PHOTOCHEMISTRY OF NON-CONJUGATED KETONES IN SOLUTION

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The basic tenet of photochemistry may be adequately summarized by the statement that an electronically excited molecule represents a new chemical species with its own structure and reactivity. While u.v.-spectroscopy of small, non-conjugated, ketones laid the foundation for the concept of $n \rightarrow \pi^*$-excitation, the photochemistry of larger carbonyl compounds is making a welcome contribution to our knowledge of the electronic distribution in these molecules and its chemical consequences. *Figure 1* represents the light-induced α-cleavage of ketones which contain a tetrahedral C-α-atom. Such a reaction appears plausible considering the change of electron configuration during the $n \rightarrow \pi^*$ transition, shown schematically in *Figure 2* as an atomic orbital approximation. The weak absorption of the carbonyl chromophore in the region of 2900 Å causes a promotion of one electron to the antibonding π^* orbital from an essentially localized, non-bonding, orbital on the oxygen atom. With increasing overlap of this *p*-orbital, with its odd electron, with one of the C–R bonds in the same plane the alkyl radical R is released and the acyl radical is formed[1].

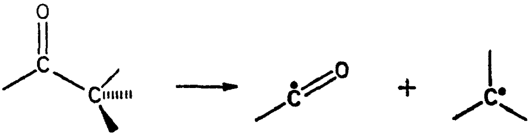


Figure 1

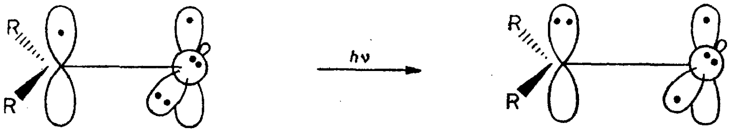


Figure 2

In solution, the α-cleavage involves the adjacent atom which is the more highly substituted by alkyl groups[2]. This is worth mentioning because, for a light-induced reaction, it is by no means obvious that the more stable of two products formed by comparable paths will be favoured. The product of the primary photochemical process is an alkyl/acyl radical pair, of the type which has been encountered in gas-phase photolysis studies with saturated ketones[3].

It is generally assumed that, in the condensed phase, the photolytic dissociation is retarded by collision deactivation and that the radicals formed are removed, at least in part, because of the cage effect postulated by Franck and Rabinowitch. If the rate of recombination of the radicals produced is not faster than the rate with which the alkyl radical centre loses its original dissymmetry, racemization should be observed with a ketone which has an asymmetric arrangement at the C-α-atom. In the early forties Butenandt and his colleagues[4] found that 17-ketosteroids on u.v.-irradiation suffer a partial racemization at C–13 (*Figure 3*). Wehrli and Schaffner[5] recently observed photo-epimerization using unfiltered light from a medium pressure mercury lamp. Since the regions of u.v.-absorption are not completely identical for both epimers, a dependence of the photostationary state on the wavelength of the light used is to be expected. The photo-epimerization can easily be explained by assuming the intermediate formation of an alkyl/acyl biradical (*Figure 3*). To study other reactions that might successfully compete with the radical coupling of this hypothetical intermediate we chose cyclic ketones. In those with a 17-ketosteroid, two intramolecular hydrogen abstractions are to be expected, and both of them have been observed[2, 6] (*Figure 4*). Open chain ketenes and unsaturated aldehydes are the products of these photoisomerizations.

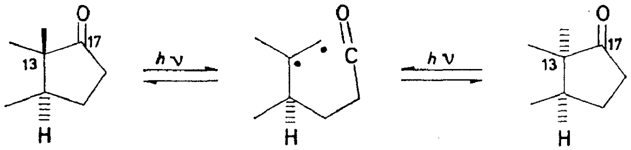


Figure 3

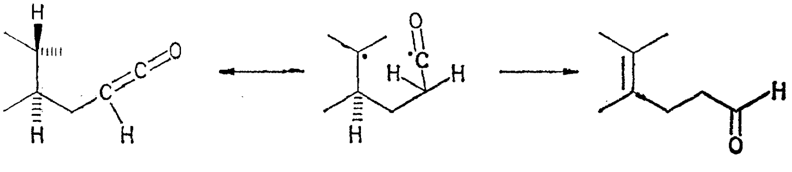


Figure 4

The intramolecular nature of these reactions has been demonstrated by using suitably deuterated ketones. A 17-ketosteroid, bisdeuterated at C–16 (*Figure 5*), furnishes a ketene[7] and, in the presence of water, a carboxylic acid, which also contain two deuterium atoms per molecule. Only one of

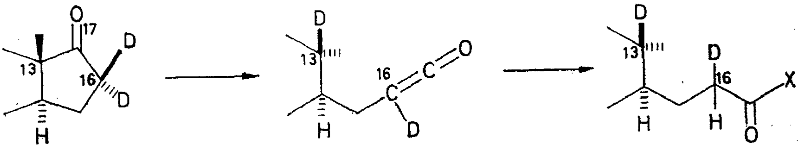
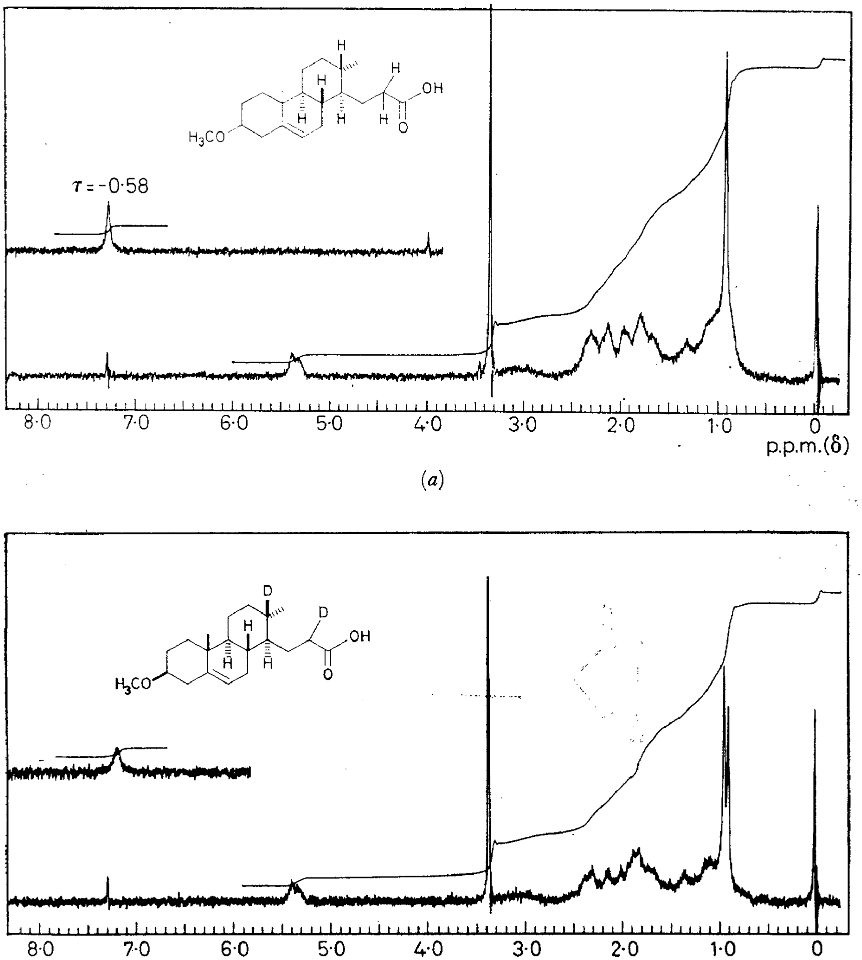


Figure 5

these is, however, still at C–16. Comparison of the n.m.r.-spectra of the bisdeuterated carboxylic acid derivatives and the corresponding undeuterated compounds strongly suggests that the other deuterium atom has migrated to C–13[7] (*Figure 6*).

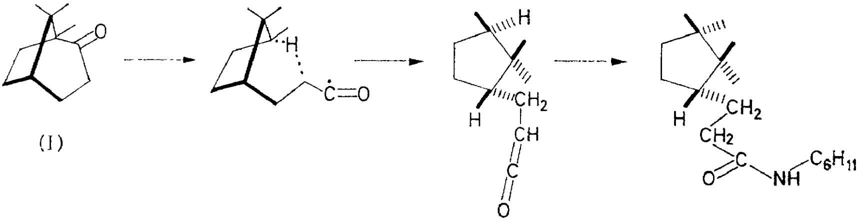


(*a*)

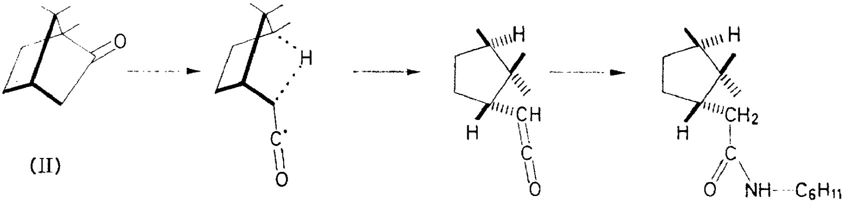
(*b*)

Figure 6. In the section of the spectra shown in the upper part of each figure, the sweep was offset 200 c/s.

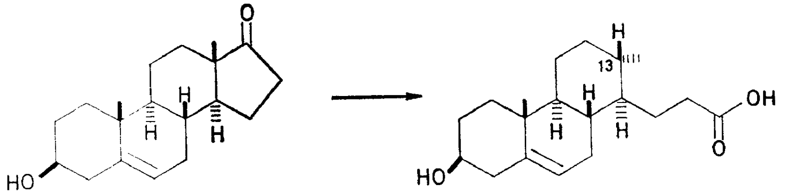
The following facts can be considered as an additional support for the intramolecular character of the disproportionation. The extent of the photoisomerization is greater with 6-ring than with 5-ring ketones[8]. The irradiation of homocamphor (I) in the presence of cyclohexylamine affords an amide in at least 17 per cent yield; on the other hand, the lower homologue (II), under the same conditions, leads to the corresponding cyclohexylamide with a yield not exceeding 1 per cent. Similarly, the photochemical ring cleavage of the ketonic D-homosteroid (III) gives an acidic product in about 45 per cent yield, whereas the acid from the 17-ketosteroid (IV) is formed in *ca.* 28 per cent yield. Moreover the formation of the carboxylic acids or their derivatives is stereoselective. In the case of camphor (II) the transfer of hydrogen, because of geometrical restrictions in the cyclic transition state of the ketene formation, must occur in such a way that the two substituents of the amide at the original bridgehead positions in the starting material are in a *trans* configuration to each other. The same argument applies of course to the configuration of the cyclohexylamide from homocamphor (I). The 17-ketosteroid (IV) gives exclusively the carboxylic acid (V) with the methyl group at C–13 in the α-configuration. The higher



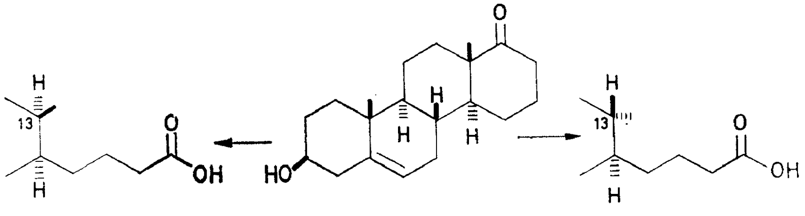
(I)



(II)



(IV) (V)



(VII) (III) (VI)

homologous carboxylic acid (VI), with the identical configuration at C–13 is formed as the main product from the D-homoketone (III); in addition, the epimeric acid (VII) is obtained[8]. The ring strain in the cyclic transition state of the hydrogen migration must be at least partly responsible for the observed stereoselectivity. If the formation of the epimer *E* (in *Figure 7*), with the methyl group at C–13 in the α-configuration, were caused only by the greater thermodynamic stability of the biradical configuration *A*, with the equatorial arrangement of the methyl group, compared with *B*, the homologous five- and six-ring ketones (IV) and (III) should show no difference in their stereoselective behaviour. But, as mentioned above, this is definitely not the case. The assumption of greater ring strain in the transition state *D*, with *trans* fused rings, compared with *C* seems to be plausible.

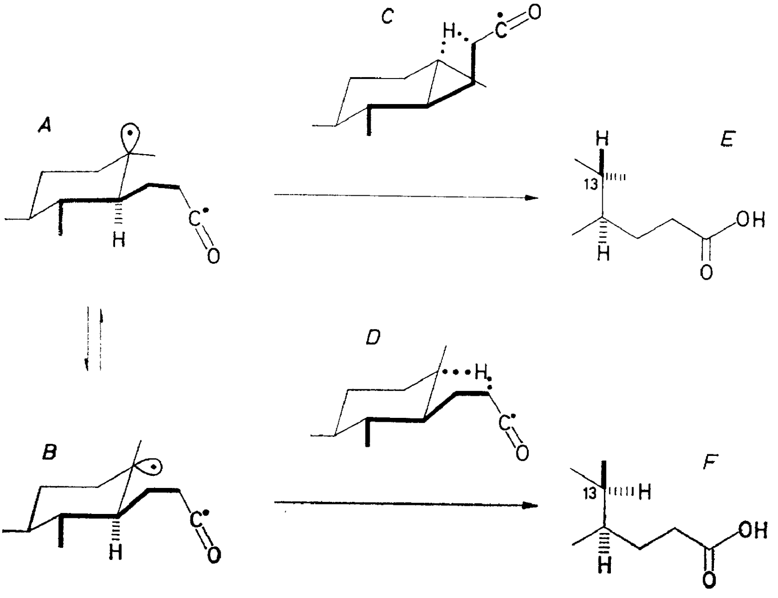
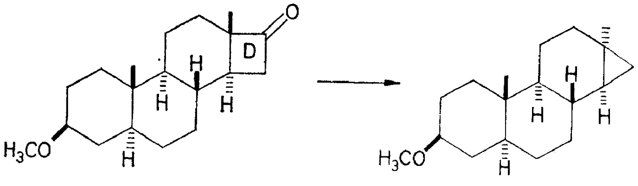


Figure 7

Of special interest is the irradiation of the lower ketosteroid homologue (VIII), with a four membered ring D. In addition to other products the



(VIII) (IX)

cyclopropane (IX), is formed in nearly 30 per cent yield. Its structure is assigned from a consideration of its elemental analysis, and n.m.r. and i.r.

spectra (*Figures 8* and *9*). The photo-elimination of carbon monoxide in the gas phase at elevated temperatures is typical of saturated ketones[3]. Under these conditions the reaction may be used as a preparative method for the production of alkyl radicals and their secondary products. It is especially useful for the formation of cyclic hydrocarbons[9].

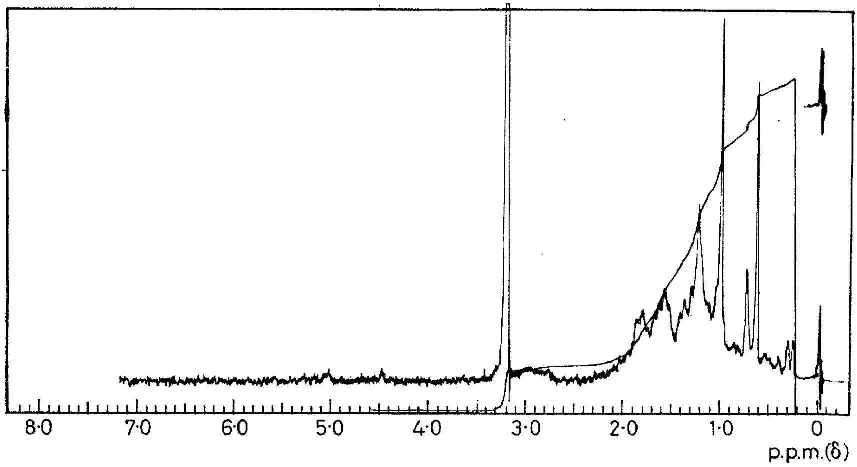


Figure 8

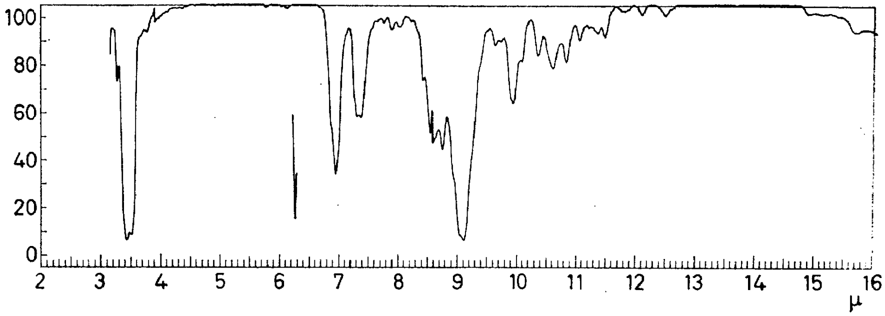
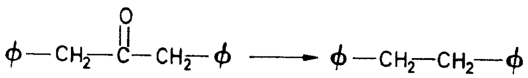


Figure 9

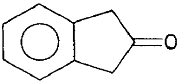
In the condensed phase, and at room temperature, there is little, if any, photodecarbonylation. Ketones which, formally at least, furnish in the primary photodissociation acyl radicals, the decomposition of which requires only a low activation energy, provide interesting exceptions[10]. Thus dibenzyl ketone (X) is decarbonylated rapidly and almost quantitativly to dibenzyl



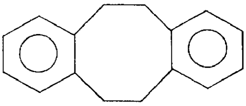
$$\phi{-}CH_2{-}\overset{O}{\overset{\|}{C}}{-}CH_2{-}\phi \longrightarrow \phi{-}CH_2{-}CH_2{-}\phi$$

(X) (XI)

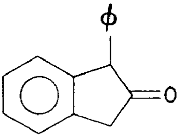
(XI). Stabilization by π-delocalization of the species produced in the light-induced decarbonylation controls the ease of the reaction. This is demonstrated with a series of β-indanone derivatives. The unsubstituted compound (XII) on irradiation in benzene looses less than 10 per cent carbon monoxide. Dibenzocyclo-octadiene (XIII) can be isolated in low yield, in addition to polymeric material. A benzene solution of α-phenyl-β-indanone (XIV) reacts under the same conditions with an almost complete loss of carbon monoxide. The racemic and *meso* configurations of the vicinal diphenyl-substituted dibenzocyclo-octadiene (XV) are obtained in a yield greater than 50 per cent. These compounds are not completely stable in light and slowly fragment with the formation of *cis*-stilben and dihydro phenanthren. α,α'-Diphenyl-β-indanone (XVI) undergoes the decarbonylation practically quantititively to give a mixture of *cis* and *trans* diphenylbenzocyclobutene (XVII). The ratio of these two isomers in the reaction product depends on the irradiation conditions. Using a glass filter, light which would be absorbed by the hydrocarbons can be excluded and four times as much of the *trans* as of the *cis* product is formed. On irradiation with unfiltered light the content of the *cis* compound increases with the reaction time up to 40 per cent of the hydrocarbon mixture. The elimination of carbon monoxide from (XVI) emphasizes the preparative value of photodecarbonylation. The resulting compounds in this case are interesting since both the isomers form adducts with dienophiles. The *trans* compound reacts quantitatively and smoothly with *N*-phenylmaleimide at room temperature. The *cis* isomer is less reactive; in two weeks at room temperature it forms an adduct with the same dienophile in 70 per cent yield. The formation of such adducts could



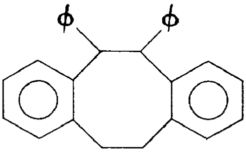
(XII)



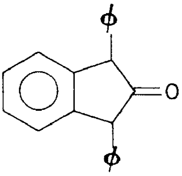
(XIII)



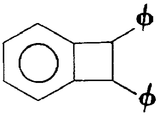
(XIV)



(XV)

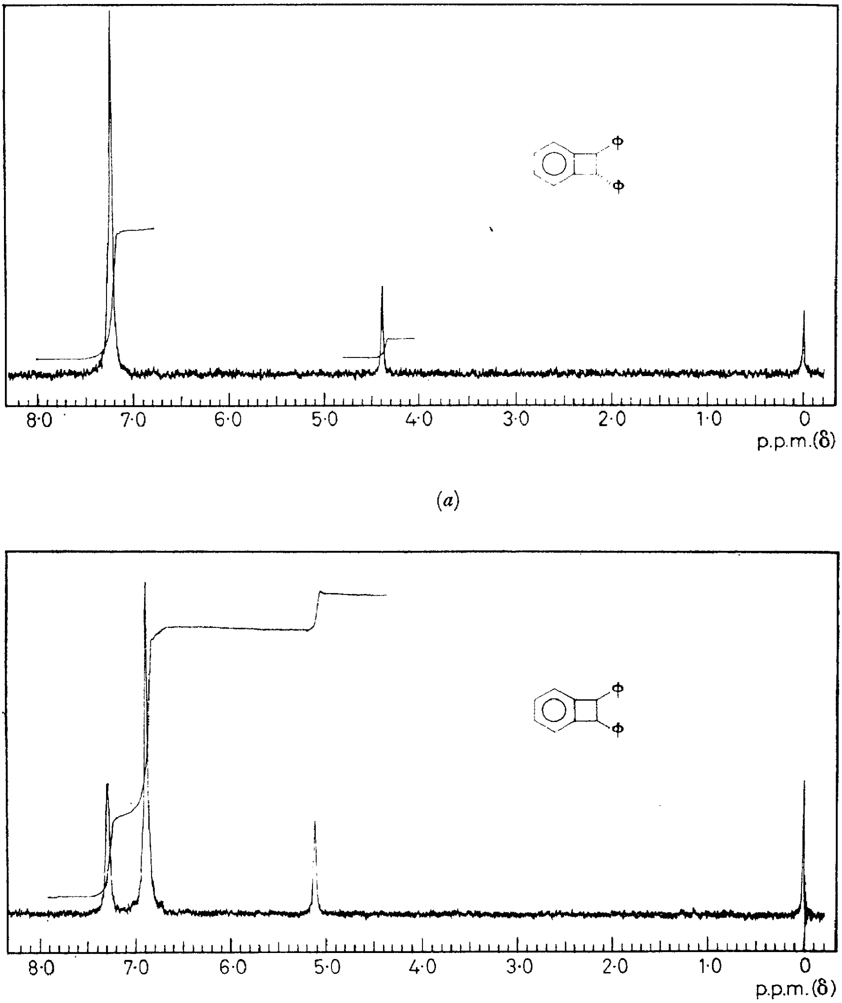


(XVI)



(XVII)

conceivably occur by a four-centre type mechanism, or by an initial equilibration between the benzocyclobutene and an *o*-quinonoid form[11]. Since the two hydrocarbons, whose configurations are known from their n.m.r. spectra (*Figure 10*) give two different adducts with *N*-phenyl maleimide, this reaction seemed suitable for settling the point, provided that the reaction is assumed to occur by *cis* addition of the two reagents. The *trans* isomer (XVIIb), would give the adduct (XVIIIc), with the *trans* arrangement of the two phenyl groups on the central ring, if the reagent reacts directly with the hydrocarbon. The *cis* isomer (XVIIa), would lead to *anti*– *cis*– *anti* (XVIIIa) and *syn*– *cis*– *syn* (XVIIIb) diastereoisomers. On

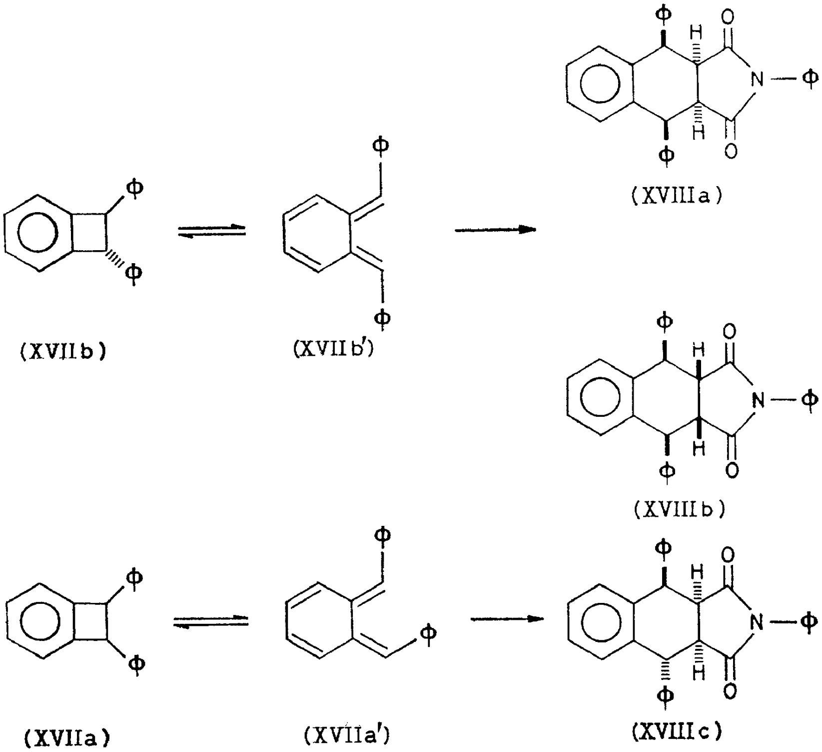


(*a*)

(*b*)

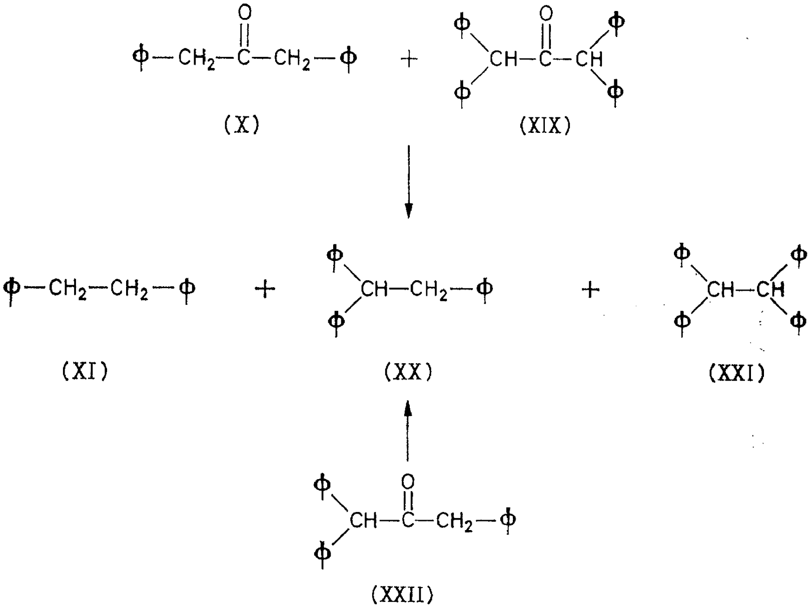
Figure 10

the other hand, if there were an initial equilibration with quinonoid forms (XVIIa′ and XVIIb′) then because of the steric relationship within the two pairs of valence tautomers, the *trans*-cyclobutene derivative (XVIIb) would lead to the two diastereoisomers (XVIIIa) and (XVIIIb). The *cis* compound (XVIIa), would give only the one adduct (XVIIIc). In practice



(XVIIb) gave two adducts in the ratio of 15 to 1, and (XVIIa) gave only one adduct. This is in agreement with the addition of the dienophile to the valence tautomers (XVIIa′) and (XVIIb′).

It has been demonstrated experimentally that the photodecarbonylation occurs *via* free radicals; this is true at least for the open chain α,α′-phenyl substituted ketones[10]. The irradiation product obtained from an equimolecular mixture of the symmetrically substituted di- and tetraphenyl acetone derivatives (X) and (XIX), consists of a mixture of (XI), (XX) and (XXI). A slight deviation from the product ratio 1 : 2 : 1 in favour of the symmetrically substituted hydrocarbons can easily be explained by the faster decarbonylation of (X) compared with (XIX). The same products, in the required proportions, are obtained from (XXII) by light-induced elimination of carbon monoxide. It is not quite clear whether the radical producing photodissociation of the phenyl-substituted acetone derivatives is a one-step reaction, or whether acyl radicals are intermediates. There is, perhaps, no parallel here with the well-known behaviour of aliphatic ketones since the activation energy for the decomposition of an acyl radical obviously decreases with increasing stabilization by π-delocalization.



The different types of photochemical reactions of cyclic non-conjugated ketones referred to, the photo-epimerization, the two different routes of photoisomerizations, and finally the photodecarbonylation, can reasonably be interpreted as involving intermediate biradicals formed as dissociation products in the primary photochemical process. It should be emphasized, however, that their existence is based purely on analogy and has not been proved experimentally.

After consideration of Butenandt's photo-epimerization, Schenck[12] has brought up again Werner's mechanism of racemization[13]. He has now applied this mechanism to an electronically excited molecule while discussing the possibility that a change of configuration at an asymmetric atom might occur without cleavage of a bond to that centre. At present there is no compelling evidence in favour of such a process.

Srinivasan[9] has expressed some doubt as to whether an alkyl/acyl biradical is an intermediate during the photolysis of cyclic ketones leading to unsaturated aldehydes. His objection consists of the experimental observation that oxygen has no quenching effect on the formation of any of the reaction products. The basis for such an argument is the high reactivity of alkyl radicals with molecular oxygen, and certainly any alkyl/acyl biradical intermediate must have a reduced reactivity if it fails to combine with this radical scavenger. A remarkable decrease in reactivity, though only for intermolecular processes, has been reported as characteristic for biradicals. From polymer chemistry it is known[14] that such species obtainable from cyclic disulphides and cyclic azo-compounds, with the two reactive centres not too far apart and not in adjacent or in conjugated positions, behave as highly inefficient initiators for polymerization; intramolecular reactions, such as coupling or disproportionations, are much faster than addition to an olefinic monomer. Furthermore, the production of short branches during the high temperature radical polymerization of ethylene is considered as an intramolecular hydrogen transfer commonly known as "back biting"[15] (*Figure 11*).

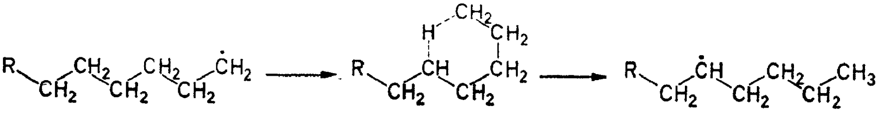
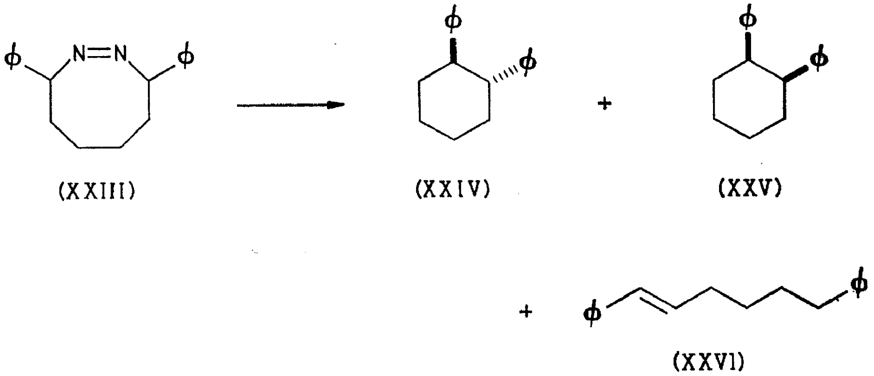
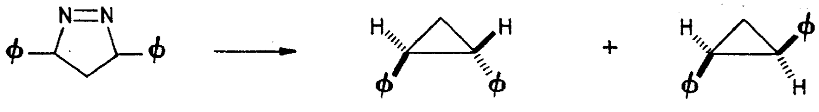


Figure 11

To investigate the problem of the intermolecular reactivity of a biradical especially with molecular oxygen, we irradiated two cyclic azo-compounds in the absence, and in the presence, of oxygen[16]. Under u.v. irradiation the eight membered cyclic azo-compound (XXIII)[17] eliminates nitrogen and affords the three hydrocarbons (XXIV), (XXV) and (XXVI), which can easily be explained as arising from an intermediate biradical, in 77 per cent yield. In the presence of oxygen the yield of these products is not lowered. An analogous result is obtained on the photoelimination of nitrogen from the five-membered cyclic azo-compound (XXVII)[18]. In the absence, and in the presence, of oxygen the total yields of the two hydrocarbons (XXVIII) and (XXIX) are 72 and 73 per cent respectively. If biradicals are involved in these reactions they behave quite differently from what would be expected for a doubled monoradical.

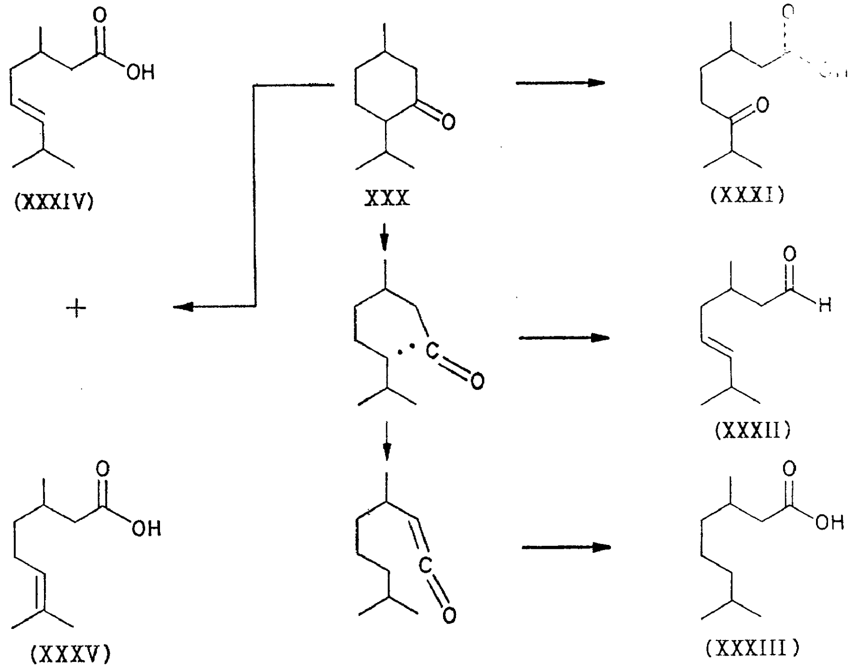


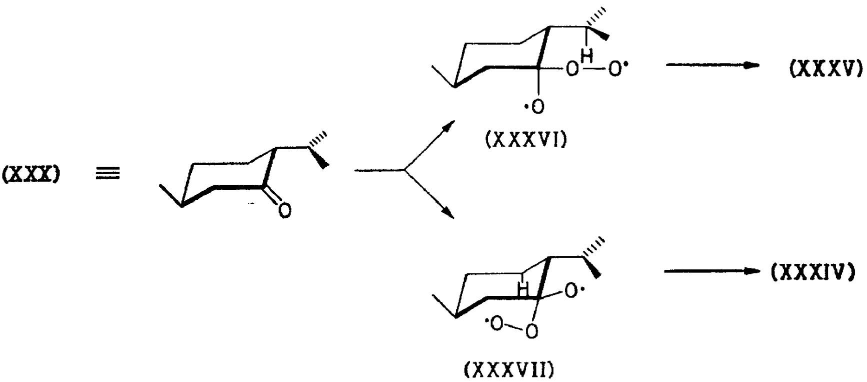
(XXIII) (XXIV) (XXV) (XXVI)



(XXVII) (XXVIII) (XXIX)

We had chosen azo-compounds, and not ketones, for the examinations of the effect of oxygen on possible intermediates in order to avoid a reaction of molecular oxygen with the photo-activated ketone itself. In the literature there are indications of such light-induced autoxidations, and on the irradiation of cyclic ketones in benzene solution in the presence of oxygen we obtained new compounds in addition to those known to be formed in the absence of oxygen[6]. More than fifty years ago Ciamician and Silber[19] observed that menthone (XXX), in aqueous alcoholic solution, is transformed by sunlight to the unsaturated aldehyde (XXXII), and to the saturated carboxylic acid (XXXIII); the latter is certainly formed *via* the corresponding ketene. In the presence of oxygen, in addition to these compounds, the keto acid (XXXI), was isolated by the Italian workers. It is not known at present exactly how the latter compound is produced, but we believe that the aldehydic photoisomerization product can be excluded





as a precursor. When oxygen was passed through an irradiated solution of menthone in benzene we were able to isolate the two unsaturated carboxylic acids (XXXIV) and (XXXV). The aldehyde (XXXII) can again be excluded as an intermediate[20]. Postulation of a reaction between the excited ketone and molecular oxygen leads to the correct formal relationship between the structure of the starting material (XXX), and the structures of the unsaturated acids isolated. If in some way hydroxy hydroperoxy biradicals (XXXVI) and (XXXVII) were formed in the primary photochemical process they could rearrange with the formation of two unsaturated peroxy acids quite similar in structure to the observed carboxylic acids. These transformations are generalized in *Figure 12*.

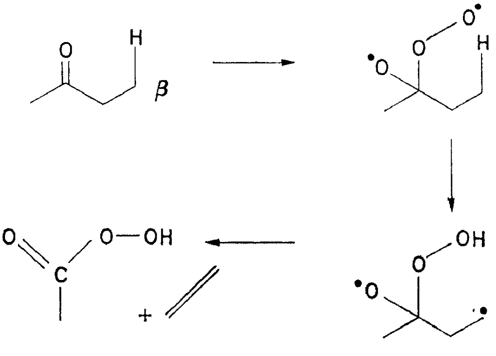
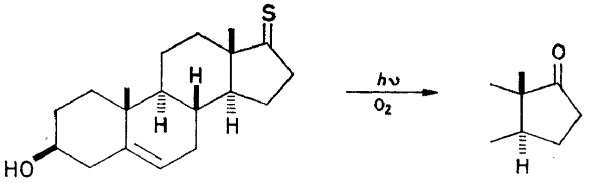


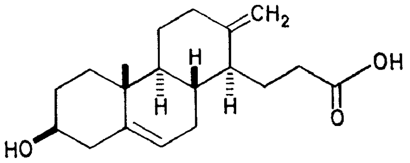
Figure 12

Photo-oxidations by reaction of an electronically excited molecule and molecular oxygen are known and are of special interest because they probably have no parallel with thermal reactions. An obvious case is the transformation of the pink coloured steroid thione (XXXVIII)[21], into (IV), which is



(XXXVIII) (IV)

caused by visible light in the presence of oxygen[22]. Since the absorbed energy in this case is not sufficient to break a C–C or a C–H bond it must be the excited thione group itself which reacts with oxygen. For carbonyl



(XXXIX)

compounds a photochemical exchange of oxygen cannot normally be observed. By using $^{18}O_2$, Srinivasan and Noyes[23] were able to demonstrate this reaction in acetone.

In agreement with the formal mechanistic picture of a photo-oxidative fragmentation, the 17-ketosteroid (IV), and its C–13 epimer are both transformed in 20 per cent yield into the unsaturated acid (XXXIX), in addition to the carboxylic acid (V), discussed earlier. According to *Figure 12*, any ketone with at least one hydrogen atom in the C–β position, and a cisoid arrangement of the extreme centres H and O, should undergo the cleavage reaction which starts with a hydrogen transfer *via* a six-membered cyclic transition state. The 1,4 biradical thereby formed undergoes a fragmention characteristic of such a species with the formation of a C–C double

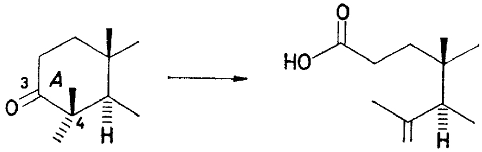
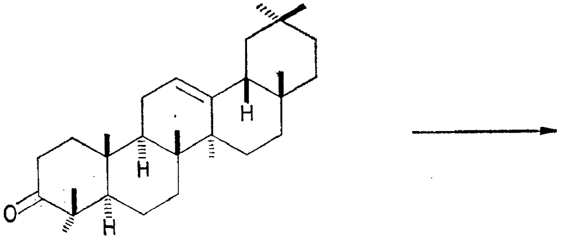


Figure 13



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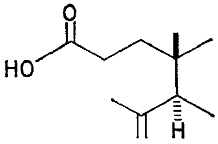
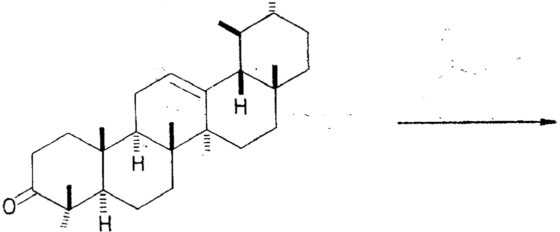
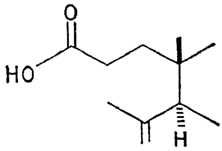


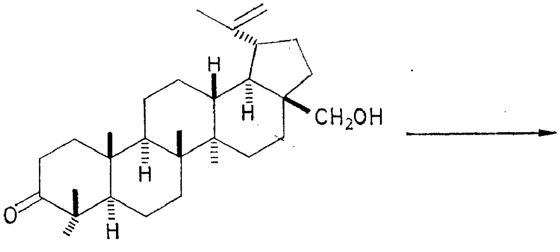
(XLI)



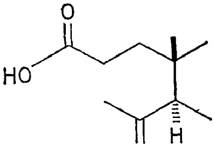
(XLII)



(XLIII)



(XLIV)



bond and a peroxy-acid grouping. It is, of course, conceivable that the whole process is concerted. The practical utility of this reaction is illustrated in *Figure 13* for 3-keto-4,4-dimethyl isoprenoids[6]. These compounds are biogenetically related to carboxylic acids of the same structural type, but with an opened ring *A* and a terminal double bond. Compounds belonging to this class have recently been found in nature.

On irradiation of β-amyrone (XL) in a benzene solution through which oxygen was passed, nyctanthic acid (XLI), was obtained in *ca.* 20 per cent yield. Similarly α-amyrone (XLII) was transformed into roburic acid, (XLIII). Betulone (XLIV), gave in about the same yield the carboxylic acid (XLV). We believe the latter to be a natural product, but it has not yet been isolated from natural sources.

Finally, I should like to express my gratitude to all my young colleagues who carried out the work described above.

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