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SPECIFICITY IN PHOTOCHEMICAL CYCLOADDITIONS

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The photodimers obtained from a variety of 4,6-diene-3-ketosteroids have recently (1,2) been assigned the structure I (or II) involving addition of the α,β-double bond of one monomer unit to the γ, δ-double bond of a second. In spite of the reversibility of these reactions and the fact that they occur in homogeneous solution, only one of the twenty possible dimers (2) has been observed. The behaviour of 3,5-diene-7-ketosteroids has now been examined in order to determine if the observed specificity and mode of dimerization represent a characteristic property of heteroannular dienones or resulted from the specific environment of the chromophore in the cases investigated previously.

Irradiation (3) of ethyl acetate solutions of $\Delta^{3,5}$-androstadiene-7,17-dione (III) resulted in crystallization of a single dimeric product, VI, (4) m.p. 263-4°, (88% yield) which reverted to III upon heating above its melting point[b]. VI was also obtained, to the exclusion of any other

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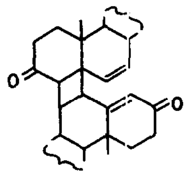
[a] National Science Foundation Summer Fellow, 1963

[b] This thermal reversal excludes the possibility of photochemical epimerization at C-13 or other reactions involving the 17-ketone.



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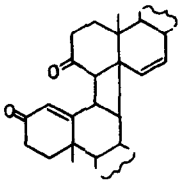

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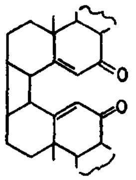

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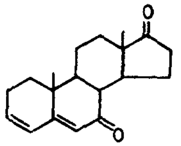

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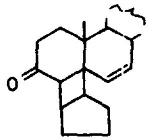

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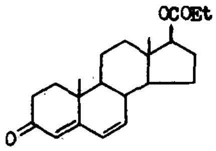

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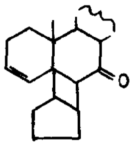

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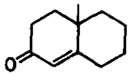

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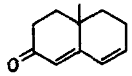

X

dimeric products, by irradiation of benzene solutions of III which remained homogeneous throughout irradiation. Under similar conditions, VI was converted to III, establishing the photochemical reversibility of this cycloaddition also. The structure assigned to VI[c], resulting from cyclobutane formation between the γ, σ-double bonds of two molecules of III, was established by the presence of two olefinic protons in the n.m.r. (singlet, 4.01τ), two conjugated carbonyl groups (6.02 μ; 248 mμ (24,200)), and the cyclopentanone carbonyls (5.75 μ). Products of structure analogous to VI were obtained from $\Delta^{3,5}$-androstadiene-7-one-17β-ol acetate (IV) and $\Delta^{3,5}$-cholestadiene-7-one (V). In all cases only a single dimeric product could be isolated.

Clearly, the mode of dimerization of these heteroannular dienones

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c. The head-to-tail isomer is, a priori, an equally likely possibility giving rise to a total of four possible isomers.

(and possibly the specificity as well) must be due to the specific environment of the chromophore in the two types of systems. Since the concentration of photoexcited molecules must be small relative to the concentration of ground (electronic) state molecules in these reactions (0.1 M solutions), it seems reasonable to assume that the dimerization process involves one molecule in each state. The "unsymmetrical" nature of I (or II) allows a distinction as to which are the reacting bonds in the two states. Evidence on this point was provided by irradiation of $\Delta^{4,6}$-androstadiene-3-one-17β-ol propionate (VII) in benzene-cyclopentene solution (5) which afforded a 1:1 adduct, 4,5-(6',7'-bicyclo[3,2,0]heptano)-Δ^{6}-androstene-3-one-17β-ol propionate (VIII), m.p. 164-5°, (70% yield), which reverted to VII upon heating above its melting point. The structure assigned to VIII was consistent with the presence of unconjugated carbonyl groups (5.77-5.81 μ; 285 mμ (125)) and two olefinic protons (doublets 4.08[d], 4.31 τ (J_{AB} = 10 cps.)). Assuming that the mechanisms of dimerization and cyclopentene addition are similar (5), it would appear that the dimerization of 4,6-diene-3-ones involves addition of the α, β-double bond of a photoexcited molecule to the less hindered γ, δ-double bond of a ground state molecule[e].

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d. This doublet exhibited secondary splitting, J = 2 cps.

e. Addition at the γ,δ-double bond of VII might also be predicted if the reacting site in the excited species possessed appreciable anionoid character. However, recent evidence suggests (6) that the excited species in photochemical reactions of homoannular dienones has negative character localized on oxygen and positive character distributed through the conjugated system of the carbon skeleton.

A similar experiment with V in benzene-cyclopentene solution did not yield the product of addition to the γ,δ-double bond which would have been predicted on the basis of the dimerization of V. Instead, the single 1:1 adduct obtained, 5,6-(6',7'-bicyclo[3,2,0]heptano)-Δ^3-cholestene-7-one (IX), m.p. 116-8°, was the product of addition at the α,β-double bond of V as shown by the absence of conjugation (5.83 μ, 290 mμ (110)) and the presence of two olefinic protons (doublets, 4.17, 4.51 τ (J_{AB}= 10 cps.)). Like the other cyclobutane derivatives obtained in this work, IX reverted to V upon heating above its melting point.

These results can be accomodated by the assumption that steric hindrance plays a determining role in these photochemical cycloadditions, completely hindering addition of a second bulky steroid to the α,β-double bond of V but still allowing the smaller cyclopentene molecule to approach this apparently preferred site[f]. A more detailed interpretation requires knowledge of the stereochemistry of the various photoproducts which is not presently available. Attempts to investigate the reactions of hetero-annular dienones in simpler systems which might be more readily amenable to stereochemical studies have not been fruitful. For example, irradiation of 9-methyl-6-dehydro-Δ^4-3-octalone (X) afforded no dimeric product; only non-crystalline material of high molecular weight being obtained. Similar observations have been made by Butenandt et al. (7) and confirmed in this work in the photoirradiation of the 9-methyloctalone XI which afforded uncharacterized, high molecular weight products (even with careful exclusion

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f. Support for this view was provided by the observation that both cyclopentene additions and dimerizations of 3,5-diene-7-ketones were appreciably slower than the corresponding reactions of 4,6-diene-3-ketones.

of oxygen) in contrast to analogous Δ^4-3-ketosteroids (7) which readily afford photodimers.

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(2) M. B. Rubin, G. E. Hipps, and D. Glover, J. Org. Chem., **29**, 68 (1964).

(3) Reactions were performed in a nitrogen atmosphere in pyrex vessels using a high pressure mercury vapor lamp as the light source.

(4) Satisfactory molecular weights and elemental analyses were obtained for the new compounds described.

(5) This experiment was suggested by the report of P. E. Eaton, J. Am. Chem. Soc., **84**, 2454 (1962) that irradiation of cyclopentenone in cyclopentene solution leads to formation of the cyclobutane derivate, cis, trans, cis-tricyclo[5.3.0.0^{2,6}]decane-3-one. No products which might have arisen by energy transfer from photoexcited ketone to cyclopentene were detected. The use of benzene-cyclopentene mixtures in the experiments described in this work was dictated by solubility considerations. The photodimerization of cyclopentenone afforded two of the four possible dimers of the cyclobutane type.

(6) O. L. Chapman and L. F. Englert, J. Am. Chem. Soc., **85**, 3028 (1963); M. H. Fisch and J. H. Richards, Ibid., **85**, 3029 (1963).

(7) A. Butenandt, L. Poschmann, G. Failer, U. Schiedt, and E. Biekert, Ann., **575**, 123 (1951).