THE DIELS–ALDER DIENE SYNTHESIS

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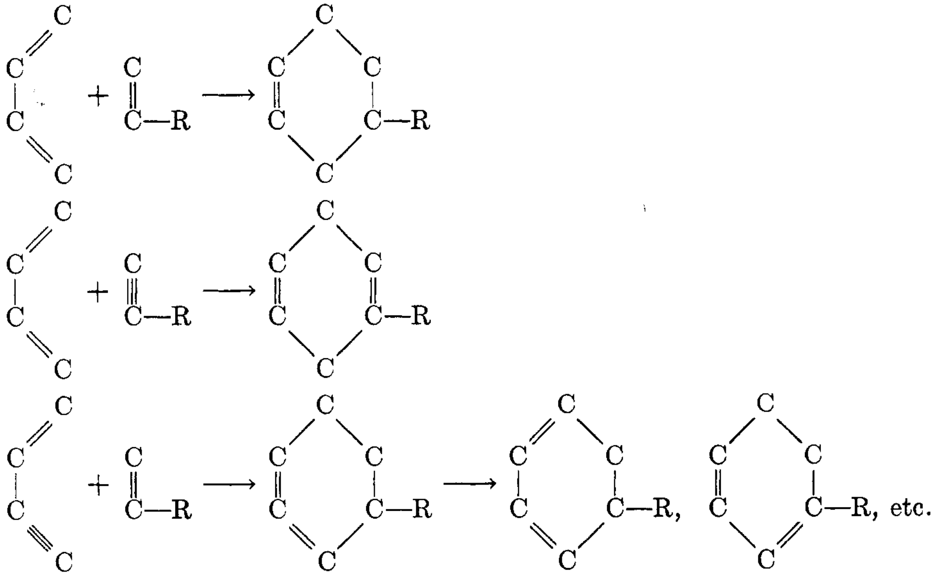
I. INTRODUCTION

A. Definition

The diene synthesis (often termed the Diels–Alder reaction or the Diels–Alder diene synthesis) is more than the name implies. Enynes and diacetylenes may also undergo typical diene synthesis reactions. Basically, the great majority of these syntheses may be classified under one of the following types:



R in the above examples is usually of the types which terminate in a carbonyl group attached directly to one of the olefinic or acetylenic carbon atoms. Representative dienophiles of this type are acids, their anhydrides, esters, and halides, and also aldehydes, ketones, or quinones. The carbonyl group is not a necessary structural feature, however. It will be shown later that R may be acetoxyl (as in vinyl acetate), nitro, sulfonyl, cyano, amino, vinyl, or even hydrogen. Diene syntheses proceed with greatest facility, however, when R contains the carbonyl group in the manner indicated above.

B. Nomenclature

The compound which acts in the capacity of C═C—R or C≡C—R is designated as the *philodiene* or *dienophile*; the latter term seems less confusing. The etymology of these terms from the Greek is apparent. The other compound involved in the reaction, whether it be diene, polyene, enyne, or diyne, will be referred to as the *diene* in this review purely for the sake of convenience. The reaction product is the *adduct* or *adject*. The *diene* and *dienophile* are often designated collectively by the term *generators*.

C. Dienes

The forms which the diene may assume are amazingly variable. For instance, the diene may be simple, as piperylene or isoprene; or it may be more complex, as furan, pyrrole, thebaine, tetraphenylcyclopentadienone, pyridine, anthracene, ergosterol, cycloheptadiene, α-naphthylacetylene, 3,4-dihydro-1-vinylnaphthalene, 1,3-menthadiene, or 1,2,5,6-dibenzanthracene. Neither thionessal (tetraphenylthiophene) nor thiophene itself has been observed to add dienophiles, and the same is probably true of the thiotolenes, thioxenes, and selenophene. The whole subject of non-addition of dienophiles by thiophene and its derivatives has, however, been reopened by Clapp's discovery (400) that one compound of this series will add dienophiles at temperatures in the neighborhood of those employed for sulfur dehydrogenation of hydroaromatic compounds. In the investigations of the other thiophene compounds it is doubtful that the temperatures used by Clapp were employed. Clapp's reaction occurs with the evolution of hydrogen sulfide as in a sulfur dehydrogenation, and it may be that other thiophenes will respond under similar conditions.

Benzene and its simpler derivatives have been observed not to add dienophiles. Compounds do exist, however, in which one of the diene double bonds is a Kekulé double bond. Anethole and α-phenylstyrene are compounds of this type; they add maleic anhydride with reduction of one of the benzene rings to a cyclohexadiene ring. α-Vinylnaphthalene acts in a similar manner. One example (9,10-anthraquinone) appears to be known in which a lone benzene ring is able to add dienophiles, but this is disputed by a negation published prior to the above report. Heterocyclic dienes containing nitrogen as a part of the ring (pyrrole or pyridine) invariably react abnormally. Elsewhere the diene synthesis usually gives products the formulas of which are in accordance with the general statement of the synthesis as given by the reaction types on page 320. It is occasionally found that certain compounds containing isolated double bonds, one double bond, or even no double bonds at all will add dienophiles.

This phenomenon usually can be explained by assumption of a preliminary isomerization or conversion of the compound in question to another substance containing isolated double bonds, and eventually to one containing conjugated double bonds which is able to add the dienophile. Such examples are found almost exclusively among the terpinoids.

Occasionally the adduct will decompose in a predictable manner when heated, or upon formation if the temperature of the reaction mixture of diene and dienophile is sufficiently high. Adducts of acetylenic dienophiles with cyclohexadienes, cyclopentadienones, and derivatives of the lactone of 1-hydroxy-4-carboxy-1,3-butadiene (cumalin) evolve ethylenes, carbon monoxide, and carbon dioxide, respectively, when pyrolyzed.

Only a limited number of enynes has been studied. Butz has done most of the existing work in this field which, though not well developed, offers considerable promise.

At least one phase of the well-known trimerization of acetylene to benzene might be regarded as a diene synthesis. This phase would be the addition of a mole of acetylene to the dimer of acetylene (vinylacetylene), yielding benzene. It should be said that there is apparently no conclusive proof that the trimerization proceeds through such a mechanism; but since no proof of any other definite mechanism appears to have been established, the author feels that the mechanism of the diene synthesis for the formation of benzene is as admissible for consideration as any other mechanism.

D. Allenes

Dienes containing the grouping C=C=C do not react directly with dienophiles. Reaction is possible through the mechanism of an initial isomerization to a conjugated system, such as could occur at elevated temperatures. A few allenes have been studied; thus, 1-cyclohexyl-2,3-pentadiene (2) was found not to react with maleic anhydride (see also 403, 404).

E. Tests for dienes

Since a transient yellow color is observed in the reaction of maleic anhydride with dienes, it had been proposed that the appearance of such a color on treatment of an unknown substance with maleic anhydride was a positive test for a conjugated dienoid system. Sandermann (323, 324) found that the test was unreliable, since positive results were secured with resorcinol, hydroquinone, pyrocatechol, benzidine, diethylaniline, diphenylamine, brucine, anethole, and carbazole, as well as with ergosterol, α-phellandrene, abietic acid, isoeugenol, anthracene, and pyrene. Apparently a negative test is of more value than a positive test.

The Fieser test (203) for conjugated dienes consists in treating the unknown with a solution of diazotized *p*-nitroaniline. If an orange color develops within a reasonable time, the test is positive. Arbuzov and Rafikov (60) believe the test to be unreliable, for in the reaction of dienes with the Fieser reagent some dinitrodiazobenzene is always formed. The structure of the coupling product with butadiene (60) is probably *p*-nitrobenzeneazo-1-butadiene, for reduction gives *p*-phenylenediamine and pyrroline. Goodway and West (229) obtained positive tests using caryophyllene, α- and β-phellandrenes, α-pinene, 3-carene, and dipentene. Save for the phellandrenes, not one of these compounds contains a conjugated system.

F. trans-Butadienoid systems

The Bredt addition rule (322, 324) postulates that in cyclic dienes, the two double bonds must be in the same ring in order that addition of dienophiles may occur according to the diene synthesis. In contradiction to this rule, it is found that bis-1-dialin (3,4,3′,4′-bis(dihydro-α-naphthyl)) adds dienophiles without double-bond wandering prior to addition; and many other similar examples may be found, such as the addition of dienophiles by 2,3,4,5,2′,3′,4′,5′-octahydrobiphenyl. The rule should be modified by stating that the two double bonds of the conjugated system must be in the *cis*-configuration with each other or else must rearrange to such a configuration before addition can occur. In the majority of cases free rotation of the single bond between the 2- and 3-carbon atoms of the butadienoid portion of the molecule makes assumption of either a *cis*- or a *trans*-configuration a simple matter. In certain cases, however, only a *trans*-butadienoid system may exist without placing a large amount of strain on the molecule. The *trans*-butadienoid systems of β-phellandrene and 3,5-cholestadiene (cholesterilene) cannot well change into *cis*-butadienoid systems without double-bond migration. Addition to these molecules proceeds with great difficulty and probably with rearrangement and polymerization. Thus, β-phellandrene and maleic anhydride give tars and a small yield of the adduct of α-phellandrene and maleic anhydride. The adduct is obtainable only on vacuum distillation of the tar (228). Cholesterilene (332) adds maleic anhydride (348) only under drastic conditions to give a product the alkali salts of which are insoluble in water (distinction from other sterol–maleic anhydride adducts), and which are probably polymeric. Certain other sterol dienes of *trans*-butadienoidal configuration have been shown not to react with maleic anhydride (405).

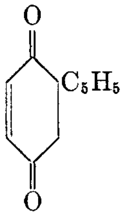
II. DISCOVERY OF THE DIENE SYNTHESIS

Isolated examples of the diene synthesis appear in the literature of the past half-century, but the extensive development of the subject did not begin until 1928, when Diels and Alder recognized that a reaction observed by Euler and Josephson (195) between *p*-benzoquinone and isoprene was strikingly similar to a reaction—observed by Diels, Blom, and Koll (157)—of azodicarboxylic ester with cyclopentadiene and also with isoprene derivatives. That the reaction was possibly of general application can be sensed from the paper of Diels, Blom, and Koll, and apparently the years 1925–1928 were devoted to experimentation designed to show that such actually was the case.

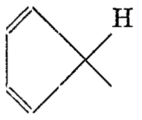
An early series of papers by Zincke and coworkers (376–378) dealt with the reactions of 1,2,4,5,5-pentachlorocyclopenten-3-one. Loss of a molecule of hydrogen chloride from this compound gave tetrachlorocyclopentadienone. Since this compound contains the structures of reactive diene and reactive dienophile, it was not isolated as such, but rather as the dimer which was formed according to the Diels–Alder diene synthesis. The dimer was an intermediate product in a series of reactions ending in octachlorohydrindone, which was easily reduced to hexachloroindone.

Staudinger (337) has made a very famous series of researches on polymerization and on compounds of high molecular weight. It was his opinion that the dimerization of cyclopentadiene occurred to give compounds containing cyclobutane rings. The dimer of cyclopentadiene was considered to be the product of the 1,2-addition of two molecules of monomer to each other. The structure of such a product would be that of a cyclobutane with two cyclopentene rings fused to it. In a brilliant series of papers on the structure of cyclopentadiene polymers, Alder and Stein showed that these were formed by the 1,4-addition of a molecule of cyclopentadiene to a double bond of cyclopentadiene monomer or polymer. The structure of cyclopentadiene dimer (dicyclopentadiene) is that of a partially hydrogenated indene possessing a methylene bridge across the 4- and 7-positions. 1,4-Addition of cyclopentadiene to this compound occurs at the double bond of the six-membered ring, giving cyclopentadiene trimer. In the production of higher polymers, 1,4-addition of cyclopentadiene to its polymer always occurs at the double bond of the terminal six-membered ring and never at the double bond of the five-membered ring.

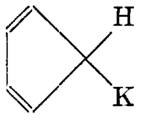
Albrecht (379) described, in 1906, certain experiments in which cyclopentadiene was caused to react with quinones and ketones. The reaction product of *p*-benzoquinone with an equimolecular quantity of cyclopentadiene was thought to be I. While the structure of the C_5H_5 group was not stated explicitly,



I



II



III

it probably was intended to be as shown in formula II, for cyclopentadiene forms a potassium derivative (III).

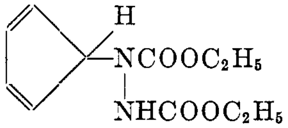
Albrecht was not altogether certain of the validity of structure I for his product. He also found that a second mole of cyclopentadiene would react with *p*-benzoquinone; the structure assigned to this product was that of 2,5-bis-cyclopentadienyl-tetrahydro-*p*-benzoquinone, although he recognized the possibility of 2,6 and 2,3 isomerism. Other quinones, such as chloranil and 1,4-naphthoquinone, were shown to react. A period of 2 hr. was required for the reaction of *p*-benzoquinone with a benzene solution of cyclopentadiene at

0°C., while chloranil required two weeks; both chloranil and 1,4-naphthoquinone would react with only 1 mole of the diene. 9,10-Anthraquinone, 9,10-phenanthrenequinone, β-naphthoquinone, benzil, benzalacetone, dibenzalacetone, phorone, and dibenzoylstyrene would not react under the mild conditions used. Since that time it has been found that β-naphthoquinone and the unsaturated ketones will react at higher temperatures.

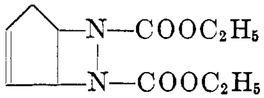
Staudinger's work suggested that the condensation product of cyclopentadiene with *p*-benzoquinone was analogous to the dimer obtained from cyclopentadiene, for the structure he assigned to the condensation product was that of a compound formed by addition of cyclopentadiene and *p*-benzoquinone by the 1,2-addition mechanism.

In 1920, Euler and Josephson (195) published the paper already referred to, which concerned the reaction of isoprene with *p*-benzoquinone. The product obtained was assigned the structure of 2,6-dimethyl-1,4,5,8,1a,4a,5a,8a-octahydro-9,10-anthraquinone. This structure was nearly correct, for it was shown later (153) that the product was really a mixture of the 2,6- and 2,7-dimethyl-1,4,5,8,1a,4a,5a,8a-octahydro-9,10-anthraquinones.

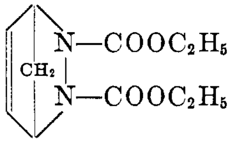
The paper of Diels, Blom, and Koll (157) was next to appear. They paid particular attention to the structure of the reaction product that was obtained from cyclopentadiene and azodicarboxylic ester. In accordance with the assumptions of Albrecht, the structure of the product was first given as shown in formula IV. The assumptions of Staudinger led to formulation of the structure as V, while the work of Euler and Josephson led to formulation of the structure as VI. Since the adduct took up only two atoms of hydrogen or bromine, structure IV was invalidated. Confirmation of formula VI was secured in several ways. First, the methylene bridge of the hydrogenated adduct (VII) was broken with hydrogen chloride to give a methylchloropiperidazine derivative (VIII). Secondly, the same hydrogenated adduct was saponified and decarboxylated to give an endomethylenepiperidazine (IX), vigorous reduction of which gave 1,3-diaminocyclopentane. No such compound could have been obtained from either compound IV or compound V.



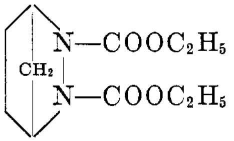
IV



V



VI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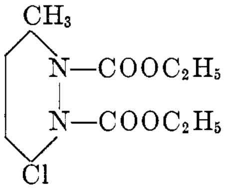
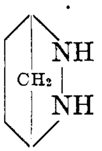

VIII


IX

These facts threw grave doubts upon the Albrecht structure for the adducts of cyclopentadiene and *p*-benzoquinone, and furnished the initiative for the beginning of a program of research marked by the appearance of the first epochal paper by Diels and Alder (136). It should be noted that a considerable number of patents on the additions of dienes and dienophiles were taken out almost simultaneously by the I. G. Farbenindustrie A.-G.

In their first paper on diene syntheses, Diels and Alder presented evidence in support of their belief that Albrecht's addition compound between cyclopentadiene and α-naphthoquinone was 1,1a,4,4a-tetrahydro-1,4-endomethylene-9,10-anthraquinone, since the corresponding adduct between α-naphthoquinone and butadiene was easily oxidized to anthraquinone. Later (146) they were able to convert the cyclopentadiene adduct itself to anthraquinone, thus meeting the objections of Staudinger who insisted that the adduct was formed by 1,2-addition of cyclopentadiene to the quinone ring of α-naphthoquinone. The views of Diels and Alder concerning the structures of their products were the subjects of intense criticism at first, for it was thought that these might conceivably be "molecular compounds" somewhat akin to the compounds of the polynuclear hydrocarbons with picric acid, 1,3,5-trinitrobenzene, and styphnic acid. This view received apparent substantiation by the discovery that certain of the adducts would decompose into their generators on distillation. However, the formation of derivatives of anthracene could not be explained by the view which assumed that the adducts were so-called molecular compounds, and eventually the differing stabilities of individual adducts were made use of in the first preparation of the acid chloride of acetylenedicarboxylic acid (172) and in other ingenious, convenient, and useful syntheses.

The study of the diene synthesis has been pursued intensively since the publication of the initial papers of Diels and Alder. It is a matter of some difficulty to find a volume of a chemical journal of today which does not contain an article which bears on some phase of the diene synthesis. Today one sees polyesters the acid fractions of which are prepared by the diene reaction between abietic acid and maleic anhydride (304). By offering means for the quantitative determination of conjugated dienes in petroleum products, the diene reaction will facilitate the perfection of processes which produce motor fuels of initially high octane ratings and high lead susceptibilities combined with improved stabilities. The number of possible practical applications of the general principle of the diene synthesis is virtually unlimited.

III. DIENOPHILES

The types of compounds which may be used as dienophiles will be considered initially, for the majority of studies in the field of the diene synthesis were based primarily on the determination of the capacity of the compound under investigation to act as a diene in the diene synthesis. Since a considerable amount of work has been conducted with regard to quinones in the diene synthesis, these dienophiles will be discussed in the section to follow.

The types of dienophilic compounds which may be employed in the diene synthesis are nearly as diverse in character as the types of compounds which may serve as dienes. They may be added to the reaction mixture as such, or prepared *in situ* (47, 239).

A. Olefinic dienophiles

As stated previously, the dienophiles which add most readily are those containing the groupings C═C—C═O or C≡C—C═O, and these have been the most extensively studied of dienophilic substances. With them, many diene syntheses occur readily at room temperature to give nearly quantitative yields of adducts. Examples of such dienophiles are crotonaldehyde, acrolein, 3,4-diketo-1-pentene, *sym*-dibenzoylethylene, 1-cyclopenten-3-one, acrylic acid, methyl acrylate, fumaroyl chloride, maleic anhydride, tetrolic acid, propiolic ester, acetylenedicarboxylic ester, *p*-benzoquinone, *α*-naphthoquinone, and *p*-toluquinone. With the exception of the nitrogen heterocycles, additions almost always occur in the manner indicated by the general rule for diene reactions as given on page 320. Thus, acrolein reacts with butadiene to give Δ^3-tetrahydrobenzaldehyde, and *α*-naphthoquinone and butadiene give 1,4,1a,4a-tetrahydro-9,10-anthraquinone (136). The nature of the solvent has no effect on the composition of the product, but ordinarily (196) reaction occurs about five times as rapidly in a polar solvent (ethanol) as it does in a non-polar solvent such as benzene.

Substituents located on the atoms of the carbon-to-carbon double bond (the "carbonylenic" (106) double bond) of the C═C—C═O group definitely decrease dienophilic character. Two exceptions to this rule are the carbonyl group (as shown by the dienophilic property of ethylenetetracarboxylic ester) and groups which may split off easily during the course or after the completion of the diene synthesis (these are notably hydroxyl and the halogens). All other substituents, with the possible exception of the cyano group, tend to decrease the dienophilic property of the carbonylenic double bond.

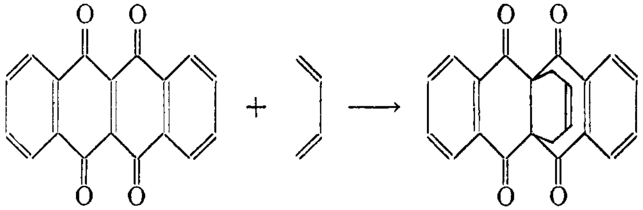
The extent to which these substituents suppress dienophilic property depends to a great extent on the type of dienophile. These may be roughly divided into four classes:

Class A: Alkyl and aryl derivatives of acrolein, maleic anhydride, acrylic acid, and methyl or other alkyl or aryl vinyl ketones. These include such compounds as cinchonic anhydride, cinnamic acid, benzalacetophenone, crotonaldehyde, etc. The decrease of dienophilic activity is not of great magnitude, and is usually manifested only in cases of dienes of low reactivity or which have groups on the 1- and 4-positions of the butadienoid system, when addition either is slow or fails to occur.

Class B: Fused-ring derivatives of acrolein, maleic anhydride, acrylic acid, and vinyl ketones. These include the adducts of equimolar quantities of diene and α,β-acetylenic acids and, generally speaking, all cyclene aldehydes, acids, and their derivatives, as well as cyclic ketones such as cyclopenten-3-one. Increase in unsaturation of the fused ring other than that of the carbonylenic group results in diminishing dienophilic properties. Thus, cyclohexene-1,2-dicarboxylic anhydride and 1,4-cyclohexadiene-1,2-dicarboxylic anhydride add butadiene with considerably greater difficulty than does maleic anhydride, while 1,3,5-cyclohexatriene-1,2-dicarboxylic anhydride (phthalic anhydride) has never been observed to add any dienes whatsoever.

Class C: Alkyl- or aryl-substituted quinones. Alkyl or aryl substituents of *p*-benzoquinone suppress the dienophilic activity of the carbonylenic group to which they are attached, but have little or no effect on the activity of the other carbonylenic group. Thus, *p*-toluquinone adds butadiene readily to give an adduct which does not possess an angular methyl group. This primary product of addition will add a second mole of butadiene to give an octahydroanthraquinone possessing an angular methyl group, but the addition takes place only with considerable difficulty.

Class D: Quinones with fused rings. These resemble Class B dienophiles. Thus, 1,4,5,8-tetrahydroanthraquinone will add dienes with considerable difficulty, and anthraquinone and phenanthrenequinone add no dienes whatsoever. However, fusion of two quinone rings to each other is actually the substitution of —CO— groups on a carbonylenic double bond, and therefore dienophilic activity is not suppressed. Naphthacenediquinone adds dienes almost as readily as does *p*-benzoquinone:



Naphthacenediquinone

To generalize broadly, it may be said that dienes and dienophiles will tend to react, as far as possible, to give adducts which do not possess angular, geminal, or spirane groupings on the carbon atoms which formerly were the carbon atoms of the carbonylenic double bond.

B. Acetylenic dienophiles

The above steric hindrance factors apply but little to the acetylenic dienophiles, since angular, geminal, or spirane groupings are not formed when these substances add dienes. Addition to eneynes will give benzene derivatives directly, while addition of these dienophiles to diynes has not been attempted. The structure of the product from such a reaction, if reaction occurs, is indeed a matter for conjecture. Certain acetylenic derivatives, including acetylene itself, have been added to highly reactive dienes such as phencyclone (1,4-diphenyl-2,3-(*o*,*o*′-biphenylene)cyclopentadienone), but the most thoroughly studied derivatives have been those possessing *carbonylynic* groups, such as propiolic acid, acetylenedicarboxylic acid, and their methyl and ethyl esters. The adducts derived from the interaction of equimolecular quantites of acetylenic dienophile and *true* diene possess the carbonylenic grouping (if derived from the acetylenic acids) and are potentially able to add a second mole of diene. These primary adducts are dienophiles of Class B (see page 328) and are subject to the limitations of reaction rates of that class. The fact that these primary adducts may be isolated, usually in good yields, indicates that the second mole of diene is added with considerably greater difficulty than the first. This is reminiscent of the increasing difficulty in the progressive introduction of nitro groups into the aromatic nucleus.

It will be noted that the aliphatic dienophiles which add dienes readily are of the same type as those which add ammonia, amines, and hydrogen cyanide with ease.

C. Non-carbonylenic dienophiles

Dienophiles which possess neither the carbonylenic nor the carbonylynic group usually require elevated temperatures and occasionally an antioxidant (hydroquinone) to minimize polymerization of the diene. Temperatures as high as 200°C. may be required, but dienophiles with strongly acid groups attached to the carbon atoms of the double bond do not require conditions which are quite that drastic.

Dimerization of dienes forms a special case wherein the diene acts as its own dienophile. This is perhaps the earliest known type of diene synthesis, and sufficient study has been made of the subject to warrant its being treated separately.

Table 1 summarizes the work accomplished with the addition of non-carbonylenic dienophiles to dienes. It will be noted that β-naphthol is capable of adding dienes, since its keto tautomer possesses the carbonylenic group.

Referring to table 1, it will be seen that secondary addition of cyclopentadiene to the normal adduct occurred in a number of cases, particularly those in which the reaction temperatures were higher than 100–110°C. Since the primary adducts are non-carbonylenic dienophiles, and since cyclopentadiene is a particularly reactive diene, addition to form secondary products is not surprising. The fact that considerable amounts of such products are formed indicates that the dienophilic activity of the dienophile employed in any one of these reactions is not much greater than that of the primary adduct with cyclopentadiene.

TABLE 1

Diene additions of non-carbonylenic dienophiles

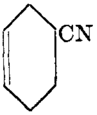
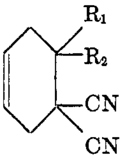
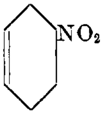
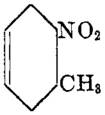
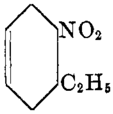
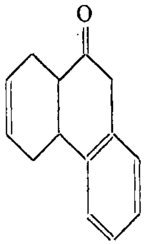
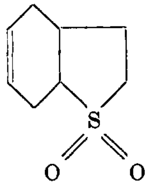
DIENE	DIENOPHILE	TEMPERATURE °C.	PRODUCT	REFERENCE
Butadiene..........	Acrylonitrile			(371)
Butadiene, isoprene.	Methylenemalononitrile derivatives			(382)
Butadiene..........	Nitroethylene	100–110		(20)
Butadiene..........	1-Nitro-1-propene	100–110		(20)
Butadiene..........	1-Nitro-1-butene	100–110		(20)
Butadiene..........	β-Naphthol			(321)
Butadiene..........	Dihydrothiophene dioxide	100–110		(20)

TABLE 1—*Continued*

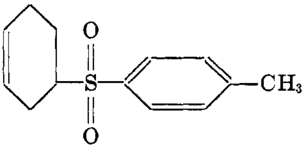
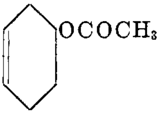
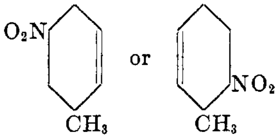
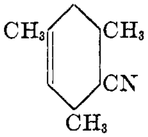
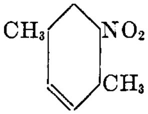
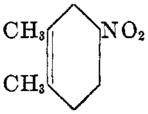
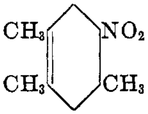
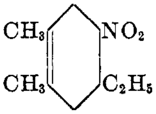
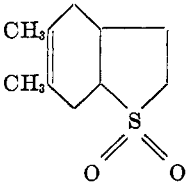
DIENE	DIENOPHILE	TEMPERATURE °C.	PRODUCT	REFERENCE
Butadiene..........	Vinyl-*p*-tolyl sulfone	100–110		(20)
Butadiene*.........	Vinyl acetate	180		(19)
Piperylene	Nitroethylene	100–110		(20)
1,3-Dimethylbutadiene...........	Crotononitrile			(246)
1,4-Dimethylbutadiene...........	Nitroethylene	100–110		(20)
2,3-Dimethylbutadiene...........	Nitroethylene	100–110		(20)
2,3-Dimethylbutadiene...........	1-Nitro-1-propene	100–110		(20)
2,3-Dimethylbutadiene...........	1-Nitro-1-butene	100–110		(20)
2,3-Dimethylbutadiene...........	Dihydrothiophene dioxide	100–110		(20)

TABLE 1—*Continued*

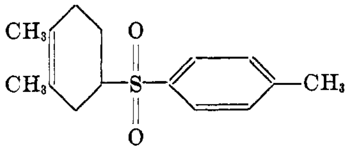
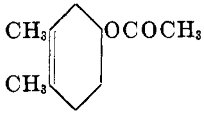
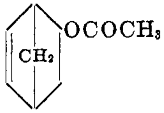
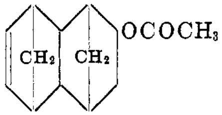
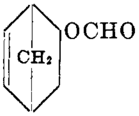
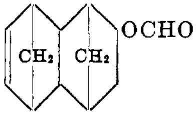
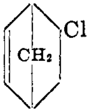
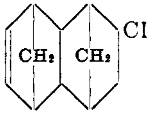
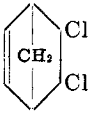
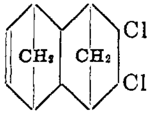
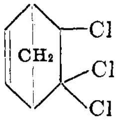
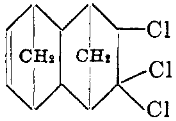
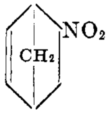
DIENE	DIENOPHILE	TEMPERATURE °C.	PRODUCT	REFERENCE
2,3-Dimethylbutadiene...........	Vinyl-*p*-tolyl sulfone	100–110		(20)
2,3-Dimethylbutadiene...........	Vinyl acetate	180		(19)
Cyclopentadiene† ..	Vinyl acetate	185–190	 and 	(19)
Cyclopentadiene† ..	Vinyl formate	180	 and 	(19)
Cyclopentadiene† ..	Vinyl chloride	185	 and 	(19)
Cyclopentadiene† ..	1,2-Dichloroethylene	185	 and 	(19)
Cyclopentadiene† ..	Trichloroethylene	185	 and 	(19)
Cyclopentadiene‡ ..	Nitroethylene	100–110		(20)

TABLE 1—*Continued*

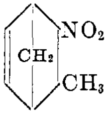
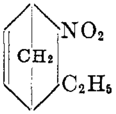
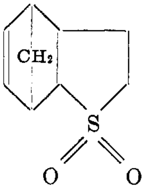
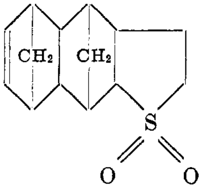
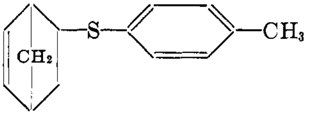
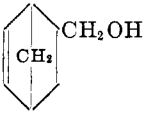
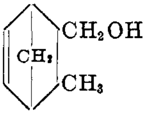
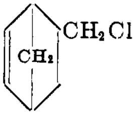
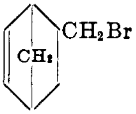
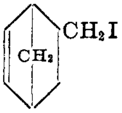
DIENE	DIENOPHILE	TEMPERATURE °C.	PRODUCT	REFERENCE
Cyclopentadiene . . .	1-Nitro-1-propene	100–110		(20)
Cyclopentadiene . . .	1-Nitro-1-butene	100–110		(20)
Cyclopentadiene† . .	Dihydrothiophene dioxide	180	 and 	(20)
Cyclopentadiene . . .	Vinyl-*p*-tolyl sulfide	100		(20)
Cyclopentadiene . . .	Allyl alcohol	175–180		(40)
Cyclopentadiene . . .	Crotyl alcohol	175–180		(40)
Cyclopentadiene . . .	Allyl chloride	175–180		(40)
Cyclopentadiene . . .	Allyl bromide	175–180		(40)
Cyclopentadiene . . .	Allyl iodide	100		(40)

TABLE 1—*Continued*

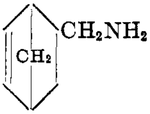
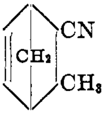
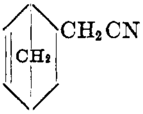
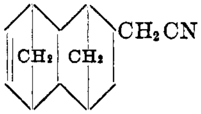
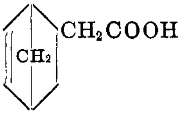
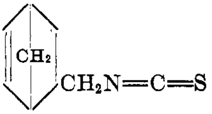
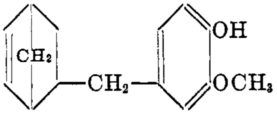
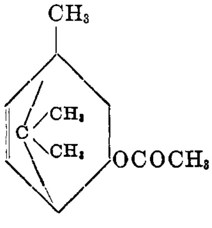
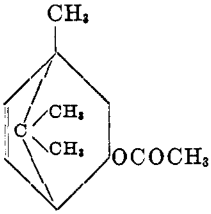
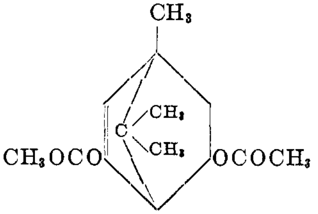
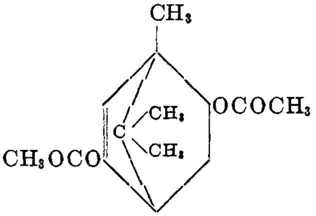
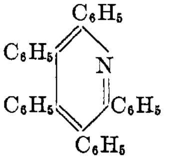
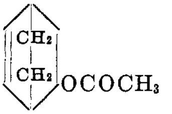
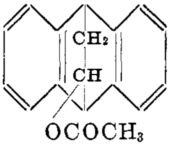
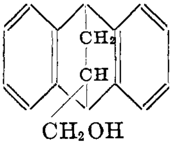
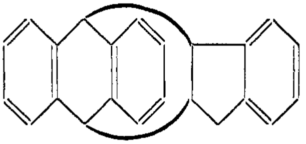
DIENE	DIENOPHILE	TEMPERATURE	PRODUCT	REFERENCE
		°C.		
Cyclopentadiene§ . .	Allylamine	175–180		(40)
Cyclopentadiene . . .	Crotononitrile			(246)
Cyclopentadiene† . .	Vinylacetonitrile	175–180	 and 	(40)
Cyclopentadiene . . .	Vinylacetic acid	175–180		(40)
Cyclopentadiene . . .	Allyl isothiocyanate	175–180		(40)
Cyclopentadiene . . .	Eugenol	175–180		(40)
1,1,2-Trimethylcyclopentadiene¶.	Vinyl acetate	235–240	 + 	(44)

TABLE 1—*Concluded*

DIENE	DIENOPHILE	TEMPERATURE	PRODUCT	REFERENCE
		°C.		
Methyl β-camphylate	Vinyl acetate	230	 or 	(44)
Tetraphenylcyclopentadienone	Benzonitrile	Reflux	 + CO	(181)
1,3-Cyclohexadiene	Vinyl acetate	180		(19)
Anthracene	Vinyl acetate	180		(19)
Anthracene	Allyl alcohol	210–220		(40)
Anthracene	Indene	200–210		(291)

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* Product is mainly 4-vinylcyclohexene, formed by dimerization of butadiene.

† The second product results from the addition of cyclopentadiene to the first product.

‡ Catalytic reduction of the adduct gave a nitro compound which yielded norbornylamine on reduction with zinc dust and acetic acid.

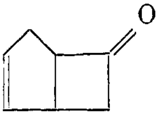
§ This adduct undergoes ring enlargement on treatment with nitrous acid, yielding 1,4-endomethylene-2-cyclohepten-6-ol.

¶ The *dl*-dehydrobornyl acetate was reduced and the product degraded to camphor.

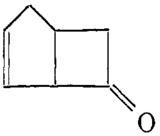
D. Ketenes

Ketene, $H_2C{=}C{=}O$, bears the same relationship to the carbonylenic dienophiles as the allenes bear to the conjugated dienes. Addition of dienes to the ketenes does not occur according to the diene synthesis. In a number of cases, 1,2-addition of dienes to ketenes does occur to form fused-ring derivatives of cyclobutanone. This reaction differs in no essential respect (Staudinger) from the reactions of ketenes with monoölefinic compounds, for these types also form fused-ring derivatives of cyclobutanone if the olefin itself is cyclic. Straight-chain olefins and diolefins form straight-chain cyclobutanone derivatives.

Cyclopentadiene has been reported to react with ketene (96), but this is disputed by Smith and his students (336). Brooks and Wilbert (96) obtained a cyclobutanone derivative, in which the location of the double bond is uncertain. The compound may have either structure I or structure II.

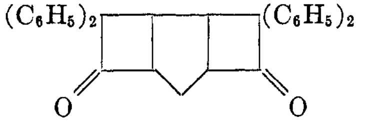


I

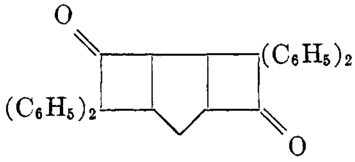


II

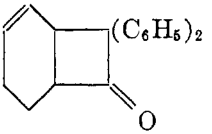
Diphenylketene and cyclopentadiene react at room temperature to yield the diphenyl derivative of I, according to Smith (336); Farmer and Farooq (198) report the product to be the diphenyl derivative of II. Reaction at higher temperatures results in the addition of a second mole of diphenylketene during a period of nine days (336) to give either III or its isomer IV. 1,3-Cyclohexadiene (198) gives V. By way of comparison, cyclopentene (336) gives VI and cyclohexene (198) gives VII.



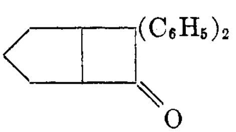
III



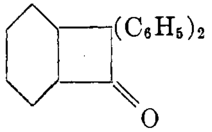
IV



V

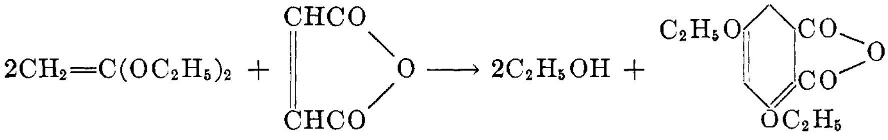


VI



VII

Ketene acetals may react in a unique manner with certain dienophiles. Condensation between 2 moles of ketene diacetal and 1 mole of maleic anhydride gives a diethoxydihydrophthalic anhydride (415):



Dimethylmaleic anhydride does not react, and the reactions with *p*-benzoquinone and with benzalacetophenone proceed normally to give cyclobutane derivatives, but acetylenedicarboxylic ester yields 3,5-diethoxyphthalic ester (415).

E. Quinones as dienophiles

The majority of diene syntheses employing *p*-benzoquinone and α-naphthoquinone will be discussed in connection with the reactions of the various dienes and enynes. There are also a few other quinones mentioned elsewhere in this review, particularly with reference to the reactions of polynuclear hydrocarbons as dienes.

The quinones to be discussed include the true quinones—those which may be derived from aromatic compounds by direct oxidation—and those partially hydrogenated quinones which result from interaction of a diene and a true quinone. Of the various types of quinones and quinonoid substances, those derived from or benzologous with *p*-benzoquinone have been studied most extensively. Some work has been done with quinones derived from or benzologous with *o*-benzoquinones, and certain compounds such as the quinonoid form of 2,4-dinitrobenzeneazo-*p*-phenol have been shown to possess dienophilic properties.

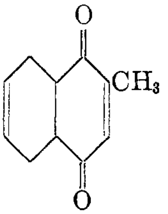
(1) p-Quinones: There are definite limitations as to the types of quinones which will act as dienophiles by virtue of the quinonoid structure. While *p*-benzoquinone will add 2 moles of a diene, the addition of the second mole occurs with somewhat greater difficulty than the addition of the first. Fusion of a completely aromatic ring to the *p*-benzoquinone nucleus will completely suppress addition of the second mole of diene, although there is little or no effect on the addition rate for the first mole. α-Naphthoquinone and 1,4-anthraquinone therefore add but 1 mole of diene. Direct fusion of two completely aromatic rings to the *p*-benzoquinone nucleus will suppress all dienophilic properties. Thus 9,10-anthraquinone will not add dienes, but one finds that the two carbonyl groups activate the benzene rings sufficiently so that 9,10-anthraquinone will add a mole of dienophile (153). This is practically the sole case in which a lone benzene ring will add dienophiles, and the case is open to dispute (295). If the ring fused to the *p*-benzoquinone ring is also a *p*-benzoquinone ring, dienophilic properties of the fusion atoms are not destroyed, for naphthacenediquinone adds dienes readily.

Substituents in the *p*-benzoquinone ring other than fully aromatized rings exhibit a marked hindering effect on the speed of addition of dienes, and often suppress reaction entirely. Addition of dienes to such quinones would result in the formation of adducts possessing angular groups. This is analogous to the effect of substituents attached to the ethylenic carbon atoms of aliphatic dienophiles, which exhibit a less marked hindering effect on the reaction speed, and which also result in the formation of angular or geminal groups and, in one or two cases, spiranes. An exception is observed when the substituent is a group which promotes the entry of an ethylenic compound into the diene reaction, notably the carbonyl group. Groups (such as halogens or hydroxyl) which can be easily eliminated from the adduct usually have but little hindering effect on the addition.

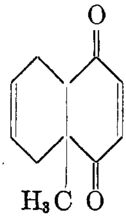
Despite the slowness of the additions observed with quinones possessing substituents attached to the carbon atoms of the carbonylenic double bond, Fieser is most optimistic concerning the possible uses of such quinones for the preparation of compounds related to sterols. This is due, no doubt, to the fact that other methods of synthesizing the sterol ring system are long and tedious and have low over-all yields.

In general, the extent to which quinones possess dienophilic properties (208) parallels their oxidation–reduction potentials. Quinones with high potentials possess greater additive power than those with lower potentials.

Certain of the foregoing statements are well illustrated by the addition of *p*-toluquinone to butadiene (103). One mole of butadiene may add to 1 mole of *p*-toluquinone to give one or both of two possible products, VIII and IX, the latter containing an angular methyl group. The fact that the product does not contain such a group is to be anticipated. This addition occurs at temperatures well below 100°C., but the addition of the second mole of butadiene requires temperatures of 150°C. or higher. In spite of the fact that adducts tend to decompose into their generators on heating, the higher temperature is necessary in order to allow the formation of detectable quantities of adduct in reasonable time and also to minimize the polymerization of excess butadiene to 1-vinyl-3-cyclohexene and octahydrobiphenyl.



VIII



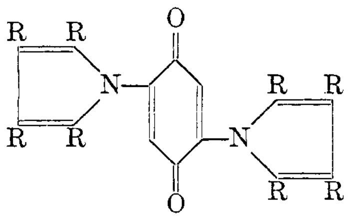
IX

Addition of butadiene to *p*-xyloquinone must necessarily result in the formation of an adduct containing an angular methyl group. The hindering effect of two methyl groups is so great that Chang-Kong and Chin-Tsien (103) observed no addition at 150°C. with benzene as solvent. Adler (7) noted only 10 per cent addition under the same conditions. By using ethanol containing a trace of acetic acid as the reaction medium, Fieser and Seligman (222) were able to add a mole of butadiene to *p*-xyloquinone. 2,3-Dimethylbutadiene was also added to *p*-xyloquinone by the same technique.

A number of patents covering quinone additions (240–245, 247–250) are owned by the I. G. Farbenindustrie Aktiengesellschaft. Most of these were issued at or near the time of the appearance of the first paper by Diels and Alder. These patents cover various phases of the addition of typical dienes to *p*-benzoquinone, α-naphthoquinone, and to their immediate alkyl, hydroxyl, and halogen derivatives. One patent (245) covers the addition of 1 mole of a diene to *p*-benzoquinone, followed by the addition of a second mole of the same or a different diene to give a hydrogenated 9,10-anthraquinone. The patent is sufficiently broad to cover the additions of tetralinquinone and the other *Bz*-partially hydrogenated α-naphthoquinones.

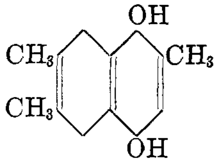
Quinone additions appear to show steric and electronic hindrance effects to a greater degree than other types of diene syntheses. In addition to steric hindrance effects arising from substituents on the *p*-benzoquinone ring, decrease of dienophilic activity is often noted when substituents are introduced into the benzene rings which may be fused to the quinone ring. Progressive hydroxylation or acetoxylation of the benzene ring of α-naphthoquinone results in diminishing dienophilic activity. Furthermore, substitution in the 1- and 4-positions of the conjugated diene may hinder progress of the diene reaction. If this substituent is joined to both the 1- and the 4-positions so as to form a cyclic diene, activity is usually enhanced. This is probably due to the conjugated system being forced to remain in the (active) *cis*-configuration. Open-chain dienes, such as butadiene, can revert to a *trans*-configuration easily, and the net effect is to halve the concentration of reactive form as compared to cyclopentadiene or cyclohexadiene. Ring formation by bridging a carbonyl group between the 1- and 4-positions of the butadienoid system leads to markedly enhanced ability of the diene to add all types of dienophiles, as strikingly exhibited by the derivatives of cyclopentadienone (*vide infra*). But simple alkyl groups, as in piperylene or 2,4-hexadiene, usually lead to restricted addition of quinones. Arbuzov and Spektermann (62) could obtain addition of only 1 mole of piperylene or of 2,4-hexadiene to *p*-benzoquinone.

As indicated in the section on nitrogen heterocycles, the reactions of pyrroles with quinones are abnormal. *p*-Benzoquinone adds 2 moles each of 2,5-dimethylpyrrole, 2,3,4-trimethylpyrrole, and 2,4-dimethyl-3-ethylpyrrole (305) to give compounds of the general structure shown in formula X. The by-product in all three cases is quinhydrone, formed by oxidation of the initial product (the *Bz*-tetrahydro derivative of X) by quinone. 2,5-Dibromo-*p*-benzoquinone reacts similarly to give the *BQ*-2,5-dibromo derivatives of the compounds indicated by the general structure X. Apparently the expected loss of hydrogen bromide from the initial product does not occur, and oxidation occurs preferentially to give the *BQ*-2,5-dibromo derivatives. *p*-Toluquinone appears to react with but 1 mole of 2,5-dimethylpyrrole, giving 2-(2,5-dimethyl-*N*-pyrryl)-5-methyl-*p*-benzoquinone (305). This may be the 4-methyl isomer.

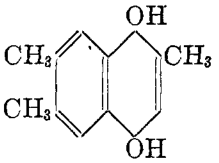


X

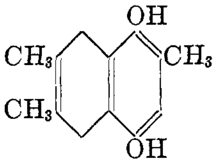
Toluquinone will add piperylene as well as butadiene (103, 222). A trace of hydrogen bromide will rearrange the adduct with 2,3-dimethylbutadiene (85, 103) into a hydroquinone (XI), while heating at 170°C. rearranges the same adduct to a mixture of XII and XIII:



XI



XII

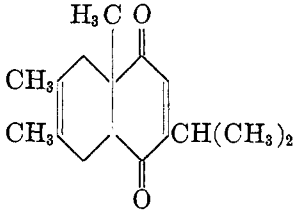


XIII

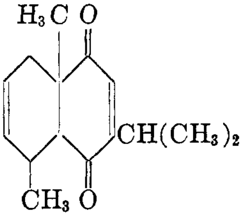
2,3-Diethoxybutadiene adds *p*-toluquinone (255) to give 2-methyl-6,7-diethoxy-5,5a,8,8a-tetrahydronaphthoquinone.

As indicated previously, *p*-xyloquinone will add dienes slowly (7) if at all (103), except under certain solvent conditions (222). The 10 per cent addition obtained by Adler (7) in the addition of butadiene to *p*-xyloquinone was the result of heating four mole proportions of diene with one of the quinone, the diene being in the form of a 20 per cent benzene solution. Heating was conducted at 160–170°C. for 10 hr.

p-Thymoquinone would be expected to behave in much the same manner as *p*-xyloquinone. It adds 2,3-dimethylbutadiene with considerable difficulty to give an oil which presumably has the structure shown in formula XIV. Piperylene is also added (222) to give an adduct assumed to be XV on the assumption that steric factors would prevent proximation of methyl groups. In the assignment of structures XIV and XV it was also assumed that, because the methyl group is of smaller size than the isopropyl group, less difficulty would be encountered in the formation of an angular methyl group than in the formation of an angular isopropyl group.

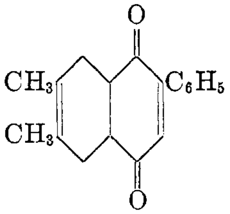


XIV

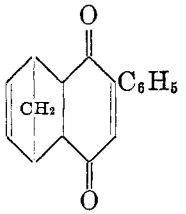


XV

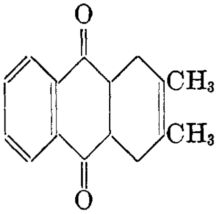
Phenyl-*p*-benzoquinone adds dienes in a manner similar to that of toluquinone, in that the product does not contain an angular group (85). At 100°C. addition occurs with 2,3-dimethylbutadiene and with cyclopentadiene, giving XVI and XVII, respectively. In contrast to the anthraquinone series, in which air oxidation of XVIII yields XIX, atmospheric oxidation of XVI gives XX in a reaction not unlike the formation of hydroxyjuglone from juglone.



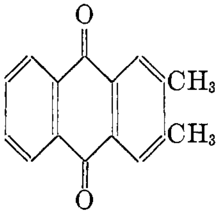
XVI



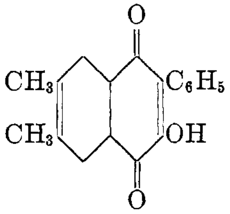
XVII



XVIII



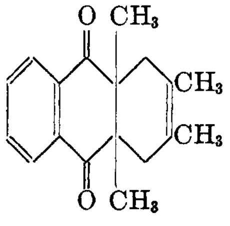
XIX



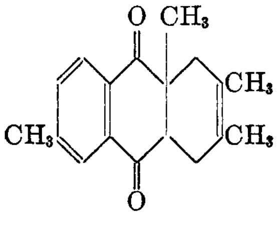
XX

1,4-Naphthoquinones exhibit the same types of steric hindrance effects as do the *p*-benzoquinones. α-Naphthoquinone itself (290) adds nearly all dienes easily. For example, it adds butadiene to give 1,1a,4,4a-tetrahydro-9,10-anthraquinone (136), 2,3-dimethylbutadiene to give 2,3-dimethyl-1,1a,4,4a-tetrahydro-9,10-anthraquinone (223), cyclopentadiene to give 1,4-endomethylene-1,1a,4,4a-tetrahydro-9,10-anthraquinone (153), and 1,3,5-hexatriene (99) to give what is believed to be 1-vinyl-1,1a,4,4a-tetrahydro-9,10-anthraquinone. Atmospheric oxidation of the hexatriene adduct gives 1-vinyl-9,10-anthraquinone.

Several alkylated α-naphthoquinones have been studied. All these have at least one methyl group in the 2-position. Because of this, addition to dienes occurs with some difficulty. 2,3-Dimethyl-1,4-naphthoquinone (221) exhibits a very slow reaction with 2,3-dimethylbutadiene, probably forming XXI. This product reverts into its generators when distilled *in vacuo*. 2,6-Dimethyl-1,4-naphthoquinone (221) reacts somewhat more readily than its isomer, giving XXII.



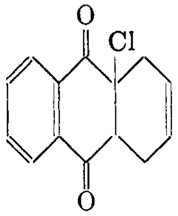
XXI



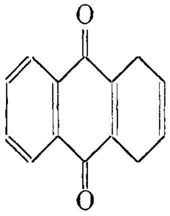
XXII

When α-naphthoquinone is substituted in the 2-position by the hydroxyl group, an adduct is formed which loses water readily to form a 1,4-dihydro-9,10-anthraquinone. Thus 2,3-dimethylbutadiene (208, 222) gives the 2,3-

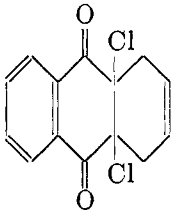
dimethyl derivative. A similar effect is shown by the 2- and 3-halogenated α-naphthoquinones, which lose hydrogen halide to yield more or less fully aromatized 9,10-anthraquinones. Accordingly, butadiene and 2-chloro-1,4-naphthoquinone (208) add to give XXIII, which loses hydrogen chloride easily to give XXIV; and butadiene reacts with 2,3-dichloro-1,4-naphthoquinone to give XXV, which loses 2 moles of hydrogen chloride to give anthraquinone.



XXIII



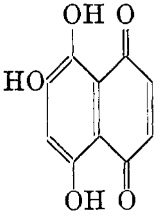
XXIV



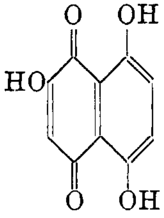
XXV

It was noted previously that progressive hydroxylation or acetoxylation of the benzene nucleus of α-naphthoquinone led to decreased dienophilic activity. Juglone (5-hydroxy-1,4-naphthoquinone) adds 2,3-dimethylbutadiene less readily than does α-naphthoquinone (208). Naphthazarin (5,8-dihydroxy-1,4-naphthoquinone) adds 2,4-hexadiene, piperylene, and alloöcimene (59) with some difficulty; a 6-hr. heating period was necessary to obtain an 83 per cent yield of adduct with 2,3-dimethylbutadiene, whereas only 20 min. heating was necessary in order to obtain a 95 per cent yield of adduct from juglone and 2,3-dimethylbutadiene (208).

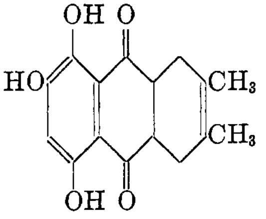
Naphthopurpurin may exist in two tautomeric forms, XXVI and XXVII:



XXVI



XXVII

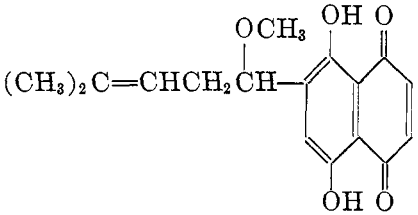


XXVIII

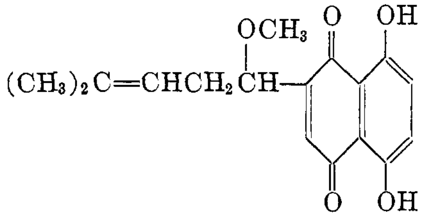
Since XXVII has an inhibiting group attached to the p-benzoquinone nucleus, the structure of the naphthopurpurin adduct with 2,3-dimethylbutadiene (208) may be predicted correctly as being XXVIII.

Juglone acetate (208) gives 5-acetoxy-1,1a,4,4a-tetrahydro-2,3-dimethyl-9,10-anthraquinone with 2,3-dimethylbutadiene. Naphthazarin diacetate adds piperylene to yield 1-methyl-5,8-diacetoxy-1,1a,4,4a-tetrahydro-9,10-anthraquinone (175); isoprene gives the 2-methyl isomer. Isomerization of these initial products occurs at the temperature (100°C.) employed to effect these additions, so that the final product obtained is 1-(or 2)-methyl-5,8-diacetoxy-1,2,3,4-tetrahydro-9,10-anthraquinone.

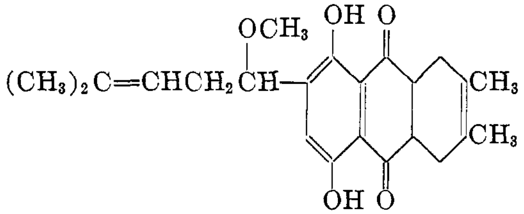
Heating naphthopurpurin triacetate with 2,3-dimethylbutadiene for a period of 27 hr. is necessary in order to obtain the same yield of adduct that may be obtained by heating naphthazarin diacetate with the same diene for a period of only 3 hr. (208). A partially acetylated methylnaphthopurpurin, 2-methyl-8-hydroxy-5,6-diacetoxy-1,4-naphthoquinone (208), will add 2,3-dimethylbutadiene, but only with considerable difficulty. The methyl ether of alkannin (307) is a derivative of naphthazarin and probably exists in two tautomeric forms, XXIX and XXX. It forms an adduct with 2,3-dimethylbutadiene, which is probably XXXI rather than XXXII.



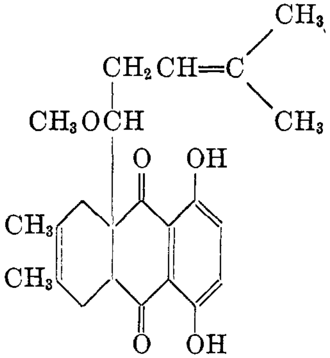
XXIX



XXX



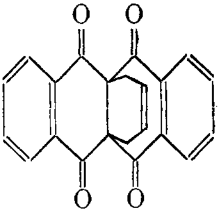
XXXI



XXXII

The only *p*-quinone derived from aromatic hydrocarbons of three or more fused rings which has been studied with respect to dienophilic properties (aside from 9,10-anthraquinone, which does not add dienes) is 9,10,11,12-naphthacenediquinone. No reports have been found concerning 1,4-anthraquinone, 1,4-naphthacenequinone, 1,4-phenanthrenequinone, or 9,10-naphthacenequinone. It is to be anticipated that all the 1,4-quinones will add dienes, and if the report of the addition of dienophiles to 9,10-anthraquinone can be confirmed, then it is likely that 9,10-naphthacenequinone will also add dienophiles. The addition of 1 mole of anthracene to *p*-benzoquinone gives an adduct which is a derivative of 1,4-anthraquinone; this is 1a,4a,9,10-tetrahydro-9,10-endo-(*o*-phenylene)-1,4-anthraquinone; it is easily oxidized to the 9,10-dihydro derivative. Both of these quinones add dienes.

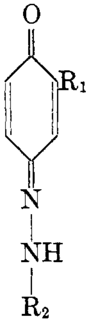
9,10,11,12-Naphthacenediquinone (202, 203) adds butadiene and 2,3-dimethylbutadiene readily. This addition shows that the fusion of two *p*-benzoquinone rings to each other does not suppress addition of dienes to the carbon atoms involved in the fusion, for the structure of the butadiene adduct is as shown in formula XXXIII. A similar structure can be assigned to the adduct with 2,3-dimethylbutadiene. This structure follows from the fact



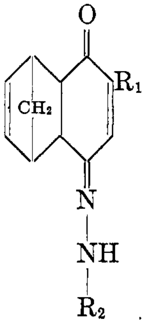
XXXIII

that, by atmospheric oxidation in alkaline solution, phthalic acid and 1,4-dihydro-9,10-anthraquinone are formed.

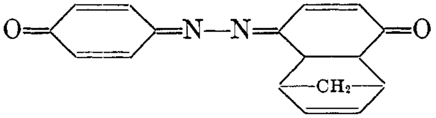
(*2*) *Quinonoid compounds:* Among the nitrogenous analogs of *p*-benzoquinone which add dienes in the diene synthesis (274) are quinone azine and various derivatives of 2,4-dinitrobenzeneazo-*p*-phenol, which exist partly in the tautomeric form (XXXIV). This tautomeric form is the active form in the diene synthesis. In the compounds investigated, R_1 is hydrogen, methyl, or bromine, and R_2 is an aromatic ring which must possess not less than two nitro



XXXIV



XXXV



XXXVI

groups. The adducts of compounds of this type with cyclopentadiene are of the general structure XXXV. The cyclopentadiene adduct of quinone azine has the structure shown in formula XXXVI.

(*3*) *o-Quinones:* The derivatives of *o*-benzoquinone have been investigated recently with regard to their capacities to act as dienophiles. It has been found that those ortho-quinones which possess a comparatively high degree of heat stability will give adducts with dienes. *o*-Benzoquinone and β-naphthoquinone are too unstable toward heat to give anything but tarry decomposition products, but a number of substituted β-naphthoquinones and certain 1,2- and 3,4-phenanthrenequinones have been shown to possess dienophilic properties. It has been found that 3-substituted 1,2-naphthoquinones add dienes more readily than do 2-substituted 1,4-naphthoquinones. Certain of these additions are complete in 1 hr. at 100°C. (204, 221).

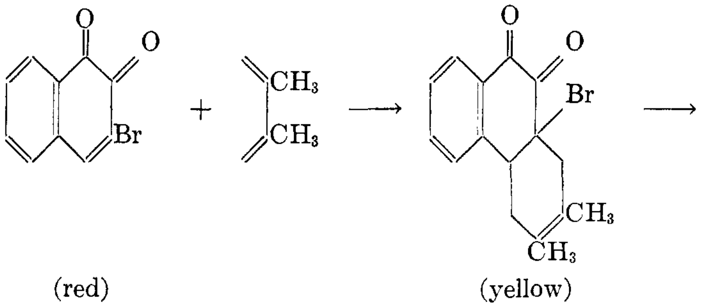
4-Substituted 1,2-naphthoquinones add dienes less readily than do their 3-substituted isomers. The addition of 2,3-dimethylbutadiene and 3-chloro-1,2-naphthoquinone is made complete by heating the components at 100°C. for 1 hr. (204, 221) in chloroform or methylene chloride solution; the product, 1a-chloro-1,1a,4,4a-tetrahydro-2,3-dimethyl-9,10-phenanthrenequinone, will lose hydrogen chloride fairly easily to give 1,4-dihydro-2,3-dimethyl-9,10-phenanthrenequinone. When the adduct is stored in a vacuum desiccator at 10°C., it decomposes to give a green-black amorphous mass. When this material is shaken in air with alcohol or ether, 2,3-dimethyl-9,10-phenanthrenequinone is produced (208).

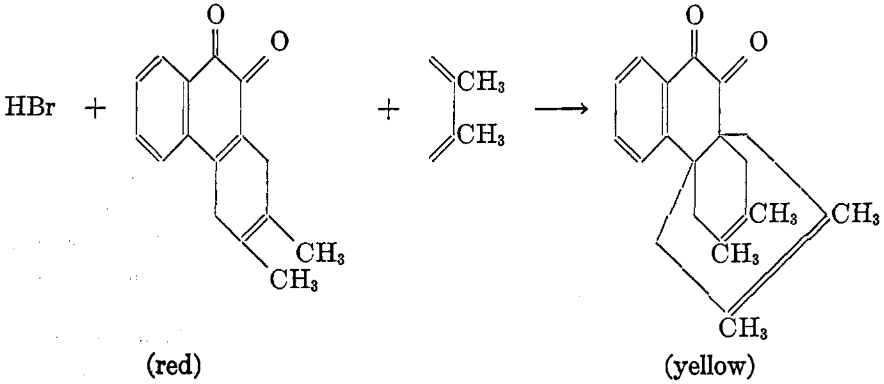
4-Chloro-1,2-naphthoquinone adds to 2,3-dimethylbutadiene much less readily than does the 3-chloro isomer. The adduct, probably 4a-chloro-1,1a,4,4a-tetrahydro-2,3-dimethyl-9,10-phenanthrenequinone (208), was not isolated; it loses hydrogen chloride more readily than the 1a-chloro isomer, giving the same dihydrodimethylphenanthrenequinone.

3,4-Dichloro-1,2-naphthoquinone (208) adds 2,3-dimethylbutadiene when heated in chloroform solution for three days at 100°C. The adduct thereby obtained, 1a,4a-dichloro-1,1a,4,4a-tetrahydro-2,3-dimethyl-9,10-phenanthrenequinone, loses hydrogen chloride much less readily than does either of the two preceding adducts. When this does occur, the product is 2,3-dimethyl-9,10-phenanthrenequinone.

Care must be exercised in the preparation of adducts from the chloro-1,2-naphthoquinones, for traces of alcohol are especially deleterious. For this reason medicinal chloroform cannot be used as solvent. Other impurities in the materials used likewise have a deleterious effect on the progress of the reaction, and highly purified materials are required in order to assure good results.

An interesting sequence of reactions may be observed in the addition reaction of 3-chloro-1,2-naphthoquinone (209) and 2,3-dimethylbutadiene. 3-Bromo-1,2-naphthoquinone acts in a similar manner. The halogenated quinone is red; when it is heated with the diene, the color fades to yellow. This is the color of the 1a-halo-1,1a,4,4a-tetrahydro-2,3-dimethyl-9,10-phenanthrenequinone. On further heating, especially in direct sunlight, the red color reappears. Introduction of a second mole of 2,3-dimethylbutadiene, followed by further heating, causes a second fading of the color to yellow. The cause of this sequence of color changes is shown in the skeleton reactions:





The adduct with 2 moles of 2,3-dimethylbutadiene usually loses a mole of the diene in preference to undergoing other reactions. Attempted formation of an oxime results in the loss of a mole of 2,3-dimethylbutadiene and formation of the dioxime of 2,3-dimethyl-1,4-dihydro-9,10-phenanthrenequinone. Pyrolysis in the presence of a mild oxidizing agent results in loss of 2,3-dimethylbutadiene and formation of 2,3-dimethyl-9,10-phenanthrenequinone.

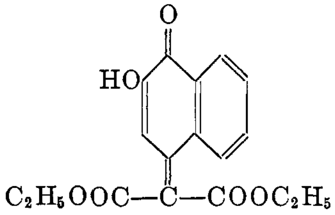
6-Bromo-1,2-naphthoquinone (208) adds 2,3-dimethylbutadiene to give a product which is probably 6-bromo-2,3-dimethyl-1,1a,4,4a-tetrahydro-9,10-phenanthrenequinone.

Although 3,7-dimethyl-1,2-naphthoquinone adds dienes less readily than does 3-chloro-1,2-naphthoquinone, it adds a number of dienes which are not added by 2-methyl-1,4-naphthoquinone (204, 208, 221). A period of three days is required for addition of this quinone to 2,3-dimethylbutadiene by heating in alcoholic solution at 100–105°C., and less drastic conditions result in no addition. The product, 1a,2,3,7-tetramethyl-1,1a,4,4a-tetrahydro-9,10-phenanthrenequinone, is of importance in that it contains an angular methyl group.

In the α-naphthoquinone series it was found that progressive hydroxylation of the benzene ring resulted in decreasing dienophilic activity. The same is true of the β-naphthoquinone series. No reaction was observed (208) between 2,3-dimethylbutadiene and either 6- or 7-hydroxy-1,2-naphthoquinone.

4-Benzyl-1,2-naphthoquinone adds 2,3-dimethylbutadiene in a slow reaction (221) to give an adduct containing an angular benzyl group; the adduct is 1,1a,4,4a-tetrahydro-2,3-dimethyl-4a-benzyl-9,10-phenanthrenequinone.

4-(1,2-Naphthoquinonyl)malonic ester may be capable of isomerization into a 1,4-quinone structure (221):

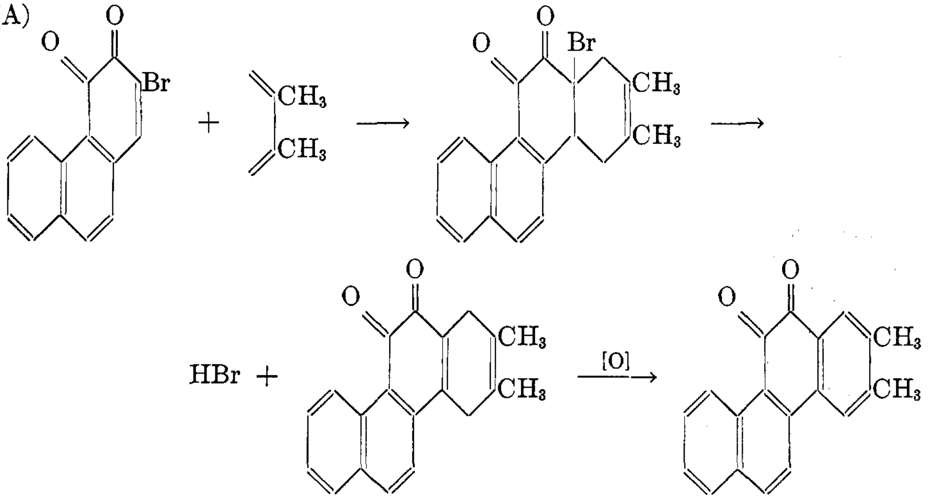


The compound adds 2,3-dimethylbutadiene, but Fieser appears to be reluctant to commit himself as to the structure of the adduct. The adduct may be derived from either the 1,4- or the 1,2-quinonoid structure. One may draw a tentative opinion from the fact that forced addition is usually required to obtain adducts of 4-substituted 1,2-ortho-quinones, and also from the fact that a hydroxyl group attached to the carbonylenic doubly bound carbon atoms does not greatly suppress dienophilic property. This would lead to the opinion that addition would tend to occur with the 1,4-quinonoid form rather than with the 1,2-form. If this be so, then the adduct should lose water on heating, and the product thus formed should be a 1,4-dihydro-2,3-dimethyl-9-methyleneanthrone derivative, decarboxylation and suitable dehydrogenation of which should give the methyleneanthrone itself.

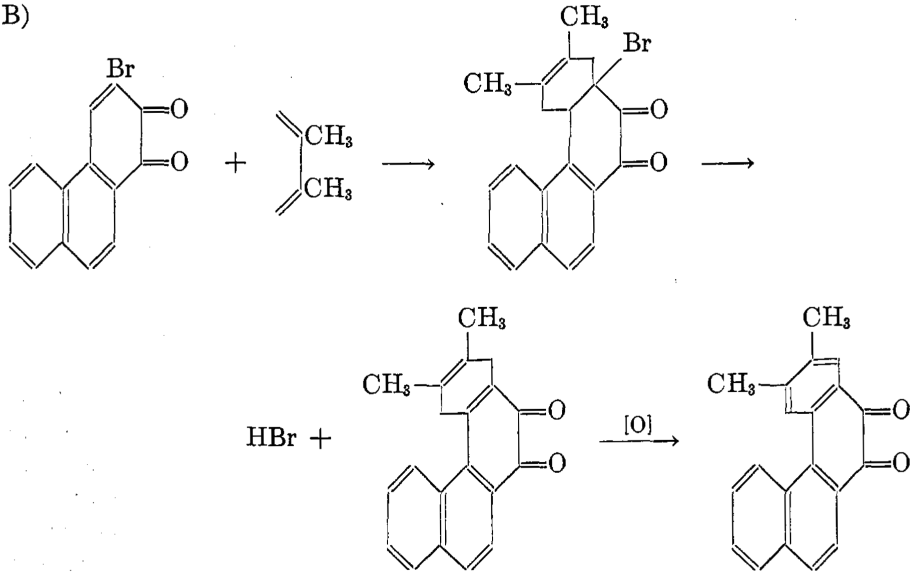
9,10-Phenanthrenequinone does not add dienophiles, and it is also indifferent to dienes. Certain derivatives of 1,2- and 3,4-phenanthrenequinones have been examined by Fieser and Dunn (210); the adducts obtained were identified by degradation to chrysenequinones and benzophenanthrenequinones. The adduct of 2-bromo-3,4-phenanthrenequinone with 2,3-dimethylbutadiene was oxidized to 8,9-dimethyl-5,6-chrysenequinone, hydrogen bromide being eliminated in the first step of the degradation. The yield was 90 per cent on the basis of the generators. 3-Bromo-1,2-phenanthrenequinone gave with dimethylbutadiene an adduct which was oxidized with chromic acid to give 6,7-dimethyl-3,4-benz-9,10-phenanthrenequinone in an over-all yield of 58 per cent, based on the generators. By using butadiene, 3,4-benz-9,10-phenanthrenequinone was prepared from 3-bromo-1,2-phenanthrenequinone. It was found that 1,2-phenanthrenequinone would add 2,3-dimethylbutadiene, but at a slower rate than did the 3-bromo derivative. The latter was easily prepared by direct bromination of 1,2-phenanthrenequinone.

The courses of these syntheses with 2-bromo-3,4-phenanthrenequinone and with 3-bromo-1,2-phenanthrenequinone are given in skeleton equations (A and B) below:

(A)



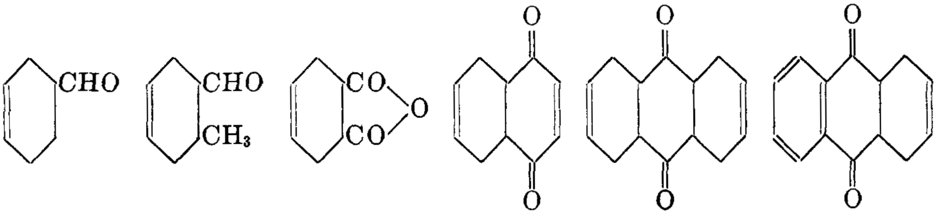
(B)



IV. DIENES: BUTADIENE AND SIMPLE DERIVATIVES

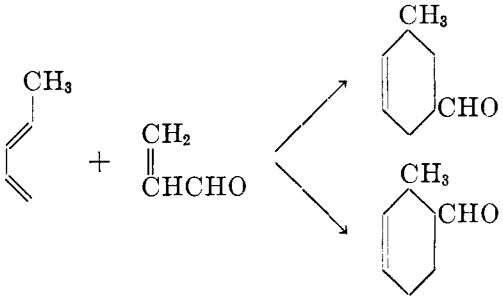
A. Simple derivatives of butadiene

The parent hydrocarbon, butadiene, reacts readily with acrolein (104, 105, 136, 144), crotonaldehyde (144), maleic anhydride (136), *p*-benzoquinone (23, 293), α-naphthoquinone (136), and many other dienophiles to give adducts of formulas which may be anticipated from the general rules for adduct structures which were given on page 320 of this review. The structures of the compounds formed are, respectively:



Piperylene (2,4-pentadiene) reacts with maleic anhydride (144) and with acrolein (63). The product of the latter reaction is illustrative of many cases of adducts the structures of which are problematical. This is always the case when both diene and dienophile do not possess a symmetrical structure with respect to the conjugated system or to the carbonylenic double bond, as the case may be. If either the diene or the dienophile is symmetrical, then the product of a normal diene reaction is of known structure.

The unsymmetrical diene and dienophile, as represented by piperylene and acrolein, may react to give one or both of two possible products:



In this case, the structure of the product can be determined by dehydrogenation to the corresponding xylene. The boiling-point difference between *o*- and *m*-xylenes is not large; hence further confirmation would be desirable, such as oxidation of the xylene to the corresponding phthalic acid. Arbuzov (63) did not employ such a proof, but he gives the structure of the adduct of piperylene and acrolein as that of the meta-aldehyde. The structure of the adduct of maleic anhydride and piperylene may be deduced from the general rules for adduct formation.

There appears to be a substantial difference (309) in the rates of addition of maleic anhydride by the *cis*- and *trans*-isomers of piperylene. The analysis of a pure mixture of *cis*- and *trans*-piperylenes was attempted by Robey and his coworkers, who found that addition ceases between 65 and 78 per cent of completion. This was ascribed to differences in the rates of addition of dienophiles by the two isomers. Arguments for and against their belief that the unreactive form (which was isolated) is the *cis*-isomer may be found in the section dealing with the mechanism and stereochemistry of the diene synthesis (see page 496)[1].

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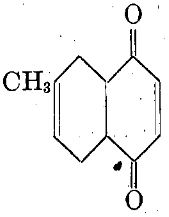
[1] After this review had gone to press, Craig presented a paper before the 104th Meeting of the American Chemical Society at Buffalo, New York. In this paper, Craig showed quite convincingly that *trans*-piperylene (formed by gentle thermal decomposition of piperylene sulfone) adds maleic anhydride readily according to the general rules of diene syntheses. It was also shown that *cis*-piperylene will polymerize before it adds maleic anhydride, thus confirming previous observations. It must be considered, therefore, that the non-addition of maleic anhydride by *cis*-piperylene is a thoroughly established fact. Although cyclopentadiene is certainly of *cis*-configuration, it adds maleic anhydride with great avidity. A possible explanation for the apparent anomaly may be that while the butadienoid configuration of cyclopentadiene is forced to be *cis*, the butadienoid configuration of *cis*-piperylene may be either *cis* or *trans*, or a dynamic equilibrium between the two forms. If the methyl group of *cis*-piperylene exerts a steric hindrance effect upon the free rotation of the vinyl group around the bond linking carbon atoms 3 and 4 (considering *cis*-piperylene to be 2,4-pentadiene), then the butadienoid configuration of *cis*-piperylene may be largely or even exclusively a *trans*-butadienoid configuration at ordinary temperatures. Temperatures required to produce appreciable amounts of the *cis*-butadienoid form or of *trans*-piperylene may be as high as or higher than those required to induce polymerization under the acidic conditions employed (owing to the acid character of maleic anhydride). This question of steric control of the proportions of *cis*- and *trans*-butadienoid forms of a given 1,3-butadiene derivative is deserving of much further study.

Care must be taken in distinguishing between *cis*- and *trans*-isomers of a diene such as piperylene, and *cis*- and *trans*-butadienoid systems. Each isomer of piperylene may exist in both *cis*- and *trans*-butadienoid forms, which probably exist in dynamic equilibrium with each other. Thus *cis*-piperylene exists in *cis*- and *trans*-forms which are in dynamic equilibrium with each other, owing to free rotation about the single bond joining the 2- and 3-carbon atoms of the butadienoid system. In a *cis–trans*-butadienoid system such as this, in which the forms are spontaneously interconvertible, the existence of such a system may be disregarded for all practical purposes.[1]

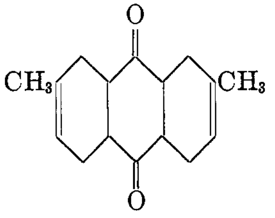
The purest sample of 3,6-dihydrophthalic acid ever made is claimed by Diels and Alder, who prepared it by the addition of acetylenedicarboxylic acid to butadiene in dioxane solution (11). This preparation had a melting point nearly 13°C. higher than the preparation of von Baeyer.

Isoprene reacts with maleic anhydride (144), *p*-benzoquinone (153), and also with itself in dimerization and trimerization reactions (136, 275, 345, and 349) which differ sharply from its polymerization reactions. This dimerization reaction will be considered more fully in a later section (see page 430), but it will be of interest to note here that it and other dimerization reactions (except those of sorbic acid and the cyclopentadienones) are examples of additions which show that the dienophile need not contain double bonds of the carbonylenic type.

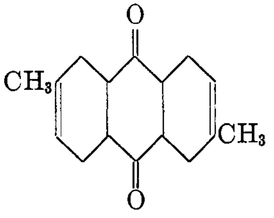
The reaction of isoprene with *p*-benzoquinone is entirely analogous to the reaction of butadiene with this dienophile. The first product of addition (I) may add another mole of isoprene to give either II or III:



I



II



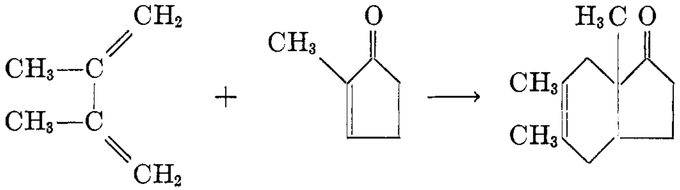
III

Actually, both products were obtained (153). Structures were proved by atmospheric oxidation to the corresponding dimethylanthraquinones.

2,4-Hexadiene reacts with crotonaldehyde, acrolein, and maleic anhydride (63, 144), but *p*-benzoquinone will add only 1 mole of the diene (62). Owing to the symmetrical nature of the diene, only one structure is possible for each of the adducts obtained thus. However, stereoisomerism is possible in the adducts. This phase of the structure of the adduct appears not to have been investigated.

1,3-Dimethylbutadiene is easily prepared by the method of the Saytzews (325), who obtained a hexadiene through the interaction of acetone, allyl bromide, and an alkali metal. The constitution of the product was not definitely established at the time, but the possibilities were limited to 1,3-dimethylbutadiene and 2-methyl-1,4-pentadiene. The latter substance does not possess the conjugated system required of dienes which undergo the diene synthesis. Inasmuch as Diels and Alder (144) found that the diene reacted with maleic anhydride to give 3,5-dimethyl-1,2,3,6-tetrahydrophthalic anhydride, the structure of the Saytzew diene was established. The same diene was also obtained by pyrolysis of the phosphate of 2-methyl-2,4-diaminopentane (144) and also by dehydration of 2-methylpentene-2,4-glycol (144), as proved by the mutual identities of the adducts of maleic anhydride and also of crotonaldehyde with the products from each of the three sources.

2,3-Dimethylbutadiene has been well studied, both because of its symmetry and because of its ease of preparation. It reacts with 3-hexen-2,5-dione (227), 2-methylcyclopenten-3-one (93), maleic anhydride (144, 199), and acrolein (139, 144) to give adducts of anticipated structures. Of particular interest in this connection is that an angular methyl group is formed in the case of 2-methylcyclopenten-3-one:



2,3-Dimethylbutadiene

2-Methyl-
cyclopenten-
3-one

When dienophiles are employed which lead to the formation of angular, geminal, or spirane groups, the diene reaction often proceeds more slowly than if the potentially angular, etc., groups of the dienophile were absent. This subject was covered earlier in this review. Thus, the above reaction of 2-methylcyclopenten-3-one with 2,3-dimethylbutadiene is much slower than the reaction of butadiene with cyclopenten-3-one. Even the addition of diacetylethylene is much more rapid than the addition of 1,2-diacetyl-1-propene (227). Where the mode of addition is optional, as in the addition of butadiene to *p*-toluquinone, the product does not contain an angular methyl group.

Having illustrated the simple diene syntheses by citing a number of typical examples, there should be no need of further elucidation of these simple types. For reference and informative purposes, however, there are listed in table 2 the simple butadiene derivatives which have been studied, together with the dienophile employed, the structure of the adduct, and the references to the literature.

With reference to table 2, it should be stated that in some cases the adduct structures are assumed, either by the author of this review or by the original investigators. Several cases will be noted in which addition fails to occur or else gives polymeric products. It may be that normal reaction will occur in a number of cases, provided the proper experimental conditions are determined and employed.[1]

TABLE 2

Diene syntheses with butadiene and simple derivatives

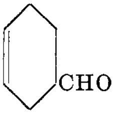
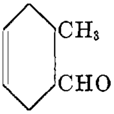
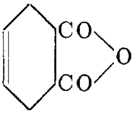
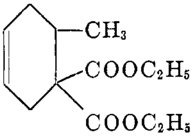
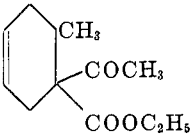
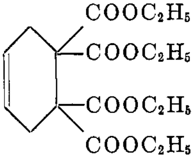
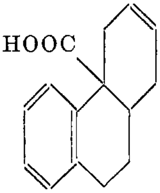
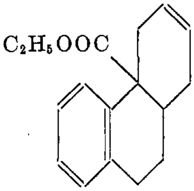
DIENE	DIENOPHILE	PRODUCT	REFERENCE
Butadiene*.......	Acrolein		(104, 105, 136, 144)
Butadiene‡.......	Crotonaldehyde		(105, 144)
Butadiene*.......	Maleic anhydride		(136, 199)
Butadiene‡.......	Ethylidenemalonic ester		(18)
Butadiene‡.......	Ethylideneacetoacetic ester		(18)
Butadiene‡.......	Ethylenetetracarboxylic ester		(18)
Butadiene‡.......	3,4-Dihydro-1-naphthoic acid		(219)
Butadiene‡.......	3,4-Dihydro-1-naphthoic ester		(218)

TABLE 2—*Continued*

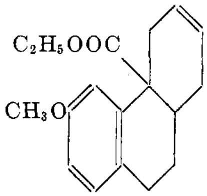
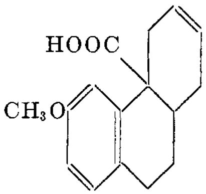
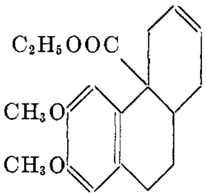
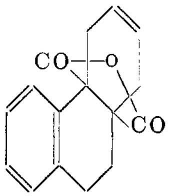
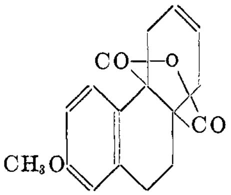
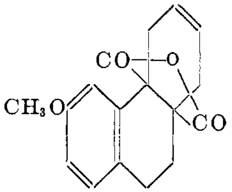
DIENE	DIENOPHILE	PRODUCT	REFERENCE
Butadiene‡	7-Methoxy-3,4-dihydro-1-naphthoic ester		(218)
Butadiene‡	7-Methoxy-3,4-dihydro-1-naphthoic acid		(219)
Butadiene‡	6,7-Dimethoxy-3,4-dihydro-1-naphthoic ester		(218)
Butadiene‡	3,4-Dihydro-1,2-naphthalic anhydride		(214, 216)
Butadiene‡	6-Methoxy-3,4-dihydro-1,2-naphthalic anhydride		(217)
Butadiene‡	7-Methoxy-3,4-dihydro-1,2-naphthalic anhydride		(217)

TABLE 2—*Continued*

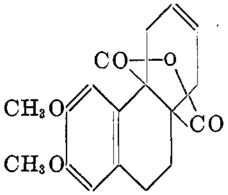
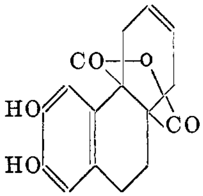
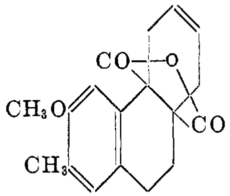
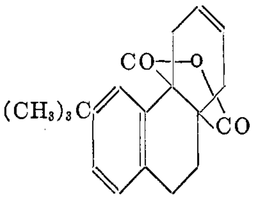
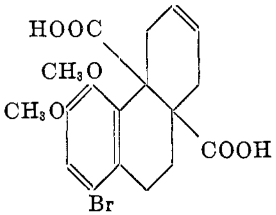
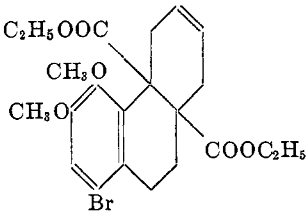
DIENE	DIENOPHILE	PRODUCT	REFERENCE
Butadiene‡	6,7-Dimethoxy-3,4-dihydro-1,2-naphthalic anhydride		(217)
Butadiene‡	6,7-Dihydroxy-3,4-dihydro-1,2-naphthalic anhydride		(217)
Butadiene‡	6-Methyl-7-methoxy-3,4-dihydro-1,2-naphthalic anhydride		(217)
Butadiene‡	7-*tert*-Butyl-3,4-dihydro-1,2-naphthalic anhydride		(220)
Butadiene‡	7,8-Dimethoxy-5-bromo-3,4-dihydro-1,2-naphthalic acid		(218)
Butadiene‡	7,8-Dimethoxy-5-bromo-3,4-dihydro-1,2-naphthalic ester		(218)

TABLE 2—*Continued*

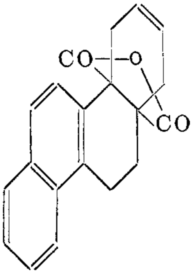
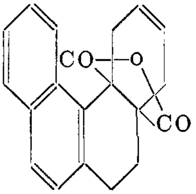
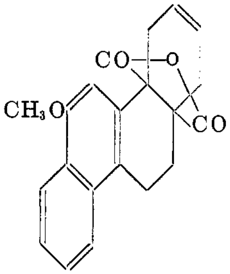
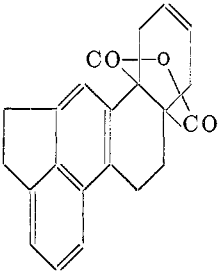
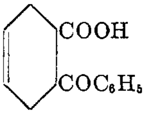
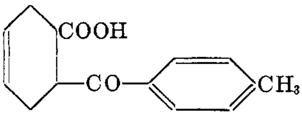
DIENE	DIENOPHILE	PRODUCT	REFERENCE
Butadiene‡	3,4-Dihydrophenanthrene-1,2-dicarboxylic anhydride		(212, 213, 216)
Butadiene‡	1,2-Dihydrophenanthrene-3,4-dicarboxylic anhydride		(213, 216)
Butadiene‡	9-Methoxy-3,4-dihydrophenanthrene-1,2-dicarboxylic anhydride		(217)
Butadiene‡	8,9-Ethylene-3,4-dihydrophenanthrene-1,2-dicarboxylic anhydride		(213)
Butadiene‡	β-Benzoylacrylic acid		(211, 215)
Butadiene‡	β-*p*-Toluoylacrylic acid		(215)

TABLE 2—*Continued*

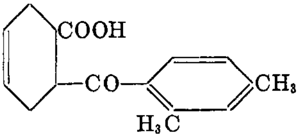
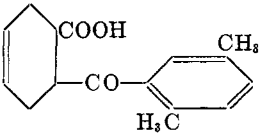
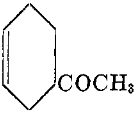
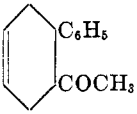
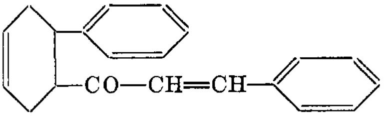
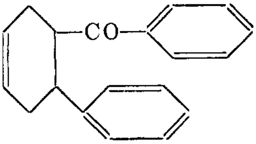
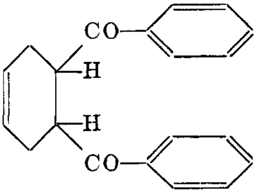
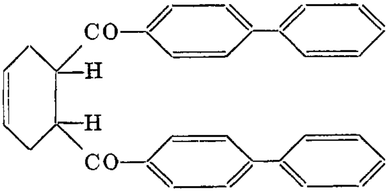
DIENE	DIENOPHILE	PRODUCT	REFERENCE
Butadiene‡	β-(2,4-Dimethylbenzoyl)acrylic acid		(215)
Butadiene‡	β-(2,5-Dimethylbenzoyl)acrylic acid		(215)
Butadiene‡	Acetylethylene		(420)
Butadiene‡	Benzalacetone		(297)
Butadiene	Ethylene	Cyclohexene	(411)
Butadiene‡	Dibenzalacetone		(297)
Butadiene‡	Benzalacetophenone		(297)
Butadiene‡	*trans*-1,2-Dibenzoylethylene		(3, 6)
Butadiene‡	*trans*-1,2-Dixenoylethylene		(4)

TABLE 2—*Continued*

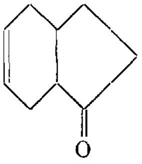
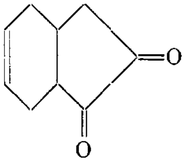
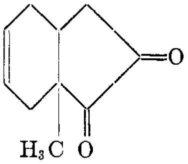
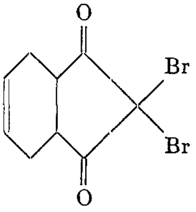
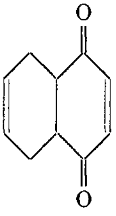
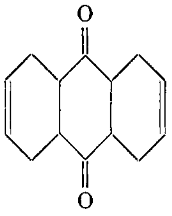
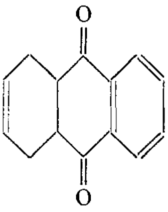
DIENE	DIENOPHILE	PRODUCT	REFERENCE
Butadiene‡	1-Cyclopenten-3-one		(129)
Butadiene‡	1-Cyclopenten-3,4-dione		(134)
Butadiene‡	2-Methyl-1-cyclopenten-3,4-dione		(132)
Butadiene‡	4,4-Dibromo-1-cyclopenten-3,5-dione		(129)
Butadiene*	*p*-Benzoquinone	 and 	(23, 293)
Butadiene*	1,4-Naphthoquinone		(136)

TABLE 2—*Continued*

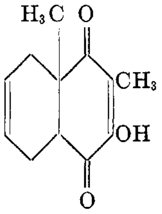
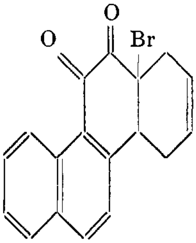
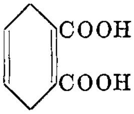
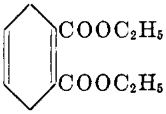
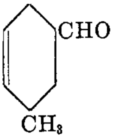
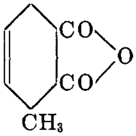
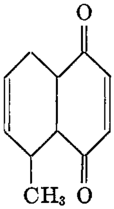
DIENE	DIENOPHILE	PRODUCT	REFERENCE
Butadiene†.......	2,6-Dimethyl-3-hydroxy-1,4-benzoquinone		(132)
Butadiene‡.......	2-Bromo-3,4-phenanthrenequinone		(210)
Butadiene‡.......	Acetylenedicarboxylic acid		(11)
Butadiene‡.......	Acetylenedicarboxylic ester		(11)
Piperylene*.......	Acrolein		(63)
Piperylene‡.......	Maleic anhydride		(144)
Piperylene‡.......	*p*-Benzoquinone		(62)

TABLE 2—*Continued*

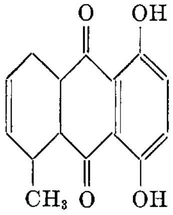
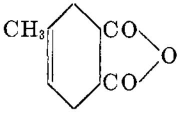
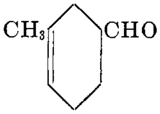
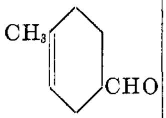
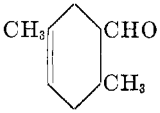
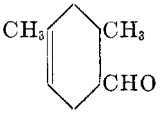
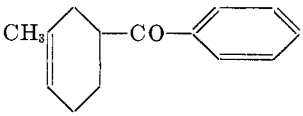
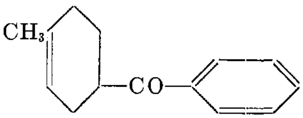
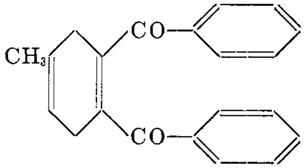
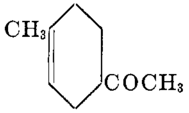
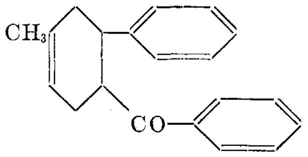
DIENE	DIENOPHILE	PRODUCT	REFERENCE
Piperylene‡	Naphthazarin		(59)
Isoprene*	Maleic anhydride		(144)
Isoprene	Acrolein	 and/or 	(139)
Isoprene	Crotonaldehyde	 and/or 	(144)
Isoprene	Benzoylethylene	 or 	(47)
Isoprene‡	Dibenzoylacetylene		(193)
Isoprene†	Acetylethylene		(420)
Isoprene†	Benzylideneacetophenone		(297)

TABLE 2—*Continued*

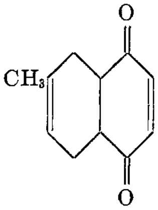
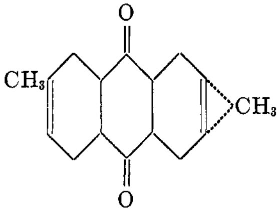
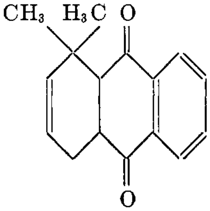
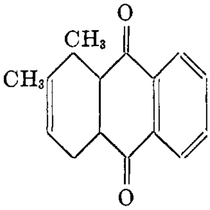
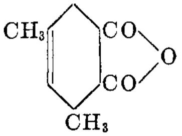
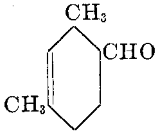
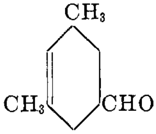
DIENE	DIENOPHILE	PRODUCT	REFERENCE
Isoprene*.........	*p*-Benzoquinone	 and both 	(153, 195)
1,1-Dimethyl butadiene‡.....	Maleic anhydride	"Waxy polymeric anhydride"	(68, 390)
1,1-Dimethylbutadiene‡..........	1,4-Naphthoquinone		(224)
1,2-Dimethylbutadiene‡.....	1,4-Naphthoquinone		(223)
1,3-Dimethylbutadiene‡.....	Maleic anhydride		(68, 105, 278, 390)
1,3-Dimethylbutadiene†.....	Acrolein	 or 	(139, 331)

TABLE 2—*Continued*

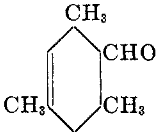
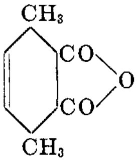
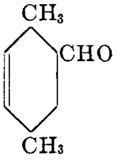
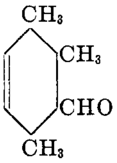
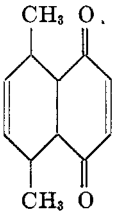
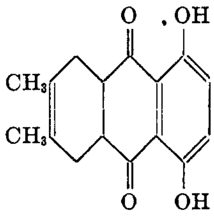
DIENE	DIENOPHILE	PRODUCT	REFERENCE
1,3-Dimethylbutadiene†.....	Crotonaldehyde		(105, 139, 144)
1,4-Dimethylbutadiene‡.....	Maleic anhydride		(63, 283)
1,4-Dimethylbutadiene‡.....	Acrolein		(63)
1,4-Dimethylbutadiene‡.....	Crotonaldehyde		(105, 331)
1,4-Dimethylbutadiene‡.....	*p*-Benzoquinone		(62)
1,4-Dimethylbutadiene‡....	Naphthazarin		(59)
2,3-Dimethylbutadiene.......	Ethylene	1,2-Dimethylcyclohexene	(411)

TABLE 2—*Continued*

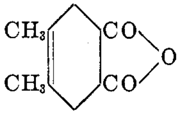
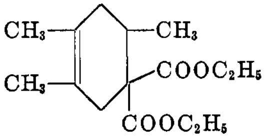
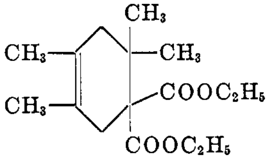
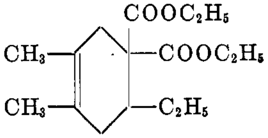
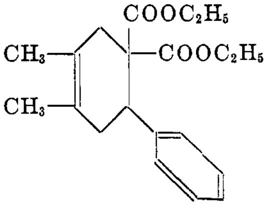
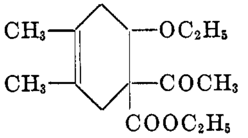
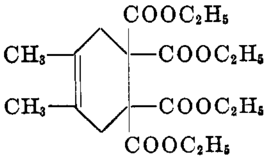
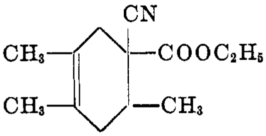
DIENE	DIENOPHILE	PRODUCT	REFERENCE
2,3-Dimethylbutadiene‡.....	Maleic anhydride		(105, 199)
2,3-Dimethylbutadiene‡......	Ethylidenemalonic ester		(18)
2,3-Dimethylbutadiene‡.....	Isopropylidenemalonic ester		(18)
2,3-Dimethylbutadiene‡.....	*n*-Propylidenemalonic ester		(18)
2,3-Dimethylbutadiene‡.....	Benzylidenemalonic ester		(18)
2,3-Dimethylbutadiene‡.....	Ethoxymethyleneacetoacetic ester		(18)
2,3-Dimethylbutadiene‡.....	Ethylenetetracarboxylic ester		(18)
2,3-Dimethylbutadiene‡.....	Ethylidenecyanoacetic ester		(18)

TABLE 2—*Continued*

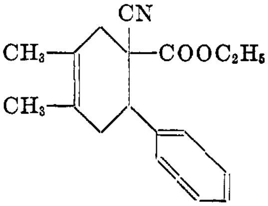
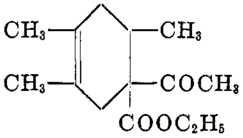
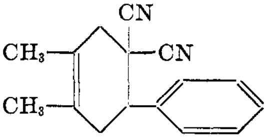
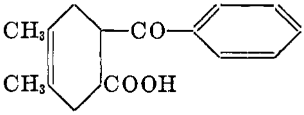
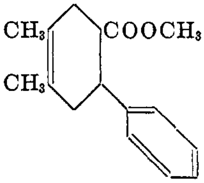
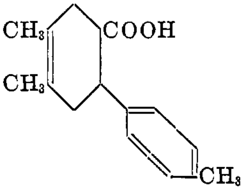
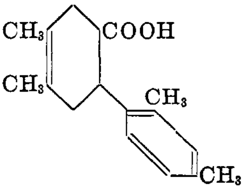
DIENE	DIENOPHILE	PRODUCT	REFERENCE
2,3-Dimethylbutadiene‡.....	Benzylidenecyanoacetic ester		(18)
2,3-Dimethylbutadiene‡.....	Ethylideneacetoacetic ester		(18)
2,3-Dimethylbutadiene‡.....	Benzylidenemalononitrile		(18)
2,3-Dimethylbutadiene‡.....	β-Benzoylacrylic acid		(211, 215)
2,3-Dimethylbutadiene‡.....	Methyl β-benzoylacrylate		(47)
2,3-Dimethylbutadiene‡.....	β-*p*-Toluylacrylic acid		(211, 215)
2,3-Dimethylbutadiene‡.....	β-(2,4-Dimethylbenzoyl)acrylic acid		(211, 215)

TABLE 2—*Continued*

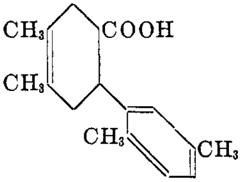
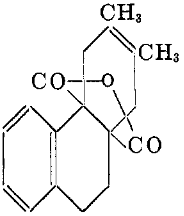
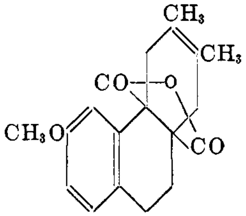
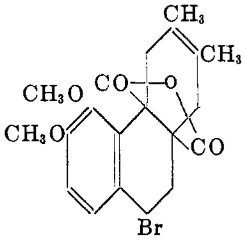
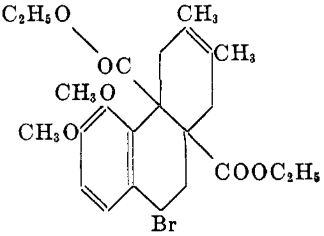
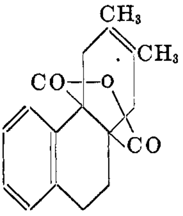
DIENE	DIENOPHILE	PRODUCT	REFERENCE
2,3-Dimethylbutadiene‡.....	β-(2,5-Dimethylbenzoyl)acrylic acid		(211, 215)
2,3-Dimethylbutadiene‡.....	3,4-Dihydro-1-naphthoic acid		(219)
2,3-Dimethylbutadiene‡.....	7-Methoxy-3,4-dihydro-1-naphthoic acid		(219)
2,3-Dimethylbutadiene‡.....	4-Bromo-7,8-dimethoxy-3,4-dihydro-1-naphthoic acid		(218)
2,3-Dimethylbutadiene‡.....	4-Bromo-7,8-dimethoxy-3,4-dihydro-1-naphthoic ester		(218)
2,3-Dimethylbutadiene‡.....	3,4-Dihydro-1,2-naphthalic anhydride		(213, 214, 216)

TABLE 2—*Continued*

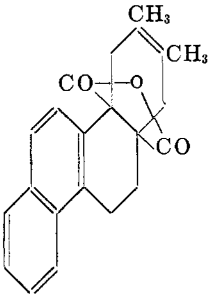
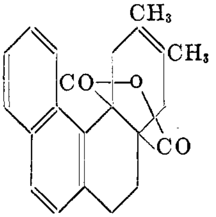
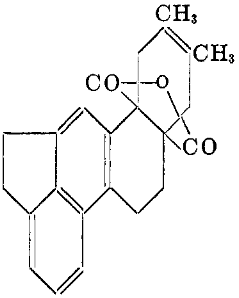
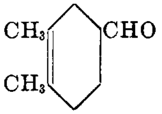
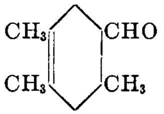
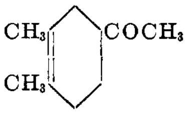
DIENE	DIENOPHILE	PRODUCT	REFERENCE
2,3-Dimethylbutadiene‡.....	3,4-Dihydrophenanthrene-1,2-dicarboxylic anhydride		(213, 216)
2,3-Dimethylbutadiene‡.....	1,2-Dihydrophenanthrene-3,4-dicarboxylic anhydride		(213, 216)
2,3-Dimethylbutadiene‡.....	8,9-Ethylene-3,4-dihydrophenanthrene-1,2-dicarboxylic anhydride		(209, 213)
2,3-Dimethylbutadiene‡.....	Acrolein		(105, 139)
2,3-Dimethylbutadiene‡.....	Crotonaldehyde		(139, 331)
2,3-Dimethylbutadiene‡	Acetylethylene		(420)

TABLE 2—*Continued*

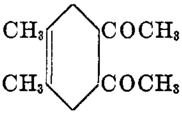
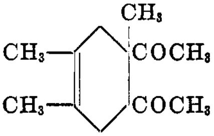
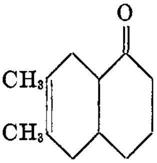
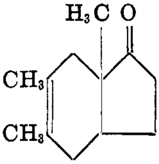
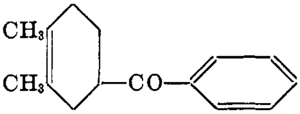
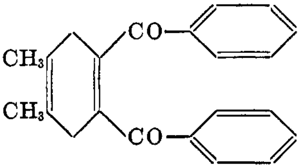
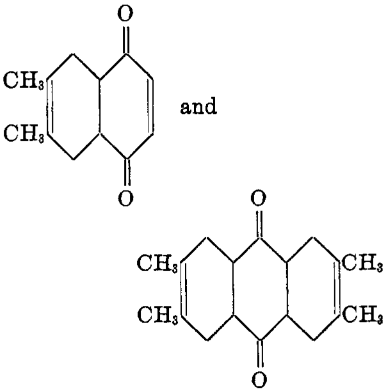
DIENE	DIENOPHILE	PRODUCT	REFERENCE
2,3-Dimethylbutadiene‡.....	1,2-Diacetylethylene		(227)
2,3-Dimethylbutadiene‡.....	1,2-Diacetyl-1-propene		(227)
2,3-Dimethylbutadiene‡.....	Cyclohexen-3-one		(76)
2,3-Dimethylbutadiene‡.....	2-Methylcyclopenten-3-one		(93)
2,3-Dimethylbutadiene‡.....	Benzoylethylene		(47)
2,3-Dimethylbutadiene‡.....	Dibenzoylacetylene		(193)
2,3-Dimethylbutadiene‡.....	*p*-Benzoquinone		(23)

TABLE 2—*Continued*

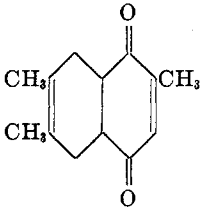
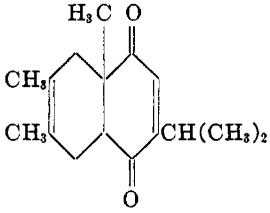
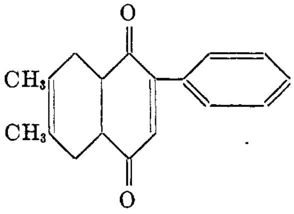
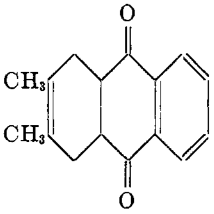
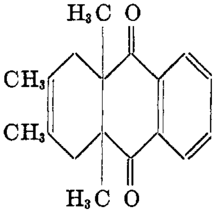
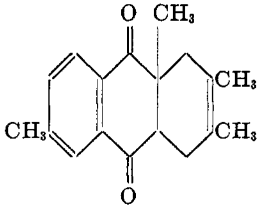
DIENE	DIENOPHILE	PRODUCT	REFERENCE
2,3-Dimethylbutadiene‡	*p*-Toluquinone		(85, 103)
2,3-Dimethylbutadiene‡	*p*-Thymoquinone		(222)
2,3-Dimethylbutadiene‡	Phenyl-*p*-benzoquinone		(85)
2,3-Dimethylbutadiene‡	α-Naphthoquinone		(223)
2,3-Dimethylbutadiene‡	2,3-Dimethyl-1,4-naphthoquinone		(221)
2,3-Dimethylbutadiene‡	2,6-Dimethyl-1,4-naphthoquinone		(221)

TABLE 2—*Continued*

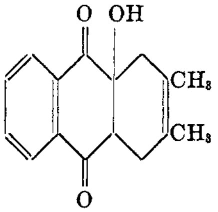
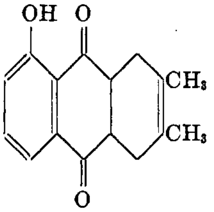
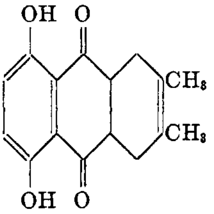
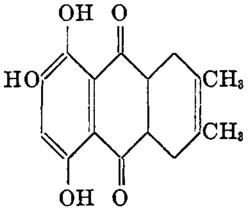
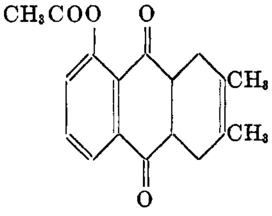
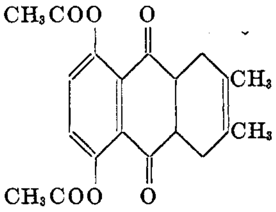
DIENE	DIENOPHILE	PRODUCT	REFERENCE
2,3-Dimethylbutadiene‡.....	2-Hydroxy-1,4-naphthoquinone		(208, 222)
2,3-Dimethylbutadiene‡.....	Juglone		(208)
2,3-Dimethylbutadiene‡.....	Naphthazarin		(208)
2,3-Dimethylbutadiene‡.....	Naphthopurpurin		(208)
2,3-Dimethylbutadiene‡.....	Juglone acetate		(208)
2,3-Dimethylbutadiene‡.....	Naphthazarin diacetate		(208)

TABLE 2—*Continued*

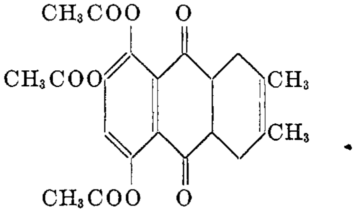
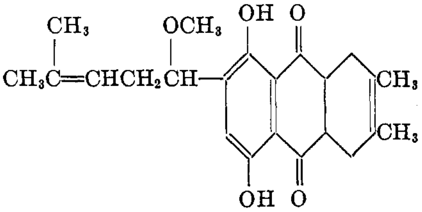
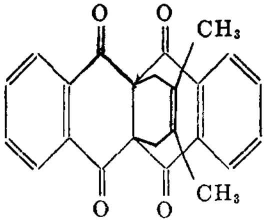
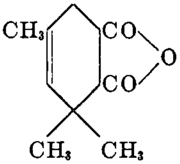
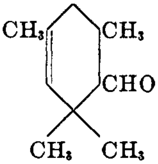
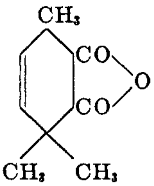
DIENE	DIENOPHILE	PRODUCT	REFERENCE
2,3-Dimethylbutadiene‡.....	Naphthopurpurin triacetate		(208)
2,3-Dimethylbutadiene‡.....	Alkannin methyl ether		(307)
2,3-Dimethylbutadiene‡.....	Naphthacenediquinone		(202, 203)
1,1,3-Trimethylbutadiene†.....	Maleic anhydride		(144)
1,1,3-Trimethylbutadiene†.....	Crotonaldehyde		(144)
1,1,4-Trimethylbutadiene‡.....	Maleic anhydride		(68)

TABLE 2—*Continued*

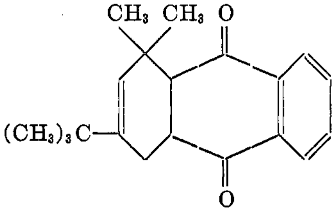
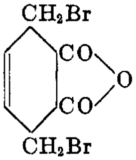
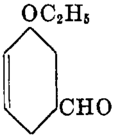
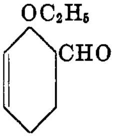
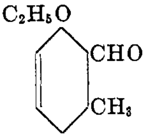
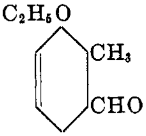
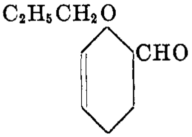
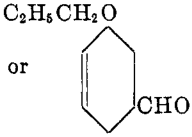
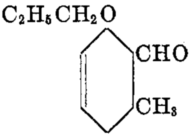
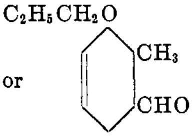
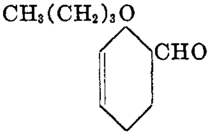
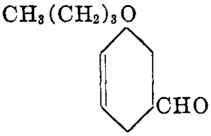
DIENE	DIENOPHILE	PRODUCT	REFERENCE
1-Isopropylbutadiene	Maleic anhydride	"Waxy polymeric adduct"	(68)
3-*tert*-Butyl-1,1-dimethylbutadiene‡	α-Naphthoquinone		(224)
1,4-Di(bromomethyl)butadiene‡	Maleic anhydride		(137)
1-Ethoxybutadiene†	Acrolein	 or 	(358)
1-Ethoxybutadiene†	Crotonaldehyde	 or 	(358)
1-*n*-Propoxybutadiene†	Acrolein	 or 	(358)
1-*n*-Propoxybutadiene†	Crotonaldehyde	 or 	(358)
1-*n*-Butoxybutadiene†	Acrolein	 or 	(358)

TABLE 2—*Continued*

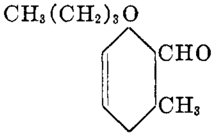
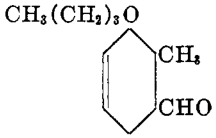
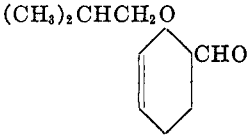
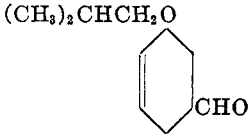
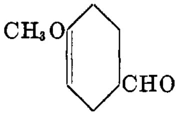
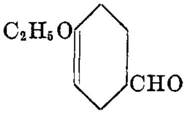
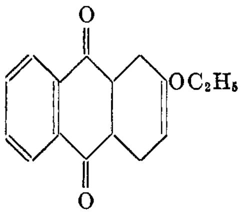
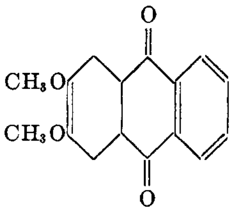
DIENE	DIENOPHILE	PRODUCT	REFERENCE
1-*n*-Butoxybutadiene†..........	Crotonaldehyde	 or 	(358)
1-Isobutoxybutadiene†..........	Acrolein	 or 	(358)
2-Methoxybutadiene†..........	Acrolein		(419)
2-Ethoxybutadiene†..........	Acrolein		(419)
2-Ethoxybutadiene†..........	α-Naphthoquinone		(402)
2,3-Dimethoxybutadiene‡.....	α-Naphthoquinone		(255)

TABLE 2—*Continued*

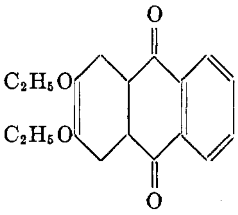
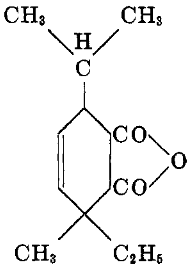
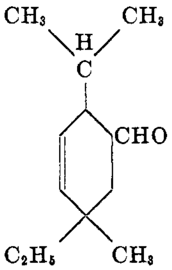
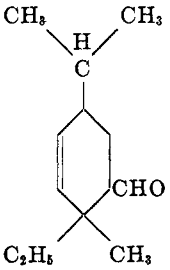
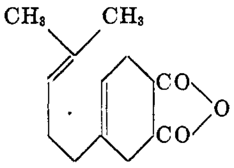
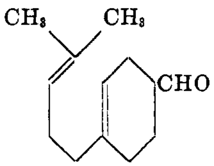
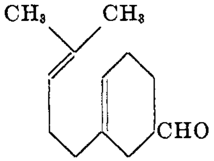
DIENE	DIENOPHILE	PRODUCT	REFERENCE
2,3-Diethoxybutadiene‡	α-Naphthoquinone		(255)
2,6-Dimethyl-3,5-octadiene‡	Maleic anhydride		(192)
2,6-Dimethyl-3,5-octadiene†	Acrolein	 or 	(192)
Myrcene‡	Maleic anhydride		(43, 144, 407)
Myrcene†	Acrolein	 or 	(139)

TABLE 2—*Continued*

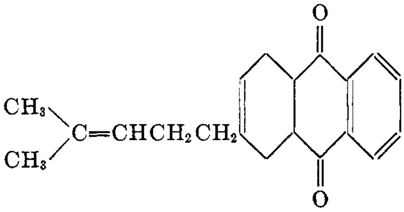
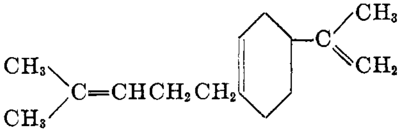
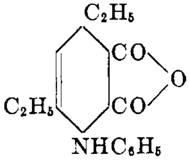
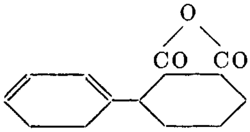
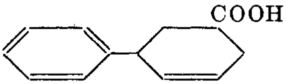
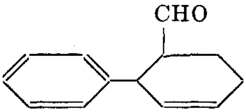
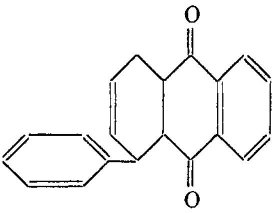
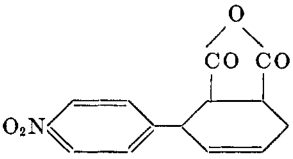
DIENE	DIENOPHILE	PRODUCT	REFERENCE
Myrcene†.........	α-Naphthoquinone		(224)
Myrcene†.........	Isoprene	 or isomers	(315)
1,3-Diethyl-4-(*N*-anilino) butadiene...........	Maleic anhydride		(423, 424)
1-Phenylbutadiene‡..........	Maleic anhydride		(17, 152)
1-Phenylbutadiene*..........	Acrylic acid		(277, 281)
1-Phenylbutadiene*..........	Acrolein		(277, 281)
1-Phenylbutadiene‡..........	α-Naphthoquinone		(153)
1-*p*-Nitrophenylbutadiene‡......	Maleic anhydride		(88)

TABLE 2—*Continued*

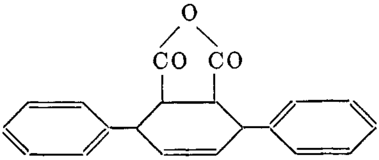
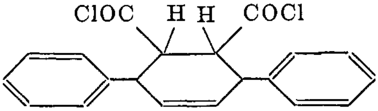
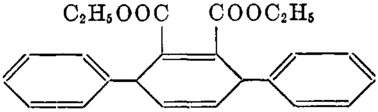
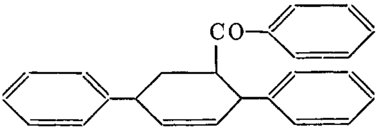
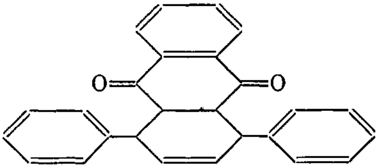
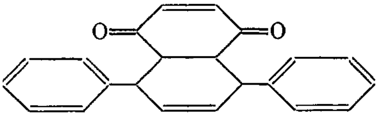
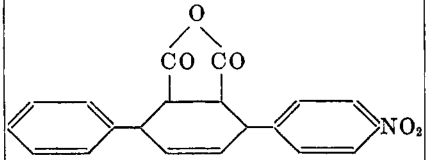
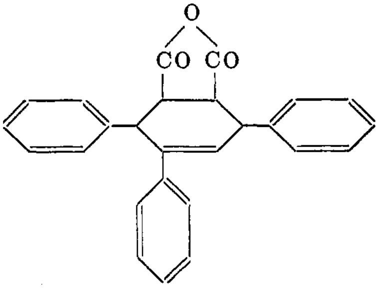
DIENE	DIENOPHILE	PRODUCT	REFERENCE
1,4-Diphenylbutadiene‡......	Maleic anhydride		(273)
1,4-Diphenylbutadiene‡.....	Fumaroyl chloride		(273)
1,4-Diphenylbutadiene‡.....	Acetylenedicarboxylic ester		(288)
1,4-Diphenylbutadiene‡.....	Benzoylethylene		(47)
1,4-Diphenylbutadiene‡........	*α*-Naphthoquinone		(425)
1,4-Diphenylbutadiene‡........	*p*-Benzoquinone		(425)
1-Phenyl-4-(*p*-nitrophenyl) butadiene‡........	Maleic anhydride		(88)
cis-1,2,4-Triphenylbutadiene‡........	Maleic anhydride		(87)

TABLE 2—*Continued*

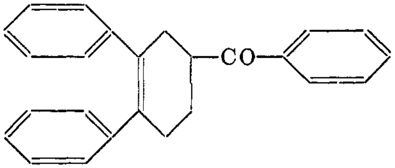
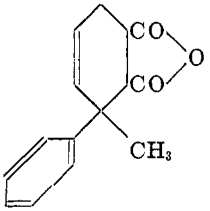
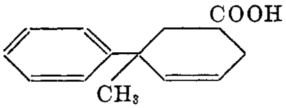
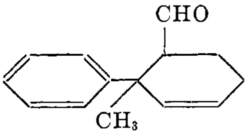
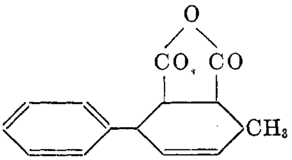
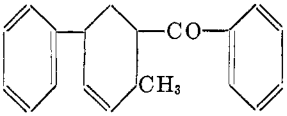
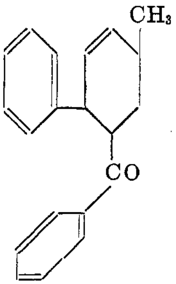
DIENE	DIENOPHILE	PRODUCT	REFERENCE
trans-1,2,4-Triphenylbutadiene	Maleic anhydride	No reaction	(87)
2,3-Diphenylbutadiene‡	Benzoylethylene		(47)
1-Phenyl-1-methylbutadiene‡	Maleic anhydride		(279)
1-Phenyl-1-methylbutadiene†	Acrylic acid		(279)
1-Phenyl-1-methylbutadiene*	Acrolein		(277, 279)
1-Phenyl-4-methylbutadiene‡	Maleic anhydride		(144)
1-Phenyl-4-methylbutadiene†	Benzoylethylene	 or 	(47)

TABLE 2—*Continued*

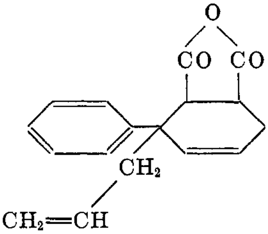
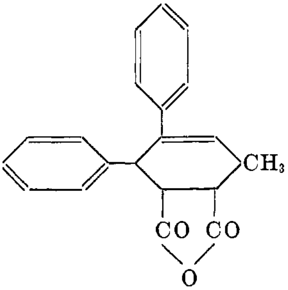
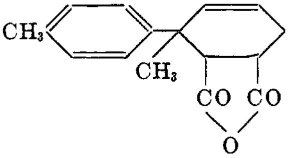
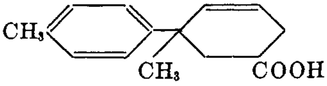
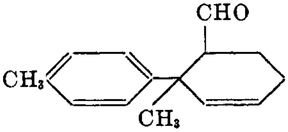
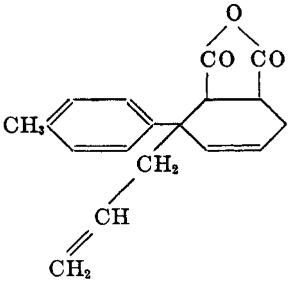
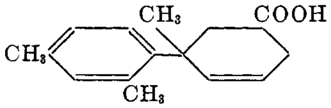
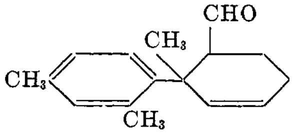
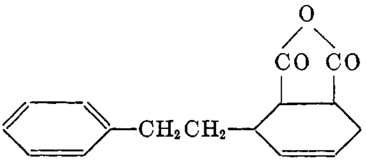
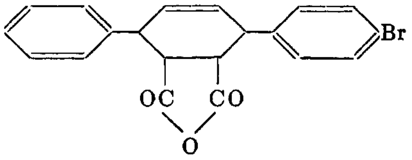
DIENE	DIENOPHILE	PRODUCT	REFERENCE
1-Phenyl-1-allylbutadiene‡......	Maleic anhydride		(280)
1,2-Diphenyl-4-methylbutadiene‡........	Maleic anhydride		(87)
1-*p*-Tolyl-1-methylbutadiene‡........	Maleic anhydride		(279)
1-*p*-Tolyl-1-methylbutadiene†........	Acrylic acid		(279)
1-*p*-Tolyl-1-methylbutadiene†........	Acrolein		(277, 279)
1-*p*-Tolyl-1-allylbutadiene‡......	Maleic anhydride		(280)

TABLE 2—*Concluded*

DIENE	DIENOPHILE	PRODUCT	REFERENCE
1-(4-*m*-Xylyl)-1-methylbutadiene†	Acrylic acid		(279)
1-(4-*m*-Xylyl)-1-methylbutadiene†	Acrolein		(277, 278, 281)
1-(2-Phenylethyl)-butadiene‡	Maleic anhydride		(122)
1-(2-Phenylethyl)-1-methylbutadiene	Maleic anhydride	Amorphous powder at 110 C.	(122)
1-(2-(*m*-Methoxyphenyl)ethyl)-butadiene	Maleic anhydride	No reaction	(122)
1,2,3,4-Tetraphenylbutadiene	Maleic anhydride	No reaction	(425)
1,4-Di(*p*-anisyl)-butadiene	Maleic anhydride	No reaction	(425)
1-Phenyl-4-*p*-bromophenylbutadiene	Maleic anhydride		(410)
1-(2-(*m*-Methoxyphenyl)ethyl)-butadiene	Acrolein	No reaction	(122)
1,4-Bis(*o*-biphenylene)butadiene	Maleic anhydride	No reaction	(346)

* Structure of adduct proved in literature cited.

† Structure of adduct assumed.

‡ Structure of adduct considered evident because only one structure is possible by the general rules (page 320) of adduct formation.

Referring again to table 2, the adduct of 1-phenyl-1-methylbutadiene and acrylic acid was found in two forms. Theoretically, one might obtain two acids, for it is theoretically possible for the carboxyl group to become located either ortho or meta to the geminal grouping. Each of these two acids should exist in two forms, depending on whether the carboxyl group is *cis* or *trans* with respect to the methyl (or the phenyl) group of the geminal system. Hence four acids are theoretically possible through the addition of acrylic acid to 1-phenyl-1-methylbutadiene. Furthermore, each of the four acids should be resolvable into *d*- and *l*-forms. The above assumes that the *cis*-form of cyclohexene is the only form capable of existence. Now the structure of the adduct resulting from the interaction of 1-phenyl-1-methylbutadiene and acrolein was proved. If the acrylic acid adducts have the formula given in table 2, then oxidation of the acrolein adducts should give one or both of the acids obtained by acrylic acid addition. Oxidation was accomplished by a Cannizzaro reaction (279), and two acids were produced. One of these was identical with an acid obtained by acrylic acid addition, but the other was not. Presuming that the acrolein is added to give a mixture of the *cis*- and the *trans*-forms of the compound given in table 2, then a logical conclusion is that acrylic acid adds to 1-phenyl-1-methylbutadiene to give a mixture of one of the ortho acids with one of the meta acids. While this explains the findings of Lehmann (279), it has not been proved conclusively. The case of 1-phenylbutadiene is related to this specific problem. Its acrolein adduct has the aldehyde group ortho to the geminal system, while its acrylic acid adduct has the carboxyl group meta to that system.

Parallel situations are found in the cases of the acrolein and acrylic acid adducts of 1-*p*-tolyl-1-methylbutadiene and of 1-(2,4-dimethylphenyl)-1-methylbutadiene, and may be amenable to the same explanation. Each forms one acrolein and two acrylic acid adducts. Two acids are formed upon oxidation of the acrolein adduct, only one of which is identical with one of the acrylic acid adducts. Structures of the acrolein adducts were not proved, however.

The structure of the product obtained from *p*-benzoquinone and 1-phenyl 1-methylbutadiene is assumed to be the oxidized adduct shown, because of the extensive reduction of excess quinone to hydroquinone and quinhydrone. The adducts of butadiene with *p*-benzoquinone are easily oxidized to naphtho- and anthra-quinones, the structures of which are those of 5,8-dihydro-1,4-naphthoquinone and 1,4,5,8-tetrahydro-9,10-anthraquinone; this may be accomplished in an alkaline medium at room temperature with atmospheric oxygen. It is logical, therefore, to assume that in the case of 1-phenyl-1-methylbutadiene and *p*-benzoquinone, the hydrogenated quinone ring of the original adduct is completely aromatized by the excess *p*-benzoquinone.

Addition of maleic anhydride to 1,4-diphenylbutadiene appeared to give four isomeric acids melting in the range 198° to 203°C. The form melting at 198°C. decomposed into its generators on distillation. From a stereochemical point of view, two anhydride adducts could be produced in which the phenyl groups are para and *cis* to each other, and one anhydride adduct could be produced in which the phenyl groups are *trans* to each other. The two *cis*-forms and the one *trans*-form explain three of the four acids observed. The fourth acid may be formed by a change of one of the acids (all of which possess carboxyl groups *cis* to each other) into an acid in which the carboxyl groups are *trans* to each other. For reasons to be discussed later, it is not likely that the anhydride possessing *trans*-phenyl groups is formed in the diene synthesis; therefore it seems more likely that certain of the four acids are the result of isomerizations of the *cis*-phenyl-*cis*-acids which are presumed to be formed initially.

TABLE 3

Reaction of chlorinated dienes with dienophiles

DIENE	REACTION*	REFERENCE
1-Chloro-1,2-butadiene	Negative	(101)
Chloroprene (2-chlorobutadiene)	Positive	(102)
3-Methylchloroprene	Positive	(121)
1-Alkylchloroprenes	Positive	(121, 254)
3,4-Dimethylchloroprene	Positive	(121)
2,3-Dichlorobutadiene	Positive	(89, 121)
1,2,3,5-Tetrachloro-2,4-pentadiene	Negative	(121)
1,3,4-Trichloro-2,4,5-hexatriene	Negative	(121)
3,4-Dichloro-1,2,4,5-hexatetraene	Negative	(121)
1-Chlorobutadiene (α-chloroprene)	Negative	(121)
4-Chloro-1,2,3,4-hexatetraene	Negative	(121)
1,4-Dichloro-2,3,5-hexatriene	Negative	(121)
1,2-Dichlorohexa-3-yne-5-ene	Negative	(121)
3,4-Dichloro-1,3,5-hexatriene	Negative	(121)
1,6-Dichloro-2,3,4-hexatriene	Negative	(121)
4-Chloro-1,2,3,5-hexatetraene	Negative	(121)
1-Chloromethylchloroprene	Positive	(202)
1-Bromomethylchloroprene	Positive	(201)
1-Chloro-5-methoxy-2,3-pentadiene	Negative	(403, 404)
1-Methoxy-3-chloro-2,4-pentadiene	Positive	(403, 404)

* In the eight cases in which addition occurred, the formulas of the products were in accord with those postulated by application of the general rules of adduct formation.

B. Halogenated dienes

Some work has been done on halogenated dienes, particularly by Carothers and his coworkers. With respect to the ability of these dienes to add maleic anhydride or α-naphthoquinone, the following generalizations may be drawn: (*a*) Dienes of the structure $\mathrm{Cl{-}C{=}C{-}C{=}C}$ or $\mathrm{C{=}C(Cl){-}C(Cl){=}C}$ do not add dienophiles. (*b*) Dienes of the structure $\mathrm{C{=}C(Cl){-}C{=}C}$, in the absence of other chlorine atoms in the molecule, usually add dienophiles as well as do the parent hydrocarbons.

Table 3 lists chlorodienes which were tested with respect to their ability to add 1,4-naphthoquinone or maleic anhydride. In those cases where reaction occurs, the structure of the product is that predicted by the general rules of adduct formation. It will be noted that one of these compounds is an allene, while certain others combine the structures of allenes and conjugated dienes.

The conclusion of Carothers was that when the diene reaction is used as a test for conjugation, it is conclusive only when positive. Even so, this may not be strictly true unless reaction is observed at or near room temperature, particularly in the cases of terpenes and sterols. Further, the diene synthesis will not detect *trans*-butadienoid configurations as such. In the cases of terpenes, certain additions occurred when the "diene" contained an isolated-double-bond system or a lone double bond; in one case, the "diene" was a fully saturated compound. All additions in these cases were conducted at elevated temperatures and the same adduct could, in certain instances, be obtained from several different "dienes," which is conclusive proof of isomerization in one or more stages of the addition. These materials did not react readily at room temperature, although the end products postulated for the isomerization of the materials prior to undergoing the diene synthesis reacted readily at room temperature.

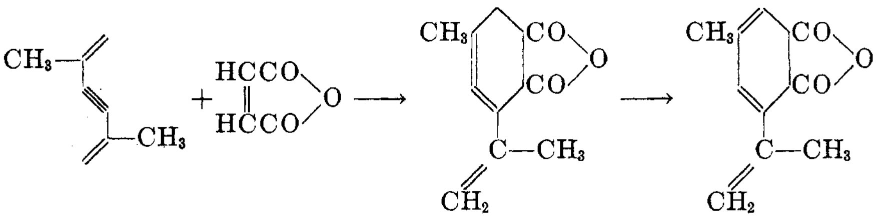
C. Allenes

Dienes containing the grouping C═C═C do not react with dienophiles, provided (*a*) isomerization to a conjugated system does not occur under the conditions of the experiment, and (*b*) the compound under investigation does not contain a conjugated system in addition to the allene system, as in the skeletons C═C═C—C═C and C═C═C—C—C═C—C═C. Certain of these compounds were investigated by Carothers and reported in table 3. The only other studies made were those of 1-cyclohexyl-2,3-pentadiene, which does not add maleic anhydride (2), and of 1-phenyl-1,2-butadiene, which adds neither maleic anhydride nor 1,4-naphthoquinone (1).

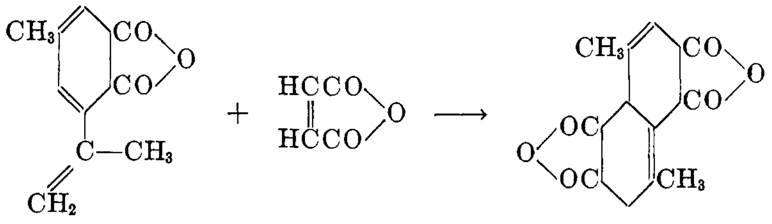
D. Enynes

As indicated in the earlier portions of this review, only a few enynes have been studied. Most of those studied belong to the dienyne class. The field is being opened up, however, by Lewis and Eleanore Butz and their coworkers. At this writing their latest paper is to be read at the 102nd Meeting of the American Chemical Society, and it will deal with enynes in the diene synthesis.

The addition of 2,5-dimethylhexa-1,5-dien-3-yne (100) and maleic anhydride proceeds, probably in two steps, to give a reduced naphthalenetetracarboxylic dianhydride:

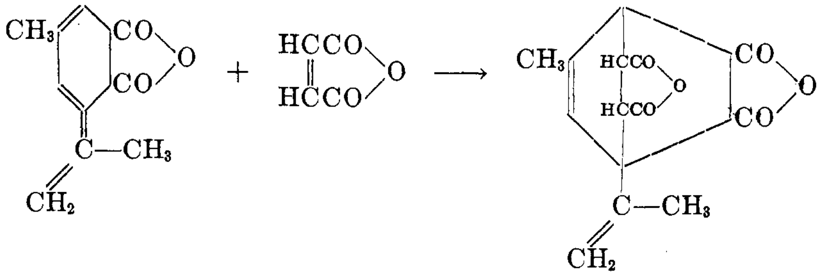


(1)

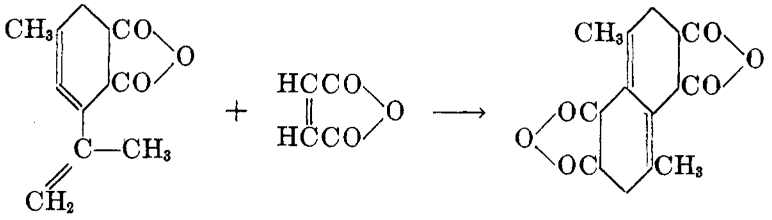


(2)

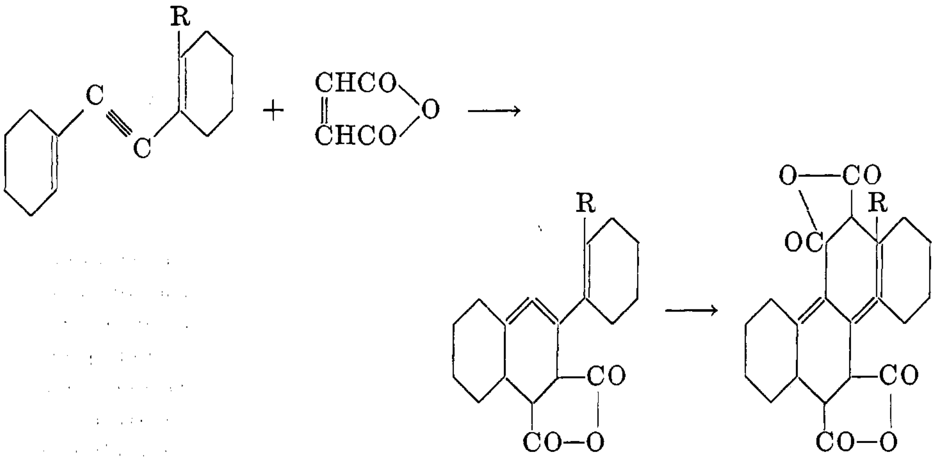
The mechanism given is that proposed by Butz; however, it seems unnecessary and indeed undesirable to postulate the isomerization of the first adduct before addition of the second mole of maleic anhydride. The author is not aware of the certainty of the locations of the double bonds in the final product as claimed by Butz. If isomerization must occur before the second mole of dienophile is added, then the substance obtained would be a mixture of the product indicated by Butz with the final product indicated immediately below:



That this conclusion is not unreasonable may be seen when it is pointed out that 1,3-cyclohexadienes are slightly more active in the diene synthesis than are open-chain dienes. If isomerization does not occur prior to addition of the second mole of maleic anhydride, the product would be that indicated below, barring subsequent isomerization:

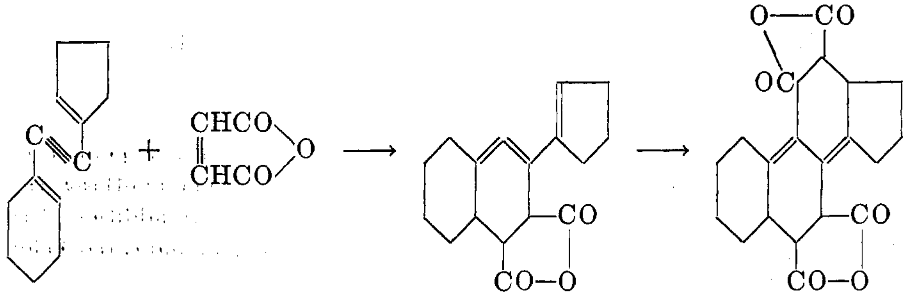


A recent paper by Joshel, Butz, and Feldman (412) describes the diene syntheses accomplished with di(1-cyclohexenyl)acetylene and 1-cyclohexenyl(2-methyl-1-cyclohexenyl)acetylene, each of which adds 2 moles of maleic anhydride. The formula of the product is given as that which might be expected if no rearrangement of double bonds occurs between the additions of the first and the second moles of maleic anhydride:



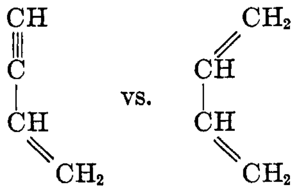
(R = H or CH_3)

Butz and Joshel (398) have been able to synthesize compounds containing the sterol-ring structure by employing 1-cyclohexenyl-1-cyclopentenylacetylene in the diene synthesis. With maleic anhydride, the reaction appears to proceed as follows:



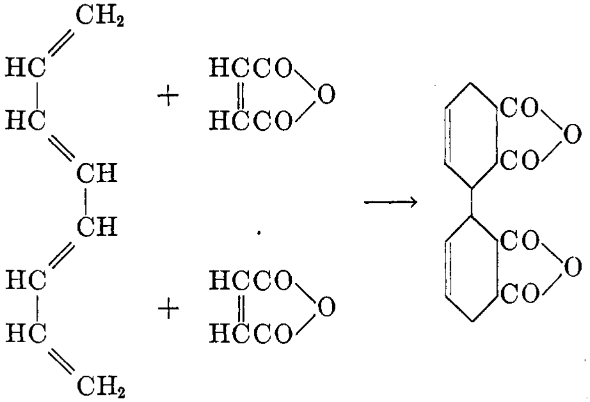
Dimethyl and diethyl fumarates have been added (399) to the above two cyclic dienynes to give adducts of structures similar to those with maleic anhydride.

The yields of adducts from these diene syntheses are not usually very high, since carbon atoms 1 and 4 of the vinylacetylene residue are further apart than in dienes. This is because acetylene is a straight-line molecule, while ethylene is more angular. In vinylacetylene and butadiene a comparison may be drawn. The inference is that proximity of carbon atoms 1 and 4 favors the diene synthesis:



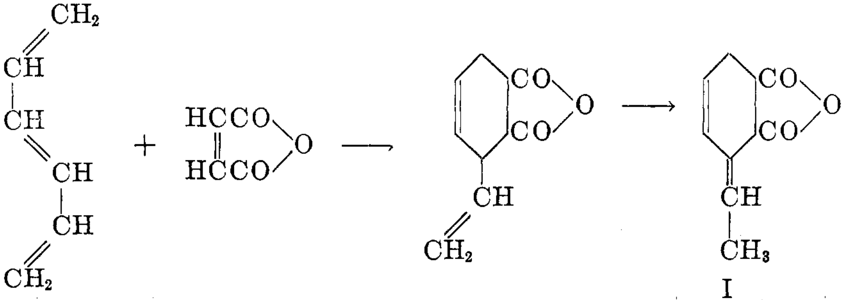
V. POLYENES

Since the conjugated polyenes possess the structure C═C—C═C, it is possible for them to add dienophiles. Further, in a triene such as hexatriene, it is of great importance to determine if the addition of a dienophile takes place at the 1,4- or 1,6-positions, or both; or in higher polyenes, to determine if addition takes place in the 1,4-, 1,6-, 1,8-, or even 1,10-positions. Indications are that, irrespective of the length of the conjugated system, addition invariably takes place at the 1,4-positions, and that each pair of conjugated double bonds in the system acts as an independent unit. Thus 1,3,5,7-octatetraene would add two mole proportions of maleic anhydride to form 1,2,3,4,1′,2′,3′,4′-octahydro-2,3,2′,3′-tetracarboxydiphenyl dianhydride:



A. *Trienes, tetrenes, etc.*

The simplest conjugated triene, 1,3,5-hexatriene, has been studied more thoroughly than any other polyene. It was first studied by Farmer and Warren (199), who obtained adducts with both *cis*- and *trans*-hexatrienes. They assigned structure I to the adduct obtained with maleic anhydride, the formation of which involves a rearrangement of the unattacked terminal double bond as well as the usual double-bond shift of a 1,4-addition to a conjugated diene. Kharasch, Nudenberg, and Sternfeld (267) claim that the structure is not that given by Farmer and Warren, but is that of 3-vinyl-1,2,3,6-tetra-

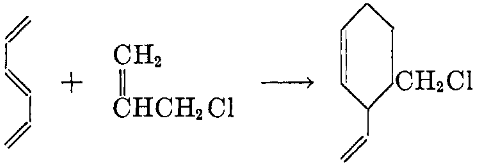


I

hydrophthalic anhydride, evidence being adduced from spectroscopic data. If conditions of the addition are drastic enough to cause the double-bond shift postulated by Farmer and Warren, it would seem that they would be sufficiently drastic to cause further wandering into the ring, since in the terpenes semicyclic double bonds such as this exhibit a marked tendency to wander into the ring, particularly under the influence of acids. The resulting product is usually a conjugated cyclic diene, which adds dienophiles with great avidity. Since hexatriene adds but 1 mole of maleic anhydride, support is given the Kharasch structure. Although the Farmer and Warren adduct structure is that of a conjugated diene, it would not be expected to add maleic anhydride without a preliminary double-bond rearrangement, because of the fixed *trans*-butadienoid structure of this compound.

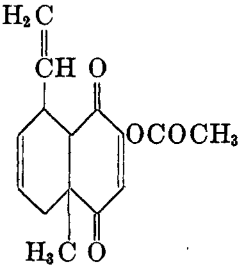
Much of the confusion may be cleared up by the discovery that the 1,3,5-hexatriene of Farmer and Warren contained cyclohexadiene (397).

Kharasch and Sternfeld (268) prepared 1,3,5-hexatriene by the reaction of allyl chloride with a solution of sodium amide in liquid ammonia. In this preparation a diene reaction was noted between hexatriene and allyl chloride:

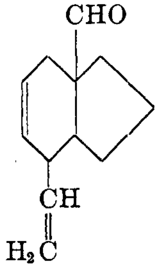


The product could have been the meta-isomer, but this was proved not to be the case. This reaction is quite unusual, for it occurs at −33°C. with a dienophile which does not possess the activating carbonyl group.

Butz and his coworkers have studied additions of other dienophiles to 1,3,5-hexatriene. α-Naphthoquinone (99) gave 1,1a,4,4a-tetrahydro-1-vinyl-9,10-anthraquinone, in agreement with Kharasch's postulates concerning the structure of the side chain of hexatriene adducts. 4-Hydroxytoluquinone acetate and 1-aldehydocyclopentene give compounds which are thought to be II and III, respectively:



II



III

In the case of II, the obvious alternative is an adduct containing an angular acetoxyl group. Presumably the facility of formation of angular groups is inversely proportional to their size. Since the methyl group is smaller than the acetoxyl group, the angular methyl group should be formed preferentially; actually, both are formed.

The adduct with α-naphthoquinone may be oxidized by air to α-vinyl-9,10-anthraquinone. Butz (98, 99) opines that the structures given for the adducts with 4-hydroxytoluquinone acetate and with 1-formylcyclopentene are the "most probable" structures (II and III), but says that the structure assigned to III is tentative. It is certain, however, that angular groups exist in the compounds represented by II and III.

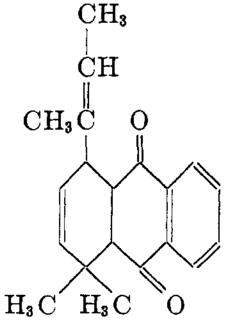
Robinson, Walker, and Todd (310) assert that 1,3,5-hexatriene does not add 1-methyl-1-cyclohexen-3-one.

Kharasch and his students (267) have extended their hexatriene synthesis to the preparation of 2,5-dimethyl-1,3,5-hexatriene, using methallyl chloride (3-chloro-2-methyl-1-propene). This adds maleic anhydride, giving the expected compound, 1,2,3,6-tetrahydro-4-methyl-6-isopropenylphthalic anhydride.

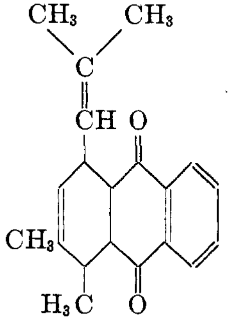
Vitamin A and related compounds, such as bixin, the carotenes, lycopene, and the xanthenes, should be capable of adding one or more moles of maleic anhydride by virtue of their long-chain conjugated systems. Kuhn and Wagner-Jauregg (273) have demonstrated addition of maleic anhydride to dyes of the bixin and carotene series. Vitamin D_2 (calciferol) is a highly substituted ring-fused hexatriene which adds maleic anhydride (368). It reacts much less readily, however, than does vitamin A (124). A separation of the vitamin D of fish-liver oils from the accompanying vitamin A and carotene (124) is based upon this fact.

Arbuzov (54, 57) has added α-naphthoquinone to alloöcimene. Though the structure of the product was not proved, evidence was secured which indicated that the structure was IV rather than V. Alloöcimene also adds crotonaldehyde and acrolein, but Arbuzov (58) neither proved the structure nor made an assumption or suggestion as to which of the four possible structures for each adduct was the correct one. The adducts appeared to be chemical individuals rather than mixtures.

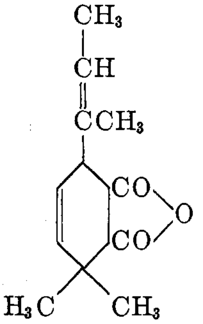
Alloöcimene adds maleic anhydride (192, 238, 407) to give a product presumed to be VI, although the alternative structure (VII) has not been disproved.



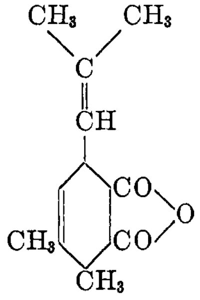
IV



V



VI



VII

Diphenylpolyenes were investigated by Diels, Alder, and Pries; also by Kuhn and Wagner-Jauregg (152, 273). 1,6-Diphenyl-1,3,5-hexatriene adds maleic anhydride in the 1- and 4-positions. 1,8-Diphenyloctatetraene adds 1 mole of maleic anhydride in boiling xylene at the 1- and 4-positions; by fusing the generators together, 2 moles of maleic anhydride were added. In boiling xylene 2 moles of maleic anhydride are added to give an isomer which yields *p*-tetraphenyl on decarboxylation and oxidation, thus showing that the second mole of maleic anhydride adds at the 5- and 8-positions. The tetraene also added 2 moles of fumaroyl chloride.

1,10-Diphenyl-1,3,5,7,9-decapentaene adds 2 moles of maleic anhydride. Decarboxylation and oxidation of the two isomeric products formed gave a material which appeared to be 1,2-bis-*p*-xenylethylene, indicating that the 2 moles of maleic anhydride had added at the 1-, 4-, 7-, and 10-positions. 1,12-Diphenyl-1,3,5,7,9,11-dodecahexaene appeared to add 3 moles of maleic anhydride; oxidation and decarboxylation of the product gave a material which appeared to be *p*-quinquephenyl. The important conclusions of the investigators were (*a*) that the diphenylpolyenes add maleic anhydride in positions which correspond with those in butadiene and (*b*) that the positions nearest the phenyl groups are the most reactive. This latter conclusion arose from the fact that degradation of the adducts from 1,10-diphenyldecapentaene appeared to give 1,2-bis-*p*-xenylethylene rather than ω-(*p*-xenyl)styrene.

B. Dienynes

Several dienynes were discussed on pages 380–382 as examples of enynes, for that particular field has not been well developed as yet. Rapid progress is being made, however. Two other dienynes have been studied,—namely, 6,9-dimethyltetradeca-5,9-dien-7-yne (92), and 4,7-di-*n*-propyldeca-3,7-dien-5-yne (100). These react with 2 moles of maleic anhydride, but the products appear to be amorphous and not well established. Referring to page 382, the ring structure of the adduct of 2,5-dimethylhexa-1,5-dien-3-yne and maleic anhydride (100) was proved by degradation to 1,5-dimethylnaphthalene.

VI. HOMOCYCLIC DIENES

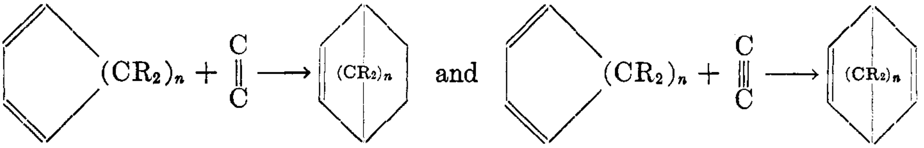
A. General

Under this heading are discussed dienes which contain their dienic double bonds in a ring composed exclusively of carbon atoms, such as cyclopentadiene and cyclopentadienone; also, compounds in which one dienic double bond is situated in a ring and the other is situated either in a side chain or else in a second ring which usually is not fused to the first ring. All rings are aliphatic in character; compounds in which one or both of the dienic double bonds are situated in a completely aromatic ring are reserved for later discussion.

1,3,5-Cyclohexatriene (benzene) has never been observed to add dienophiles, although a number of cases are known in which one of the dienic double bonds is located in a lone benzene ring and one case (9,10-anthraquinone) appears to be known in which both dienic double bonds are located in a lone benzene ring.

The first recorded addition of a dienophile to cyclopentadiene (aside from its polymerization reaction, studied by Staudinger (337) and by Bergel and Widmann (81)) was made by Albrecht (379) in 1906, using certain quinones and unsaturated ketonic compounds. Diels and Alder (136) clarified the structure of the adducts, and other illustrations of the diene synthesis with cyclic dienes were published shortly thereafter.

The general statement postulated for the diene synthesis (page 320) holds true for the homocyclic dienes, and may be written in the forms

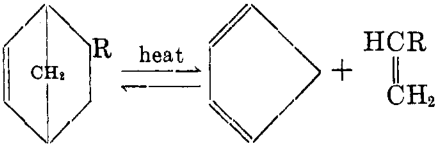


where R may be hydrogen, oxygen, or nearly any alkyl or aryl radical. Theoretically, n may be any number, but the highest value studied appears to be 3.

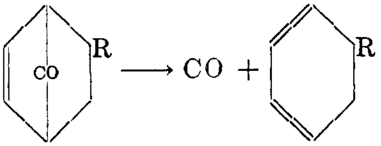
The adducts obtained from these cyclic dienes have a most interesting behavior on distillation at atmospheric pressure. Adducts of cyclopentadiene and its homologs either distil unchanged or else decompose into their generators. Adducts of cyclopentadienones usually evolve carbon monoxide, and the resulting product is either a benzene derivative (if derived from an acetylenic dienophile) or else a substituted cyclohexadiene which is easily oxidized to such a derivative. Occasionally the cyclohexadiene dehydrogenates spontaneously on heating (Allen). Adducts of 1,3-cycloheptadienes either distil unchanged or else decompose into their generators. The adducts of 1,3-cyclohexadienes with acetylenic dienophiles decompose on distillation to give an olefin and a benzene derivative. Fusion of adducts of cyclohexadienes and quinones in the presence of air leads to simultaneous oxidation and splitting of olefin. If a temperature is employed which is below that required to split out olefin, then oxidation occurs to give a compound which splits out olefin at the higher temperature. The products of olefin-splitting are aromatic quinones. Dismutation of partially hydrogenated quinone adducts may be brought about by acetic anhydride in certain instances. When adducts of cyclohexadienes with olefinic dienophiles are distilled, more or less deep-seated changes occur. The usual reaction is to give a benzene derivative and the reduced dienophile. In this manner, the adducts of α-phellandrene and of 1,3-menthadiene (α-terpinene) with maleic anhydride give succinic anhydride and *p*-cymene.

Below is a summary of the reactions indicated in the preceding paragraph:

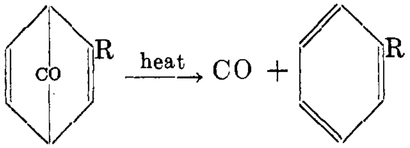
(1)



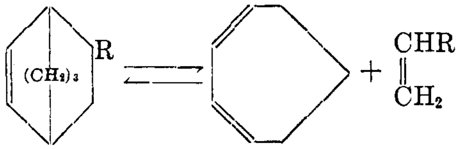
(2)



(3)



(4)



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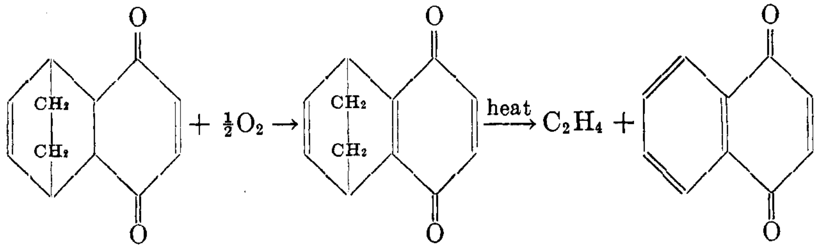
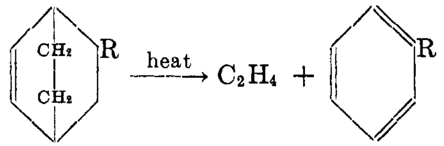


(6)



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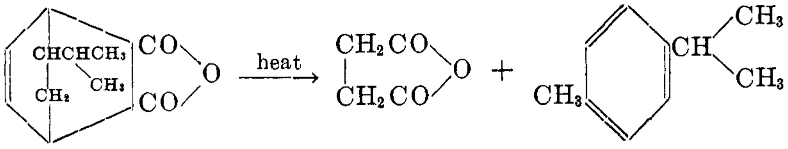
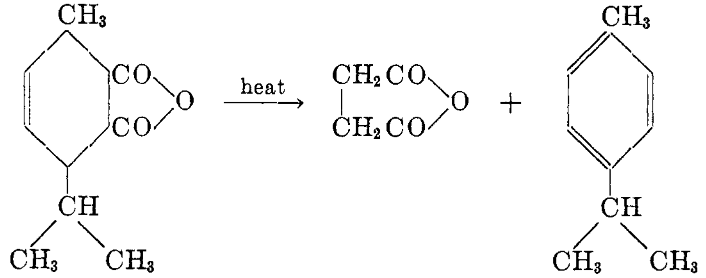


(8) 

Specific examples of the foregoing reaction types are the decomposition of the cyclohexadiene–acetylenedicarboxylic ester adduct to give ethylene and diethyl phthalate (18); the fusion of the adduct from 2 moles of cyclohexadiene and 1 mole of *p*-benzoquinone to give ethylene and 9,10-anthraquinone (34), atmospheric oxidation occurring simultaneously; the decomposition of the adduct of α-phellandrene and acetylenedicarboxylic ester to give isopropylethylene and 4-methylphthalic ester (147); and the dismutation by acetic anhydride of a partially hydrogenated adduct of cyclopentadiene with α-naphthoquinone to give α-naphthohydroquinone diacetate, cyclopentadiene, and water (which appears as acetic acid) (153).

The ethylene and carbonyl bridges are not the sole types which split out on heating, however. Lactone bridges (—CO—O—) will split out carbon dioxide on heating; this bridge is not particularly heat-stable. A good example of this reaction is found in the addition of maleic anhydride to cumalin and its derivatives, discussed elsewhere in this review. Another type is the splitting of ethylene from the partially hydrogenated adducts of certain furan derivatives with acetylenedicarboxylic ester to give dicarboxylated furan esters.

B. Cyclopentadienes

The most extensively studied of the homocyclic dienes is cyclopentadiene itself. It has been found to react with a wide variety of dienophiles, giving the anticipated products. Most of these reactions are listed in table 4; others may be found in tables 1 and 2. Polymerization reactions of the compound are discussed in a subsequent section devoted to dimerization (see page 430).

An interesting reaction of the adduct with azodicarboxylic ester is the splitting of the endomethylene bridge by hydrogen chloride to give the adduct of 1-methyl-4-chlorobutadiene and azodicarboxylic ester:

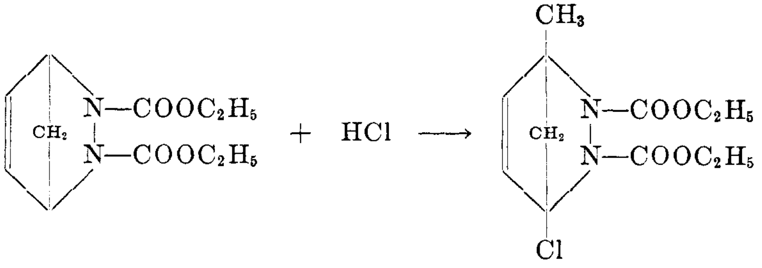


TABLE 4

Additions of dienophiles to cyclopentadiene

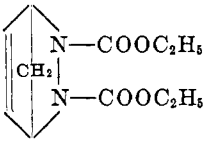
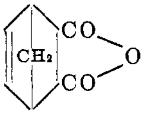
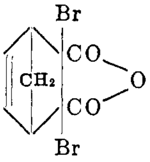
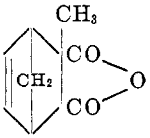
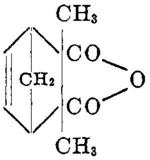
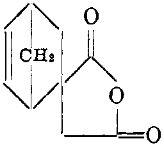
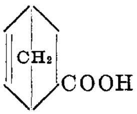
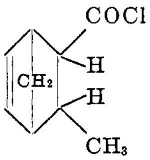
DIENOPHILE	ADDUCT	REFERENCE
Ethylene	3,6-Endomethylenecyclohexene	(411)
Azodicarboxylic ester		(157)
Maleic anhydride		(136, 137, 166)
Dibromomaleic anhydride		(151)
Citraconic anhydride		(136)
Pyrocinchonic anhydride		(146, 166)
Itaconic anhydride		(136)
Acrylic acid		(35, 37, 136)
trans-Crotonoyl chloride		(35)

TABLE 4—*Continued*

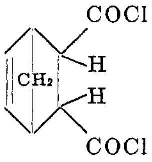
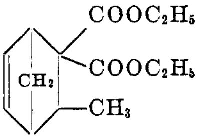
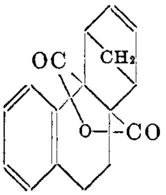
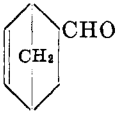
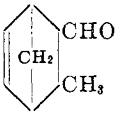
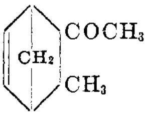
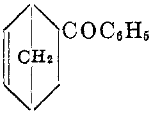
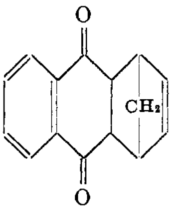
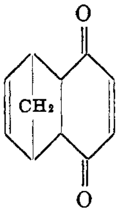
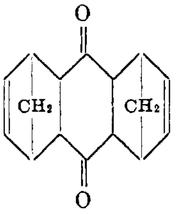
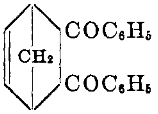
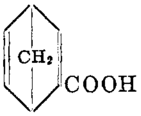
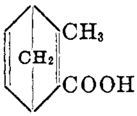
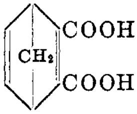
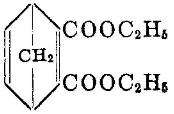
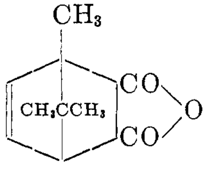
DIENOPHILE	ADDUCT	REFERENCE
Fumaroyl chloride		(35)
Ethylidenemalonic ester		(18)
1,2-Dihydro-3,4-naphthalic anhydride		(213)
Acrolein		(35, 136, 144, 150, 263)
Crotonaldehyde		(114, 150)
Ethylideneacetone		(139)
Benzoylethylene		(47)
α-Naphthoquinone		(153)

TABLE 4—*Concluded*

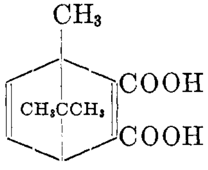
DIENOPHILE	ADDUCT	REFERENCE
p-Benzoquinone	 and 	(23, 153, 196)
cis- and *trans*-1,2-dibenzoylethylenes		(3, 6)
Propiolic acid		(39)
Tetrolic acid		(166)
Acetylenedicarboxylic acid		(147)
Acetylenedicarboxylic ester		(147)

Certain homologs and derivatives of cyclopentadiene have been investigated. Damsky (128) prepared a trimethylcyclopentadiene by distillation of the calcium salt of either α- or β-camphylic acid. Wandering of a methyl group or of a double bond (43) occurs during the pyrolysis, and the product is not 1,1,2-trimethyl-2,4-cyclopentadiene; however, it does contain a conjugated system, inasmuch as it adds vinyl acetate (44) at elevated temperatures and adds maleic anhydride and acetylenedicarboxylic ester more easily (45). If the decarboxylations of the α- and β-camphylic acids are conducted in quinoline with a copper chromate catalyst, the reactions take place at a temperature which is too low to result in isomerization of the product, and 1,1,2-trimethyl-2,4-cyclopentadiene is obtained (45). This diene is useful for the synthesis of terpinoid derivatives of bornane.

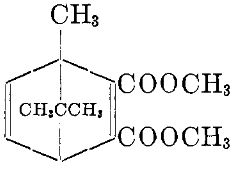
At elevated temperatures, vinyl acetate adds to 1,1,2-trimethylcyclopentadiene to give a mixture of *dl*-dehydrobornyl acetate and *dl*-dehydroepibornyl acetate. Hydrogenation, hydrolysis, and oxidation of the former adduct give *dl*-camphor. The diene also adds maleic anhydride, acetylenedicarboxylic acid, and acetylenedicarboxylic dimethyl ester to give the adducts I, II, and III:



I

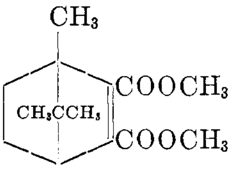


II

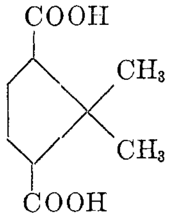


III

Adduct III may be partially reduced by platinum and hydrogen to give IV, oxidation of which by nitric acid gives a trimethylcyclopentanedicarboxylic acid (V).

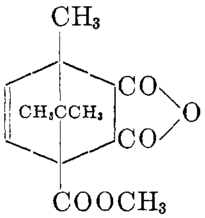


IV

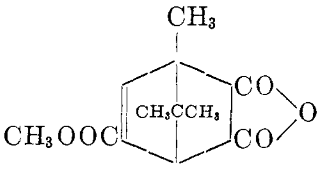


V

The camphylic acid esters add maleic anhydride, vinyl acetate, acetylenedicarboxylic acid, and acetylenedicarboxylic esters to give adducts of anticipated structures (44, 45). The maleic anhydride adducts of methyl α- and β-camphylates are VI and VII, respectively.



VI

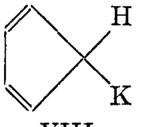


VII

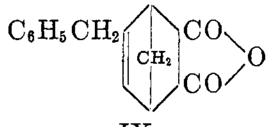
Owing to the fact that two structures are theoretically possible through the use of vinyl acetate as a dienophile, the structures of the vinyl acetate addition products are not certain.

Potassium powder, suspended in benzene or other suitable medium, reacts with cyclopentadiene to give potassium cyclopentadiene, presumably VIII.

This reacts with benzyl chloride to give a mixture of the 2- and 3-benzylcyclopentadienes, which react with maleic anhydride to give the expected adducts (12, 13). Oxidation of the adduct derived from the 3-benzyl isomer (IX) gives benzoic acid and *cis-*,*cis-*,*cis-*,*cis-*1,2,3,4-cyclopentanetetracarboxylic acid (21).



VIII



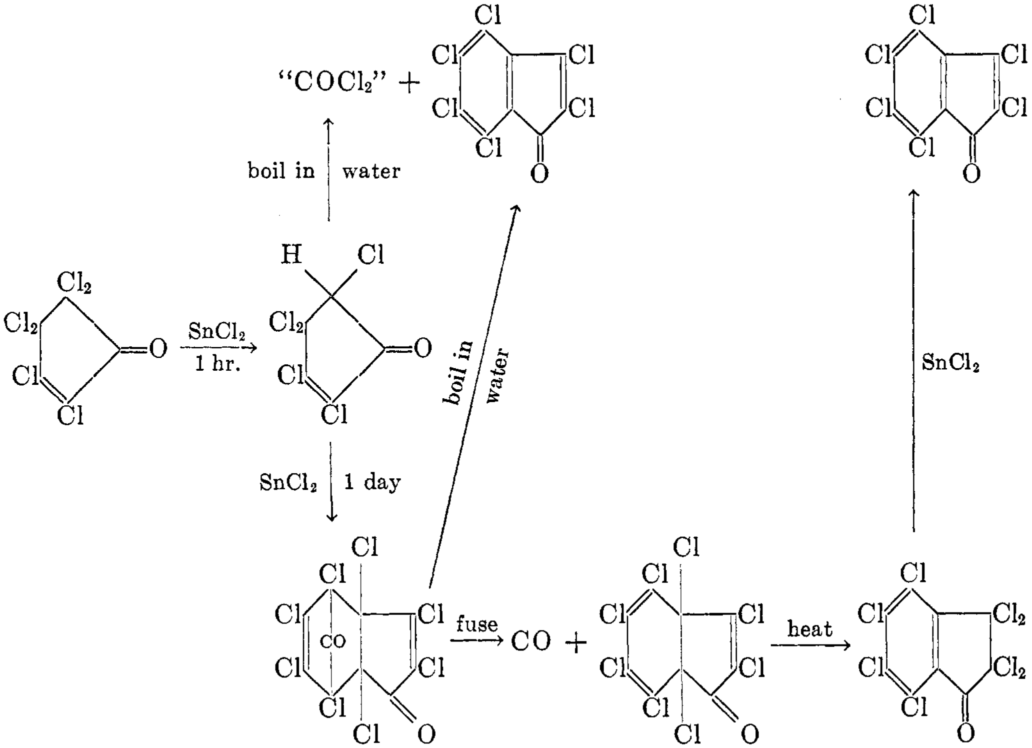
IX

C. Cyclopentadienones

Of particular interest are the reactions of the phenyl- and chloro-substituted cyclopentadienones, for these combine the structures of reactive diene and reactive dienophile. The simpler members of the series are so reactive that they have not been isolated in the monomeric state, although their transitory existence may be demonstrated. The higher members of the series are still highly reactive, adding such inert dienophiles as acetylene, butadiene, benzonitrile, and acenaphthylene. Those cyclopentadienones with phenyl groups substituted on the 1- and 4-positions of the butadienoid system of cyclopentadienone do not dimerize, probably because of the stereochemical difficulties involved. These compounds are a fine example of the fact that the carbonyl group will enhance the reactivity of a diene as well as that of a dienophile.

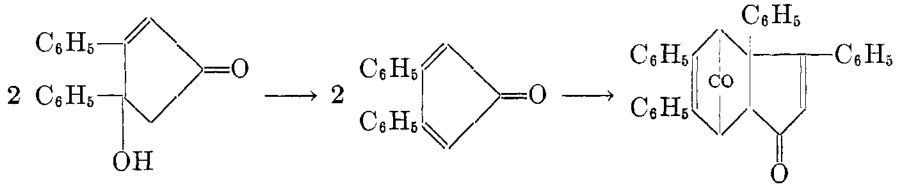
The first of these cyclopentadienones to be investigated was tetrachlorocyclopentadienone, by T. Zincke and his collaborators in the period 1893–1912 (376, 377, 378). It was first observed that hexachlorocyclopenten-3-one was reducible to 1,2,4,5,5-pentachlorocyclopenten-3-one by stannous chloride during the course of 1 hr. When boiled with water, this substance lost hydrogen chloride to form tetrachlorocyclopentadienone; this compound dimerized immediately to a compound which lost the elements of phosgene (apparently the phosgene was hydrolyzed by water to carbon dioxide and hydrogen chloride) and formed hexachloroindone. It was found later that prolonged reduction (one to two days) of hexachlorocyclopenten-3-one by stannous chloride at room temperature gave the dimer of tetrachlorocyclopentadienone. The stannous chloride probably served no useful function after the initial reduction; mere standing in water was no doubt sufficient for the tetrachlorocyclopentadienone to form and dimerize. Boiling the dimer with water gave hexachloroindone, carbon dioxide, and hydrogen chloride.

In 1912 it was found that phosgene was not liberated as such. It was shown that the dimer of tetrachlorocyclopentadienone loses carbon monoxide at its melting point to form an octachlorodihydroindone, and that further heating causes double-bond rearrangement to octachlorohydrindone. This is easily reduced by stannous chloride to give hexachloroindone. Hence the formation of hexachloroindone by boiling the dimer of tetrachlorocyclopentadienone with water is due, in part at least, to reduction of octachlorohydrindone by carbon monoxide or one of its immediate precursors. The various reactions are shown below diagrammatically:

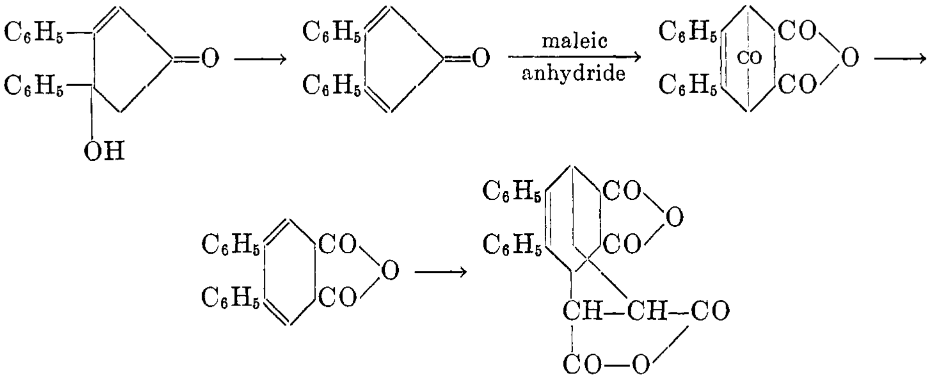


The phenylated 2,4-cyclopentadienones which have been studied include 3,4-diphenyl-, 2,3,4-triphenyl-, 2,3,5-triphenyl-, and 2,3,4,5-tetraphenyl-cyclopentadienones. The last named is also known as tetracyclone. Allied to these purely phenyl-substituted cyclopentadienones are 2,5-diphenyl-3,4-(*o*,*o*′-biphenylene)cyclopentadienone (phencyclone), and 2,5-diphenyl-3,4-(peri-naphthylene)cyclopentadienone (acecyclone). None of the 2,5-diphenylated compounds dimerizes even under extreme conditions of temperature. It is possible, therefore, to obtain all but the first two cyclopentadienones listed above in the monomeric state. These monomers are all highly colored substances.

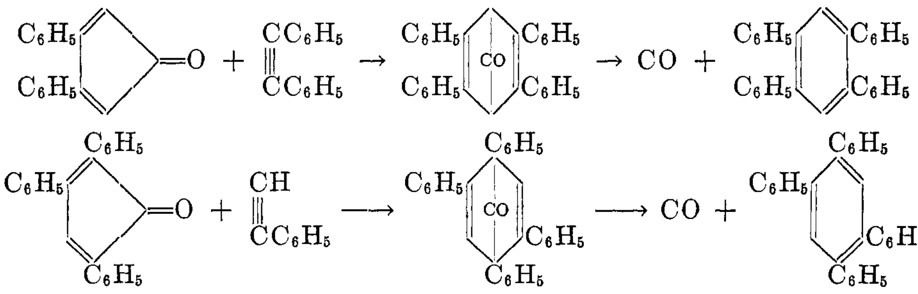
3,4-Diphenylcyclopentadienone is formed from anhydracetonebenzil in several ways (50, 51), one being by dehydration with acid. It enjoys only a transitory existence, however, dimerizing almost immediately under the conditions employed:



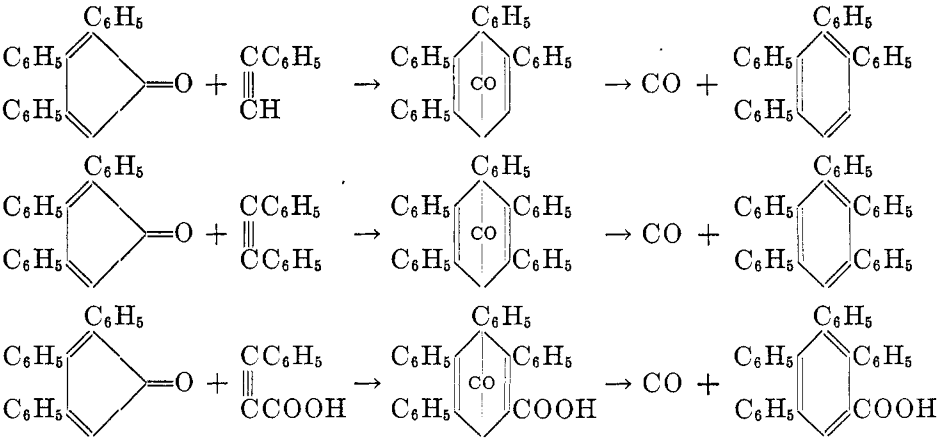
By using a large excess of maleic anhydride as the dehydrating agent, the existence of the monomeric form of 3,4-diphenylcyclopentadienone may be shown (52) by the formation of considerable quantities of an adduct derived from maleic anhydride and the monomer:



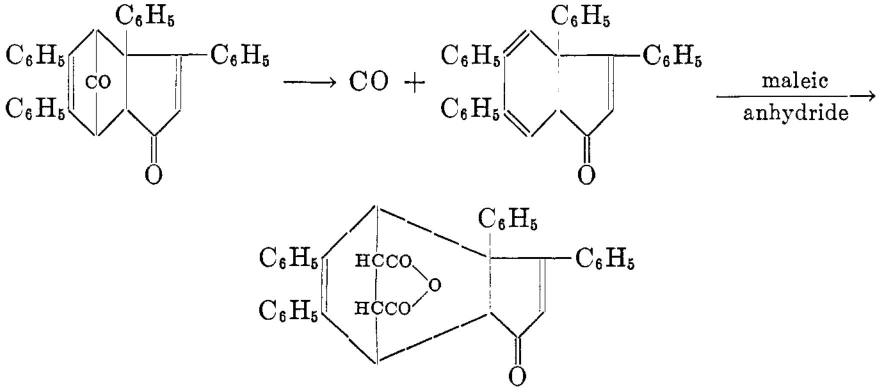
In similar fashion (178), the heating of a mixture of anhydracetonebenzil with diphenylacetylene will yield a small amount of 1,2,4,5-tetraphenylbenzene, together with much 3,4-diphenylcyclopentadienone dimer and its pyrolysis products. The same product, 1,2,4,5-tetraphenylbenzene, may be obtained in quantitative yield by the reaction of 2,3,5-triphenylcyclopentadienone (178) with phenylacetylene. The other product which is theoretically possible (1,2,3,5-tetraphenylbenzene) is not produced:



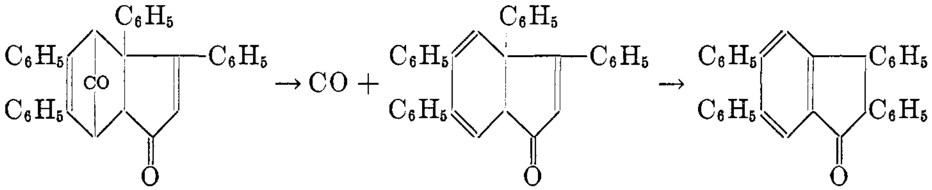
2,3,4-Triphenylcyclopentadienone is not known in the monomeric state, and dimerizes almost on formation. As in the case of 3,4-diphenylcyclopentadienone, its transitory existence may be shown by heating triphenylcyclopentenolone with phenylacetylene, phenylpropiolic acid, or diphenylacetylene. The products formed with these three dienophiles are 1,2,3,4-tetraphenylbenzene, 2,3,4,5-tetraphenylbenzoic acid, and pentaphenylbenzene, respectively (178):



It will be noted that loss of the endocarbonyl bridge occurs in each of the above syntheses. With acetylenic dienophiles this is especially true, the resulting carbonyl bridge being highly unstable toward heat. This is true to a lesser degree with the endoethylene and endolactone bridges. In the above cases, the instability of the carbonyl bridge is so great that these intermediates usually cannot be isolated. When the dienophile is an acid, the endocarbonyl compound can sometimes be obtained. Room-temperature dimerization of those cyclopentadienones which are capable of dimerization likewise gives endocarbonyl compounds. In this fashion the dimer of 3,4-diphenylcyclopentadienone loses carbon monoxide at about 230°C. to give 1,5,6,9-tetraphenyl-9,10-dihydroindone (52) and carbon monoxide. If maleic anhydride is present, an adduct is formed with this cyclohexadiene derivative:



In the absence of maleic anhydride, continued heating of 1,5,6,9-tetraphenyl-9,10-dihydroindone at 250°C. results in rearrangement to 1,2,5,6-tetraphenylhydrindone. Care is required, therefore, for success in isolating the isomeric 9,10-dihydro compound, for heating at 230°C. for any considerable length of time will also result in extensive rearrangement (52):

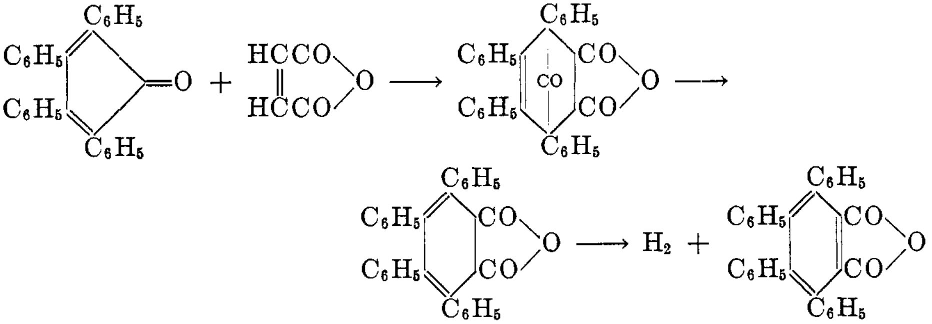


This rearrangement is analogous to that observed by Zincke (*vide supra*). The structure of the final product was confirmed by degradation to *o*-terphenyl. By heating the 9,10-dihydro compound with sulfur, 1,5,6-triphenylindene and thiophenol were formed (52). This is one of the few cases on record in which an angular aryl group is removed by sulfur dehydrogenation.

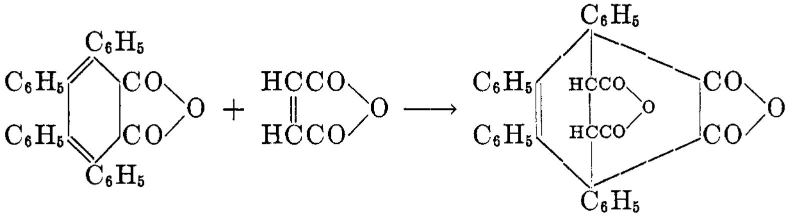
Tetracyclone (2,3,4,5-tetraphenylcyclopentadienone) was first prepared by Ziegler and Schnell (374) and almost simultaneously by Loewenbein and Ulich (287). It is a highly colored compound (red), as are all the monomeric arylated cyclopentadienones. Dilthey (180) prepared the compound by reaction of benzil with dibenzylketone to give a diphenylanhydracetonebenzil which could be dehydrated easily to tetracyclone. By substituting phenanthrenequinone or acenaphthalenequinone for benzil, one obtains phencyclone or acecylone (180).

Tetracyclone is a very reactive dienic compound, though it does not dimerize. It not only adds comparatively unreactive dienophiles with ease, but it reacts with unsaturated substances which are not ordinarily thought of as dienophiles. Accordingly, it reacts with benzonitrile, liberating carbon monoxide and forming pentaphenylpyridine (181). A reaction is also shown with sulfur, the reaction products being carbon monoxide and thionessal (tetraphenylthiophene); a similar reaction is shown by 2-(*p*-anisyl)-3,4,5-triphenylcyclopentadienone, which gives carbon monoxide and the corresponding *p*-methoxythionessal (181; see also J. prakt. Chem. [2] **151**, 185 (1938)).

Maleic anhydride adds to tetracyclone, and here the various intermediates may be isolated. The first product is 3,6-endocarbonyl-1,2,3,6-tetrahydro-3,4,5,6-tetraphenylphthalic anhydride; at higher temperatures this loses carbon monoxide to form 3,4,5,6-tetraphenyl-1,2-dihydrophthalic acid. At still higher temperatures, hydrogen is evolved and 3,4,5,6-tetraphenylphthalic acid is formed (49, 51, 182, 184):



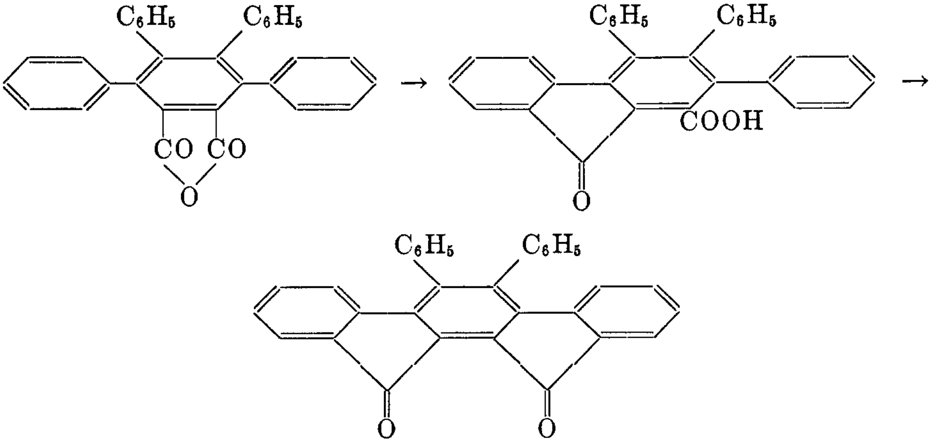
The conversion of the dihydro acid to tetraphenylphthalic acid is best accomplished by use of a dehydrogenating agent, such as sulfur, or by using an oxidizing solvent (nitrobenzene) for the reaction mixture. If the formation of tetraphthalic acid is carried out in one step from tetracyclone and maleic anhydride, the final product contains small amounts of the adduct of maleic anhydride with the dihydrophthalic acid:



A considerable number of other dienophiles has been added to tetracyclone. Indeed, this compound has been the most thoroughly studied of the cyclopentadienones with regard to activity in the diene synthesis. Benzalacetophenone was reported (49) not to add to tetracyclone, but it was shown later that addition would occur under forcing conditions (47), the products being carbon monoxide and 2,3,4,5,6-pentaphenylbenzophenone. Acetylene is added, even at 100°C., to give carbon monoxide and 1,2,3,4-tetraphenylbenzene (182). Phenylacetylene gives carbon monoxide and pentaphenylbenzene (182), and stilbene gives hydrogen, carbon monoxide, and hexaphenylbenzene of melting point 426°C. (182). The same product was obtained without evolution of hydrogen by the use of diphenylacetylene in place of stilbene (178, 181, 182). The melting point of the hexaphenylbenzene thus obtained was nearly 200°C. higher than that reported previously in the literature, which corresponded more closely with that of 1,2,4,5-tetraphenylbenzene. The previous preparation was made by the interaction of phenylmagnesium bromide with hexachlorobenzene; duplication of this work gave a similar compound (177). Molecular-weight determinations showed that the previously reported hexaphenylbenzene was in reality a tetraphenylbenzene, while the compound produced by the addition of diphenylacetylene or stilbene to tetracyclone had an observed molecular weight agreeing with the theoretical value for hexaphenylbenzene. It has an uncorrected melting point of 426°C. The previous report of the synthesis of hexaphenylbenzene must be regarded as an error.

Diphenylbutadiyne (181) also adds to tetracyclone with evolution of carbon monoxide and the product is (pentaphenylphenyl)phenylacetylene. Further reaction, which would produce decaphenylbiphenyl, does not appear to occur. With butadiene (181), such double addition does occur; carbon monoxide is evolved and the product is a mixture of octaphenylbiphenyl with various hydrogenated octaphenylbiphenyls. Cyclohexene adds in a forced reaction (181), giving carbon monoxide, hydrogen, and *Bz*-tetraphenyltetralin. Phenylbromoacetylene (181) adds easily to give pentaphenylbromobenzene. Acenaphthylene (176) gives 2,3,4,5-tetraphenyl-1,6-(peri-naphthylene)benzene. Benzoylethylene (47) adds, with evolution of carbon monoxide and hydrogen, to give 2,3,4,5-tetraphenylbenzophenone. Phenylpropiolic aldehyde (182) gives carbon monoxide and pentaphenylbenzaldehyde, and phenylpropiolic nitrile gives carbon monoxide and pentaphenylbenzonitrile.

The additions of unsaturated dibasic acids and certain of their esters to tetracyclone often result in products which contain the carbonyl bridge. The bridge can be removed by further heating and finally an aromatic acid or ester may be formed. This was shown to be the case in the addition of maleic anhydride to tetracyclone. True adducts containing the carbonyl bridge are rarely isolable in other cases. Of the dienophiles mentioned above, none undergoes reaction at temperatures lower than the temperatures required for complete decomposition of their adducts, save for maleic anhydride. Additions of the methyl and ethyl esters of acetylenedicarboxylic acid require too high a temperature to allow isolation of such intermediates (49, 184), and the products are methyl and ethyl tetraphenylphthalates. The same products are obtainable from the corresponding esters of maleic acid. While no endocarbonyl intermediate can be obtained with dimethyl maleate, such may be obtained with diethyl maleate and with dimethyl fumarate (49), because the temperatures required for reaction with the latter two esters are lower than the decomposition temperatures of the adducts resulting from such addition. Strong heating of these adducts also gives tetraphenylphthalic esters. These esters, being derived from hindered aromatic acids, are difficult to hydrolyze (49), and the ethyl ester of tetraphenylphthalic acid is stable to molten alkali at 360°C. The corresponding acid anhydride, from tetracyclone and maleic anhydride or acetylenedicarboxylic acid, condenses to a fluorenone on treatment with aluminum chloride in boiling benzene (184); more drastic treatment gives a difluorenone.



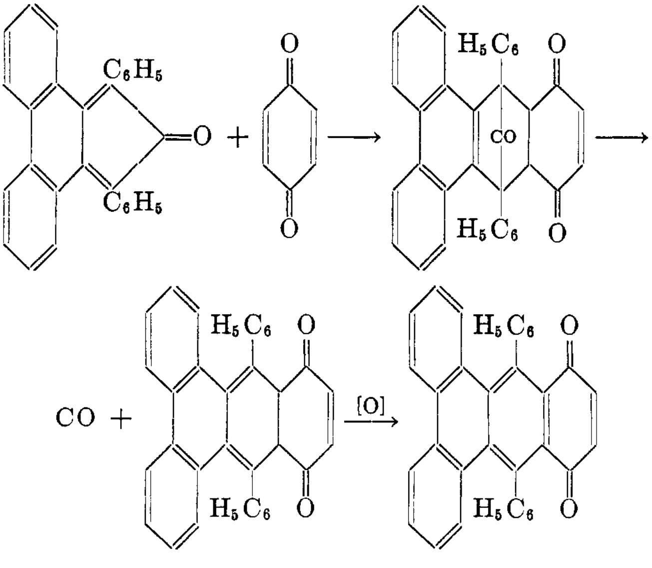
Phenylpropiolic methyl ester (184) requires a high temperature for addition to tetracyclone; consequently the intermediate carbonyl-bridged adduct is not obtainable. The corresponding acid (182, 184) also requires a high temperature for addition; it yields pentaphenylbenzoic acid. This latter acid can be condensed (184) with aluminum chloride to give 1,2,3,4-tetraphenylfluorenone. Tetrolic acid or its ethyl ester (184) gives tetraphenyl-*o*-toluic acid or its ester.

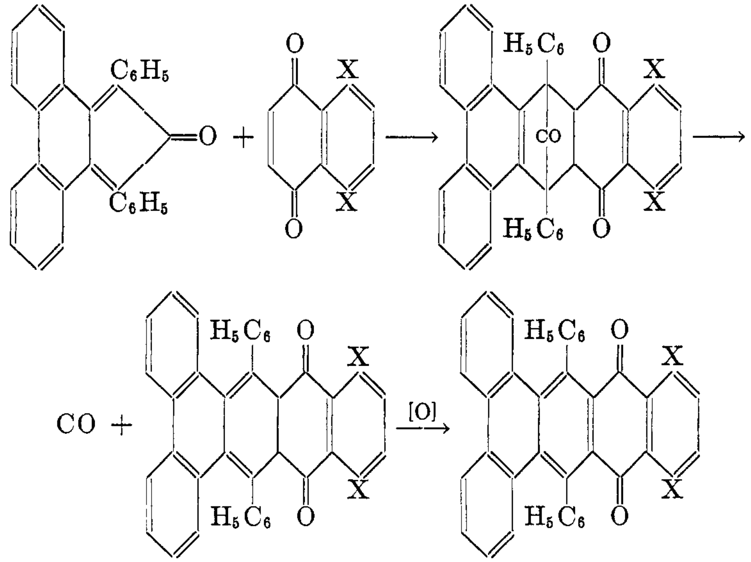
Diphenylketene does not react (49) with tetracyclone. This supports Staudinger's hypothesis (81) that diphenylketene undergoes 1,2-addition to conjugated and isolated double bonds. Quinones appear not to have been investigated, at least with tetracyclone, but the fact that adducts containing endocarbonyl bridges may be prepared with phencyclone and quinones lends support to the prediction that such will also be found to be the case with tetracyclone.

Grummitt and coworkers (408) report that tetracyclone adds a mole of cyclopentadiene to give a carbonyl-bridged adduct. In attempting to remove the carbonyl bridge by heating, preferential dissociation took place to give the original generators. No reaction was noted between tetracyclone and furan, pyrrole, *N*-methylpyrrole, or thiophene.

Allen and van Allan (387) describe 2,5-dimethyl-3,4-diphenylcyclopentadienone as being midway between 3,4-diphenylcyclopentadienone and tetracyclone. This substance is not known in the monomeric form, but in solution its dimer reacts as if it were monomeric. This dissociation of the dimer should be compared with 3,4-diphenylcyclopentadienone, which dimerizes completely and permanently, and with tetracyclone, which does not dimerize at all. Thus, the dimer of 2,5-dimethyl-3,4-diphenylcyclopentadienone will add acetylene, phenylacetylene, β-nitrostyrene, vinyl phenyl ketone, maleic anhydride, and other dienophiles because of the preliminary dissociation to the monomeric form.

Phencyclone (180) reacts with *p*-benzoquinone, naphthoquinone, naphthazarin, and naphthazarin diacetate to give adducts containing carbonyl bridges. Heating to elevated temperatures causes loss of carbon monoxide, and dihydroquinones are formed which may be dehydrogenated by atmospheric oxygen or other dehydrogenating agents to give fully aromatic quinones. In order to isolate these intermediates, it is essential that one operate in an inert atmosphere (carbon dioxide). *p*-Benzoquinone finally gives 1,2,3,4-dibenz-9,10-diphenyl-5,8-anthraquinone; α-naphthoquinone gives 1,2,3,4,6,7-tribenz-9,10-diphenyl-5,8-anthraquinone; and naphthazarin or its diacetate gives 1,4-diphenyl-2,3-(*o*,*o*′-biphenylene)-5,8-dihydroxy-9,10-anthraquinone or its diacetate:



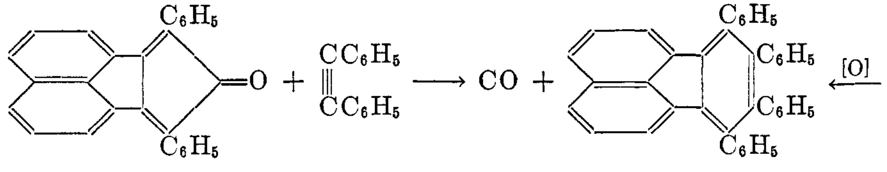


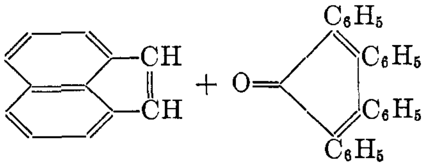
(X = hydrogen, hydroxyl, or acetoxyl)

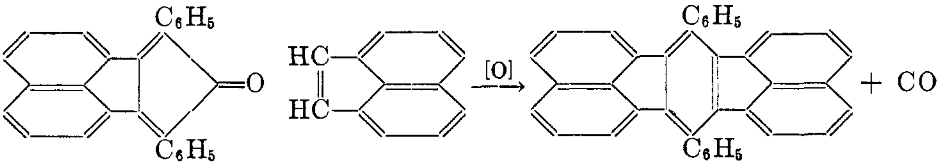
Reduction of these quinones from *p*-benzoquinone and from *α*-naphthoquinone would give the corresponding hydrocarbons. It can be seen, therefore, that this method offers means of preparing diphenylated dibenzanthracenes and naphthacenes and related hydrocarbons, some of which may be carcinogenic.

Phencyclone has been added to fumaric acid, maleic acid, and maleic anhydride (183), phenylpropiolic acid (176), phenylacetylene (176), diphenylacetylene (176), and benzoylethylene (47) to give products corresponding with those obtained from tetracyclone. It also reacts with sulfur, but the reaction is more complex than that with tetracyclone; the product is of more or less indefinite composition, for the amount of sulfur utilized ranges between four and five atoms per molecule of phencyclone. When distilled, this sulfurized product affords a 20 per cent yield of biphenylenediphenylthiophene, there being evolved carbon dioxide, carbon monoxide, carbon oxysulfide, and hydrogen sulfide.

Acecyclone shows no reaction whatever with sulfur. It has been shown to add benzoylethylene (47), acetylene (176), and phenylacetylene (176); the structures of the products correspond with those of the tetracyclone series. The adduct with diphenylacetylene (176) is identical with the adduct obtained from tetracyclone and acenaphthylene; acecyclone also adds acenaphthylene to give carbon monoxide and 1,4-diphenyl-2,3,5,6-bis(peri-naphthylene)benzene (176):





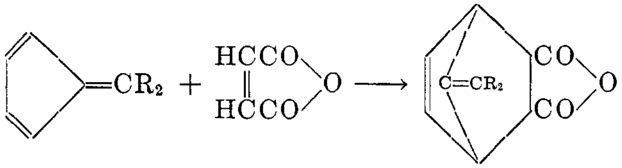


Benzalacetophenone, diphenylketone, and 1,2-dibenzoylethylene could not be added to either phencyclone or acecyclone (49).

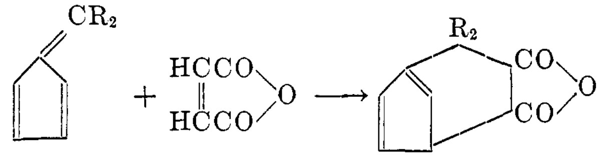
D. Fulvenes

Fulvenes are the 1-alkylidenecyclopentadienes, and contain one more double bond than cyclopentadiene. This double bond is conjugated with each of the two double bonds of the cyclopentadiene ring, and at first sight one might think that ambiguity might arise in determining which of the two possible routes (A or B) might be followed by the addition of dienophiles to fulvenes:

(A)



(B)



The fact that the postulated addition represented by reaction B would occur through addition to a *trans*-butadienoid system (see page 323) and that addition A would occur through addition to a *cis*-butadienoid system strongly suggests that addition A occurs rather than B. Further, the hypothetical reaction product of B possesses a 1,3-cyclopentadiene ring and therefore should be capable of adding a second mole of dienophile. Only 1 mole of dienophile adds to the fulvenes.

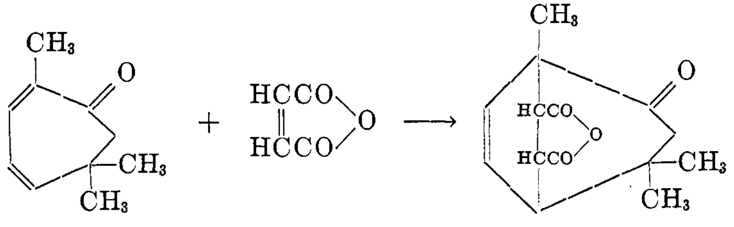
An outstanding characteristic of fulvene adducts is the fact that they are usually dissociated to a greater or less extent when in solution, though stable in the solid state. The extent of dissociation can be estimated colorimetrically in many cases, since the sole colored material in the equilibrium mixture is the fulvene (270). Oftentimes molecular-weight determinations are employed for estimation of the degree of dissociation of these adducts. Equilibrium is attained slowly in these solutions, as may be shown by the gradual increase in color of a solution of a fulvene adduct on standing.

Dimethylfulvene and diphenylfulvene react with maleic anhydride to give adducts which dissociate in solution, as do the maleic anhydride adducts of tetra- and penta-methylenefulvenes (which are prepared from cyclopentadiene and cyclopentanone or cyclohexanone (27, 270)). An interesting case is that of β-styrylfulvene (270), which contains both the fulvene and straight-chain butadiene structures: $C_6H_5CH{=}CH{-}CH{=}C({=}C_4H_4)$. This compound could add maleic anhydride across either the cyclopentadiene ring or the butadienyl side chain, or both. Circumstantial evidence indicates that addition occurs across the ring, for the maleic anhydride adduct is dissociated in solution (270). A more stable adduct, which would involve the butadiene structure, might be formed at elevated temperatures. Formation of such an adduct appears to have been neither attempted nor reported.

E. Cyclohexadienes and cycloheptadienes

The liberation of an olefin and simultaneous formation of a benzene derivative on pyrolysis of adducts of acetylenic dienophiles with cyclohexadienes serves to distinguish cyclohexadienes from cyclopentadienes and cycloheptadienes (13). The test is not conclusive unless it is shown that both the olefin and the benzene derivative are formed, since the partially reduced adducts of acetylenedicarboxylic ester with furan or sylvan (2-methylfuran) and also the decarboxylated adduct of anthraquinone and maleic anhydride evolve ethylene on pyrolysis (14, 153). This property of evolution of olefins and formation of a benzene derivative is perhaps the most important chemical property of adducts of cyclohexadienes.

Cycloheptadiene adds acetylenedicarboxylic esters (14, 33) to give esters of 3,6-endopropylene-3,6-dihydrophthalic acid, which are either stable to heat or else decompose into their generators. Eucarvone (33, 357) is a cycloheptadienone; it adds maleic anhydride as follows:



Eucarvone

Cyclohexadiene additions have been rather well studied, though not as thoroughly as cyclopentadiene additions. Certain terpadienes, such as α-phellandrene, are conjugated cyclohexadienes. The decomposition of their acetylenedicarboxylic ester adducts to easily identified olefins and esters of phthalic acid and its homologs affords a convenient general method for structure determination of the original cyclohexadiene.

TABLE 5

Cyclohexadienes in the diene synthesis

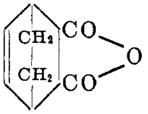
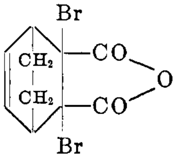
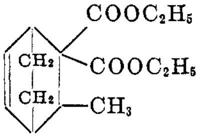
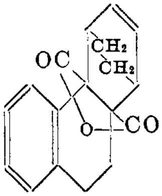
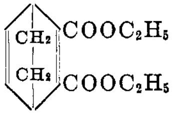
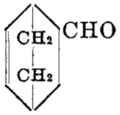
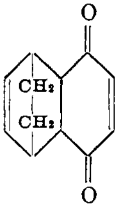
DIENE	DIENOPHILE	PRODUCT	REFERENCE
Cyclohexadiene....	Maleic anhydride		(136, 146, 199)
Cyclohexadiene....	Dibromomaleic anhydride		(151)
Cyclohexadiene....	Ethylidenemalonic ester		(18)
Cyclohexadiene....	1,2-Dihydro-3,4-naphthalic anhydride		(213)
Cyclohexadiene....	Acetylenedicarboxylic diethyl ester		(13, 14, 147)
Cyclohexadiene....	Acrolein		(151)
Cyclohexadiene....	Benzoylethylene	No reaction	(47)
Cyclohexadiene....	*p*-Benzoquinone		(23, 153)

TABLE 5—*Continued*

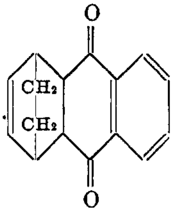
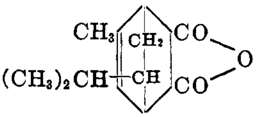
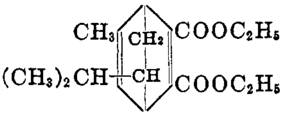
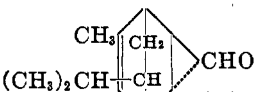
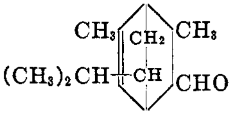
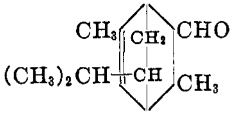
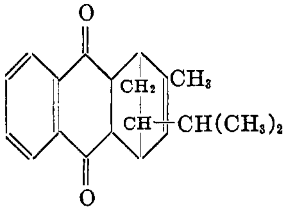
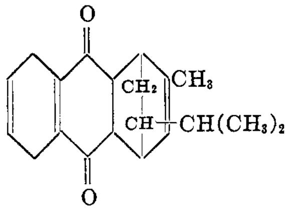
DIENE	DIENOPHILE	PRODUCT	REFERENCE
Cyclohexadiene....	α-Naphthoquinone		(153)
α-Phellandrene	Maleic anhydride		(136, 418)
α-Phellandrene	Acetylenedicarboxylic diethyl ester		(13)
α-Phellandrene	Acrolein	 (or)	(144)
α-Phellandrene	Crotonaldehyde	 or 	(144)
α-Phellandrene	Benzoylethylene	"A hopeless mass"	(47)
α-Phellandrene	α-Naphthoquinone		(153)
α-Phellandrene	5,8-Dihydro-1,4-naphthoquinone		(135)

TABLE 5—*Continued*

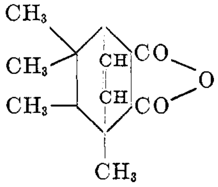
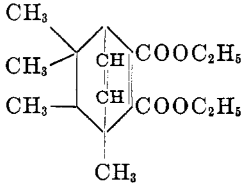
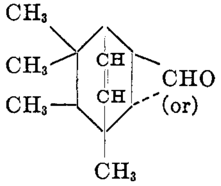
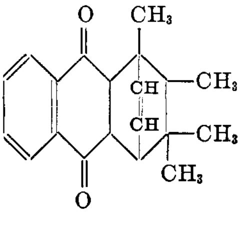
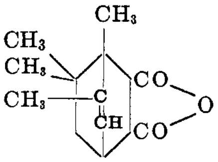
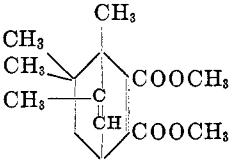
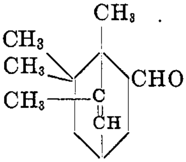
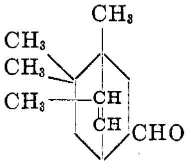
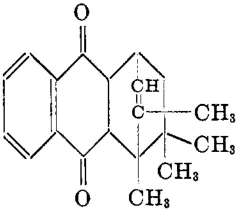
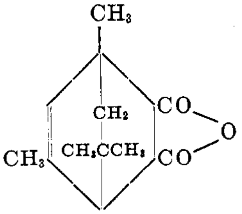
DIENE	DIENOPHILE	PRODUCT	REFERENCE
α-Pyronene........	Maleic anhydride		(190, 238, 407)
α-Pyronene........	Acetylenedicarboxylic dimethyl ester		(191)
α-Pyronene........	Acrolein		(190)
α-Pyronene........	Dibenzoylacetylene	No reaction	(191)
α-Pyronene........	*p*-Benzoquinone	No reaction	(191)
α-Pyronene........	α-Naphthoquinone		(191)
β-Pyronene........	Maleic anhydride		(190, 407)

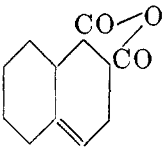
TABLE 5—*Concluded*

DIENE	DIENOPHILE	PRODUCT	REFERENCE
β-Pyronene........	Acetylenedicarboxylic methyl ester		(191)
β-Pyronene........	Acrolein	 (or) 	(190)
β-Pyronene........	Dibenzoylacetylene	No reaction	(191)
β-Pyronene........	*p*-Benzoquinone	No reaction	(191)
β-Pyronene........	α-Naphthoquinone		(191)
1,3,5,5,-Tetramethylcyclohexadiene........	Maleic anhydride		(413)

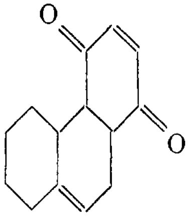
β-Phellandrene, though not a cyclohexadiene, is isomeric with α-phellandrene, and differs from the latter only in double-bond arrangement. One of these double bonds is semicyclic and is conjugated with the other. Refluxing with maleic anhydride (228) gives a resinous reaction product, high-vacuum distillation of which affords an 8 per cent yield of the adduct of α-phellandrene and maleic anhydride. This adduct could be detected only as the result of distillation and probably is formed on pyrolysis of the resin rather than by any direct interaction of maleic anhydride and β-phellandrene. This indicates that normal diene syntheses to *trans*-butadienoidal configurations do not occur without rearrangement, and is evidence for the rule given on page 323.

F. "Semicyclic" and dicyclic dienes

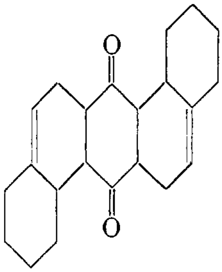
These include dienes such as 1-vinylcyclopentene and bis-1-cyclohexenyl. Of the first type, 1-vinylcyclohexene itself has been shown (126) to add maleic anhydride to give 1,2,3,5,6,7,8,8a-octahydro-1,2-naphthalic anhydride (IX) and to add *p*-benzoquinone to give 5,6,7,8,10,1a,4a,5a-octahydro-1,4-phenanthrenequinone (X) and also 1,1a,4,4a,5,5a,8,8a-*Bz*-(1,2,3,4)-*Bz'*-(1,2,3,4)-hexadecahydro-1,2,5,6-dibenz-9,10-anthraquinone (XI):



IX

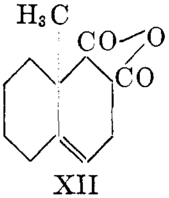


X

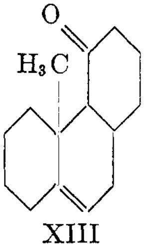


XI

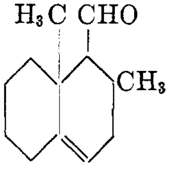
That these types of dienes are quite active is shown by the fact that 1-vinyl-2-methylcyclohexene adds maleic anhydride, cyclohexen-3-one, and crotonaldehyde (293) to give adducts XII, XIII, and XIV, respectively, all of which contain angular methyl groups.



XII

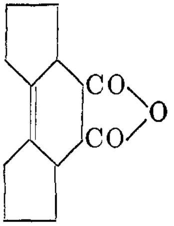


XIII

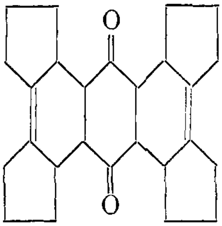


XIV

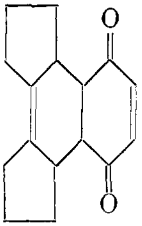
Bis-1,1'-cyclopentenyl (74) adds maleic anhydride to give the dicarboxylic acid (XV). In boiling methanol, *p*-benzoquinone adds 1 mole of the diene to give XVI; if the two compounds are boiled together for a minute or less (74), 2 moles of the diene are added to give XVII. α-Naphthoquinone adds 1 mole of the diene in boiling ethanol, giving XVIII.



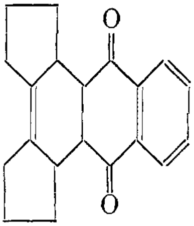
XV



XVI

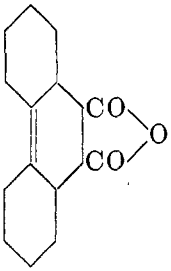


XVII

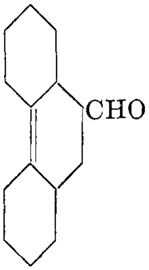


XVIII

The corresponding compound with six-membered rings, bis-1-cyclohexenyl, adds maleic anhydride (5, 74, 232) to give the reduced 9,10-phenanthrenedicarboxylic anhydride (XIX). Acrolein gives the reduced 9-aldehydophenanthrene (XX). *p*-Benzoquinone yields the reduced 9,10-benz-1,4-phenanthrenequinone (XXI) (74) when the generators are dissolved in boiling ethanol. When the generators are boiled together without any solvent, the product is the reduced 1,2,3,4,5,6,7,8-tetrabenz-9,10-anthraquinone (XXII). α-Naphthoquinone gives the reduced 1,2,3,4-dibenzanthraquinone (XXIII).



XIX



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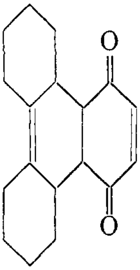
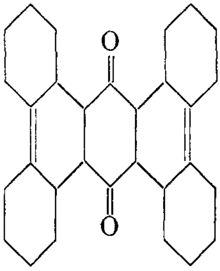
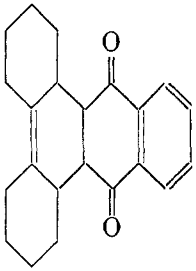


XXI



XXII



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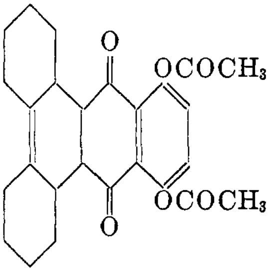
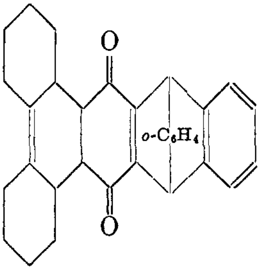
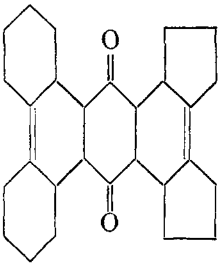


XXIV



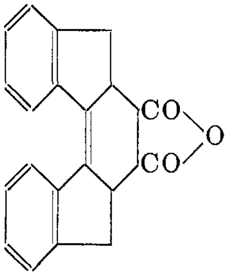
XXV



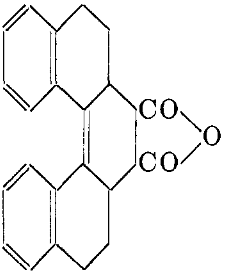
XXVI

Bis-1-cyclohexenyl is also added by naphthazarin diacetate (74) to give XXIV, and by 9,10-dihydro-9,10-endo-*o*-phenylene-1,4-anthraquinone (74) to give XXV. The quinone XVI, formed from bis-1-cyclopentenyl and *p*-benzoquinone in boiling methanol, will add a mole of bis-1-cyclohexenyl when the two are refluxed together (74), yielding XXVI.

Benzologs of the two above dienes have been studied. Bis-1-indenyl (340) has been shown to add maleic anhydride to give the reduced anhydride (XXVII), and 1,1′-bidialin (bis-3,4-dihydro-1-naphthyl) likewise gives the reduced anhydride (XXVIII). The bidialin addition does not take place as readily as does the bis-1-cyclohexenyl addition (297, 352). Barnett (74) reported failure to obtain a pure maleic anhydride addition product with bidialin, and stated that no reaction was observed between bidialin and *p*-benzoquinone or α-naphthoquinone.



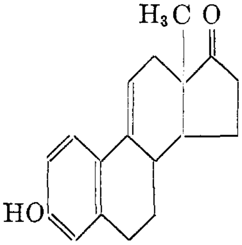
XXVII



XXVIII

Benzologs of 1-vinyl-1-cyclohexene have also been studied. 6-Methoxy-1-vinyl-3,4-dihydronaphthalene has been studied extensively, because the products formed are of importance in that they are preliminary products obtained in the rapidly developing field of sterol syntheses by diene reactions (93, 129, 130, 131, 132, 133). By choice of suitable dienophiles, adducts possessing the sterol-ring structure may be prepared, as shown in table 6.

The adduct of 2-methylcyclopenten-3,4-dione given in table 6 has been converted (132) into an isomer of estrone (XXIX).



XXIX

The semicyclic enynes, 3,4-dihydro-1-naphthylacetylene and its 6-methoxy derivative, add ethylenic and acetylenic dienophiles; the latter type of dienophile gives derivatives of 9,10-dihydrophenanthrene as adducts. Propiolic acid (130) gives a mixture of 9,10-dihydrophenanthrene-1- and 2-carboxylic acids on reac-

TABLE 6

Diene syntheses of 6-methoxy-1-vinyl-3,4-dihydronaphthalene

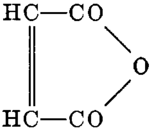
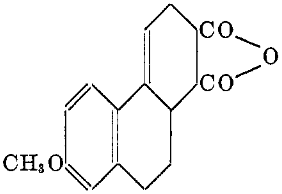
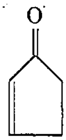
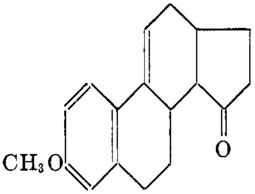
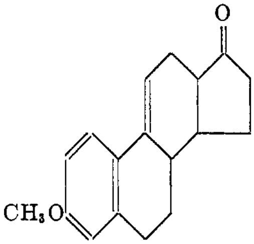
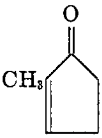
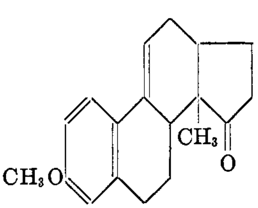
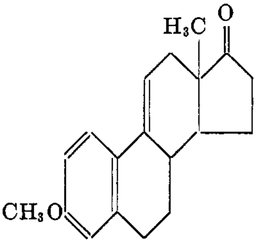
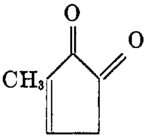
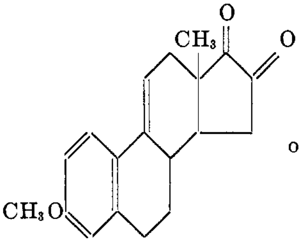
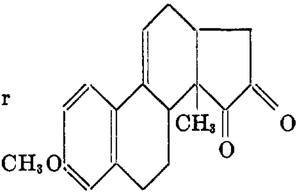
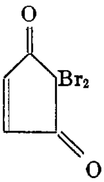
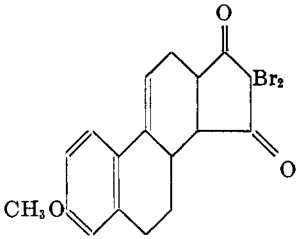
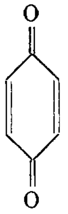
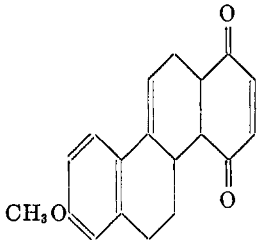
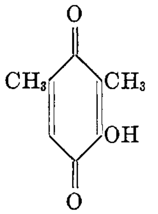
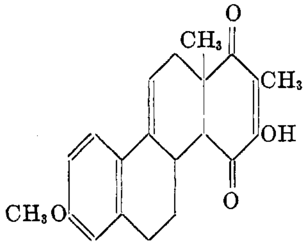
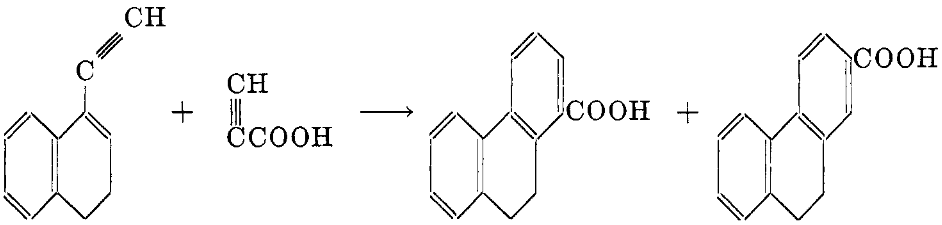
DIENOPHILE	PRODUCT
	
	 or 
	 or 
	 or 
	

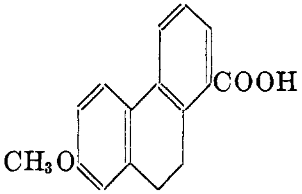
TABLE 6—*Concluded*

DIENOPHILE	PRODUCT
	
	

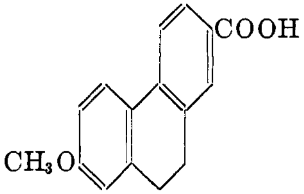
tion with 3,4-dihydro-1-naphthylacetylene, the 1-carboxylic acid being formed in greater amount.



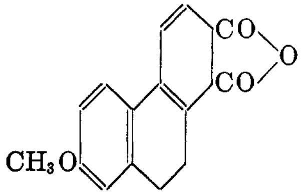
6-Methoxy-3,4-dihydro-1-naphthylacetylene adds propiolic acid (130) to give both XXX and XXXI. It does not add *p*-benzoquinone (130), but does add maleic anhydride (131), giving XXXII.



XXX

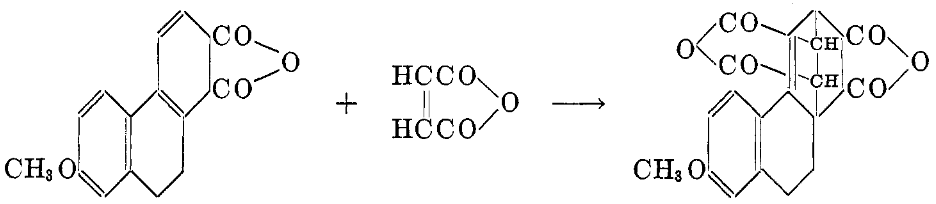


XXXI



XXXII

Since XXXII contains the 1,3-cyclohexadiene ring, it should be capable of adding further quantities of dienophiles. *p*-Benzoquinone does not add, but interaction occurs (130) in which the quinone is reduced to hydroquinone and XXXII is converted into the anhydride of phenanthrene-1,2-dicarboxylic acid. The hydroquinone appears in the form of quinhydrone. On the other hand, maleic anhydride is added to give a bridged dianhydride (131):



In this manner it may be seen that 3,4-dihydro-1-naphthylethylene and 3,4-dihydro-1-naphthylacetylene and their derivatives offer excellent possibilities as intermediates in the syntheses of the sterols and their derivatives. The reactions of the sterols themselves in the diene synthesis will be considered next.

VII. STEROLS

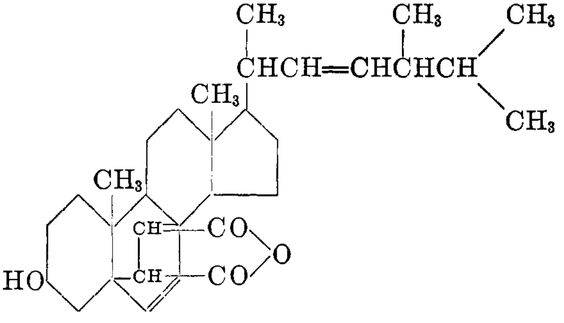
A. Ergosterol and derivatives

In the investigation of the various sterols and sterol derivatives from the standpoint of the diene synthesis, maleic and citraconic anhydrides have been almost the sole dienophiles employed. Certain of the irradiation products of ergosterol are active toward dienophiles. Lettré (282) indicates the successive formation of irradiation products as follows:

$$\begin{tikzcd}
 & \text{Lumisterol} \arrow[d] & & \text{Toxisterol} \\
\text{Ergosterol} \arrow[ur] \arrow[dr] & & \text{Vitamin D}_2 \arrow[ur] \arrow[r] \arrow[dr] & \text{Suprasterol I} \\
 & \text{Tachysterol} \arrow[ur] & & \text{Suprasterol II}
\end{tikzcd}$$

The use of acidic dienophiles in the investigations of the activities of the sterols in the diene synthesis is evident when one considers that the sterol adducts derived from such dienophiles are also acids. The adducts may therefore be separated from unchanged sterol simply by extracting with alkali, filtering from unchanged sterol, and precipitating with acid. Excess maleic or citraconic acid remains dissolved in the aqueous mother liquors.

Ergosterol adds maleic anhydride (282, 363, 366), best at a temperature of 135°C. Addition hardly occurs at room temperature and only slowly at 80°C. The same holds true for ergosteryl acetate (252, 366). The maleic anhydride adduct of ergosterol has structure I, and the corresponding adduct of ergosteryl acetate has a similar structure (253, 364). However, ordinary ergosteryl acetate shows only partial reaction with maleic anhydride (366), for a residue of dihydroergosteryl acetate remains unattacked. Distillation of the adduct of ergosteryl acetate and maleic anhydride in high vacuum gives maleic and succinic anhydrides, and a portion of the ergosteryl acetate may be recovered (366).



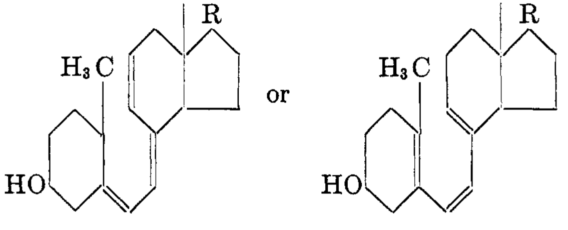
I

This recalls the formation of succinic anhydride and *p*-cymene by distillation of the adducts of maleic anhydride with α-phellandrene and with 1,3-menthadiene (page 388). Apparently a portion of the ergosteryl acetate appears as a dehydroergosteryl acetate, which probably possesses an aromatic ring. Reduction of the ergosteryl acetate–maleic anhydride adduct leads to initial hydrogenation of the double bond in the side chain. When ergosterol itself is reduced, the conjugated system is attacked first. By reduction of the ergosteryl acetate adduct and heating, 22-dihydroergosteryl acetate is produced, saponification of which gives 22-dihydroergosterol (364). 22-Dihydroergosterol, of course, adds maleic anhydride (362) to give a compound identical with I, except that the side chain is saturated. Windaus and Lüttringhaus (366) dispute this addition to a certain extent by saying that "dihydroergosterol" does not add maleic anhydride. There are three possible dihydroergosterols, only one of which has the conjugated-double-bond system required for the diene synthesis.

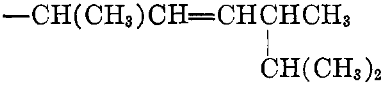
A tetrahydroergosteryl acetate (235) has been reported to add maleic anhydride. If this can be repeated, then the way is paved for an investigation of the mechanism of the reaction, for presumably the tetrahydroergosteryl acetate contains but one double bond.

Dehydroergosteryl acetate (235) adds maleic anhydride to give an adduct which appears to exhibit dimorphism. It may be distilled unchanged at 220°C. and in the cathode-glow vacuum (10^{-4} mm. of mercury), but decomposition into the generators occurs at 240°C. Dehydroergosterol itself also forms an adduct with maleic anhydride (234).

Tachysterol contains four double bonds and is formed from ergosterol on irradiation, when the central six-membered ring is opened. Lettré (282) suggests two alternative structures for the sterol, as shown below:



where R is



$$-\mathrm{CH(CH_3)CH{=}CH\underset{\substack{|\\ CH(CH_3)_2}}{C}HCH_3}$$

Lettré calls attention to the fact that, while ergosterol requires a temperature of 135°C. for the addition of maleic anhydride, tachysterol will add citraconic anhydride at room temperature (282). This adduct contains only two double bonds and its formation is interpreted as meaning that two molecules of citraconic anhydride have added, probably by addition of one molecule of citraconic anhydride followed by wandering of a double bond in the resulting product to give a conjugated system which then adds the second molecule of citraconic anhydride. It is difficult to understand how such a wandering could occur readily at room temperature, however.

The next product in the irradiation sequence is vitamin D_2 (calciferol). It and its acetate add maleic anhydride (296, 368). Calciferol, like tachysterol, possesses an isolated double bond and three conjugated double bonds. There have been no reports to the effect that calciferol adds two molecules of maleic anhydride, however.

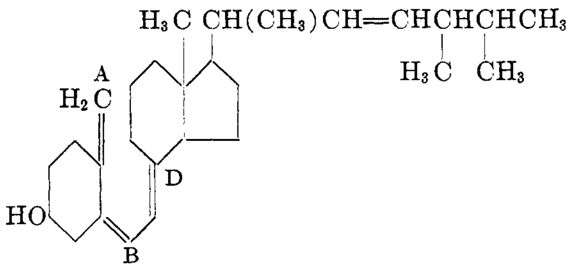
Heating calciferol to 190°C. results in ring closure and disappearance of a double bond with the formation of two isomeric products, isopyrovitamin and pyrocalciferol. Two double bonds are present in a single ring in each isomer, and each adds maleic anhydride (296).

Irradiated ergosterol was found to have lost its antirachitic power when treated with maleic anhydride or citraconic anhydride (367), thus indicating that vitamin D_1 contains conjugated double bonds. An earlier observation (361) indicated that maleic anhydride would not react with irradiated ergosterol, which led to the conclusion that the conjugated system of ergosterol is destroyed by irradiation. This is false, as was shown above.

The reaction of citraconic anhydride with irradiated ergosterol is incomplete, some 10 to 20 per cent remaining unattacked. The tachysterol which may be isolated from irradiated ergosterol reacts nearly as readily with citraconic anhydride (369) as it does with maleic anhydride.

Pure vitamin D_2 adds citraconic anhydride very slowly (365) and it is to be expected that the maleic anhydride addition proceeds more rapidly (368).

Windaus and Thiele (368) give the formula of calciferol as



and they state that maleic anhydride adds to carbon atoms A and B rather than to B and D. If the latter addition did occur, a ring with gem-substitution (a spirane) would be formed. This reaction would be expected to be much slower than the reaction between maleic anhydride and the combination of A and B.

Windaus and Lüttringhaus (366) divide the ergosterol derivatives into three classes according to their abilities to add dienophiles. Class I compounds react readily with maleic anhydride on staining at room temperature for several days, and include tachysterol, dehydroergosterol, one of the three isoergosterols, and certain irradiation products of ergosterol. Class II compounds, comprising ergosterol and its acetate, barely exhibit reaction at room temperature but react readily at 135°C. Class III compounds show no reaction, and comprise a dihydroergosterol, ergosterols D and F, the other two isoergosterols, and the products of the over-irradiation of ergosterol.

When ergosteryl acetate is treated with hydrogen chloride, the reaction products may be separated to some degree through the use of maleic anhydride (360). The adducts are separated by solution in caustic alkali and are decomposed into their generators by heating in high vacuum.

B. Cholesterol and derivatives

Cholesterol derivatives have been investigated only slightly with regard to their abilities to add dienophiles. 2,4-Cholestadiene adds maleic anhydride readily in boiling xylene solution (339). The mixture termed "cholesterilene," —the main constituent of which is probably 3,5-cholestadiene,—adds maleic anhydride to some extent, but the product appears to be abnormal (194, 338). 3,5-Cholestadiene itself possesses a *trans*-butadienoidal configuration, and it adds maleic anhydride only under drastic conditions (338, 347). The product obtained is probably polymeric, for its alkali salts are insoluble in water (distinction from other sterol–maleic anhydride adducts). 2,4-Cholestadiene is claimed to give an abnormal addition product with maleic anhydride (194), although it contains the 1,3-cyclohexadiene ring. This claim has been disputed (339).

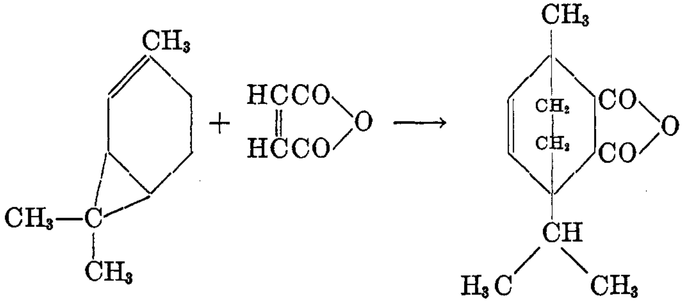
Coprastadienol (365) adds maleic anhydride easily to give an adduct which is best isolated in the form of the acetate by treatment of the adduct with acetic anhydride, since the adduct acetate crystallizes far better than does the original adduct.

$\Delta^{6,8(14)}$-Cholestadiene and $\Delta^{7,9(11)}$-cholestadiene possess *trans*-butadienoidal configurations; they do not add maleic anhydride (405). On the other hand, $\Delta^{7,14}$-cholestadiene possesses a *cis*-butadienoidal configuration and is able to add maleic anhydride.

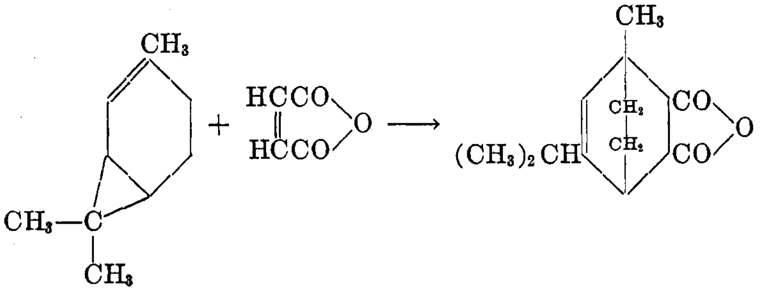
VIII. TERPENES AND TERPINOID BODIES IN THE DIENE SYNTHESIS

The terpenes often react as dienes, and sometimes even if they do not contain conjugated double bonds. It is likely that isomerization takes place prior to the consummation of the diene reaction; a somewhat satisfactory explanation can be advanced on this basis for most of the reactions.

Hultzsch (238) obtained addition of maleic anhydride to α-pinene, limonene, terpinolene, and 3-carene at reflux temperatures. None of the adducts appeared to be identical. On the other hand, when maleic acid was employed as dienophile, all the adducts were identical, and were the same as the adduct obtained from 1,3-*p*-menthadiene and maleic acid. Diels (162) observed that 3-carene[2] formed an adduct with maleic anhydride, which did not appear to be identical with the adduct from 1,3-*p*-menthadiene and maleic anhydride. He took the view that, inasmuch as the cyclopropane ring often acts as a double bond (as in the addition of hydrogen bromide or bromine to cyclopropane; see, however, Kharasch, Fineman, and Mayo (266)), the cyclopropane ring could function as a double bond and be in conjugation with the double bond of what he called 3-carene[2].



Diels apparently neglected to consider the equally likely mechanism:



A somewhat more satisfactoy rexplanation for certain of these observations may possibly be found in the application of generally known facts of terpene

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[2] There is controversy in the literature regarding the carenes. Goodway and West (228) state that 3-carene does not contain a cyclopropane ring in conjugation with the double bond, while Hultzsch (238) states that Diels used 4-carene in his reaction. Hultzsch obtained addition with both 3-carene and 4-carene.