ON PHOTOCHEMICAL TRANSFORMATIONS OF STEROIDS

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ABSTRACT

Some of the photochemical reactions of steroids which the authors have been investigating during the past years are reviewed. Emphasis is placed on light-induced substitutions, eliminations, and rearrangements which in view of their high selectivity and chemical yields are of preparative utility.

INTRODUCTION

Extensive work directed towards the synthesis of steroids with functionalized angular methyl groups, formed part of the foremost efforts in steroid chemistry in the mid 1950's. Special attention was focused on finding laboratory routes to the difficultly accessible hormone aldosterone which bears a C-18 aldehyde function. As an alternative to total syntheses or partial degradation and reconstruction of the ring system (of ring D in steroids and of ring E in conessine, in particular), methods allowing direct and selective substitution of the 'non-activated' angular methyl groups appeared worthwhile for the investigation (as synthetic short-cuts). For this purpose functional groups at easily accessible positions of the steroid skeleton had to be chosen that were both capable of attacking non-activated alkane hydrogens, and assured selectivity owing to their sterically suitable location relative to the envisaged site of attack. This general concept of selective functionalization by use of intramolecular reactions, as advocated by us in the years 1958–1960†‡, was not new at the time. However, it had not been exploited systematically in complex molecules and it represented a challenging problem for synthetic organic chemistry during that period. Accordingly, other researchers had recognized this concept as a promising approach and made important contributions by the application of known processes and of novel reactions within this frame. Special mention be made of Professors D. H. R. Barton and E. J. Corey and their coworkers for pioneering work, and of the groups at CIBA, Schering, and Syntex, for perfection and extension of such achievements‡.

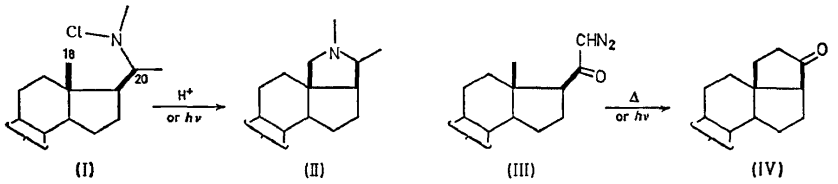
As a brief recapitulation, the first successful efforts at ETH in this field may be summarized here. The first functionalizations of methyl group 18 were achieved by acid-catalyzed transformation of a 20-chloramino derivative (I→II; Hofman–Löffler–Freytag reaction)§,[3] and by pyrolytic[5] and photolytic[6] decomposition of

†Lectures by O. Jeger at, *e.g.*, the Chemical Society, Zürich; CIBA Ltd., Basle; and the Imperial College of Science and Technology, London

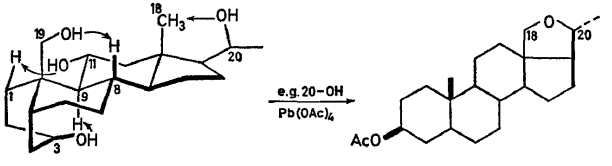
‡For reviews see, *e.g.*, Schaffner, Arigoni, and Jeger[1], on the early efforts in this field, and Heusler and Kalvoda[2] for a more recent comprehensive coverage.

§An analoguos photochemical transformation was reported simultaneously by Corey[4].

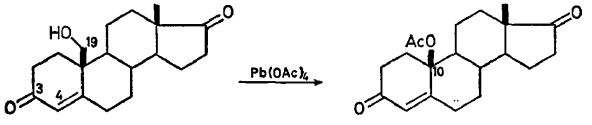
diazoketones of type III which furnished, though in unsatisfactory yields, cyclopentanones (IV). A smooth method for direct substitution by oxygen in frequently high product yields became available when it was found that lead tetraacetate oxidation of monohydric alcohols results in the ready formation of cyclic ethers[7]. In formula (V) a choice of specific examples of such intramolecular cyclizations is indicated. In certain cases of lead tetraacetate oxidation, fragmentations may compete successfully with intramolecular oxide formation. Occasionally as with the transformation of Δ^4-3-oxo-19-alcohols to 10β-acetoxy-19-nor compounds (VI → VII)[8], practically quantitative yields of fragmentation products can be obtained.



(I) (II) (III) (IV)



(V)



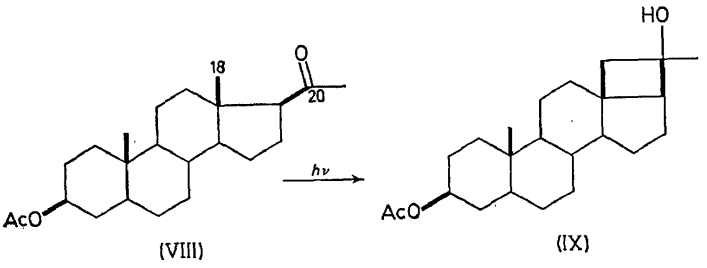
(VI) (VII)

PHOTOCHEMICAL CYCLIZATION OF 20- AND 11-OXO STEROIDS

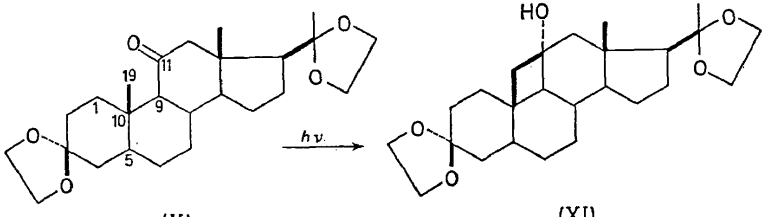
At the dawn of what is sometimes called the Renaissance of Organic Photochemistry, it was an attractive venture to test the applicability of photochemically induced intramolecular reactions of the general type discussed above in complex molecules. In view of the high energies absorbed by a chromophore group it appeared questionable at that time, whether direct photochemical substitution reactions could be achieved which would compare favourably with the selectivity and preparative yields obtainable by ground state processes. That such was indeed the case could be demonstrated by the t-cyclobutanol formation upon ultraviolet irradiation of 20- and 11-oxo steroids (cf. VIII→IX [9,10] and X → XI [11]).

The cyclizations of the 11-oxo series (5α, 5β, and $\Delta^{5,6}$) exhibit a particularly interesting feature of selectivity. The reaction is initiated by the abstraction of a hydrogen by the carbonyl oxygen in the n,π^* excited state, and most likely by its electron-deficient non-bonding p orbital which should be localized mainly in the carbonyl plane. The hydrogens at the two positions within reach of the oxygen (CH_2-1 and CH_3-19) are above and below this plane by about equal margins. Surprizingly, then, a primary methyl hydro-

gen is abstracted selectively. While the ring strain which would be introduced by cyclobutanol formation upon an attack at the alternative position CH_2-1 should be more severe than in the actual case observed (attack at CH_3-19), the process could have been expected to result in a fragmentation of the 9,10-bond (Norrish type II process). In search for the factor(s) directing this selectivity our attention is presently focused on the hypothesis that the excited carbonyl group is non-planar and bends preferably 'upwards' approaching the axial 11β-configuration.†



(VIII) (IX)



(X) (XI)

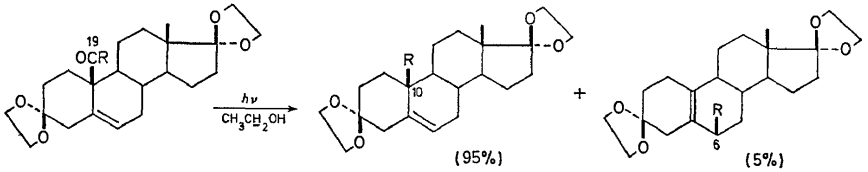
The successful application of this type of ketone photochemistry to highly selective steroid transformations (which in the above case led to a ready access to, e.g., 19-hydroxy-11-ketones on fragmentation of the t-cyclobutanols by lead tetraacetate oxidation) encouraged the search for other photochemical reactions as the key steps in synthetic steroid chemistry.

PHOTOCHEMICAL DECARBONYLATION OF Δ^5-UNSATURATED 19-ALDEHYDES

An essentially quantitative reaction was found on the irradiation of Δ^5-unsaturated 19-aldehydes (XII) which decarbonylate neatly to a ~19:1 mixture of the double bond isomers (XIV) and (XVI)[12]. The reaction is largely insensitive to the nature of solvents used. The corresponding deutero-aldehyde (XIII) yields, despite the use of ehtnaol—a relatively efficient hydrogen donor—as a solvent, the fully deuterated product (XV) and the

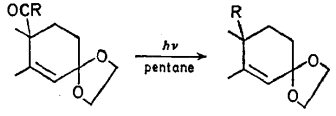
† Note ref. 43 for the equally selective hydrogen abstraction from CH_3-19 in 11-oxolanostanol. The photochemical *t*-cyclobutanol formation of this triterpenoid analogue of (X) does *not* deviate from the reaction course in the steroids as has been assumed previously[44] on the basis of erroneous claims in the literature.

minor isomer (XVII) with still 90 per cent of the original isotope content. A more detailed investigation[13] disclosed that this photodecarbonylation is a unimolecular excited singlet state process of high quantum efficiency. It is a quite general reaction for β-unsaturated (including cyclic and aliphatic β-aryl) aldehydes which show appreciable conjugation attributable to the overlap of the olefinic or aromatic π orbital with both the non-bonding p and the anti-bonding π^* orbitals of the carbonyl group. From the extensive work on this particular reaction, only one additional example be mentioned briefly. Compound (XVIII) approximates a monocyclic



(XII) R=H ..... (XIV) R=H
(XIII) R=D ..... (XV) R=D (100%)

(XVI) R=H
(XVII) R=D (90%)



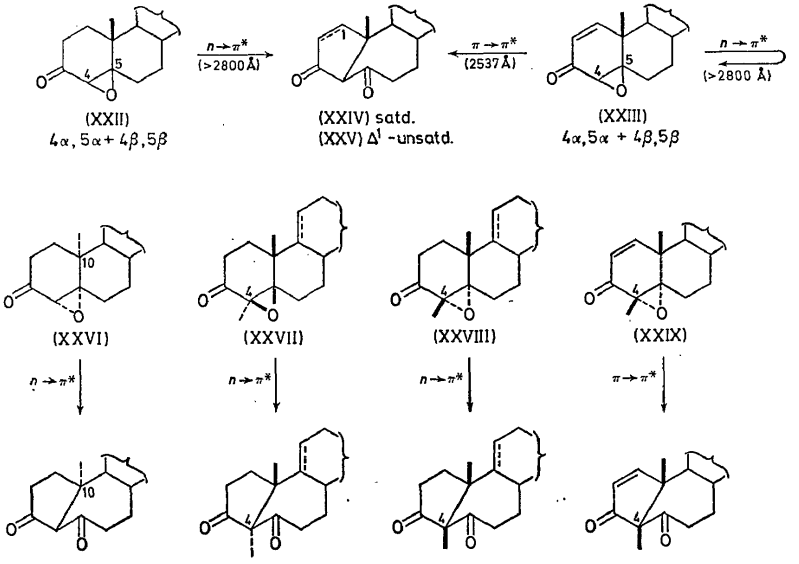
(XVIII) R=H
(XIX) R=D

(XX) R=H
(XXI) R=D (91%)

model of the steroidal aldehyde (XII). Smooth transformation of (XVIII) to (XX) is observed in t-butanol, pentane, and 1,3-pentadiene solutions, without significant differences of the respective rates of conversion. The decarbonylation of the deuteroaldehyde (XIX) to (XXI) in pentane is accompanied by the incorporation of 9 per cent hydrogen, which amount increases to 21 per cent if the reaction is carried out in the presence of about 2 M tri-*n*-butyl stannane. It is to be noted that here no double bond shift as in (XII) → (XVI) was detectable. Also, ethanol is a generally less efficient hydrogen donor in (XIII) → (XV) + (XVII) than pentane is in (XIX) → (XXI), and the difference between 9 and 21 per cent of external hydrogen addition does not at all correspond to the difference in inherent hydrogen donating capacity between pentane and stannane, an especially efficient hydrogen donor. One may conclude, therefore, that the intramolecular hydrogen transfer to the α- and γ-positions depends on the extent to which the formyl group is held rigidly in an axial position relative to the unsaturated ring moiety [the cyclohexene derivative (XVIII) is conformationally more mobile than ring B of (XII), and the formyl substituent need not have a strong preference for the axial position].

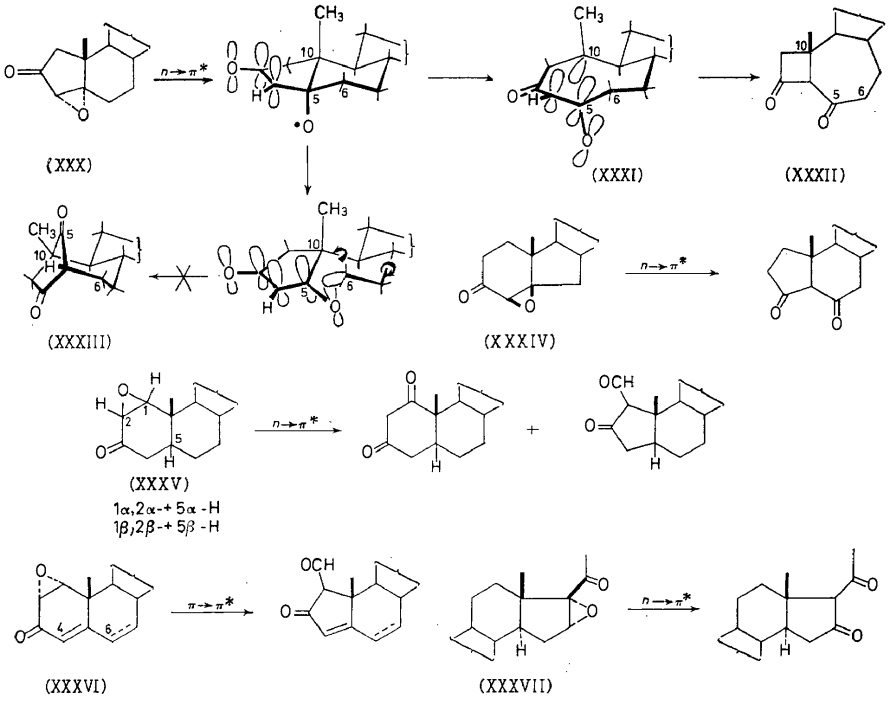
PHOTOCHEMICAL TRANSFORMATIONS WITH α,β-EPOXY-KETONES

Another photoreactive system, the α,β-epoxyketones, proved of considerable synthetic interest[14]. $n \rightarrow \pi^*$ Excitation of the two 4,5-diastereoisomeric testosterone acetate epoxides (XXII) effects a smooth photorearrangement to the enolizable β-diketone (XXIV). Remarkably, neither the analogous reaction nor any other photochemical transformation takes place when the corresponding Δ^1-unsaturated epoxyketones (XXIII) are irradiated in the long-wavelength $n \rightarrow \pi^*$ absorption band. The structurally analogous overall rearrangement (XXIII) → (XXV) is, however, effected on selective $\pi \rightarrow \pi^*$ excitation with 2537 Å light[15]. The rearrangement, i.e. the migration of C-10 from C-5 to C-4, is fully stereospecific. This is documented, e.g., by the results with (XXVI)–(XXIX) which show that the configuration of



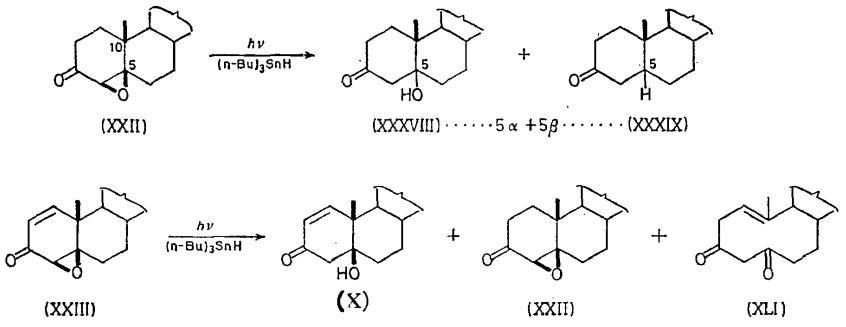
the migrating C-10 is retained and that of C-4 is inverted[16]. A model inspection of the molecular changes involved reveals that subsequent to the homolytic C_α—O oxide bond cleavage (the assumed reversible primary photochemical process) the stereoelectronics of the rearrangement of the intermediate diradical are favourable for a concerted 1,2-alkyl shift maintaining continuous orbital overlap and electron redistribution at the participating centres. Alternative alkyl shifts (e.g., of CH_2-6 from C-5 to C-4, which would result in the formation of a bridged β-diketone) requiring dissociation to free alkyl radicals for structural reasons, are not observed. A particularly informative illustration of this point is furnished by the case of A-nor epoxyketone (XXX) where the concerted migration of C-10 to form the cyclobutanone derivative (XXXII) [cf. transition state (XXXI)] is chosen exclusively rather than dissociation to a free C-6 radical and reclosure to a much less strained bridged diketone (XXXIII).

An extensive study of the epoxyketone photoisomerization revealed its quite general scope. *Inter alia*, a large number of steroidal examples with product yields ranging from 50 to over 90 per cent was reported (for a choice see XXXIV–XXXVII)[14–17].



While hydrogen-donating solvents such as primary and secondary alcohols and ethers do not interfere with the epoxyketone rearrangement, the use of tri-*n*-butylstannane in benzene results in a competitive hydrogen addition, which in the case of (XXII) leads to a mixture of the stereoisomeric hydroxyketones (XXXVIII) and ketones (XXXIX) instead of diketone (XXIV) formation [18,19]. The irradiation of the Δ^1-unsaturated epoxyketone (XXIII) under the same conditions results in an even more complex product mixture which consists mostly of compounds (XXII), (XL), and (XLI). Both the ring cleavage to (XLI) and the partial inversion of configuration at C-5 in (XXXVIII) may be reconciled with postulation of an intermediate 4-alkyl-5-oxydiradical which undergoes (reversible) fragmentation of the 5,10 bond.

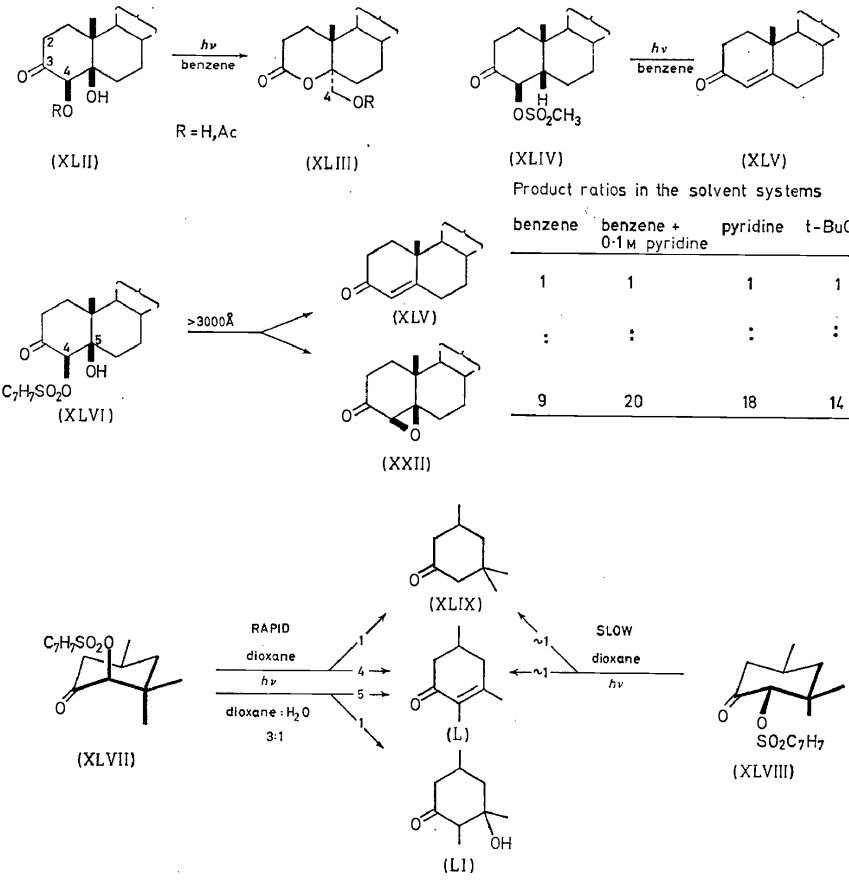
The photolytic cleavage of bonds attached to the α-carbon, as exemplified above by the C_α—O bond cleavage of α,β-epoxyketones, is frequently encountered in ketones possessing electronegative substituents or cyclopropyl groups in the α-position. The reaction has been attributed to a π^*-assisted process of the n,π^*-excited carbonyl group[20]. In fact, the antibonding orbital may in some cases extend to the single bond attaching the leaving substituent or atom[19]. The following examples serve to demonstrate that the competition



between different modes of primary photochemical processes may be controlled to a high degree by the nature of α-substituents and eventually be used to conduct highly selective transformations in excellent preparative yields. On irradiation in benzene solution, α,β-dihydroxy- and α-acetoxy-β-hydroxyketones of type (XLII) are readily isomerized to the corresponding hydroxy and acetoxy lactones (XLIII) in 81 per cent and 87 per cent yields, respectively[21]. The molecular mechanism responsible for these reactions is obviously an α-cleavage between C-3 and C-4, followed by an intramolecular hydrogen transfer from C-2 to C-4 to form a hydroxymethyl group and a ketene which subsequently lactonizes with the angular hydroxy group. When, however, the α-hydroxy group of the starting material is esterified with a sulphonic acid, photolytic elimination processes predominate to the exclusion of the α-cleavage. Thus, (XLVI) yields a mixture of epoxyketone (XXII) and of unsaturated ketone (XLV). The ratio of the two products depends to some extent on the polarity of the solvent used in the irradiation.† This observation is in accordance with the proposal[21] that the product formations (XLVI) → (XLV) and (XLVI) → (XXII) are indicative of two competing photochemical pathways: on one hand, a homolytic C_α—O fission resulting in the expulsion of tosyloxy radical from C-4 and, subsequently, of hydroxy radical from C-5 and in the formation of enone (XLV), and on the other hand, a heterolytic elimination of tosylate anion, followed by cyclization of the resulting 5-hydroxy-4-carbonium ion and deprotonation to the epoxyketone (XXII). While the photolysis of (XLVI) is thus primarily of mechanistic interest, irradiation of simple α-sulphonyloxyketones such as (XLIV) yield the corresponding enone (XLV) in preparative yields of over 80 per cent.

A direct proof of the existence of a keto-carbonium ion intermediate as well as information pertaining to the importance of steric criteria for the photoreaction were obtained with the monocyclic compounds (XLVII) and (XLVIII)[22]. On irradiation in dry dioxane solution, (XLVII) was converted rapidly to a 1:4 mixture of the unsaturated ketone (XLIX) and the rearranged enone (LI), respectively. The formation of (XLIX) is possibly

†The β-diketone (XXIV) is formed as a third photoproduct on irradiation of (XLVI). It has not yet been established whether it originates in part directly from the photolysis of (XLVI) or solely from a subsequent photoisomerization of the epoxyketone (XXII). In the above product ratios the yields of compound (XXIV) are included in those of (XXII).



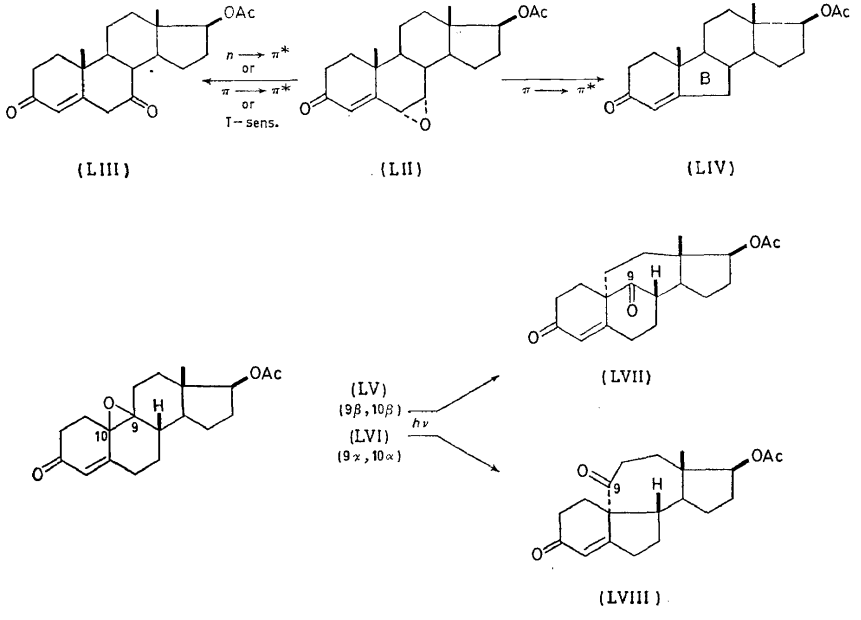
Product ratios in the solvent systems

benzene	benzene + 0·1 M pyridine	pyridine	t-BuOH
1	1	1	1
:	:	:	:
9	20	18	14

due to hydrogen abstraction by the carbonyl oxygen from the solvent and the subsequent elimination of the α-substituent from the ketyl radical. The transformation to the rearranged enone, however, results obviously from a direct sulphonyloxy elimination to an intermediate which is capable of undergoing a 1,2 methyl shift and form enone (L). That indeed at least part of this primary product is a keto-carbonium ion follows from the irradiation of (XLVII) in aqueous dioxane where, after the rapid methyl migration, the precursor of (L) is trapped by hydration to give hydroxyketone (LI) at the expense of (L). Contrary to the relatively rapid phototransformation of the axial sulphonyloxyketone (XLVII), the equatorial isomer (XLVIII) reacted only very slowly in dry dioxane to a 1:1 mixture of (XLIX) and (L). This decrease in efficiency conforms with the model of a π^*-assisted cleavage mode which should be sterically optimal if axial σ-bonds are broken, and unfavourable if equatorial bonds are involved.

A considerable array of diverse phototransformations has been observed with α,β-unsaturated ketones. One of these types of reaction includes the cleavage of a bond attached to the γ-carbon of the enone system and consti-

tutes a formal double-bond homologous extension of the cleavage discussed above for saturated ketones. Quite a close analogy to the rearrangement of saturated α,β-epoxyketones is provided by the almost quantitative isomerization of the α,β-unsaturated γ,δ-epoxyketone (LII) to the ene-dione (LIII) on irradiation in the $n\rightarrow\pi^*$ band with light above 3100 Å or on sensitization using acetophenone[14, 23]. The triplet energy of (LII) (*ca.* 55 kcal/mole) is considerably lower than that of similar cyclohexenones† and the triplet conversion (LII) → (LIII) is therefore not affected by the addition of 1,3-pentadiene and naphthalene which act efficiently as triplet quenchers in the case of testosterone acetate (XLV, see below). When the irradiation of (LII) is carried out with monochromatic light of 2537 Å, also B-nortestosterone acetate (LIV) is formed in about 30 per cent yield in addition to (LIII). This result opened the hitherto best synthetic approach to (LIV), and constitutes yet another specifically $\pi\rightarrow\pi^*$-induced reaction of an enone. A search for possible intermediates participating in the reaction path (LII) → (LIV) has failed until now to provide mechanistic information.



An investigation of the two unsaturated epoxyketones (LV) and (LVI) shows that each diastereoisomer is converted specifically to one ene-dione,‡

†See reference 24 for, e.g., testosterone acetate (XLV).

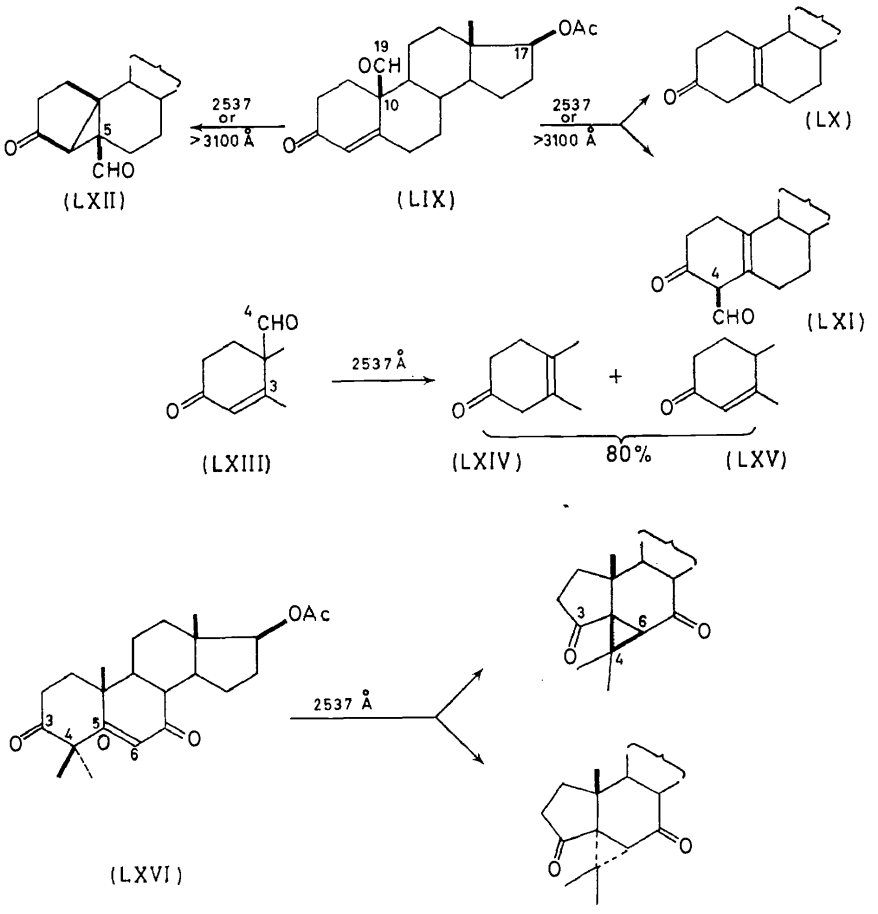
‡ More recent results show that the 9β,10β-epoxyketone (LV) rearranges in fact to *two* photoisomers, i.e. (LVII) and the 10α-stereoisomer of (LVIII) which conforms equally well to the structural restrictions imposed by the reaction mechanism discussed above.

(LVII) and (LVIII), respectively. The result confirms that these rearrangements follow a basically analogous course as the $\delta \rightarrow \gamma$ hydrogen shift in (LII) → (LIII), and that they are subject to a stereospecific control similar to that encountered with the transformations of epoxyketones (XXVII)–(XXIX). It is possible, therefore, to predict product structures on this basis[25].

The photochemical behaviour of the α,β-unsaturated γ-aldehydoketone (LIX) is less specific[26]. In fact two primary processes have been found to occur when the conjugated ketone chromophore is excited with monochromatic light of wavelength 2537 Å. A cleavage process producing an allylic and a formyl radical pair, and a competing rearrangement to the cyclopropyl aldehydoketone (LXII) are observed. Intramolecular recombination of the radical pair leads to the partly enolized isomer (LXI) (formally equivalent to a suprafacial 1,3 formyl migration) and presumably back to starting material as well. Complete dissociation causes decarbonylation to (LX) after uptake of a hydrogen atom from the medium by the intermediate allyl radical. The second primary photoreaction can be formulated as a bonding process between the β-carbon of the enone (C-5) and the aldehyde carbon C-19†. Cleavage of the resulting cyclopropyl diradical can either regenerate (LIX) or form (LXII). As a mechanistic alternative, the isomerization (LIX) → (LXII) may be viewed as a concerted orbital symmetry allowed ($\pi^{2a} + \sigma^{2a}$) addition[35]. The two primary processes, responsible for (LIX) → (LX) + (LXI) and (LIX) → (LXII), respectively, can be quenched by naphthalene in solid solution at 77°K. At room temperature in liquid solution, however, they proceed too rapidly to allow diffusion controlled triplet quenching. An experimental distinction between the two processes was possible on the basis of differential isotope effects using the 17,19-dideutero (LIX). The photolysis of the monocyclic analogue (LXIII) furnishes in about 8 per cent yield the decarbonylation products (LXIV) and (LXV)[28]. A plausible rationalization for the almost exclusive occurrence of the dissociative reaction mode is available if one resorts to a similar explanation as was considered above to account for the reactivity differences between (XII) and (XVIII). Owing to the greater conformational flexibility of (LXIII), the formyl group is not fixed rigidly in the axial position as it is in the steroid molecule (LIX). Concurrently, the disposition for an intramolecular 1,3 formyl shift on radical fission on one hand, and for 3,4′-bonding on the other hand, would be sterically less stringent.

A rearrangement, which is formally analogous to (LIX) → (LXII), is observed when the α,β-unsaturated δ-diketone (LXVI) is excited to the triplet state [including selective irradiations in the enone $\pi \rightarrow \pi^*$ (2537 Å) and $n \rightarrow \pi^*$ (3660 Å) absorption bands]. The rearrangement to the two stereoisomeric cyclopropyldiketones can be quenched entirely by 0·5 M naphthalene. Selective labelling of the 4α-methyl group (CD_3) in (LXVI) was used to show that the rearrangement is a stepwise process capable of configurational scrambling of the diastereotopic *gem*-methyls, and that reversible cleavage of the 3,4-bond in (LXVI) is not important. The most

†Analogous bonding between the β-carbon of photoexcited enones and a π-system in the δ-position has been proposed for related rearrangements; see, e.g., the discussion of the photoisomerization of $\Delta^{1,5}$-3-oxo steroids[27].

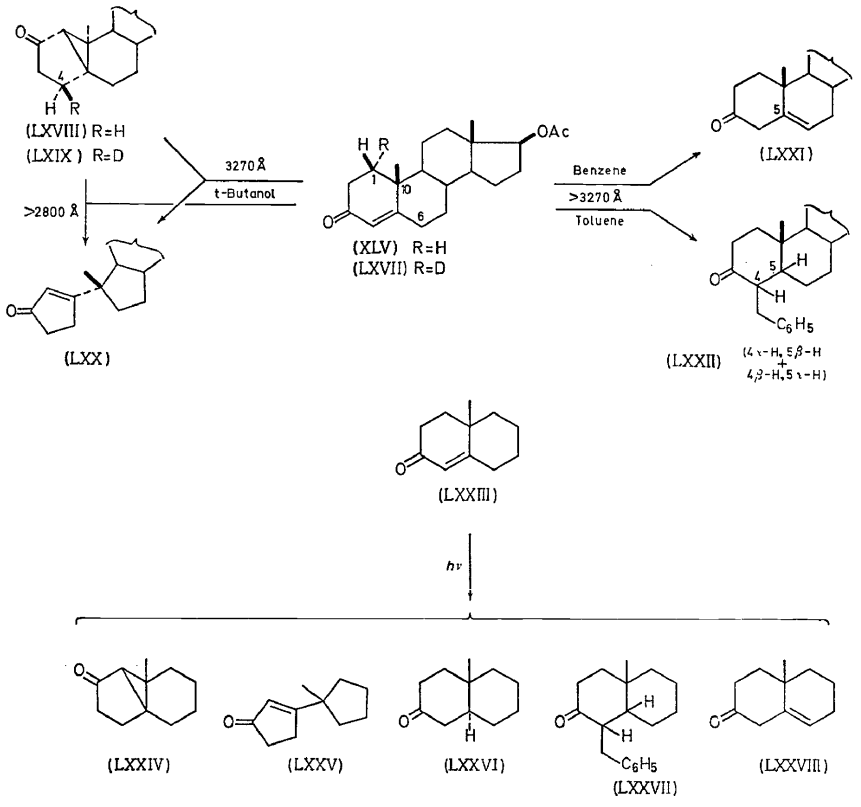


(LXII) (LIX) (LX) (LXI) (LXIII) (LXIV) (LXV) (LXVI)

likely photochemical process is therefore bonding between C-3 and C-5 to form two stereoisomeric 3,5-bridged 3-0,6-diradical intermediates[29].

PHOTOCHEMICAL TRANSFORMATIONS OF STEROIDAL CYCLOHEXENONES

The first example of a cyclohexenone → bicyclo[3.1.0]hexan-2-one rearrangement has been reported by Gardner with cholestenone and, at about the same time, has been elaborated in some more detail with testosterone acetate (XLV) by our group and by Chapman[30,31]. Irradiation in t-butanol using a mercury medium pressure light source and quartz or pyrex filter results in the rearrangements (XLV) → (LXVIII) + (LXX). A more thorough reinvestigation in our laboratory showed recently[32] that in fact a photostationary equilibrium (XLV) $\rightleftarrows$ *hν* $\rightleftarrows$ (LXVIII) is formed which is gradually drained by the isomerization to (LXX). A dramatic change in the photochemical behaviour of (XLV) is observed when t-butanol is replaced by benzene as the solvent. Instead of the above rearrangements the isomeriza-



Solvent	*Product yields*				
	(LXXIV)	(LXXV)	(LXXVI)	(LXXVII)	(LXXVIII)
t-Butanol	80%	*ca.* 5%	3%	—	11%
Isopropanol	31%	*ca.* 3%	35%	—	6%
Toluene	3%	(†)	19%	40%	2%
Benzene	14%	(†)	6%	—	45%

(†) Yields too small for quantitative determination

tion to the β,γ-unsaturated ketone (LXXI) occurs as the virtually exclusive photochemical process. It has been shown that this transformation is due to a bimolecular photoreaction in which the oxygen of an excited enone abstracts a hydrogen from C-6 of a non-excited partner molecule. Yet another almost complete change in products is observed when the irradiation of (XLV) is carried out in toluene solution. The main reaction in this solvent is toluene addition to (LXXII), accompanied to a small extent by double bond migration (→LXXI) and double bond reduction with concomitant formation of dibenzyl. This strong solvent dependence of the photo-transformations of (XLV) provides an interesting tool to direct specifically certain reactions of the same molecule. It is paralleled by the qualitatively

similar but not as exclusive solvent-dependant product formation of the octalone analogue of testosterone, see (LXXIII) → (LXXIV) — (LXXVIII).†

The transformations of both (XLV) and (LXVIII) as well as those of the bicyclic series are triplet reactions. Accordingly, they can be quenched completely using naphthalene, dienes, and stilbene at moderate concentrations. Furthermore, sensitization of (XLV) and of (LXXIII) by acetophenone in the corresponding solvents leads to the same product distributions as the direct irradiations. The rearrangements, the double bond reduction, and the toluene addition have been attributed to primary photochemical processes of the π,π^* enone triplet, and the double bond isomerization to an n,π^* triplet reaction. These assignments are based on the observation of differential quenching of the two reaction categories, and on arguments relating to mechanistic implications derived from the two hydrogen abstraction modes (assuming hydrogen abstraction capacity of the oxygen in the n,π^* state, and of the β-carbon in the π,π^* state) and to the specific triplet energy dependence on the solvent nature.

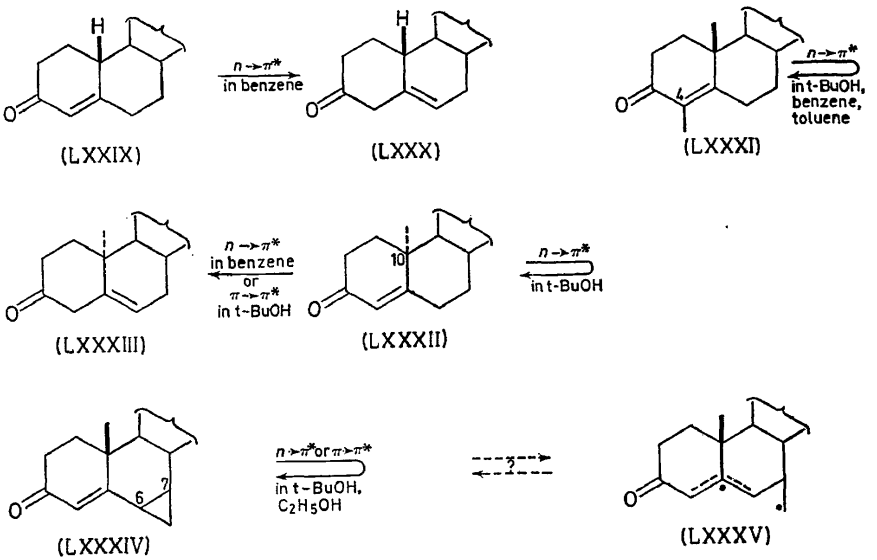
On direct irradiation and on acetophenone sensitization of 1α-deutero testosterone acetate (LXVII) the 4β-deutero cyclopropylketone isomer (LXIX) is formed. This result proves that the rearrangement is stereospecific‡ with retention of configuration at C-1 and inversion at C-10. It excludes the possibility that the (C-10 → C-5)-shift of C-1 proceeds through fission of the 1,10 single bond to a diradical intermediate, but it does not distinguish between a stepwise overall process involving a synchronous 1,2 shift and a subsequent ring closure to cyclopropane, and a concerted $[\sigma^2a + \pi^2a]$ addition which would be in accordance with the Woodward–Hoffmann rules of orbital symmetry conservation for a photoexcited state process[35]. We may note in this connection that the geometry of the enone (XLV) in its π,π^* triplet state, which is most likely non-planar[24], appears to be quite favourable for orbital overlap as required for a concerted process.

Apparently slight changes in the molecular structure of steroidal cyclohexenones can alter their photochemical behaviour drastically. 19-Nortestosterone (LXXIX) is not rearranged to the 19-nor analogue of (LXVIII) on irradiation in t-butanol[36], but in benzene solution it undergoes a ready double bond shift to the $\Delta^{5,6}$-isomer (LXXX) which is prepared only with difficulty using other methods[37]. 4-Methyltestosterone acetate (LXXXI) proved in our hands almost completely photostable when irradiated in t-butanol, in benzene, and in toluene[32].

10α-Testosterone acetate (LXXXII)[38], for the synthesis of which yet another photochemical reaction of high yield (the cross-conjugated cyclohexadienone → bicyclo[3.1.0]hexenone rearrangement[39]) had been applied as the key step, isomerizes readily to (LXXXIII) in benzene solution as do (XLV) and (LXXIX)[40]. In t-butanol, however, (LXXXII) remained essentially photostable when irradiated in its $n \rightarrow \pi^*$ transition. On the other hand, excitation with 2537 Å light in the same solvent results in proton elimination

†Recently, the rearrangement to (LXXIV) to has been reported erroneously to represent the almost exclusive photoreaction of (LXXIII) in *t*-butanol and in benzene[33].

‡The analogous rearrangement of 12-methyl-1,2,3,5,6,12-hexahydrophenanthrone-(3) has been shown to proceed stereospecifically by Chapman[34].



from C-6 in a specifically $\pi \rightarrow \pi^*$ induced process which furnishes again the β,γ-unsaturated ketone (LXXXIII)[40, 41].

PHOTOSTABILIZATION

Photostabilization can be achieved by efficient and entirely reversible photoreactions. The two diastereoisomeric 6,7-methylene testosterone acetates (LXXXIV) may well be examples of such behaviour. Irradiation in either of their two ultraviolet absorption bands and in t-butanol as well as in ethanol does not lead to any detectable molecular change which is quite in contrast to the photochemistry of the lower homologue (XLV)[42]. It has been proposed that this apparent stability is due to a neatly reversible fission of the three-membered ring (cf. LXXXIV $\leftrightharpoons$ LXXXV), which would involve selectively the 'axial' peripheral bond in the γ-position to the enone moiety and would thus also account for the non-interconversion of the two stereoisomers.

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References

[1] K. Schaffner, D. Arigoni, and O. Jeger. *Experientia* **16,** 169 (1960).
[2] K. Heusler and J. Kalvoda. *Angew. Chem.* **76,** 518 (1964); *Angew. Chem.* (*Int. Ed.*) **3,** 525 (1964).

[3] P. Buchschacher, J. Kalvoda, D. Arigoni, and O. Jeger, *J. Am. Chem. Soc.* **80,** 2905 (1958).
[4] E. J. Corey and W. R. Hertler. *J. Am. Chem. Soc.* **80,** 2903 (1958).
[5] F. Greuter, J. Kolvoda, and O. Jeger. *Proc. Chem. Soc.* 349 (1958).
[6] F. Kaplan, K. Schaffner, and O. Jeger. Unpublished results (1960).
[7] G. Cainelli, M. Lj. Mihailović, D. Arigoni, and O. Jeger. *Helv. Chim. Acta* **42,** 1124 (1959), and subsequent papers.
[8] M. Amorosa, L. Caglioti, G. Cainelli, H. Immer, J. Keller, H. Wehrli, M. Lj. Mihailović, K. Schaffner, D. Arigoni, and O. Jeger. *Helv. Chim. Acta* **45,** 2674 (1962).
[9] P. Buchschacher, M. Cereghetti, H. Wehrli, K. Schaffner, and O. Jeger. *Helv. Chim. Acta* **42,** 2122 (1959), and subsequent papers on 20-oxo steroids.
[10] N. C. Yang and D.-D. H. Yang. *Tetrahedron Letters.* No. 4, 10 (1960).
[11] H. Wehrli, M. S. Heller, K. Schaffner, and O. Jeger. *Helv. Chim. Acta* **44,** 2162 (1961), and subsequent papers on 11-oxo steroids.
[12] J. Iriarte, J. Hill, K. Schaffner, and O. Jeger. *Proc. Chem. Soc.* 114 (1963).
J. Hill, J. Iriarte, K. Schaffner, and O. Jeger. *Helv. Chim. Acta* **49,** 292 (1966).
[13] E. Baggiolini, H. P. Hamlow, K. Schaffner, and O. Jeger. *Chimia* **23,** 181 (1969).
E. Baggiolini, H. P. Hamlow, and K. Schaffner. *J. Am. Chem. Soc.* **92,** in press (1970), and H. P. Hamlow, H. Küntzel, H. Wolf, and K. Schaffner. Unpublished results (1965–1970).
[14] Part of the phototransformations of steroidal epoxyketones has been reviewed earlier by O. Jeger, K. Schaffner, and H. Wehrli. *Pure Appl. Chem.* **9,** 555 (1964).
[15] C. Lehmann, K. Schaffner, and O. Jeger. *Helv. Chim. Acta* **45,** 1031 (1962).
H. Wehrli, C. Lehmann, P. Keller, J.-J. Bonet, K. Schaffner, and O. Jeger. *Helv. Chim. Acta* **49,** 2218 (1966).
[16] H. Wehrli, C. Lehmann, K. Schaffner, and O. Jeger. *Helv. Chim. Acta* **47,** 1336 (1964).
H. Wehrli, C. Lehmann, T. Iizuka, K. Schaffner, and O. Jeger. *Helv. Chim. Acta* **50,** 2403 (1967).
[17] J. Pfister, C. Lehmann, and H. Wehrli. *Helv. Chim. Acta* **51,** 1505 (1968).
[18] P. Keller, G. Eggart, H. Wehrli, K. Schaffner, and O. Jeger. *Helv. Chim. Acta* **50,** 2256 (1967).
[19] For a previous review see K. Schaffner. *Pure Appl. Chem.* **16,** 75 (1968).
[20] For discussions see, e.g., H. E. Zimmerman. *Adv. Photochemistry* **1,** 183 (1963).
L. D. Hess, J. L. Jacobson, K. Schaffner, and J. N. Pitts, Jr. *J. Am. Chem. Soc.* **89,** 3684 (1967).
[21] G. Hüppi, G. Eggart, S. Iwasaki, H. Wehrli, K. Schaffner, and O. Jeger. *Helv. Chim. Acta* **49,** 1986 (1966).
A. Tuinman, A. Ghosh, K. Schaffner, and O. Jeger. *Chimia* **23,** 180 (1969).
[22] S. Iwasaki and K. Schaffner. *Helv. Chim. Acta* **51,** 557 (1968).
[23] J. A. Saboz, T. Iizuka, H. Wehrli, K. Schaffner, and O. Jeger. *Helv. Chim. Acta* **51,** 1362 (1968).
[24] G. Marsh, D. H. Kearns and K. Schaffner. *Helv. Chim. Acta* **51,** 1890 (1968).
[25] M. Debono, R. M. Molloy, D. Bauer, T. Iizuka, K. Schaffner, and O. Jeger. *J. Am. Chem. Soc.* **92,** 420 (1970).
[26] D. E. Poel, H. Wehrli, K. Schaffner, and O. Jeger. *Chimia* **20,** 110 (1966).
E. Pfenninger, D. E. Poel, C. Berse, H. Wehrli, K. Schaffner, and O. Jeger. *Helv. Chim. Acta* **51,** 772 (1968).
[27] B. Nann, H. Wehrli, K. Schaffner, and O. Jeger. *Helv. Chim. Acta* **48,** 1680 (1965), and references therein.
[28] H. P. Hamlow, E. Pfenninger, K. Schaffner, and O. Jeger. Unpublished results (1965 and 1969).
[29] S. Domb, G. Bozzato, J. A. Saboz, and K. Schaffner. *Helv. Chim. Acta* **52,** 2436 (1969).
S. Domb and K. Schaffner. *Helv. Chim. Acta* **52,** in press (1970).
B. A. Shoulders, W. W. Kwie, W. Klyne, and P. D. Gardner. *Tetrahedron* **21,** 2973 (1965).
[30] B. Nann, D. Gravel, R. Schorta, H. Wehrli, K. Schaffner, and O. Jeger. *Helv. Chim. Acta* **46,** 2473 (1963).
O. L. Chapman, T. A. Rettig, A. A. Griswold, A. I. Dutton, and P. Fitton. *Tetrahedron Letters* 2049 (1963).
[31] W. W. Kwie, B. A. Shoulders, and P. D. Gardner. *J. Am. Chem. Soc.* **84,** 2268 (1962).
H. Dutler, C. Canter, H. Ryf, E. C. Utzinger, K. Weinberg, K. Schaffner, D. Arigoni, and O. Jeger. *Helv. Chim. Acta* **45,** 2346 (1962), footnote 14.
[32] D. Belluš and K. Schaffner. *Chimia* **23,** 182 (1969).
D. Belluš, D. R. Kearns, and K. Schaffner. *Helv. Chim. Acta* **52,** 971 (1969).
[33] H. E. Zimmerman, R. G. Lewis, J. J. McCullough, A. Padwa, St. W. Staley, and M. Semmelhack. *J. Am. Chem. Soc.* **88,** 1965 (1966)..
[34] O. L. Chapman, J. B. Sieja, and W. J. Welstead, Jr. *J. Am. Chem. Soc.* **88,** 161 (1966).
[35] R. B. Woodward and R. Hoffmann. *Angew. Chem.* **81,** 797 (1969).

[36] M. Maçzka and C. Ganter. Unpublished results (1967). W. G. Dauben, G. W. Shaffer, and N. D. Vietmeyer. *J. Org. Chem.* **33,** 1390 (1968).
[37] H. G. Berscheid, D. Belluš, and K. Schaffner. Unpublished results (1968).
[38] R. Wenger, H. Dutler, H. Wehrli, K. Schaffner, and O. Jeger. *Helv. Chim. Acta* **45,** 2420 (1962).
[39] For a review see K. Schaffner. *Adv. Photochemistry* **4**, 81 (1966).
[40] S. Kuwata and K. Schaffner. *Helv. Chim. Acta.* **52,** 173 (1969).
[41] H. Wehrli, R. Wenger, K. Schaffner, and O. Jeger. *Helv. Chim. Acta* **46,** 678 (1963).
[42] J. Pfister, H. Wehrli, and K. Schaffner. *Helv. Chim. Acta* **50,** 166 (1967).
[43] R. Imhof, W. Graf, H. Wehrli, and K. Schaffner. *Chem. Comm.* 852 (1969).
[44] E. Altenburger, H. Wehrli, and K. Schaffner. *Helv. Chim. Acta* **48**, 704 (1965).