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PHOTOCHEMICAL TRANSFORMATIONS - XIII. THE MECHANISM OF THE REACTION OF $\Delta^{3,5}$-CHOLESTADIENE[1,2]

William G. Dauben and Fred G. Willey[3]
Department of Chemistry, University of California,
Berkeley 4, California

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FAIRLY extensive studies of the photochemistry of cisoid conjugated dienes have established that ultraviolet irradiation of such systems usually leads to formation of a new bond between carbon atoms 1 and 4 of the diene to yield a cyclobutene or, in the special case of some six-membered rings, to bond cleavage to form a hexatriene.[4] These two types of reactions are virtually impossible with a diene held in a transoid conformation, since to bond carbon atoms 1 and 4 would require introduction of excessive strain, and to open a ring appears

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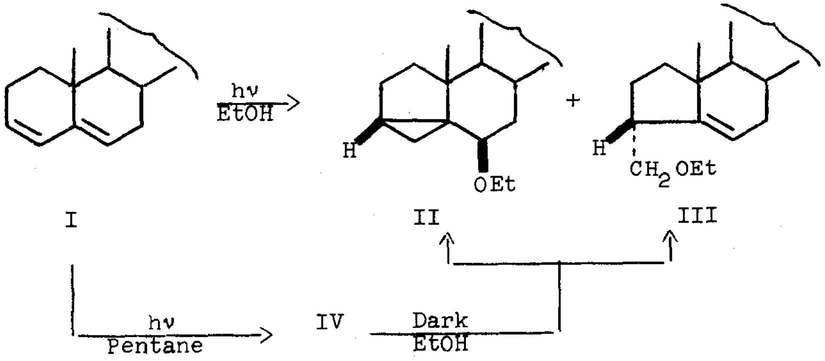
[1] For Paper XII, see W. G. Dauben and Fred G. Willey, J. Am. Chem. Soc. 84, 1497 (1962).

[2] This work was supported, in part, by Grant No. A-709, U.S. Public Health Service.

[3] National Science Foundation Predoctoral Fellow, 1959-1962.

[4] P. de Mayo, Quart. Revs. 15, 383 (1961); W. G. Dauben and R. L. Cargill, Tetrahedron 15, 197 (1961); O. L. Chapman, D. J. Pasto, G. W. Borden, and A. A. Griswold, J. Am. Chem. Soc. 84, 1220 (1962); W. H. Schuller, R. H. Moore, J. E. Hawkins, and R. V. Lawrence, J. Org. Chem. 27, 1178 (1962).

to require proximity of the ends of the system. Indeed, in the two cases of direct irradiation of a *transoid* diene reported in the literature, quite different reactions occur. It was found that abietic acid, upon irradiation in the absence of oxygen, yielded a mixture of di- and tetrahydroxyabietic acid, but it was postulated that the reaction was induced by acetaldehyde formed from the photochemical decomposition of the solvent, ethanol.[5] $\Delta^{3,5}$-Cholestadiene (I), however, undergoes 1,3-addition of protic solvents upon irradiation in aqueous or alcoholic solutions to yield the 3,5-*cyclo*-steroid (II).[6]



Although there are no analogies upon which to base a prediction of the type of reaction a *transoid* diene might undergo upon irradiation, the cholestadiene result is surprising in at least two respects. First, simple molecular orbital theory

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[5] R. F. Brown, G. B. Bachman, and S. J. Miller, J. Am. Chem. Soc. 65, 623 (1943).

[6] W. G. Dauben and J. A. Ross, J. Am. Chem. Soc. 81, 6521 (1959)

applied to conjugated dienes[7] predicts that the molecular orbital to which an electron is promoted in going to the first electronically excited state is one which allows bonding between the first and fourth and between the second and third carbon atoms, but not between the first and third and between the second and fourth carbon atoms of the diene system. Second, the solvent addition reaction must have a negative entropy of activation, since it is bimolecular, and it proceeds with complete stereospecificity. A molecule undergoing a bimolecular reaction of an average entropy of activation requires as many as 10^6 collisions to react.[8] Based upon the extinction coefficient[9] of the absorption band at 235 mμ (ε 22,000), the lifetime of the excited cholestadiene singlet must be of the order of $10^{-8}$$10^{-9}$ second during which time the molecule can undergo only about 10^4 collisions. Thus, for a bimolecular reaction to occur in the excited state, a long-lived excited species might be required, and such a species has not been observed.[10]

For these reasons, it was of interest to study this photoreaction in more detail. It has now been found that $\Delta^{3,5}$-cholestadiene disappears at the same rate upon irradiation

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[7] A. Streitwieser, Jr., Molecular Orbital Theory for Organic Chemists, John Wiley and Sons, New York, N. Y., 1961.

[8] A. A. Frost and R. G. Pearson, Kinetics and Mechanism, John Wiley and Sons, Inc., New York, N. Y., 2nd Edition, 1961, p. 104, 144.

[9] C. Reid, Excited States in Chemistry and Biology, Butterworth Scientific Publications, London, 1957.

[10] E. Havinga, R. J. de Kock, and M. R. Rappoldt, Tetrahedron **11**, 276 (1960).

under aprotic conditions in a helium atmosphere as it does upon irradiation in protic solvents. A solution of 7.84 g. of $\Delta^{3,5}$-cholestadiene in 750 ml. of spectral-grade pentane under a helium atmosphere was irradiated with a G.E. AH-6 high pressure mercury arc lamp in a water-cooled quartz probe for 10 hrs. at the end of which time, 98% of the diene had reacted. The solvent was removed under a stream of dry nitrogen at room temperature and the residue dried at 0.01 mm. at the same temperature. The clear syrup[11] (Anal. C, 87.30; H, 12.10. Calcd. for $C_{27}H_{44}$: C, 88.04; H, 11.86; Calcd. for $C_{27}H_{44}O$: C, 84.38; H, 11.46) is unstable towards moisture, air, and heat and has the following properties: $[\alpha]_D$-17° (CCl_4); apparent molecular weight, 434 ±26 (osmometric in CCl_4); NMR spectrum, no absorption above 9.25τ (C-13 angular methyl), absorption at 4.5τ (vinyl H) corresponding to 0.6 ±0.1 proton; infrared spectrum, shoulder at 3018 cm.$^{-1}$, no band in hydroxyl or carbonyl region and no medium or strong absorption below 1350 cm.$^{-1}$; ultraviolet spectrum, ϵ_{200}~4500. When a solution of the material in hexadecane (b.p. 287°) is refluxed briefly, the compound is converted to a conjugated diene.

Attempts to isolate a pure compound from this photomixture were soon abandoned due to the instability of the material. However, it was found that treatment of the total crude product with ethanol in the dark afforded exactly the same products as obtained by direct irradiation of the diene in ethanol. The

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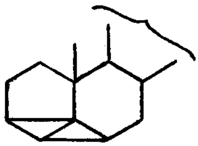
[11] The analytical sample of the glassy solid gained weight noticeably as it was being weighed.

crude mixture obtained by the two routes exhibited identical IR, UV, and NMR spectra, optical rotations, and thin-layer chromatograms.

Chromatography of the mixture obtained by ethanol treatment of the product from irradiation of $\Delta^{3,5}$-cholestadiene in pentane on activity III neutral alumina readily separated the ether II in 60% yield, and a new ether, III ($C_{29}H_{50}O$, m.p. 63-65°, $[\alpha]_D$-48.7°) in 15% yield. II was identified by comparison with an authentic sample prepared by direct irradiation of $\Delta^{3,5}$-cholestadiene in ethanol,[6] and III was identified as 3α-hydroxymethyl-Δ^5-A-norcholestene ethyl ether by comparison with a sample prepared by the action of ethyl tosylate on the sodium salt of the known 3α-hydroxymethyl-Δ^5-A-norcholestene.[6] Re-examination of the mixture obtained from direct irradiation of the diene in ethanol resulted in the isolation of the A-nor ether III in about the same yield, and the two homoallylic isomers have been shown not to be interconvertible under the conditions used for formation and isolation.

The above evidence indicates that $\Delta^{3,5}$-cholestadiene is converted by ultraviolet irradiation primarily to a monomeric, saturated hydrocarbon which contains neither cyclopropyl methylene groups nor oxygen functions and which readily undergoes net 1,3 and 1,1 addition of ethanol in the dark. The only structure which we believe can meet such requirements is a 3,5-4,6-*bis*-*cyclo*steroid as IV.



IV

The only data which have been obtained to date which may argue against such a structure are the absorption due to about 0.6 vinyl protons in the NMR spectrum and the magnitude of the end absorption in the ultraviolet. It must be recalled, however, that the apparent molecular weight indicates the presence of 18 ±7% of a dimer. The dimer may well be of the same type as one formed from fluorescein-sensitized irradiation of $\Delta^{3,5}$-cholestadiene, namely, a <u>bis</u>-$\Delta^{2,5}$-steroid.[12] Such a compound contains three vinyl protons per equivalent, and 18 ±7% of such a compound would contribute 0.5 ±0.2 vinyl protons to the NMR spectrum of a mixture, a value in agreement with the observed 0.6 ±0.1. Based on the ultraviolet spectra of Δ^{2}- and Δ^{5}-cholestene,[13] such a <u>bis</u>-steroid would have an extinction coefficient of about 11,000 at 200 mμ, and 18 ±7% of the dimer should contribute between 1200-2700 to the extinction of the photo-mixture at this wavelength. If IV has an ε of 2300-3700, it could readily account for the 1800-3300 residual absorption, and such a molar extinction is not

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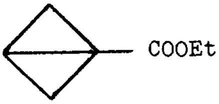
[12] J. L. Owades, <u>Experientia</u> 6, 258 (1960).

[13] R. A. Micheli and T. H. Applewhite, <u>J. Org. Chem.</u> 27, 345 (1962).

unexpected, since the related tricyclo[4.1.0.0.^{2,7}]heptane (V), a bicyclobutane possessing less strain and fewer substituents than IV, has ϵ_{200} 1320.[14]

The differences in reactivity of the bicyclobutane system represented by IV in comparison to V and VI[15] may be rationalized on the basis of the greater strain energy present in IV which is introduced by fusion of the ring system into a steroid molecule.

V



VI

Since the addition of solvent to irradiated $\Delta^{3,5}$-cholestadiene occurs as a dark reaction of a species in the ground electronic state, the earlier concern about the lifetime of the excited state in relationship to a bimolecular reaction is no longer present. It still remains to reconcile 1,3-bond formation with the prediction of simple molecular orbital theory that such an interaction is prohibited. It may be that the electronically excited molecule, after undergoing a number of vibrations, attains a geometrical configuration such that the original wave functions are modified to permit 1,3 bonding.

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[14] W. R. Moore, H. R. Ward, and R. F. Merritt, J. Am. Chem. Soc. 83, 2019 (1961).

[15] K. B. Wiberg and R. P. Ciula, J. Am. Chem. Soc. **81**, 5261 (1959).