acetophenone. After dissolving both components in benzene, 2 g. anhydrous $AlCl_3$ were added. After refluxing for three hours on the water bath, the color had changed from red to greenish-black. On the addition of water to decompose the cinnamal acetophenone-aluminium chloride complex and the excess chloride, the benzene layer turned emerald green. The two layers were separated and the aqueous layer was extracted two more times. Anhydrous soda ash was added to the extract and left to stand for two hours. The color changed slowly to orange-red, taking ten to thirty minutes. The solvent closest to the Na_2CO_3 changed color more quickly. The change was accelerated by warming.

A red, viscous mass was obtained from the benzene extract.

This was taken up in dry ether, all but a small amount of a flocc-ulent material dissolving. This green flocculent mass was filtered off and left to dry. On the evaporation of the solvent, it lost a great deal of its bulk, turned black and was left as a tarry blob.

Ligroin was added to a portion of the filtrate, precipitat-ing a brown flocculent material in what appeared to be a very good yield. However, on drying, it also shrivelled up to a very small quantity of black amorphous material, somewhat oily to the feel. It could not be purified sufficiently by washing with ligroin or ether to render a melting point determination possible. Using petrol ether instead, the substance was obtained again, save that the brown color remained on drying.

A second portion of the filtrate was allowed to stand until the ether had evaporated off. Alcohol was added, some of the red gummy residue dissolving. The non-soluble portion appeared as a heavy oil, less viscous than the original viscous mass. It was in-soluble in benzene and ether as well, and but slightly in chloro-form. This would suggest that the alcohol-soluble portion of the red gummy material had solvent action upon the non-soluble fraction. The latter, in chloroform solution, could not be precipitated by dry HCl gas. On allowing the alcohol to evaporate off from the soluble fraction, treatment with HCl gas resulted in the precipit-ation of a red gummy material.

Dry HCl gas was slowly bubbled into a third portion of the filtrate, with constant stirring. A reddish-black, very glue-like flocculent material was precipitated in considerable yield. This was filtered off. On allowing to stand, the flocculent character disappeared, the filtered material becoming tarry blobs, black in color. The filter paper turned green for a few millimeters around

the blobs. The latter were scraped off and dissolved in 95% ethanol.
On the addition of water to part of this alcoholic solution, a
yellow somewhat crystalline substance, melting at 120°, was prec-
ipitated. With dilute ammonia, the same material was precipitated
from the second portion, but in a yellower condition and melting
at 122°.

Some of this material was dissolved in dry ether and dry HCl
gas passed in, precipitating a green powder melting at 112° and
giving a definite lowering on taking a mixed melting point. Pre-
sumably the 122° material is a free base, the 112° substance being
its hydrochloride.

The green salt could not be re-crystallized from the usual
solvents. In order to purify the free base, the brown particles
were thoroughly washed with water to remove excess ammonia or
any ammonium chloride formed. The only solvent which could be used
was petrol ether. A few reddish-orange crystals were obtained,
melting at 92°, shortly after dissolving. No more could be obtained
on allowing the mixture to stand until the petrol ether had been
completely evaporated. As it evaporated, a red oil was seen to
creep up the sides of the beaker. This oil was left after no more
solvent was left. It could not be purified by vacuum distillation
as it went gummy, nor could it be crystallized, even on standing
six months. Re-dissolving the free base in dry ether, followed by
passing in dry ammonia gas gave a small yield of the yellow part-
icles, but not enough to warrant using this method as a means of
purifying the substance. The amount of crude base could not be
increased above 0.2 g. for 5.4 g. cinnamal acetophenone and 3.6.g.
benzal aniline.

2. ANTHRACENE AND BENZAL ANILINE.

(a) In Benzene.

Equimolecular proportions of anthracene (1.0 g.) and of benzal aniline (1.0 g.) were refluxed in benzene, on the water bath, for six hours. On allowing part of the solvent to evaporate off, 0.5 g. of yellowish crystals were obtained, melting at 215° and giving no depression in a mixed melting point with anthracene (m.p. 216°). Three successive crops of anthracene were filtered off, melting at 209°, 194° and 181°, respectively. On washing with ether these values rose to 210-214°. On the basis of a mixed melting point with pure anthracene, the crystals were identified. Further examination of the residue indicated that a condensation reaction with benzal aniline had not taken place.

(b) In Xylol.

The two reaction components (1.0 g. of each) were refluxed in xylol for five hours, part of the solvent being then distilled off and the remainder allowed to evaporate off more slowly in order to facilitate fractional crystallization of the reaction mixture. Within the course of a week, 0.9 g. of anthracene was recovered. A reaction could not be observed.

(c) Fusion.

Following fusion at 180-200° on the oil bath for twelve hours, the reaction mixture was dissolved in benzene and allowed to crystallize out. The entire amount (1.0 g.) of anthracene used was recovered, again proving that no reaction had taken place.

3. CINNAMAL ACETOPHENONE AND PHENYL ISOCYANATE.

(a) Fusion.

Cinnamal acetophenone and phenyl isocyanate were fused at

100° for two hours, the amounts used being one gram of each. This would correspond to two moles of isocyanate to one of diene. The fusion was carried out on the water bath, the reactants being contained in a round bottom flask to which was attached an upright air condenser. After leaving overnight, the excess isocyanate was washed out with dry ether, lemon yellow crystals being left. These were dissolved in boiling ether and recrystallized from it, giving a melting point of 102°. They were identified as cinnamal aceto-phenone by means of a mixed melting point. The first crop weighed 0.6 g., two successive crops amounting to 0.2 and 0.1 g., melting at 100° and 98°, respectively. No condensation could be detected.

The reaction was carried out as before, but the heating was prolonged to eight hours. About 0.7 - 0.8 g. of cinnamal aceto-phenone were filtered off, melting at 99° and giving no lowering of melting point with cinnamal acetophenone of m.pt. 102°.

A third attempt was made, using 1.0 g. each of cinnamal acetophenone and phenyl isocyanate, fusing the reactants on the oil bath at 150° for seven hours, and allowing the mixture to stand over the week-end. The excess of phenyl isocyanate was then washed out with dry ether and the residue, somewhat reddish in color, was dissolved in hot benzene, with the exception of a small amount of buff-colored crystals. On washing with benzene and drying, the latter were found to melt at 235°. On the basis of a mixed melting point with carbanilide (m.p. 238°), the buff-colored crystals were converted to a bromine derivative. The method used was as follows: 0.05 g. were dissolved in 10 ccs. hot alcohol, cooled, and a drop of liquid bromine added. On dilution, a yellowish precipitate was formed which, on washing with cold 95% ethanol, gave white silky crystals subliming at 291°. This then verified the identity of the

buff-colored crystals as carbanilide. About 0.5 g. was obtained.

The filtrate from which the carbanilide had been removed was allowed to evaporate to dryness, yielding a red, viscous mass. This was dissolved in dry ether and dry HCl gas was bubbled through it. A slight amount of carbanilide was precipitated.

In order to avoid the possibility that water, either from the air or from the reagents, had been responsible for the formation of carbanilide, another attempt was made ~~out~~, using well-dried materials. 1.0 g. of cinnamal acetophenone which was dried for four days in a vacuum dessicator was placed in a dry, round-bottomed flask, and 1.0 g. of phenyl isocyanate was added. An upright air condenser was attached to the flask and a drying tube, containing $CaCl_2$, was filled up to the free end of the condenser. The reaction was carried out at 150° for eleven hours and the mixture was left over the week-end. The excess of phenyl isocyanate was washed out several times with sodium-dried ether and set aside in a beaker in the fume cupboard. After standing a week, all that was found in the beaker was a slight amount of orange-red gummy material, but not trace of carbanilide.

The contents of the flask were then refluxed with benzene for a few minutes, cooled and filtered, yielding 0.4 g. of carbanilide, melting at 236°. On further evaporation of the benzene, another 0.2 g. of carbanilide was filtered off, the filtrate drying to a red gummy mass. The latter could not be identified or crystallized.

(b) Activation with Anhydrous Aluminium Chloride.

A fusion was carried out on the water bath at 100° for two and a half hours with 1.0 g. cinnamal acetophenone, 1.0 g. phenyl isocyanate and 0.5 g. anhydrous $AlCl_3$, and leaving overnight to crystallize. A reddish, gummy mass containing yellow crystals

.was obtained. The excess of phenyl isocyanate was removed by washing several times with dry ether. The yellow crystals were separated from the reddish mixture manually, recrystallized from ether and dried. Their melting point (99°) and mixed melting point (98°) showed them to be cinnamal acetophenone.

The reddish gummy material was dissolved in benzene, water being added to effect the solution of the $AlCl_3$ salt. The benzene layer was then separated, dried over anhydrous Na_2CO_3 and filtered. By distilling off a portion of the benzene, a yellowish crystalline mass separated. On filtering and drying, this was found to melt at 233°. It was identified as carbanilide by means of a mixed melting point with carbanilide (m.pt. 238°) and by the formation of a silky-white bromine derivative subliming at 291°.

The carbanilide must have been formed during the addition of the water used to dissolve the $AlCl_3$. Had it been present prior to that, it would not have been completely soluble in the amount of cold benzene used to dissolve the red gummy mass.

The benzene filtrate containing the reddish material was allowed to evaporate down completely. No crystallization took place. The residue was therefore redissolved and a few cubic centimeters of conc. HCl were added to the benzene solution. The benzene layer was separated, dried and allowed to evaporate to dryness. The reddish mass was again obtained. This was dissolved in dry ether and treated with dry HCl gas. This precipitated a slight amount of carbanilide. On extraction of the HCl layer, after neutralization with 10% NaOH solution, using ether as the solvent, no material was obtained save a slight amount of a dirty, yellowish-black residue.

With the exception of carbanilide-formation, no reaction was observed that might be interpreted as a "diene synthesis".

4. ANTHRACENE AND BENZONITRILE.

(a) In Benzene.

Anthracene (0.9 g.) and benzonitrile (0.5 g.) were refluxed on the water bath in benzene solution for four hours. The solution was then set aside to evaporate. Within the course of several days the entire weight of anthracene used was recovered, proving that no reaction had taken place under these conditions.

(b) In Toluene.

The above reaction was repeated, using toluene as the solvent, and heating for four hours over an open flame. Part of the toluene was distilled off and, on cooling, 0.4 gms. of anthracene separated out. The solution was set aside to evaporate down further, another 0.4 g. being recovered. There was no evidence of a reaction.

(c) Fusion.

A fusion was carried out on the oil bath for ten hours at 170°, using the same amounts of materials as in (a) above. The fusion mixture was left over the week-end to crystallize. It was then dissolved in benzene and fractionally crystallized by slow evaporation of the solvent. By the end of the week, 0.8 g. of anthracene had been recovered and identified by a melting point (215°) and by a mixed melting point. There was no reaction.

(d) Activation with conc. Sulfuric Acid.

Equimolecular weights of the two components were thoroughly mixed in a beaker and covered with conc. sulfuric acid. On the addition of the acid, the mixture turned brownish, frothing up after standing about five minutes and turning greenish-black. The frothing was accompanied by the evolution of sulfur dioxide fumes.

After standing three days, the mixture was poured into an excess of water and extracted six times (due to the slight solubility of the substance being extracted) with ether. The solution was dried over anhydrous Na_2CO_3, filtered, and the excess of ether distilled off. The residual solvent was allowed to evaporate off slowly, brownish-white platelets separating out. These were recrystallized from ether, dried and a melting point taken (128°).

The platelets contained nitrogen, were soluble in hot water, gave a neutral reaction to moist litmus paper and were decomposed by means of conc. NaOH solution with evolution of ammonia. The substance was identified qualitatively by the system of Clarke[134] as benzamide. Confirmation was obtained by means of a mixed melting point.

The aqueous (acid) residual solution was made alkaline with an excess of 10% NaOH solution and extracted with ether. On drying and evaporation of part of the solvent, no residue was left.

The formation of benzamide is explained by a partial hydrolysis of the benzonitrile by the sulfuric acid.

5. CINNAMAL ACETOPHENONE AND BENZONITRILE.

(a) In Benzene.

1.2 g. of cinnamal acetophenone were refluxed with 0.5 g. of benzonitrile in benzene solution for three hours. The solution was then poured into a beaker and set aside to evaporate. In the course of the next five days the entire weight of cinnamalacetophenone used was recovered from the reaction mixture, proving that no reaction had taken place.

(b) In Chloroform.

The above reaction was repeated, the components being re-

fluxed on the water bath for five hours, in chloroform. The sol-
ution was then set aside to evaporate. Three successive crops of
cinnamal acetophenone crystals were filtered off, amounting to 1.0
g. and melting at 102°, 101° and 99°, respectively. Confirmation
was obtained by mixed melting points.

No reaction could be observed.

(c) Fusion.

The two reaction components were fused at 100° for four
hours on the water bath, a reddish color being observed to develop.
The mixture was then dissolved in ether and allowed to crystallize.
Of the 1.2 g. cinnamal acetophenone used, 1.0 g. was recovered and
identified by a mixed melting point, following re-crystallization
from ether. There was no reaction under these conditions.

The fusion was repeated at 150°, the time of heating being
prolonged to five and a half hours. The reaction mixture was left
overnight to crystallize. It was then taken up in ether and allow-
ed to crystallize out slowly. Although the red color was more
pronounced than before, indicating a certain amount of decomposition
or hetero-polymerization, 1.0 g. of the 1.2 g. of cinnamal aceto-
phenone used was recovered and identified by re-crystallization
and by mixed melting points. No reaction was observed.

(d) Activation with conc. Sulfuric Acid.

A two-phase reaction was carried out, using 1.2 g. of cinn-
amal acetophenone and 0.5 g. of benzonitrile, the components being
covered by a layer of conc. sulfuric acid. The reaction was done in
a round-bottomed flask, lightly stoppered. A red-green fluorescence
was observed due to the action of the acid. After standing a week,
the mixture was poured into an excess of water and extracted with

300 ccs. of ether. The ethereal solution was dried over anhydrous Na₂CO₃, part of the solvent was distilled off, and the rest was allowed to evaporate off slowly. Whitish crystals melting at 126-8° separated. They were identified as benzamide by means of a mixed melting point. Their formation is due to the hydrolytic action of the sulfuric acid on the benzonitrile.

The acid residue was made alkaline with 10% NaOH solution and extracted with ether. On drying and evaporation of the solvent, no residue of a crystalline nature was obtained.

A condensation had therefore not taken place.

6. CINNAMAL ACETOPHENONE AND CINNAMAL ANILINE.

The cinnamal aniline used was made by mixing equimolecular weights of freshly distilled aniline (9.3 g.) and cinnamic aldehyde (13.2 g.). Considerable heat was evolved, accompanied by the formation of a yellow crystalline mass. The product was re-crystallized several times from alcohol and dried. The melting point was 108°; the yield amounted to 20 g.

(a) In Ether.

Equimolecular weights of the two components (0.5 g. each) were dissolved in ether, refluxed on the water bath for two hours and left overnight. By fractional re-crystallization from ether, more than half of the cinnamal acetophenone was separated from the cinnamal aniline and identified by a mixed melting point. No reaction occurred under these conditions.

(b) In Benzene.

The reaction was repeated, refluxing the two substances in benzene for four hours on the water bath. The mixture was poured into a beaker and set aside to evaporate. About .3 g. of cinnamal

acetophenone was recovered and identified by a melting point and a mixed melting point. Examination of the residue indicated that no new material had been formed, the bulk of the cinnamal aniline and some cinnamal acetophenone alone being present.

(c) In Chloroform.

Reaction (b) was repeated, using chloroform as the reaction medium, the time of heating being four hours. On cooling and partial evaporation of the solvent, some cinnamal acetophenone was recovered and identified by a melting point and mixed melting point. Further evaporation yielded more of the diene component, until 0.4 g. was recovered. No reaction was observed.

(d) Fusion.

Cinnamal acetophenone (1.0 g.) and cinnamal aniline (1.0 g.) were fused on the oil bath at 150° for five hours. The reaction mixture, reddish in color, was cooled, dissolved in benzene and set aside to evaporate. A mixture of both components crystallized out. These were separated by means of their solubility relationships and identified by their melting points and mixed melting points. 0.7 g. of cinnamal acetophenone and 0.8 g. of cinnamal aniline were recovered. No reaction was noted.

The reaction was repeated, except that thetfusion was prolonged to ten hours. With the exception that the fusion mixture possessed a ddeeper color, the identical results were obtained.

B. THE NITROGEN ATOM IN THE UNSATURATED ANIL.

1. CINNAMAL ANILINE AND ANTHRAQUINONE-1,4.

(a) In Benzene.

One gram of anthraquinone and 0.8 g. of cinnamal aniline were dissolved in benzene and refluxed on the water bath for five hours. The solution was poured into a beaker and allowed to evaporate. Crystals of anthraquinone separated out, 0.8 g. being recovered. They were identified by their melting point (273°) and mixed melting point. No reaction was noted.

(b) In Chloroform.

The reaction was repeated in chloroform solution, the time being three hours. The solution was set aside to evaporate, 0.9 g. anthraquinone being recovered. No reaction took place.

Extension of the time of heating to five hours, gave the very same result.

(c) In Xylol.

A fourth attempt was made, using xylol as the solvent, since a constant temperature of 138-139° could be successfully maintained. The time of the reaction was six hours. Most of the xylol was distilled off, the solution being then set aside to evaporate slowly. In the course of the next ten days, 0.9 g. of anthraquinone was recovered. The desired reaction did not take place.

(d) Fusion.

Equimolecular amounts of anthraquinone (1.0 g.) and of cinnamal aniline (0.8 g.) were heated on the oil bath at 180° for fifteen hours. It was extremely difficult to effectively fuse the two substances due to the high melting point of the anthraquinone and to the fact that it sublimed easily at the temperature of the fusion. It was therefore necessary to carry the reaction out in a sealed hard-glass tube which was completely immersed in the hot paraffin.

The reaction mixture, which had become reddish in color, was

to cool. It was stirred up with cold ether so that the residue was
left colorless, the colored component being present in the solvent.
The residue wasre-crystallized from benzene and identified as
anthraquinone by means of a melting point (273°) and a mixed melting
point. The ethereal solution was set aside to evaporate, yielding
about 0.2 g. of anthraquinone, after which about 0.7 g. of cinnamal
aniline was filtered off.

The ethereal solution was then evaporated down to dryness and
re-dissolved in dry ether. Dry HCl gas was passed in, precipitating
a reddish-black substance, amorphous in nature and amounting to 0.1
g. This substance may be a decomposition of polymerization product
of the cinnamal aniline. Its nature could not be revealed due to the
small yield and to the fact that it could not be re-crystallized.

2. CINNAMAL ANILINE AND CINNAMIC ALDEHYDE.

(a) In Ether.

Equimolecular weights of cinnamal aniline (0.8 g.) and of
cinnamic aldehyde (0.6 g.) were used in an attempt to bring about
a diene reaction between them. They were refluxed on the water bath
in ethereal solution for two hours and were then left over the
week-end. The ether was allowed to evaporate off, facilitating the
recovery of the entire 0.8 g. of cinnamal aniline used.

(b) In Benzene.

The reaction was repeated, using benzene as the reaction sol-
vent and heating for five hours on the water bath. The mixture was
allowed to evaporate down, cinnamal aniline being recovered in
successive crops. The entire amount of cinnamal aniline was recovered
and identified by means of a melting point and mixed melting point.
The reddish liquid residue was identified as cinnamic aldehyde by

the formation of a semicarbazone melting at 215°.

(c) Fusion.

0.8 g. of cinnamal aniline and 0.6 g. of cinnamic aldehyde were used on the water bath at 100° for five hours. The reaction mixture turned dark red in color. It was left overnight to cool and was then dissolved in benzene and set aside in a beaker to evaporate. 0.5 g. of cinnamal aniline separated and were identified by a melting point and mixed melting point. The residual solution was somewhat viscous in nature, but by careful manipulation, 0.2 g. more of cinnamal aniline were recovered. No reaction was noted.

The same result was obtained by carrying out a fusion for two hours at 100°, save that the reaction mass was not as darkly colored, while the ethereal solution was less viscous. By repeating for ten hours, the indications of a slight decomposition or side reaction (color and viscosity) were more marked, but no reaction could be observed as in both cases 0.7-0.8 g. of cinnamal aniline were recovered.

A third fusion was carried out at 150° on the oil bath for five hours, while a fourth fusion at 150° was effected for ten hours. The color was deeper and the viscosity more noticeable at the higher temperature and longer time of reaction. The reaction masses were dissolved in ether and allowed to evaporate down. In neither case could more than 0.6 g. of cinnamal aniline be recovered due to the increasing viscosity of the ethereal solution. The latter was found to contain a large amount of aldehyde, probably cinnamic aldehyde, since a very pronounced reaction was obtained with ammoniacal silver solution and with Fehling's solution. A semicarbazone was prepared, melting at 215°. No diene synthesis was observed.

3. CINNAMAL ANILINE AND QUINONE.

The p-benzoquinone used in the subsequent reactions was prepared by the oxidation of hydroquinone with sodium dichromate and sulfuric acid[135]. Approximately 80 g. of quinone could be obtained from 100 g. of hydroquinone, the melting point of the product, after re-crystallization from benzene, was 113-115°.

(a) In Ether.

Cinnamal aniline (2.0 g.) and quinone (1.0 g.) were dissolved in ether, refluxed on the water bath for two hours and then left over the week-end. The odor of quinone was still distinctly felt. On evaporation of the ether, a mixture of quinone and cinnamal aniline was obtained, save that the solid matter was colored black. The color appeared only on removal of the solvent and exposure of the solute to the atmosphere. On re-solution of the crystalline material, the ethereal solution was dark in color, as contrasted to the pale yellow tint of the original solution. By refluxing for three hours and leaving a week, the same result was obtained.

(b) In Benzene.

Cinnamal aniline and quinone were refluxed in equimolecular proportions, as before, for five hours, using benzene as the solvent. The color of the benzene solution was not appreciably changed at the conclusion of the operation. On evaporation of some of the solvent, some quinone and cinnamal aniline separated from solution and were identified by melting points and mixed melting points. On evaporation of the remainder of the solvent, the residue became black in color, while re-solution resulted in a very dark colored solution. The color of the benzene solution became darker somewhat on leaving for a week to ten days in a sealed flask, probably due to oxidation

by air dissolved in the benzene.

It was impossible, however, to detect any new substance in the reaction mixture due to the fact that slow evaporation of the solvent resulted in the separation and recovery of 1.7 g. of cinnamal aniline and 0.8 g. of quinone.

(c) Fusion.

Equimolecular amounts of cinnamal aniline and quinone were fused on the brine bath at 100-110⁰ for two hours. The fusion mixture turned black. It was left overnight to crystallize and was then treated with hot ligroin in order to dissolve any unchanged cinnamal aniline or quinone. That either of these was present seemed unlikely due to the complete absence of any odor of quinone. On evaporation of the ligroin a yellow-orange viscous mass resulted. This could not be crystallized or identified.

The black reaction mixture was then treated several times with hot alcohol and filtered. Brown flakes melting at 150⁰ were obtained. On re-crystallization from alcohol, the melting point was raised to 187⁰.

The black residue which was insoluble in the hot alcohol melted at 253⁰. It was refluxed with chloroform in an attempt to separate it into its component parts on the basis of their solubilities. Only a slight amount dissolved, the insoluble residue melting at 285⁰. On evaporation of some of the chloroform, black crystals melting at 250⁰ were obtained, whereas the same substance could be precipitated from the chloroform by the addition of a small amount of petrol ether. The crystals obtained by the latter procedure melted at 245⁰ but gave no depression in a mixed melting point with the 250⁰ sample.

Re-crystallization of each of the three black residues, of

melting points 253°, 285° and 250°, respectively, from nitrobenzene,
gave the same product, purplish flakes melting at 327°. By means of
a second re-crystallization, the melting point was raised to 337°.
Further purification was effected by sublimation in vacuo.

The method used was as follows: The high-melting substance was
re-crystallized once from nitrobenzene and then boiled in benzene
several times in order to remove the excess nitrobenzene. The
purified material was dried for two days in a vacuum dessicator. A
hard glass test tube (large size) was scrupulously cleaned and into
it was placed a clean combustion boat containing the high-melting
substance. The open end of the tube was fitted with a stopper through
which was placed a piece of hard glass tubing. The latter was conn-
ected with the suction pump. When the air pressure withing the tube
was approximately 10 mms. of mercury, a Bunsen flame was gently
played over that portion of the tube containing the combustion boat,
causing the purple crystals to sublime on the cooler parts of the
tube, a certain amount of fused material invariably remaining in the
boat. After cooling, the boat was carefully removed and the sublimate
shaken out. The latter was placed in a vacuum dessicator for two days
and a melting point taken. The value obtained was 339°. By re-
crystallizing again from nitrobenzene, refluxing with benzene, and
drying, no further elevation was attained.

(i) Identification of the 187° substance.

This substance was easily soluble in acetone and glacial
acetic acid but could be dissolved in alcohol, ether, benzene and
ligroin with considerable difficulty. It turned litmus paper blue,
indicating faint basic properties. It was insoluble in dilute HCl,
but was soluble in conc. sulfuric acid with blood red color. It was
insoluble in 10% NaOH solution, although soluble in alcoholic KOH

with the development of an orange-red color.

The 187° substance was dried over the week-end in a vacuum dessicator and then analysed for nitrogen by the Kjeldahl method.

(a) Weight sample = 0.2000 gms.

Mean volume of 0.10 N NaOH req'd to neutralize excess of sulfuric acid after absorption of ammonia = 30.95 ccs. (corr.).

The 50.0 ccs. H_2SO_4 used to trap the ammonia evolved was equivalent to 46.7 ccs. of 0.10 N NaOH.

Hence, the volume of ammonia evolved = 46.7 - 30.95 = 15.75 ccs. (0.10 N).

$$\therefore \% N = \frac{(15.75)(14)(0.10)(100)}{(1000)(0.2000)} = 11.02$$

(b) Weight sample = 0.2122 gms.

Mean volume 0.10 N NaOH req'd = 30.2 ccs. (corr.).

Volume 0.10 N ammonia evolved = 46.7 - 30.2 = 16.5 ccs.

$$\therefore \% N = \frac{(16.5)(14)(0.10)(100)}{(1000)(0.2122)} = 10.87$$

These values found (11.02%, 10.87%) agree to a certain extent with the amount of nitrogen present in 2,5-dianilino-quinone-mono-anil (11.54% theoretically). Due to difficulties encountered in re-crystallizing the sample of the 187° material, it was not possible to obtain a greater degree of purity. However, on the basis of the solubility relationships and the fairly close nitrogen content, this substance must be accepted as 2,5-dianilino-quinone-monoanil.

The method of Jackson and Koch[136] was employed in preparing a sample of the monoanil for comparison and for mixed melting point tests. 1.1 gms. of quinone and 0.9 gms. of aniline were dissolved in chloroform and refluxed for an hour on the water bath under an upright condenser. On cooling, a purplish crystalline solid separated. This was 2,5-dianilino-quinone in an impure condition. It was re-

fluxed several times with acetone, yielding a reddish solution and leaving the 2,5-dianilino-quinone undissolved. On partial evaporation of the acetone, a reddish powder was obtained, melting at 185°. Re-crystallization from acetone or alcohol caused this to rise to 197-200°.

A mixed melting point of the monoanil of m.pt. 200° with the 187° substance gave a reading of 190° (using equal quantities of each).

(ii) Identification of the 339° substance.

A pure sample of the 339° substance was prepared according to the method outlined on p. 99. Analyses were carried out on this to determine the carbon, hydrogen and nitrogen contents, respectively.

The results obtained in combustions are as follows:

(a) Weight sample = 0.1742 gms.

Weight carbon dioxide absorbed = 0.4730 gms.

Weight water absorbed = 0.0709 gms.

$$\therefore \% C = \frac{(12)(0.4730)(100)}{(44)(0.1742)} = 74.06$$

$$\% H = \frac{(2)(0.0709)(100)}{(18)(0.1742)} = 4.63$$

(b) Weight sample = 0.1776 gms.

Weight carbon dioxide absorbed = 0.4826 gms.

Weight water absorbed = 0.0715 gms.

$$\therefore \% C = \frac{(12)(0.4826)(100)}{(44)(0.1776)} = 73.91$$

$$\% H = \frac{(2)(0.0715)(100)}{(18)(0.1776)} = 4.47$$

The theoretical values for 2,5-dianilino-quinone are: carbon 74.49%, hydrogen 4.83%.

The purified sample was analysed according to the Kjeldahl technique for nitrogen content:

(a) Weight sample = 0.2277 gms.

Mean volume 0.10 N NaOH req'd. = 32.3 ccs. (corr.).

Volume 0.10 N ammonia evolved = 46.7 - 32.3 = 14.4 ccs.

$$\therefore \ \% \ N = \frac{(14.4)(14)(0.10)(100)}{(1000)(0.2277)} = 9.76$$

(b) Weight sample = 0.2575 gms.

Mean volume 0.10 N NaOH req'd = 32.4 ccs. (corr.).

Volume 0.10 N ammonia evolved = 46.7 - 32.4 = 14.3 ccs.

$$\therefore \ \% \ N = \frac{(14.3)(14)(0.10)(100)}{(1000)(0.2575)} = 9.50$$

The theoretical value for 2,5-dianilino-quinone is 9.66 % of nitrogen.

The molecular weight of the 339° substance was carried out by the method of Rast, using camphor as the substance whose melting point is to be lowered. The depression constant (K) for camphor is 40,000 while its melting point was found to be 178°.

(a) Weight of 339° substance = 0.0062 gms.

Weight camphor = 0.0702 gms.

Melting point of mixture = 165°.

Melting point depression (observed) = 13°.

$$\therefore \ \text{Molecular weight} = \frac{(6.2)(40,000)}{(13)(70.2)} = 271.9.$$

(b) Weight of 339° substance = 0.0067 gms.

Weight camphor = 0.0731 gms.

Melting point of mixture = 178°.

Melting point depression (observed) = 14°.

$$\therefore \ \text{Molecular weight} = \frac{(6.7)(40,000)}{(14)(73.1)} = 261.9.$$

(c) Weight of 339° substance = 0.0067 gms.

Weight camphor = 0.0731 gms.

Melting point of mixture = 165°.

Melting point depression (observed) = 13°.

∴ Molecular weight = $\frac{(6.7)(40,000)}{(13)(73.1)}$ = 282.1.

The molecular weight of 2,5-dianilino-quinone is 290.

On dissolving the 339° substance in conc. sulfuric acid, a fuchsin red color was obtained[130]. By pouring this solution into cold water, yellow particles were precipitated. These were filtered and dried for several days in a vacuum dessicator. The melting point was 334-6°. This is a test for 2,5-dianiline-quinone.

Another test carried out was an alkaline hydrolysis[137]. A gram of the high-melting purple substance was placed in a round-bottomed flask and refluxed with 50 ccs. of 20% alcoholic KOH for three hours on the water bath. The mixture was poured into water and extracted ten times with 50 cc. portions of ether. The ethereal solution was dried over anhydrous $CaCl_2$, most of the ether distilled off and the rest allowed to evaporate off slowly. Orange-red crystals were obtained in an impure condition in a small yield. It was, however, possible to re-crystallize them from ethyl acetate, a melting point of 204° being obtained. This would indicate that the crystals formed were 2,5-dioxy-quinone, which are dark-yellow needles, melting at 215-220°. Further confirmation of this conclusion was drawn from the solubility relationships of the 204o material. It was soluble in alcohol and slightly soluble in hot water and ether.

The alkaline portion of the reaction mixture, from which the 2,5-dioxy-quinone had been extracted, was acidified with dil. H_2SO_4 and extracted with ether several times. The ethereal solution was dried and crystallized as in the previous case, yielding more 2,5-dioxy-quinone (m.pt. 203-5°).

The final reaction carried out with the 339° substance was heating 1.0 gms. with 3.0 gms. of aniline hydrochloride on the oil bath at 150° for five hours[138]. On cooling, dark purple-red crystals were obtained in an impure condition. These were dried and then boiled with alcohol to remove any alcohol-soluble impurities. The crystals were then re-crystallized from benzol. Their melting point was 233°, while that of azophenin was 236-7°. A melting point depression could not be obtained by mixing equal amounts of each.

The azophenin prepared (233°) was insoluble in alcohol, ether and cold benzol, but was soluble in hot benzol and in chloroform. It was insoluble in 10% KOH and colored hot conc. hydrochloric acid violet without dissolving. The crystals were soluble in conc. H_2SO_4 with a violet coloration, becoming suddenly sky blue at 300°. The sulfuric acid solution gave a carmine red fluorescence on dilution with water.[139,140]

The azophenin used for purposes of comparison was prepared according to the method of Jackson and Porter[139], by heating 2,5- -monoanil dianilino-quinone/for six hours with an excess of aniline at 180-200° on the oil bath, cooling, filtering, and re-crystallizing twice from benzene. The melting point obtained was 234°.

The above tests established the identity of the 339° compound as 2,5-dianilino-quinone.

(iii) Identification of cinnamic aldehyde.

On p. 98 it was pointed out that evaporation of the ligroin solution resulting by boiling the cinnamal aniline-quinone reaction mixture with ligroin to remove soluble materials had yielded a yellow-orange viscous mass which could not be crystallized or identified. By using larger quantities (8.6 gms. cinnamal aniline and 5.4 gms. quinone) and heating at 100-110° for one hour, it was

possible to obtain a ligroin solution in the same way, in which
cinnamic aldehyde could be identified. In this case, after the
reaction mixture had solidified, ligroin was added and stirred into
the solidified mass with a glass rod. This procedure was repeated
several times, using altogether about 30 ccs. of ligroin. The solvent
was not allowed to evaporate off, but was diluted with an equal volume
of 95% ethanol. Ten ccs. of this solution was tested for reducing
properties with Fehling's solution, giving a positive reaction.

The remaining 50 ccs. was treated with semicarbazone hydro-
chloride, in the usual manner, and on adding a small amount of water,
a dirty grey flocculent precipitate settled out. This was twice re-
crystallized from alcohol, yielding a flaky material melting at 215°.
This gave no depression with the semicarbazide of cinnamic aldehyde.

(iv) Benzal aniline and quinone.

The mechanism of the reaction of quinone on cinnamal aniline
has been presented on p. 68 as involving hydrolysis of the cinnamal
aniline into cinnamic aldehyde and aniline, followed by a substit-
ution reaction of the aniline on the quinone. Cinnamic aldehyde has
been identified but no trace of hydroquinone could be found, this
being a by-product of the substitution reaction. It could only have
been present in the ligroin solution or in the alcoholic solution
containing the monoanil. After removal of the monoanil from the
alcoholic solution, the latter was evaporated down, but no hydro-
quinone separated in a condition suitable for further analysis. Only
a slight brown residue (0.1 gms.) was obtained, but this could not
be re-crystallized or identified.

But the substitution course of the reaction was verified by an
analogous reaction, involving the hydrolysis of benzal aniline,
quinone being used as before. Equimolecular amounts of benzal aniline

(0.9 gms.) and of quinone (0.5 gms.) were dissolved in 30 ccs. of
95% ethanol and refluxed for half an hour on the water bath. The mix-
ture was left overnight and filtered. A yield of 0.6 gms. of 2,5-
dianilino-quinone was obtained, melting at 328°, and possessing a
distinctive metallic sheen. On re-crystallization from nitrobenzene,
the melting point rose to 334°.

The alcoholic solution was allowed to evaporate down slowly,
crystals of hydroquinone (m.pt. 169°) being obtained and identified
by means of the Schotten-Baumen reaction, the benzoyl derivative
formed melting at 202°.

The reaction was repeated, using 3.6 gms. benzal aniline and
2.0 gms. quinone. After filtration of the 2,5-dianilino-quinone, the
residual solution was subjected to distillation at a pressure of
10-15 mms. of mercury in the hope of obtaining aniline in the dist-
illate. The distillate was partially evaporated to remove the
alcohol and was then tested with semicarbazide hydrochloride and
sodium acetate. A semicarbazide was not obtained, however.

The reaction was repeated by fusion on the water bath at 100°
for one hour. On cooling the black reaction mass solidified completely.
It was re-crystallized from nitrobenzene twice, yielding 2,5-di-
anilino-quinone, melting at 333°.

(d) In Chloroform.

Cinnamal aniline (3.4 gms.) and quinone (2.2 gms.) were re-
fluxed in 50 ccs. chloroform for two and a half hours on the water
bath. After cooling and filtering, 0.7 gms. of 2,5-dianilino-quinone
were obtained, melting at 324°. These crystals had a slight greenish
tinge and gave no depression with a pure sample of melting point 338°.

The filtrate was allowed to evaporate down further, two more
crops of 2,5-dianilino-quinone being obtained, until 1.1 gms. had

been filtered off. The filtrate was evaporated to dryness and boiled several times with benzene. A reddish-purple powder was obtained from the benzene solution, melting at 188°. On re-crystallization four times from benzene, the melting point rose to 233°. A melting point depression was not obtained with azophenin prepared from 2,5-dianilino-monoanil.

Hydroquinone was obtained in small yield (0.2 gms., melting at 168°) by extraction from the benzene-soluble residue, after evaporation of the solvent, by means of ether. A benzoyl derivative was obtained with the hydroquinone, melting at 201-202°.

(e) In Alcohol.

Equimolecular amounts of cinnamal aniline (6.0 gms.) and of quinone (3.8 gms.) were dissolved in 50 ccs. of 95% ethanol and refluxed on the water bath for thirty minutes to one hour. The color of the solution turned purple-black in the course of a few minutes heating. Superheating was very pronounced, with considerable bumping. It was deemed advisable to use a 500 ccs. round bottom flask in which to carry out the reaction in order to prevent the mixture from shooting out through the condenser. The addition of glass beads or of pieces of porous pot did not help very much in preventing bumping. The time of heating was not of much importance, since substantially the same yields of products were obtained by heating from thirty to sixty minutes. The ratio of components used was, however, important, as will be pointed out presently.

The mixture was left overnight, dark purple crystals of 2,5-dianilino-quinone being filtered off, melting at 320°. On re-crystall-ization from nitrobenzene, the melting point rose to 329°. No depression was obtained with a sample of m.pt. 339°.

On allowing the solvent to evaporate off slowly, a dark tarry

mass containing a certain amount of crystalline material was deposited. Due to the solubility relationships of the tar and the crystalline material, it was not possible to effect a separation with the common organic solvents. However, a slight amount of crystalline matter could be obtained by precipitation from alcoholic solution by the addition of small quantities of water. The tar was dissolved in alcohol and water was added in ten cc. portions, stirring thoroughly after each addition, warming slightly, and immediately filtering on the suction pump. In this way, a considerable amount of tar was separated and set aside for further examination. The filtrate was treated with water as before until it acquired a maroon colour. By this time, very little tar came down on the further addition of water. The maroon or cherry-red solution was allowed to crystallize.

Cherry-red crystals separated out, and on drying were found to melt over a range of 80-100°, indicating considerable impurity. The color and general appearance of the crystals varied considerably with the method of precipitation from the alcoholic solution. When a large amount of tar was present, the solid material appeared black to brown or purple in color, often containing light brown needle-like crystals. With more effective separation, the color of the crystals became lighter. The degree of crystallinity varied also. Some of the crystals were small in size, while others were well-formed and needle-like. The impure crystals were set aside for further examination.

The filtrate, after removal of the cherry-red crystals, was extracted several times with ether, yielding a considerable amount of hydroquinone melting at 169° (following re-crystallization from benzene) and forming a dibenzoate melting at 198-199°.

The yield of 2,5-dianilino-quinone appeared to be fairly con-

stant for mixtures of cinnamal aniline and quinone in the ratios of
1:1 to 2:1. The yields of the cherry-red substance were not constant,
however, as indicated in the following table:

Wt. cinnamal aniline (C)	Wt. quinone (Q)	Ratio C/Q	Yield 2,5-dianilino-quinone	Yield cherry-red substance
6.0 gms.	3.8 gms.	1:1	0.6 gms.	1.2 gms.
"	3.0	5:4	"	1.5
"	2.5	3:2	"	2.2
"	1.9	2:1	"	1.9

Thus, the yield of the cherry-red substance increases with
increasing proportions of cinnamal aniline in the reaction mixture,
the best yields being favored by a ratio (cinnamal aniline to
quinone) of 2:1 or, preferably, 3:2.

From the point of view of yield, the tarry material seemed
to be the chief product of the reaction. Several experiments to
determine its nature were therefore carried out.

A portion of the tar was boiled with water and filtered hot
through a fluted filter paper. The filtrate was cooled and extracted
several times with ether. The ether was dried with anhydrous Na_2CO_3,
filtered, and set aside to evaporate. A slight amount of black
amorphous matter, melting at 64-69°, was obtained. It possessed a
pleasant fruity odor. Due to its high solubility in the organic
solvents available, it could not be purified sufficiently for
purposes of identification.

The portion of the tar which did not dissolve in the hot
water (i.e., the residue after filtration) was placed in a flask
and treated with live steam. It could not be steam distilled.

Vacuum distillation at 14 mms. pressure was next carried out
on the tar, a cubic centimeter of an oily liquid being collected
with the distillate. This was proved to be cinnamic aldehyde due to
the formation of a well-defined semicarbazone melting at 214°.

Several attempts were made to convert the tar into a cryst-
alline derivative. These were: reduction, treatment with acetic
anhydride, and with hydroxylamine. A portion of the tar was diss-
olved in benzene and refluxed for half an hour on the water bath
with Zn and dilute HCl, while a second portion was similarly treated
with $SnCl_2$ and HCl. The color of the benzene solution did not
change. The benzene layers in both cases were separated from the
acid by means of a separatory funnel, dried over anhydrous $CaCl_2$,
and allowed to evaporate. The tar was obtained in both cases. The
acid layers were then neutralized with 10% NaOH and extracted with
ether. After drying and evaporation of the solvent, no residue was
found.

A few grams of the tar were refluxed with acetic anhydride for
an hour, cooled and poured into water. The tar separated unchanged.

A gram of tar was dissolved in 95% ethanol and treated with
hydroxylamine hydrochloride and anhydrous sodium acetate, heated to
boiling, cooled, and then treated with cold water. The tarry material
separated.

A more intensive investigation of the cherry-red substance
showed a very close relationship between it and the tar. The former
was boiled with benzene and filtered, thereby separating it effect-
ively from the insoluble 2,5-dianilino-quinone. By the method of
precipitating with alcohol it was not possible to completely separate
the two, although extraction with benzene proved satisfactory. After
evaporation of the benzene, the cherry-red substance appeared black
in color. It was dissolved in strong ethyl alcohol and re-precipitated
as before by the addition of water. Great care must be observed if
the crystallization is to be properly made. In fact, this appeared
to be the most critical stage of the investigation, for unless due

precautions were taken it was simply impossible to obtain a pure

sample for analysis.

The best method seemed to be the use of small quantities of

the crude material, not more than three grams. Due to the nature

of the substance, three grams occupied more than half of a 100-cc.

beaker. It was necessary to carry out the re-crystallization in an

open beaker, in spite of the fact that alcohol was being used, in

order that the solution could be filtered very hot. The material

was dissolved in the minimum amount of alcohol, heating gently at

intervals to facilitate solution. A few cubic centimeters of water

were added drop by drop, stirring after every few drops. At first,

the color would not change, but as more water was added, the color

became lighter. As soon as this was observed, the solution was

carefully heated, with stirring. The color darkened on heating. More

water was added, very carefully, and the mixture was again heated

until any precipitated matter had dissolved. The process was repeated

until the color of the solution (when hot) was maroon in color.

This appeared to be at a concentration of about 40% of alcohol. The

addition of more water would precipitate the tar. It was not found

advisable to dissolve the cherry-red substance directly in the 40%

alcohol, due to difficulties encountered in the process of solution

and to the danger of precipitating the tar. It is impossible to

give absolute directions for the process described; that must beleft

to the experimenter.

After the proper concentration of solvent had been attained,

the solution was filtered hot through a small suction funnel, care

being taken with the last few cubic centimeters which would invar-

iably contain a small amount of black liquid tar. The tar itself was

poured back with the rest of the impure cherry-red material, while the

filtrate was poured into a beaker before it could cool. Here again certain care must be taken since it was noted that the last few cubic centimeters of the filtrate contained a small amount of liquid black tar. On cooling, the latter would solidify. It did not necessarily yield a black tarry solid mass; occasionally, fawn-colored material, somewhat like a number of tiny mushrooms appeared throughout its surface.

By dissolving the black tarry liquids or solids mentioned in the last paragraph in alcohol and repeating the precipitation with water, the tar could be made to crystallize out in fawn-colored crystals in the same way that the mass of the cherry-red material. This indicated that the tar and cherry-red substance (which is fawn-colored when pure) are identical or interchangeable. The one could be converted into the other by varying the strength of the alcohol-water solution, the heat of solution, and the method of filtration. Considerable practise is essential in mastering the technique outlined.

The polarizing microscope was made use of in the investigation of the cherry-red substance. Samples of the impure material which had been re-crystallized but once were examined in both water and Canada Balsam. The particles appeared somewhat leaf-like, white to yellow in color, and contaminated with a dark brown substance adhering very closely to the particles. The crystalline nature of the substance could not be clearly determined. Samples which had been re-crystallized four times and which were not brown, but light fawn, in color, were definitely crystalline, showing strong blues and reds with rotation of the nicols. Whereas the first sample was contaminated to the extent of 20-30% with the dark brown impurity, the second sample was only contaminated to the extent of a few per cent.

It was impossible to absolutely remove this last trace of impurity, even by ten re-crystallizations. And in view of the interchangeability of the tarry material and the cherry-red substance, it seemed probable that the fawn-colored material was the true crystalline form, while the tarry condition represented an amorphous state. The reason for the lack of color in the sample first examined by polarized light may be that a small amount of the amorphous tar had formed a solid solution with the crystal, thereby masking its strongly bi-refractive nature.

The fawn-colored crystals were orthorhombic in form and strongly birefractive, giving striking colors on rotating the nicol. The crystals were bi-axial and optically positive, the plane of cleavage being perpendicular to the acute bisectrix.

The crystals gave a violet color reaction with conc. H_2SO_4 and a yellow with conc. HCl and HNO_3. They dissolved with difficulty in 10% NaOH and were easily soluble in benzene, chloroform, acetone and slightly soluble in ether and ligroin. They were insoluble in water.

The melting point was found to be 112°.

The results of elementary analysis for carbon and hydrogen are given below. The samples used were the purest obtainable, having been re-crystallized seven times, and were a light fawn in color. They were dried over the week-end in a vacuum dessicator. In this connection it should be pointed out that the dessicator was not completely evacuated on the suction pump since such a procedure would cause the crystals to be converted partially to the tar. A moderate vacuum only could be tolerated. It was also necessary to leave the dessicator in a cool place as a further precaution.

(a) Weight of sample = 0.0936 gms.

Weight of carbon dioxide formed = 0.2898 gms.

Weight of water vapor formed = 0.0531 gms.

$$\therefore \% C = \frac{(12)(0.2898)(100)}{(44)(0.0936)} = 84.44$$

$$\% H = \frac{(2)(0.0531)(100)}{(18)(0.0936)} = 6.30$$

(b) Weight of material = 0.0801 gms.

Weight of carbon dioxide produced = 0.2494 gms.

Weight of water produced = 0.0448 gms.

$$\therefore \% C = \frac{(12)(0.2494)(100)}{(44)(0.0801)} = 84.92$$

$$\% H = \frac{(2)(0.0448)(100)}{(18)(0.0801)} = 6.21$$

The results obtained by Kjeldahl analysis for nitrogen are noted below. These analyses were carried out on the purest sample obtainable, blanks being run on the reagents.

(a) Weight sample = 0.8335 gms.

Volume of 0.10 N NaOH used = 16.5 ccs. (corr.).

Volume of 0.10 N ammonia evolved = 30.2 ccs. (i.e., 46.7 - 16.5)

$$\therefore \% N = \frac{(30.2)(14)(0.10)(100)}{(1000)(0.8335)} = 5.07$$

(b) Weight sample = 0.3774 gms.

Volume of 0.10 N NaOH req'd. = 33.2 ccs. (corr.).

Volume of 0.10 N ammonia evolved = 13.5 ccs. (i.e., 46.7 - 33.2)

$$\therefore \% N = \frac{(13.5)(14)(0.10)(100)}{(1000)(0.3774)} = 5.01$$

As a check on the identity and purify of the cherry-red substance, a second analysis (Kjeldahl) was carried out on a second sample of material, with the exception that in this case the purified material was dissolved in strong alcohol and re-crystallized, but in such a way as to encourage the formation of a small amount of tar, the latter solidifying with the fawn-colored needles. The proportions of the two forms were approximately equal. The solidified material

was pulverized in a mortar and dried in the vacuum dessicator (at partial vacuum only) for three days.

(a)   Weight sample = 0.1397 gms.

Volume 0.10 N NaOH req'd. = 41.5 ccs. (corr.).

Volume 0.10 N ammonia evolved = 5.2 ccs. (i.e., 46.7 - 41.5).

$$\therefore \ \% N = \frac{(5.2)(14)(0.10)(100)}{(1000)(0.1397)} = 5.21$$

(b)   Weight sample = 0.1674 gms.

Volume 0.10 N NaOH req'd. = 40.9 ccs. (corr.).

Volume 0.10 N ammonia evolved = 5.8 ccs. (i.e., 46.7 - 40.9).

$$\therefore \ \% N = \frac{(5.8)(14)(0.10)(100)}{(1000)(0.1674)} = 4.85$$

The slight discrepancy in the results obtained (0.36) may be due to experimental error or to some slight chemical decomposition in the sample. However, the two results check closely enough to suggest that the tarry solid is closely related, if not identical, to the fawn-colored crystals. Further evidence of the relationship between these two forms is seen from the fact that the same reduction product is obtained on appropriate treatment. Similarly, both yielded the same bromine derivative and the same semicarbazone. These will be dealt with in subsequent paragraphs.

In order to get a correct molecular formula, the freezing point method was employed for the determination of the molecular weight. The solvent used in this case was benzene of high purity. The depression constant (K_f) for benzene is 5.12.

(a)   Weight sample = 0.0841 gms.

Freezing point of benzene = 6.02⁰.

Freezing point of solution = 5.93⁰.

Freezing point depression = 0.09⁰.

Weight of solvent = 21.77 gms.

$$\therefore M = \frac{(.0841)(5.12)(1000)}{(21.77)(0.09)} = 276.7$$

(b) Weight sample = 0.1793 gms.

Freezing point of solvent = 6.020°.

Freezing point after addition of sample = 5.845°.

Freezing point depression = 0.175°.

$$\therefore M = \frac{(0.1793)(5.12)(1000)}{(21.77)(0.175)} = 241.0$$

(c) Weight sample = 0.2742 gms.

Freezing point of solvent = 6.020°.

Freezing point after addition of sample = 5.770°.

Freezing point depression = 0.250°.

$$\therefore M = \frac{(0.2742)(5.12)(1000)}{(21.77)(0.250)} = 258.0$$

On the basis of these results, the formula of the 112° substance is $C_{19}H_{17}ON$.

The oxygen atom in the 112° compound was found to be ketonic in character since it did not reduce Fehling's solution, Schiff's reagent or an ammoniacal silver solution, but formed a silvery grey semicarbazone on treatment with semicarbazide hydrochloride. The yield was small in view of the fact that less than a gram of the 112° substance was available for the reaction. Hence it was only possible to carry out a Kjeldahl analysis for nitrogen. The sample analysed was re-crystallized twice from benzene and dried for four days in the vacuum dessicator. It melted sharply at 218°. An identical melting point was obtained on crystallizing from alcohol.

(a) Weight sample = 0.0769 gms.

Volume 0.10 N NaOH used = 42.4 ccs. (corr.).

Volume 0.10 N ammonia evolved = 4.3 ccs. (i.e., 46.7 - 42.4).

$$\therefore \% N = \frac{(4.3)(14)(0.10)(100)}{(0.0769)(1000)} = 7.83$$

(b) Weight sample = 0.0927 gms.

Volume 0.10 N NaOH req'd. = 41.6 ccs. (corr.).

Volume 0.10 N ammonia evolved = 5.1 ccs. (i.e., 46.7 - 41.6).

$$\therefore \% N = \frac{(5.1)(14)(0.10)(100)}{(0.0927)(1000)} = 7.70$$

A bromine derivative was prepared by dissolving 0.3 gms. of the 112° substance in 10 ccs. strong ethanol, cooling, and adding a few drops of liquid bromine. After standing half an hour, the bromine derivative was precipitated out by the addition of a few drops of water. It was re-crystallized by dissolving in alcohol and re-precipitating with water. The sample was creamy-white in color and melted, when dry, at 126-128°. Due to a lack of sufficient material, it was not possible to prepare enough of the bromine derivative for analysis.

The same bromine substance was prepared from a sample of the dried tarry material. In this case, the tar was prepared by dissolving the 112° substance in alcohol and precipitating with water under such conditions that the tar came down. This was separated from the remainder of the solution by decanting the latter, and dried on cooling. The reason for preparing the tar in this manner, rather than using the crude tar, was that the intention of the investigator was to obtain additional proof as to the relationship between the tar and the 112° compound.

The presence of a keto-oxygen atom in the molecule of the 112° substance suggested the fact that reduction would convert it either into a phenol or into an alcohol group (OH). If such a derivative could be obtained in the pure state, the difficulties of working with the fawn-colored material would be eliminated. The determination of the basic structure of the substance would be facilitated since reduction would only affect the degree of oxidation of the O-atom.

The 112° substance was dissolved in a minimum amount of benzene,
filtered, and the filtrate treated with a solution of SnCl$_2$ contain-
ing a little dilute hydrochloric acid. A yellow solid was precipitated.
This could also be obtained with SnCl$_2$ alone, indicating the ease of
the reduction. The latter reaction might be promoted by some HCl
formed by hydrolysis of the salt, although the extent of such hydro-
lysis would be very small. The reduction product was filtered twice
with a 5% HCl solution and then with six washings of distilled water,
until the filtrate no longer produced a precipitate with silver
nitrate solution. The lemon-yellow solid was scraped off with a
spatula and transferred to a beaker. It was left over the week-end
to dry in a vacuum dessicator.

The only solvent which could be used for re-crystallization
of the reduction product was benzene, although this manipulation
was accompanied by extreme difficulty due to the very slight solub-
ility of the compound. The benzene used was dried overnight in a
flask containing anhydrous CaCl$_2$. On re-crystallization, the color
of the crystals darkened to orange-yellow. They were small and well-
formed, melting at 158°, sharply, after four crystallizations. They
possessed a slight sheen or glitter.

The reduction product was easily soluble in acetone and alco-
hol, less soluble in hot benzene, chloroform and water, and insol-
uble in ether, petrol ether and ligroin. It showed an intense yellow
color with conc. sulfuric acid. Acid permanganate solution is decol-
orized in the cold, as is bromine water, the latter reaction being
accompanied by the production of a slight milkiness, but not by the
evolution of HBr. The reduction product was soluble in dilute HCl
with the production of a yellow color, but did not seem to dissolve
in 10% NaOH solution. Ammoniacal vapors were produced on heating with

a 50% KOH solution.

Two combustions were carried out on a sample of the 158° reduction product that had been re-crystallized four times from benzene and then dried in the vaccum dessicator for two days. It was, however, noticed that an inorganic residue was left in the combustion boat, probably $SnCl_2$. The presence of this impurity was not suspected in view of the sharp melting point and in view of the number of crystallizations carried out. Further, the melting point was the same after the second, third and fourth re-crystallizations. One possibility considered was that a compound was formed with the true reduction product, but this was not borne out by the variation in the amount of tin salt in the 158° material. In the two samples burned out in the combustions for carbon and hydrogen, the amounts of inorganic residue were 23.35 and 19.26 per cent.After making allowance for the fact that the samples contained only 76.65% and 80.74% of the reduction compound, respectively, the calculations of carbon and hydrogen content showed the following values: carbon 56.50 amd 52.40%; hydrogen 6.01 and 4.57%. These results are mentioned in passing, but are not submitted as accurate analyses of the reduction product. It was not possible, due to the small amount of material, to prepare more of the reduction compound, although by means of a different procedure. This would be necessary if a correct determination of carbon and hydrogen is to be obtained.

Kjeldahl analysis for nitrogen gave the values 3.48 and 3.55%, but these can not be accepted due to the fact that the samples contained the inorganic impurity. On the basis of an 80% organic content, these figures could be corrected to read about 4.5%.

There could be no doubt that treatment of the 112° substance with acid stannous chloride had been accompanied by reduction of the

keto-oxygen atom. A Schotten-Baumen reaction was carried out on two

grams of the impure reduction product, using a 10% NaOH solution to

assist the reaction. An unusually large amount of heat was evolved,

accompanied by the formation of a light brown benzoyl derivative.

This was extracted from the stannous chloride by means of boiling

benzene, dried with anhydrous $CaCl_2$, and filtered. Well-defined

crystalline flakes separated out on evaporation of the benzene,

melting at 160-161°. Due to their different crystalline nature,

color, solubility relationships and a considerable lowering in a

mixed melting point test, these were shown to be different from the

158° reduction product.

Several grams of the benzoyl derivative were re-crystallized

twice from benzene and set aside to dry in a vacuum dessicator.

These crystals melted sharply at 161° and appeared suitable for

elementary analysis. The results obtained for nitrogen by the

Kjeldahl method are as follows:

(a) Weight sample = 0.1234 gms.

Volume 0.10 N NaOH req'd. = 41.0 ccs. (corr.).

Volume 0.10 N ammonia evolved = 5.7 ccs. (i.e., 46.7 - 41.0).

$$\therefore \% N = \frac{(5.7)(14)(0.10)(100)}{(0.1234)(1000)} = 6.47$$

(b) Weight sample = 0.1400 gms.

Volume 0.10 N NaOH req'd. = 40.4 ccs. (corr.).

Volume 0.10 N ammonia evolved = 6.3 ccs. (i.e., 46.7 - 40.4).

$$\therefore \% N = \frac{(6.3)(14)(0.10)(100)}{(0.1400)(1000)} = 6.30$$

Combustions for carbon and hydrogen revealed the following

values:

(a) Weight sample = 0.838 gms.

Weight carbon dioxide evolved = 0.2427 gms.

Weight water evolved = 0.0428 gms.

$$\therefore \% C = \frac{(12)(0.2427)(100)}{(44)(0.0838)} = 78.89$$

$$\% H = \frac{(2)(0.0428)(100)}{(18)(0.0838)} = 5.67$$

(b) Weight sample = 0.0854 gms.

Weight carbon dioxide absorbed = 0.2480 gms.

Weight water absorbed = 0.0424 gms.

$$\therefore \% C = \frac{(12)(0.2480)(100)}{(44)(0.0854)} = 79.22$$

$$\% H = \frac{(2)(0.0424)(100)}{(18)(0.0854)} = 5.52$$

The molecular weight of the benzoyl derivative was determined by the micro method of Rast, using camphor of melting point 178° and depression constant 40,000.

(a) Weight sample = 0.0060 gms.

Weight camphor = 0.0724 gms.

Melting point of mixture = 163°.

Melting point depression = 15°.

$$\therefore M = \frac{(6.0)(40,000)}{(15)(72.4)} = 221.0$$

(b) Weight sample = 0.0064 gms.

Weight camphor = 0.0690 gms.

Melting point of mixture = 162°.

Melting point depression = 16°.

$$\therefore M = \frac{(6.4)(40,000)}{(16)(69.0)} = 232.0$$

On the basis of the above results, the formula of the 158° substance has been calculated as $C_{14}H_{12}ON$.

SUMMARY.

SUMMARY.

1. A comprehensive review of the "diene synthesis" or "Diels-Alder reaction" has been presented and a number of its more important applications have been discussed.

2. A series of experiments have been carried out in an endeavour to effect a diene synthesis between a conjugated diene and a nitrogen-containing philodiene component, by 1,4-addition. The pairs of reactants employed were: cinnamal acetophenone and benzal aniline; anthracene and benzal aniline; cinnamal acetophenone and phenyl isocyanate; anthracene and benzonitrile; cinnamal acetophenone and benzonitrile; and cinnamal acetophenone and cinnamal aniline. A diene reaction could not be detected, although products were obtained with cinnamal acetophenone and benzal aniline, one melting over 300° and the other at 122°. Due to the small yields, these could not be analysed. The reaction of phenyl isocyanate on cinnamal acetophenone was accompanied by the formation of carbanilide, even under strictly anhydrous conditions.

3. A series of experiments have been carried out in an endeavour to effect a diene synthesis by means of 1,4-addition between an anil conjugated with an olefinic linkage and a non-nitrogenous philodiene component. The reaction pairs used were: cinnamal aniline and anthraquinone-1,4; cinnamal aniline and cinnamic aldehyde; and cinnamal aniline and quinone.

4. The reaction of cinnamal aniline and quinone by fusion gave rise to 2,5-dianilino-quinone and 2,5-dianilino-quinone-monoanil, with hydroquinone and cinnamic aldehyde as by-products. The reaction

in chloroform yielded azophenin instead of 2,5-dianilino-
quinone-monoanil. By carrying out the reaction in alcohol, 2,5-
dianilino-quinone was produced, accompanied by a fawn-colored
substance, melting at 112^0, and possessing the composition
$C_{19}H_{17}ON$. The latter yielded a semicarbazone melting at 218^0,
a bromine derivative melting at $126-128^0$ and a reduction
product containing an OH group. The semicarbazone has been
analysed for nitrogen, while the reduction product has been
found to be impure, due to a very close association with $SnCl_2$.
The reduction product has been converted to a benzoyl derivative
of formula $C_{14}H_{12}ON$, melting at $160-161^0$.

5. No reaction of the "diene" type has been found to occur, under
the conditions employed.

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