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THE SYNTHESIS OF CONDENSED RING COMPOUNDS. IX. THE REACTION OF 5-ACETOXY-1,4-TOLUQUINONE WITH CON-JUGATED DIENES, AND THE RULES OF ALDER¹

ELEANORE W. J. BUTZ AND LEWIS W. BUTZ

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In order to prepare methylvinyloctalones similar to I for use in a projected synthesis of steroids (1) we have studied the reaction of 5-acetoxy-1,4-toluquinone (II) with 1,3,5-hexatriene. If the enol acetate (III) were a product of this reaction and were convertible to the isomer IV, we should have an intermediate useful for the synthesis of steroids with a hydroxyl or a keto group at position 3 and a methyl group at position 10, the type most frequently en-



countered among naturally occurring steroids. We have already reported (2) the isolation of a substance $C_{15}H_{16}O_4$ from the products of this reaction and assumed that it had either structure III or V. It is still uncertain whether III can be readily converted to IV, and IV then condensed with a derivative of cyclopentene to produce a steroid. Dane and co-workers (3) in recent years have prepared several steroids by the addition of cyclopentene derivatives to

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Some of this material was presented before the Organic Chemistry Division of the American Chemical Society, Atlantic City, September 10, 1941. analogous vinyldihydronaphthalenes. The chances that the scheme of synthesis outlined in (1) may be practical are increased by the observations that 1,5-diene-3-ynes add maleic anhydride (4, 5) and quinones (6), because adducts from acetoxytoluquinone and dienynes, such as VI and VII, already would contain a reactive diene system, whereas III must be converted to IV. We wish at this time to present descriptions of the products formed in the reaction of acetoxytoluquinone with hexatriene, still incomplete descriptions, but demonstrating much of their structure and indicating what types of compound may be accessible through the reaction of the same quinone with dienynes.



Although a Diels-Alder reaction of acetoxytoluquinone with hexatrien cane yield 16 primary products, four structural isomers each in four stereoisomeric (racemic) forms, we did not hesitate to utilize the reaction for synthetic purposes, since it is well known that it proceeds with a high degree of selectivity. This prognosis was found to be correct; two products were obtained in substantial yield (45% and 21%). This reaction of acetoxytoluquinone with hexatriene provides an interesting test of the relative reactivities of the acetoxyethene and methylethene systems. If the size of the substituent group at the dienophile double bond is the controlling factor, the chief products should be the enol acetates III and V. One or both of these is undoubtedly formed but it, or they, is extremely unstable, and only occasionally has an enol acetate been isolated although many batches were run. This instability of the enol acetates and some of the other products has complicated the study of the reaction. Its completion has been further hindered by the difficulty of preparing adequate quantities of hexatriene of assured purity. The preliminary work (2) was done with hexatriene prepared by the pyrolysis of sym-divinylglycol with formic acid according to van Romburgh (7). It was then found that the dehydration of 1,5-hexadiene-3-ol gave better yields of hexatriene (8) and most of the work here reported was done with hexatriene from this source. After much of the experimental work had been done, it was discovered (9) that this hexatriene probably contained some 1,3-cyclohexadiene, which would also in all likelihood react with acetoxytoluquinone to give products isomeric with those from hexatriene. The difficulties arising from this circumstance were controlled by including a study of the reaction of acetoxytoluquinone with pure 1,3-cyclohexadiene and with hexatriene prepared by the low temperature method of Kharasch and Sternfeld (10) which had appeared in the meantime.

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It will be shown that three compounds, and possibly a fourth, can be isolated from the products of reaction of acetoxytoluquinone with hexatriene; that each of the three are formed both from hexatriene prepared by the method we previously described (8) and that of Kharasch and Sternfeld (10); and finally that each of these compounds differs from each of three which can be obtained by the reaction of acetoxytoluquinone with cyclohexadiene. The description of an adduct obtained from acetoxytoluquinone and 2,3-dimethyl-1,3-butadiene will also be given.

When acetoxytoluquinone and hexatriene are heated together in ethanol at 70° or 95° the colorless substance, $C_{15}H_{16}O_4$, previously (2) reported, cannot always be isolated from the product mixture, and when it is found, the quantity is much smaller than that of either of two other products which have since been obtained. The product obtained in highest yield (45%) is a faintly yellow crystalline compound, C₁₅H₁₆O₄, melting at 109-110°, which gives no color with ferric chloride and which could not be hydrolyzed to any product giving such a color. When heated at 200° at reduced pressure it gave acetic acid and tarry products which were not characterized. Enol acetates are usually not resistant to hydrolysis, and structures III and V probably do not represent this substance. Addition of hexatriene to the acetoxyethene link of the quinone would lead to compounds VIII and IX and these structures are compatible with the properties of the acetate melting at $109-110^{\circ}$. After the descriptions of the other compounds prepared in this work have been presented, it will be apparent that this substance, the major product of the reaction between acetoxytoluquinone and hexatriene, is an angular acetate, VIII or IX. The product formed



in next largest amount is a colorless crystalline compound, $C_{13}H_{14}O_3$, which begins to decompose at 195° and melts at 206–210°. It dissolves in cold dilute aqueous sodium hydroxide and can be recovered unchanged from this solution by precipitation with hydrochloric acid. This behavior suggests an enolic structure, which is confirmed by the purple-black to brown-black solutions which the substance gives with ferric chloride. A part of the hexatriene has therefore added to the methylethene link in the quinone, and under the conditions of the addition reaction or the subsequent isolation of products the acetate thus formed has become hydrolyzed to an enol. Whether this enol has structure X or XI, XII or XIII, or one of a number of other tautomeric structures we do not know. The fact that the substance does not decompose until a rather high temperature (195°) is reached in the melting point determination perhaps indicates a dienol structure such as XII or XIII. The third compound, $C_{15}H_{16}O_4$, was isolated in very small quantity from only one batch. After recrystallization from ether it melted unsharply at about 135-140° and gave a deep green solution with ferric chloride. When heated with water for a short time, part of it dissolved and the filtered hot solution deposited a colorless material on cooling. This suspension gave a brown-black solution with ferric chloride similar to that obtained from the free enol. This enol was isolated from the part which did not pass into the hot water solution, and the close relationship of the acetate melting at 135-140° to the enol decomposing at 195° and melting at $206-210^{\circ}$ was thus demonstrated. Whether the acetate has structure III or V or some tautomeric structure such as XIV cannot be decided on the basis of available evidence. It can be concluded, however, that the addition of hexatriene to acetoxytoluquinone does yield an enol acetate with an angular methyl group which is hydrolyzed with ease to an enol. On the basis of crystalline material actually isolated, this acetate appears to be a minor product and the angular acetate (VIII or IX) seems to be the chief product, but this apparently lower yield of enol acetate and enol may be due in part to the diffi-



culty of isolating the enol acetate. The identity of the compound $C_{15}H_{16}O_4$ reported previously (2) is in doubt. When heated it decomposed at 161–162° to a yellow solid which melted at 192–195°. On the addition of tenth-normal aqueous sodium hydroxide it dissolved within a few minutes in the cold. Its behavior with ferric chloride was not observed. Since the solubility in

alkali indicated that the substance was an enol acetate, and since the melting point of the product of pyrolysis (at $161-162^{\circ}$ in the capillary tube) was close to that of the enol $C_{13}H_{14}O_3$, which has been obtained pure and from many batches, it is suggested that it may have been largely converted to this enol during the melting point determination. The difficulty of purifying such enol acetates and of obtaining the two preparations in quantity has made it impossible to determine whether this compound previously reported and the acetate which melts at $135-140^{\circ}$ are the same or isomeric.



When heated together at 65°, acetoxytoluquinone and cyclohexadiene gave three crystalline compounds which were different from those just described. Therefore, it would seem that the pyrolytic hexatriene used in this work contained little if any cyclohexadiene (9). The adduct obtained in largest yield (up to 55%) is faintly yellow, melts at 123–124° and has the composition $C_{15}H_{16}O_4$. This is not an enol acetate for it gives no colored solutions with ferric chloride, either before or after exposure to hydrolytic conditions, and does not dissolve readily in aqueous sodium hydroxide. The only probable structure is that represented by XV. This was conclusively shown to be correct by examination of the products of pyrolysis. It seemed likely that a compound XV



would split out acetic acid readily when heated to give XVI and it will be recalled (11) that compounds containing this 1,4-ethano-2,5-cyclohexadiene system are often decomposed at about 150° with the formation of ethylene and an aromatic ring. When we heated the substance melting at 123–124° at about 200° and under reduced pressure, acetic acid and 2-methyl-1,4-naphthoquinone (XVII) were obtained. Accordingly, under the conditions employed, cyclohexadiene adds to the acetoxyethene link of the quinone to a greater extent than to the methylethene link. These conditions are mild and it would have been predicted that a group as large as the acetoxyl group would retard considerably the addition of the diene to the dienophile. Some other factor must therefore be present which facilitates this particular addition, and later on we will propose what this factor may be.

Under the same experimental conditions cyclohexadiene adds to the methylethene link, for it has been possible to isolate a very small quantity of an enol which must have structure XVIII or a tautomeric one. This substance, $C_{13}H_{14}O_8$, melted at 152–153°, was soluble in dilute aqueous sodium hydroxide and gave a brown solution with ferric chloride, and evidently had been formed by hydrolysis of an enol acetate. The third product from this reaction is a faintly yellow compound which melts at 84–87°. The highest yield obtained was 6%. The composition is that of the expected enol acetate, $C_{15}H_{16}O_4$, but this cannot be its structure for it not only fails to hydrolyze to the enol of melting point 152–153° or another enol, but it also decomposes on heating to give 2methyl-1, 4-naphthoquinone and acetic acid, just as does the isomer which melts at 123–124°. The structure of this substance must also be XV and we shall therefore call it XV-B.



Since neither XV-B nor the higher-melting isomer (XV-A) has enolic properties, their isomerism cannot be explained by assigning the tautomeric structure XIX to one of them. Nor can it be alleged that the one isomer is a trans-decalin type (XX), formed by conversion of the cis isomer which would be the primary product of the Diels-Alder addition. According to Alder and Stein, such a trans structure is probably incapable of existence because of the presence of the ethano bridge at the adjacent carbon atoms (12). The stereoisomerism here is probably of the endo-exo type discussed by Alder and Stein (13) in connection with the products of addition of dienophiles to cyclopentadiene and certain fulvenes.

Under a given set of conditions these workers found that cyclopentadiene and diphenylfulvene (the phenyl groups replacing the hydrogens of the methylene of fulvene) each reacted with maleic anhydride to give one compound in 100%yield. On the other hand, the analogous dimethylfulvene and pentamethylenefulvene each gave two compounds, one in about 60% yield and the other in about 40% yield. They were able to show conclusively that the compound from cyclopentadiene is the bicycloheptenedicarboxylic acid (XXI) which is quite different from the stereoisomer XXII which they obtained by another method.



When, instead of cyclopentadiene, dimethylfulvene or pentamethylenefulvene reacts with maleic anhydride, the reaction no longer follows a single course, but proceeds to the formation of two stereoisomeric compounds in unequal amounts. This Alder and Stein attributed to the presence of the additional double bond. They proposed the hypothesis that in cases in which a diene and a dienophile can lead to more than one stereoisomer, the molecules of diene and dienophile prior to reaction tend to assume that relative orientation which corresponds to the maximum density of doubly bonded atoms. Upon reaction that isomer is formed which follows from this orientation. For this reason cyclopentadiene and maleic anhydride give only the endo isomer XXI in which the two carboxyls are relatively close to the annular double bond. In the attraction of the carboxyl groups, the methylene group offers no competition to the double bonds of the diene system. For a similar reason diphenylfulvene and maleic anhydride give only one product, XXIV (R is phenyl), in which the carboxyls are now oriented toward the C:RR group which contains seven double bonds. But in dimethylfulvene or pentamethylenefulvene the group R contains no double bonds; the carboxyls are attracted to both the diene system and the semicyclic double bond, two competing reactions ensue, and two products, XXIII and XXIV, are formed.



The existence of the two forms, exo and endo, in this type of stereoisomerism depends on the rigidity of the molecules with the 1,4-bridge. Cyclohexadiene gives analogous products. Now in the reaction of acetoxytoluquinone and cyclohexadiene, structures are involved which could give rise to two isomeric angular acetates of the endo-exo type. In this case the competing unsaturated centers, the carbonyls and the acetoxyl, are in the dienophile reactant. Since

one of the competing systems has two double bonds and the other but one, the isomers can be expected in unequal yield. Actually 55% of the higher-melting compound (XV-A) and 6% of the lower-melting compound (XV-B) were isolated. Unlike Alder and associates, we have not proved the structures of the two isomers in this regard, but it will be subsequently shown that according to the rule of Alder and Stein the major product (XV-A) should have structure XXV. The acetate XV-B then must be XXVI.



Only one product was isolated from the reaction mixture from acetoxytoluquinone and 2,3-dimethyl-1,3-butadiene. This reaction was studied less thoroughly than the other two. It is being included because it has been found that here again the diene has added to the acetoxyethene link. The addition was carried out in ethanol at 95° and gave 42% of a faintly yellow crystalline compound which melts at 116–117°. This compound is an acetate, $C_{15}H_{18}O_4$, which is not converted to an enol by heating with dilute aqueous acetic acid. In view of the similarity in properties to some of the acetates from hexatriene and cyclohexadiene, we were curious to know how it would behave toward heat. At about 200° and under reduced pressure the products were acetic acid and a crystalline residue from which a small quantity of a nearly white compound was isolated. This melted at 170-175° and was soluble in hot water. Apparently it was a hydroquinone, but was not characterized further. The crude crystalline residue was oxidized with ferric chloride to give 2.6.7-trimethyl-1.4-naphthoquinone in good yield. The structure of the adduct is therefore to be represented by XXVII, and the probable course of the pyrolysis by XXVII \rightarrow XXVIII.



The outstanding result of this work is the observation that these dienes react with the acetoxyethene link of the quinone to an equal or greater extent than with the methylethene link. The methyl group at the dienophile link as a rule retards but does not prevent a Diels-Alder addition. The observation that dienes will add to an acyloxyethene link is not new. Nylén and Olsen (14) found that cyclopentadiene adds to acetoxymaleic anhydride, but not to ethyl *beta*-acetoxycrotonate. Alder and Rickert (15) were able to add vinyl acetate to many dienes. However, it was not to be expected that the acetoxyethene link would be the preferred site of reaction when a methylethene link is available. That this is the case was demonstrated by the preparation of 2-methyl-1,4naphthoquinone from cyclohexadiene and 2,6,7-trimethyl-1,4-naphthoquinone from dimethylbutadiene just described. With the quantity of material on



hand we could not find conditions suitable for the corresponding preparation of 2-methyl-5-vinylnaphthoquinone (XXXII) or 2-methyl-8-vinylnaphthoquinone (XXXIII) from hexatriene. Either the tetrahydronapthalenedione (VIII) or (IX) was recovered unchanged or dark, extensively decomposed products resulted from which no crystalline compounds could be isolated. This failure is perhaps to be charged to the probable instability of the vinyl derivatives (XXIX) (XXX) (XXXI) in the presence of the acetic acid formed in equivalent amount at the high temperature of the pyrolysis. In the pyrolysis of the dione (VIII or IX) two-thirds of the theoretical quantity of acetic acid was collected and determined by titration of the distillate. A comparison of the properties of the acetoxymethylvinyltetrahydronaphthalenedione of melting point $109-110^{\circ}$ with the other compounds prepared (Table I) leaves no doubt that the substance has structure VIII or IX.

EXPERIMENTAL

The melting points for new compounds are corrected.

The ferric chloride enol test was performed by the addition of 2 drops of 0.15% FeCl₃ in ethanol to 1 cc. of dilute solution of the unknown substance.

5-Acetoxy-1, 4-toluquinone (II). The procedure of Thiele and Winter (21) was followed. The guinone was used after three crystallizations from hexane; m.p. 75-76°.

Anal. Calc'd for C₉H₈O₄: C, 60.0; H, 4.5.

Found: C, 60.1; H, 4.6.

1,3,5-Hexatriene. (By Adam M. Gaddis.) Most of the hexatriene was made by the dehydration of 1,5-hexadiene-3-ol with phthalic anhydride at 160-200° (8). That employed

TABLE I

The Properties of Compounds Formed in the Reaction of 5-Acetoxy-1,4-toluquinone WITH 2,3-DIMETHYL-1,3-BUTADIENE (A), 1,3-CYCLOHEXADIENE (B),

COMPOUND	A-I	B-I	B-II	B-III	C-I	C-II	C-III
Melting point, °C. Color	116–117 pale yellow	123–124 pale yellow	84-87 pale yellow	152–153 white	109-110 pale yellow	135–140 pale yellow	206-210 white
Soluble in cold aque- ous 0.1 N sodium hydroxide	no	no	no	yes	no ^b	yes	yes
Color with ferric chloride	none	none	none	pink- brown	none	green	brown- black
Composition	$C_{15}H_{18}O_4$	$C_{15}H_{16}O_{4}$	C15H16O4	$\mathrm{C}_{13}\mathrm{H}_{14}\mathrm{O}_{3}$	$C_{15}H_{16}O_4$	$C_{15}H_{16}O_4$	$C_{13}H_{14}O_3$
Pyrolyzed to a naph- thoquinone	yes	yes	yes		? •		
Position of maximum absorption in ultra- violet ²	2360 Å	2300 Å	2350 Å		2350 Å		2560 Å

AND 1,3,5-HEXATRIENE (C)

^a Complete absorption curves for the ultraviolet region have been determined for these compounds by Russell E. Davis and Harry Bastron of the Bureau of Animal Industry. These will be published by Dr. Davis and Mr. Bastron in collaboration with us in a future paper dealing with the application of absorption spectra to some problems incidental to the synthesis of condensed ring compounds. It will be enough to recall here that Wassermann (27) found a maximum at 2220 Å for 5,8-methano-4a,5,8,8a-tetrahydronaphthalene-1,4-dione.

^b Color becomes reddish-brown.

• Only acetic acid isolated.

for the preliminary (2) work was prepared according to Romburgh (7). A small quantity was prepared by the low-temperature method of Kharasch and Sternfeld (10); it was possible to convert this preparation² to 1-vinyl-9,10-anthraquinone (22).

1,3-Cyclohexadiene. This was prepared from cyclohexene by the procedure of Hofmann and Damm (23). The purified product boiled at 80-81°; n_2^{20} 1.474. Kistiakowsky (24) reported $n_{\rm D}^{20}$ 1.4740.

2,3-Dimethyl-1,3-butadiene. (By Adam M. Gaddis.) This was prepared according to the method of Fieser and Seligman (25). The product boiled at 66-71°.

² We are indebted to Mr. Melvin Goldberg for this preparation of hexatriene and for the conversion to vinylanthraquinone.

4a-Acetoxy-2-methyl-5-vinyl-4a,5,8,8a-tetrahydronaphthalene-1,4-dione (VIII) or its 8vinyl isomer (IX). Three moles of hexatriene (from hexadienol) and acetoxytoluquinone in four volumes of ethanol were kept in sealed tubes filled with CO₂ at 66-74° for 39 hours. The products from six tubes (7.9 g. of hexatriene and 5.8 g. of acetoxytoluquinone) were worked up together. Removal of the more volatile components at 60° and reduced pressure gave 8.7 g. (10%) of crude products. Addition of benzene to this gave no crystalline material (except after long standing in the refrigerator, in which case crystalline enol C₁₃H₁₄O₃ separated), but addition of 2-3 cc. of ether gave 2.4 g. of crystals (A) which were filtered off. Removal of the ether and 0.5 g. of other volatile material by holding at 90° and 9 mm. for 2 hours failed to yield more crystals. Repeated extraction of this uncrystallized portion with hot heptane gave solutions which deposited 2 g. of crystalline product (B) upon cooling. A and B were identical and were combined; m.p. 103-104°, 45%. Two recrystallizations from petroleum ether gave 1.4 g., faintly yellow, m.p. 109-110°.

Anal. Calc'd for C₁₅H₁₆O₄: C, 69.2; H, 6.2.

Found: C, 69.4; H, 6.5.

This compound becomes more deeply yellow in color and partially liquefied after storing in the dark for many months. This deteriorated product can be repurified by crystallization from hexane. Cold tenth-normal aqueous sodium hydroxide does not dissolve it. Hot aqueous alkalies slowly give deeply colored solutions. In ethanol it gives no colored solution with ferric chloride.

Pyrolysis of VIII (or IX). Upon heating 179 mg. at 200-215° and 80 mm. for 7 minutes, some material was driven off and the contents of the flask became very black. On reducing the pressure to 15 mm., solid acetic acid was condensed in a trap at -40° . Titration of this condensate with 0.05 N sodium hydroxide showed 30.84 mg. of acetic acid or 67%. Oxidation of the black residue with ferric chloride gave material from which no crystalline quinone could be isolated. When the period of heating was reduced to 2 minutes, unchanged starting compound was recovered, and again no solid products of pyrolysis were obtained.

2-A cetoxy-4a-methyl-5-vinyl-4a, 5, 8, 8a-tetrahydronaphthalene-1, 4-dione (III), its 8-vinyl isomer (V), or tautomer. Acetoxytoluquinone (4.2 g.) was heated with 5.5 g. or 3 moles of hexatriene (from hexadienol) in 33 cc. of absolute ethanol at 92-97° for 16 hours. The volatile components were removed at 50° under reduced pressure. Addition of 10 cc. of benzene to the residual gum (7.2 g.), boiling, and cooling gave no crystalline material (thus differing from some other experiments in which crystalline enol separated at this point). As further additions of benzene and refrigeration for several days yielded no crystals, the benzene solution (30 cc.) was poured into 800 cc. of petroleum ether and the resulting gum and dilute solution were separated. The gum weighed only 0.4 g. and was discarded. The petroleum ether was evaporated from the solution to give a partially crystalline residue. Trituration with 150 cc. of petroleum ether gave an insoluble fraction A and a solution B. Slow evaporation of B gave 0.6 g. of the angular acetate described in the preceding section (m.p. 105-106°, no color with ferric chloride) and 2 g. of oil which did not crystallize. A was purified by slow evaporation of its solution in 100 cc. of petroleum ether-diethyl ether mixture (2:1) which gave 0.4 g. of a crystalline compound, m.p. 135-140° (from ether), green color with ferric chloride.

Anal. Calc'd for C15H16O4: C, 69.2; H, 6.2.

Found: C, 69.2; H, 6.2.

This acetate (III, V, or tautomer) was hydrolyzed slowly by heating with water at 80-100°. A minor portion passed into solution and precipitated as colorless enol on cooling. The products of hydrolysis were dissolved in aqueous sodium hydroxide, the solution extracted with ether, hydrochloric acid added to the aqueous layer until red to litmus and Congo papers, the precipitate washed with water, dissolved in ether, and dried with sodium sulfate. Evaporation of the ether gave colorless crystals, m.p. 200-205°; m.p. of mixture with authentic enol (m.p. 206-210°), prepared as described below, was 203-207°; brown color with ferric chloride. This acetate, which was isolated from only one batch, is therefore hydrolyzed with ease to the enol which was obtained from many batches, and it probably is the acetate of this enol, although the possibility of tautomerization during hydrolysis must be recognized.

2-Hydroxy-4a-methyl-5-vinyl-4a, 5, 8, 8a-tetrahydronaphthalene-1, 4-dione (X), its 8-vinyl isomer (XI), or a tautomer. One and three-tenths grams of acetoxytoluquinone, 1.7 g. of hexatriene from the hexadienol, and 10 cc. of absolute ethanol were heated in a sealed tube at 66-73° for 39 hours. Evaporation of the ethanol at reduced pressure in a stream of carbon dioxide gave a partly crystalline residue which was stirred with 5 cc. of warm benzene, cooled, and filtered. Concentration of the filtrate to 4 cc. gave another crop of crystalline enol. Yield, 0.4 g., 21%. Often separation of crystals did not occur until after addition of benzene and refrigeration of the benzene solution for several days. Two recrystallizations from benzene gave glistening white crystals, decomposing at 195°, m.p. 206-210°.

Anal. Calc'd for C13H14O3: C, 71.6; H, 6.4.

Found:

C, 71.6; H, 6.6.

This compound gives a brown-to-black color with ferric chloride in water or ethanol. It is soluble in hot water, from which solution it precipitates on cooling, and is soluble in cold 0.1 N aqueous sodium hydroxide. It can be recovered unchanged from the aqueous solution of the sodium salt. To 127 mg. of the enol was added 8.35 cc. of 0.1 N sodium hydroxide, whereupon a nearly colorless solution resulted in a few minutes. Addition of 0.09 N hydrochloric acid precipitated a solid which, after washing, drying, and recrystallizing from benzene weighed 70 mg., melted at 208-210° and did not depress the m.p. of the original enol.

Reaction of acetoxytoluquinone with hexatriene prepared from allyl chloride and sodamide in liquid ammonia (10). One gram of hexatriene, with the boiling range 75–90°, and 0.75 g. of acetoxytoluquinone were heated together in 10 cc. of absolute ethanol at 70° for 40 hours. The ethanol was removed and the residue was separated into a part soluble in benzenepetroleum ether mixture (1:4) (A), and a part insoluble therein (B). B on recrystallization from benzene gave 30 mg. of colorless product, which gave a brown-black color with ferric chloride and did not depress the melting range of a specimen of the enol of m.p. 206-210° described in the preceding section. Cooling the solution of A, filtering off a little impure enol, evaporating the filtrate to dryness, extracting the residue with 3 cc. of cold petroleum ether, and allowing this solution to stand for several days gave 30 mg. of faintly yellow crystals, m.p. 104-108°, which after being dried on tile gave no depression in melting point with the angular acetate, m.p. 109-110°, prepared from pyrolytic hexatriene.

The two diastereoisomeric 4a-acetoxy-5,8-ethano-2-methyl-4a,5,8,8a-tetrahydronaphthalene-1,4-diones (XV-A) and (XV-B), and 5,8-ethano-2-hydroxy-4a-methyl-4a,5,8,8a-tetrahydronaphthalene-1,4-dione (XVIII). Acetoxytoluquinone (1.4 g.), with 1.4 g. (2.3 moles)of cyclohexadiene in 4 cc. of absolute ethanol for 65 hours at 65° gave, after removal of the volatile components, a residue which crystallized well after seed had been obtained by grinding. The products were taken up in 10 cc. of ether and the solution was cooled well in a solid carbon dioxide-Cellosolve bath. The faintly yellow product (XV-A), m.p. 123-124° after recrystallization from methanol and ethanol, gave no color with ferric chloride in ethanol. Yield 1.0 g.; 55%.

Anal. Calc'd for C₁₅H₁₆O₄: C, 69.2; H, 6.2.

Found: C, 69.1; H, 6.4.

The ether was removed from the mother liquor from XV-A, the residue was leached out with successive portions of warm ligroin (b. 60-70°), the ligroin evaporated from the combined extracts, and the residue therefrom taken up in a mixture of petroleum ether (b. 30-60°) and ether. When cooled very gradually, 100 mg. of crystals was deposited, m.p. 82-87°. Recrystallization from the same solvent mixture gave XV-B, faintly yellow, m.p. 84-87°; yield, 6%.

Anal. Calc'd for C₁₅H₁₆O₄: C, 69.2; H, 6.2. Found: C, 69.2; H, 6.2. XV-B like XV-A gave no colored solution with ferric chloride. It was shown not to be a mixture of XV-A with an enol acetate, by an unsuccessful attempt to hydrolyze it to an enol. Ten milligrams was heated one hour in 6 cc. of ethanol and 3 cc. of 12 N aqueous hydrochloric acid. After careful neutralization with sodium hydroxide solution, the addition of ferric chloride failed to give a color. The enol acetate III or V was hydrolyzed to a chromogenic enol by merely heating with water. That the treatment with hydrochloric acid, or the presence of the sodium chloride resulting from the neutralization did not inhibit the customary enolic response to ferric chloride was demonstrated by a parallel experiment with the enol X or XI. In the latter case no color could be produced with ferric chloride in the presence of free hydrochloric acid, but after neutralization the usual colored solution was obtained.

Although no enol acetate was ever isolated from the reaction products of acetoxytoluquinone with cyclohexadiene, the enol XVIII was found in one batch. The material in the angular acetate mother liquor was distilled at 1-2 mm. At bath temperature $210-220^{\circ}$, a fraction of approximate b.p. 130° passed over and condensed to a red crystalline mass. Successive recrystallization from ether and petroleum ether-ether mixture gave white crystals, m.p. 152-153°. This substance was soluble in cold dilute sodium hydroxide and gave a pink-brown colored solution with ferric chloride in ethanol. It smelled of hickory wood smoke.

Anal. Calc'd for $C_{13}H_{14}O_3$: C, 71.6; H, 6.4.

Found: C, 71.3; H, 6.7.

Pyrolysis of XV-A to 2-methyl-1,4-naphthoquinone and acetic acid. Two hundred and twenty-two milligrams of XV-A, m.p. 123-124°, was heated in a small tubular flask attached to a receiver cooled to -40° for 20 minutes at 100-110 mm. and at bath temperature 210-215°. Trapping of the ethylene formed was not attempted, nor was a quantitative recovery of the acetic acid. After the period of heating, the flask was brought slowly to room temperature and the pressure reduced to 14 mm. for 10 minutes. In this way an amount of acetic acid was transferred to the receiver which required 11.30 cc. of 0.0505 N sodium hydroxide for neutralization. This is 34.2 mg. of acetic acid; 67% yield. The yellow oil on the sides of the flask and the charred residue at the bottom were worked up separately. The yield of 2-methyl-1,4-naphthoquinone, m.p. 103° from ether-ligroin was 51%; it did not depress the m.p. (105°) of an authentic specimen.

Pyrolysis of XV-B to 2-methyl-1,4-naphthoquinone and acetic acid. The isomer of m.p. $84-87^{\circ}$ (XV-B) (114.6 mg.) was pyrolyzed in the same way as XV-A. The decomposition proceeded less smoothly than that of XV-A. The recovery of acetic acid as indicated by titration was 7.9 mg. or 29%. The yield of pure 2-methyl-1,4-naphthoquinone was smaller than that from XV-A. It melted at 102° (from ligroin); m.p. of mixture with the authentic specimen (m.p. 105°) was 103°.

4a-Acetoxy-2,6,7-trimethyl-4a,5,8,8a-tetrahydronaphthalene-1,4-dione (XXVII). (By Adam M. Gaddis.) Acetoxytoluquinone (3.6 g.), 2.4 g. (1.5 moles) of 2,3-dimethyl-1,3butadiene, and 18 cc. of ethanol were heated at 95° for 14 hours. Concentration of the reaction mixture to one-half volume at reduced pressure gave 1.9 g. of crystalline material which after recrystallization from ether-hexane and then from hexane gave 1.29 g., faintly yellow, m.p. 116-117°. Evaporation of the original alcohol mother liquors, extraction of the residue with ether and hexane, and crystallization of the residue, obtained by the removal of solvents from this extract from methanol gave a further crop of the same product. Yield, 2.2 g.; 42%.

Anal. Calc'd for C15H18O4: C, 68.7; H, 6.9.

Found: C, 68.9; H, 7.2.

This compound does not dissolve completely in cold 0.1 N aqueous sodium hydroxide, gives no colored products with ferric chloride, and was not hydrolyzed to products giving such color with ferric chloride when heated with 30% acetic acid in water at 95° for one hour.

Pyrolysis of XXVII. Two hundred and sixty milligrams of XXVII, m.p. 116-117°,

was heated at $210-215^{\circ}$ and 80-85 mm. for 15 minutes. While the reaction flask was cooling, the pressure was reduced to 15 mm. The condensed acetic acid required 16.1 cc. of 0.0505 N sodium hydroxide, which is equivalent to 48.8 mg. of acetic acid; yield, 80%. The residue from the pyrolysis crystallized on cooling.

A small portion was recrystallized from ether-ligroin, yielding a white substance with a tinge of violet, m.p. 170–175° with decomposition, which was soluble in hot water. This was not analyzed, but presumably was 2,6,7-trimethylnaphthalene-1,4-diol (XXVIII). For characterization the crude product of pyrolysis was oxidized by warming for a few minutes with 3 g. of ferric chloride hexahydrate in 15 cc. of ethanol. The ethanol solution was poured into 250 cc. of water, allowed to stand 15 minutes, the yellow crystals filtered off, and recrystallized successively from aqueous methanol and ligroin. Yield, 100 mg.; m.p. 107.5–108.5°. Bergmann and Bergmann (26) give m.p. 110° for 2,6,7-trimethyl-1,4-naphthoquinone.

Anal. Calc'd for C₁₃H₁₂O₂: C, 78.0; H, 6.0. Found: C, 78.0; H, 6.5.

APPLICATION OF THE RULE OF ALDER AND STEIN TO THE PREDICTION OF ISOMERIC PRODUCTS OF THE DIELS-ALDER REACTION

On the basis of about ten thoroughly investigated reactions, which were all of the type leading to products with endo bridges, Alder and Stein (13) proposed the following rule: Upon mixing a 1,3-diene and a dienophile the molecules tend to assume that mutual orientation which corresponds to the greatest accumulation of double bonds, and that product is formed in larger amount which is to be expected from the preferred pre-reaction orientation. The reactants of Alder and Stein presented only one dienophile link and could yield only two diastereoisomeric products. They were rather simple cases, and it was possible for Alder and Stein to apply the rule by merely inspecting the conventional structural formulas suitably juxtaposed. It is the purpose of this section to show how the rule may be applied to more complicated cases such as the reactions of acetoxytoluquinone. Three general cases will arise: (A) The maximal density of double bonds will be determinable by inspection of conventional formulas drawn to scale³ and suitably juxtaposed. (B) The maximal density of double bonds cannot be determined as in (A), but can be determined by making measurements of such drawings and supporting these by simple calculations. (C) In the presence of double bonds in mobile groups, the position of nearest approach of the mobile double bond to the other double bonds must be determined, and the measurements and calculations then made as in (B).

Acetoxytoluquinone is a bifunctional dienophile, the two olefin links carrying different groups. Therefore, the reaction acetoxytoluquinone + 2,3-dimethylbutadiene could yield two products which are position isomers, and the relative amounts to be expected in the product-mixture might be predictable by the Alder-Stein rule. The reaction acetoxytoluquinone + hexatriene could give four position isomers as well as diastereoisomeric forms of each. Acetoxytoluquinone and cyclohexadiene could yield two position isomers, each in the endo and exo configuration. The pre-reaction orientations leading to these four

³ By employing the currently available values for interatomic distances and interbond angles.

products are illustrated in Figure 1 by means of the type of representations used by Alder and Stein. An additional complication offered in the cases of reactions with acetoxytoluquinone or with hexatrene is that one of the orienting double bonds is a component of a freely rotating group. Therefore, in applying the



Fig. 1. The Four Alder-Stein Orientations of Cyclohexadiene and Acetoxytoluquinone

Two coplanar positions of the acetoxyl group are shown. The line R_0R_{150} is the diameter of the circle described by the moving point R.

rule in these cases the probable position of the acetoxyl and the vinyl group must be determined and considered.

It might be profitable before analyzing the acetoxytoluquinone reactions to apply the rule to a case taken from the literature in which both position-isomeric and diastereoisomeric products are possible, but in which no mobile double bonds are involved. The reaction of cyclopentene-3-one with 1,2-dihydro-7-methoxy4-vinylnaphthalene studied by Dane and Eder (16) is of this type. The structure of the product isolated was not demonstrated or discussed by Dane and Eder, but Robinson and Rydon (17) had the following to say about it: "If, as seems probable, the Diels reaction is initiated by the coupling of the more anionoid end of the diene system with a cationoid β -carbon atom of a catio-enoid system, then the choice between these alternatives can be made if we can locate the more reactive anionoid C-atom in I"—the vinyldihydronaphthalene—"The circumstances are somewhat complex in this cross-conjugated system and the most that can be said is that the more aliphatic site of the vinyl group favors IV,"—here designated as XXXVI—"whereas the combined effect of two unsaturated conjugated centres on the naphthalene double bond, as well as the influence of the methoxyl group, and any steric factor favors III"—(XXXVII).



It is noteworthy that Robinson and Rydon were not only unable to decide on a choice between the two position isomers, but also ignored the question of stereoisomerism, *i.e.*, the relative configuration at carbons 8 and 14 in both XXXVI and XXXVII.

Now the rule of Alder and Stein permits a prediction of the relative amounts of some of these four products by mere inspection of juxtaposed formulas⁴ as in Figure 2. It can be readily seen that in orientation A, the accumulation of double bonds is greater than in orientations B, C, or D. Therefore the isomer XXXVI-A would be expected in greatest yield. It can also be seen that XXXVII-A (from orientation B) should be formed in larger amount than XXXVII-B (from orientation D). Likewise XXXVI-B should be formed in larger amount than XXXVII-B. It seems impossible to determine whether orientation B or orientation C corresponds to the greater density of double bonds by merely inspecting these formulas. It will therefore be necessary to use

⁴ Neither Alder and Stein nor others have discussed application of the rule in any detail, and no complete critique will be given in this paper. However, the following assumptions seem to be implied in the rule as stated by Alder and Stein (13): 1. In directing orientation all types of double bonds, C—C, H—C—O, RO—C—O, etc., are quantitatively equivalent. 2. The effective directing force is localized at some point, *e.g.*, the midpoint of the double bond. 3. It is unnecessary to consider the many possible random orientations of the reactant molecules; only the standard orientations illustrated by the formulas in parallel planes as juxtaposed by Alder and Stein need be compared, in order to determine which correspond to the greater density of double bonds.



Fig. 2. The Four Orientations of the Compounds of Dane and Eder

formulas drawn to scale and actually measure the double bond density in order to decide this point. A method of doing this is outlined below in connection with an analysis of the acetoxytoluquinone reactions. The Alder and Stein rule, therefore, predicts that the order of yields will be XXXVI-A > XXXVI-B > XXXVII-B, and XXXVI-A > XXXVII-A > XXXVII-B. Only a complete experimental study of the Dane-Eder reaction can demonstrate what validity the rule has in this case.



Dane and Schmitt (18) investigated the reaction of the same vinyldihydronaphthalene derivative with 1-methylcyclopentene-4,5-dione. This case can be analyzed in exactly the same way as the reaction of Dane and Eder. The rule predicts that the 8,14-cis stereoisomer of the steroid XXXVIII, with angular methyl at carbon 14, would be the chief product. Dane and Schmitt (28) by appropriate reactions converted the adduct which they obtained from this reaction to the corresponding non-olefinic 17-monoketone. The latter was not identical with the methyl ether of estrone (XL) and indeed could not be, aside from stereochemical considerations, if their adduct had structure XXXVIII rather than XXXIX.



Another reaction in this same category was studied by Butz (2) with a view to the synthesis of 13-formyl steroids, namely the addition of cyclopentene-1aldehyde to hexatriene. Here again, if the rule of Alder and Stein holds, the major product would be the intermediate (9-formyl-4-vinylhexahydroindene) of possible use in the synthesis, not of 13-formyl, but of 14-formyl steroids.

The reaction of acetoxytoluquinone and cyclohexadiene may yield four

acetoxyethanomethyltetrahydronaphthalenediones, two diastereoisomeric 2acetoxy compounds, and two diastereoisomeric 4a-acetoxy compounds. At least three of these were formed: one product of addition to the acetoxyethene link (XV-A), yield 55% or more; another product of addition to the acetoxyethene link (XV-B), yield 6% or more; and a product of addition to the methylethene link, the acetate of the enol XVIII (XXXIV or XXXV), yield 39% or less. The evidence does not exclude the possibility that a second enol acetate was formed. Thus one compound was formed in larger amount than all others combined and 61% or more of the total reaction occurred at the acetoxyethene link. Could these results have been predicted on the basis of the Alder-Stein rule?





XXXV

By reference to Figure 1,⁵ a choice can be made in the same way as in the case of the products of the reaction studied by Dane and Eder, *provided*, *that*

⁵ In this figure the formulas are drawn to scale (one inch = one Ångstrom) using the following values for the bond lengths and interbond angles:

a	= c = 1.36 Å	$ab = bc = 121^{\circ}$
b	= 1.46 Å	af = $cd = 123^{\circ}$
\mathbf{d}	= f = 1.50 Å	$de = ef = 116^{\circ}$
е	= 1.54 Å	$gh = ij = jk = lg = 121^{\circ}$
g	= j = 1.32 Å	$hi = kl = 118^{\circ}$
h	= i = k = l = 1.50 Å	$hn = in = km = lm = 121^{\circ}$
\mathbf{m}	= n = 1.14 Å	io $= 117^{\circ}$
q	= s = 1.54 Å	$jo = 122^{\circ}$
0	= p = 1.41 Å	$op = 108^{\circ}$
r	= 1.33 Å	$pr = 122^{\circ}$

the carbon and oxygen atoms of the carbonyl part of the acetoxyl group are in the plane of the quinone ring. This will be true for only the two positions of the acetoxyl group which are shown in Figure 1. Since free rotation of the acetyl group about bond p and free rotation of the acetoxyl group about bond o are possible, the double bond r can take an infinitely large number of positions. For the position of r shown nearer to n, to be designated as R at 180° from an arbitrary origin, inspection of the figure shows that the order of orientation preference according to the Alder and Stein rule is B > A or D > C. It is found by actual measurement of the distances between double bonds in the figure that the order is B > A > D > C; while for the other position of r shown (in which r is more remote from n, R at 0°, *i.e.*, at the arbitrary origin), the preferred orientation order is B > A = D > C.

This result was arrived at as follows: Just prior to reaction, the essentially flat molecules of diene and quinone are found in two parallel planes with an interplanar distance x. The molecules become mutually oriented, partly according to A, partly according to B, etc., so that a line in the plane of the diene joining the terminal carbon atoms of the diene system when projected on the plane of the quinone coincides exactly with bond g or j. Designating the midpoints of the various bonds by capital letters corresponding to the bond letters in Figure 1, the fourteen distances between mutually movable double bonds which are needed for calculating the double bond densities can be designated as AG, MR, etc. These distances in the case of GR, JR, MR, NR, or their projections on the plane of the quinone ring (A'G, A'J, A'M, A'N, A'R, C'G, C'J, C'M, C'N, C'R) in the case of the remainder are measured directly from the drawings by dividers. The values found are recorded in columns A-I, B-I, C-I, and D-I (Table II). The interplanar distance x is then assigned a value, and the actual distances AG, AJ, etc., are calculated from A'G, A'J, etc., and are recorded in columns A-II, B-II, C-II, and D-II. The preferred orientation order will be the same for all values of x; x = 1.39 Å⁶ was taken as a reasonable value. It is now possible by finding the sum of the distances in the II columns, to compare the double bond densities in the four orientations, A, B, C, and D. From Table II it is seen that, for this one position of R, the sum of distances between all the double bonds which are free to approach one another is smallest (40.17 Å) for orientation B. B is therefore the preferred orientation since it corresponds to the greatest density of double bonds. The values for the other orientations are A, 41.38 Å; D, 44.48 Å; C, 47.34 Å. C is therefore the least probable orientation.

Thus it is evident that by an operation consisting of drawing structural formulas to scale, measuring certain distances on the drawing and making some simple calculations, it has been possible to make a choice between orientations A and D for a particular position of the bond r. This choice appeared impossible by mere inspection of the drawings.

These are taken from "The Theory of Organic Chemistry" by Branch and Calvin (19) or are based upon the values for bond lengths and interbond angles in closely related compounds. A suitable value for b was obtained by calculation after the others were chosen. This was necessary in order to ensure a closed ring of required dimensions. Carbon-hydrogen bonds are omitted from the formulas but might have to be considered if any steric question should arise.

 $^{^{6}}$ Taking the carbon-carbon distance of the new bonds formed in the addition reaction as 1.54 Å, the interplanar distance will be 1.39 Å at the moment of formation of these new bonds.

For the second position of R in which r is coplanar wis the quinone ring (R more remote from N; called R_0 in a later discussion), it was found that B was again the most preferred orientation and C the least preferred. For this position of R, orientations A and D were found to be equally probable. The actual sums computed were: B, 41.45 Å; A, 43.79 Å; D, 43.62 Å; C, 50.17 Å. The difference of 0.17 Å between the sums in A and D is of about the same magnitude as the sum of errors involved in obtaining these sums (about 0.20 Å), and is therefore too small to be taken as indicative of a preference between the two orientations.

Thus it is seen that the numbers which have been taken as a measure of the density of double bonds are different in a given orientation for different positions

TABLE II

The Distances, in Ångstrom Units, between Fourteen Pairs of Double Bonds in Four Mutual Orientations of Acetoxytoluquinone and Cyclohexadiene at $R = 180^{\circ}$

	ORIENTA	TION A	ORIENTATION B		OBIENTATION C		ORIENTATION D	
	I	11	I	II	I		I	II
AR180	2.83	3.12	1.98	2.42	3.87	4.11	1.96	2.40
CR_{180}	4.60	4.87	4.12	4.35	5.32	5.50	4.13	4.36
GR_{180}	4.05	4.05	4.00	4.00	4.07	4.07	4.08	4.08
JR_{180}	2.94	2.94	2.92	2.92	3.07	3.07	3.04	3.04
MR_{180}	5.15	5.15	5.15	5.15	5.23	5.23	5.21	5.21
NR_{180}	1.72	1.72	1.75	1.75	1.76	1.76	1.77	1.77
AG	1.20	1.84	2.25	2.64	1.23	1.85	3.36	3.62
AJ	2.28	2.65	1.22	1.85	3.34	3.62	1.24	1.87
$\mathbf{A}\mathbf{M}$	3.15	3.44	3.17	3.44	3.60	3.86	3.60	3.88
\mathbf{AN}	1.15	1.80	1.14	1.80	2.08	2.45	2.10	2.45
CG	1.25	1.87	2.30	2.69	1.25	1.87	3.33	3.62
CJ	2.27	2.64	1.25	1.87	3.33	3.62	1.22	1.85
$\mathbf{C}\mathbf{M}$	1.15	1.80	1.14	1.80	2.10	2.45	2.07	2.45
\mathbf{CN}	3.20	3.49	3.20	3.49	3.63	3.88	3.60	3.88
Sum	•••••	41.38		40.17		47.34		44.48

(INTERPLANAR DISTANCE = 1.39 Å)

of the double bond r. For one position, orientation A is definitely more probable than orientation D; for another position, the probability of A is about equal to that of D. Conceivably, therefore, there may be positions which r can take, in which the order of preference B > A > D > C > may not hold. In order to apply the rule of Alder and Stein in such cases, all the positions of r must be investigated.

What position does r have in acetoxytoluquinone alone and in the presence of cyclohexadiene (in orientations A, B, C, and D) in the absence of any additional solvent or in an indifferent solvent?⁷ The reasonable assumption can be made

⁷ A consideration of possible effects of the solvent on the orientation will be most interesting, but is outside the scope of this paper. All of the reactions with acetoxytoluquinone were carried out in nearly anhydrous ethanol, with the exception of one experiment with cyclohexadiene in which there was no additional solvent.

that in acetoxytoluquinone alone, the rule of Alder and Stein is already valid, and that in most of the molecules, the bond r is not necessarily in the plane of the quinone ring, but occupies whatever position corresponds to the maximum density of double bonds in the molecule. This position can be found from the following considerations, assuming that there is no rotation of the acetyl group about bond p from the position shown in Fig. 1:⁸

Let R_o be the midpoint of bond r when this bond is in the position coplanar with the quinone ring and more remote from N (Fig. 1). Now bond r (as a part of the acetoxyl group) can rotate freely about bond o, the midpoint R taking all possible positions on a circle (Fig. 3). As r rotates about o from the position stated, R passes through an arc of 180° until r again is coplanar with the quinone ring. This is the other coplanar position of r and r is now nearer to N. The midpoint of r in this position will be designated R_{180} . If a line $R_o R_{180}$ be drawn connecting these two points, the midpoint T (Fig. 1) will be the center of the circle which R describes. These relationships are clearly seen from Figure 3.

The positions of R may now be described in terms of the angle ϕ which TR_{ϕ} makes with TR_{ϕ} . In order to determine the approximate position of R in the acetoxytoluquinone alone, it is only necessary to determine the distances GR, JR, MR, and NR and find their sum for a sufficiently large number of values of ϕ . The distance TR_{ϕ} was measured from the



Fig. 3. Construction Drawing for the Determination of RR' for any Value of Angle ϕ

drawing (Fig. 1) and found to be 1.87 Å. Since the projections of R on the plane of the quinone ring for different values of ϕ all fall on the line R_0R_{180} , the distances TR'_{ϕ} will be 1.87 cos ϕ . Having calculated these and marked them off on R_0R_{180} , it was possible to measure GR', JR', MR', and NR' for various values of ϕ . GR, JR, MR, and NR could then be calculated since $RR' = 1.87 \sin \phi$. The results are given in the first column of Table III. It is seen that the sum of distances between double bonds is the minimum when ϕ is about 170°, *i.e.*, when the acetoxyl group is about 10° out of the plane of the quinone ring and near bond n.

⁸ There is evidence from dipole moment data that such rotation will not occur (29). Vector addition of the ketone and ether moments in the acetoxyl group leads to the conclusion that rotation of the acetyl group about bond p is restricted with a single minimum in the position in which the moments are oppositely directed and the carbon and oxygen atoms of the acetoxyl group and the 5-carbon atom of the quinone ring are all in one plane. It would be interesting to calculate whether the same restriction in positions of the acetyl group would follow from the rule of Alder and Stein. Such a calculation would seem to require a knowledge of the position of some point U at which all the Alder-Stein effects of the several fixed double bonds could be considered localized. Once U were located, the distance RU could then be related to the angle ϕ (measuring rotation about the bond o) and an angle θ which would measure the rotation about bond p, and it should then be possible to determine the values for RU, ϕ , and θ at which RU is a minimum.

As the cyclohexadiene molecule approaches, the position of the acetoxyl double bond will change by virtue of the influence of two new double bonds, a and c. For any given distance of the plane of a and c from the plane of the quinone ring, *e.g.*, 1.39 Å, the minimum sum of distances between double bonds can be determined for different values of ϕ providing rotation about p does not occur or is adequately described.⁸ The necessary distances are shown in Figure 4. For distances involving G, J, M, and N, it is only necessary to measure GR',

TABLE 1	I	I
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The Sums of the Distances Between the Double Bonds in Acetoxytoluquinone and in Various Mutual Orientations of Cyclohexadiene and Acetoxytoluquinone for Various Values of ϕ

φ ACETOXY (DEGREES) NONE	ACETOXYTOLUQUI-	ORIENTATION OF ACETOXYTOLUQUINONE AND CYCLOHEXADIENE				
	NONE ALONE	A	В	С	D	
0	15.09	43.79	41.45	50.17	43.62	
15						
30	15.06	43.09	40.49	49.44	42.45	
45	15.10	42.78	40.16	49.18	42.24	
60	15.11				42.06	
75	15.02	42.18	39.71	48.43	41.98	
90	14.92	41.95	39.52	47.99	42.11	
105	14.82	41.62	39.48	47.69	42.43	
120	14.65	41.43	39.55	47.43	42.84	
135	14.43	41.25	39.63	47.11	43.21	
150	14.19	41.16	39.75	46.85	43.45	
165	13.62	41.07	39.65	46.49	43.48	
180	13.86	41.38	40.17	47.34	44.48	





RR'= 1.87 \$10\$

FIG. 4. CONSTRUCTION DRAWINGS FOR THE DETERMINATION OF AR, CR, AND GR, JR

JR', MR', NR', A'G, etc. RR₁ = 1.87 sin ϕ . For the distances AR and CR, it is necessary to measure A'R' and C'R', and to calculate y which is RR' – AA' or 1.87 cos ϕ – 1.39. The fourteen distances have been calculated for a number of values of ϕ and the results are given in Table III.

It is seen that at any value of ϕ which was investigated, B is the most preferred orientation; and therefore the rule says that the compound obtained in the largest yield is the angular acetate XXV.⁹ Likewise at all values of ϕ , C was

⁹ The values in Table III are plotted in Fig. 5. It is seen to be unlikely that the B curve would ever rise above the A, D, or C curves. Investigation of further values of ϕ is there-

the least preferred orientation. The relation of the sums in A and D change with ϕ , but at all angles from 105° to 180°, the sum of the distances is less in A; and therefore A can be considered the preferred orientation with respect to D, since ϕ is 170° just before reaction.

From the values in Table III or the curves in Figure 5 it is not possible to determine ϕ at the minimum sums of distances with precision because of the small variation in these sums with change in ϕ at some portions of the curves. Although precise values for these angles could possibly be determined by methods



FIG. 5. GRAPHIC REPRESENTATION OF PART OF TABLE III

Abscissae: Values of angle ϕ in degrees. Ordinates: Sums of the distances in Å. units between the double bonds in various mutual orientations of cyclohexadiene and acetoxy-toluquinone.

of calculus, such procedure may not be necessary in many cases to determine the order of preferred orientation.

DISCUSSION

According to the rule of Alder and Stein, on mixing acetoxytoluquinone and cyclohexadiene most of the molecules will become oriented according to B (Figure 1) with bond r lying in a plane nearly perpendicular to the planes of the rings. The angular acetate (XV-A) of m.p. $123-124^{\circ}$ which was the chief prod-

fore unnecessary. Orientation C is seen to have a very low probability, while D is definitely more probable than A only in the range $\phi = 100^{\circ}$ to 180° .

uct should therefore have structure XXV, and the angular acetate (XV-B) of m.p. 84–87° must be the isomer XXVI. The enol of m.p. 152–153° may be related to the acetate XXXIV, since this structure results from orientation A, and only one enol was isolated. The least probable product is the compound XXXV. The experimental findings in the case of this reaction are in good agreement with predictions which one could make from the rule.

It would next be valuable to analyze the reaction of acetoxytoluquinone and hexatriene from the standpoint of the rule since we wish to know which of the theoretically possible structures should be assigned to the angular acetate (some diastereoisomer of VIII or IX), obtained in 45% yield, and to the enol acetate (some diastereoisomer of IV or V), the enol of which was obtained in 21% yield.



Fig. 6. Four Alder-Stein Orientations of Trans-hexatriene and Acetoxytoluquinone

Two coplanar positions of the acetoxyl group are shown. The products to be expected from each are shown.

Such an analysis will be much more difficult than in the case of the acetoxytoluquinone-cyclohexadiene reaction, and it is still far from completed. In the first place it is unknown whether the hexatriene used consisted of the cis or trans isomer or a mixture of the two (10). The analysis will be somewhat simpler if it is assumed that trans-hexatriene is reacting. By inspection of formulas drawn to scale (Fig. 6), it can be seen that orientation A is preferred to C, and B is preferred to D. Here, in addition to the free rotation of the acetoxyl group already considered, free rotation is possible about bonds b and d of the triene molecule. It would appear that, in order to achieve maximal density of double bonds, the acetoxyl group would take some position corresponding to a considerably greater value of the angle ϕ than 90°, due to the presence of the double bond e which was not present in cyclohexadiene. Likewise the vinyl group would rotate about d so that the bond e would approach the acetoxytoluquinone molecule. This mutual approach of e and r would presumably cease some time before the distance ER became zero, because of the mutual interference in space between the acetoxyl and the vinyl groups. Rotation of the dienyl system abc about d and the vinyl group including a about b would also occur in the direction of the quinone molecule. Accordingly the hexatriene molecule, as well as the quinone molecule, would almost certainly not remain in the planar configuration which Figure 6 suggests. However, whatever the magnitude of these probable rotations, the orientations A and B appear the two most probable, and A is preferred to B.

Orientation A leads to the angular acetate VIII in which the acetoxyl group is ortho to the vinyl. Trans-hexatriene, therefore, is predicted to give more of VIII than of the position isomer IX; and since only one angular acetate was obtained, the compound of m.p. 109–110°, this substance may have structure VIII. VIII can exist in two diastereoisomeric forms; we have been unable to make a



FIG. 7. Two Alder-Stein Orientations of Cis-hexatriene and Acetoxytoluquinone

Two coplanar positions of the acetoxyl groups are shown. The products to be expected from each are indicated.

choice between these two by inspection of formulas and we leave this question open for future analysis.

Orientation B leads to the enol acetate V, which may represent the structure of the enol acetate, m.p. 135–140° which yields on hydrolysis the enol, m.p. 206–210°. These compounds can also exist in two diastereoisomeric forms; here again we feel unable to make a selection without comparing the sums of distances involved in various configurations of the reactant molecules.

The rule predicts then that trans-hexatriene will yield VIII rather than IX and V rather than IV. If structural analysis of the angular acetate and enol, which seems feasible, should confirm this prediction, we should have evidence that the hexatriene used was the trans isomer, for cis-hexatriene can be expected to give nearly equal amounts of VIII and IX (Fig. 7). Nearly equal amounts of IV and V should also be obtained from cis-hexatriene.

In this connection the dimerization of hexatriene observed by Kharasch and Sternfeld (10) is of interest because only one isomer was isolated and this in over 50% yield. The adduct was 4-butadienyl-3-vinylcyclohexene (Fig. 8). If the 3,5-isomer was not formed, this would be evidence, granting the validity of the Alder-Stein rule under the conditions of the dimerization, that only transhexatriene reacted, for trans-hexatriene can give only the 3,4-dimer, while cishexatriene should give nearly equal amounts of the 3,4- and 3,5-dimers.

Alder and Windemuth (20) have found that diene additions occur selectively even when no double bonds are present other than the three which take part in the formation of the new ring. They suggest that in such cases there is a tendency for the reactant molecules to orient themselves so that there is a maximum accumulation of groups containing unshared electron pairs. This rule of Alder and Windemuth should be applied in conjunction with that of Alder and Stein. In many reactions both orienting double bonds and unshared electron pairs are present. In the case of the acetoxytoluquinone-cyclohexadiene reaction we venture to say that the unshared electron pairs (at the oxygen atoms) are so



FIG. 8. ALDER-STEIN ORIENTATION DIAGRAMS SHOWING THE DIMERIZATION OF HEXATRIENE A and B: trans-hexatriene plus trans-hexatriene. C and D: trans-hexatriene plus cishexatriene. E and F: cis-hexatriene plus cis-hexatriene. The expected butadienylvinylcyclohexenes are indicated.

placed that taking them into account will not appreciably alter the conclusions already drawn regarding the order of preferred orientations. However, this will not be true for all reactions.

SUMMARY

When 1,3-cyclohexadiene and 1,3,5-hexatriene react with 5-acetoxy-1,4toluquinone, addition occurs at both the acetoxyethene and the methylethene links. The principal product is an angular acetate in each case. An angular acetate was the sole product isolated after reaction of 2,3-dimethyl-1,3-butadiene with acetoxytoluquinone. This preferred addition to the acetoxyethene link is predictable by application of the rule of Alder and Stein. Three of the four theoretically possible isomers were isolated from the reaction products of cyclohexadiene and acetoxytoluquinone. Two of these were angular acetates and one was an enol. The structures of the endo and exo angular acetates were proved by conversion to 2-methyl-1,4-naphthoquinone. The structure of the angular acetate from dimethylbutadiene was proved by conversion to 2,6,7-trimethyl-1,4-naphthoquinone.

Hexatriene and acetoxytoluquinone gave an angular acetate and an enol in substantial yields. The structures were not proved. According to the rule of Alder and Stein the acetoxyl and vinyl groups should be *ortho* in the angular acetate and the methyl and vinyl groups *meta* in the enol.

It would seem profitable to employ the rules of Alder and Stein and Alder and Windemuth in the prediction of products and as a guide in structural analysis, when necessary by actual calculation of the distances between the various pairs of double bonds and unshared electron pairs.

Beltsville, Md.

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