

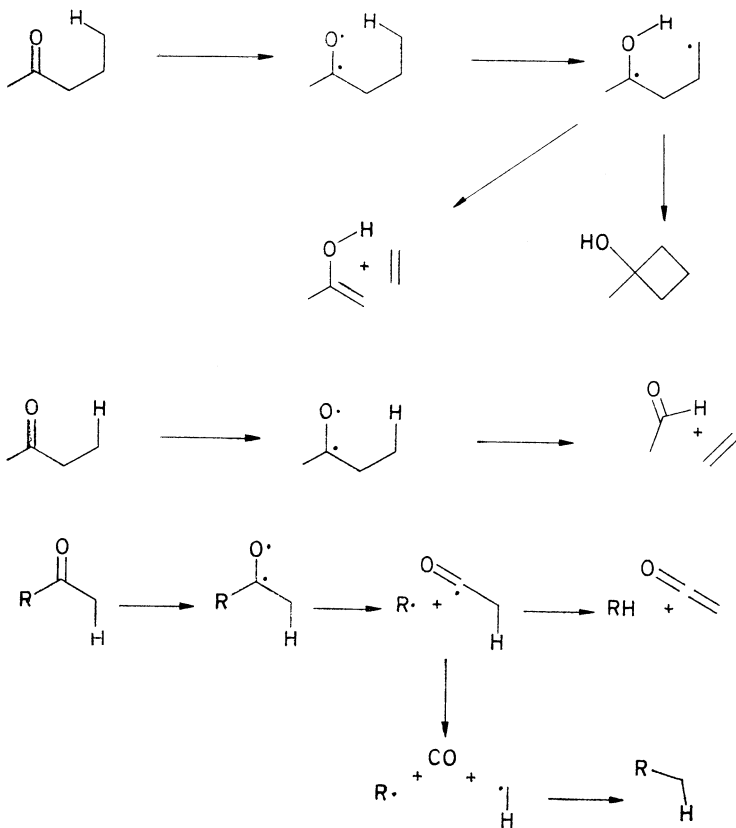
STEREOSPECIFICITY IN PHOTOCHEMICAL REACTIONS OF KETONES

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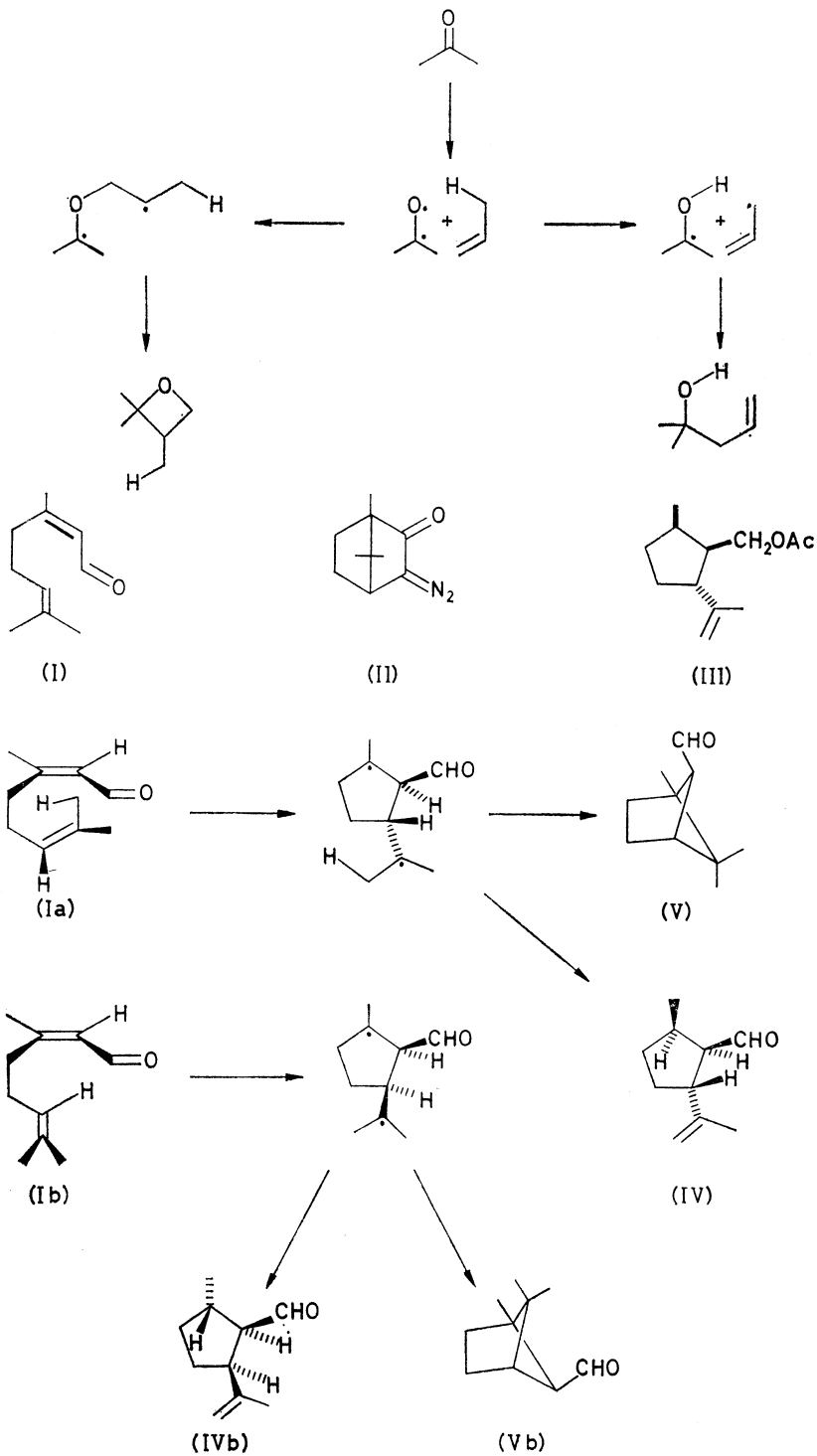
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Some of the more important reactions, not involving rearrangement, that follow $n \rightarrow \pi^*$ excitation of ketones are summarized in the following diagrams. Although in some cases there is no decisive evidence on whether reaction proceeds through the $n - \pi^*$ singlet or triplet state the triplet mechanisms are illustrated, leading to radical intermediates. This mode of reaction is certainly common, if not universal[†].

Isomerization following $n \rightarrow \pi^*$ excitation of citral (I) brings out some



[†] The excited singlet and triplet may react in quite different ways¹, as, of course, may the triplet $n - \pi^*$ and $\pi - \pi^*$ states of conjugated ketones².

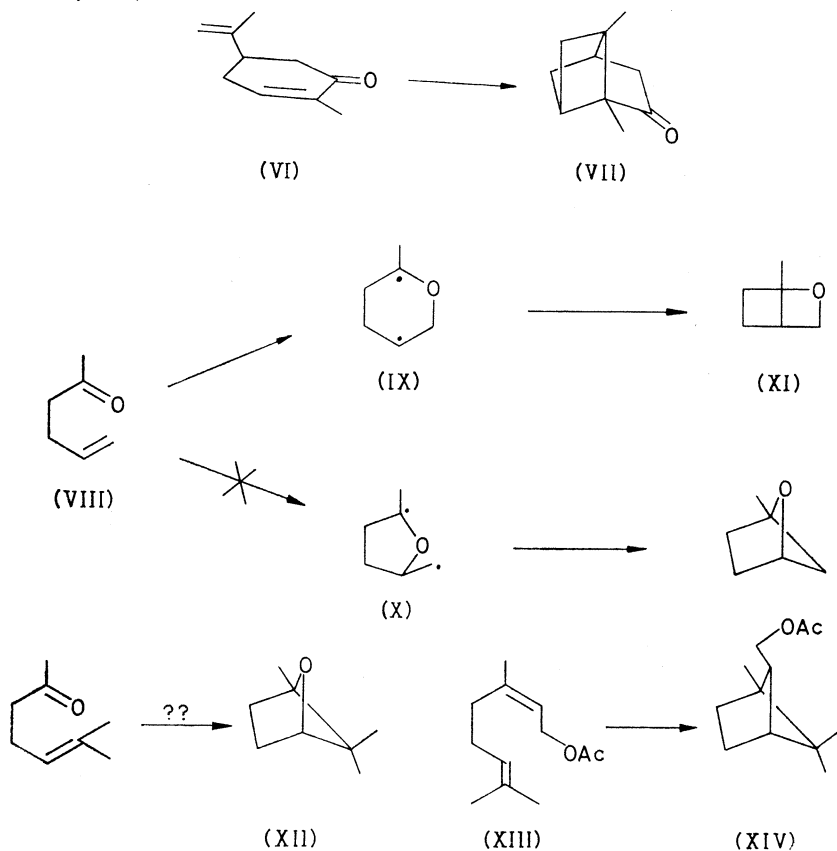


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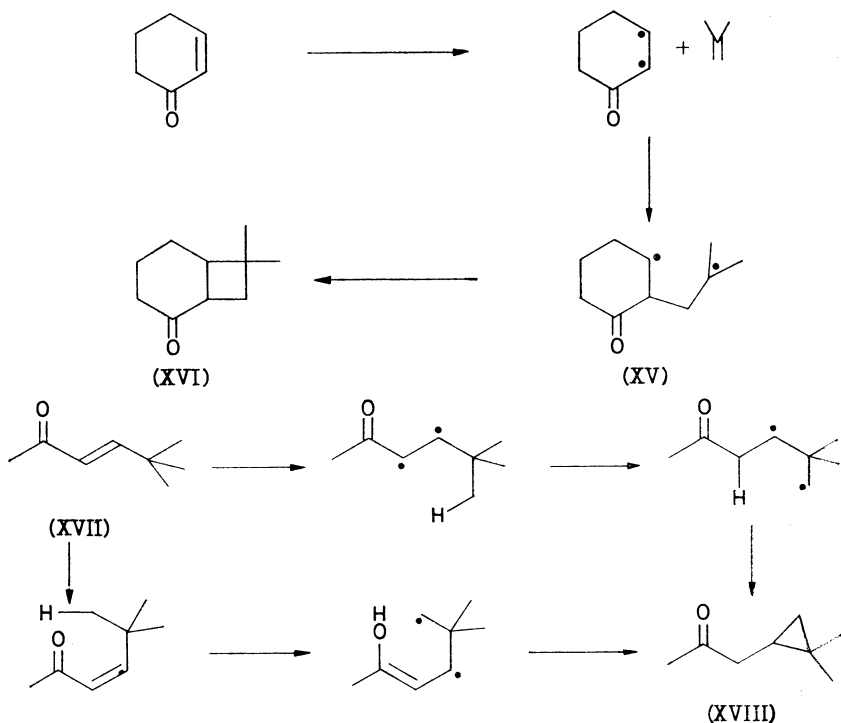
important characteristics in reactions of this kind, and, therefore, this transformation is taken as the starting point of this paper.

The most striking aspect of the reaction is the relation of the stereochemistry of the principal products, photocitral-A(IV) and B(V). The stereochemistry of the latter was established³ by comparison with a sample made *via* ring-contraction of diazo-camphor (II) and the author and his colleagues have recently been able to settle that of the former by comparison of the derived acetate⁴ (III) with samples of all the possible stereoisomers, which have now been synthesized in Dr Wolinsky's laboratory.

Formation of photocitral-B is an example of the familiar intramolecular addition of double bonds to give a cyclobutane⁵, and it is structurally analogous to the conversion of carvone (VI) to carvone-camphor⁶ (VII) (9 per cent yield). On the other hand, the oxygen analogue (VIII) adds the ends of the two double bonds the other way round⁷, to form (XI). If this reaction proceeds through the $n - \pi^*$ triplet the oxygen atom may add to give the more stable diradical (IX not X). The dimethyl derivative for the same reason might then give the analogue (XII) of photocitral-B. 90 per cent of the volatile product from benzophenone-photosensitized cyclization of neryl acetate (XIII) is the acetate of the same stereochemistry in the B-series⁴ (XIV).



Formation of photocitral-A is more unusual. It is a photochemical example of Alder's thermal ene-reaction⁸. While there is no conclusive evidence yet on the mechanism of the reaction, a scheme³ for which there is analogy assumes that the triplet $n - \pi^*$ unsaturated aldehyde group in conformation (Ia) adds to the other double bond to give a diradical that after spin-inversion can either cyclize to photocitral-B (V) or transfer a hydrogen atom to give photocitral-A (IV). On the other hand, conformation (Ib) would give a diradical leading to (Vb) and (IVb), which are not observed. The diradical from (Ib) has the dimethylmethyl radical in an equatorial-like position, which can react further only by rotation into an axial-like conformation, attained directly from (Ia). It is possible that photocitral-A is formed directly from the $n - \pi^*$ singlet state in a concerted reaction: that would also explain the lack of any member of the B-series from photosensitized irradiation of neryl acetate (XIII). On the other hand, it may be formed from a vibrationally excited $n - \pi^*$ triplet which loses its excess energy before it can react further in conformation (Ib); and the prosaic explanation, that *cis*- and *trans*- citral equilibrate and each cyclize to the monocyclic diradical with maximum separation between CHO and the terminal CH₃, still has to be tested. It is hoped that work now going on will clarify these points.



Another reaction in which the orientation of the product seems to be controlled by the addition of the α -carbon atom of an excited ($n - \pi^*$ triplet??) α,β -unsaturated ketone to the less substituted end of an olefinic double bond has recently been reported⁹: the enone thus behaves as a true

vinyllogue of the carbonyl group. Cyclohexenone adds isobutene to give (XVI) with none of the structural isomer. A concerted addition *via* the singlet would, of course, give only the *cis* isomer of (XVI), but addition *via* the triplet (in which the α -carbon is more electrophilic than the β -) forms the diradical (XV) which must last long enough to allow the initially axial side-chain radical to become equatorial. Better orbital-overlap and less steric repulsion then result from closure to the *trans* isomer, the predominant product.

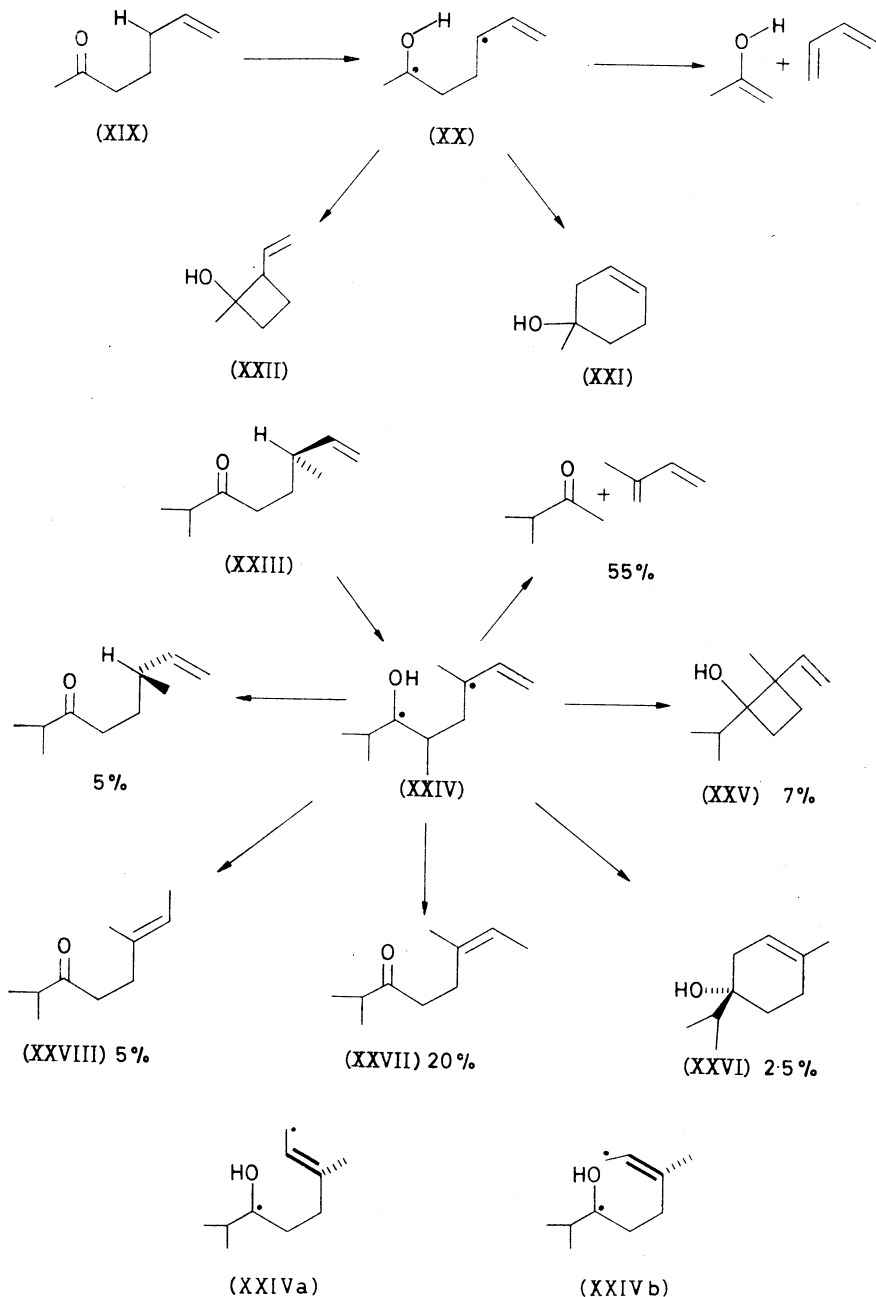
A reaction that appears to involve hydrogen-abstraction by an α -carbon atom is the interesting synthesis of cyclopropanes reported by Yang¹⁰, in which irradiation of (XVII) yields (XVIII). (The alternative mechanism, involving a seven- rather than five-membered cyclic transition state is still possible: intermolecular reaction seems much less likely.)

Another reaction of Yang's that must be mentioned is the photocyclization of the heptenone (XIX) to the cyclohexenol (XXI), for it is another photochemical ene-reaction, the carbonyl group filling the rôle of the α,β -double bond in citral (I). Although some of them may stem from the singlet state, each of the products may arise from the diradical¹¹ (XX) formed from the $n - \pi^*$ triplet. Further insight into this reaction has just been provided by experiments¹² on an optically active derivative (XXIII). Again all the products can be formulated as coming from the diradical (XXIV) derived from the $n - \pi^*$ triplet. However, the stereochemical results (recovered XXIII 76.5 per cent racemized; only one isomer of XXV; XXVI 62 per cent optically pure), especially the higher optical purity of the cyclohexenol (XXVI) after shorter irradiation, lead Schulte-Elte and Ohloff¹² to favour separate one-step, concerted reactions for the formation of (XXVI) and (XXV). This presumably implies direct reaction of the excited singlet state.

In the absence of further evidence that is quite possible, but the products and their stereochemistry can still be interpreted in terms of diradical intermediates, if one stretches the theory to allow that planar allyl radicals are stereochemically stable¹³, so that two separate intermediates (XXIVa) and (XXIVb) may be involved, according to the initial conformation of the triplet ketone (XXIII), and that reversal of electron spin and cyclization can proceed as fast as, or even faster than, rotation about single bonds. If the allyl radicals remain almost planar, (XXIVa), formed from triplet (XXIII) in the conformation where the vinyl group is at right angles to the C—H bond being broken and nearly eclipsing the CH₃ group, can give the cyclobutanol (XXV) but not the cyclohexenol (XXVI) or (XXVII), and hardly (*via* an entirely unstrained intramolecular transfer) (XXVIII) which is formed in only small amounts. On the other hand (XXIVb) with the vinyl group opposed to the CH₂CH₂ chain could give the cyclobutanol (XXV), the cyclohexenol (XXVI), the isomer (XXVII), but not (XXVIII), while maintaining the allyl radical planar. Rotation of the isopropyl group upward and the hydroxyl down in (XXIVb) would produce the cyclohexenol (XXVI): the opposite rotation would pass a conformation that might be diverted by transfer of hydrogen to give (XXVII) before proceeding far enough to produce the epimer of (XXVI).

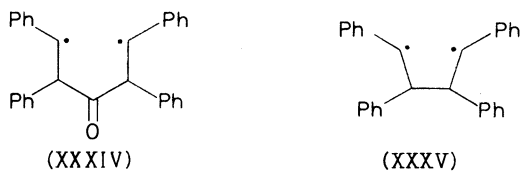
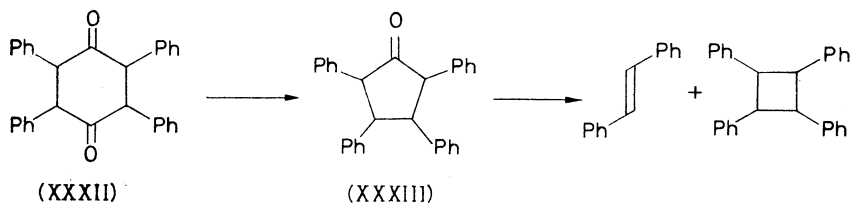
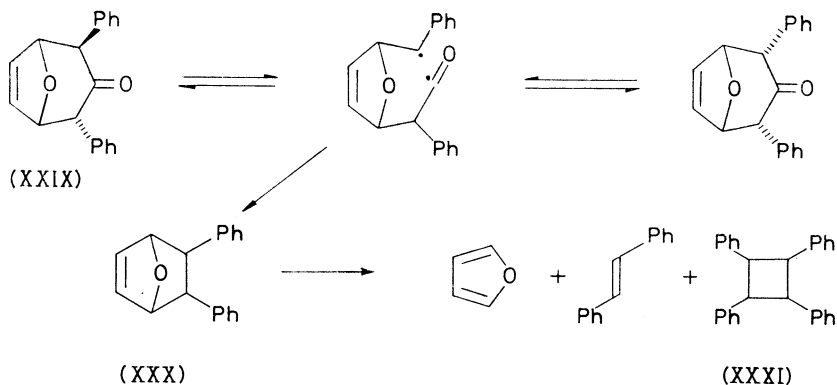
And now, the rest of this paper will discuss some reactions of a quite different class, those in which the bond between the carbonyl group

and the α -carbon atom is broken. This process seems to involve cleavage of the CO—C bond in the triplet to give a diradical that either loses CO to leave two radicals that combine, or undergoes hydrogen-migration to give a ketene¹⁴ (process *A* in the first set of formulae). For



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example¹⁵, irradiation of the α,α' -diphenyl ketone (XXIX) interconverts the two isomers and then leads *via* loss of CO to the unstable intermediate (XXX) that breaks up into furan and stilbene, accompanied by its cyclobutane photo-dimer (XXXI). The reaction takes the same course with the dihydro-derivative of (XXIX) and in the analogue with a CH₂ bridge in place of O, but the decarbonylated products are then, of course, stable. The diketone (XXXII) undergoes decarbonylation to give the monoketone



(XXXIII), *cis* and *trans* stilbene, and the dimer (XXXI). Since irradiation of the monoketone (XXXIII) also yields stilbenes and dimer, it might have been assumed to be an intermediate in their production from the diketone (XXXII). However, the ratio of stilbenes to dimer (about 12:1 from XXIX and XXXII, or from irradiation of stilbene in presence of dihydro XXIX, but 1:1 from XXXIII) shows that this is not so: much dimer (XXXI) must be formed directly from the monoketone (XXXIII) but not from the diketone (XXXII). The diradical (XXXIV) from (XXXII) can cyclize to the monoketone (XXXIII) or fragment, perhaps in two steps, to CO and

stilbene; the diradical from (XXXIII) correspondingly can cyclize to the dimer (XXXI) directly or fragment to monomeric stilbene.

Even when the radicals are not stabilized by phenyl groups, the configuration at the α -carbon atom is usually lost. For example, photo-decarbonylation of the bridged-ring ketone (XXXVI) gives both stereoisomeric hydrocarbons¹⁶ (XXXVIII and XXXIX). It is interesting that the main product, the ketene (XL), can be formed from a diradical (XXXVII) only after ring-inversion to bring the hydrogen atom within reach of the α -radical centre. Quinkert¹⁷ has shown that 17-keto-steroids with either configuration of the angular methyl group give the same acid (through the ketene) with the more stable equatorial methyl group (XLI).

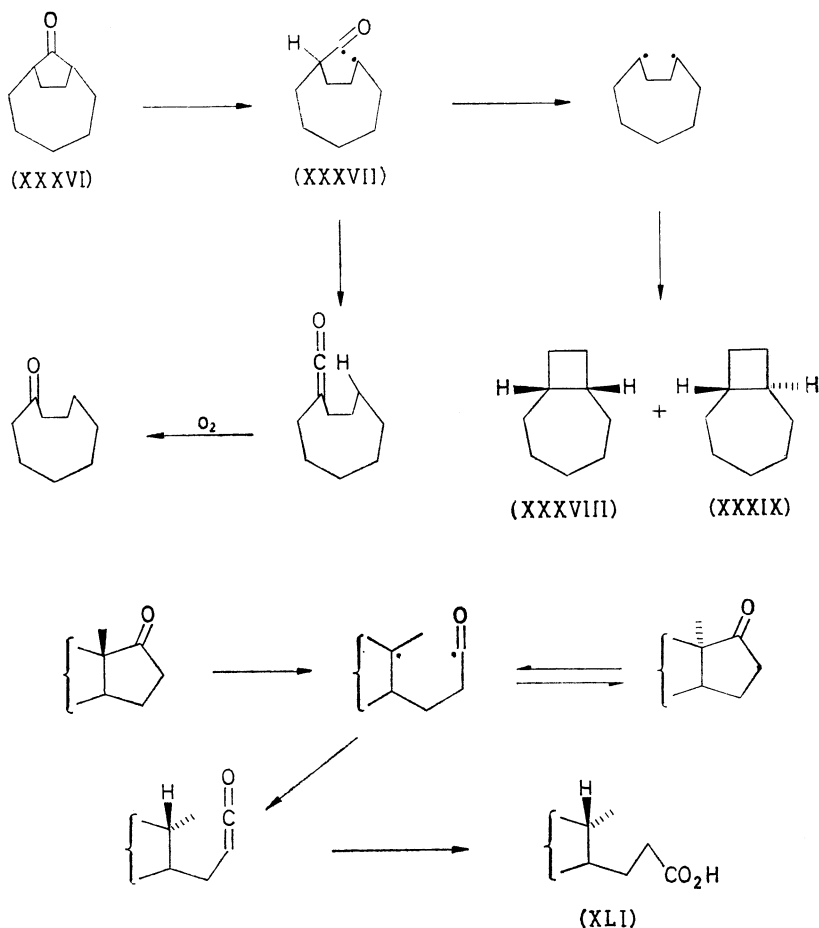
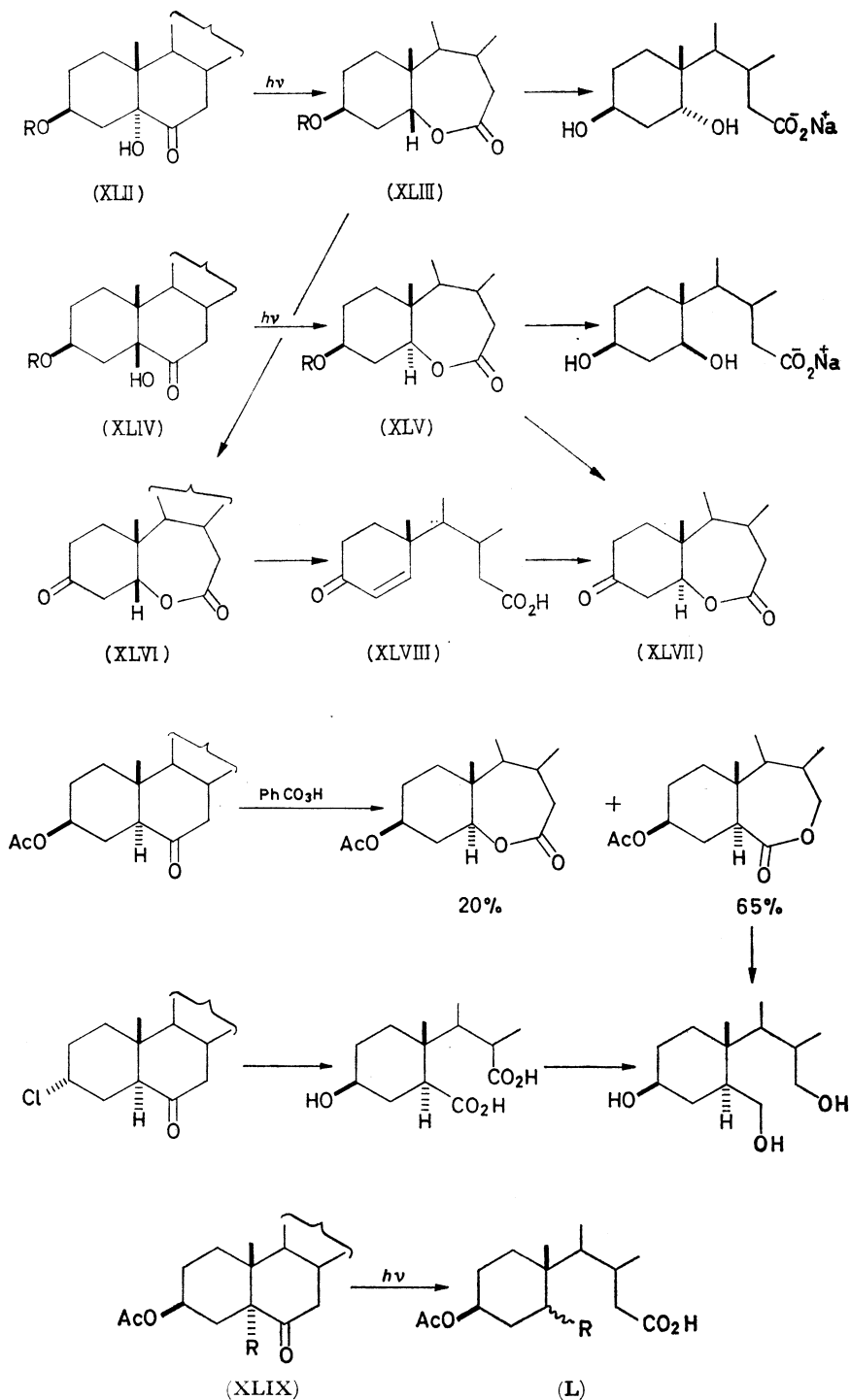


Photo-hydrolysis of 3 β -acetoxycholestan-6-one (XLIX, R = H), forms the *seco*-acid (L, R = H) in a typical reaction of the sort, and the 5 α -acetoxy-derivative (XLIX, R = OAc) yields a mixture of the two epimeric *seco*-acids (L, R = α - and β -OAc), as usual.

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In sharp contrast to this are the completely stereospecific photo-isomerizations of α -ketols to lactones¹⁸. Thus, 3 β ,5 α -dihydroxycholestan-6-one (XLII) gives only the lactone (XLIII) and the 5 β -epimer (XLIV) gives only the lactone (XLV). The two derived ketones (XLVI and XLVII) can be equilibrated (greatly in favour of XLVII) through the unsaturated ketone (XLVIII) and their structures are proved *inter alia* by the reactions shown on the previous page.

Photolysis of the *O*-deutero-derivatives (XLII and XLIV) in *O*-deutero-ethanol has been used¹⁸ to find out whether the hydrogen atom at C-5 in the lactones (XLIII and XLV) comes from the OH or from the 7-CH₂ group. In fact it comes entirely by intramolecular transfer from the latter, because the products (XLIII and XLV) carry the deuterium at C-7, not at C-5. Although the reaction is thus closely related to the cleavage of ketones to ketenes, its stereospecificity shows that it cannot proceed through *free* radicals, and suggests that the singlet $n - \pi^*$ state may react directly (unless inversion of electron-spin is much faster than rotation about single bonds).

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