

AN ABSTRACT OF THE THESIS OF

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Title KINETIC STUDIES OF SOME THERMAL REARRANGEMENTS

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cis-2, cis-4, cis-6-Octatriene (Ia), trans-2, cis-4, cis-6-octatriene (IIa) and trans-2, cis-4, trans-6-octatriene (IIIa) were prepared and subsequently characterized by carbon-hydrogen analyses, ultraviolet spectra, infrared spectra and by nuclear magnetic resonance spectra of both the trienes and their 4, 5-dideuterio analogs.

Valence isomerization of IIIa was shown to yield cis-5, 6-dimethyl-1, 3-cyclohexadiene:  $k = 4.45 \times 10^{-5} \text{ sec}^{-1}$  at  $132^\circ$ ,  $k = 2.45 \times 10^{-4} \text{ sec}^{-1}$  at  $152^\circ$ ,  $k = 7.02 \times 10^{-4} \text{ sec}^{-1}$  at  $165^\circ$ ,  $E_a = 29.4 \text{ kcal/mole}$  and  $\Delta S^\ddagger = -7 \text{ e. u.}$  at  $149^\circ$ . Thermal interconversion of Ia and IIa was observed:  $k = 2 \times 10^{-5} \text{ sec}^{-1}$  at  $109.5^\circ$  (Ia  $\rightarrow$  IIa) and  $K = 5.5$  (IIa/Ia). Valence isomerization of a mixture of Ia and IIa yielded trans-5, 6-dimethyl-1, 3-cyclohexadiene:  $k = 1.5 \times 10^{-5} \text{ sec}^{-1}$  at  $178^\circ$ ,  $k = 6.4 \times 10^{-5} \text{ sec}^{-1}$  at  $196^\circ$ ,  $E_a = 33 \text{ kcal/mole}$  and  $\Delta S^\ddagger = -9 \text{ e. u.}$  at  $185^\circ$  for the disappearance of the mixture. Both cis- and trans-5, 6-dimethyl-1, 3-cyclohexadiene were shown to rearrange to 1, 6-dimethyl-1, 3-cyclohexadiene:  $k = 0.8 \times 10^{-5} \text{ sec}^{-1}$  at  $182^\circ$ ,

$k = 3.6 \times 10^{-5} \text{ sec}^{-1}$  at  $200^\circ$ ,  $E_a = 36 \text{ kcal/mole}$  and  $\Delta S^\ddagger = -3 \text{ e. u.}$   
at  $190^\circ$  for the disappearance of the trans isomer, and  $k = 1.85 \times 10^{-5} \text{ sec}^{-1}$  at  $178^\circ$ ,  $k = 4.59 \times 10^{-5} \text{ sec}^{-1}$  at  $189^\circ$ ,  $E_a = 34 \text{ kcal/mole}$   
and  $\Delta S^\ddagger = -7 \text{ e. u.}$  at  $183^\circ$  for the disappearance of the cis isomer.  
Thermal rearrangement of 1,6-dimethyl-1,3-cyclohexadiene yielded o-xylene, p-xylene, ethylbenzene and some unidentified components.

Rearrangement of cis-2-(o-hydroxyphenyl)pent-3-ene in deuterium oxide yielded the trans isomer with one deuterium atom in the gamma-olefinic position. Slow incorporation of deuterium was also detected in the alpha-methyl group. The rate of cis to trans isomerization for cis-2-(o-hydroxyphenyl)pent-3-ene was shown to equal the rate of olefinic deuterium incorporation. These two studies establish that the abnormal Claisen rearrangement of cis-2-(o-hydroxyphenyl)pent-3-ene is a stereospecific reaction.

Kinetic studies of the equilibrium of cis- and trans-2-(o-hydroxyphenyl)pent-3-ene in water showed  $E_a = 33 \text{ kcal/mole}$  and  $\Delta S^\ddagger = -13 \text{ e. u.}$  for cis  $\rightarrow$  trans and  $E_a = 35 \text{ kcal/mole}$  and  $\Delta S^\ddagger = -12 \text{ e. u.}$  for trans  $\rightarrow$  cis. A deuterium isotope effect ( $k_{\text{OH}}/k_{\text{OD}}$ ) of 2.7 at  $205^\circ$  was calculated from the rates of rearrangement.

KINETIC STUDIES OF SOME THERMAL REARRANGEMENTS

by

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# KINETIC STUDIES OF SOME THERMAL REARRANGEMENTS

## INTRODUCTION

Organic reaction mechanisms can be classified into ionic, radical, and molecular processes. Ionic and radical reactions are well known, and methods for studying the mechanisms of these reactions have long existed. Although molecular reactions have been recognized for some time, many of the ordinary methods for studying the mechanisms of other types of reactions have not proved fruitful when applied to this class.

These molecular reactions are characterized by their (1) susceptibility to thermal induction, (2) inertness to free radical initiators and inhibitors, (3) insensitivity to acid and base catalysis, (4) insensitivity to solvent effects, (5) definite stereochemical requirements, and (6) first-order kinetics.

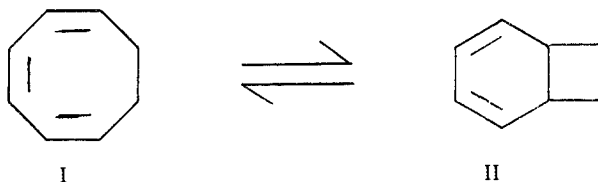
The work described in this thesis is concerned with expanding the available information on the mechanisms of some molecular reactions. The kinetic studies herein are devoted to two separate examples of molecular reactions: the valence isomerism of conjugated trienes, and the abnormal Claisen rearrangement.

## HISTORICAL

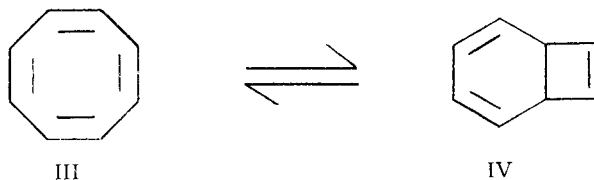
Valence Isomerism of Conjugated Trienes

The classic example of the valence isomerization between cis trienes and cyclohexadienes is the equilibrium between 1, 3, 5-cis,cis, cis-cyclooctatriene (I) and bicyclo-[4.2.0]-octa-2, 4-diene (II) (12).

These two isomers readily



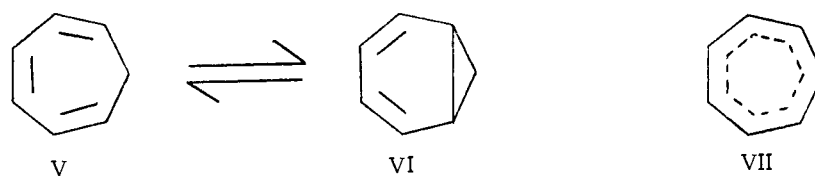
interconvert at elevated temperatures, yet they may be isolated in pure form and characterized at room temperature. A similar valence isomerization has long been postulated as the first step in the formation of Diels-Alder adducts by cyclooctatetraene (III). The reality of this process has recently been demonstrated by two independent groups. Vogel, Kiefer and Roth succeeded in isolating bi-



cyclo-[4.2.0]-2, 4, 7-octatriene (IV) and showed that this substance undergoes a ready isomerization to its isomer (III) (76). Huisgen

and Mietzch have determined that the equilibrium concentration of the bicyclic isomer (IV) at 100° is 0.01%, and that this is indeed the first step in adduct formation by cyclooctatetraene (III) (44).

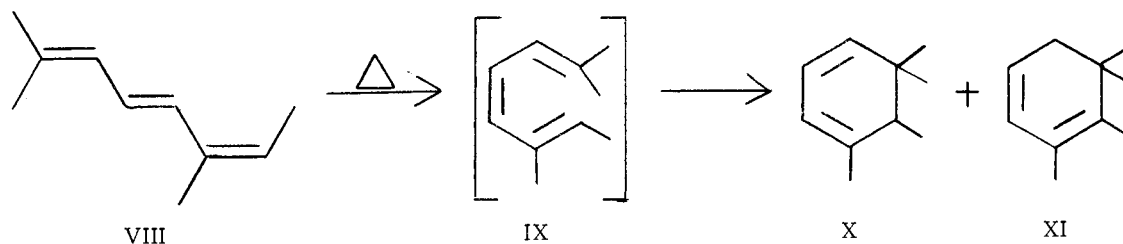
The existence of valence isomers in the tropilidene system (V and VI) is still open to question. The X-ray diffraction pattern of



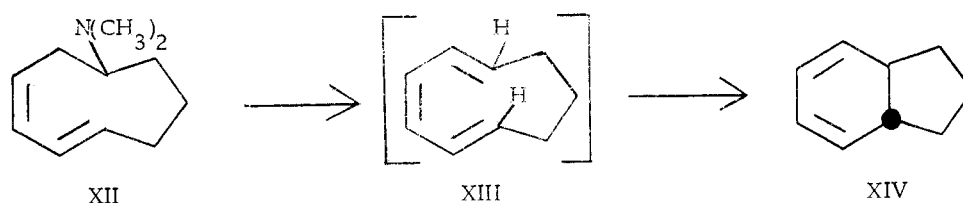
tropilidene molybdenum tricarbonyl has been interpreted as consistent with only the 1, 3, 5-cycloheptatriene structure (V) (19). However, many of the reactions of tropilidene derivatives yield products which have been rationalized as derived from the norcaradiene structure (VI) (4, 13, 14, 15). Although the coexistence of the isomers V and VI has not been unequivocally demonstrated, Berson and Willcott were able to rationalize the thermally induced skeletal rearrangements of substituted tropilidenes on the basis of an equilibrium between the simple analogs of V and VI (7). Vogel and coworkers were also able to rationalize spectral data of some tropilidene analogs on the basis of a similar equilibrium (74, 77). The pseudo-aromatic structure VII has also been postulated for tropilidenes (18). The Raman and infrared spectra (23), resonance energy of 9-10 kcal/mole (72), and n. m. r. spectrum (18) of tropilidene have all been

interpreted as being consistent with its formulation as a pseudo-aromatic structure. Thus, the structure of tropilidene (V and VI versus VII) is still not resolved.

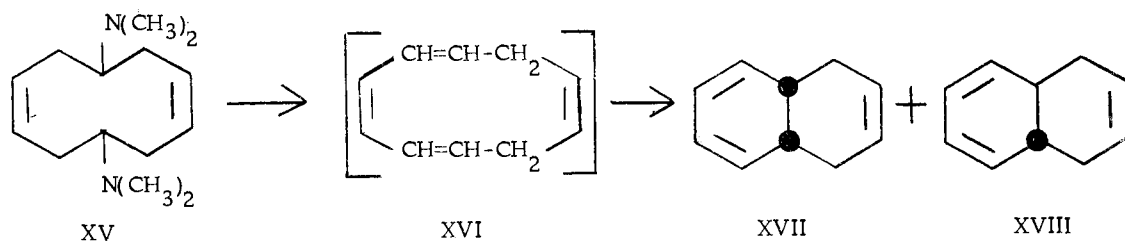
Parker and Goldblatt carried out the thermal pyrolysis of allo-ocimene (VIII) (62). The major products of the reaction were identified as  $\alpha$ -pyronene (X) and  $\beta$ -pyronene (XI). The  $\beta$ -pyronene (XI) was shown to arise directly from the  $\alpha$ -pyronene (X). The cyclization of allo-ocimene (VIII) was rationalized by a prior isomerization to the cis isomer IX, followed by valence isomerization to  $\alpha$ -pyronene (X).



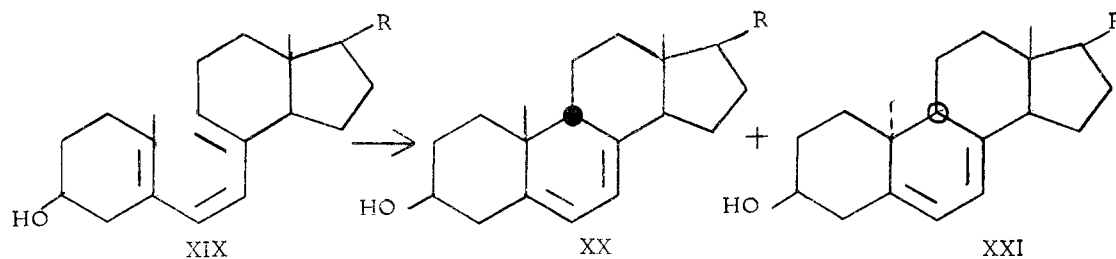
Alder and Dortmann postulated a valence isomerization to account for the observed results of their attempted preparation of 1, 3, 5-cyclononatriene (XIII) by the stepwise Hofmann degradation of homopseudopelletierine (XII) (3). The major product of the reaction was trans-bicyclo-[4. 3. 0]-nona-2, 4-diene (XIV) which is a valence isomer of the desired triene (XIII).



Similar results were obtained by Grob and Schiess in both the Hofmann degradation and N-oxide elimination of 1,6-bis(dimethylamino)-3,8-cyclodecadiene (XV) (33). The products of these reactions were tentatively identified as a mixture of the cis- and trans-bicyclo-[4.4.0]-deca-2,4,8-trienes (XVII and XVIII, respectively). The authors suggested that these products arise by valence isomerization of the initially formed tetraene (XVI).

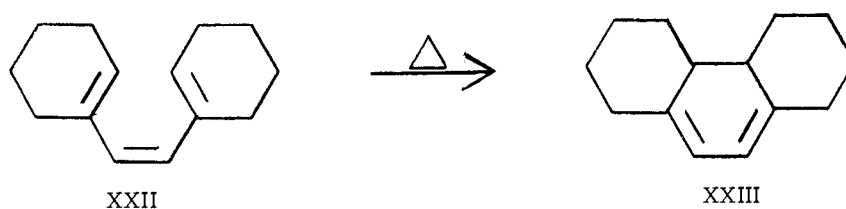


Havinga and Schlatmann have suggested that pyro- (XX) and isopyrocalciferol (XXI) are formed by the heating of precalciferol (XIX) (37). If pyro- (XX) and isopyrocalciferol (XXI) are indeed formed

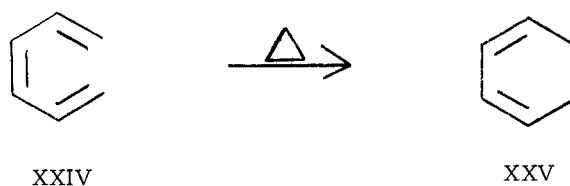


from precalciferol (XIX), then this reaction provides a further example of this type of valence isomerism.

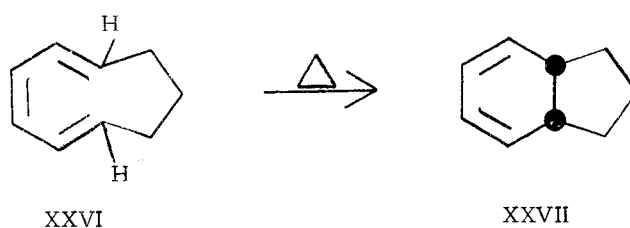
Several additional examples of valence isomerism in conjugated trienes have recently been demonstrated. Pippin provided some evidence that cis-1,2-di-(1'-cyclohexenyl)-ethene (XXII) readily isomerizes to a decahydrophenanthrene (XXIII) at 180° (64). The



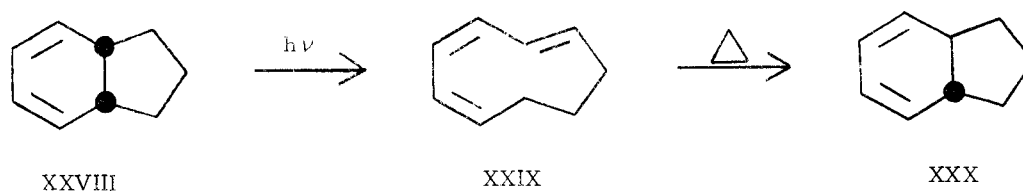
thermal cyclization of *cis*-1, 3, 5-hexatriene (XXIV) to cyclohexa-1, 3-diene (XXV) was carried out by Lewis and Steiner in an investigation of the mechanism of the reaction (54). Glass, Watthey and



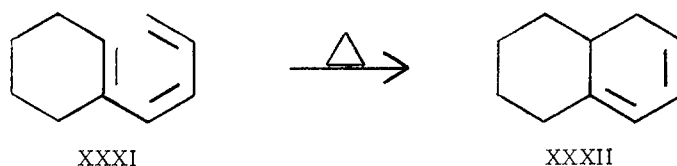
Winstein have converted *cis, cis, cis*-1, 3, 5-cyclononatriene (XXVI) to its valence isomer, *cis*-bicyclo-[4. 3. 0]-nona-2, 4-diene (XXVII) (31). A triene which is most probably the *trans, cis, cis* isomer of



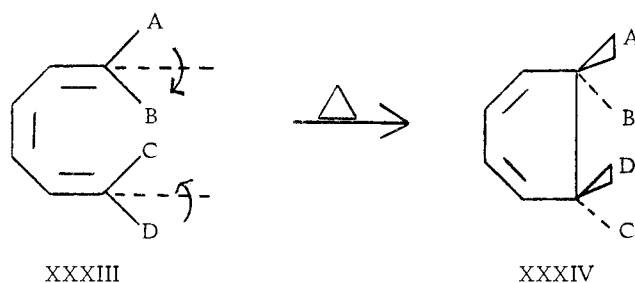
XXVI has recently been isolated by Vogel, Grimme, and Dinne (75) from photolysis of the bicyclic diene XXVIII. This isomer (XXIX)



was shown to cyclize thermally to trans-bicyclo-[4.3.0]-nona-2,4-diene (XXX). Ring closure occurred when the triene XXXI was passed through a gas chromatographic column (60).



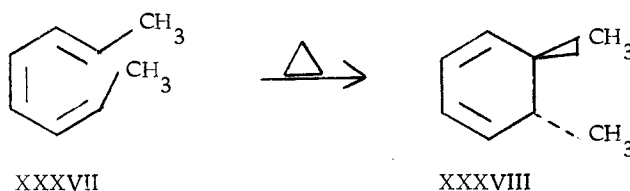
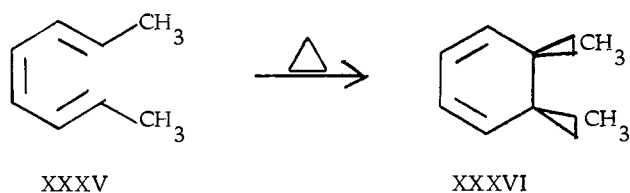
Woodward and Hoffmann have recently proposed a method for predicting the stereochemistry of electrocyclic reactions from molecular orbital theory (80). Among other predictions of stereochemical behavior, Hoffmann and Woodward have postulated that the thermal cyclization of all hexatrienes (XXXIII) to cyclohexadienes (XXXIV) is a disrotatory process, as illustrated. This prediction



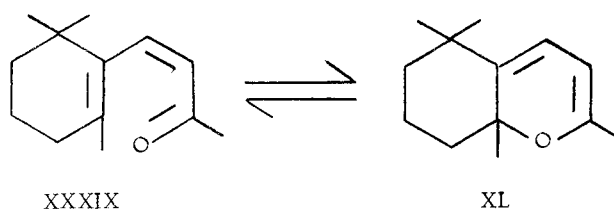
has been verified by a number of experimental examples. These include the previously reported thermal transformation of precalciferol (XIX) to pyro- (XX) and isopyrocalciferol (XXI) (37) and the thermal cyclizations of trans, cis, trans-1,6-dimethylhexa-1,3,5-triene (XXXV) to cis-1,2-dimethylcyclohexa-3,5-diene (XXXVI) and trans, cis, cis-1,6-dimethylhexa-1,3,5-triene (XXXVII) to



trans-1, 2-dimethylcyclohexa-3, 5-diene (XXXVIII) (58, 75).



A recent and exceedingly interesting example of valence isomerism in a heteroatomic system analogous to the conjugated trienes has been uncovered by Marvell and coworkers (61). These workers were able to show that the cis-dienone XXXIX and the  $\alpha$ -pyran XL exist in equilibrium and that the rates of the two valence isomerization processes are enormously faster than those of their all carbon analogs.

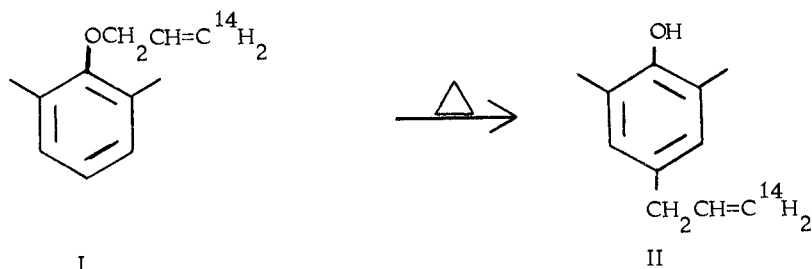


### Abnormal Claisen Rearrangement

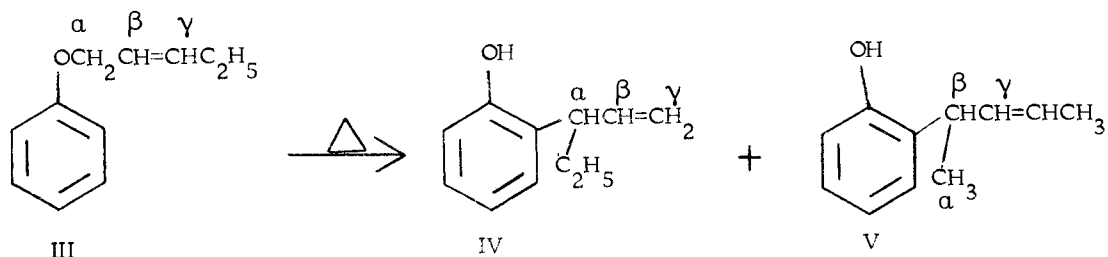
The rearrangement known today as the Claisen rearrangement was discovered in 1912 (10). The structural requirements for this rearrangement are satisfied by allyl ethers of either enols or

phenols. These compounds rearrange to the corresponding C-allyl derivatives in the absence of a catalyst when subjected to elevated temperatures.

With phenyl allyl ethers migration goes exclusively to an ortho position, with the exception that when both ortho positions possess substituents other than hydrogen, further migration to the para position may be observed. Para migration occurs exclusively without inversion of the allyl chain as is illustrated by the rearrangement of the C<sup>14</sup> labeled ether I (69). However, migration to the ortho posi-



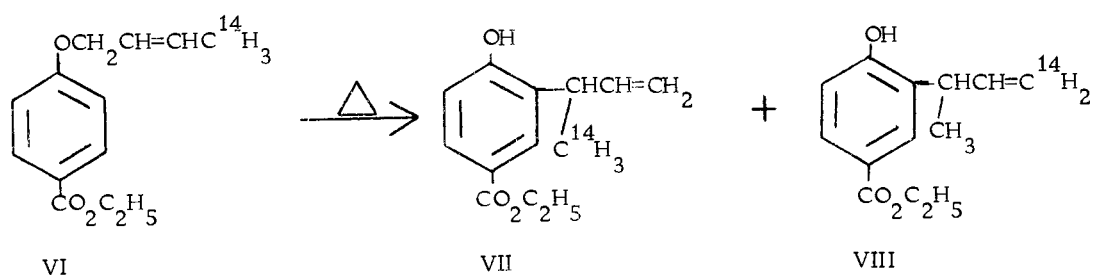
tion involves inversion of the allyl group as is illustrated by the rearrangement of the ether III (45) to give compound IV. Both a normal product (gamma carbon attached to the aromatic nucleus) and an



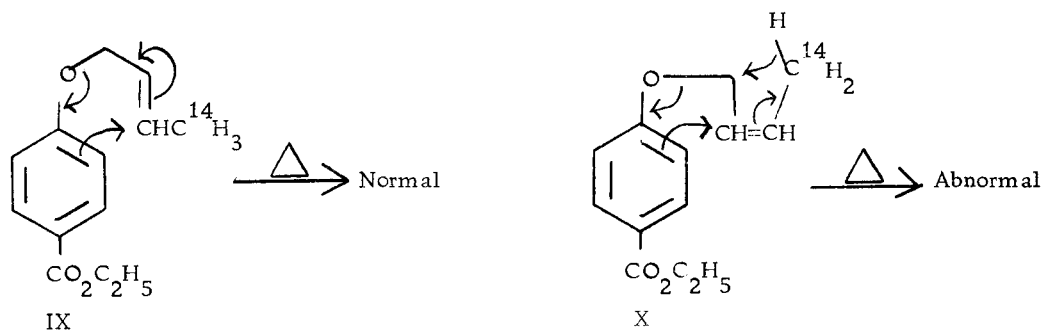
abnormal product (beta carbon attached to the aromatic nucleus) are formed during rearrangement of III. The nature of the products from the rearrangement is dependent upon the substitution pattern in the

allylic portion of the rearranging molecule. Alkyl groups substituted on the alpha carbon give ethers which yield exclusively the normal product. However, alkyl groups substituted on the gamma carbon give ethers which yield both the normal and abnormal products.

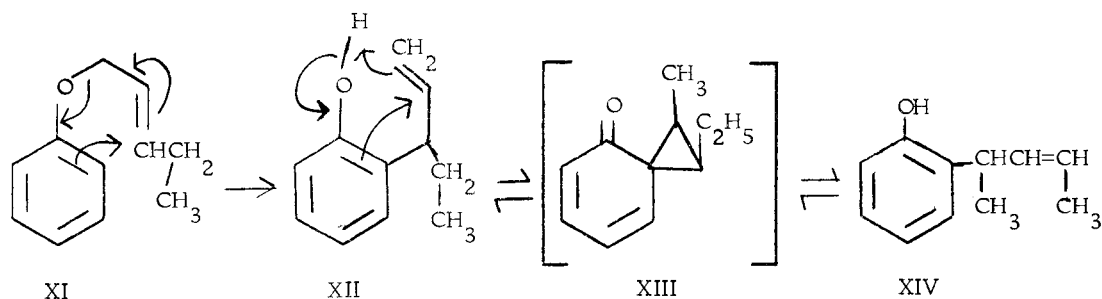
Lauer and Filbert first showed that the abnormal product was produced by the rearrangement of gamma-ethylallyl phenyl ether (III) (51). It was subsequently shown by Hurd and Pollack that both the normal (IV) and abnormal (V) products were formed in this reaction (45). Lauer and Ungnade have examined the rearrangement of allylic ethers of ethyl-4-hydroxybenzoate and determined that the product of this reaction also consists of both normal and abnormal products (52). More recently, Lauer and coworkers examined the rearrangement of crotyl-delta C<sup>14</sup>-p-carbomethoxyphenyl ether (VI) (53). The appearance of the C<sup>14</sup> label in two different positions in the product (VII and



VIII) confirmed that once again two products were being formed, and these workers suggested two independent pathways for producing the normal (IX) and abnormal (X) products from the ether.

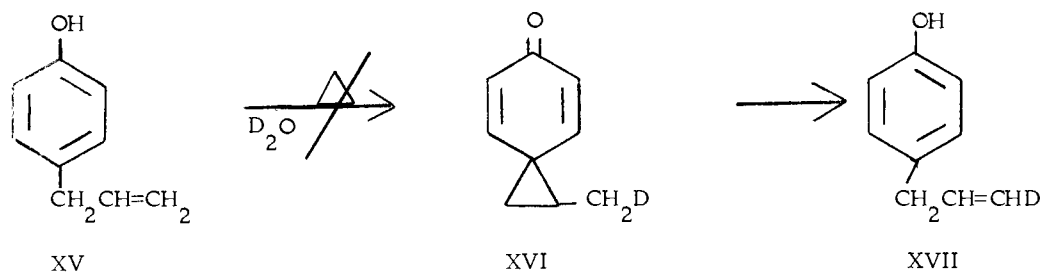


However, Marvell, Anderson, and Ong have shown through kinetic studies that the abnormal rearrangement product is formed from the ether by a consecutive series of reactions involving the normal product as an intermediate (57). Thus, these latter workers were able to demonstrate that the 3-(o-hydroxyphenyl)pent-1-ene (XII) obtained by the Claisen rearrangement of the corresponding ether (XI) rearranges to 4-(o-hydroxyphenyl)pent-2-ene (XIV). They postulated the spiro-dienone (XIII) as an intermediate in the abnormal Claisen rearrangement.



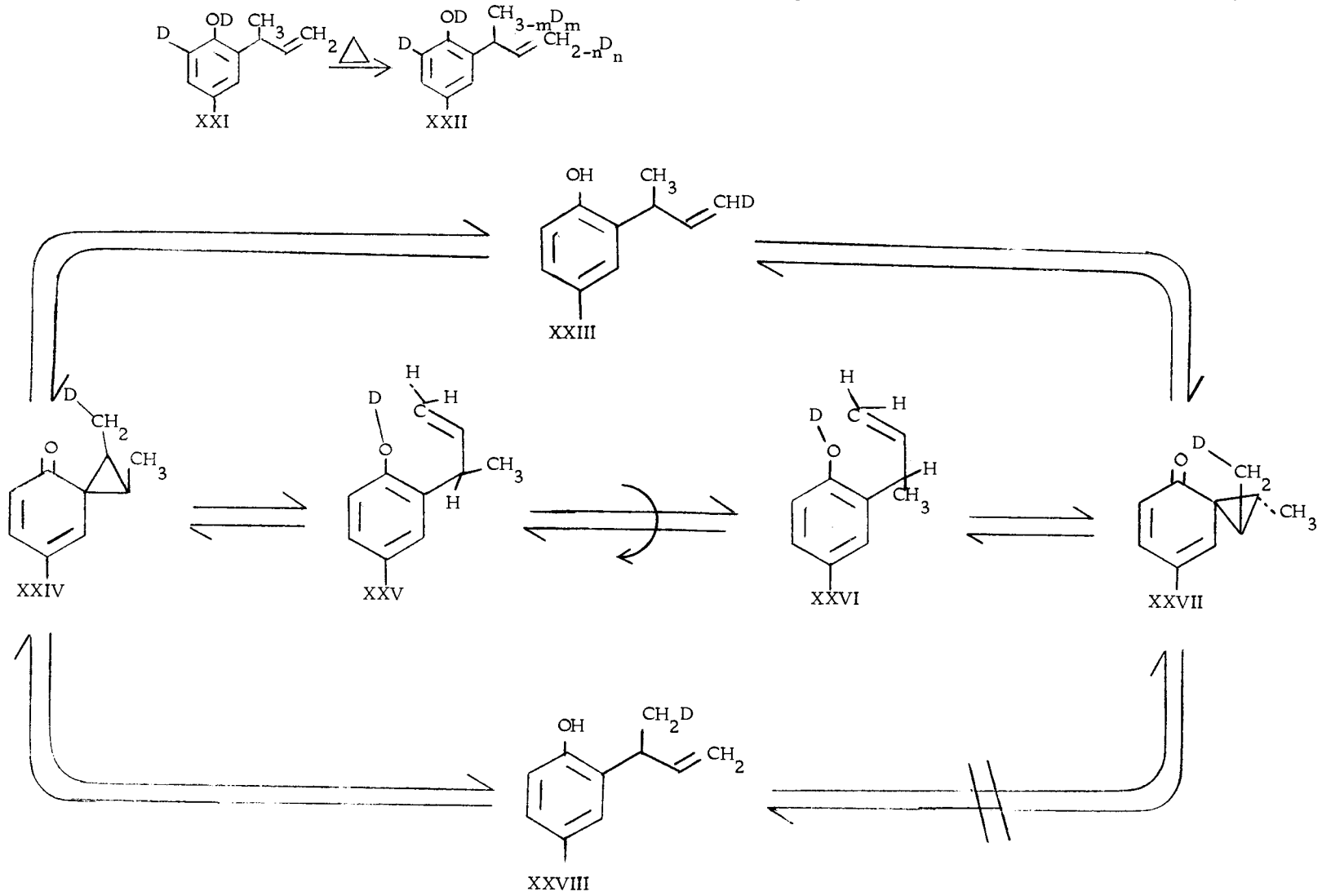
Subsequently, Schmid and coworkers (34) examined the kinetics of the rearrangement of crotyl- $\delta$ - $C^{14}$ -p-methylphenyl ether and concluded that their experimental data were in complete agreement with the mechanism postulated by Marvell. Further studies by Schmid

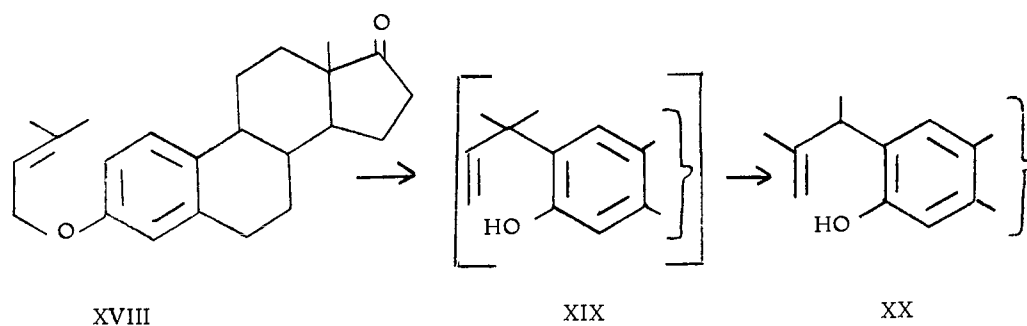
and coworkers on the abnormal Claisen rearrangement involved re-arrangement of the dideuterated phenol (XXI) in deuterium oxide (35, 68). By determination of both the position and the extent of deuteration in XXII, Schmid was able to provide evidence in support of the mechanism shown in Scheme I. Schmid and coworkers also demonstrated that XXIV and XXVII are the only intermediates in the rearrangement, and that the formation and further reaction of these intermediates are intramolecular processes. In agreement with these findings attempts to produce a reaction analogous to the abnormal Claisen rearrangement with p-allylphenols (XV, XVI, and XVII) led only to failure.



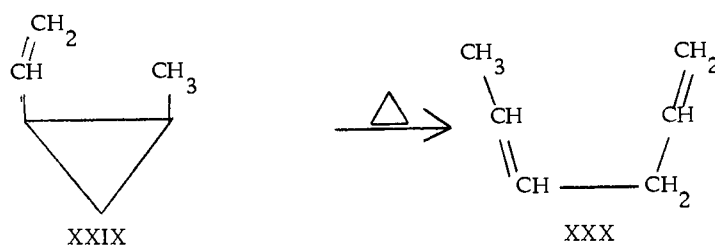
The thermal rearrangement of 3,3-dimethylallyl estrone ether (XVIII) to the phenol (XX) was recently demonstrated by Jefferson and Scheinmann (47). The formation of a product with this structure was rationalized by assuming the intervention of an abnormal Claisen rearrangement. These workers were able to demonstrate by trapping experiments that the normal Claisen rearrangement product (XIX) was an intermediate in the reaction.

Scheme I. Proposed Mechanism for Abnormal Claisen Rearrangement

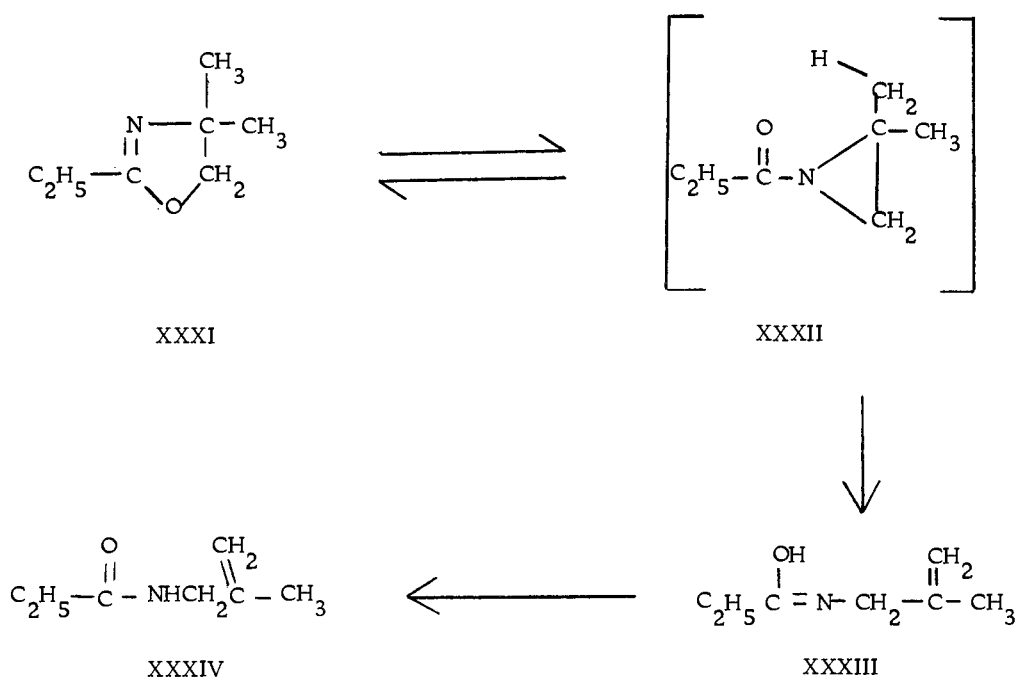




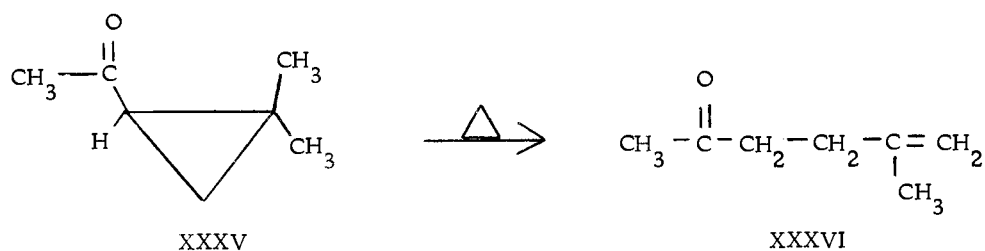
The recent literature includes several examples of thermal rearrangements which are analogous to the abnormal Claisen rearrangement. These rearrangements all involve as the structural essential, a *cis*-1-alkyl-2-vinylcyclopropane system or any heteroanalog of this. Thus, Ellis and Frey have reported the rearrangement of *cis*-1-methyl-2-vinylcyclopropane (XXIX) to *cis*-hexa-1,4-diene (XXX) (22). Wehrmeister has carried out the rearrangement of 2-ethyl-



4,4-dimethyl-2-oxazoline (XXXI) to *N*-methylallylpropionamide (XXXIV) (78). This rearrangement can be rationalized via the conversion of the oxazoline (XXXI) to *N*-propionyl-2,2-dimethylaziridine (XXXII) which then undergoes thermal isomerization (24, 25, 26, 38, 39, 48, 71) to the enol of *N*-methylallylpropionamide (XXXIII). Roberts and Landolt have demonstrated the isomerization of



1-acetyl-2, 2-dimethylcyclopropane (XXXV) to ( $\beta$ -methylallyl)-acetone (XXXVI) (65). Roberts and coworkers have also shown that this re-



action is reversible (66). Other workers have carried out similar studies on the thermal isomerizations of 1-acetyl-2-methylcyclopropane to allylacetone (11) and of 1-carbomethoxy-2-methylcyclopropane to methyl pent-4-en-1-oate (9).



## DISCUSSION

Valence Isomerism of 2, 4, 6-OctatrienesIntroduction

The studies reported in this section of the thesis had two objectives, (1) to synthesize and characterize the isomeric cis- or trans-2, cis-4, cis- or trans-6-octatrienes (Ia, IIa, and IIIa) and (2) to study the thermal valence isomerizations of cis-2, cis-4, cis-6-octatriene (Ia) and trans-2, cis-4, cis-6-octatriene (IIa). Each of these two trienes (Ia and IIa) would be expected to undergo a thermal isomerization analogous to that established previously for trans-2, cis-4, trans-6-octatriene (IIIa) (8).

Synthesis and Structure Identification

Preliminary studies (8) had previously established a method of synthesis applicable to the preparation of cis- or trans-2, cis-4, cis- or trans-6-octatrienes (Ia, IIa, and IIIa). The general synthetic

scheme is shown in Table 1. Initially the synthesis was carried through from cis-2-octen-4-yn-7-ol (IX) (8) to cis-2, cis-4, cis-6-octatriene (Ia) and trans-2, cis-4, cis-6-octatriene (IIa). An amount of the triene mixture sufficient only for the characterization of these compounds was obtained. The acetylenic compound (IX) was hydrogenated (deuterated) over Lindlar catalyst and the product (Xa) was converted without purification directly to the tosylate (XIa). The final elimination step gave a mixture of hydrocarbons. This mixture was separable by gas chromatography (g. p. c.) and was ultimately shown to contain 14% cis-2, cis-4, cis-6-octatriene (Ia), 57% trans-2, cis-4, cis-6-octatriene (IIa), 10% cis-2, cis-6-octadien-4-yne (XVI), 14% trans-2, cis-6-octadien-4-yne (XVII), and 5% unidentified components. It was later found that over-hydrogenation of the acetylenic compounds (IX and XIII) by 15% reduced the amount of acetylenic material present and greatly facilitated g. p. c. separation of the hydrocarbon mixture.

In order to obtain larger quantities of Ia and IIa to complete the studies, the synthetic scheme was carried through directly with the mixture of isomeric pentenynes (VIII and XII). Preparative g. p. c. was again utilized to obtain the pure compounds.

One hydrocarbon product isolated (8) from the synthetic process starting with XII showed an ultraviolet spectrum characteristic of conjugated trienes (20), cf. Table 2. This compound is that one of

Table 1. Synthesis of 2, 4, 6-octatrienes.

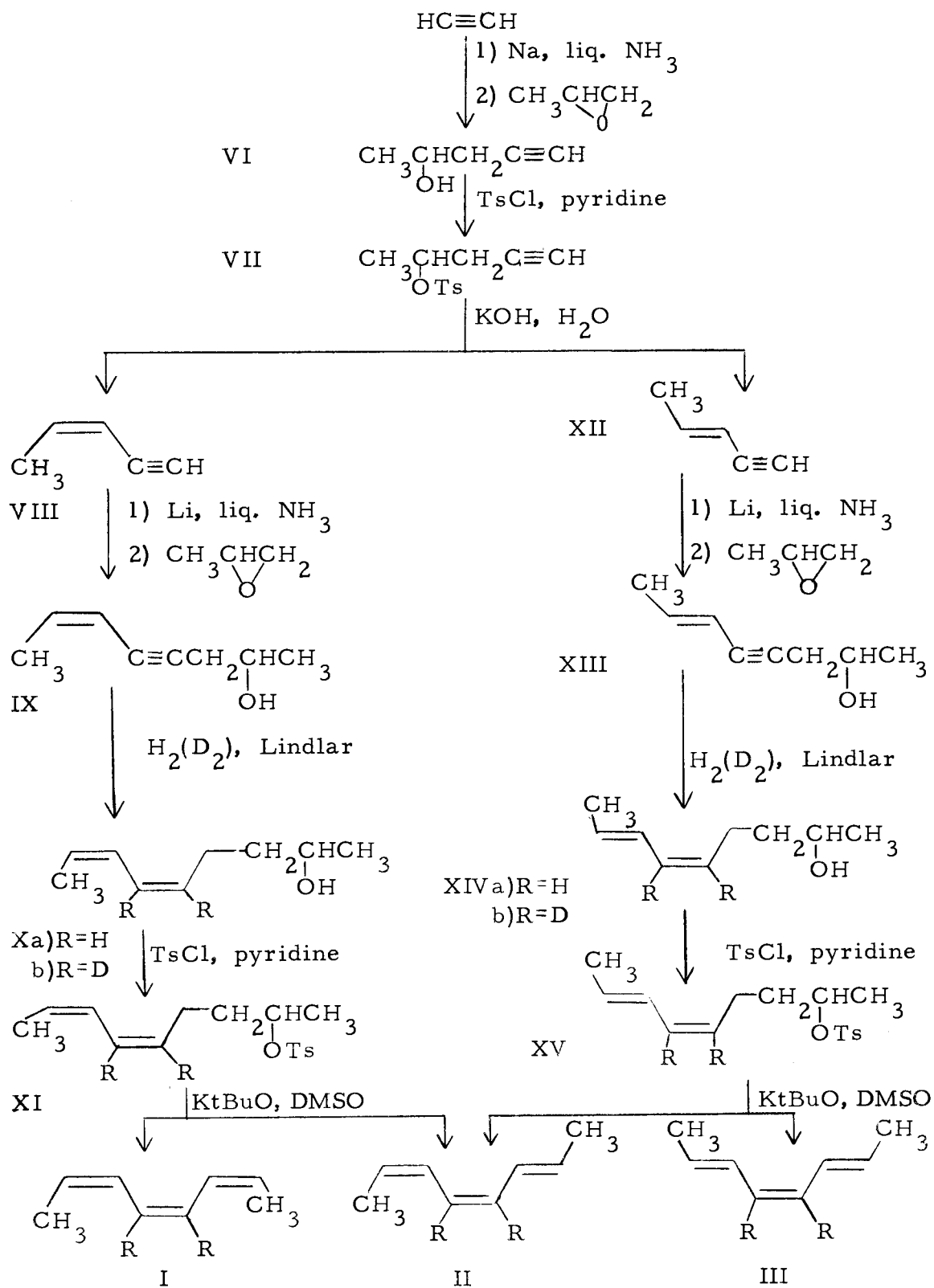


Table 2. Spectral characterization of Ia, IIa and IIIa.

Compound (% Purity)	U. V.		I. R.	N. M. R.			4, 5-dideuterio N. M. R.			
	$\lambda_{\max}$ m $\mu$	$\epsilon$	$\nu$ , cm <sup>-1</sup>	Splitting	$\delta$ , ppm.	Area	Pattern	$\delta$ , ppm.	J, cps.	
Ia (>96%)	262	26, 200	3040, 3015,	multiplet	5.22-6.72	6	ABX <sub>3</sub>	A=5.47	AX=7.0	
	270	32, 500	2970, 2845,	multiplet	1.68-1.91	6		B=6.35	AB=11.0	
	280	24, 500	1628, 688					X=1.75	BX=1.5	
IIa (>99%)	257	32, 000	3030, 2959,	multiplet	5.30-6.74	6	ABX <sub>3</sub>	A=5.61	AX=6.5	
	265	38, 600	2849, 1629,	multiplet	1.64-1.90	6		B=6.32	AB=15.5	
	276	29, 200	957, 699					X=1.77	BX=1.5	
								CDY <sub>3</sub>	C=6.30	CY=1.5
									D=5.42	CD=11.0
									Y=1.73	DY=7.0
IIIa (>96%)	255	33, 000	3030, 3005,	multiplet	5.28-6.78	6	ABX <sub>3</sub>	A=5.58	AX=6.5	
	267	41, 000	2965, 2885	multiplet	1.62-1.98	6		B=6.40	AB=15.0	
	277	30, 000	1643, 960, 706					X=1.76	BX=1.5	

two trienes, ultimately isolated and identified as products of this synthesis, which is obtained in larger amounts. Thus on synthetic grounds alone it can be assigned the structure IIIa. The assignment was completely confirmed by spectral and chemical methods. The n. m. r. spectrum of this substance shows absorption in two regions of the spectrum, the two having relative areas of 1:1. In the region characteristic of allylic methyls, there appear four lines with  $J_{AX} = 6.5$  cps.,  $J_{BX} = 1.5$  cps., while the olefinic region is too complex for first order analysis. Simplification of the latter region was achieved by introduction of deuterium in place of hydrogen at  $C_4$  and  $C_5$ . The dideuterio triene (IIIb) shows an olefinic proton spectrum which is the AB part of an  $ABX_3$  spectrum with  $J_{AB} = 15.0$  cps. This coupling is characteristic of trans double bonds (46). Hence this is a symmetric molecule having both terminal double bonds of trans configuration.

That the central double bond is indeed cis is indicated both by the facile ring closure to a cyclohexadiene (8) and by the difference in its ultraviolet spectrum from that of the known all trans octatriene (2). Lewis and Steiner (54) have shown that trienes with a central trans double bond will not undergo a ring closure at temperatures below  $300^\circ$ . The infrared spectrum is in complete agreement with this assignment, and the following vibrational assignments can be made: vinyl C-H stretch at 3030 and 3005  $\text{cm}^{-1}$ , methyl C-H stretch

at 2965 and 2885  $\text{cm}^{-1}$ , C=C stretch at 1643  $\text{cm}^{-1}$ , trans double bond C-H out-of-plane deformation at 960  $\text{cm}^{-1}$ , and a cis double bond C-H out-of-plane deformation at 706  $\text{cm}^{-1}$ .

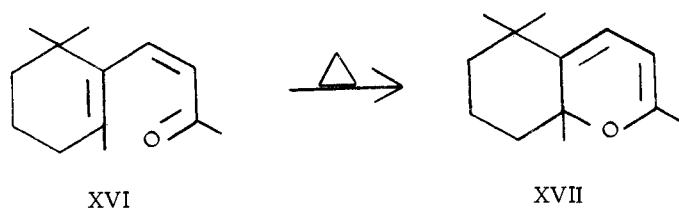
As is indicated in Table 1, there were obtained from each of the two parallel synthetic processes, starting respectively with IX and XII, two trienes. An analysis of the data of Table 2 in exactly the same fashion as in the paragraphs above provides convincing proof of the structures and stereochemistry of the other two isomeric trienes obtained.

### Valence Isomerization

Reaction of trans-2, cis-4, trans-6-Octatriene (IIIa) (8). A 0.67 M solution of IIIa in pentane was heated in a sealed tube at 132°. Rearrangement gave a single product which was isolated via preparative g. p. c. The u. v. spectrum of this product showed  $\lambda_{\text{max}} = 261 \text{ m}\mu$  ( $\epsilon = 4,100$ ) which is characteristic (20) of a homoannular diene. The n. m. r. spectrum of the product showed a singlet at  $\delta = 5.88 \text{ ppm}$  (four olefinic protons), the A part of an  $\text{AXY}_3$  pattern at  $\delta = 2.42 \text{ ppm}$  (two allylic protons), and a doublet at  $\delta = 0.97 \text{ ppm}$  (six methyl protons). Spectral data thus indicate that the product must be a 5,6-dimethyl-1,3-cyclohexadiene. Ozonolysis of the product followed by peroxide oxidation produced meso-2,3-dimethylsuccinic acid. The product is therefore cis-5,6-dimethyl-1,3-cyclohexadiene (IV).

Rate studies for this valence isomerization were carried out on samples containing equimolar quantities of IIIa and toluene dissolved in cyclohexane. Aliquots of the prepared solution were sealed under a nitrogen atmosphere in Pyrex glass bombs. The bombs were immersed in a constant temperature bath and removed at various time intervals. Analysis of the rearranged samples was by g. p. c.

The observed rate constants for this valence isomerization were  $4.45 \times 10^{-5} \text{ sec}^{-1}$  at  $132^\circ$ ,  $2.45 \times 10^{-4} \text{ sec}^{-1}$  at  $152^\circ$ , and  $7.02 \times 10^{-4} \text{ sec}^{-1}$  at  $165^\circ$ . The energy of activation was calculated to be 29.4 kcal/mole and the entropy of activation - 7 e. u. at  $149^\circ$ . The negative entropy of activation denotes a higher degree of order in the transition state than in the reactants. Formation of a cyclic intermediate from a noncyclic reactant is always accompanied by a negative entropy change (30). Thus, for the valence isomerization of XVI to XVII, an entropy of activation of - 14 e. u. was found (61).

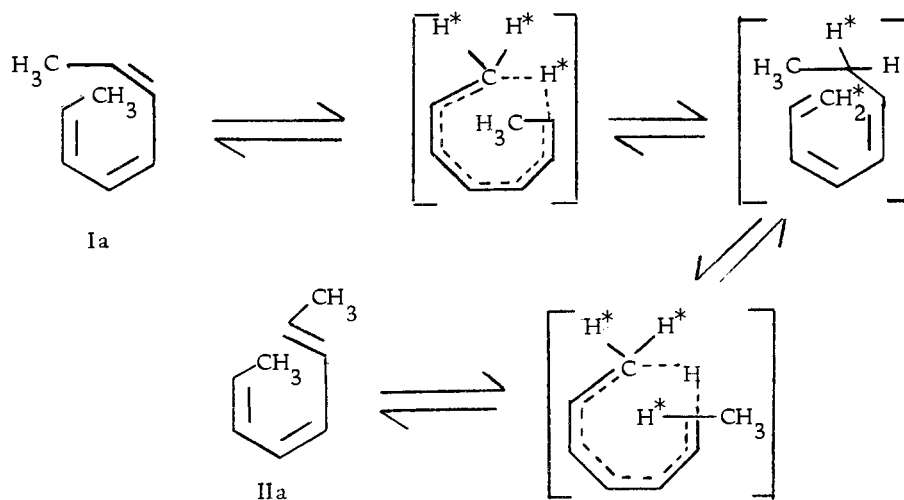


The absence of cis-trans interconversion in the valence isomerization of IIIa to IV is shown by the absence of the all trans isomer in the product since, if produced, it would be stable under the reaction conditions. Thus it appears that the mechanism of

valence isomerism is not related to cis-trans interconversion.

Reactions of trans-2, cis-4, cis-6-Octatriene (IIa) and cis-2, cis-4, cis-6-Octatriene (Ia). Preliminary studies on the valence isomerizations of trans-2, cis-4, cis-6-octatriene (IIa) and cis-2, cis-4, cis-6-octatriene (Ia) showed that the behavior of these compounds was much more complex than the behavior found for IIIa. It was found that thermal interconversion of Ia and IIa occurred readily at 100°. The rate constant for this interconversion (Ia → IIa) at 109.5° was  $2 \times 10^{-5} \text{ sec}^{-1}$  (8), while the equilibrium constant ( $K = \text{IIa}/\text{Ia}$ ) was 5.5.

The thermal interconversion of Ia and IIa can be rationalized through consecutive 1,7 hydrogen shifts. An important 1,7 thermal



hydrogen shift in an open-chain system has been known for some time in the precalciferol-calciferol equilibrium (67). Experimental proof for a 1,7 hydrogen shift in the above system ( $\text{Ia} \rightleftharpoons \text{IIa}$ ) has not been



obtained.

It is somewhat surprising that 1, 5 hydrogen shifts are not observable during the interconversion of Ia and IIa. These same 1, 5 hydrogen shifts are well known in both cyclic triene (32) and 1, 3-diene systems (79). Failure to observe 1, 5 hydrogen shifts in the present system may be attributed to a higher free energy requirement for the 1, 5 than for the 1, 7 hydrogen shift. An alternative explanation may be that the 1, 5 shift results in disruption of the conjugation in the system, and no 1, 3, 6-triene is present in sufficient quantity at equilibrium to be observed.

The valence isomerization of a mixture of Ia and IIa was carried out in cyclohexane at 178°. Three products were observed (g. p. c.). The first product was identified (vide supra) as cis-5, 6-dimethyl-1, 3-cyclohexadiene (IV). The product IV was shown to be derived from trans-2, cis-4, -trans-6-octatriene (IIIa) which was present in the starting material in the amount of 6% (g. p. c. analysis). The rapid disappearance of impurity IIIa and simultaneous appearance of product IV were observed before the valence isomerization of the equilibrium mixture (Ia + IIa) had proceeded to a measurable extent. The second product was identified (8) as trans-5, 6-dimethyl-1, 3-cyclohexadiene (XVIII) by u. v., infrared, and n. m. r. spectra, and by ozonolysis followed by peroxide oxidation to yield dl-2, 3-dimethylsuccinic acid. The third product was identified (8) as

1,6-dimethyl-1,3-cyclohexadiene (XIX) by u. v., infrared, and n. m. r. spectra. This product (XIX) was subsequently shown (vide infra) to be derived from XVIII and is not a direct product of the reaction of the equilibrium mixture ( $Ia \rightleftharpoons IIa$ ).

Kinetic studies were carried out as previously described on samples of the mixture (Ia and IIa) and toluene dissolved in cyclohexane. Analysis (g. p. c.) showed that the disappearance of the mixture (Ia and IIa) was first order with respect to the sum of Ia and IIa (Figures 1 and 2). The kinetic study showed that  $k = 1.5 \times 10^{-5} \text{ sec}^{-1}$  at  $178^\circ$ ,  $k = 6.4 \times 10^{-5} \text{ sec}^{-1}$  at  $196^\circ$ ,  $E_a = 33 \text{ kcal/mole}$ , and  $\Delta S^\ddagger = -9 \text{ e. u.}$  at  $185^\circ$  for the disappearance of the mixture.

The kinetic study carried out at  $196^\circ$  (Table 10 and Figure 2) indicates that a comparatively fast reaction precedes the valence isomerization. This fast initial reaction is attributed to the presence of peroxides which are readily formed from the oxygen sensitive trienes. The linear correlation obtained from the rate study at  $178^\circ$  (Table 9 and Figure 1) indicates that peroxides were not present in the samples initially, but that the peroxides were formed upon storage of the trienes prior to the kinetic run at  $196^\circ$ .

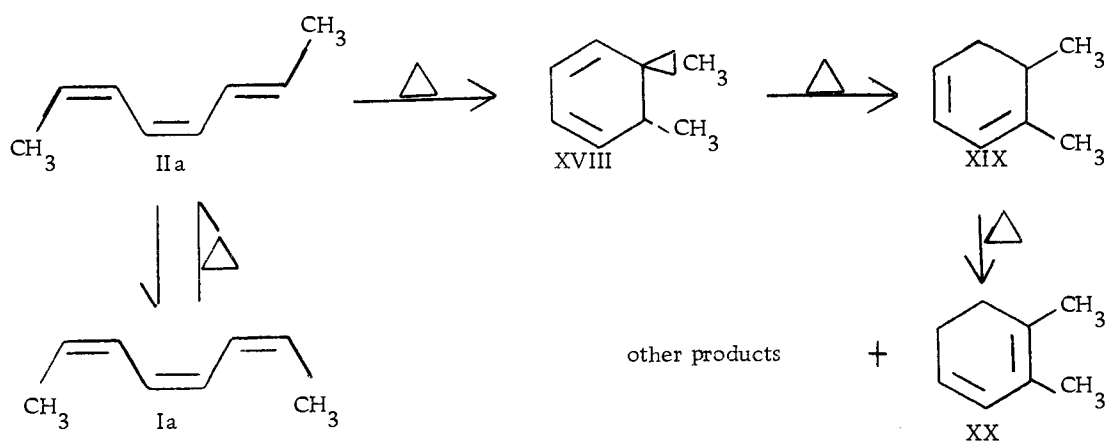
The infinity points (Tables 9 and 10) for the above two kinetic runs showed that 20% of the triene remained unreacted. When pure XVIII was heated, no trienes (Ia and IIa) could be found in the product. Thus no equilibrium between XVIII and (Ia + IIa) exists. If 1, 5

hydrogen shifts occurred under the reaction conditions, isomerization of the central double bond could result. Trienes possessing a central trans double bond cannot yield ring closed products, and this could explain the observed infinity point. However, if this were true, one would expect more 1,5 hydrogen shift (and therefore a greater amount of unreacted triene at the infinity point) in the kinetic run at 196° than at 178°. Since the reaction at both temperatures yields the same infinity point, the 1,5 hydrogen shift is not a satisfactory explanation. The alternative remains that the infinity reading is due to an unreactive impurity in the original triene mixture. Such a large amount of impurity is unexpected from the gas phase chromatogram of the starting materials. The confirmed presence of 6% trans-2, cis-4, trans-6-octatriene (IIIa) in the starting material cannot be part of the 20% impurity since IIIa immediately cyclizes to IV under the conditions of the present reaction. Dienenyne impurities have also been shown (g. p. c.) to be absent from the starting material. The possibility that small amounts of trienes with a central trans double bond may be present in the synthetic mixture is not excluded. Hydrogenation with Lindlar catalyst of conjugated enynes has previously been shown to result in the formation of some trans double bond (60). Elimination of the tosylate with KtBuO has also previously been shown (8) to result in base catalyzed isomerization of double bonds when the molar ratio of base to tosylate exceeds 1:1. The

g. p. c. retention times of compounds with a central trans double bond are unknown in comparison with the retention times of the trienes Ia, IIa, and IIIa. Although trienes with a central trans double bond may be present and would not undergo ring closure, it was not proven that the observed infinity point was due to their presence.

In the valence isomerization reaction the secondary product XIX can arise from the primary product XVIII by a 1,5 hydrogen shift. Some 1,5 hydrogen shifts have previously been observed for these compounds (XVIII and XIX), but no kinetic data have been published (63). Kinetic studies on XVIII (g. p. c. pure) showed that the disap-

Scheme II. Sequence of Reactions



pearance of this compound was first order (Figures 3 and 4, Tables 11 and 12):  $k = 0.8 \times 10^{-5} \text{ sec}^{-1}$  at  $182^\circ$ ,  $k = 3.6 \times 10^{-5} \text{ sec}^{-1}$  at  $200^\circ$ ,  $E_a = 36 \text{ kcal/mole}$ , and  $\Delta S^\ddagger = -3 \text{ e. u.}$  at  $190^\circ$ . The main product of the reaction of XVIII was the previously identified 1,6-dimethyl-1,3-cyclohexadiene (XIX). A small amount of 1,2-dimethyl-

1, 3-cyclohexadiene (XX) was also identified (8) as a product of this reaction. Thermal rearrangement (8) of cis-5, 6-dimethyl-1, 3-cyclohexadiene (IV) also yielded XIX along with small amounts of XX. This reaction was first order with respect to IV and exhibited  $k = 1.85 \times 10^{-5} \text{ sec}^{-1}$  at  $178^\circ$ ,  $k = 4.59 \times 10^{-5} \text{ sec}^{-1}$  at  $189^\circ$ ,  $E_a = 34 \text{ kcal/mole}$ , and  $\Delta S^\ddagger = -7 \text{ e. u.}$  at  $183^\circ$  (8).

The presence of 1, 2-dimethyl-1, 3-cyclohexadiene (XX) in the products of the thermal rearrangement of both XVIII and IV suggests that this product (XX) is derived from 1, 6-dimethyl-1, 3-cyclohexadiene (XIX) by a second 1, 5 hydrogen shift. Thermal rearrangement of XIX (g. p. c. pure) yielded mainly XX along with lesser amounts of o-xylene (8), p-xylene (8), ethylbenzene (8), and some unidentified components. Kinetic studies of this reaction showed that the disappearance of XIX was not a first order process and no satisfactory rate correlation could be obtained for this reaction. These data on 1, 5 hydrogen shifts are in qualitative agreement with the previous work (63). However, the work discussed here is an extension of that previous work and establishes the rate constants and kinetic order for these reactions.

Assuming the mechanism shown in Scheme II ( $\text{Ia} \rightleftharpoons \text{IIa} \rightarrow \text{XVIII} \rightarrow \text{XIX}$ ), calculation of the concentration of XVIII at various times during the kinetic run can be made using the measured rate constants (30). Although this concentration term is not particularly

sensitive to the ratio of the rate constants for the last two steps, a reasonable fit to the experimental points is obtained (Table 3). The data are in good accord with the assumption that XVIII is the primary product of the rearrangement of IIa.

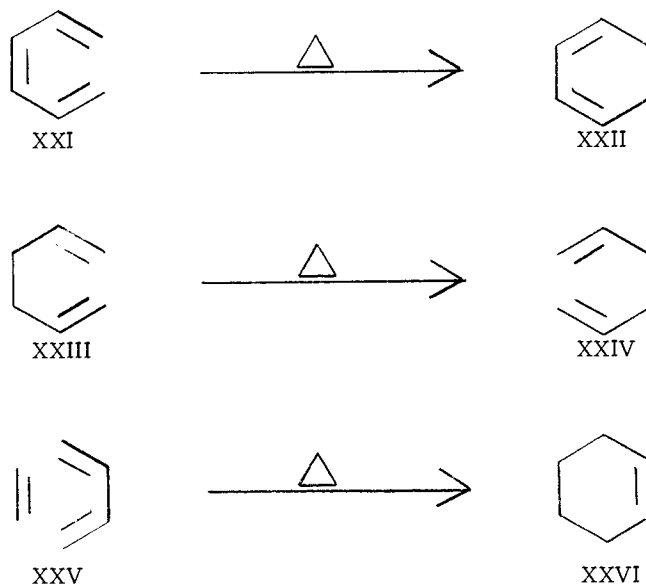
Table 3. Comparison of calculated and experimental concentrations.

Sample	Time, sec	Calc. $\frac{(\text{XVIII})}{(\text{Ia} + \text{IIa})}$	Exper. $\frac{(\text{XVIII})}{(\text{Ia} + \text{IIa})}$
1	5,460	0.07	0.06
2	16,800	0.18	0.17
3	26,700	0.27	0.23
4	45,000	0.37	0.37
5	84,500	0.48	0.40

The rate constant for the valence isomerism of IIa (corrected for the equilibrium between IIa and Ia) is  $1.9 \times 10^{-5} \text{ sec}^{-1}$  at  $178^\circ$ . This is slower than the reaction of the trans, cis, trans isomer (IIIa) by a factor of at least 100. This slower rate is attributed to a steric effect due to the cis methyl group on one of the terminal double bonds. It is quite reasonable that Ia with two cis methyl groups should undergo valence isomerization to a cyclohexadiene so much more slowly than IIa, that Ia is converted to XVIII through the path  $\text{Ia} \rightarrow \text{IIa} \rightarrow \text{XVIII}$  rather than undergoing a direct ring closure.

## General Conclusions

Formally the ring closure reaction which converts a *cis*-triene (XXI) to a cyclohexadiene (XXII) resembles both the molecular rearrangements such as the Claisen and Cope reactions (XXIII to XXIV) and the well-known bimolecular Diels-Alder reaction (XXV to XXVI). The difference in the first case involves addition of a new



pi bond to the biallylic system. In the second case it involves joining diene and dienophile by a new sigma bond. It is of interest to consider how far this formal analogy provides a useful insight into real similarities and differences in these reactions.

It is rather well-accepted today that the Claisen and Cope rearrangements as well as the Diels-Alder reaction are concerted processes. The kinetic data provided by the present work indicate

that the thermal valence isomerization reactions described here belong to the same type of reaction. Should some sort of rotation about the central double bond convert the triene to a non-orthogonal pair of allyl radicals as an intermediate, one would expect some cis-trans interconversion to occur. Also the activation energy would have to equal or exceed the energy required to break a pi bond (ca. 65 kcal/mole) minus the stabilization energy of two allyl radicals (ca. 25 kcal/mole). The radical intermediate can be excluded on both counts. Thus it seems reasonable to assume that the ring closure is a concerted process.

It is interesting to compare all these reactions with respect to their activation parameters. In the Cope reaction one single bond is broken and a new one is formed. The triene valence isomerization converts one pi bond to a sigma bond, while a Diels-Alder reaction converts two pi bonds to two sigma bonds. For the unsubstituted six carbon systems the initial and final states are of equal energy for the Cope reaction, the final state is ca. 12-14 kcal/mole more stable in the triene valence isomerization, and is some 38 kcal/mole more stable in the Diels-Alder process. Based on a naive application of the Evans-Polanyi picture (30) of a reaction, this would suggest that the activation energy of the Diels-Alder process should be the lowest of the three processes, and the Cope should be the highest. As Table 4 shows these conclusions are not completely borne out by



experimental data, but it should be kept in mind that the data in the table are not completely comparable since substituent influences have not been taken into account.

Table 4. Comparison of activation parameters.

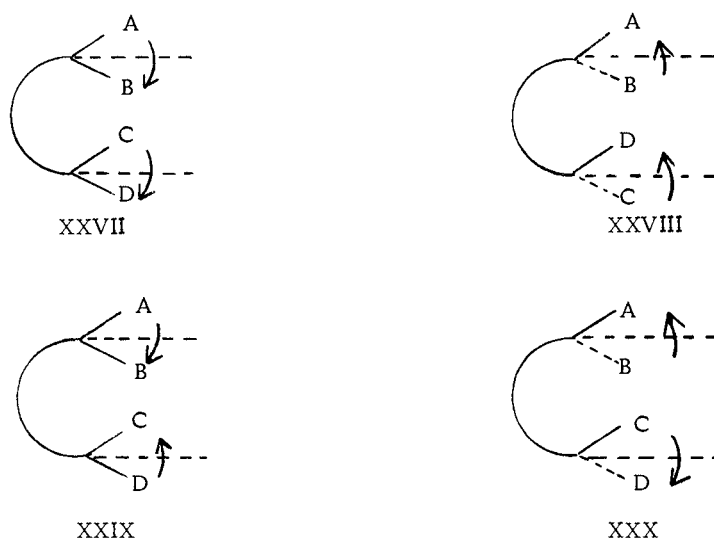
Reaction	$E_a$ , kcal/mole	$\Delta S^\ddagger$ , e. u.
Valence isomerization	29-33	- 7 to - 9
Diels-Alder (30)	20-29	-13 to -26
Claisen (17)	30-34	- 2 to -16
Cope (29)	26-29	-11 to -14

The entropies of activation all fit quite reasonably with the expectations of theory for the concerted processes under consideration. Thus the bimolecular Diels-Alder reaction shows the largest negative  $\Delta S^\ddagger$ . The rather rigid cis-triene and allyl phenyl ethers show the lowest negative  $\Delta S^\ddagger$  values, and the mobile diallyl molecules have intermediate values.

Perhaps the most important feature which these reactions have in common is their high degree of stereoselectivity. The study made here shows that IIIa undergoes the ring closure reaction in a stereospecific manner, and while the data will not permit more than an estimate to be made in the case of IIa, it is better than 90% stereoselective. These values correspond quite favorably with the results reported for the Claisen and Cope (17) and the Diels-Alder (56)

reactions.

Shortly after this work was completed Woodward and Hoffmann (80) suggested a theoretical basis for predicting the stereochemical course of the triene ring closure. Since the fixed geometrical isomerism imposed upon the open-chain system is related to the rigid tetrahedral isomerism in the cyclic compound, electrocyclic reactions may proceed by either a conrotatory (XXVII and XXVIII) or a disrotatory (XXIX and XXX) process. From the symmetry of the



highest occupied molecular orbital in the open-chain compound it is predicted that these electrocyclic reactions ( $1 \pi$ -bond  $\rightarrow$   $1 \sigma$ -bond) will be thermally conrotatory and photochemically disrotatory for  $m = 4q$  ( $m$  = number of  $\pi$ -electrons,  $q$  = an integer), and thermally disrotatory and photochemically conrotatory for  $m = 4q + 2$ . In agreement with these predictions the thermal isomerization of cyclobutenes and the photochemical cyclization of hexatrienes have both

been shown (1, 16, 28, 36, 37, 73) to be conrotatory. The stereochemistry of the thermal cyclization of hexatrienes (IIa and IIIa) has been established as disrotatory in this thesis and is also in agreement with the predictions of Woodward and Hoffmann. Thus, trans-2, cis-4, trans-6-octatriene (IIIa) isomerized thermally to cis-5, 6-dimethyl-1, 3-cyclohexadiene (IV) and trans-2, cis-4, cis-6-octatriene (IIa) yielded trans-5, 6-dimethyl-1, 3-cyclohexadiene (XVIII). The thermal cyclization of cis-2, cis-4, cis-6-octatriene (Ia) could not be carried out due to the facile rearrangement of Ia to IIa. Cyclic cis, cis, cis trienes have previously been shown (12, 31, 44, 76) to isomerize thermally by a disrotatory process to the cis-cyclohexadiene derivative. However, these latter cyclic examples may not be indicative of unencumbered reaction stereochemistry since the ring imposes important and perhaps determinative restraints on the reaction course.

This orbital symmetry correlation with the stereochemical mode of reaction has been extended more recently to the Diels-Alder (41, 42), Claisen and Cope (43, 81), and related processes (41, 43, 81). The agreement of theory with experimental data is highly encouraging for this approach. Two other groups (55, 82) have subsequently shown that it is possible to draw similar conclusions from slightly different approaches.

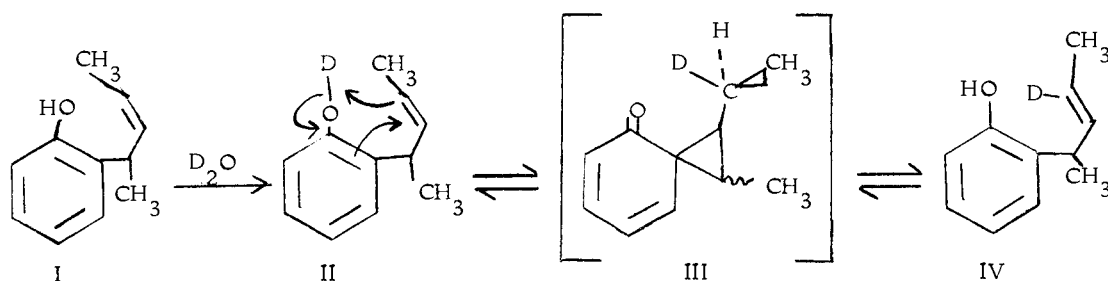
## Abnormal Claisen Rearrangement

### Introduction

A mechanism has previously been postulated (57) for the abnormal Claisen rearrangement. Subsequent work (34, 35) on this rearrangement has been interpreted as in agreement with the proposed mechanism. However, two important sources of information were not examined in previous investigations of this reaction.

When *cis*-2-(o-hydroxyphenyl)pent-3-ene (I) is rearranged in the presence of a suitable source of deuterium, the postulated mechanism (Scheme III) for the abnormal Claisen rearrangement requires that the isomerization of the *cis* to *trans* double bond be accompanied by the simultaneous incorporation of an olefinic deuterium. According to Scheme III the *trans*-phenol (IV) must contain one

Scheme III. Proposed Mechanism



olefinic deuterium atom, and the rate of *cis* to *trans* isomerization must equal the rate of olefinic deuterium incorporation. The degree of stereospecificity for this reaction can then be determined by

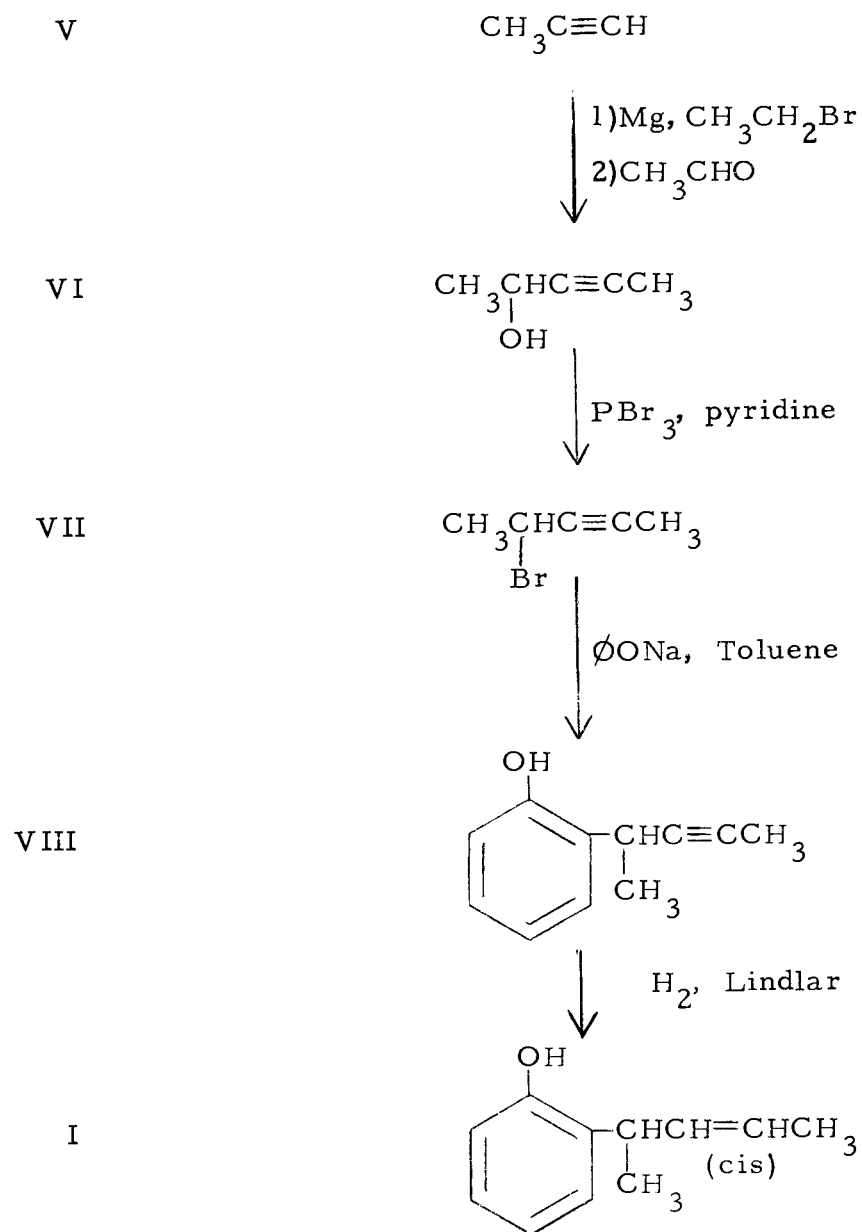
examination of these two experimental points. Since the proposed mechanism requires complete stereospecificity for the rearrangement, evidence for (or against) this mechanism may be obtained.

The kinetic order and activation parameters of the abnormal Claisen rearrangement have not previously been obtained. These data must also be in agreement with the proposed mechanism. Scheme III shows a proton transfer for the formation of the spiro-dienone intermediate (III). If a proton transfer is involved in the rate determining step of this reaction, a substantial deuterium isotope effect would also be expected.

The purpose of the present work is then to carry out studies on the degree of stereospecificity and the kinetics, and to determine the extent of their agreement with the postulated mechanism for the abnormal Claisen rearrangement.

### Synthesis

The compound chosen for study of the abnormal Claisen rearrangement is the known (59) *cis*-2-(o-hydroxyphenyl)pent-3-ene (I). This phenol (I) was synthesized according to Table 5. The synthetic method satisfies the requirements that the side chain occupy only the ortho position, that the site of attachment to the aromatic nucleus is allylic, and that the configuration of the double bond is *cis*.

Table 5. Synthesis of *cis*-2-(o-hydroxyphenyl)pent-3-ene (I).

The preparation of 2-hydroxypent-3-yne (VI) (Table 5) was carried out according to the method of Marvell, Stephenson, and Ong (59). Treatment of the alcohol (VI) with phosphorus tribromide as described by Smith and Swenson (70) yielded 2-bromopent-3-yne (VII). The key step in the scheme is the heterogeneous C-alkylation procedure of Kornblum and Lurie (49) in which the alkylation occurs exclusively at the ortho rather than at the para position. Heterogeneous alkylation of sodium phenoxide with 2-bromopent-3-yne (VII) proceeded smoothly to give good yields of the 2-(o-hydroxyphenyl)-pent-3-yne (VIII). Although no infrared band at  $2250\text{ cm}^{-1}$  (triple bond) was observed, the assignment of structure for VIII is supported by the elemental analysis, subsequent reduction over Lindlar catalyst to the corresponding cis-phenol (I), and by the infrared bands at  $3475\text{ cm}^{-1}$  (hydroxyl group) and  $747\text{ cm}^{-1}$  (mono-ortho substitution). The cis-2-(o-hydroxyphenyl)pent-3-ene (I) was obtained by stereospecific reduction of the acetylenic compound (VIII) using Lindlar catalyst poisoned with synthetic quinoline. Introduction of the cis double bond in the last step of the synthetic scheme minimizes the possibility of cis to trans isomerization. Support for the assignment of structure I is obtained by infrared bands at  $3460\text{ cm}^{-1}$  (hydroxyl),  $750\text{ cm}^{-1}$  (mono-ortho substitution), and  $705\text{ cm}^{-1}$  (cis double bond). Furthermore, ultraviolet and nuclear magnetic resonance (n. m. r.) spectra are in agreement with structure I.

## Degree of Stereospecificity

Rearrangement of cis-2-(o-hydroxyphenyl)pent-3-ene (I) in  $D_2O$ . The degree of stereospecificity of the abnormal Claisen rearrangement of I was determined as follows. Four samples of the cis-phenol (I), each in a ten fold weight excess of deuterium oxide, were rearranged at 205°. The resulting mixtures were separated by preparative gas phase chromatography (g. p. c.) and the n. m. r. spectrum of the deuterated trans-phenol (IV) from each sample was determined (Figure 5). The n. m. r. spectra of the deuterated trans-phenols (IV) were notably different from the spectrum for trans-2-(o-hydroxyphenyl)pent-3-ene (IX) (Figure 6). The spectra of IV and IX show six types of protons: non-allylic methyl, allylic methyl, benzylic, hydroxyl, olefinic, and aromatic. The data in Table 6 show the relative integration values for these types of protons in the deuterated (IV) and undeuterated (IX) trans-phenols. From the data (Table 6) it is evident that the deuterated trans-phenols (IV) have incorporated one deuterium atom in the olefinic position. The splitting pattern of the allylic methyl group confirms that the olefinic proton adjacent to this methyl group has been replaced by deuterium. Thus, the n. m. r. spectra of the allylic methyl group has been transformed from a doublet in IX (Figure 6) to a singlet in IV (Figure 5).

Incorporation of deuterium into the aromatic ring is also



Table 6. N. M. R. integrations of trans-phenols.

Compound	Non-allylic methyl	Allylic methyl	Benzylic	Hydroxyl	Olefinic	Aromatic
IX	3.1	3.0	1.0	-	1.9	5.1*
IV, 0.7 half lives	2.9	2.9	1.0	-	1.0	3.5*
IV, 2.0 half lives	2.7	3.0	1.0	1.0	1.0	2.0
IV, 3.6 half lives	2.3	2.9	1.0	-	1.0	3.1*
IV, 4.8 half lives	1.9	2.5	0.9	-	1.0	2.8*

\* Contains hydroxyl proton

Table 7. N. M. R. integrations of cis-phenols.

Compound	Non-allylic methyl	Allylic methyl	Benzylic	Hydroxyl	Olefinic	Aromatic
I	3.3	2.8	.9	.9	1.9	4.0
0.7 half lives	2.9	3.0	1.0	-	1.9	3.5*
2.0 half lives	3.0	2.8	.9	1.0	1.6	2.0
3.6 half lives	2.8	2.8	.9	-	1.4	2.0
4.8 half lives	2.4	2.6	.9	-	1.3	2.7*

\* Contains hydroxyl proton

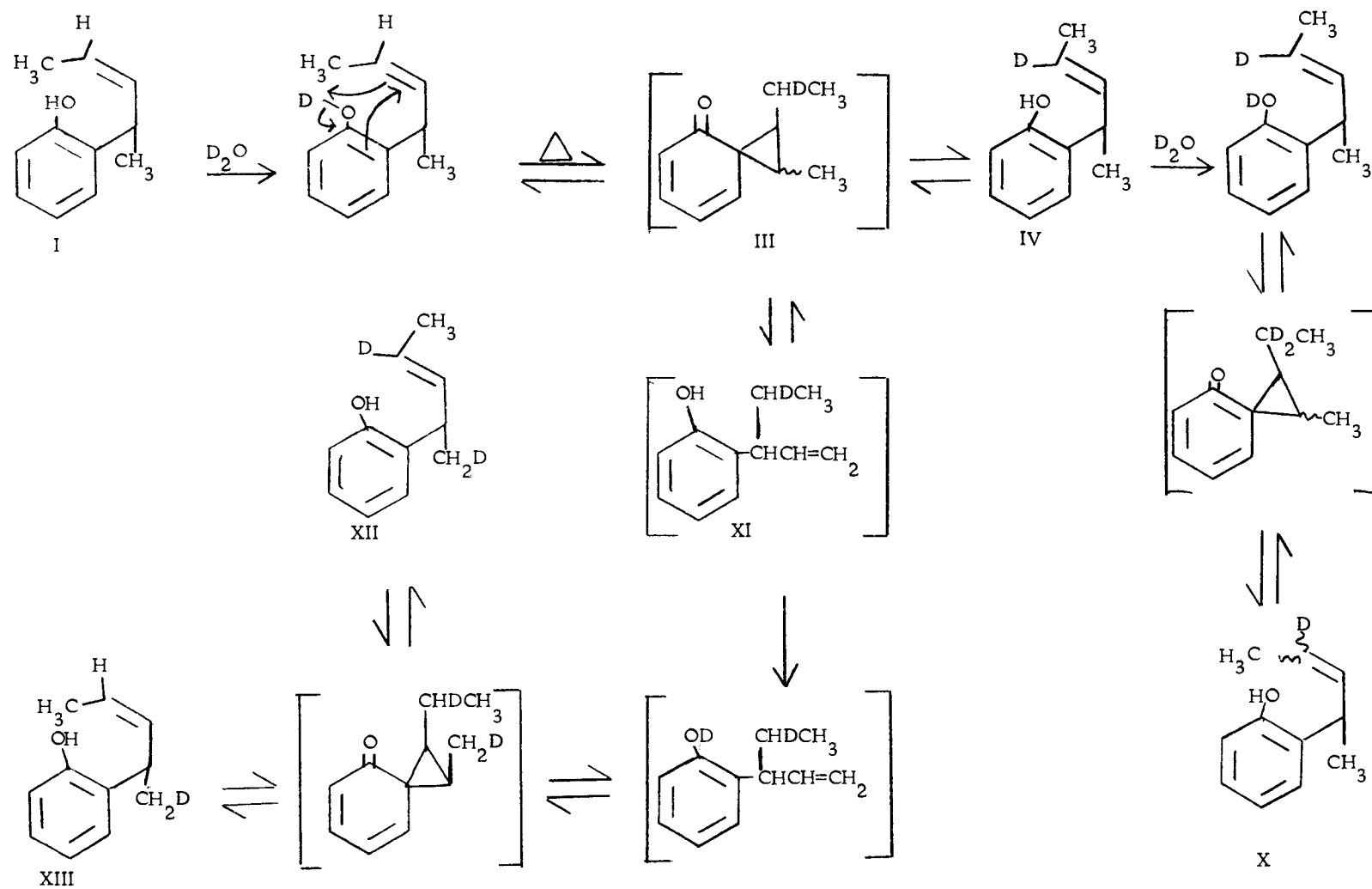
indicated from the data in Table 6. This exchange of deuterium for hydrogen is expected at the ortho and para positions of the phenol due to the activation of these positions by the hydroxyl group. However, the notable incorporation of deuterium into the non-allylic methyl group of IV is not expected and deserves some comment (vide infra).

The cis phenol was also isolated (g. p. c. ) from the above rearrangements and examined by n. m. r. The data in Table 7 indicates that partial deuteration of the olefinic position has occurred in the recovered cis phenol. This slow olefinic deuterium incorporation of the cis-phenol can be explained by an equilibrium between the cis- and trans-phenols. Thus, further reaction of the deuterated trans-phenol (IV) in the presence of  $D_2O$  results in olefinic deuterium incorporation to yield X as shown by Scheme IV.

The existence of an equilibrium between cis- (I) and trans-phenols (IX) was confirmed by heating of the trans-phenol (IX) in water at  $210 \pm 5^\circ$ . Subsequent analysis (g. p. c. ) showed that this sample reached the same equilibrium (22% I and 78% IX) as found for heating of the cis-phenol in deuterium oxide at  $205^\circ$ .

The observed incorporation of deuterium in the non-allylic methyl group of the deuterated trans-phenol (IV) (Table 6) is now also confirmed in the deuterated cis-phenol (Table 7). This incorporation of deuterium can be explained by considering an alternative reaction pathway that is available to the spiro-dienone intermediate

Scheme IV. Proposed Mechanism of Deuterium Incorporation



(III). In Scheme IV there are three reaction pathways available to III. Aromatization requires the cleavage of either one of two cyclopropyl bonds. Cleavage of one of the bonds yields either the reactant or the product (IV). Cleavage of the alternative cyclopropyl bond during aromatization yields compound XI. Subsequent rearrangement of XI yields the cis- and trans-phenols (XIII and XII) with deuterium in the non-allylic methyl group. Previous studies (5) have shown that the non-deuterated analog of compound XI is not stable under the present reaction conditions, but is rapidly converted to 2-(o-hydroxyphenyl)pent-3-ene. In agreement with this finding infrared studies on the product mixtures of the rearrangement failed to detect the presence of a vinyl group at  $905-915\text{ cm}^{-1}$  and  $985-995\text{ cm}^{-1}$ . Even though XI cannot be detected under the reaction conditions, this compound can be an intermediate in the reaction and adequately explains the deuterium incorporation of the non-allylic methyl group.

The stereospecificity of the abnormal Claisen rearrangement has now been established and is in complete agreement with the postulated spiro-dienone intermediate. Although it has been necessary to expand the original mechanism for this reaction, the observed stereospecificity is adequately explained by Scheme III.

Kinetics of the Rearrangement of cis-2-(o-hydroxyphenyl)pent-3-ene in D<sub>2</sub>O. A second method of substantiating the stereospecificity

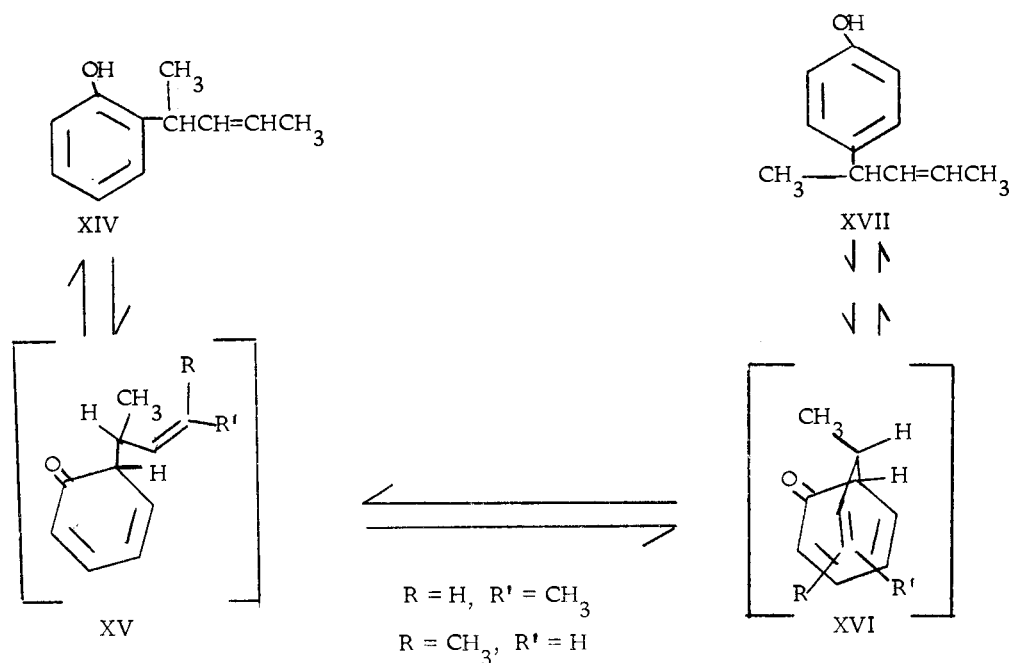
of the reaction is by comparison of the rate of cis to trans isomerization with the rate of olefinic deuterium incorporation for the cis-phenol (I). The rearrangement was carried out at 205° with samples of I in a ten fold weight excess of deuterium oxide. Each of the rearranged samples was measured for the extent of cis to trans isomerization (g. p. c. ) and for the extent of olefinic deuterium incorporation (n. m. r. ).

The accuracy of the g. p. c. analytical method was illustrated by examination of a mixture of the cis- (34%) and trans- (66%) phenols (I and IX). Analysis of this synthetic mixture yielded 36% I and 64% IX. Also, pure samples of I and IX were shown to undergo no detectable isomerization during the analysis. The experimental data (Table 13) confirm that the reaction reaches an equilibrium (vide supra). The first order kinetic plot (Figure 7) and the equilibrium constant ( $K = k_1/k_{-1}$ ) for the reaction ( $\text{cis} \xrightleftharpoons[k_{-1}]{k_1} \text{trans}$ ) allowed calculation (30) of the rate constants shown in Table 14. G.p.c. analysis of the kinetic samples also showed that competitive secondary reactions were occurring during the rearrangement. The infinity sample (8 half lives) was shown to be a mixture of the following: 1% of a mixture of 2-ethyl-3-methylcoumaran (XX) and 3-ethyl-2-methylcoumaran (XXI); 11% of 2-(p-hydroxyphenyl)pent-3-ene (XVII); 19% of the deuterated cis-phenol; and 69% of the deuterated trans-phenol (IV). Since the side products were formed quite slowly in comparison

to the rate of the observed rearrangement, they do not appreciably affect the observed rate constants.

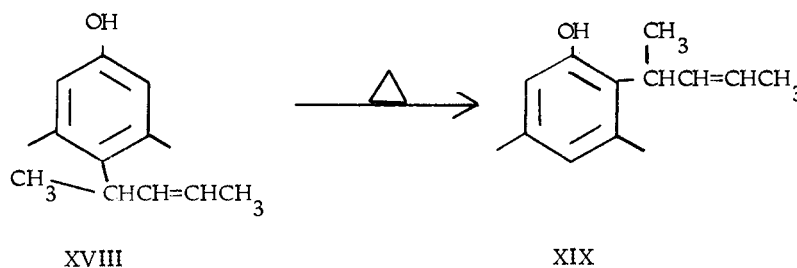
The para-phenol XVII was identified by g. p. c. comparison with an authentic sample, and by its infrared and n. m. r. spectra. Formation of XVII during the rearrangement can be rationalized by Scheme V which is equivalent to the mechanism previously proposed (68) by Schmid for the para-Claisen rearrangement.

Scheme V. Formation of 2-(p-hydroxyphenyl)pent-3-ene



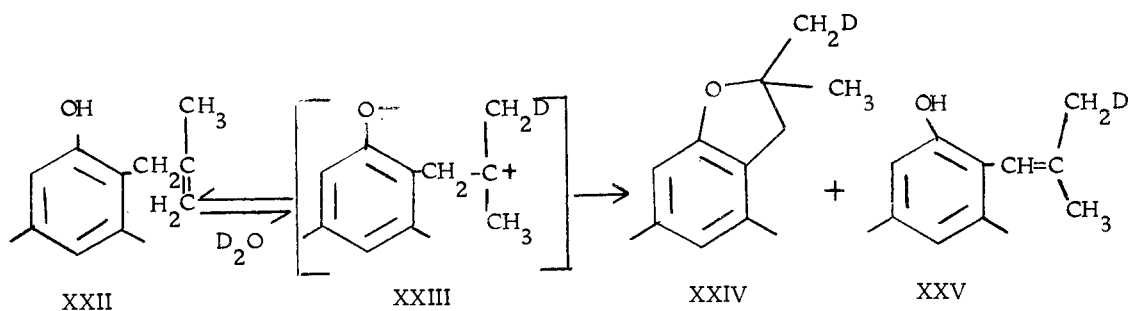
Ketonization of the ortho-phenol XIV yields a cyclohexadienone intermediate which can exist in two conformations (XV and XVI). Reaction of conformation XVI via a Cope rearrangement subsequently yields the para-phenol XVII. The rate determining step for this reaction is the ketonization of the ortho-phenol (XIV). The reaction

is probably an equilibrium since the para-phenol XVIII has previously been shown (68) to rearrange to the ortho-phenol XIX at 230°.



The mixture of coumarans (XX and XXI) was collected via preparative g. p. c. as a single peak and subsequently identified by its infrared and n. m. r. spectra. The infrared spectrum of this mixture exhibits bands at  $1228\text{ cm}^{-1}$  (aryl ether) and  $744\text{ cm}^{-1}$  (mono-ortho substitution). The  $1228\text{ cm}^{-1}$  band is in agreement with infrared bands reported to be characteristic of the coumarans (50). The n. m. r. spectrum of the coumarans (Figure 8) is satisfactorily interpreted as a 50-50 mixture of XX and XXI. Attempts to separate this mixture on several different g. p. c. columns were unsuccessful. The yield of the coumarans from the rearrangement can be increased by prolonged heating at relatively higher temperatures. The results of heating the trans-phenol (IX) in water at  $218 \pm 8^\circ$  for 161 hours are shown in Table 8.

Schmid and coworkers (35) have reported the isolation of a coumaran (XXIV) from the abnormal Claisen rearrangement of XXII. In addition to XXIV the propenyl derivative XXV was also isolated by



these workers. The appearance of XXIV and XXV as products led these workers to postulate the formation of a carbonium ion intermediate (XXIII) which competes with the abnormal Claisen rearrangement.

Table 8. Composition of rearrangement product.

Compound	Percent composition (g. p. c.)
2-( <u>o</u> -hydroxyphenyl)pent-3-ene	49
2-( <u>p</u> -hydroxyphenyl)pent-3-ene	34
coumarans XX and XXI	12
phenol	3
unidentified	2

The present study differs from the work of Schmid (35) in two important respects. No propenyl derivatives could be detected (infrared, n. m. r., or g. p. c.), and two (as opposed to one) coumarans (XX and XXI) were obtained. These results indicated that the mechanism of formation of the coumarans is not the same as that previously suggested by Schmid.

If the reaction of I or IX in water does give a 50-50 mixture of





a gradual decrease in the rate constant as the reaction progresses. This decrease in rate is attributed to the competitive secondary reaction which yields the para-phenol XVII. The proposed mechanism of formation of XVII (Scheme V) predicts that no olefinic deuterium exists in this compound. Correction of the data in Table 15 for this infinity point yields a linear first order kinetic plot (Figure 9) with  $k = 0.27 \times 10^{-5} \text{sec}^{-1}$ . This rate is equal to the rate,  $k_1 = 0.27 \times 10^{-5} \text{sec}^{-1}$ , of cis to trans isomerization ( $\text{cis} \xrightleftharpoons[k_{-1}]{k_1} \text{trans}$ ). The identical values obtained for these rate constants is in agreement with a completely stereospecific reaction as established previously.

Kinetics of the Rearrangement of cis-2-(o-hydroxyphenyl)pent-3-ene in H<sub>2</sub>O. Activation energy and entropy values for the abnormal Claisen rearrangement have not previously been reported. Activation parameters for the rearrangement of I are readily available from the rates of cis to trans isomerization. The rate of isomerization of I in water was therefore determined at two temperatures. The data in Tables 16 and 17 yield first order kinetic plots (Figures 10 and 11) for this reaction. Rate constants were calculated for the equilibrium ( $\text{cis} \xrightleftharpoons[k_{-1}]{k_1} \text{trans}$ ) in the usual manner (30) and are shown in Table 14. Calculation of the activation parameters yields  $E_a = 33 \text{ kcal/mole}$  and  $\Delta S^\ddagger = -13 \text{ e. u.}$  for cis  $\rightarrow$  trans and  $E_a = 35 \text{ kcal/mole}$  and  $\Delta S^\ddagger = -12 \text{ e. u.}$  for trans  $\rightarrow$  cis.

The previously obtained rates (Table 14) for the rearrangement of I permit calculation of the deuterium isotope effect for this reaction. At 205°  $k_H/k_D$  was 2.7. The maximum theoretical (40) isotope effect is 4.6 at this temperature. The closeness of these values indicates a primary isotope effect for the reaction. This conclusion is in agreement with the proposed mechanism (Scheme III) and indicates that the formation of the spiro-dienone is the rate determining step. However, because of the polarity of bonds to oxygen, large isotope effects can occur even when the proton is not directly transferred (30). The observed kinetic isotope effect must therefore be used with care as a tool for diagnosis of mechanism. Thus, this evidence is indicative, but not compelling.

### General Conclusions

Deuterium labeling studies have previously been carried out on the abnormal Claisen rearrangement by two different groups. The first study was by Schmid and coworkers (35) and dealt mainly with the rearrangement of 3-(2'-hydroxy-5'-methyl-phenyl)-1-butene. The second study was carried out by Roberts and coworkers (66) and pertained to the rearrangement of (α-methylallyl)acetophenone. The results reported in this thesis are in agreement with the previous observation that deuterium is transferred exclusively to the α-methyl and γ-olefinic positions, and that this deuterium

incorporation is much faster in the olefinic than in the methyl position.

Experimental support for the proposed mechanism (Scheme I) has been obtained. The complete stereospecificity of the reaction was shown by two methods and is in agreement with the spiro-dienone intermediate. First order kinetics were demonstrated for the reaction and activation parameters were obtained. The entropy of activation ( $\Delta S^\ddagger$  - 12 e. u. ) fits quite reasonably with the expectations of theory and denotes a higher degree of order in the transition state than in the reactants. The observed deuterium isotope effect supports the formation of the spiro-dienone intermediate as the rate determining step.

## EXPERIMENTAL

Valence Isomerism of 2, 4, 6-Octatrienescis-2, cis-4-Octadien-7-ol

This alcohol was prepared according to the method of Caple (8). The hydrogenation was carried out at atmospheric pressure on 4 g portions of cis-2-octen-4-yn-7-ol with 10% by weight of Lindlar catalyst in 50 ml of petroleum ether containing two drops of synthetic quinoline. The hydrogenation was stopped after the absorption of one equivalent of hydrogen and the catalyst removed by filtration. The products were combined, the solvent removed under vacuum and the residue distilled, b. p. 50-52° (0.7 mm).  $n_{D}^{23.4}$  1.4832. Yield, 55.7 g (94%). Infrared peaks: 3333, 3040, 3012, 2985, 2959, 2924, 2865, 1597, 1447, 1370, 1111, 1075, 940, 841, and 698  $\text{cm}^{-1}$ .

cis-2, cis-4-Octadien-7-ol tosylate

The tosylate was prepared under a nitrogen atmosphere according to the method of Caple (8) by addition of 27.2 g (0.22 mole) of the corresponding alcohol to 42.8 g (0.22 mole) of p-toluenesulfonyl chloride dissolved in 28 ml of anhydrous pyridine at 0°. The solution was stirred for 24 hours and treated with 80 ml of water. The product was taken up in ether and washed successively with water, dilute

phosphoric acid, dilute sodium bicarbonate, and finally twice more with water. After the solution had been dried over anhydrous sodium sulfate the solvent was removed under vacuum. The yield of the crude tosylate was 61.3 g (100%). Infrared peaks: 3058, 3040, 3021, 2976, 2924, 2865, 1590, 1350, 1185, 1170, 1090, 900, 812, 704, and  $662\text{ cm}^{-1}$ .

cis-2, cis-4, trans-6-Octatriene and cis-2, cis-4, cis-6-Octatriene

The mixture of geometric isomers was prepared according to the method of Caple (8). A suspension of 21.8 g (0.19 mole) of potassium t-butoxide in 50 ml anhydrous dimethylsulfoxide was added dropwise under a nitrogen atmosphere to 60.5 g (0.22 mole) of the corresponding tosylate in 60 ml of anhydrous dimethylsulfoxide at  $0^{\circ}$ . After having been stirred for an additional 15 minutes the solution was treated with 100 ml of water. The product was taken up in pentane, washed several times with water, and dried over anhydrous sodium sulfate. The solvent was removed under vacuum and the product distilled, b. p.  $51-54^{\circ}$  (20 mm). Yield 11.5 g (55%). The mixture was shown by gas chromatography (Perkin Elmer model 154C;  $1/8'' \times 14'$  10% carbowax 20-M on firebrick column) to consist of approximately 57% cis-2, cis-4, trans-6-octatriene, 14% cis-2, cis-4, cis-6-octatriene, 10% cis-2, cis-6-octadien-4-yne, 14% cis-2, trans-6-octadien-4-yne, and 5% unidentified components. Infrared

peaks: 3021, 2985, 2959, 2933, 2907, 2849, 1631, 1447, 1429, 978, 959, 929, 823, and  $700\text{ cm}^{-1}$ .

4, 5-d<sub>2</sub>-cis-2, cis-4-Octadien-7-ol

This compound was prepared according to the method of Caple (8) by deuteration of cis-2-octen-4-yn-7-ol at atmospheric pressure. The deuteration was carried out on 4 g portions of the acetylenic compound with 40% by weight of Lindlar catalyst in 50 ml of pentane containing one drop of synthetic quinoline. The deuteration was stopped after the absorption of one equivalent of deuterium and the catalyst was removed by filtration. The products were combined, the pentane removed under vacuum and the residue distilled, b. p.  $78-81^{\circ}$  (2.5 mm). Yield, 11.8 g (84%). Infrared peaks: 3333, 3021, 2959, 2915, 2252, 1439, 1366, 1114, 1073, 936, and  $721\text{ cm}^{-1}$ .

4, 5-d<sub>2</sub>-cis-2, cis-4-Octadien-7-ol tosylate

The tosylate was prepared under a nitrogen atmosphere according to the method of Caple (8) by the dropwise addition of 11.8 g (0.09 mole) of the corresponding alcohol into a solution of 18.1 g (0.09 mole) of p-toluenesulfonyl chloride in 15 ml anhydrous pyridine at  $0^{\circ}$ . The solution was stirred for an additional 28 hours and then treated with 40 ml of water. The product was taken up in ether and washed successively with water, dilute phosphoric acid, dilute

sodium bicarbonate, and finally twice more with water. After the solution had been dried over anhydrous sodium sulfate, the solvent was removed under vacuum. The yield of the crude tosylate was 25.9 g (100%). Infrared peaks: 3021, 2976, 2924, 2865, 2252, 1585, 1364, 1183, 1170, 915, 888, 812, 703, and 662  $\text{cm}^{-1}$ .

4, 5-d<sub>2</sub>-cis-2, cis-4, trans-6-Octatriene and 4, 5-d<sub>2</sub>-cis-2, cis-4, cis-6-Octatriene

The mixture of geometric isomers was prepared under a nitrogen atmosphere according to the method of Caple (8) by the dropwise addition of a suspension of 10.0 g (0.09 mole) of potassium t-butoxide in 25 ml of anhydrous dimethylsulfoxide to 25.9 g (0.09 mole) of the crude tosylate dissolved in 30 ml anhydrous dimethylsulfoxide at 0°. After having been stirred for an additional 20 minutes the solution was treated with 50 ml of water. The product was taken up in pentane, washed several times with water, and dried over anhydrous sodium sulfate. The pentane was removed under vacuum and the product distilled, b. p. 73-80° (40 mm). Yield, 6.8 g (69%). The mixture was shown by gas chromatography (Aerograph Auto-prep model A-700; 1/4" X 15' 20% carbowax 20-M on firebrick column) to consist of approximately 58% 4, 5-d<sub>2</sub>-cis-2, cis-4, trans-6-octatriene, 10% 4, 5-d<sub>2</sub>-cis-2, cis-4, cis-6-octatriene, 18% cis-2, cis-6-octadien-4-yne, 8% cis-2, trans-6-octadien-4-yne, and 6% unidentified



components. Infrared peaks: 3021, 2994, 2950, 2924, 2907, 2865, 2849, 2257, 1435, 955, 925, and  $717\text{ cm}^{-1}$ .

### 1-Pentyn-3-ene

This compound was prepared according to the method of Eglinton and Whiting (21). In a 200 ml three-necked flask equipped with nitrogen inlet tube, magnetic stirring bar, dropping funnel, and an exit tube leading to two consecutive dry ice-acetone traps were placed 66 ml of water, 15.8 g (0.28 mole) of potassium hydroxide and 1/8 teaspoon of "All" detergent. To the boiling aqueous solution was added dropwise 56.4 g (0.25 mole) of the p-toluenesulfonate of 1-pentyn-4-ol. The contents of the dry ice-acetone traps were then warmed, the layers separated, and the organic product dried over anhydrous sodium sulfate. The mixture of geometric isomers has been previously separated and characterized in this laboratory (8). However, the crude mixture was used directly in the preparation of 2-octen-4-yn-7-ol.

### trans-2-Octen-4-yn-7-ol and cis-2-Octen-4-yn-7-ol

The mixture of alcohols was prepared according to the method of Caple (8) from lithamide, 1-pentyn-3-ene and propylene oxide. In a two-liter three-necked round-bottomed flask equipped with mechanical stirrer, dropping funnel and a reflux condenser protected

by a soda lime drying tube were placed 500 ml of liquid ammonia and a pinch of ferric nitrate. To this solution 1.75 g (0.25 gram atom) of lithium was slowly added and the mixture stirred for one hour. The 1-pentyn-3-ene was then added dropwise and the solution stirred for one and one-half hours, whereupon 15.5 g (0.27 mole) of propylene oxide was added and the mixture stirred for an additional 24 hours. The liquid ammonia was then allowed to evaporate. A mixture of 50 ml of water and 125 ml of ethyl ether was added to the solution with mixing. The layers were separated and the organic portion washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. Distillation gave 8.8 g (28% yield based upon the p-toluenesulfonate of 1-pentyn-4-ol) of the mixture of alcohols, b. p. 82-95° (3 mm).

trans-2,cis-4-Octadien-7-ol and cis-2,cis-4-Octadien-7-ol

The hydrogenation was carried out according to the method of Caple (8) on 4 g portions of the mixture of alcohols using 10% by weight Lindlar catalyst, a few drops of synthetic quinoline and 50 ml of petroleum ether as solvent. After 1.2 equivalents of hydrogen had been absorbed, the hydrogenation was stopped and the catalyst removed by filtration. The products were combined, the petroleum ether removed under vacuum and the residue distilled, b. p. 50-52° (0.7mm). Yield, 8.3 g (99%). Infrared peaks: 3344, 3012, 2959,

2933, 1447, 1111, 1074, 977, 942, and  $694\text{ cm}^{-1}$ .

trans-2,cis-4-Octadien-7-ol and cis-2,cis-4-Octadien-7-ol  
tosylates

The mixture of tosylates was prepared according to the method of Caple (8) by addition of 8.3 g (0.06 mole) of the corresponding mixture of alcohols to 12.6 g (0.07 mole) of p-toluenesulfonyl chloride in 20 ml of anhydrous pyridine at  $0^\circ$  under a nitrogen atmosphere. The mixture was stirred for 24 hours and hydrolyzed with 35 ml of water. The product was taken up in ether and washed successively with water, dilute phosphoric acid, dilute sodium bicarbonate, and finally twice more with water. After the solution had been dried over anhydrous potassium carbonate the ether was removed under vacuum. The yield of the crude tosylate was 18.4 g (100%), and this was used directly in the preparation of the 2,4,6-octatriene mixture.

trans-2,cis-4,trans-6-Octatriene, trans-2,cis-4,cis-6-  
Octatriene, and cis-2,cis-4,cis-6-Octatriene

The geometric mixture of 2,4,6-octatrienes was prepared according to the method of Caple (8) by adding dropwise a suspension of 7.30 g (0.06 mole) of potassium t-butoxide in 20 ml of anhydrous dimethylsulfoxide to 18.4 g (0.07 mole) of the corresponding tosylate in 25 ml of anhydrous dimethylsulfoxide at  $0^\circ$ . After having been

stirred under nitrogen for an additional 15 minutes, the solution was treated with 40 ml of water. The product was taken up in pentane, washed several times with water, and dried over anhydrous sodium sulfate. The solvent was removed under vacuum and the product distilled, b. p. 51-54° (20 mm). Yield, 7.4 g (69%). The mixture was shown by gas chromatography (Aerograph Auto-prep model A-700; 1/4" X 15' 20% carbowax 20-M on firebrick column) to consist of approximately 27% trans-2, cis-4, trans-6-octatriene, 44% trans-2, cis-4, cis-6-octatriene, 10% cis-2, cis-4, cis-6-octatriene, 6% cis-2, cis-6-octadien-4-yne, 5% cis-2, cis-6-octadien-4-yne, and 8% unidentified components. Infrared peaks: 3030, 3003, 2959, 2933, 2924, 2857, 1637, 1447, 1431, 1372, 979, 960, 934, 825, and 701  $\text{cm}^{-1}$ .

#### Separation of 2,4,6-Octatriene Mixtures

The synthetic mixtures were separated into their respective components by preparative gas chromatography. An Aerograph Auto-prep model A-700 equipped with a 1/4" X 15' 20% carbowax 20-M on 30-50 mesh firebrick column was used for this separation. The u. v., infrared and n. m. r. spectra of the pure compounds are listed in Table 2. These compounds have been completely characterized in this laboratory (8).

## Kinetic Studies

All kinetic studies were carried out on 0.66 M solutions of the compound in question dissolved in cyclohexane with a known amount of standard substance added. These samples were placed in Pyrex glass bombs, sealed under nitrogen, and subjected to the temperature necessary to produce rearrangement. At arbitrary times the samples were withdrawn, cooled, and examined by gas phase chromatography to determine the progress of the reaction.

### Abnormal Claisen Rearrangement

#### 2-Hydroxypent-3-yne

The alcohol was prepared from 72 g (3.0 gram atoms) of magnesium turnings, 327 g (3.0 moles) of ethyl bromide, approximately 180 ml (3.0 moles) of methylacetylene and 180 ml (3.0 moles) of acetaldehyde according to the method of Ong (59). Distillation of the product under vacuum yielded 120 g (48%) of a colorless liquid. Purification was accomplished by redistilling through a 12" column packed with glass helices, b. p. 74-76° (65 mm),  $n_{D}^{23.5}$  1.4441. Reported: b. p. 61-61.5° (29 mm),  $n_{D}^{24}$  1.4445 (59). Infrared peaks: 3460, 2230, 1447, 1370, 1327, 1157, 1075, 1000, and 885  $\text{cm}^{-1}$ .

2-Bromopent-3-yne

The bromide was prepared from 30.0 g (0.36 mole) of 2-hydroxypent-3-yne, 10 ml of anhydrous pyridine and 45.0 g (0.17 mole) of phosphorous tribromide in 150 ml of anhydrous ether according to the method of Ong (59). Distillation through a glass helices packed 12" column yielded 33.2 g (63%) of a clear liquid, b. p. 83° (129 mm). Reported b. p. 49-49.5° (28 mm) (59). Infrared peaks: 2230, 1444, 1375, 1315, 1185, 1062, 1025, 955, and 718  $\text{cm}^{-1}$ .

2-(o-Hydroxyphenyl)pent-3-yne

This phenol was prepared from 25.2 g (0.22 mole) of anhydrous sodium phenoxide, and 33.2 g (0.23 mole) of 2-bromopent-3-yne in 435 ml of anhydrous toluene according to the method of Ong (59). Distillation yielded 22.7 g (65%) of colorless liquid, b. p. 79-81° (0.3 mm),  $n^{23.5}_D$  1.5428. Reported: b. p. 78-80° (0.3 mm),  $n^{23.5}_D$  1.5430 (59). Infrared peaks: 3475, 1595, 1485, 1450, 1340, 1325, 1270, 1215, 1085, 1036, 835, and 790  $\text{cm}^{-1}$ .

cis-2-(o-Hydroxyphenyl)pent-3-ene

This phenol was obtained by catalytic hydrogenation of 2-(o-hydroxyphenyl)pent-3-yne at atmospheric pressure. The

hydrogenation was carried out on 5-6 g portions of the acetylenic compound, 10-15% by weight Lindlar catalyst, and 50 ml of anhydrous ethyl acetate containing one drop of synthetic quinoline. The hydrogenation was stopped after the absorption of one equivalent of hydrogen and the catalyst removed by filtration. The solvent was removed under vacuum and the residue distilled, b. p. 56-60° (0.05 mm),  $n^{22}_D$  1.5336. Reported b. p. 63-65° (0.25 mm),  $n^{23.5}_D$  1.5347 (59). Infrared peaks: 3460, 1600, 1506, 1457, 1405, 1275, 1250, 930, 825, 750, and 705  $\text{cm}^{-1}$ . UV:  $\lambda_{\text{max}}$  280  $\text{m}\mu$  ( $\epsilon = 3,000$ ), 274  $\text{m}\mu$  ( $\epsilon = 3,410$ ). The n. m. r. spectrum showed a doublet centered at  $\delta = 1.30$  ppm with  $J = 7$  cps (3H), a doublet centered at  $\delta = 1.69$  ppm with  $J = 5$  cps (3H), a quintet centered at  $\delta = 3.97$  ppm with  $J = 7$  (1H), a singlet at  $\delta = 5.05$  ppm (1H), a multiplet centered at  $\delta = 5.50$  ppm (2H), and a multiplet centered at  $\delta = 6.85$  ppm (4H).

Anal: Calc. for  $\text{C}_{11}\text{H}_{14}\text{O}$ ; C, 81.44%; H, 8.69%

Found: C, 81.61%; H, 8.90%

#### trans-2-Bromopent-3-ene

The bromide was prepared from 4.9 g (0.06 mole) of 2-hydroxypent-3-ene, 2 ml of anhydrous pyridine and 2.1 ml of phosphorus tribromide according to the method of Ong (59). The product was purified by distillation through an alembic to yield 3.7 g (44%) of colorless liquid, bath temperature 88-91° (120 mm),  $n^{25}_D$  1.4729.

Reported: b. p. 65-66° (130 mm),  $n_D^{23}$  1.4721 (59). Infrared peaks: 1637, 1430, 1368, 1170, 1007, 965, and 730  $\text{cm}^{-1}$ .

trans-2-(p-Hydroxyphenyl)pent-3-ene

This phenol was prepared from 1.0 g (0.007 mole) of trans-2-bromopent-3-ene, and 0.8 g (0.007 mole) of sodium phenoxide in 6.4 ml of 40% aqueous ethanol according to the method of Schmid (6). The solvent was removed under vacuum and the residue analyzed by gas chromatography (Perkin Elmer model 154C equipped with 1/4" X 6' 15% ucon polar on firebrick column at 197°.

<u>Compound</u>	<u>Retention time</u>	<u>Exper. Comp.</u>	<u>Lit.(6) Comp.</u>
trans-2-phenoxy-pent-3-ene	1.9 min.	12%	19%
trans-2-(o-hydroxyphenyl)pent-3-ene	10.4 min.	45%	31%
trans-2-(p-hydroxyphenyl)pent-3-ene	21.4 min.	43%	50%

Yield, 69%. Reported yield, 48% (6).

Rearrangement of cis- or trans-2-(o-hydroxyphenyl)pent-3-ene in Water or Deuterium Oxide

The pure phenol was placed in Pyrex glass bombs with a ten-fold weight excess of distilled water or deuterium oxide. The bombs were flushed with nitrogen, sealed, and totally submerged in a thermostatically controlled silicone oil bath at the specified temperatures. The bombs were removed at various intervals of time,



cooled, and opened. The organic material was taken up in carbon disulfide and analyzed by gas chromatography (Aerograph Auto-prep model A-700 equipped with a 1/4" X 15' 4% FFAP on 45-60 mesh chromosorb G column) and n. m. r. (dimethylformamide external standard).

### 2-(p-Hydroxyphenyl)pent-3-ene

This compound was isolated by preparative g. p. c. from the rearrangement of trans-2-(o-hydroxyphenyl)pent-3-ene in water as previously described. Infrared peaks: 3340, 3030, 2965, 2925, 2865, 1610, 1597, 1510, 1448, 1372, 1225, 1171, 1010, 963 and 825  $\text{cm}^{-1}$ . The n. m. r. spectrum showed a doublet centered at  $\delta = 1.24$  ppm with  $J = 7$  cps (3H), a doublet centered at  $\delta = 1.65$  ppm with  $J = 5$  cps (3H), a quintet centered at  $\delta = 3.29$  ppm with  $J = 7$  (1H), a multiplet centered at  $\delta = 5.43$  ppm (2H) and a  $A_2B_2$  pattern centered at  $\delta = 6.83$  ppm (4H) which is superimposed on a singlet (1H).

### 2-Ethyl-3-methylcoumaran and 3-ethyl-2-methylcoumaran

This mixture of coumarans was isolated as a single peak by preparative g. p. c. from the rearrangement of trans-2-(o-hydroxyphenyl)pent-3-ene in water as previously described. Infrared peaks: 3030, 2965, 2920, 2860, 1228, 850, and 745  $\text{cm}^{-1}$ . The n. m. r. spectrum of the mixture is shown in Figure 8.

Table 9. Rearrangement of cis- and trans-2, cis-4, cis-6-octatriene. 178°

Sample No.	Time hrs.	<u>Triene</u> Toluene	$\log \frac{(\text{triene})_0}{(\text{triene})_t}$	$k \times 10^{-5} \text{sec}^{-1}$
0	0	2.26	0	-
1	1.50	2.17	.024	1.0
2	4.67	1.85	.116	1.6
3	7.42	1.61	.201	1.7
4	12.50	1.38	.302	1.5
5	23.50	1.00	.548	1.5
6	26.28	.85	.702	1.7
7	71.50	.50	$\infty$	-

Average  $k = 1.5 \times 10^{-5} \text{sec}^{-1}$

Table 10. Rearrangement of cis- and trans-2, cis-4, cis-6-octatriene. 196°

Sample No.	Time hrs.	$\frac{\text{Triene}}{\text{Toluene}}$	$\log \frac{(\text{triene})_o}{(\text{triene})_t}$
0	0	2.35	0
1	1.25	1.58	.235
2	2.50	1.29	.370
3	4.00	1.08	.505
4	5.25	.92	.645
5	6.50	.87	.700
6	7.78	.74	.887
7	59.25	.50	$\infty$

$$\text{Average } k = 6.4 \times 10^{-5} \text{ sec}^{-1}$$

Table 11. Rearrangement of trans-5, 6-dimethyl-1, 3-cyclohexadiene. 182°

Sample No.	Time hrs.	$\frac{\text{diene}}{\text{o-xylene}}$	$\log \frac{(\text{diene})_o}{(\text{diene})_t}$	$k \times 10^{-5} \text{ sec}^{-1}$
0	0	2.17	0	-
1	12.00	1.59	.136	.72
2	24.00	1.08	.304	.81
3	36.00	.73	.474	.84
4	48.00	.57	.582	.77
5	60.00	.43	.704	.75
6	72.00	.34	.806	.72

$$\text{Average } k = .8 \times 10^{-5} \text{ sec}^{-1}$$

Table 12. Rearrangement of trans-5, 6-dimethyl-1, 3-cyclohexadiene.  
200°.

Sample No.	Time hrs.	$\frac{\text{diene}}{\text{o-xylene}}$	$\log \frac{(\text{diene})_0}{(\text{diene})_t}$	$k \times 10^{-5} \text{ sec}^{-1}$
0	0	2.17	0	-
1	1.75	1.58	.139	5.1
2	4.00	1.25	.241	3.8
3	5.30	1.03	.325	3.8
4	7.25	.81	.428	3.7
5	9.25	.67	.511	3.5
6	12.33	.45	.684	3.5
7	26.00	0	$\infty$	-

Average  $k = 3.6 \times 10^{-5} \text{ sec}^{-1}$

Table 13. Isomerization of cis-2-(o-hydroxyphenyl)pent-3-ene in  $D_2O$  at  $205.0 \pm 0.2^\circ$ .

Sample No.	Time, hrs.	%Cis compd.	$\log \frac{C_0 - C_\infty}{C - C_\infty}$
1	12.0	86	0.087
2	24.0	79	0.137
3	36.0	69	0.221
4	48.0	63	0.280
5	60.0	58	0.337
6	84.0	50	0.446
7	96.0	45	0.531
8	132.0	39	0.663
9	144.0	34	0.814
10	168.0	32	0.893
11	194.4	28	1.115
12	231.5	25	1.416
13	266.2	23	1.893
14	306.0	22	$\infty$

Average  $k_1 = 0.27 \times 10^{-5} \text{ sec}^{-1}$

$k_{-1} = 0.08 \times 10^{-5} \text{ sec}^{-1}$

Table 14. Summary of experimental rates for cis-phenol  $\rightleftharpoons$  trans-phenol.

Rate Constant	Temperature	Process	Solvent
$k_1 = 0.27 \times 10^{-5} \text{ sec}^{-1}$	$205.0 \pm 0.2$	Isomerization	$\text{D}_2\text{O}$
$k_{-1} = 0.08 \times 10^{-5} \text{ sec}^{-1}$	$205.0 \pm 0.2$	Isomerization	$\text{D}_2\text{O}$
$k = 0.27 \times 10^{-5} \text{ sec}^{-1}$	$205.0 \pm 0.2$	Olefinic deuterium incorporation	$\text{D}_2\text{O}$
$k_1 = 0.76 \times 10^{-5} \text{ sec}^{-1}$	$204.7 \pm 0.3$	Isomerization	$\text{H}_2\text{O}$
$k_{-1} = 0.21 \times 10^{-5} \text{ sec}^{-1}$	$204.7 \pm 0.3$	Isomerization	$\text{H}_2\text{O}$
$k_1 = 3.3 \times 10^{-5} \text{ sec}^{-1}$	$226.3 \pm 0.3$	Isomerization	$\text{H}_2\text{O}$
$k_{-1} = 1.0 \times 10^{-5} \text{ sec}^{-1}$	$226.3 \pm 0.3$	Isomerization	$\text{H}_2\text{O}$

Table 15. Rate of olefinic deuterium incorporation of *cis*-2-(o-hydroxyphenyl)pent-3-ene at  $205.0 \pm 0.2^\circ$ .

Sample No.	Time, hrs.	Percent Incorporation of One Olefinic Deuterium	$\log \frac{C_0}{C}$	$k \times 10^{-5} \text{ sec}^{-1}$
1	12.0	11	.051	.27
2	24.0	21	.103	.27
3	36.0	32	.168	.30
4	48.0	34	.181	.24
5	60.0	39	.216	.23
6	84.0	48	.285	.22
7	96.0	62	.421	.28
8	132.0	65	.457	.22
9	144.0	67	.482	.21
10	168.0	67	.482	.18
11	194.4	74	.586	.19
12	231.5	83	.771	.21
13	266.2	87	.886	.22
14	306.0	91	1.046	.22

Average  $k = 0.23 \times 10^{-5} \text{ sec}^{-1}$

Table 16. Isomerization of cis-2-(o-hydroxyphenyl)pent-3-ene in  $H_2O$  at  $204.7 \pm 0.3^\circ$ .

Sample No.	Time, hrs.	%Cis compd.	$\log \frac{C_0 - C_\infty}{C - C_\infty}$
1	12.0	76	0.163
2	24.0	60	0.319
3	36.0	46	0.525
4	48.0	37	0.741
5	60.0	31	0.984
6	72.0	29	1.109
7	84.0	26	1.410
8	96.0	23	$\infty$

$$\text{Average } k_1 = 0.76 \times 10^{-5} \text{ sec}^{-1}$$

$$k_{-1} = 0.21 \times 10^{-5} \text{ sec}^{-1}$$

Table 17. Isomerization of cis-2-(o-hydroxyphenyl)pent-3-ene in  $H_2O$  at  $226.3 \pm 0.3^\circ$ .

Sample No.	Time, hrs.	%Cis compd.	$\log \frac{C_0 - C_\infty}{C - C_\infty}$
1	1.5	82	0.116
2	4.5	60	0.325
3	6.0	54	0.398
4	7.0	49	0.467
5	8.5	45	0.552
6	11.0	39	0.697
7	15.0	31	1.006
8	21.3	23	$\infty$

$$\text{Average } k_1 = 3.3 \times 10^{-5} \text{ sec}^{-1}$$

$$k_{-1} = 1.0 \times 10^{-5} \text{ sec}^{-1}$$



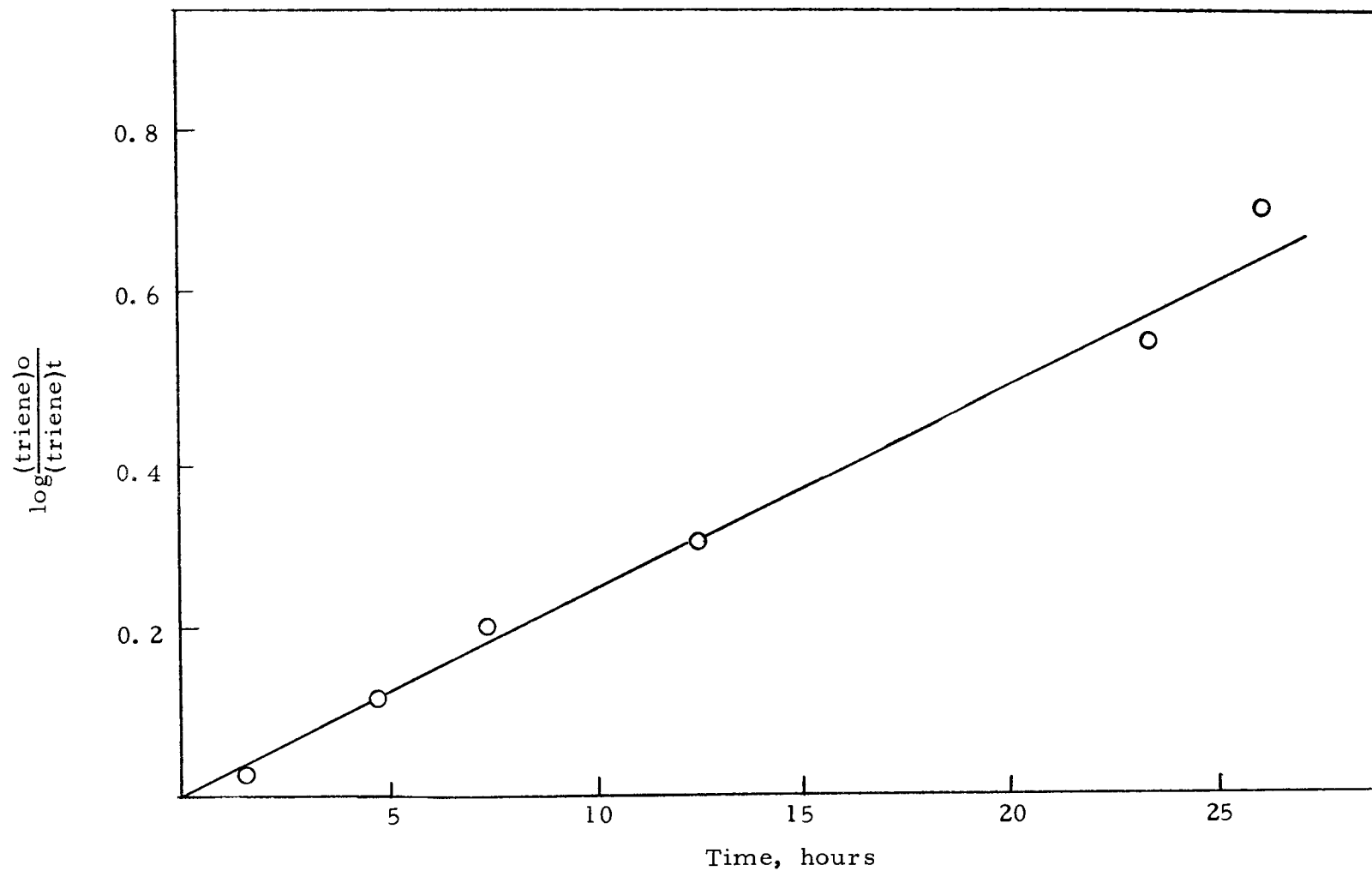


Figure 1.  $\text{Log} \frac{(\text{triene})_o}{(\text{triene})_t}$  versus time; 0.66 M (trans- and cis-2, cis-4, cis-6-octatriene) at 178°

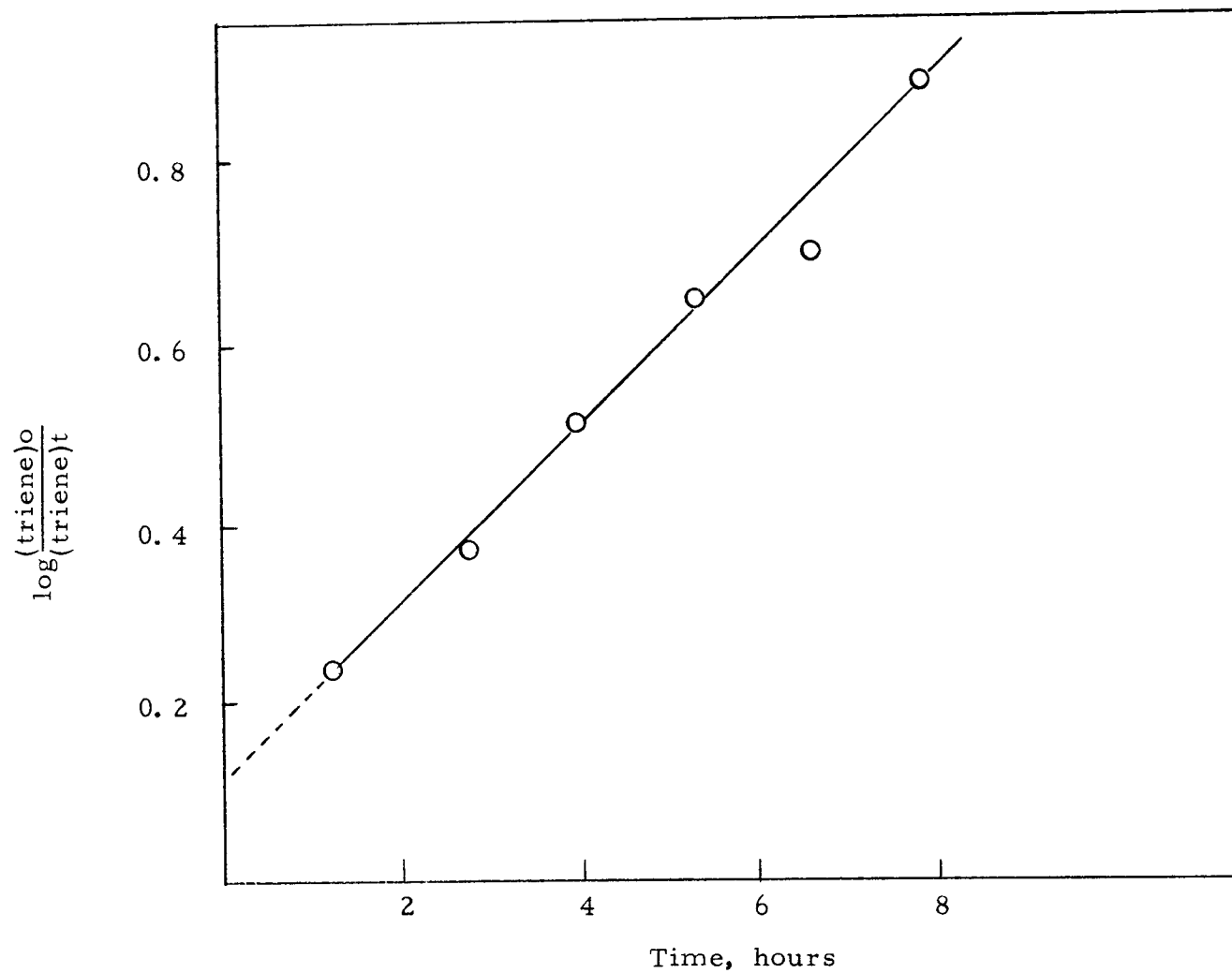


Figure 2.  $\text{Log}\frac{(\text{triene})_o}{(\text{triene})_t}$  versus time; 0.66M (trans- and cis-2, cis-4, cis-6-octatriene) at 196°

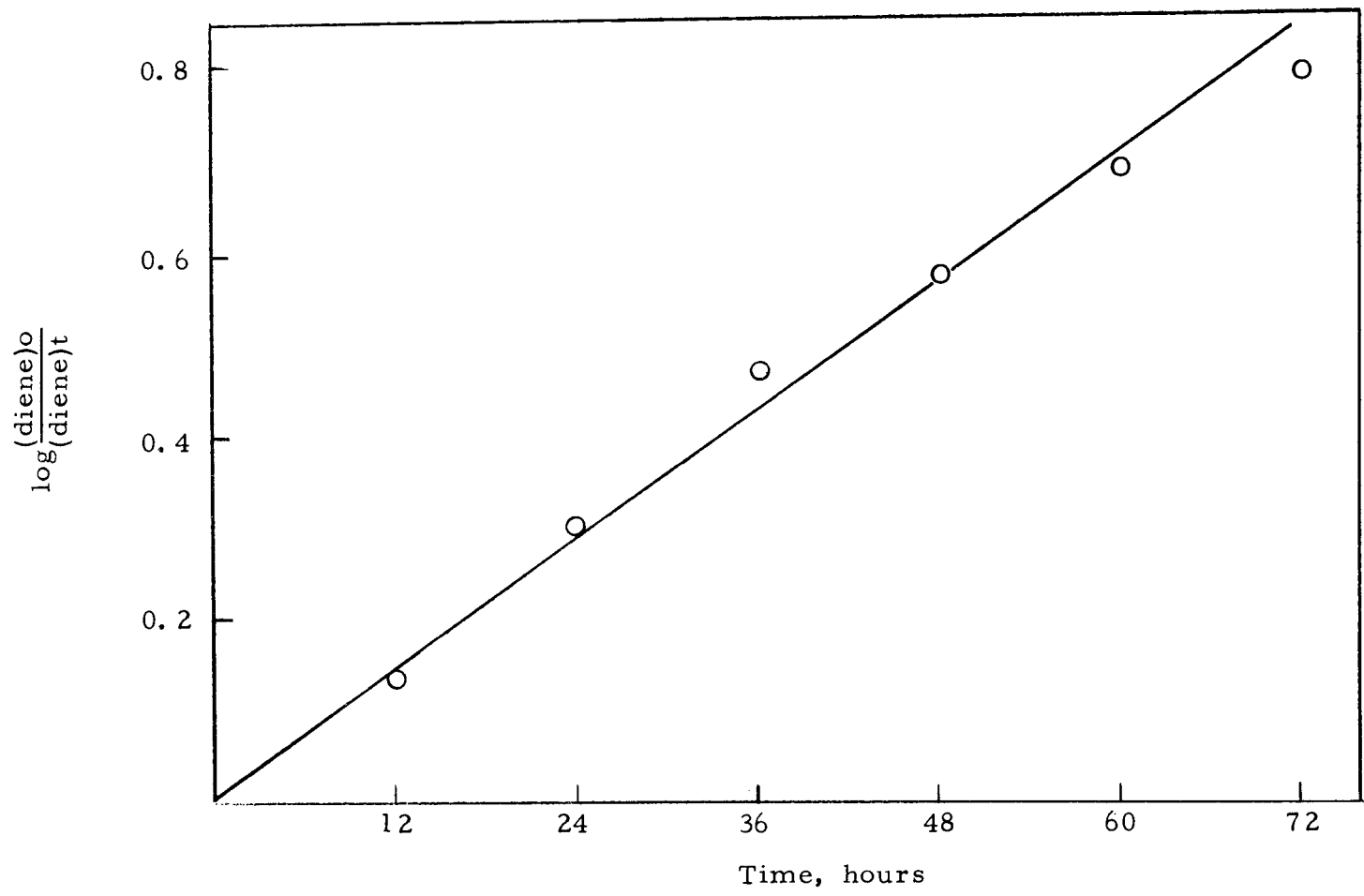


Figure 3.  $\text{Log} \frac{(\text{diene})_0}{(\text{diene})_t}$  versus time; 0.66 M trans-5,6-dimethyl-1,3-cyclohexadiene at 182°

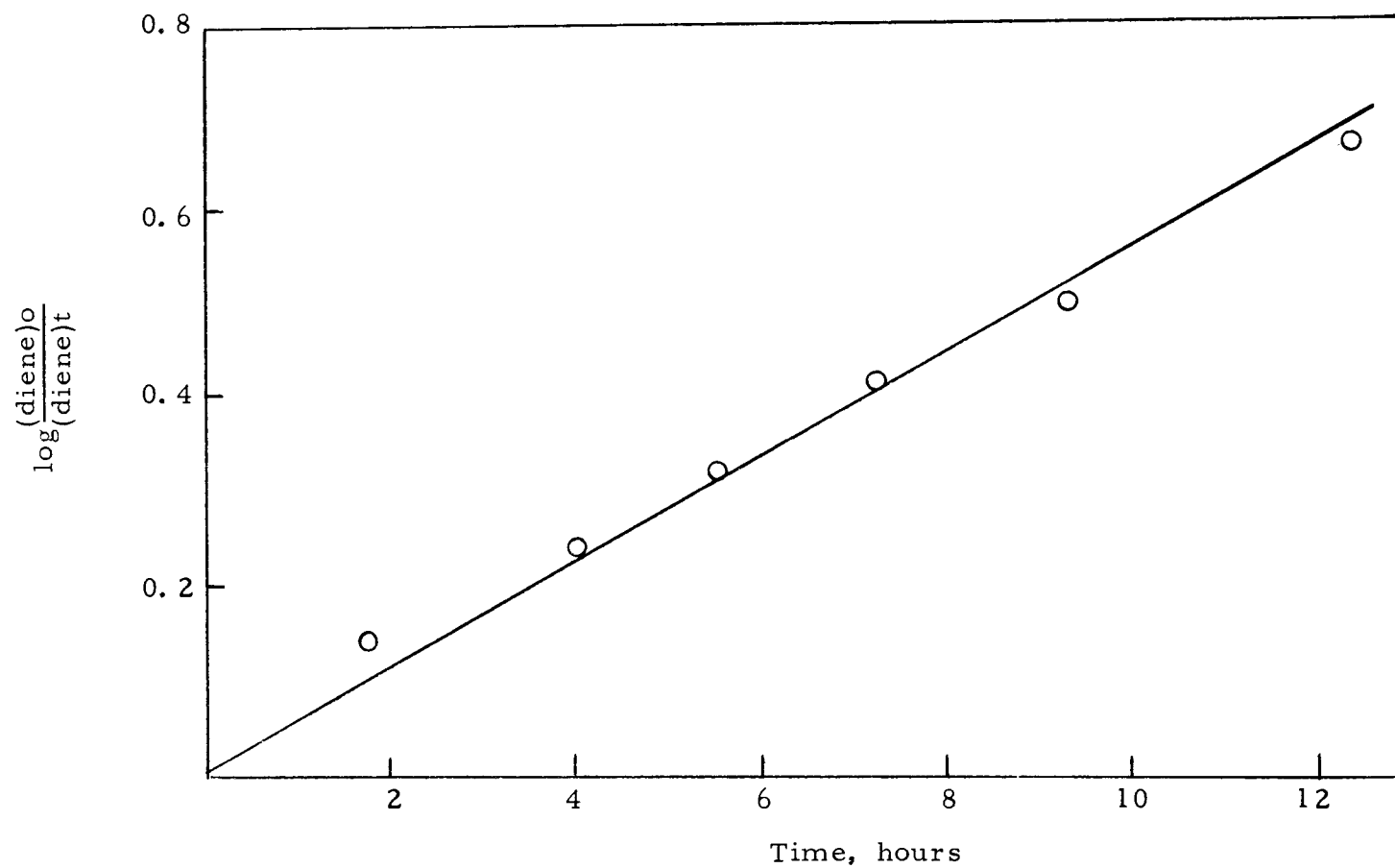


Figure 4.  $\text{Log} \frac{(\text{diene})_0}{(\text{diene})_t}$  versus time; 0.66 M trans-5,6-dimethyl-1,3-cyclohexadiene at 200°

Figure 5. N. M. R. of deuterated trans-2-(o-hydroxyphenyl)pent-3-ene

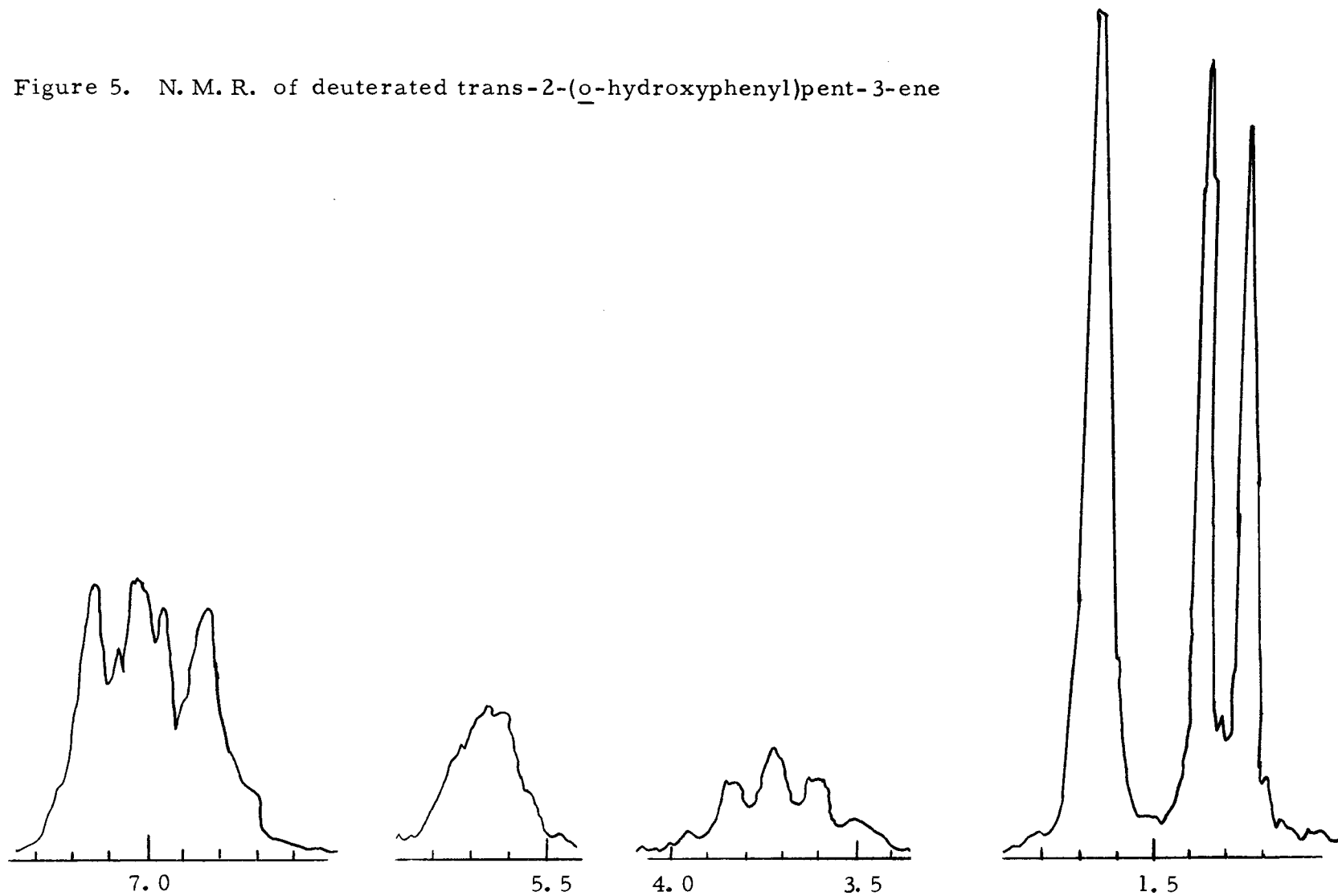
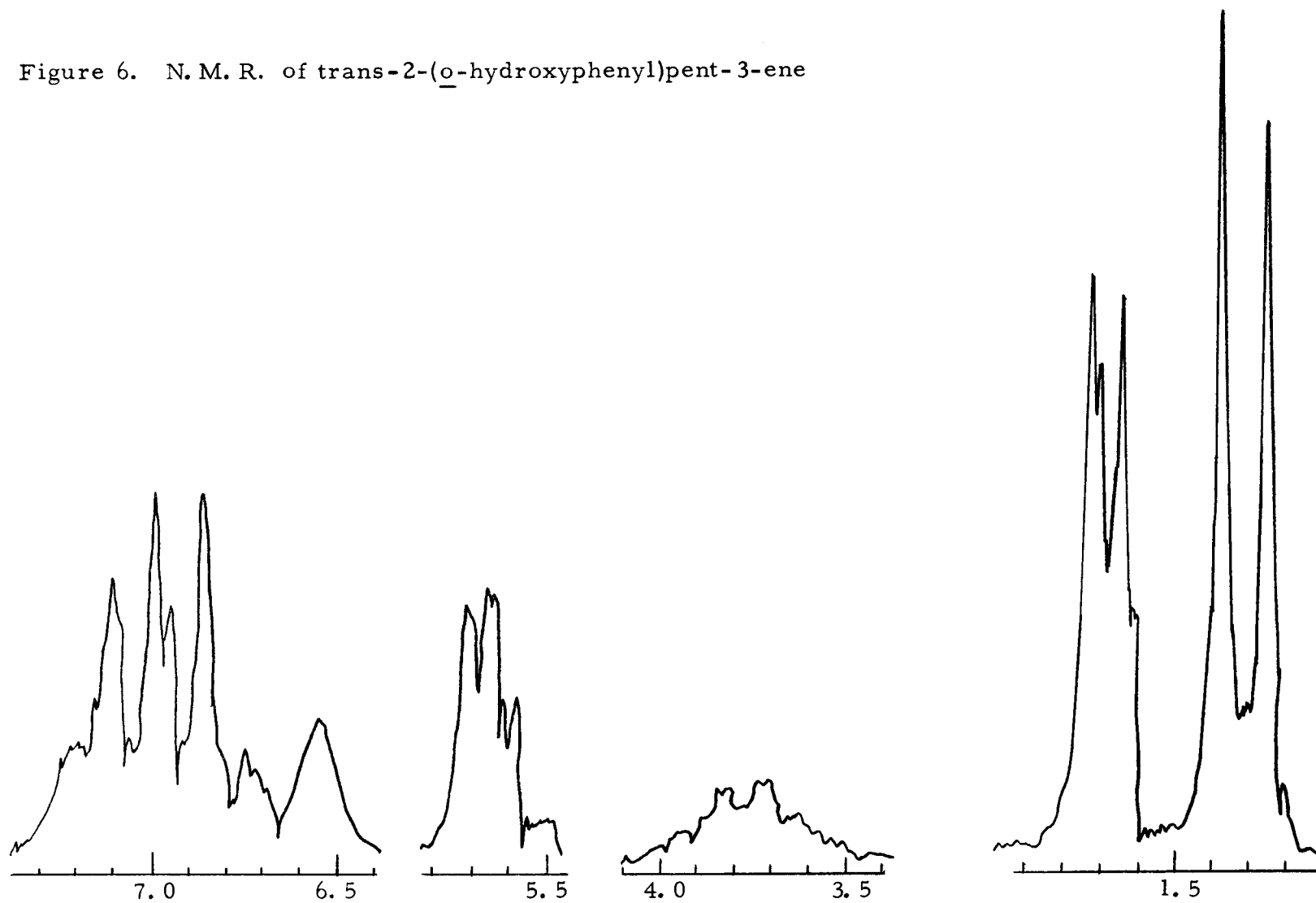


Figure 6. N. M. R. of *trans*-2-(o-hydroxyphenyl)pent-3-ene



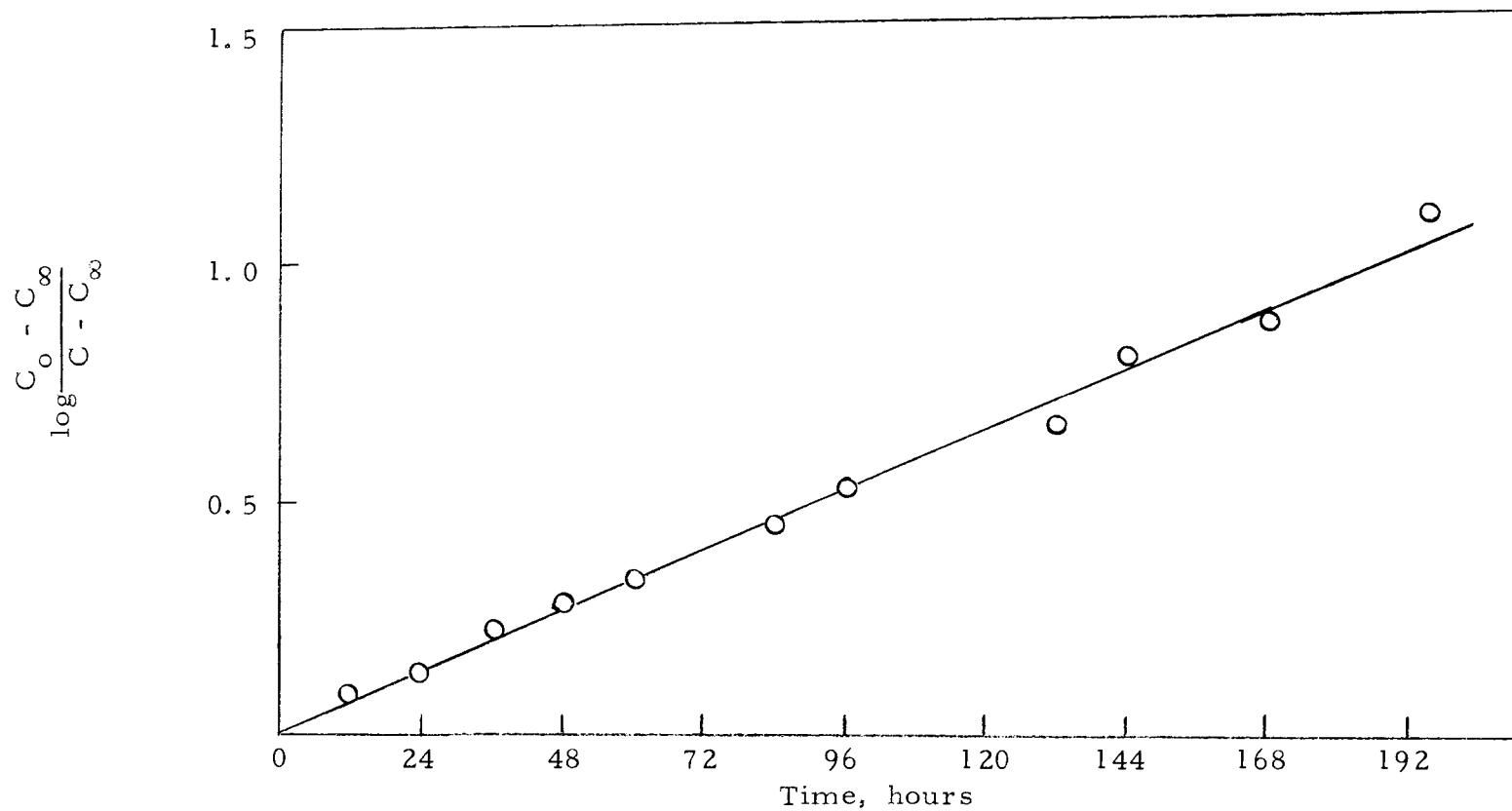
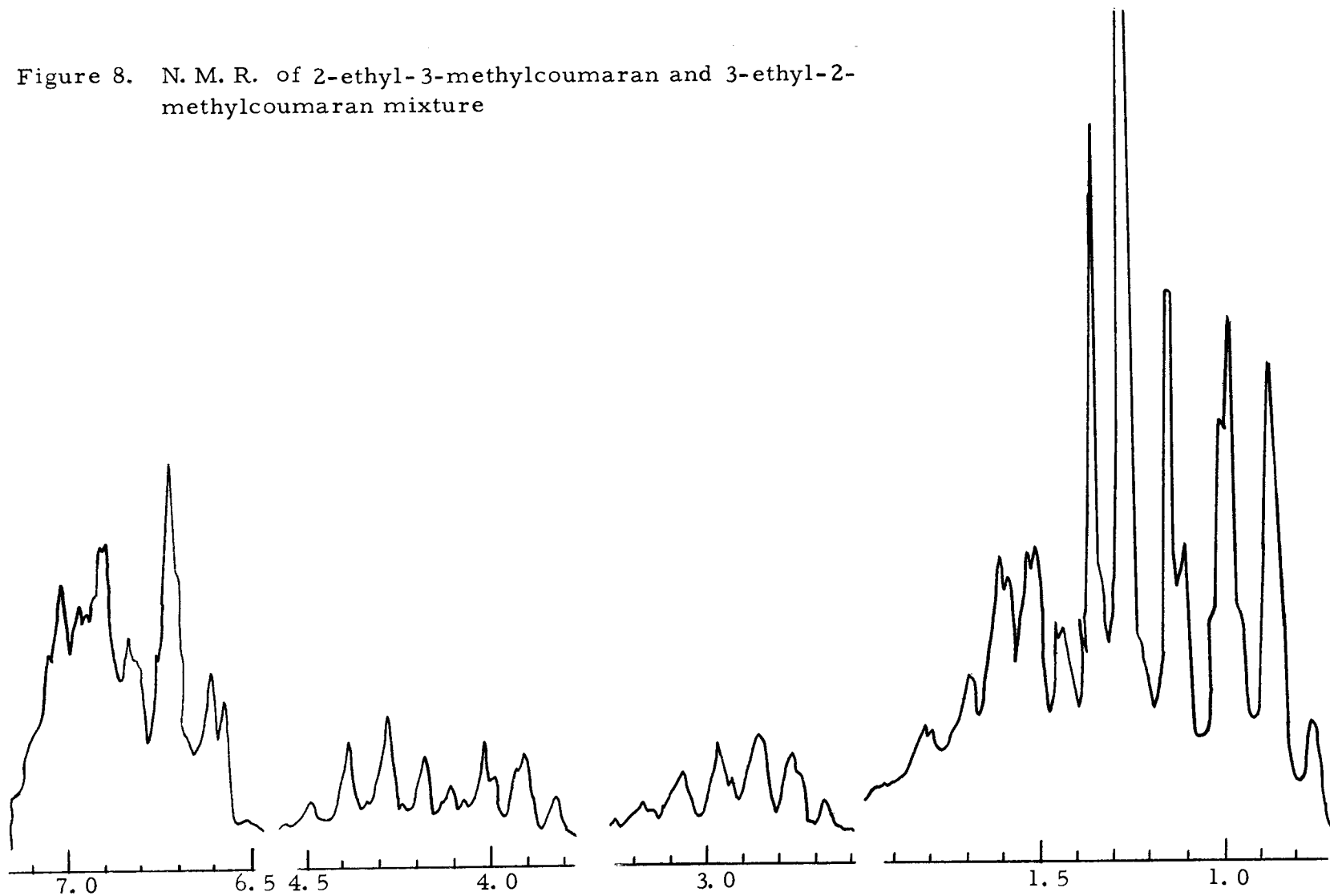


Figure 7.  $\log \frac{C_0 - C_8}{C - C_8}$  versus time for isomerization of cis-2-(o-hydroxyphenyl)pent-3-ene in  $D_2O$  at  $205.0 \pm 0.2^\circ$

Figure 8. N. M. R. of 2-ethyl-3-methylcoumaran and 3-ethyl-2-methylcoumaran mixture





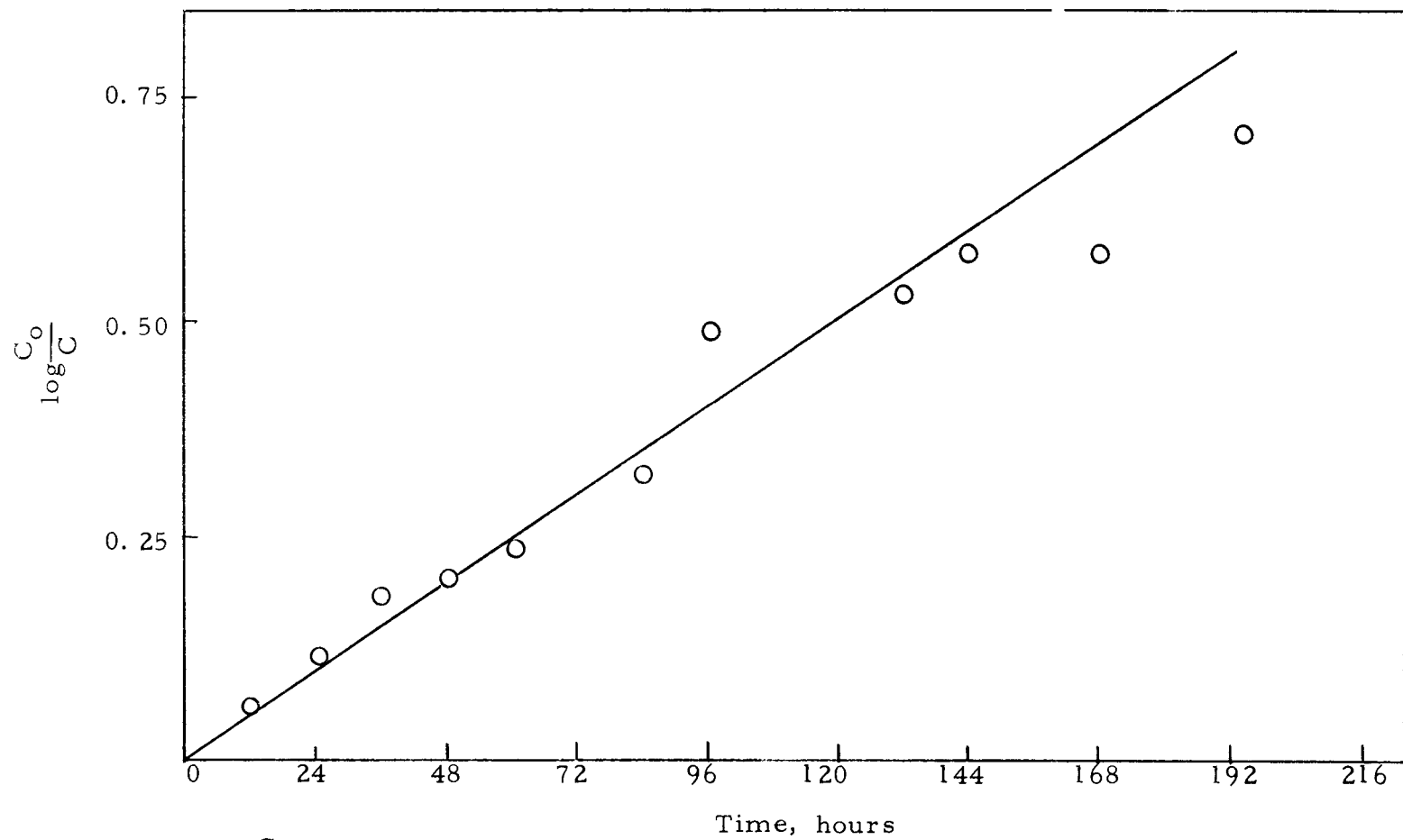


Figure 9.  $\log \frac{C_0}{C}$  versus time for olefinic deuterium incorporation of cis-2-(o-hydroxyphenyl)pent-3-ene at 205°. 88

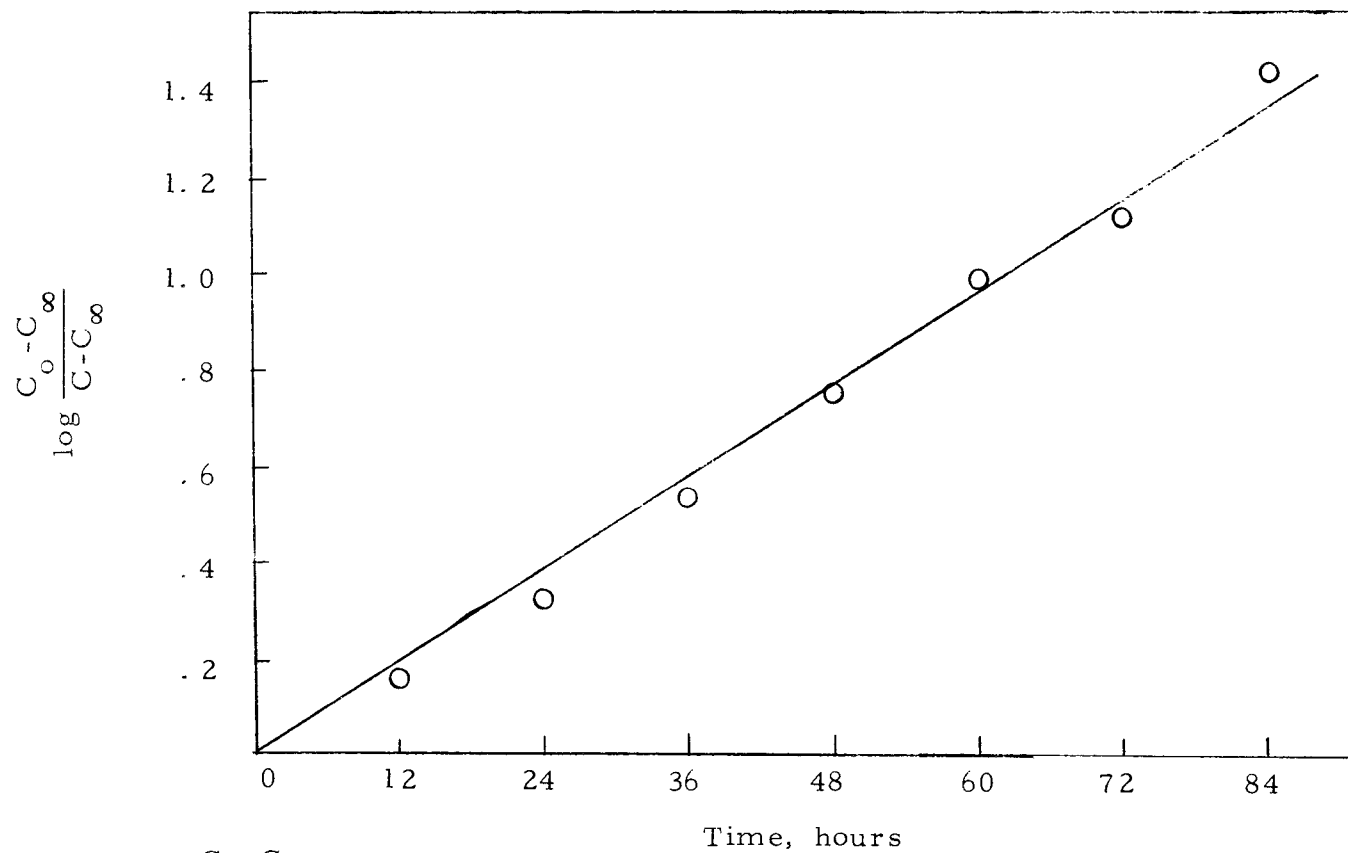


Figure 10.  $\log \frac{C_0 - C_\infty}{C - C_\infty}$  versus time for isomerization of cis-2-(o-hydroxyphenyl)pent-ene in  $H_2O$  at  $205.0 \pm 0.2^\circ$

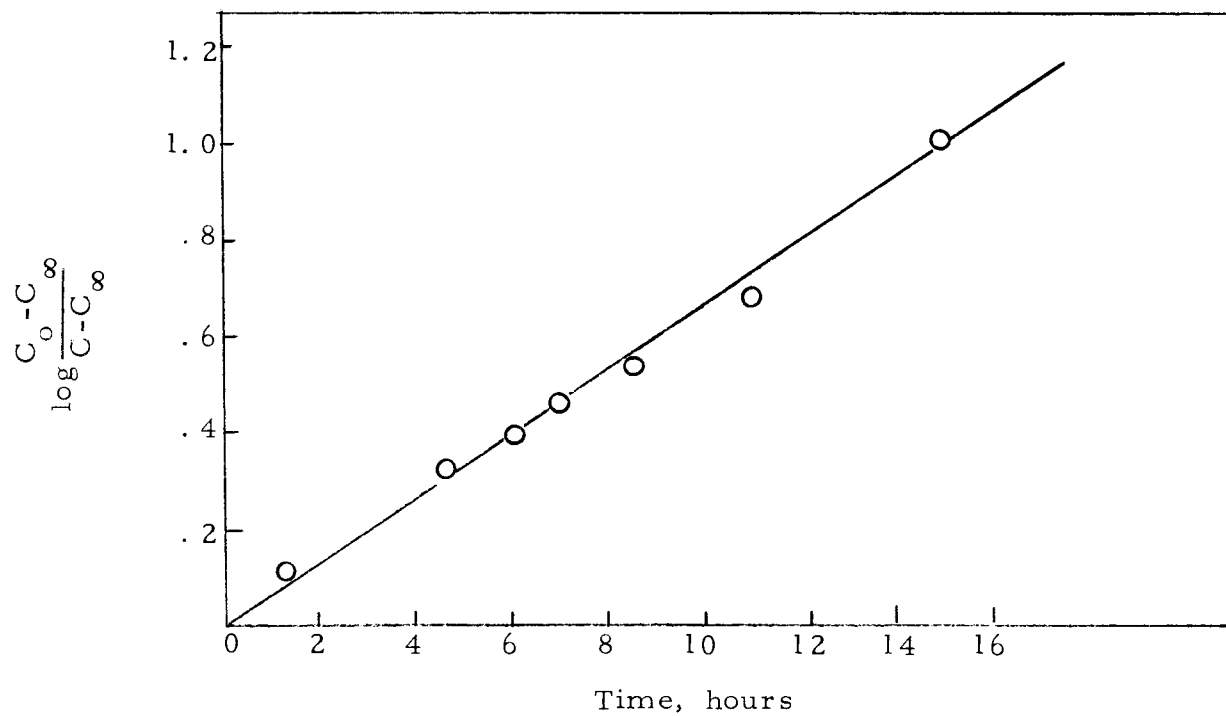


Figure 11.  $\log \frac{C_0 - C_\infty}{C - C_\infty}$  versus time for isomerization of cis-2-(o-hydroxyphenyl)pent-3-ene in  $H_2O$  at  $226.3 \pm 0.3^\circ$

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