

THE IRRADIATION OF SOME CISOID AND TRANSOID DIENES

by

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A Thesis Submitted to the Faculty of the

DEPARTMENT OF CHEMISTRY

In Partial Fulfillment of the Requirements
For the Degree of

MASTER OF SCIENCE

In the Graduate College

THE UNIVERSITY OF ARIZONA

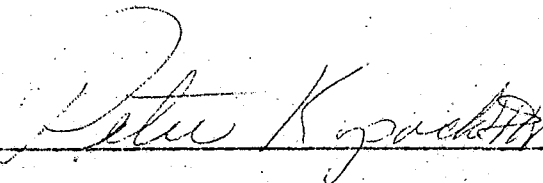
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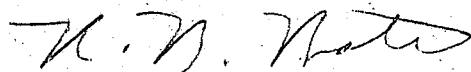
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This thesis has been approved on the date shown below:



R. B. Bates
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Date

ACKNOWLEDGMENT

The author wishes to express his gratitude to Dr. R.B. Bates for directing the course of this research, to the Petroleum Research Fund for a research assistantship and the University for a teaching assistantship.

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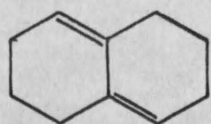
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APPENDIX-----

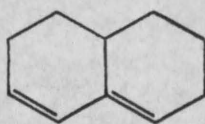
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ABSTRACT

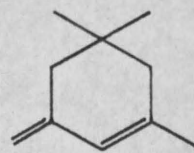
$\Delta^{1(9),5(10)}$ -hexahydronaphthalene (I),
 $\Delta^{1,8}$ hexahydronaphthalene (II) and 1,5,5-trimethyl-3-
 methylene-1-cyclohexene (III) gave no observable photo-
 chemical rearrangement when irradiated with or without
 photosensitizers. However, irradiation of 1,1,3,5-
 tetramethyl-2,4-cyclohexadiene (IV) gave a mixture of
cis- and trans-2,4,6-trimethyl-1,3,6-heptatrienes (V)
 in fair yield.



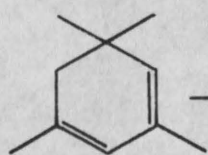
I



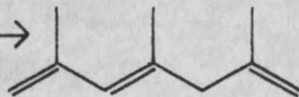
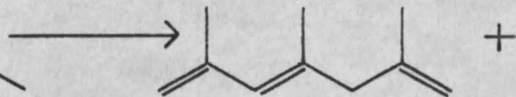
II



III

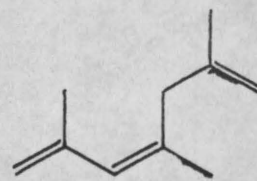


IV



Va

+

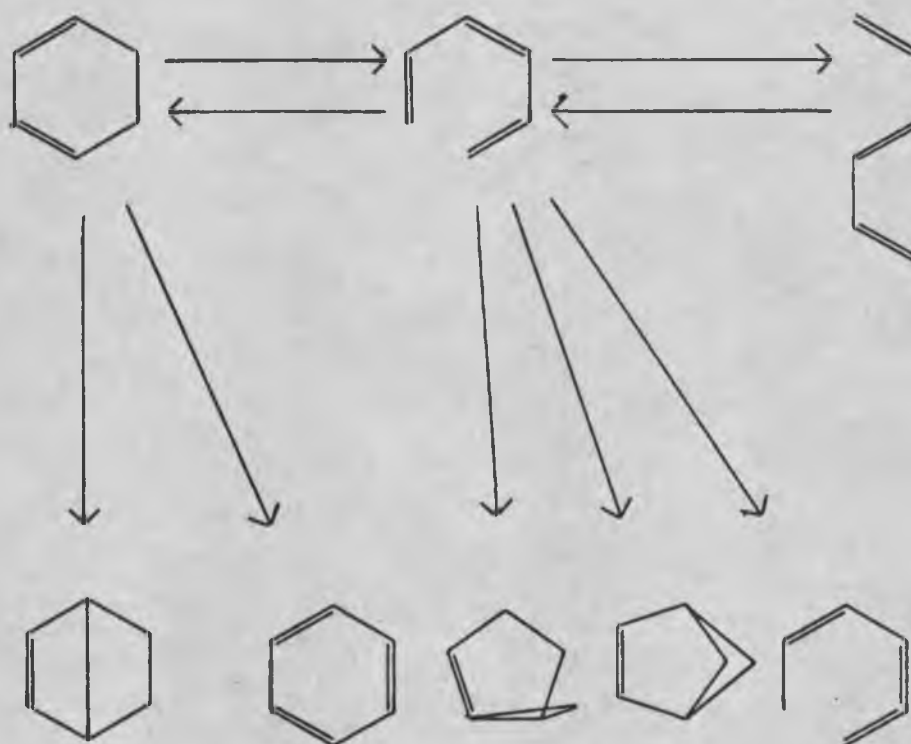


Vb

HISTORICAL

Irradiation of Cisoid Dienes

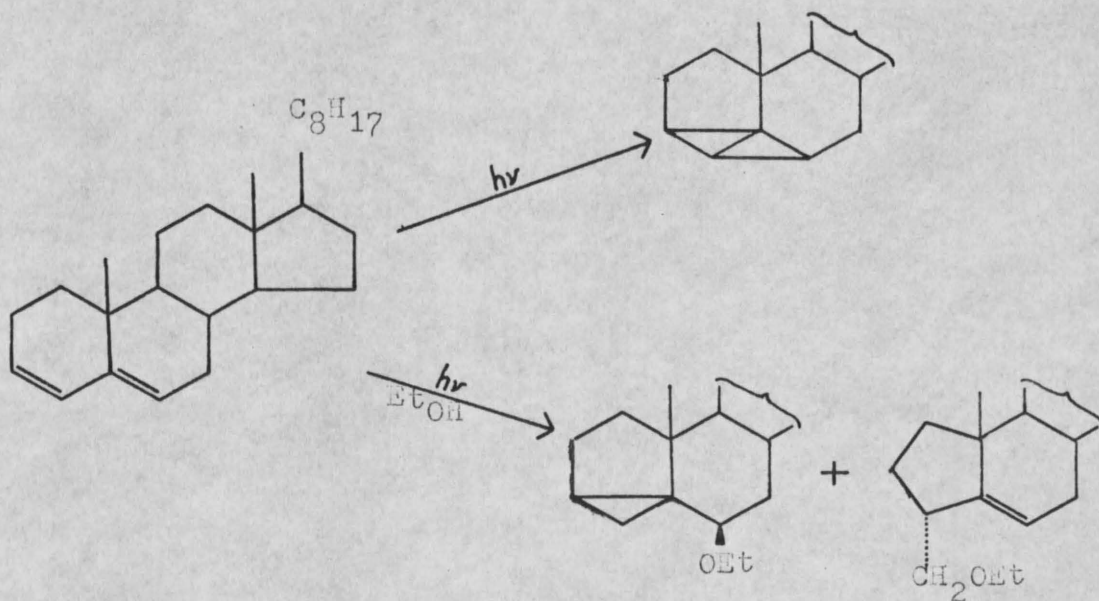
Extensive work has been done on the irradiation of endocyclic cisoid dienes (Noyes et al, 1963). The basic rearrangements are summarized below.



Irradiation of Transoid Dienes

Evidence of photochemical reactions of conjugated transoid dienes has only recently been obtained. It was found that abietic acid, upon irradiation in the absence of oxygen, yielded a mixture of the di- and tetrahydroxy-abietic acids, but it was postulated that the reaction was induced by acetaldehyde formed from the photochemical decomposition of the solvent, ethanol (Brown et al, 1943).

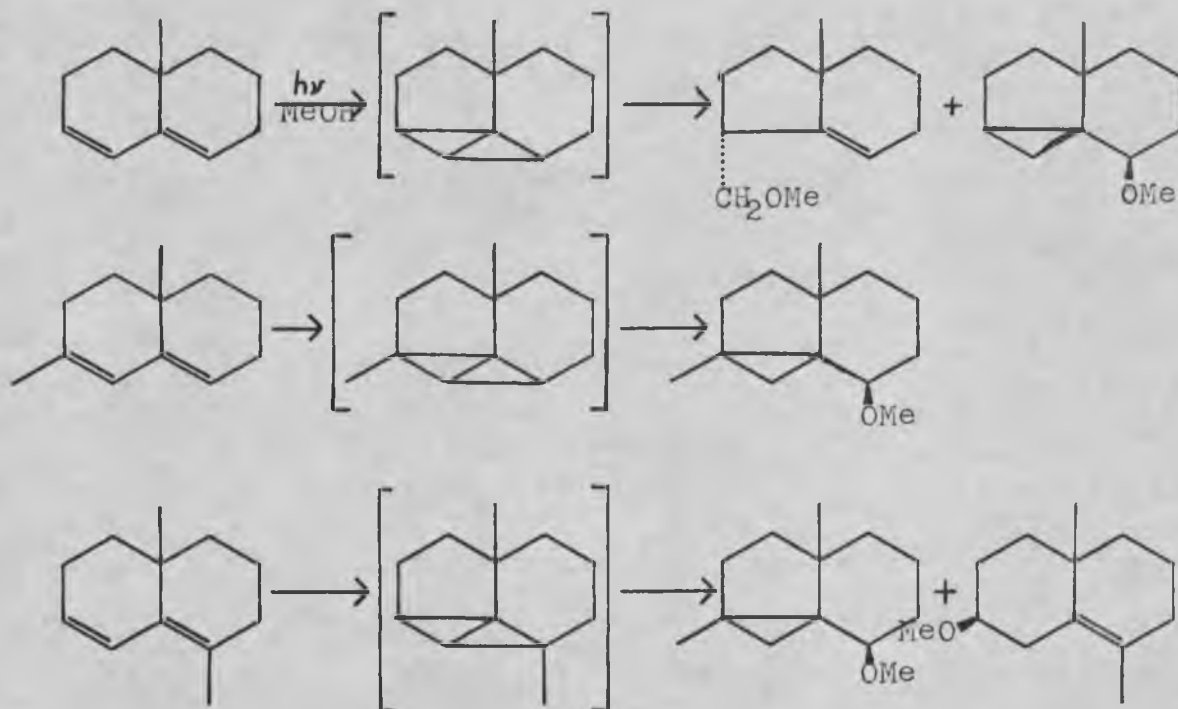
$\Delta^{3,5}$ -Cholestadiene, however, upon irradiation in aqueous or alcoholic solutions, yielded two ethers.



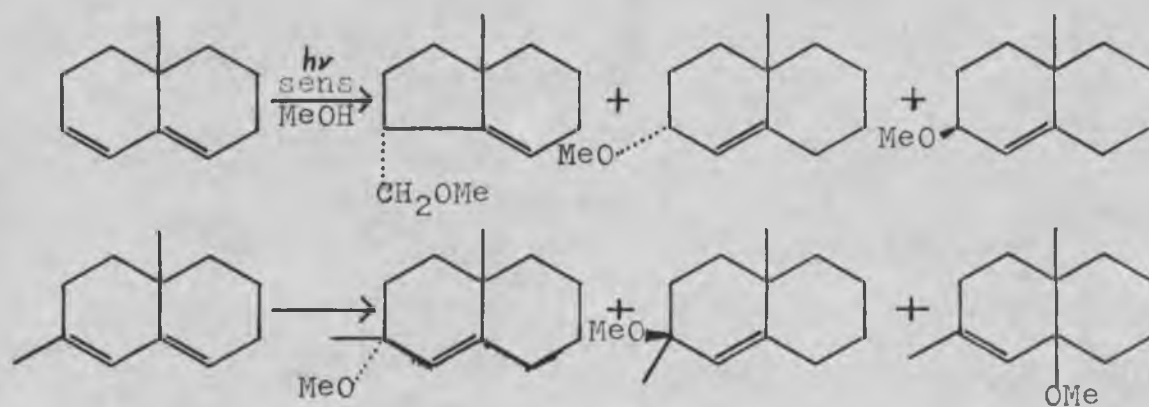
When irradiated under aprotic conditions (pentane), the intermediate 3,5-4,6-bis-cyclosteroid is isolated.

Simple molecular orbital calculations predict that such a 1,3 bond formation is prohibited (Dauben and Willey, 1962).

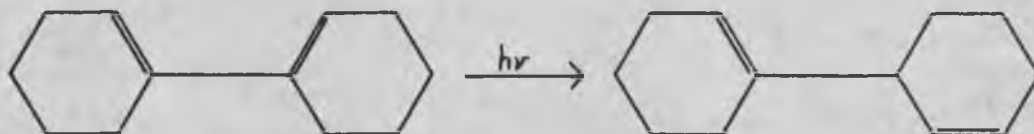
Irradiation of 9-methyl- $\Delta^{3,5}$ -hexahydronaphthalene in several dimethyl $\Delta^{3,5}$ -hexahydronaphthalenes in methanol have been studied and the products found again indicate bicyclobutane intermediates (Dauben, 1965):



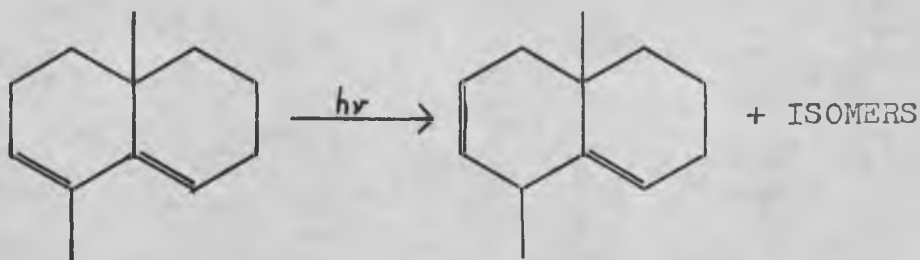
The effects of sensitizers on the products and yields have also been determined (Dauben, 1965):



Another interesting rearrangement is that of disconjugation of a conjugated diene. Only two reactions involving such a rearrangement have been reported in the literature. K.J. Crowley reported the following reaction (Crowley, 1962):



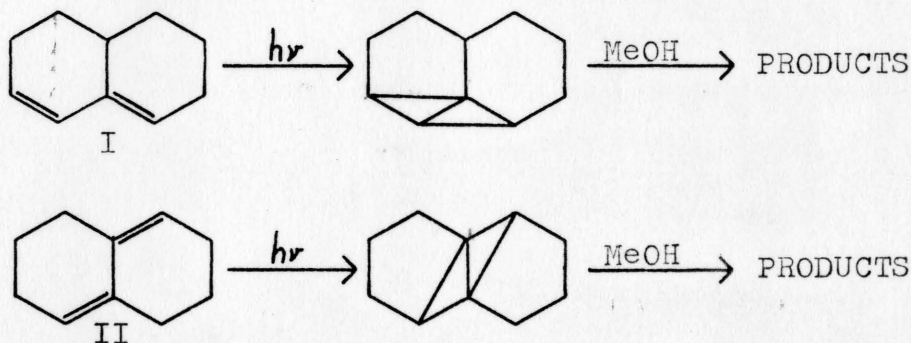
W.G. Dauben reported the same type of rearrangement when 1,10-dimethyl- $\Delta^{1,8}$ -hexahydronaphthalene is irradiated (Dauben, 1965):



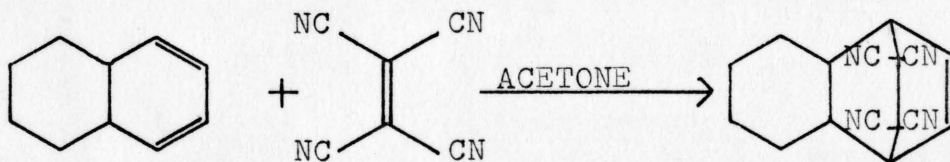
DISCUSSION

Irradiation of $\Delta^{1(9),5(10)}$ (II) and $\Delta^{1,8}$ -hexahydronaphthalene (I)

It was of interest to see whether the simplest transoid hexahydronaphthalenes would react in the same manner as observed by Dauben and Willey for hexahydronaphthalene derivatives.



The two hexahydronaphthalenes were prepared by the isomerization of $\Delta^{2,9}$ -hexahydronaphthalene. Two methods were used to isolate the dienes. In the first, the cisoid impurities were removed as their Diels-Adler adducts with tetracyanoethylene:

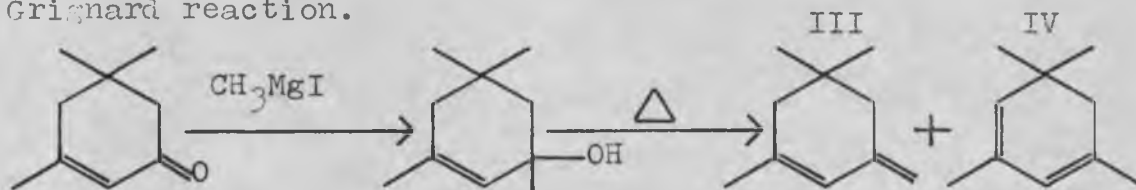


Final separation was accomplished with a preparative vapor phase chromatograph. The other method consisted of

preparative vapor phase chromatography as the only means of separation. Irradiation of the mixture in the presence of oxygen gave an unidentified yellow wax. No reaction was observed when the transoid mixture was irradiated in an inert atmosphere.

Irradiation of 1,5,5-trimethyl-3-methylene-1-cyclohexene (III)

The photochemistry of the transoid diene (III) and its cisoid isomer (IV) was investigated. These dienes were prepared concurrently from isophorone via the Grignard reaction.

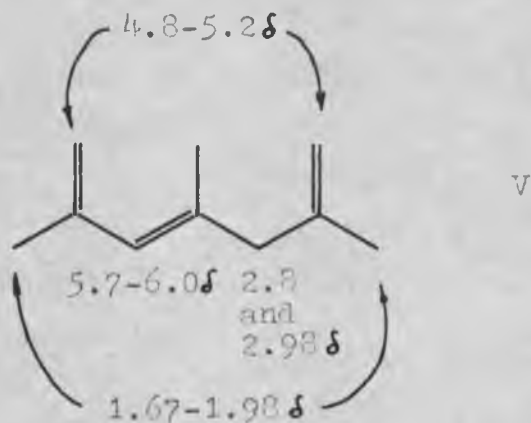


The two dienes were separated in pure form by means of preparative vapor phase chromatography. No reaction was observed when the transoid diene was irradiated in either methanol or ethanol or in the presence of a photosensitizer.

Irradiation of 1,1,3,5-tetramethyl-2,4-cyclohexadiene (IV)

Dilute solutions (to prevent intermolecular reactions) of the cisoid diene (IV) were irradiated in oxygen free systems. In all cases a decrease in the amount

of cisoid was noted by vapor phase chromatography and after 24 hours nearly all of the diene had reacted. Four major components were found after irradiation. The second and fourth components eluted from the Carbowax column were identified by retention times to be the transoid diene (III) and unreacted starting material. The presence of the transoid diene could be due in part to the thermal isomerization in the vaporization chambers of the vapor phase chromatographs or to photoisomerization of the cisoid diene. The first component eluted off the column disappeared when the photomixture was distilled under reduced pressure and did not appear in the reaction mixture at the same relative concentration for each irradiation. The third component in all irradiations was the major product. The NMR and IR showed this product to be 2,4,6-trimethyl-1,3,6-heptatriene (V):

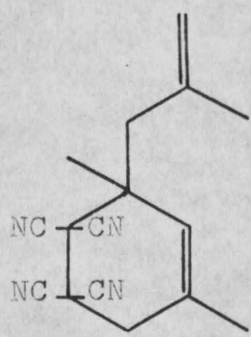


The two peaks at 2.98 and 2.80 δ together were always integrated as two protons, though their relative areas

varied with reaction times and conditions. This can best be explained by assuming that the two stereoisomers have the same retention times on the VPC column and that the observed NMR spectrum is that of a mixture of two dienes. Comparison of the NMR spectrum with that of an authentic sample purchased from Chemical Samples Company, Columbus, Ohio supported this view. This sample was also apparently a mixture of the two stereoisomers (Figure II).

The product was further characterized by the formation of the tetracyanoethylene adduct; the cis and trans dienes should give the same adduct. Both NMR and IR spectra supported the proposed structure. Elemental analysis was consistent with the empirical formula

C H N . The structure is believed to be:
 16 16 4



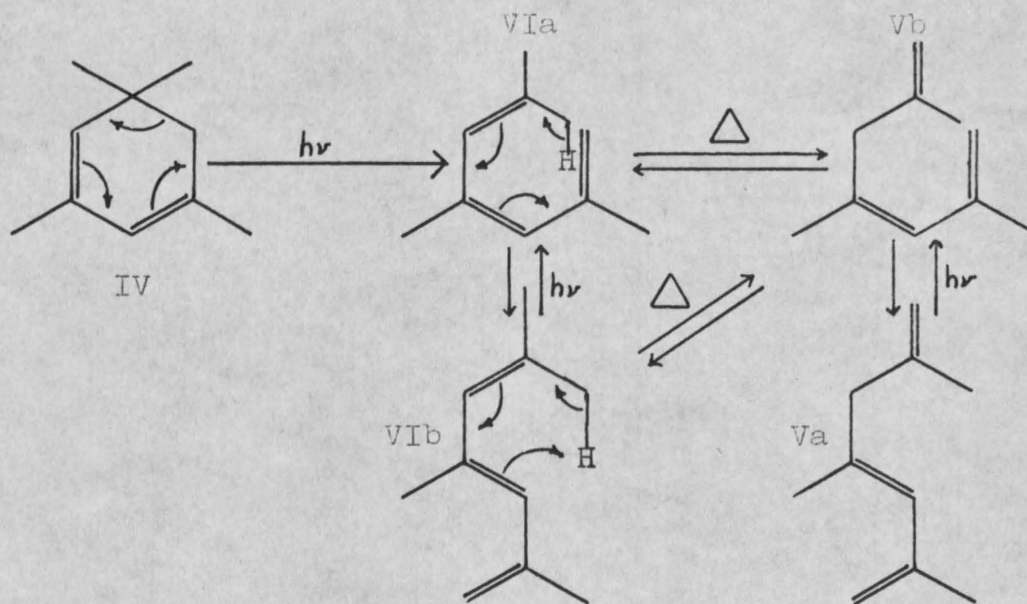
Mechanism of the Photoreaction

There is considerable doubt whether the observed product is due solely to a photochemical reaction. A

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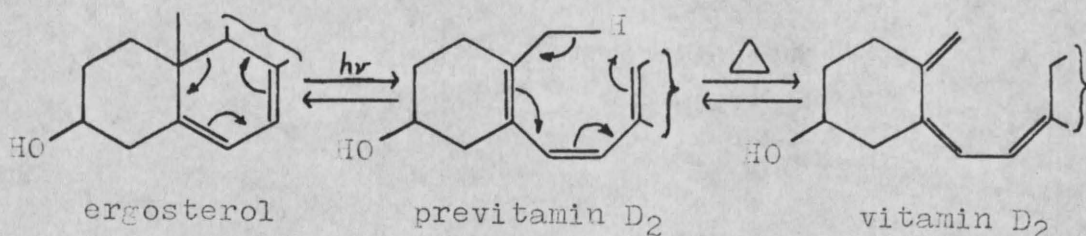
thermal post irradiation reaction could be taking place in the vaporization chamber of the vapor phase chromatograph.

A suggested scheme for the rearrangement is shown below:



The initial rearrangement to the triene (VIa) parallels many observed photochemical reactions involving conjugated cyclic dienes. The driving force for the disconjugation step would then be provided by the non-bonded steric interactions in VIa and/or VIb. Photoisomerization about the double bond could easily take place to give the observed product. The proposed thermal reaction finds some precedent in the irradiation of ergosterol, which gives previtamin D in a photochemical step; this

substance rearranges thermally slightly above room temperature, probably via the 8-membered ring transition state shown, to give vitamin D₂ (Fieser, 1959):



It might be possible to determine more regarding the course of the reaction by examining the ultraviolet spectrum of the diene solution during irradiation, and to isolate VIa and/or VIb by working at lower temperatures.

EXPERIMENTAL

Birch Reduction of Tetralin

A 101.6 g. sample (0.77 moles) of freshly distilled tetralin was reduced by the procedure of Carnighan (Carnighan, 1963). The light yellow oil remaining after evaporation of the solvent was used directly in the next reaction. VPC on a Carbowax column showed this mixture to contain about 75% of $\Delta^{2,9}$ -octalin and 25% of tetralin.

Isomerization of the Birch Reduction Mixture

The mixture (124.6 g.) prepared by the Birch reduction of tetralin as described above was isomerized as described by Carnighan by refluxing with potassium tert-amyloxide in tert-amyl alcohol for 384 hours, during which the reaction mixture separated into brown layers. An additional 200 ml. of water was added; the organic layer was extracted with 200 ml. of hexane, washed four times with 200 ml. of water, and twice with 200 ml. of concentrated brine. The solvent was removed with the rotary evaporator at room temperature under reduced pressure, leaving a light yellow liquid (60.8 g.). Vapor phase chromatography (Carbowax, 100°) showed five peaks

that were identified by comparison to a standard chromatogram:

peak #1	<u>octalins</u>	1.3%
#2	<u>cisoids</u>	12.6%
#3	<u>transoids</u>	52.3%
#4	<u>Birch product</u>	9.7%
#5	<u>tetralin</u>	24.5%

Isolation of the Transoid Dienes

#1. To 15.0 g. of the isomerization mixture in 120 ml. of dry tetrahydrofuran (THF) was added 6.0 g. (0.05 moles) of recrystallized tetracyanoethylene at room temperature. The solution, which very rapidly became warm and turned red, was allowed to stand overnight in an open container. The resulting dark, gummy mass was dissolved in 60 ml. of THF. To 10 ml. of this solution was added 10 ml. of hexane. This solution was placed on an Alumina (Merck, acid washed, 2.3x20 cm.) column and eluted with 100 ml. of hexane. The eluent was collected and the solvent removed under reduced pressure at room temperature with the rotary evaporator, leaving a clear liquid. VPC (Carbowax, 100^o) showed six peaks that were identified by retention times.

peak #1	<u>octalins</u>	3.3%
#2	<u>cisoids</u>	0.0%
#3	<u>transoids</u>	48.9%
#4	<u>Birch product</u>	0.0%
#5	<u>tetralin</u>	48.8%

A 2.0 ml. sample of this mixture was injected into a preparative VPC (Carbowax, 125°) and the transoid fraction was collected. Analytical VPC (Carbowax, 100°) showed it to be >99% pure. Comparison of the NMR spectrum of this mixture to those of the pure compounds showed two or more isomers to be present in very nearly equal amounts.

#2. The transoid dienes (I and II) were separated from the isomerization mixture by preparative VPC, but without the prior TCNE treatment. By collecting a small area of the transoid diene peak, it was possible to obtain a fraction containing 9% cisoids, 89% transoids, and 2% octalins (analytical VPC, Carbowax, 100°). Repeated attempts to improve the purity of the fraction were unsuccessful, undoubtedly due to the poor resolution of the preparative column. VPC with a QF-1 column (100°) showed a 3.6:1 ratio of $\Delta^{1(9),5}$ -hexahydronaphthalene to $\Delta^{1,8}$ -hexahydronaphthalene.

Irradiation of the Transoid Dienes (I and II)

#1. A solution of 0.9 g. of the diene mixture (procedure #1) in 75 ml. of heptane was irradiated with a General Electric sun lamp for 39 hours. The solution was

stirred in an open beaker under a stream of nitrogen and kept at a temperature of 33°. VPC (Carbowax, 100°) showed that the transoid component had completely disappeared. Removal of the solvent under pressure at room temperature with a rotary evaporator left a yellow wax insoluble in benzene, heptane, and carbon tetrachloride and soluble in THF. The IR spectrum showed strong absorption at 1700 cm^{-1} , suggesting that the dienes had reacted with the oxygen in the air.

#2. A 1% solution of the transoid diene mixture (procedure #2) in ethyl alcohol under nitrogen in a quartz test tube was irradiated for one week with a low pressure mercury arc lamp. Removal of the solvent under reduced pressure with the rotary evaporator left a light yellow liquid that was shown to be identical by NMR and IR to the starting material.

#3. A solution of 1.2 g. of the transoid diene (procedure #2) mixture in 90 ml. of ethyl alcohol under nitrogen was irradiated with a 85 watt high pressure mercury arc lamp (Figure IV) for 19 hours. VPC (Carbowax, 100°) of the solution before and after irradiation showed no detectable difference.

#4. Irradiation of 1.48 g. of the isomerization mixture in 2500 ml. of reagent grade methanol under nitrogen

for 14 hours at 5° with an immersed 450 watt Hanovia low pressure mercury arc lamp was followed by removal of the solvent at room temperature leaving a light yellow liquid. Subsequent VPC (Carbowax, 100°) and IR comparison of the starting material showed no change in the transoid components of the mixture, but a 5% reduction in the concentration of the cisoid fraction.

Preparation of the Cisoid and Transoid Dienes (III and IV) from Isophorone (After Gosselink, 1966)

A 1500 ml., three necked, round bottom flask, fitted with a mechanical stirrer, condenser, and separatory funnel, was charged with 200 ml. of anhydrous ether and 24.0 g. (0.99 moles) of magnesium turnings. The flask was swept with nitrogen. To the solution was added 161.4 g. (0.99 moles) of methyl iodide dissolved in 500 ml. of anhydrous ether over a period of 1 hour. The reaction was kept at gentle reflux by alternate cooling with an ice bath and warming. The magnesium-ether complex was decomposed slowly by stirring in a saturated solution of ammonium chloride. The organic and aqueous layers were separated with a separatory funnel and the organic layer was washed twice with 200 ml. of water. The ether was removed at room temperature under reduced pressure with a rotary

evaporator, leaving a light brown liquid. Distillation of this solution under aspirator vacuum gave 83.2 g. (0.61 moles, 62%) of a clear liquid, b.p. 78-85°. VPC (Carbowax, 100°) showed only two peaks.

Irradiation of the Mixture of the Cisoid and Transoid Dienes (III and IV)

A solution of 8.0 g. (0.59 moles) of the mixture of the two dienes dissolved in 2500 ml. of reagent grade methanol was irradiated with an immersed 450 watt Hanovia mercury arc lamp at 5° for 5 hours. The solvent was removed under reduced pressure at room temperature with the rotary evaporator, leaving a light yellow oil. An NMR was obtained with a microcell, but the spectrum was very complicated and no further work was done with this reaction product.

Separation of the Cisoid and Transoid Dienes (III and IV)

The two dienes were separated with the preparative VPC (115°). The first run through the column gave the first component in 99% purity and the second in 90%. With a second run, both components were obtained in pure form.

NMR of the two fractions showed the first component to be the cisoid diene (IV) and the second to be the transoid diene (III).

Irradiation of the Transoid Diene (III)

Irradiation of a solution of 24.4 g. (0.18 moles) of the transoid diene in 2500 ml. of reagent grade methanol with an immersed 450 watt Hanovia mercury arc lamp at 30° for 11½ hours was followed by removal of methanol under reduced pressure at room temperature. VPC (Carbowax, 100°) of the clear liquid showed only unchanged starting material.

Irradiation of a solution of 1.3 g. (0.010 moles) of the transoid diene and 0.1 g. (0.0006 moles) of benzophenone in 140 ml. of reagent grade methanol with an 85 watt high pressure mercury arc lamp at room temperature under nitrogen for 24 hours. VPC (Carbowax, 100°) showed only the solvent and a component with the same retention time as the transoid diene. Extracted the single component with benzene and evaporated the benzene off under reduced pressure. NMR of the residue showed only unchanged starting material.

Irradiation of the Cisoid Diene (IV)

#1. A solution of 1.9 g. (0.014 moles) of the cisoid diene in 130 ml. of reagent grade methanol was irradiated with an 85 watt high pressure mercury arc lamp under nitrogen for 24 hours. The methanol was removed under reduced pressure, leaving a light yellow liquid. VPC showed six peaks: the first, fourth, and sixth identified by retention times to be methanol, cisoid diene (IV) and transoid diene (III) respectively. The main peak, #5, was collected on the preparative VPC. Analytical VPC showed it to be a single peak (NMR - Figure I, IR peaks - 1649 (s), 1800 (w), 1450 (s), 895 (s) cm^{-1}), no oxygen functions; 2 double bonds, one conjugated and one not. Analysis: calculated for $\text{C}_{10}\text{H}_{16}$, %C 88.16, %H 11.84; found %C 88.20, %H 11.88.

#2. A solution of 1.4 g. (0.010 moles) of the cisoid diene (IV) and 130 ml. of methanol at room temperature was irradiated for 285 hours under nitrogen with a 85 watt mercury arc lamp. VPC of the photoproduct residue after workup showed four peaks. The largest peak (#3) was collected with a preparative VPC (Carbowax, 100°). NMR and IR spectra showed it to be identical with peak #5 above.

#3. A 52 g. (0.38 moles) sample of the cisoid diene (IV) in 130 ml. of reagent grade methanol at room temperature under nitrogen was irradiated with an 85 watt mercury arc lamp for $2\frac{3}{4}$ hours. VPC showed four main peaks of which #3 was the largest. This peak was collected using the preparative VPC (Carbowax, 100°). Its NMR spectrum was identical to the above with the exception of the peak at 2.80 δ which disappeared and the peak at 2.98 δ which integrated as 2 protons.

Tetracyanoethylene Adduct of Cisoid and Transoid

Trienes (Va and Vb)

To 0.1296 g. (0.00095 moles) of the triene mixture in 1 ml. of tetrahydrofuran was added 0.1300 g. (0.00095 moles) of tetracyanoethylene (recrystallized) in 1 ml. of tetrahydrofuran at room temperature. On standing, the solution changed from dark red to light yellow at which point the solvent was removed under reduced pressure with the rotary evaporator, leaving a dark red oil. On standing, the residual oil deposited red crystals and white needle-like crystals. Two recrystallizations from a 3:1 water methanol mixture give fine light yellow

needles, m.p. 90-92° (NMR - Figure III, IR peaks - 1649 (m), 1462 (s), 1380 (s), 945 (m) cm^{-1}).

Analysis:	Calculated for C H N :	
		16 16 4
	72.70%	C
	6.10%	H
Found:		
	72.74%	C
	6.37%	H

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APPENDIX

FIGURE I. Main photoproduct from the irradiation of 1,1,3,5-tetramethyl-2,4-cyclohexadiene (IV).

FIGURE II. 2,4,6-trimethyl-1,3,6-heptatriene. Chemical Samples Company, Columbus, Ohio.

FIGURE III. TCNE adduct of the main photoproduct from the irradiation of 1,1,3,5-tetramethyl-2,4-cyclohexadiene.

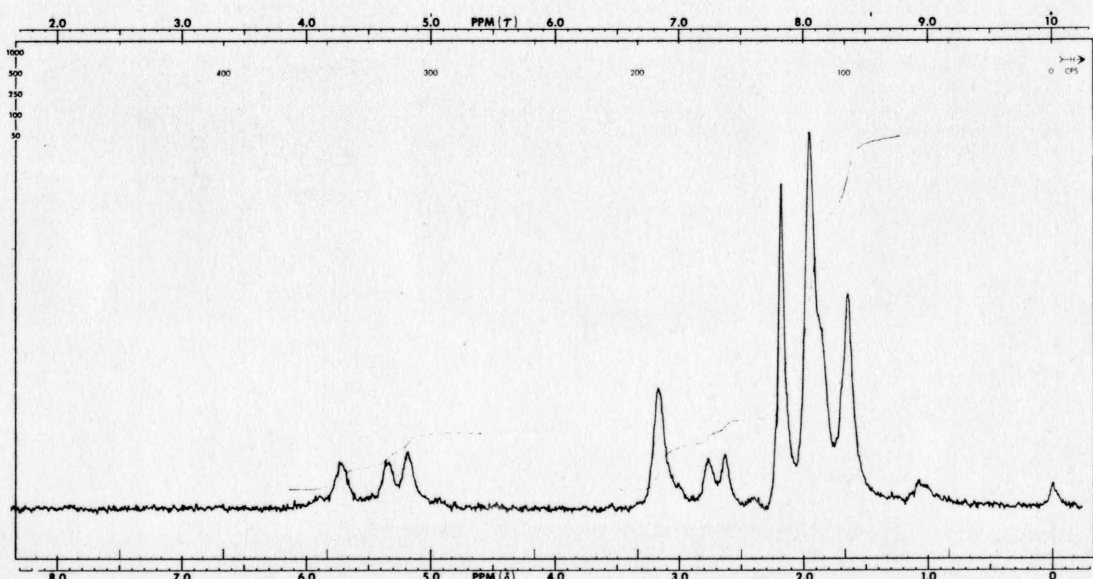
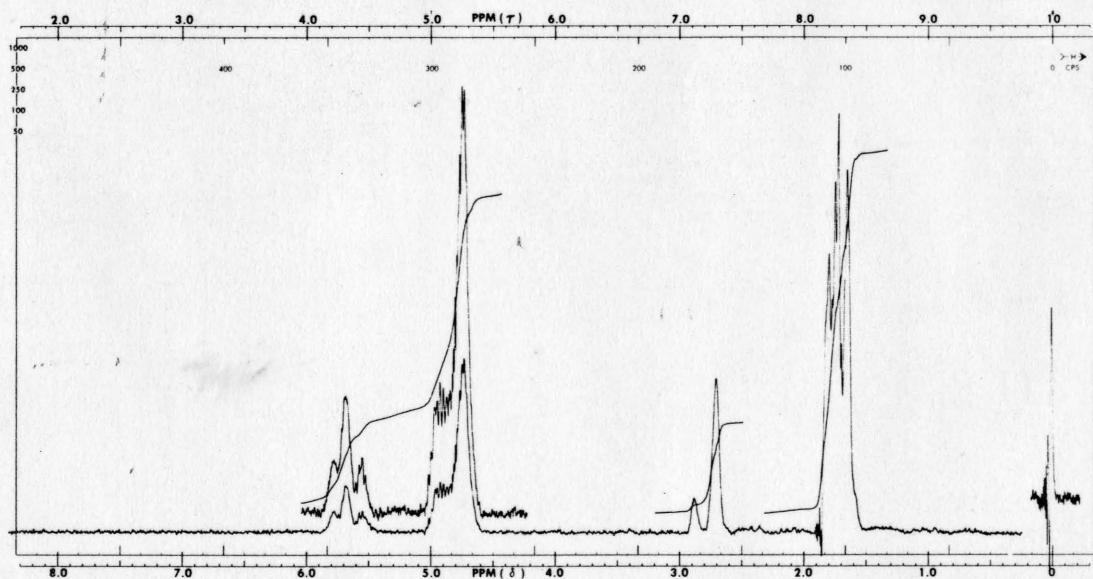
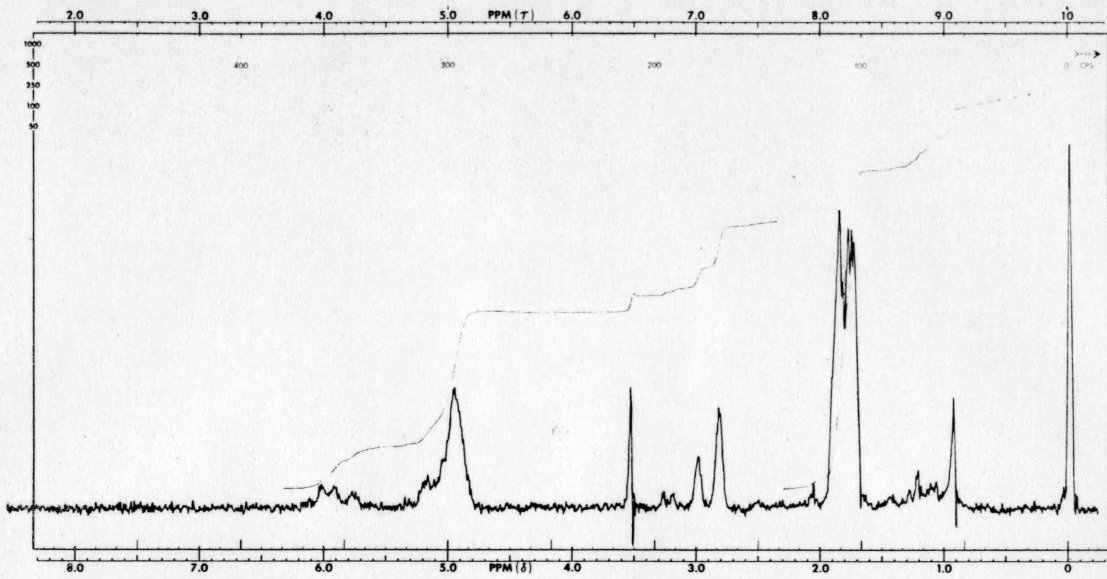


FIGURE IV. 85 watt high pressure mercury arc lamp.

- A - Coolant inlet
- B - Coolant outlet
- C - Nitrogen inlet
- D - Nitrogen outlet
- E - G.E. mercury arc lamp, 85 watt
- F - Water jacket
- G - Magnetic stirrer
- H - Reaction chamber
- I - Sealing wax
- J - Silicon cement seal

