PART – I

(Preparation and Photochemistry of Cross-Conjugated Cyclohexadienone Ring A of Friedalane Triterpene)

CHAPTER - I

(A short review on Structural Aspects of Cross-conjugated Cyclohexadienone Photochemistry)

Introduction :

The photochemical rearrangements involving cyclohexadienones in general and cross-conjugated cyclohexadienones (2,5 cyclohexadienones) in particular, are remarkably facile, but fascinatingly complicated. Light induced rearrangement of α-santonin-(1),a sesquiterpene cross-conjugated cyclohexadienone,was recorded in the literature as early as 1830. Considerable efforts have been directed by a group of Italian workers at the beginning of the last century[1]. The pioneering studies by Barton, Jeger, Vantamelen and their groups resolved the structure and stereochemistry of various photoproducts of α-santonin[2-9]. Subsequently, it was observed that photo transformations in cross-conjugated cyclohexadienones are fairly general and could be correlated with α-santonin photoproducts. Several detailed reviews[11-17] have appeared concerning this rapidly expanding research activity that unveiled the deep-seated, multistep photochemical rearrangements and also on the progress in understanding the mechanistic aspects of these reactions.

Since the field has expanded enormously and a wealth of information concerning the reaction products and mechanism have accumulated,we wish to divide the review on the photochemistry of cross-conjugated cyclohexadienone in two chapters : **Chapter-I**, that deals with the structural aspects of the plethora of photoproducts, generally obtained in this type of compounds and **Chapter II,** that deals with the mechanistic aspects of the formation of photoproducts.

Concerning **Chapter I,** so vast is the progress achieved in this field and the process has encompassed such a wide variety of molecular structural types that it is difficult to cover them in detail and photochemists look at this with awe. Thus, here, a short but comprehensive discussion has been attempted, which is representative rather than exhaustive.

Depending upon structural variations, substitution patterns, solvent polarities and different exciting wavelength used, a multitude of products are obtained through a multistep process. When a cross-conjugated cyclohexadienone is photolysed in nonpolar solvents such as dioxane or ether using exciting wavelength of 254 nm, the prinicpal product obtained is the bicyclo [3.1.0] hex-3-en-2-one, a cyclopropyl ketone (also called as lumiproduct, analogous to lumisantonin 2). On prolonged irradiatiion secondary transformation of lumiketone gives rise to several spiro-ketones and eventually phenols. Interestingly, when irradiation is effected in acidic solution the lumiproduct is not obtained, instead, the major photoproducts obtained are mixture of spiro-ketols having a spiro [4,5] ring system and hydroxyhydrazulenones (5/7 fused). Since we are concerned here with the irradiation of the cross-conjugated cyclohexadienone in anhydrous as well as aquous dioxane where lumiproduct and phenol are principal products, our review will involve the formation of lumiproducts and phenols depending upon structural variations and substitution patterns.

Since the photochemical transformation of α-santonin(1) has been studied earliest and since a lot of informations regarding structure, stereochemistry and mechanism have gathered based on this molecule, it is worthwhile to take up the discussion of α-santonin (1) first (SECTION-A). Then we discuss the monocyclic cross-conjugated cyclohexadienones (SECTION-B) followed by bicyclic (SECTION-C) and then extended to polycyclic compounds including steroids (SECTION-D). A short discussion on formation of phenolic products has been made (SECTION-E). Some heterocyclic compounds have been dwelt upon (SECTION-F). Also we have focussed on anomalous behaviour of some 2,5-cyclohexadienones (SECTION-G).

SECTION - A

(A short review on Santonin ⟶ Lumisantonin Photorearrangement)

Barton and coworkers[5] observed that irradiation of α-santonin(1) in neutral media gave an isomer lumisantonin(2). This compound was also obtained by Buchi, Jeger[2] and Cocker and their groups[3]. The structure was deduced by chemical degradation and intensive spectroscopic studies. It showed IR bands in nujol at 1765 (γ-lactone), 1703 and 1663 cm^{-1} (α,β unsaturated cyclopentenone) λmax239 nm (ε 5860) indicating an α,β-unsaturated ketone. Three C-Me groups were determined both chemically and by quantitative IR measurements.

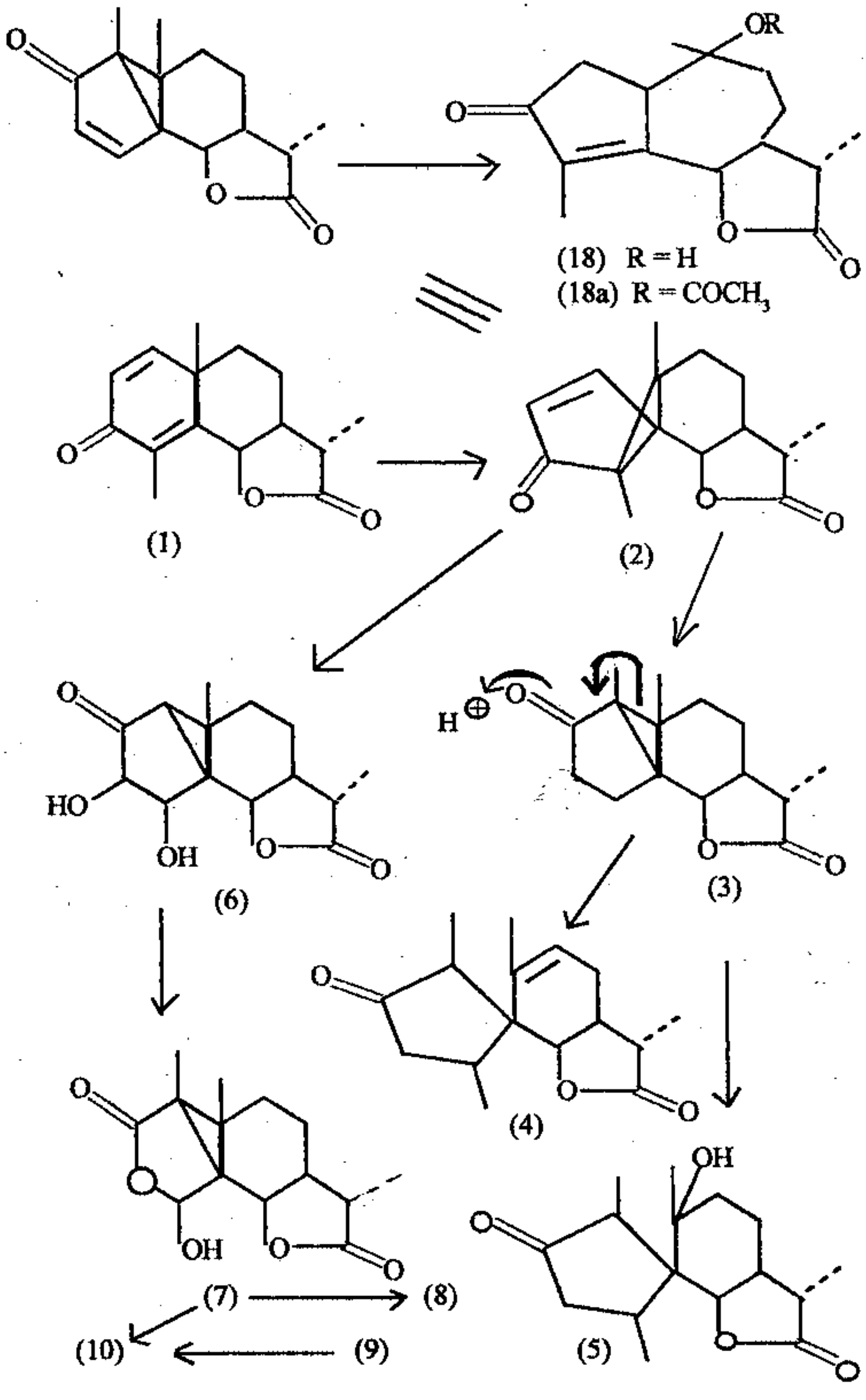
(2) was readily hydrogenated to a dihydroderivative (3) which showed IR bands at 1770 (γ-lactone) and 1703cm^{-1}. The later frequency at 1703cm^{-1} is indicative of a bicyclo [3.1.0] hexan-2-one system. On refluxing with aquous AcOH (3) furnished an isomer (4) and the corresponding tertiary alcohol(5). The compound (4) exhibited IR bands at 1765 (γ-lactone) and 1735 (normal cyclopentanone)cm^{-1}. UV showed only an isolated ethylenic linkage in its uv spectrum. The production of an additional ethylenic linkage under such mild condition, in conjunction with spectral data, provides a proof of the presence of a conjugated ketone group and cyclopropane ring in lumisantonin(2). The constitution (5) follows from its genesis and the failure to show absorption in the far ultraviolet region and appearance of IR bands at 3430 (OH), 1750 (γ-lactone) and 1726 cm^{-1} (cyclopentanone).

Treatment of (2) with OsO_4 gave a crystalline glycol (6) having IR bands at 3360(OH), 1770 (γ-lactone) and 1726 cm^{-1} (cyclopentanone) and UV absorption same as dihydrolumisantonin (5). It consumed 2 mole of periodic acid to afford a C-14 aldehydic acid which is regarded as existing in the lactol form (7), since it showed no UV or IR aldehyde absorption. It gave a positive Fehling's test and was oxidised by CrO_3 to afford an anhydride (8), IR band at 1830 (anhydride) and 1770 cm^{-1} (superimposed anhydride and γ-lactone bands). The position of the anhydride band at 1830 cm^{-1} is what might be expected for a succinic anhydride attached to cyclopropane ring. This evidence conclusively proved the presence of the grouping $(-C-CH=CH-)$ in lumisantonin. This was further confirmed by ozonolysis. (2) on treatment with ozone yielded formic acid and a compound (9) which exhibited IR band at 3440 (OH) and 1755 cm^{-1} (broad band). Alkaline H_2O_2

cleaved the compound (9) to afford [illegible] (10), the constitution of which followed when it was obtained also by opening the lactone-ring of lactol (7) with alkali.

Treatment of (2) with hydrogen bromide in AcOH for a short period gave a non-conjugated cyclopentenone (11), IR band (in CCl_4) at 1792 (γ-lactone), 1752 (Br - unsaturated cyclopentenone) and (in nujol) at 1627, 802, 752 and 722 cm^{-1} (triply substituted ethylenic linkage). Boiling in pyridine converted (11) to a new non-conjugated dienone (12) and some re-formed lumisantonin. Therefore, the opening of the cyclopropane ring is reversible. The bromoketone (11) was unstable at room temperature, it liquified and then resolidified to produce a new conjugated dienone (13) which contained three C-Me groups and registered IR bands at 1760 (γ-lactone), 1697 and 1660 (conjugated cyclopentenone) and at 1630 and 722 cm^{-1} (trisubstituted double band). UV spectrum disclosed an α,β-unsaturated ketone band at 220 nm. The ketone (13) absorbed two moles of hydrogen and furnished a saturated ketone (14).

The results described above show that lumisantonin (2) must contain the partial structure (15). The further rearrangements described below enabled Barton et al. to ascertain full structure of lumiproduct as (2). With aqueous AcOH(2) gave the 10-hydroxy compound (18) and with AcOH containing a trace of percloric acid, 10-acetoxy derivative (18a) was obtained. These rearrangements can be interpreted as in (16) or as involving an intermediate (17) which undergoes further rearrangement as indicated.


OR
(18) R = H
(18a) R = COCH3
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(2)
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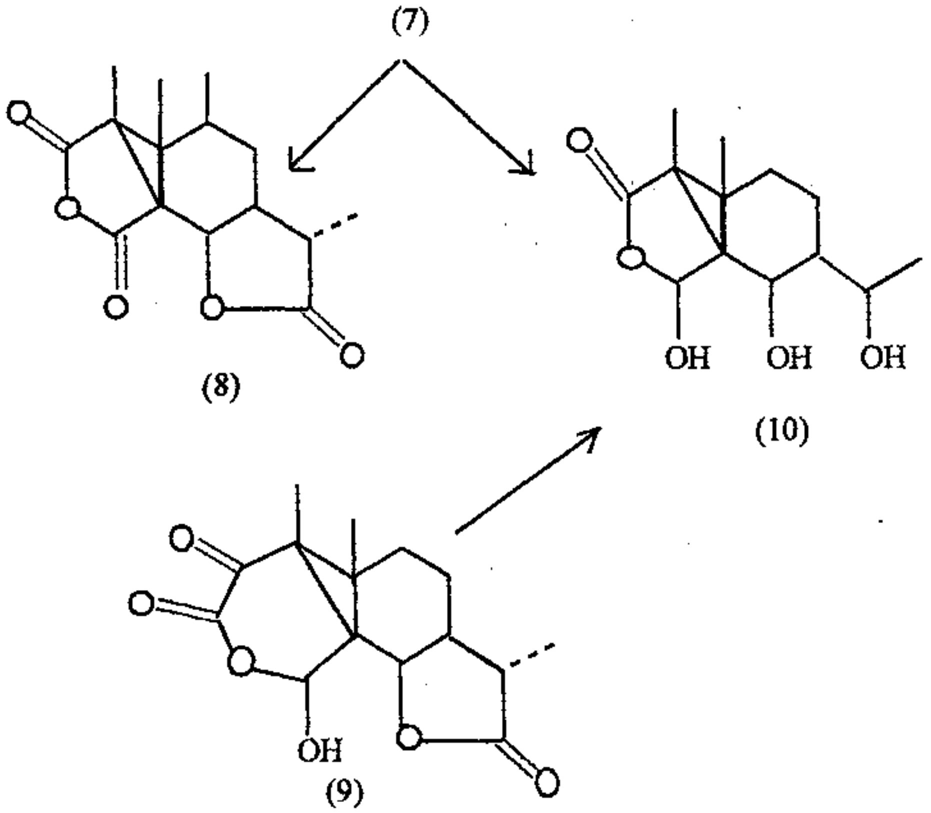
(5)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OH
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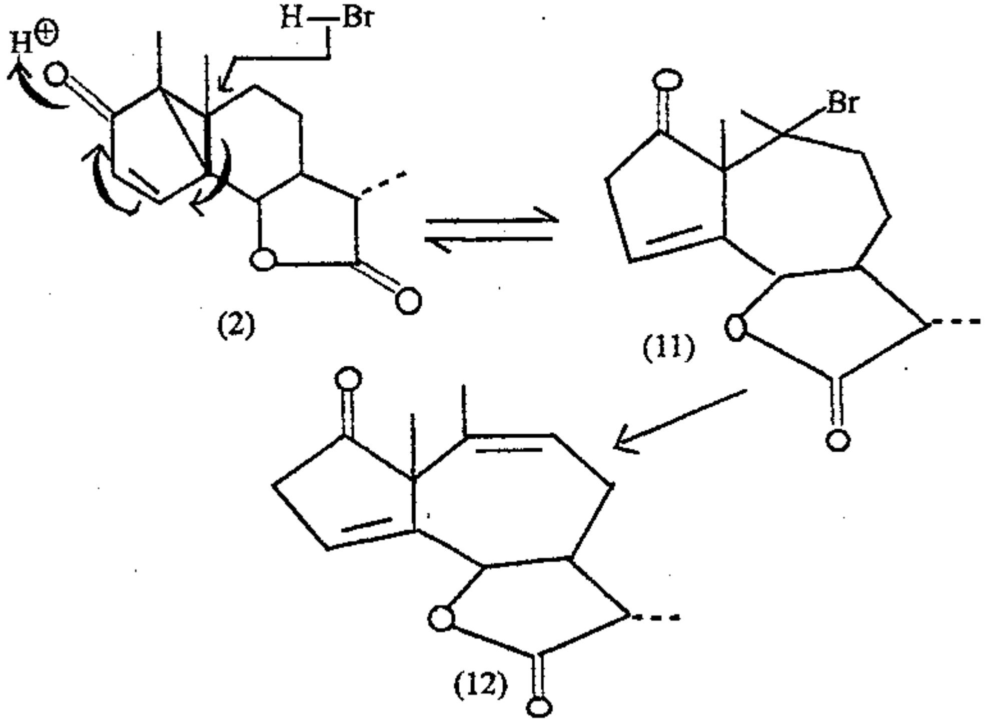
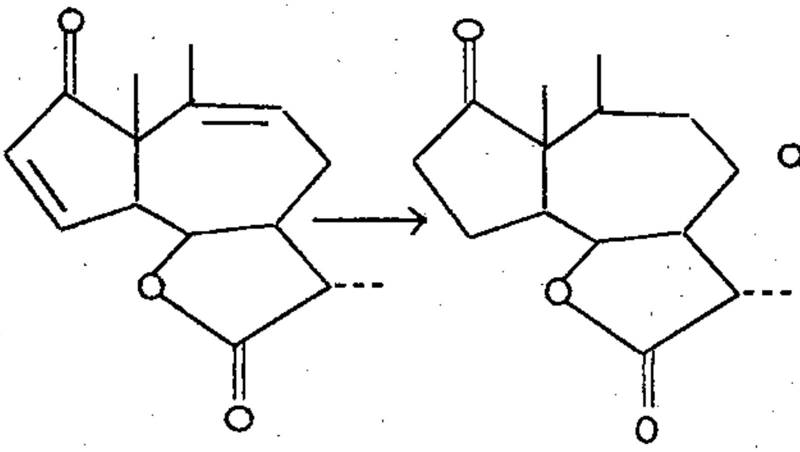

H⊕
H—Br
(2)
Br
(11)
(12)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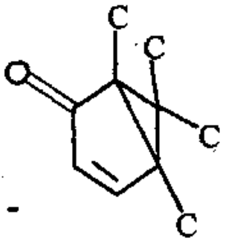
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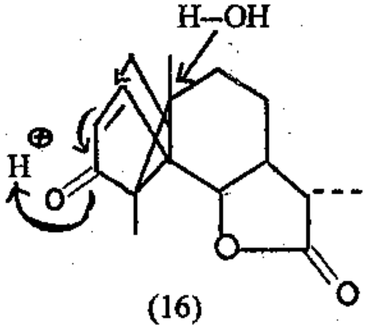

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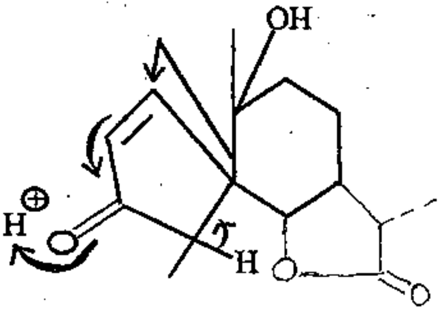


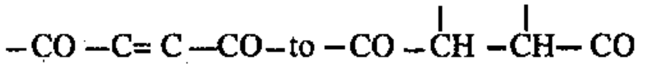
(17)

The Stereochemistry of Lumisantonin :

Barton and Gilham[6] carried out a detailed degradative study to deduce the stereochemistry of lumisantonin(2). Its stereochemistry has been evaluated at every centre of asymmetry. It has been shown that the cyclopropane ring is fused *cis* to its attached five and six-memebred rings. The photorearrangement is strerospecific with inversion of configuration at the angular methyl group.

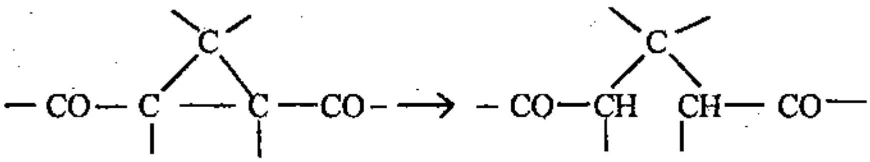
The centres of asymmetry at position 6,7 and 11 are not altered in the photoisomerisation. Since these centres do not have bonds permitting the UV absorption needed for this reaction and since all four possible santonins epimeric at C-6 and C-11 have been irradiateed and shown to furnish four different transformation products[30], a fact best explained if C-6 , C-7 and C-11 are not altered in any way on irradiation.

The *cis* relation between the 3,4 and 1,5-bonds in (2) has already been proved[5]. Thus the dicarboxylic acid obtained by opening ring A of (2) gives spontaneously the anhydride (20). This rules out the possibility of the two carboxyl groups of the acid attached in the *trans* manner to the cyclopropane ring. The reactions described below established the configuration of the Me group at C-10 in (2). Dihydrolumisantonin (19) was oxidised with CrO_3 to afford the diketo acid (22). This exhibited an interesting UV absorption λ_{max} 220nm (ε5600). By analogy with the ready reduction of the system



$-CO-C{=}C-CO-$ to $-CO-\overset{|}{C}H-\overset{|}{C}H-CO-$ by dissolving metals,

it was predicted that there would exist a cyclopropylogous reaction of the type

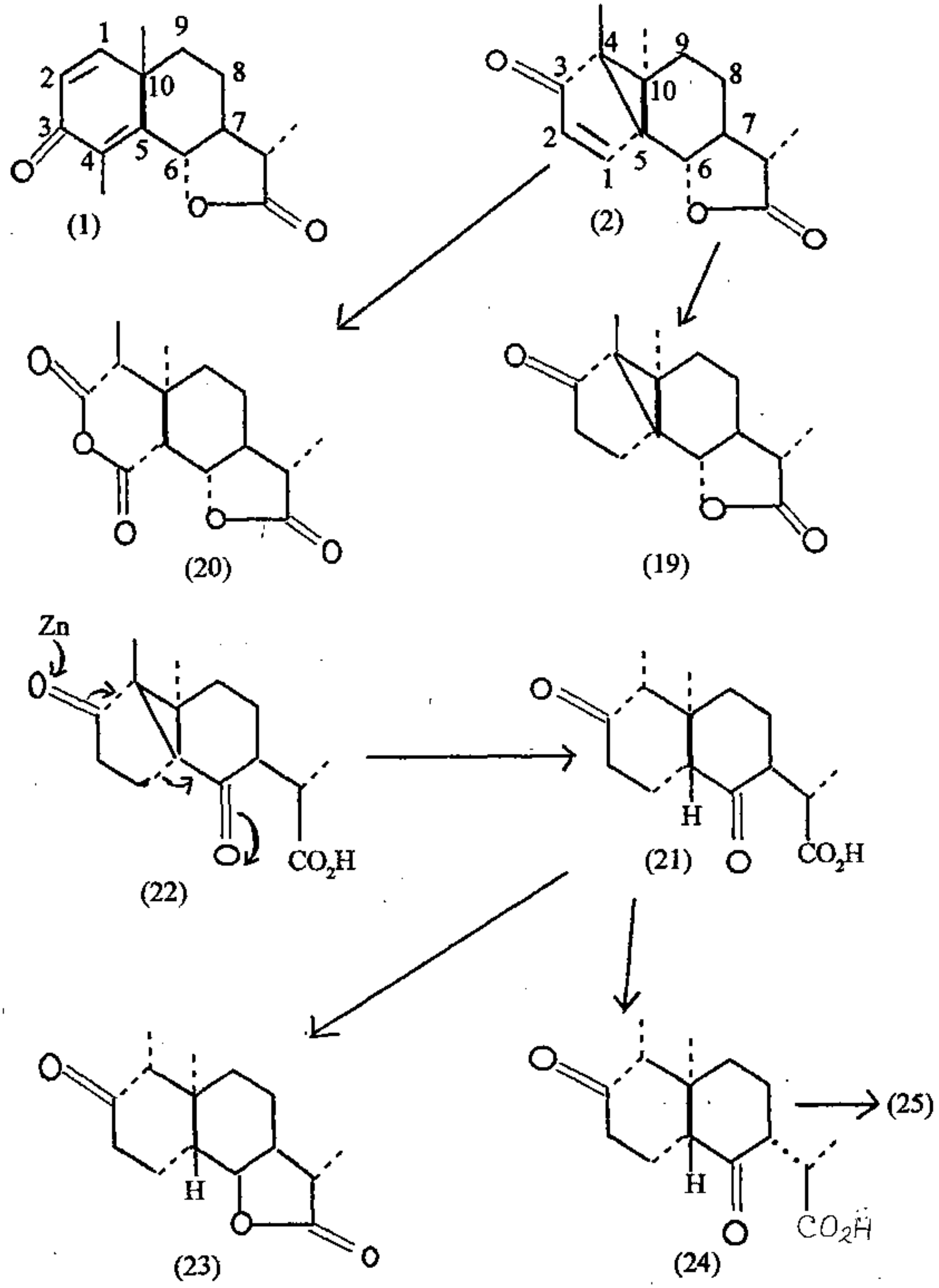


which could be applied to the diketo acid (22) that on reduction with a Zn-Cu couple in acetic acid readily furnished the diketo acid (21). The presence of two cyclohexanone carbonyl groups in this acid was shown by IR spectrum. Reduction with borohydride gave a dihydroxy acid which lactonised spontaneously. Subsequent oxidation yielded the ketolactone (23). The stereochemistry of the ring junction in this ketolactone was ascertained by comparing ORD curve, which showed a single Cotton Effect with a trough at 310 nm [M] - 2400°) with that of friedelin (26) to which it is analogous. The dispersion curve also corresponded, but with inversion of α-tetrahydrosantonin (27). Since this lactone was stable to digestion with alkali, the configuration of the ketolactone (23) at position-4 is regarded as *equatorial* (α). If it is assumed that the borohydride reduction of the diketo acid (21) and subsequent manipulations have not inverted the configuration at C- 4, then this compound must be assigned with a 4α-Me group as already indicated in (21). A non-crystalline isomer (24) was obtained by NaOH treatment of the keto acid (21) at steam-bath temperature. Reduction with borohydride produced a dihydroxy acid which spontaneously lactonized. This was oxidised, without isolation, to a new keto lactone (25) by CrO_3 oxidation. The Keto lactone (25) showed ~~A~~ an ORD curve which has a single Cotton Effect with a trough at 310nm ([M]-3800°) very similar to that recorded above for the isomer (23). These results are interpreted as follows :

Since the diketo acid has already the more stable *trans*-decalin ring fused and almost certainly, an *equatorial* Me group at C- 4, the only configuration that can be inverted by the mild treatment with alkali must be that at position C - 7. Thus the hydroxyl group and propionic side chain of (19) must, because of ring fusion, both be *axial* as shown in lumisantonin (2). This is further corroborated by the fact that lumisantoninic acid and its dihydroderivative do not lactonise unless the condition is forceful. The configuration at position-6 in the two keto-lactones(23) and (25) are regarded as β and α respectively, because of the changes in rotation they exhibit in opening of the lactone ring in alkali. The lactone rings in both these compounds are formed spontaneously from the parent hydroxy-acids. Since the propionic acid side chain of (23) is β (axial) spontaneous lactonization is, in any case, only possible if the configuration is β at position-6 (cis-lactone formation).

The configuration at position-4 in lumisantonin was determined in the following way. In their early work Barton et al.[5] demonstrated that lumisantonin on careful treatment with hydrogen bromide afforded the doubly unsaturated ketolactone (28) where the configuration of (2) at position- 4 is preserved. The ORD curve of the compound (28) showed a single Cotton Effect with a trough near 330 nm ([M] -5700°) of enantiomeric type of that of a comparable model steroid (29). The latter had a single Cotton Effect with a peak near 330 nm ([M] + 4800°). The configuration at position-4 in (2) must be, therefore, opposite to that at position-13 in (29) as written into formula (2). Thus, the stereochemistry of lumisantonin (2) at every centre of asymmetry is defined.

The structural assignment of lumisantonin (2) was also independently established by Arigoni[2] et al. and Cocker[3] et al..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(19)
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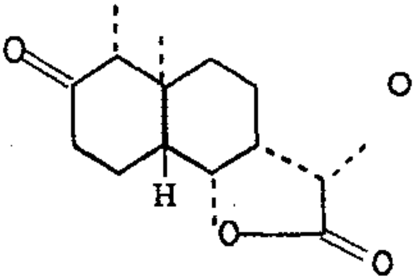
H
(23)
H
CO$_2$H
(24)
(25)



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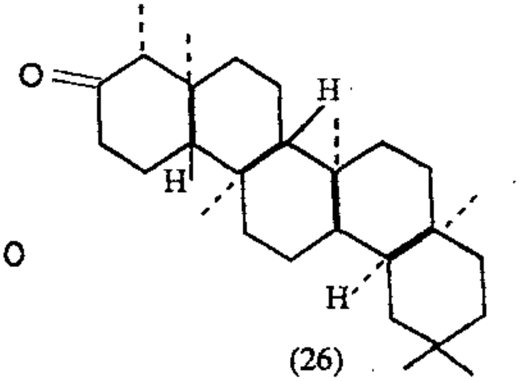

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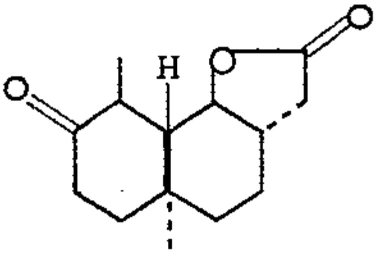

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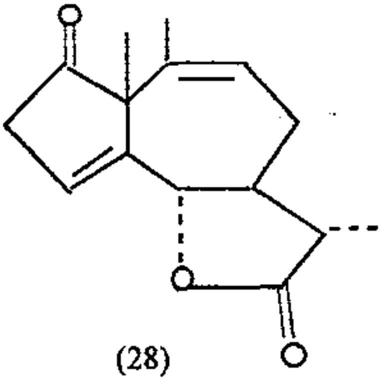

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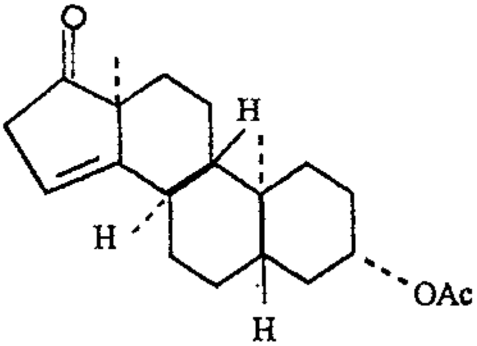
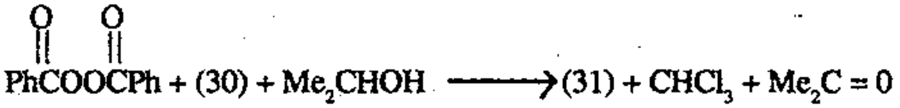


(29)

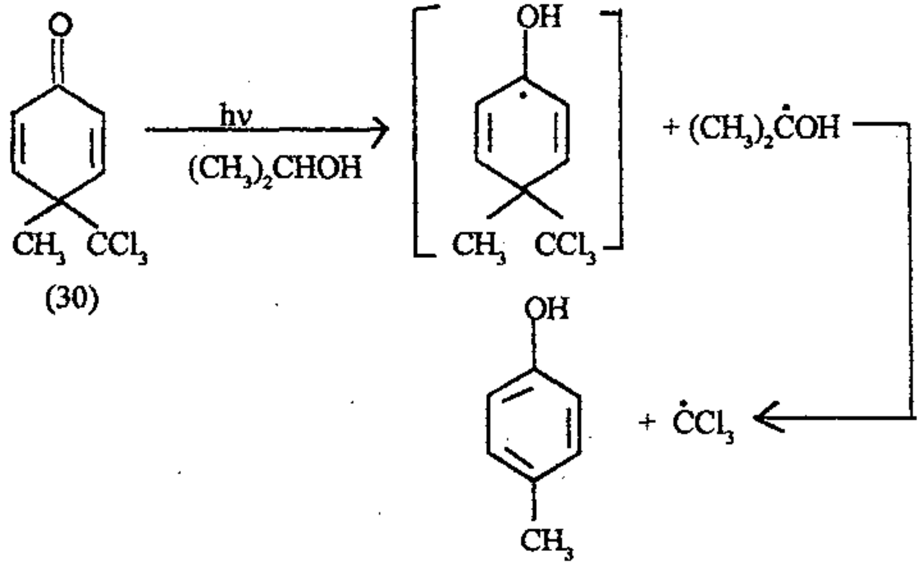
SECTION - B

(A short review on the Photochemistry of Monocyclic 2,5-Cyclohexadienones)

For extensive study Schuster and co-workers[18] have elegantly chosen the compound 4-methyl-4-trichloromethyl cyclohexadienone (30) which is easy to synthesise and has also molecular simplicity. This model compound possesses a trichloromethyl substituent at C- 4 which can be expelled readily as radical. Photolysis of (30) in ether or 2-propanol afforded p-cresol (31) and products C_2Cl_6 and $CHCl_3$ are derived from $\dot{C}Cl_3$. This supports the proposition of the primary photochemical intermediate as a radical-like species. To adduce further evidence for radical intermediate they thermally generated $Me_2\dot{C}OH$ by decomposing benzoyl peroxide at 80°C in isopropanol in which (30) was added. P-cresol (31) was obtained along with $CHCl_3$ in good amount.



$$Ph\overset{O}{\overset{\|}{C}}O O\overset{O}{\overset{\|}{C}}Ph + (30) + Me_2CHOH \longrightarrow (31) + CHCl_3 + Me_2C=0$$

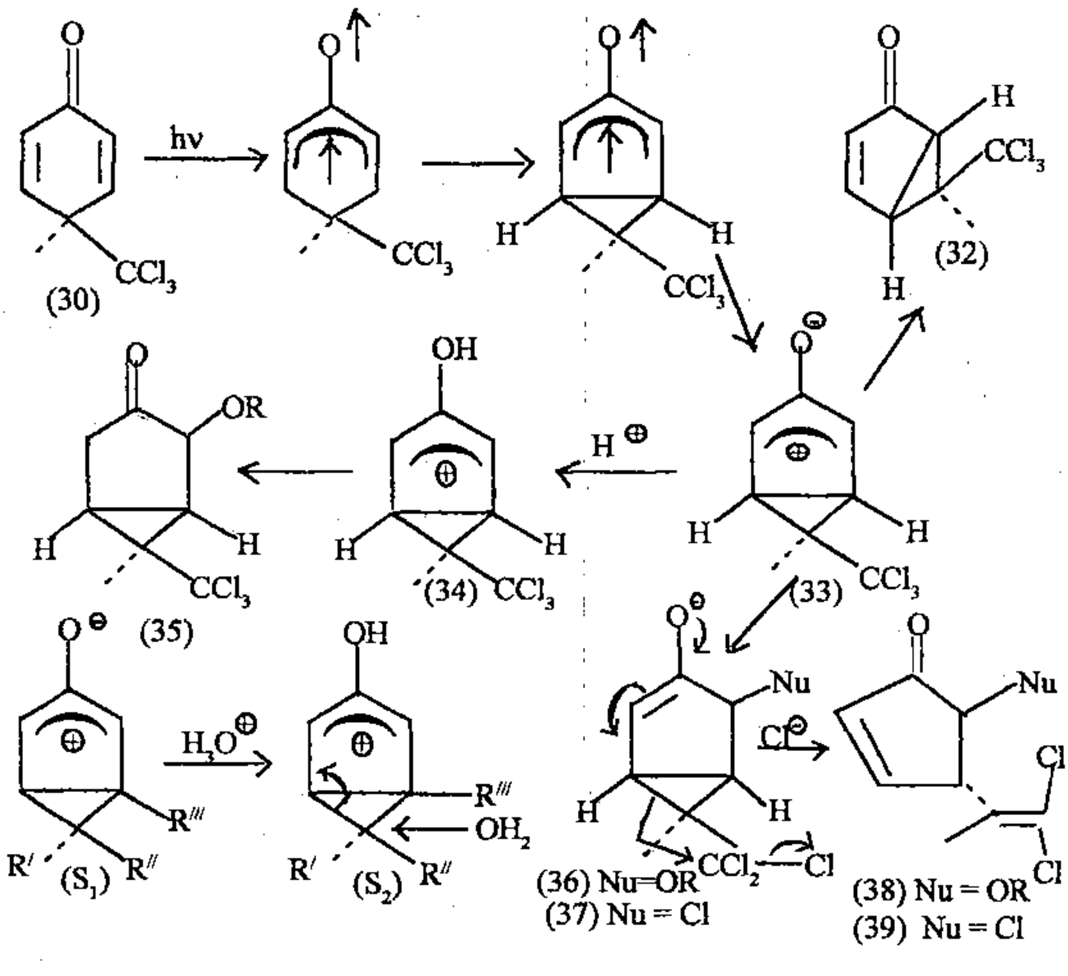


(30)

(31)

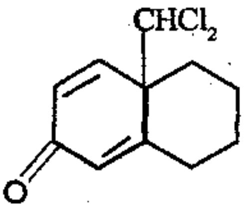
$$\dot{C}Cl_3 + \dot{H} \longrightarrow CHCl_3 \qquad 2\dot{C}Cl_3 \longrightarrow C_2Cl_6$$

On the other hand, irradiation in benzene yielded the lumiproduct (32). Schuster et al. also utilized this compound for providing uinequivocal proof for the intermediacy of zwitterion at the later stage of this deep-seated rearrangement. A close look at the structure of (30) shows that due to the presence of the electron - withdrawing trichloromethyl substituent susceptibility of this intermediate to nucleophilic trapping increases considerably in the transition state. It makes [1,4] rearrangement to lumiproduct as in (S$_1$) and the cyclopropyl cleavage as in (S$_2$) less favourable and increases the possibility of zwitterion (33) for trapping as well as kinetic study. Protonation of (33), which has been envisaged as the common intermediate for (32), (35), (38) and (39) in acidic methanol, ethanol or isopropanol gives (34) which is captured by solvent to yield the alkoxy ketone (35). The product (35) is a unique one since the postulated zwitterion skeleton is preserved in it. In the absence of an appropriate electrophile, the zwitterion is captured by nucleophile such as alcoholic solvent and added halide ion to afford (36) and (37), respectively, which subsequently fragmented to give (38) and (39) by an



anionic Grob-type process. On increasing LiCl concentration in methanol and trifluroethanol the ratio (39)/(32) and (38)/(39) increase linearly and the quantum yield of the formation of the zwitterion (33) approaches to unity.

In contrast to (30) the closely related bycyclic dienone (40) is inert under similar condition of irradiation[22]. Probably lesser stability of the dichloromethyl radical could be the reason for the failure of (40) to undergo expulsion. Also the failure to take part in lumiproduct formation can be accounted for by the destabilising election-withdrawing effect of the dichloromethyl group on the usual intermediate (41) possessing an electron deficient π-system.



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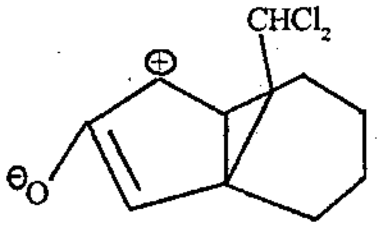
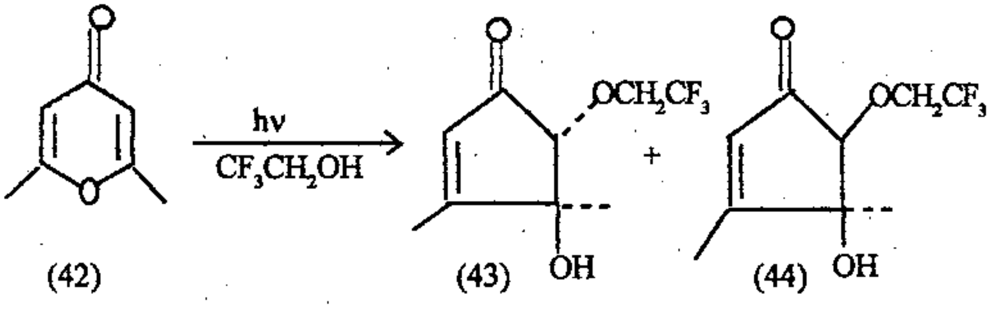
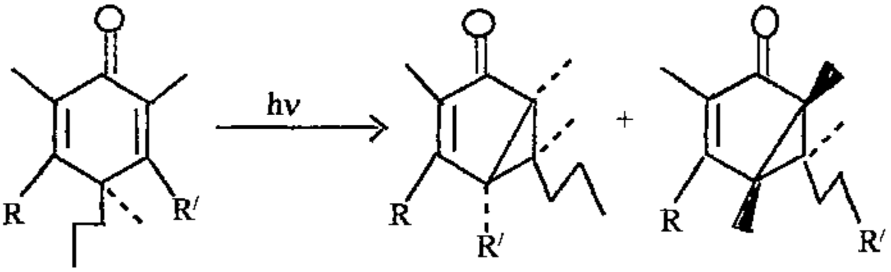


(41)

Pavlik et al.[23-24] irradiated 2,6 - dimethyl-4H-pyran-4-one (42) in 2,2,2-trifluroethanol and obtained the stereoisomeric products (43) (major isomer) and (44) (minor one). These products are formed by nucleophilic trapping and fragmentation of the zwitterion intermediate just as in the trichloromethyl analogue (33) discussed above.

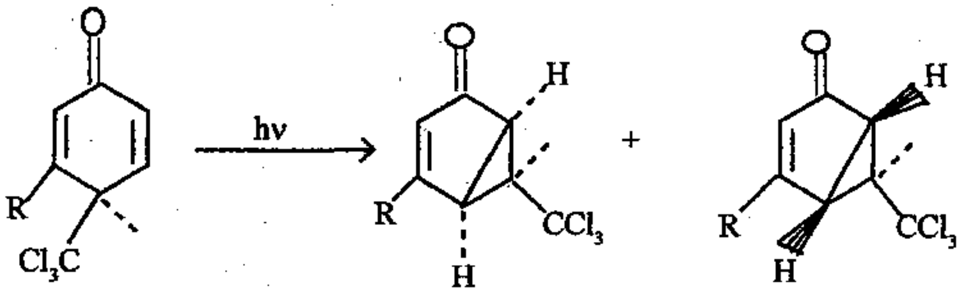


Subsequent to photoexcitation of cyclohexadienones which are generally nearplanar, β, β′ bonding is postulated which leads to puckering of the ring system. Indepth studies have been conducted to determine the factors that govern the steric and regioselective course of cyclohexadienone-bycyclohexenone photoconversion, particularly in monocyclic system. In the absence of other perturbations in the system the direction of ring puckering seems to be steric in nature. Rogers and Heart[25] observed that increased steric requirements of substituents at C-3 to C-5 may direct the bulkier of the C-4 substituents [n-propyl in (45)] into the *endo* orientation. The molecular motion leading to *exo* orientation would require the larger substituent (n-propyl) to pass by the substituent (CH_3) which becomes more difficult with their increasing size. In the series (45a) - (45c) they[25] demonstrated that the ratio of the products (46a-c)/(47a-c), as shown below, support their proposition, provided the inversion of configuration on the [1,4] shift is assumed.



(45a)R = R′=H	46a) R=R′=H	(47a)R=R′=H	$\frac{46a}{47a} = \frac{44}{56}$
(45b)R=CH_3, R′=H	(46b)R=CH_3, R′=H	(47b)R=CH_3, R′=H	$\frac{46b}{47b} = \frac{68}{32}$
(45c)R=R′=CH_3	(46c)R=R′=CH_3	(47c)R=R′=CH_3	$\frac{46c}{47c} = \frac{91}{09}$

In order to examine the relative contribution of electronic and steric effects, Schuster and coworkers[18-19] have chosen the cyclohexadienone (30) and its methyl homolog (48)[26] possessing trichloromethyl group at C- 4 which can exert steric effect due to bulky - CCl_3 group as well as electronic effect arising from columbic charge repulsion between the electron-rich CCl_3 group and the dienone π-system. The cyclohexadienone (30) afforded (32) as the sole product while (48) gave both *exo* (50) and *endo* (49) as major and minor products, respectively. The stereochemistry of the products were ascertained on the basis of spectral data, hydrogenation experiment and an X-ray crystal analysis. The results are rationalized mechanistically on the basis of competition of steric effect favouring an endo orientation in the intermediate and derived lumiketone of the bulkier substituent (CCl_3) at C - 4 and columbic effects favouring an *exo* orientation of CCl_3 and other electron-rich group. In these systems, it is clear that electronic effects dominate in the reaction course.



(30) R = H

(48)R = CH_3

(49)R = CH_3

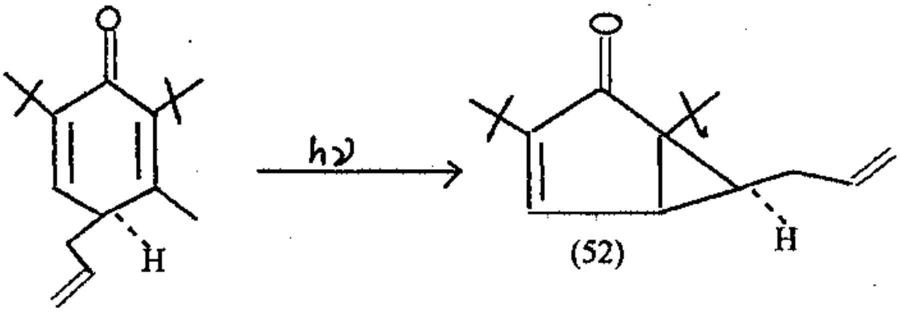
(32)R = H

(50) R=CH_3

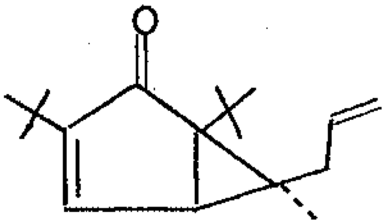
A few cases of cyclohexadienone photorearrangement have been reported in which the [1,4] shift can take place in two nonequivalent directions and in which the double bond substitution in the bicyclohexenone products seem to exert a selective infleunce in the direction in which migration proceeds. The product formation reflects a preference for α, β-di or β- monosubstituted double bond.[25-27]

Miller[28] observed that irradiation of (51) containing allyl group at C - 4 gave (52) . NMR analysis of the product showed that the cyclopropyl proton and the allyl group are on the same carbon which can only be C - 6. The geometry of C - 6 was deduced from the unusually high field absorption (τ 7.96) of the allylic methylene group. This absorption appears at approximately the same position as that of the allylic methylene group of (53), but is about 0.4 ppm higher field than the allylic methylene absorption of (54). The allyl group in (52), therefore, must be in the shielded *endo* position over the π-electron cloud of the cyclopentenone ring. Irradiation of (55) containing *trans* 2-butenyl group at C - 4 afforded (56). Its spectra indicated that the structure of the product was indeed analogous to that of

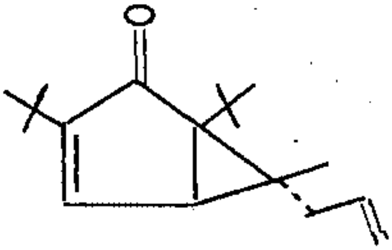
(52). Besides, the NMR spectrum clearly showed that the trans-2-butenyl group of (55) remains unchanged during the reaction.



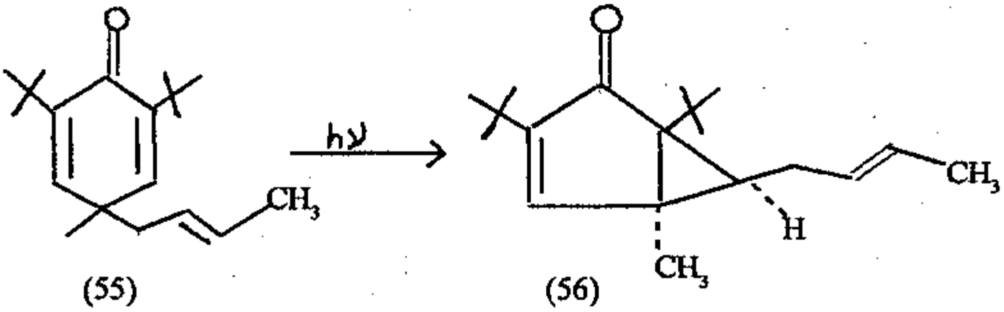
(51) (52)



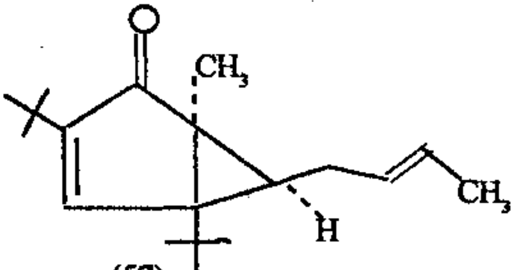
(53)



(54)



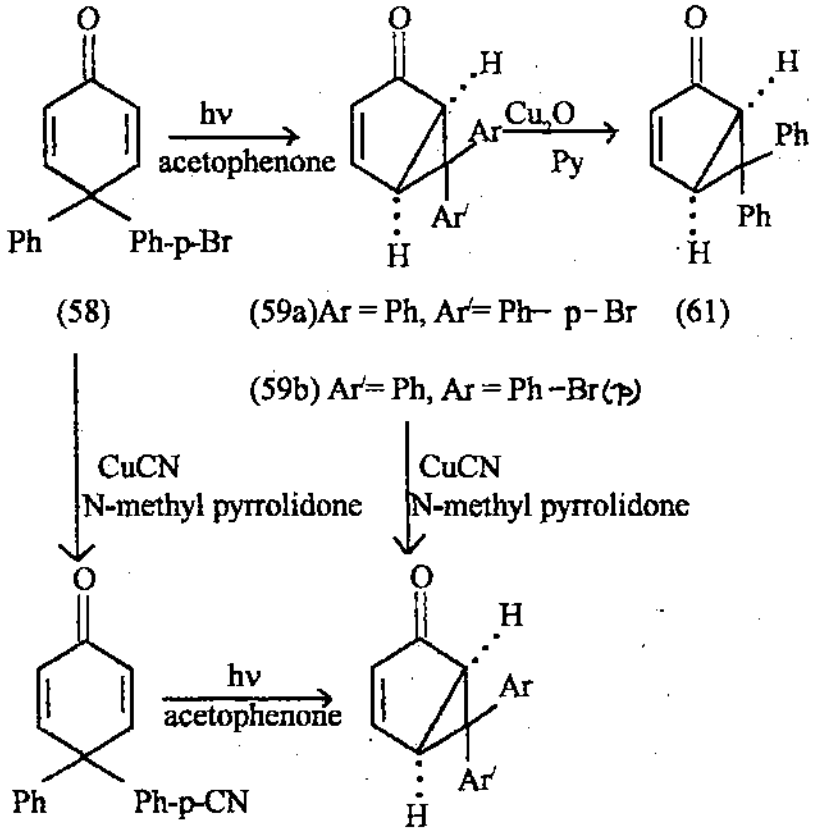
(55) (56)



(57)

The selective rearrangement of (55) to (56) combines preferential *endo* puckering with a [1,4] shift toward the product with an α-monosubstituted double bond. This reversion of the [1,4] shift trend could be due to less severe steric compression between methyl and t-butyl groups in (56) than in the alternative (57).

On irradiation of 4-p-bromophenyl-4-phenyl-2,5-cyclohexadienone (58) Zimmerman and Grunewald[29] obtained two isomeric *cis* and *trans* 6-p-bromophenyl-6-phenyl-bycyclo-[3.2.0]-hex-3-en-2-ones (59a) and (59b). That they were the stereoisomeric products was established by their reductive conversion, as shown below, to the known 6,6-diphenyl bicyclo [3.1.0] hex-3-en-2-one(61). Cuprous cyanide in N-methyl pyrrolidone resulted each to these epimeric (59a) and (59b) to the corresponding 6-p-cyano-phenyl-6-phenyl bicyclo [3.1.0] hex-3-en-2-one isomers (60a) and (60b), respectively. These were demonstrated to be identical with the products of photolysis of 4-p-cyanophenyl-4-phenyl cyclohexadienone (62). Therefore, the dienone irradiation afforded only the usual type-A photorearrangement and no C- 4 ⟶ C- 3 aryl migration.



(58)

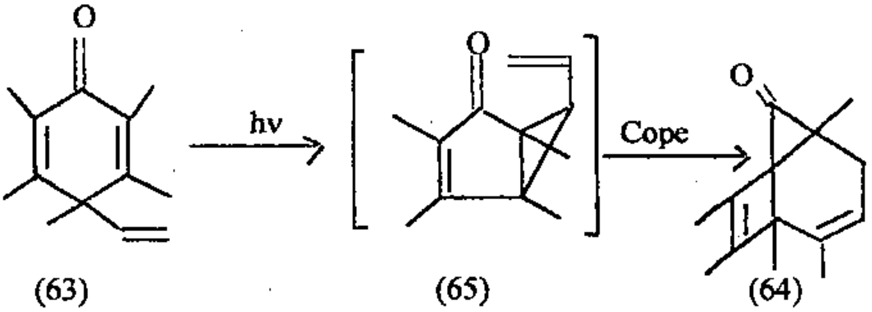
(59a) Ar = Ph, Ar' = Ph– p-Br

(61)

(59b) Ar' = Ph, Ar = Ph –Br(p)

(60a) Ar = Ph, Ar' = Ph - p - CN
(60b) Ar' = Ph, Ar = Ph - p - CN

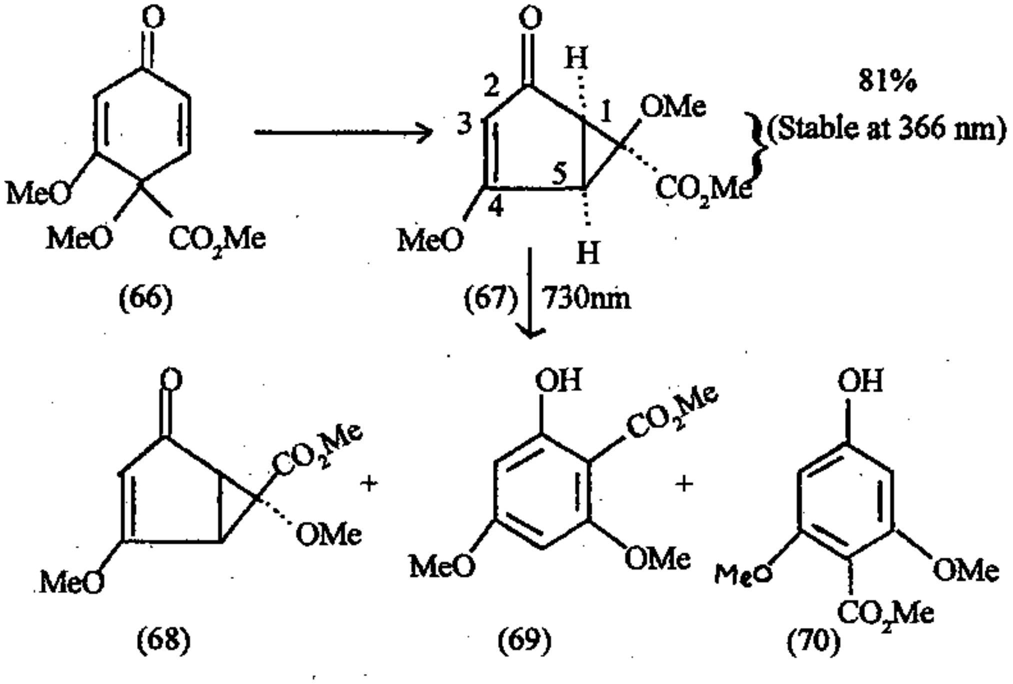
The first example of photochemistry of 2,5-cyclohexadienones with a 4-vinyl substituent was reported by Hart and Nitta.[31]. The initially formed luniproduct resulted in an unusual skeleton rearrangement.



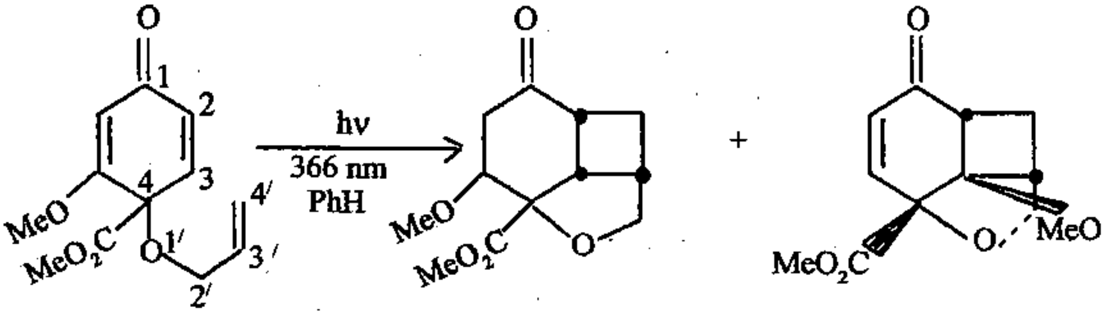
(63) (65) (64)

The structure of the product (64) was deduced from its spectral data and method of synthesis. Elemental analysis and the mass spectrum showed that (64) was an isomer of (63).The carbonylabsorption $\nu_{c=0}$ 1753 cm^{-1} and uv λ_{max} 280nm (ε 24), end absorption of spectrum at 220 nm (ε 7149) clearly eliminated the anticipated structure (65). The NMR spectrum showed one vinyl proton at δ 5.13(m), two aliphatic methyls at δ 1.03(m) three allylic methyls at δ 1.67 (m) and two additional allylic protons at δ 2.17(m), all consistent with the assigned structure (64). One plausible path from (63) to (64) is via the unstable endo-vinyl compound (65), a lumiproduct which being a cis-divinylcyclopropane spontaneously undergoes Cope rearrangement to (64).

In 1991 A.G.Schultz and R.E. Hazrington[32] reported that enantiomerically enriched 4-carbomethoxy-3,4-dimethoxy-2,5-cyclohexadien-1-one(66) undergoes a completely disastereoselective (but not enantiospecific) type A photorearrangement at 366 nm to give 6-carbomethoxy-4,6-dimethoxy bicyclo-[3,1,0^{1,5}]-hex-3-ene-2-one in 81% yield (67), which is photostable at 366 nm but rearranges to disastereoisomer (68) and phenols (69) and (70) at > 300 nm.



It is proposed that ground state conformational effects control the type A photochemistry of (66) and that rearrangement to (67) occurs in accordance with the principle of least motion in the transition state for rearrangement to diastereomerically related zwitterions of (66). Irradiation of (71) in benzene solution at 366 nm gave a 3:1 mixture of 7-oxatricyclodecenones (72) and (73). It is interesting to note that $1'$-oxa-substitution on the 4-($3'$ - butenyl) side chain is compatible with intra-molecular 2+2 photocyclo addition, which occurs to the apparent exclusion of the type A photorearrangement.



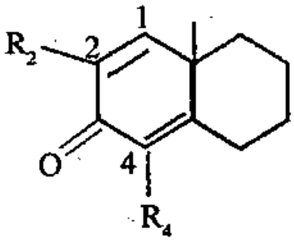
58% 18%

(71) (72) (73)

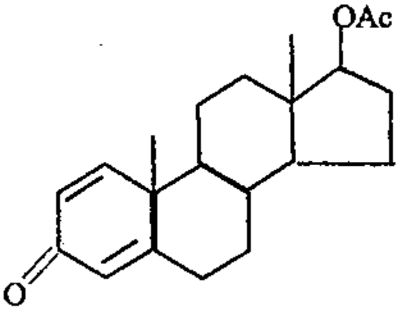
SECTION - C

(A short review on Bicyclic Cross-conjugated Cyclohexadienones)

Like photochemistry of monocyclic cyclohexadienones, bicyclic ones also have been studied intensely. Formation of lumiproduct is fairly general. It has been observed earlier that a good amount of lumiproduct can be achieved from 4-methyl dienone (74c) by using the broad energy spectrum from a high-pressure mercury lamp. In contrast, the unsubstituted (74a) or 2-methyl systems (74b) afford low yield of lumiproducts. Initially, this difference of lumproduct formation has been attributed to a basic difference in reaction pathway and various explanations have been afforded[37-40]. Later it has been observed that most of the other products obtained from the unsubstituted dienone (74a) and similar unsubstituted steroidal dienone(75)[39,40] are secondary photoproducts which are derived via the lumiproduct. Hence, the difference between unsubstituted and 4-methyl substituted systems actually stems from the basic difference in the rate of conversion of dienone to lumiproduct and the rate of destruction of lumiproduct to other secondary photoproducts and is not a fundamental difference in reaction pathway.



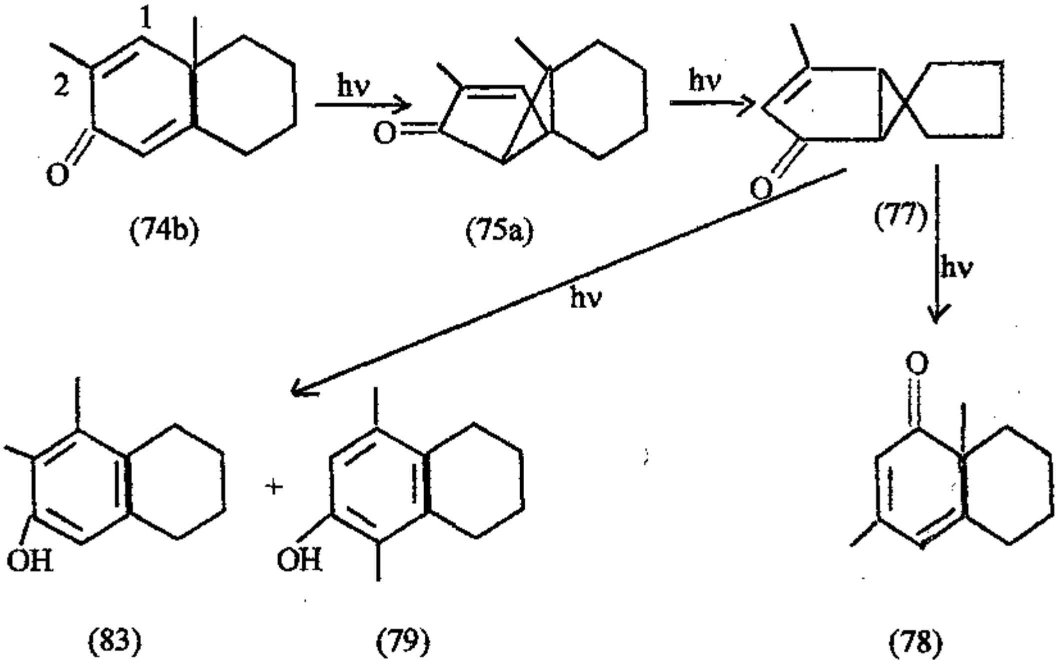
(74a), $R_2 = R_4 = H$
(74b), $R_2 = Me, R_4 = H$
(74c), $R_2 = H, R_4 = CH_3$



(75)

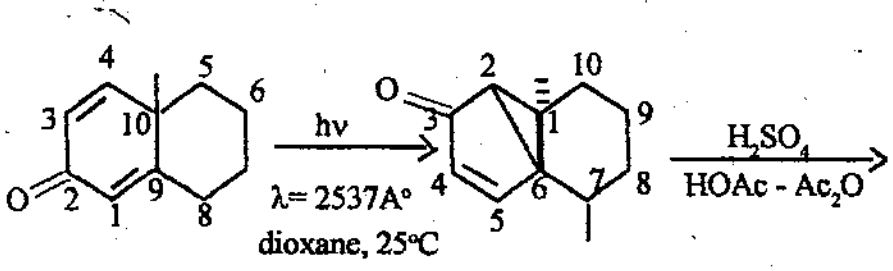
Although the photostationary concentration of the lumiproducts from many unsubstituted (74a) or 2-methyl substituted dienones (74b) are quite low in the presence of the broad spectrum of high-oressure mercury lamp, this difficulty often can be overcome by the use of monochromatic light source of 253.7 nm available from low-pressure mercury lamp[40,41]. At this particular wavelength, the absorption by the lumiproduct is usually only about a sixth of the starting dienone and hence the rate of lumiproduct formation significantly exceeds the rate of further conversion of lumiproduct to secondary photoproducts. Consequently, interruption of irradiation at the appropriate time afforded lumiproducts in good yields. This technique also improved further the yield of lumiproduct from 4-methyl substrates.

In an effort to learn more about the nature of the effects of alkyl substituents in the photochemical rearrangement of cross-conjugated cyclohexadienones, Kropp[33] studied the photochemical properties of the 2-methyl-1, 4-dien-3-one (74b) in both neutral and acidic media. Irradiation of (74b) in dioxane gave the linearly conjugated product (78) as the principal product via at least three distinct photochemical rearrangements involving the cyclopropyl ketone (75a) (lumiproduct) and (77) as intermediates.

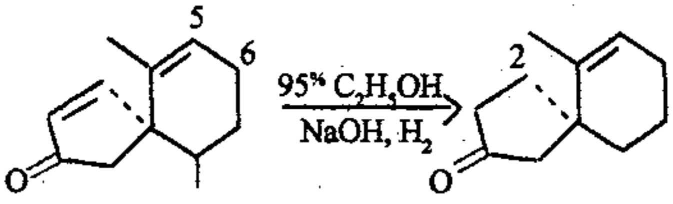


Two minor products formed in neutral as well as acidic media had been characterised as phenols (79) and (83). He also commented upon the significant role of the 2-methyl substituent in the photochemical properties of (74b).

Utilizing photochemical technique as a synthetic tool, Caine and co-workers[34] developed a convenient synthesis of a precursor to the spirovetione sesquiterpenes. They photolysed the bicyclic hexadienone and obtained the tricyclic lumiketone(75b) in good yield. Structure of (75b) was deduced by combination of physical techniques. UV spectrum showed λ_{max} 234 nm (ε 4820) , IR at 1695 cm^{-1} (conjugated cyclopentenone) and ^1H NMR signals at δ 0.96 (δ , J = 6.7 Hz, 3H, 7- CH_3), 1.18 (S, 3H, 1- CH_3), 5.82 (q, J_{AB} = 5.5, J_{BX} = 1.1 Hz; 1H, 4-H) and 7.19 (q, J_{AB} = 5.5, J_{AX} = 0.8 Hz, 1H, 5-H). Mass spectrum registered molecular ion peak at m/z 176 (M^+).



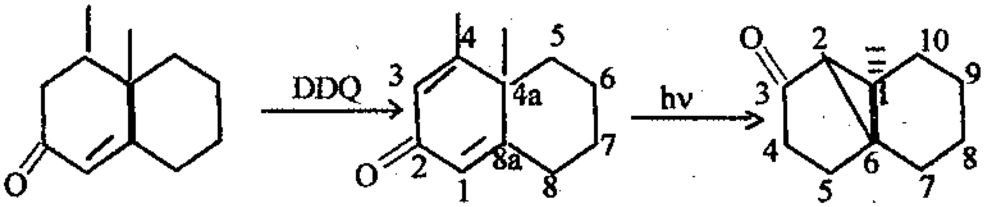
(74a) (75b)



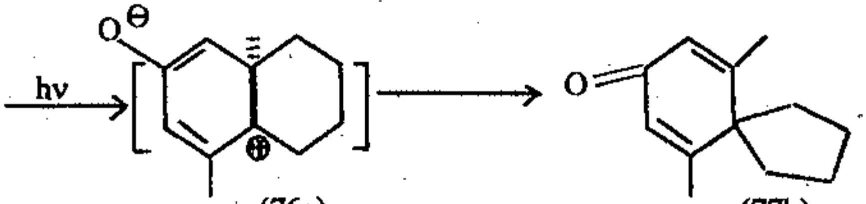
(76) (77a)

The key compound (75b) was first treated with HOAc-Ac_2O in H_2SO_4 to afford the spirodienone (76) which ultimately gave rise to the spiroenone (77a) a precursor of spirovetivone, on catalytic reduction in alcoholic alkali.

Caine et al.[35] also used this photochemical method for the interconversion of nootkatane and spirovetivone sesquiterpenes. The dienone (74d) which is related to the nootkatane system since it contains a methyl substituent at C- 4, was prepared by DDQ oxidation of the corresponding cis-dimethyl octalone[36] and irradiated in anhydrous dioxane at 254 nm to produce the lumiproduct, the tricyclodecenone (75c) in 62% yield. This primary photoproduct is itself photolabile and undergoes further rearrangement presumably via dipolar intermediates such as (76a) which is considered to arise by electron excitation, cleavage of the internal bond of the cyclopropane ring and electron demotion. The dipolar species undergo 1,2 methylene migration to yield a spiro dienone (77b).

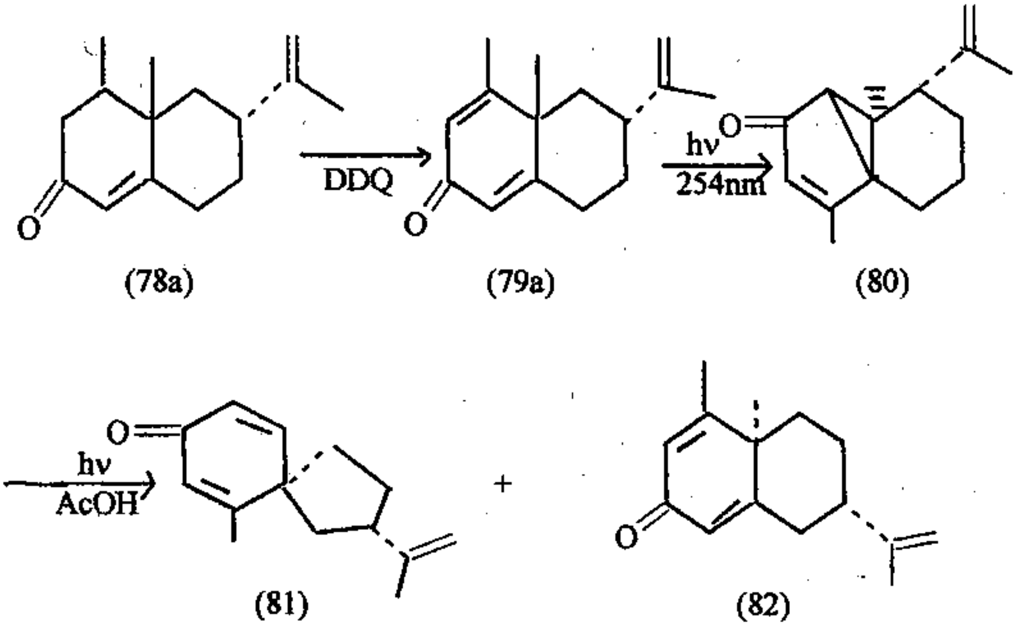


cis-dimethyl octalone (74d) (75c)



(76a) (77b)

They[35] also studied the photochemical behaviour of various bicyclic dienone with sesquiterpene carbon skeleton. 3,4-dehydronootketone (79a) which was prepared by DDQ oxidation of nootkatone (78a), on irradiation at 254nm in anhydrous dioxane afforded the lumiproduct, the tricyclodecanone (80) which on further irradiation in 45% aqueous acetic acid for 30 min using pyrex-filtered UV light yeilded the spirotrienone (81), the bicyclic trienone (82) and dehydronootketone (79a) in 46, 37 and 12% yield, respectively.

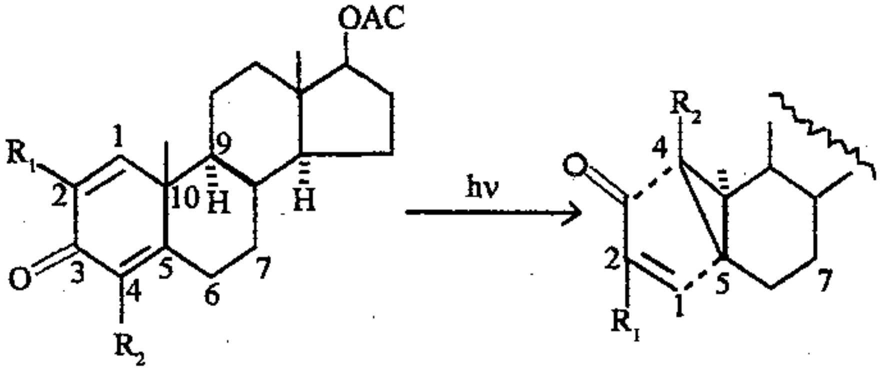

O
DDQ
O
hν
254nm
O
(78a)
(79a)
(80)
hν
AcOH
O
+
O
(81)
(82)

SECTION - D

(A short review on Photochemistry of Polycyclic Cross-conjugated Cyclohexadienones including Steroids)

We begin with steroids. Steroids are a class of substances upon which all sorts of reactions including photochemical reactions have been applied. This is mainly due to their significant biological properties.

Jeger and coworkers[42] first carried out photoreaction of O-acetyl-1-dehydrotestorterone (83a) with broad spectrum high-pressure mercury lamp in dioxane and recorded the formation of the corresponding lumiproduct(84a) in low yield (11%). Later , in same solvent but using a low pressure lamp (2537A°) Jeger et al.[43] observed the formation of lumiketone (84a) in high yield (62%). Prolonged irradiation in dioxane solution yielded a complex mixture of products from which four phenolic and five ketonic compounds including the lumiproduct (84a) were isolated. Spectral data, NMR and rotatory dispertion data were advanced in support of lumiketone structure (84a).



(83a) $R_1 = R_2 = H$

(83b) $R_1 = CH_3$, $R_2 = H$

(83c) $R_1 = H$, $R_2 = CH_3$

(83d) $R_1 = R_2 = CH_3$

(84a) $R_1 = R_2 = H$

(84b) $R_1 = CH_3$, $R_2 = H$

(84c) $R_1 = H$, $R_2 = CH_3$

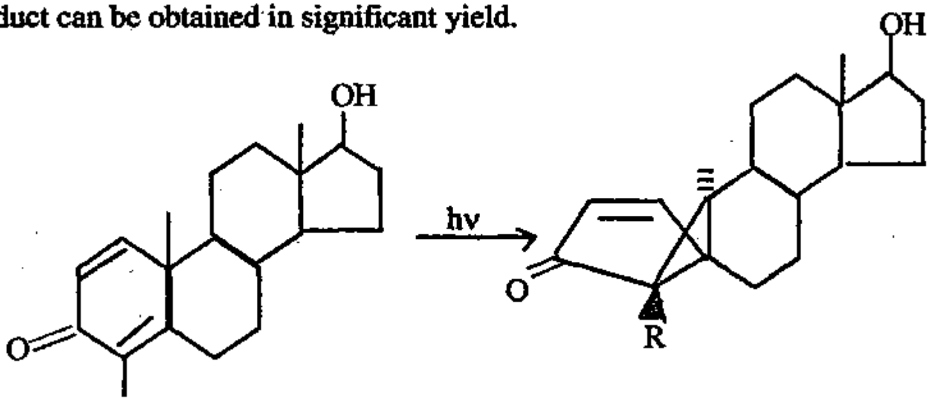
(84d) $R_1 = R_2 = CH_3$

This photoreaction has been successfully utilised to achieve the selective inversion of configuration at C-10 and the accomplished they synthesis of 10α - testosterone with unnatural angular configuration starting from (83a) in seven steps.[44]

Arigoni, Jeger[45] and their gropup studied the effect of methyl substituent at C-4 tstosterone derivative(83c) on lumiproduct formation. Upon irradition with high pressure lamp in diaxane solution (83c) they obtained corresponding lumiketone (84c) in 60-70% yield. They have also carried out photolysis of 2,4-dimethyl analogue (83d) under same irradiation condition and recorded the formation of the lumiproduct (83d) in good yield (60%). On the other hand, 1-dehydrotestosterone derivative (unsubstituted) (83a) under the same condition of irradiation yielded a mixture of 8 compounds. Thus, it appears that[45] the photochemical isomerisation of cross-conjugated steroid dienones is profoundly influenced by the presence of a methyl substituent at C - 4.

Schaffner, Jeger and coworkers[46] also noticed that on irradiation 2-methyl substituted testosterone derivative (83b) in dioxane with broad spectrum high pressure lamp afforded the corresponding lumiproduct (84b) as one of the products. Furthemore, the close relationship between the sequence of rearrangement initiated by the irradiation of (83a) and its 2-methyl homologue (83b) has been carefully observed.

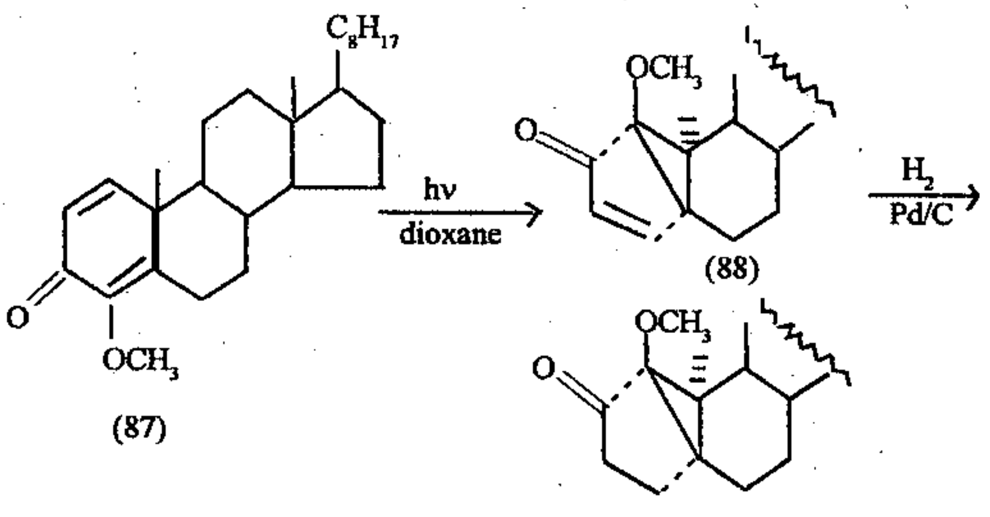
Because of the photolability of the primary photoproduct, the lumiproduct, prolonged irradiation gives rise to several secondary photoproducts. Propensity for the formation of secondary photoproducts is more pronounced at higher wavelengths of broad spectrum high pressure mercury lamp. This difficulty can be frequently circumvented by the use of low-pressure lamp emitting almost monochromatic wavelength of 2537A°. At this particular wavelength, the absorption of the lumiproduct is about one sixth of the starting dienone. Consequently, the rate of lumporoduct formation considerably exceeds the rate of further conversion of the lumiproduct to secondary photoproducts. Thus, by arresting the photoreaction at an appropriate time the lumiproduct can be obtained in significant yield.



(85) $R = H, CH_3, C_2H_5$, n-butyl isobutyl and isoamyl (86)

Schuster and Barringer[47] synthesised several 4-alkylated dehydrotestosterones (3) (R = H, CH_3, C_2H_5, n-butyl, isobutyl and isoamyl) and conducted their photolysis at 2537A° in dioxane. The corresponding lumiketones (86) were obtained with variable quantum efficiency. The photoreaction is qunched by 1,3-cyclohexadiene and trans piperylene. Low-temperature absorption and emission studies indicated the lowest triplet in such systems in the π, π* triplet. It has been suggested that the two lowest triplet states Tn,π* and Tπ,n* are in equilibrium at room temperature. Studies also showed the differential quenching capabilities of the dienes which had been ascribed to the relaxation of the spectroscopic triplet (E_t = ~70 kcal mol^{-1}) to a triplet (E_t = 60 kcal/mol) whose geometry may approximate to that of the previously postulated 3,5-bonded intermediate. Radiationless decay from the triplet was not thought to be the reason for the inefficiency in this reactions, but rather return to the starting material from some intermediate along the reaction pathway to product, had been suggested.

Pete and Wolfhugel[48] irradiated 4-methoxy-cholesta - 1,4-dien-3-one(87) in dioxane at 360 nm and got the lumiproduct (88). The structure of the photoproduct was deduced by spectroscopic methods coupled with hydrogenation to a saturated ketone (89). The uv spectrum of (88) in hexane exhibited absorption at 242 (4500) and 285(1360) nm and IR bands at 1740, 1660 and 1575 cm^{-1}. NMR spectrum showed resonances at δ3.41 (S, 3H), 5.77 (d, 1H) and 7.10 (d, 1H). The hydrogenated product (89) displayed uv absorption at 227 (34.70) nm, IR bands at 1715, 1180, 1003. 900cm^{-1} and an NMR resonance at δ3.41 (S, 3H) besides other resonances.

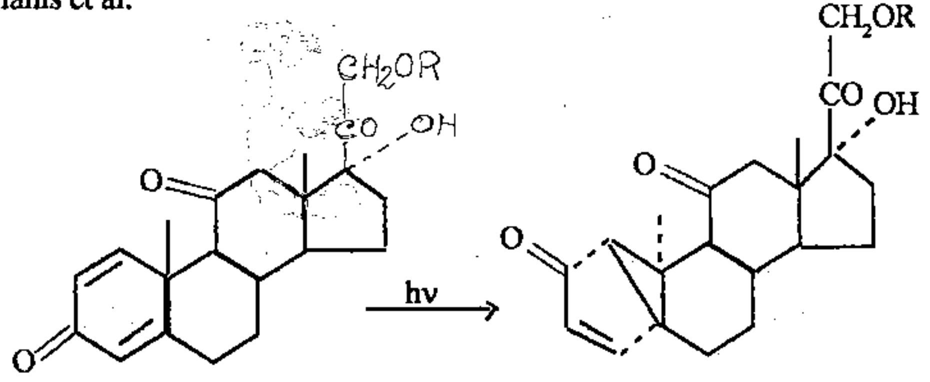


(87)

(88)

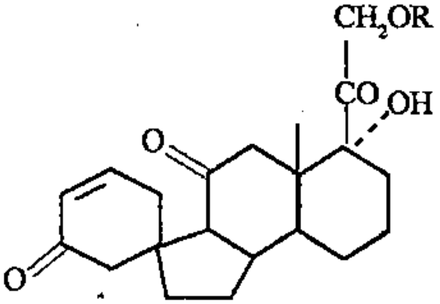
(89)

Barton and Taylor[49] first carried out the photolysis of prednisone(90a) and its acetate (90b) and assigned the structure (91a) and (91b) for the corresponding lumiproducts. Since their assigned structure differed from that expected (92a) and (92b), based on the new generally accepted methanism for photoisomerisation of cross-conjugated dienones, reinvestigations of the photochemistry were undertaken by Williams et al.[50]



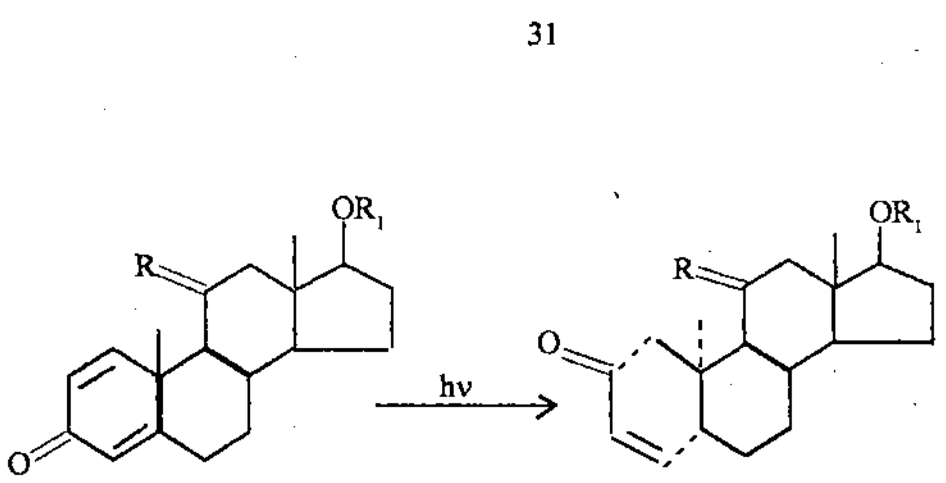
(90a) R = H
(90b) R = AC

(92a) R = H
(92b) R = Ac



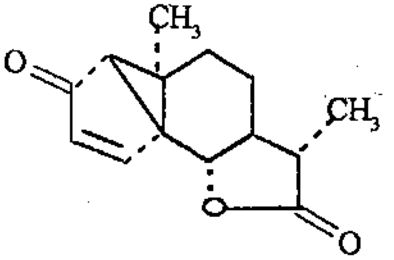
(91a) R = H
(91b) R = Ac

The assignment of the structure and stereochemistry of (92a) and (92b) was by comparison of their spectral data with those of lumiproducts (94a) and (94b), derived by photoisomerisation of 17β-acetoxy-1-dehydrotestosterones (93a)[51] and (93b)[52] in dioxane with 254 nm light. The structure of the lumiproduct (94a) was proven by chemical degradation[52] and by CD measurement.[54] The UV of the lumiproduct (92b) λ_{max} 266nm (ε 2500) is in close agreement with that of (94b) 268 nm (ε 2950)[53]. The ^1H NMR spectra of the A-ring protons in the lumiproducts(92a) and (92b) show a very characteristic coupling pattern similar to that described for (94a)[52]. Namely, in the



(93a) R = 2H, R_1 = Ac
(93b) R = O, R_1 = Ac

(94a) R = 2H, R_1 = Ac
(94b) R = O , R_1 = Ac

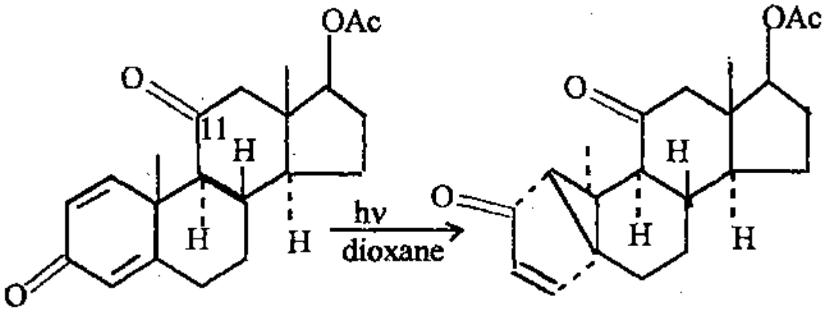


(95a)

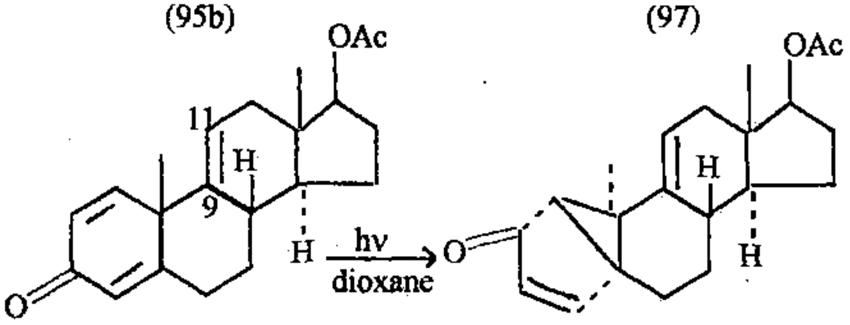
NMR spectra of (92a), (92b) there are two doublets centred at δ7.26 (7.20) and 5.87(5.86) with J = 6.0Hz, indicating the presence of an α, β-unsaturated ketone in the ring A. Double irradiation experiments indicate that the H-1 of (92a), (92b) is coupled to both the H-3 and H-4, through the carbonyl as was also observed in (94a)[52]. In ^{13}C NMR spectra for (92a), the chemical shift assignments for the carbon atoms in rings A and B of (92a) are based on those of lumisanotonine (95a) and bicyclo [3.1.0] hex-3-en-2-one and C and D rings of cortisone acetate[55]. A significantly different ^{13}C NMR signals for a radically different structure (91) would be expected. Proof of the stereochemistry of the lumiproduct was obtained from a comparison of CD of (92a) and (92b) with the model compounds (95a) and (94a). In all cases they show a negative CD of similar magnitude around 345nm followed by a positive CD around 275 nm, again of similar magnitude. The CD of structures similar to (91) show no maxima or minima with an amplitude greater than 10.3[54]. Thus, CD supports very strongly sttucture (92) and excludes the structures similar to (91), Furthermore, the absence of peaks in the mass spectra of (92a) and (92b) at M^+ - 95 and M^+ - 96 also argues against structures such as (91).

Finally, a comparison of lumiproductone acetate with that prepared by Barton and Taylor[49] showed them to be identical and hence, their structure for lumiprednisone acetate should be (92b).

Presence of a functional group in the close proximity of a reactive centre sometimes modify the course of reaction and/or reaction rate. Schaffner, Jeger and coworkers[56] conducted irradiation of steroidal A-ring cyclohexadienone containing 11-keto group (95b) and 9(11)-ene(96) in dioxane and obtained virtually quantitative photoisomerization to (97) and (98) respectively. These conversions are consistent with the previously established general scheme of cross-conjugated cyclohedadienone under neutral condition. This also revealed that a keto group at 11 or a double bond at 9(11) position did not exert any nocticeable influence on the course of this phototransformation.



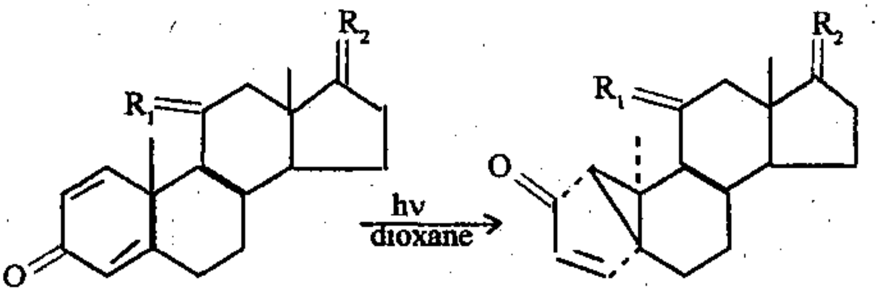
(95b) (97)



(96) (98)

In order to examine the effect of the presence of C-11α and 11β - hydroxy groups on the course of lumiproduct formation, Williams et al.[57] carried out photolysis of 21-acetoxy prednisolone (99) and 11-a hydroxy pregna-1,4- dien-3, 20-dione

(100) in neutral condition and got the expected lumiproducts (101) and (102) respectively. This led to the inference that the presence of an α- or β-hydroxyl group at the C-11 position in ring-C of a steroid does not change the general photoisomerisation path of an A ring cross-conjugated cyclohexadienone.



(99) R_1 = α-H, β-OH, R_2=α-OH, β-$COCH_2OAc$; (101) R_1 = α-H, β-OH

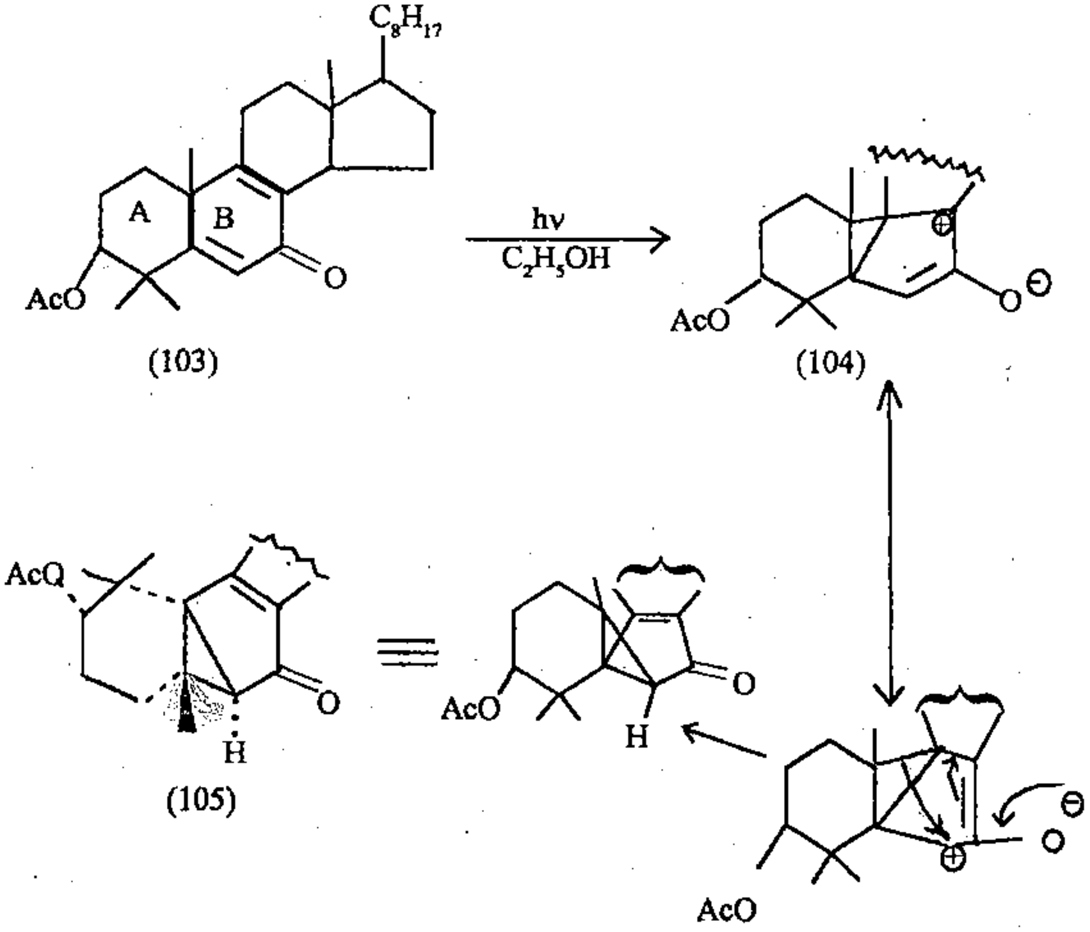
(100) R_1 = α-OH, β- H, R_2=α-H, β-$COCH_3$; R_2=α-OH, β-$COCH_2OAc$

(102) R_1 = α-OH, β-H

R_2=α-OH, β-$COCH_3$

On the other hand, the presence of a hydroxyl group at C-10 of C-19 norsteroid gives the anomalous reaction product discussed in page 64.

Cyclopropyl ketone (lumiproduct) formation is fairly general for 2,5-cyclohexadienone (cross-conjugated) and is not limited to those having the hexadienone chromophore in ring A only . Irradiation of a B-ring containing this chromophore in steroid, 3β-acetoxylanosta-5,8-dien-7-one (103), gave a product to which the structure and stereochemistry (105) was assigned[58,59]. This is the expected product from rearrangement of the cyclopropyl intermediate (104) in the usual fashion.

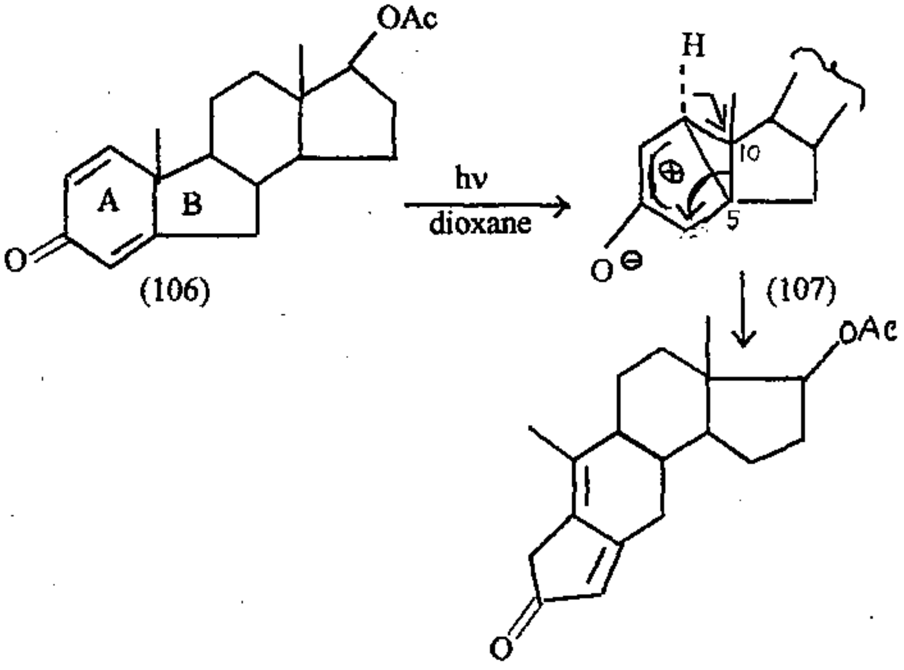


(103)

(104)

(105)

In dioxane solution, the B-nor dienone (106) is converted exclusively to the linear dienone (108). The preference for fission of the 5, 10 bond in the proposed intermediate (107) has been attributed to the relief of enhanced ring strain which is introduced by the five-membered B-ring as compared to the structurally analogous intermediate having a six-membered B-ring.

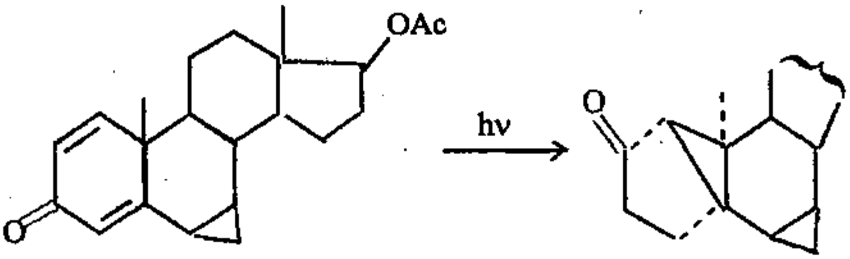


(106)

(107)

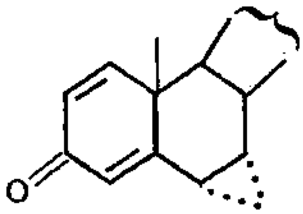
(108)

The 6β, 7β methano homolog of steroid (109), upon irradiation in dioxane isomerises readily to the bicyclohexenone (110) while the 6α, 7α- isomer (111) is extraordinarily stable toward irradiation[61].

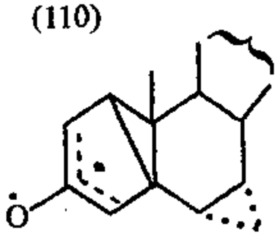


(109)

(110)

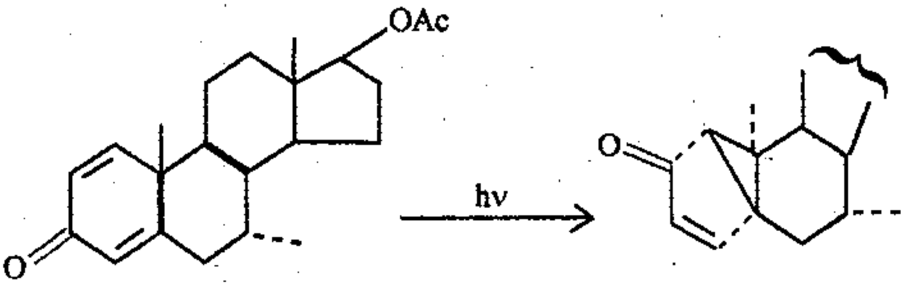


(111)



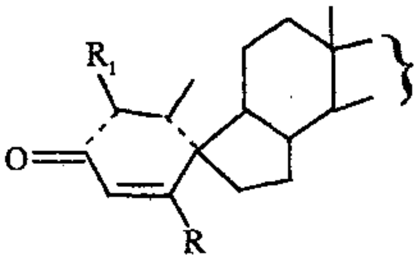
(112)

The apparent failure of (111) to react may be due to the high steric strain which would be introduced by the two adjacent three-membered rings on ring B upon 1,5-bridging. This could cause reversal of primary diradical formation (112) and corresponding zwitterion might not be formed. In contrast, a steric inhibition of similar magnitude would not arise in the reaction of (109) having a trans arrangement of the two cyclopropyl rings in the primary photochemical step prior to the rearrangement at the stage of a dipolar ground state intermediate. Interestingly, (113), the 7α-methyl hormolog of (83a), isomerizes to(114) smoothly[62]. In this case, the steric interaction in the primary product structure can be expected to be less severe than in (112).

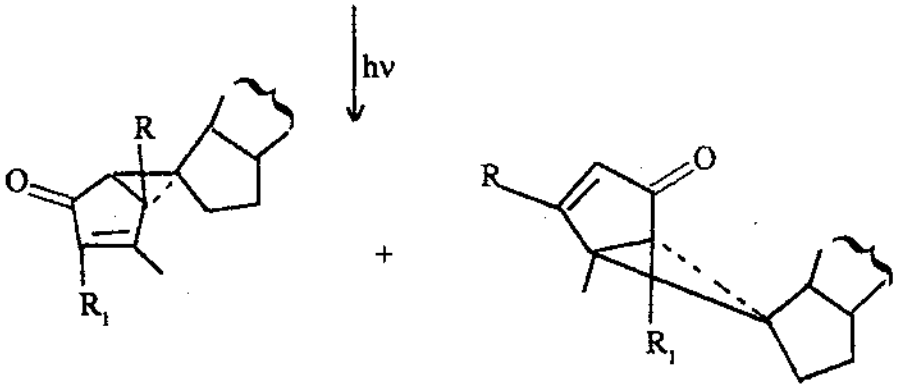


(113) (114)

Several steroidal spirodienones have been subjected to photochemical transformation. They are obtained either as secondary products during prolonged photolysis of steroidal 2,5-cyclohexadienones or by synthetic methodology. Upon irradiation, steroidal spirodienones (115a - c) afforded the principal bicyclohexenone photoproducts (116a - c) and (117a - c). Their relative distributions are 116a/117a ca. 3:1, 116b/117b ca. 1:30 and 97c/98c ca. 5:1. The reaction course of these cases can be rationalised by the steric and regioselective controls narrated by Schaffner[63,64]. The principal factors that govern the steric and regioselective courses are (i) the puckering of the ring system on β, β[1] bonding, (ii) the configurational fate of the migrating carbon in the subsequent [1, 4] shift and (iii) the direction in which this migration proceeds.



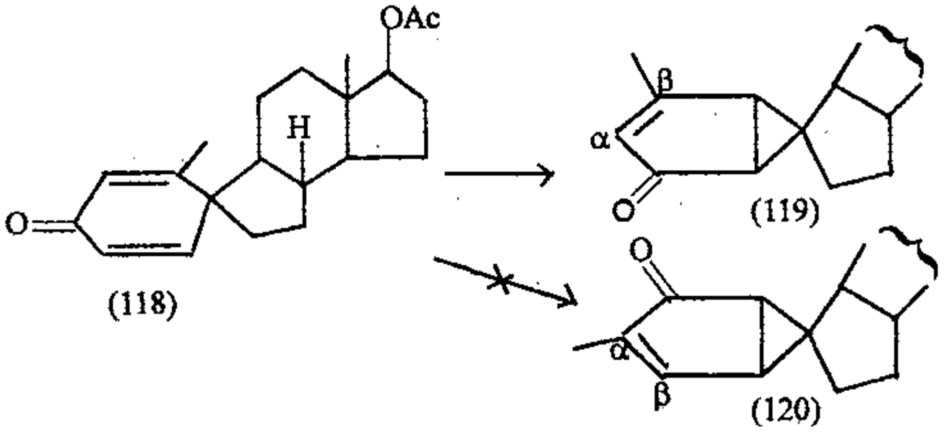
(115a) $R = R_1 = H$
(115b) $R = CH_3 = R_1 = H$
(115c) $R = H, R_1 = CH_3$



(116a) $R = R_1 = H$
(116b) $R = CH_3,\ R_1 = H$
(116c) $R = H,\ R_1 = CH3$

(117a) $R = R_1 = H$
(117b) $R = CH_3, R_1 = H$
(117c) $R = H, R_1 = CH_3$

It is interesting to note that photolysis of (118) gives rise to the photoproduct (119) in preference to the alternative possibility (120). This selectivity is perhaps attributable to a preferred formation of the more stable β-methyl-substituted-enone system of (119)[65].

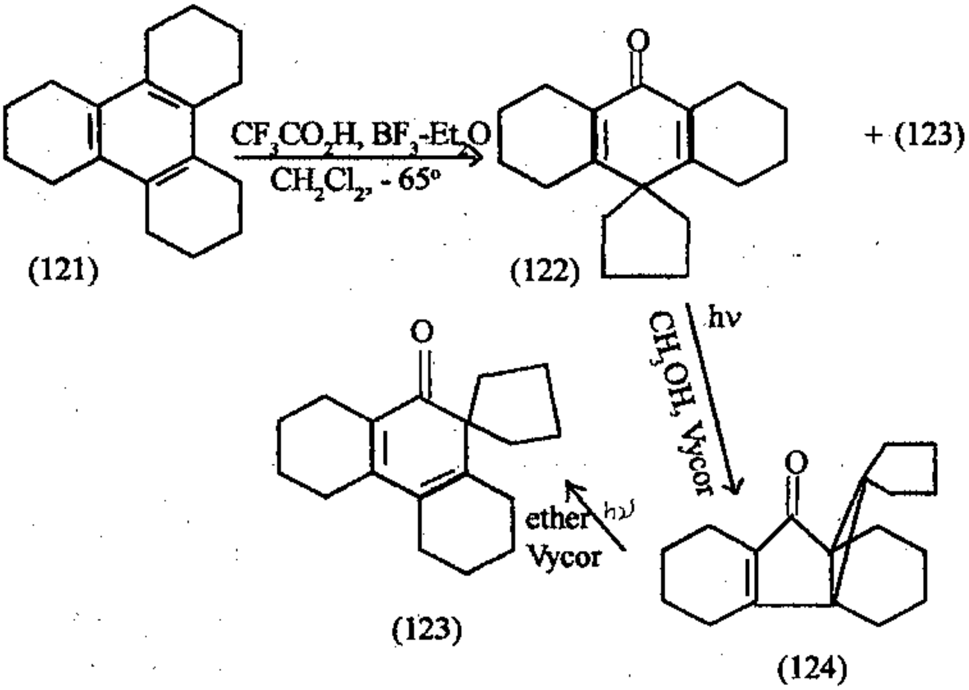


(118)

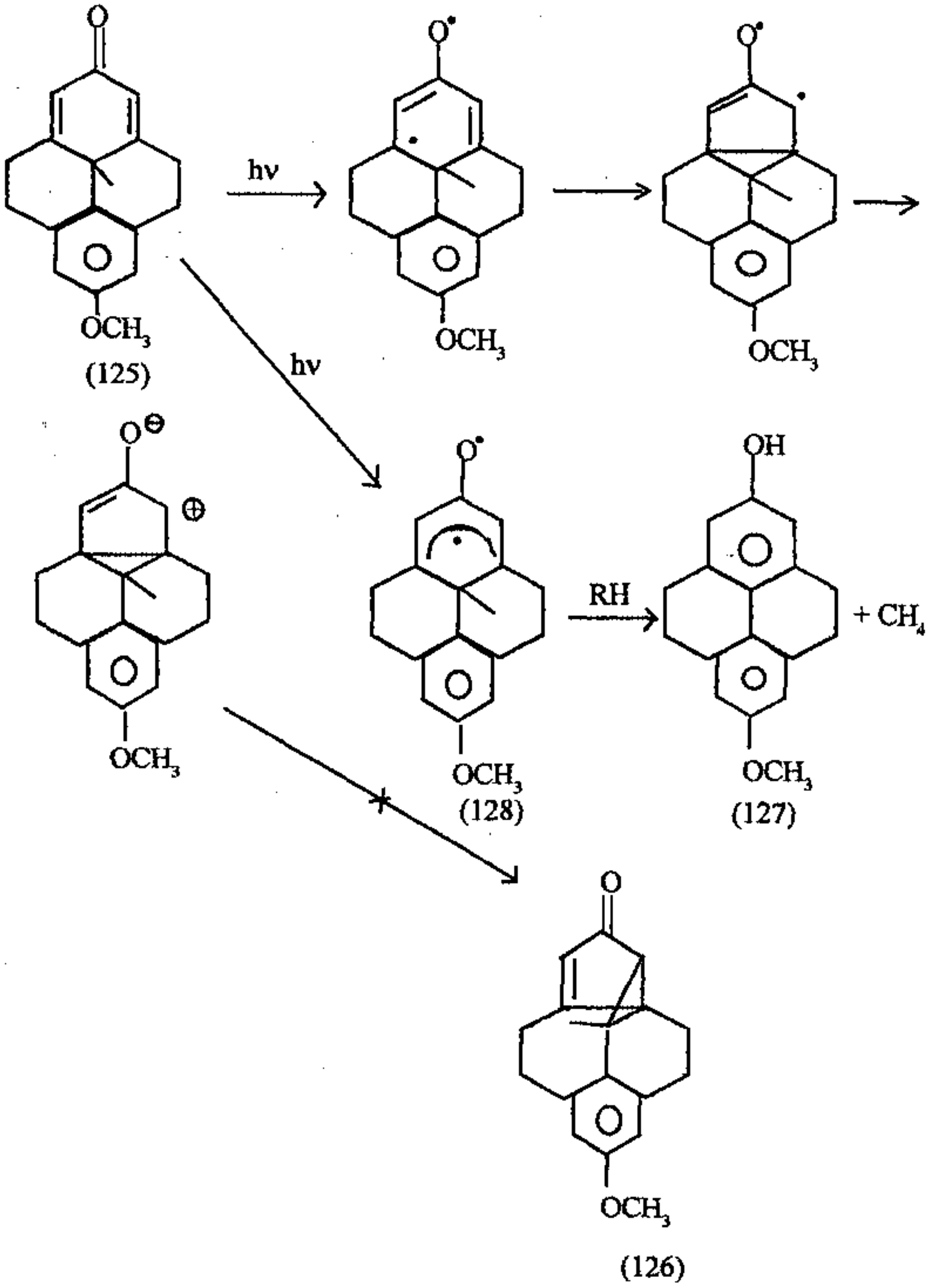
(119)

(120)

Hart and Lankin[66] observed that symmetrical dodecahydrotriphenylene (121) on oxidation with CF_3CO_2H and BF_3 afforded the polycyclic cross-conjugated spirocyclohexadienone (122) along with linearly-conjugated isomer (123). The cross-conjugate compound (122) on irradiation in methanol using a Vycor filter yielded the lumiproduct (124) in good amount. Changing the solvent from methanol to ether gave (123) which was also obtained by irradiation of (124) in ether.



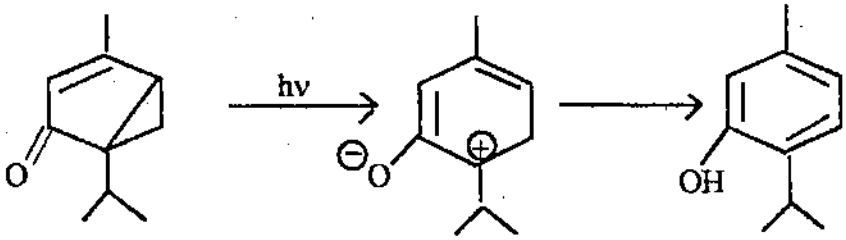
An interesting case of polycyclic cyclohexadienone (125) has been reported by Zimmerman[67]. (125) can not rearrange photochemically to afford the type A rearrangement product (126) owing to the constrain imposed by the geometry of the molecule. Here, β - β' bonding should not be inhibited, but the [1,4] migration generally accepted at the last stage of the rearrangement is geometrically impossible. Thus, instead of lumiproduct, the product phenol (127) is formed by elimination of methyl as methane caused by abstruction of hydrogen from hydrogen donating solvent at the excited dienone triplet state (128).


O
hν
O•
O•
OCH₃
(125)
OCH₃
OCH₃
hν
O⊖
⊕
O•
OH
RH
+ CH₄
OCH₃
OCH₃
(128)
OCH₃
(127)
O
OCH₃
(126)

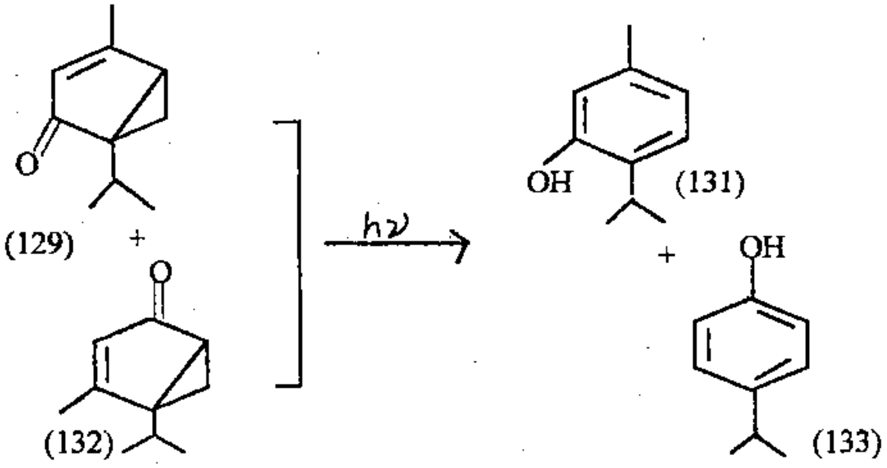
SECTION - E

(Formation of Phenolic Photoproducts)

Since the primary photoproducts i.e. lumiproducts (also called cyclopropyl ketones) possesses bicyclo [3.1.0] hex-3-en-2-one skeletone, can themselves be considered as dienone in which one of the double bonds has been replaced by a cyclopropane ring. This renders the lumiproducts photolabile and this is one of the reasons for complexity of the 2,5-cyclohexadienone phototransformations. These lumiproducts on further irradiation or 2,5-cyclohedadienones on prolonged irradiation in aqueous dioxane, alcohols or in acid give rise to phenolic compounds as ultimate products through a complicated series of intermediates involving several dienones and cyclopropyl ketone photoproducts. These transformations are initiated usually by photolysis of the internal cyclopropyl bond which forms part of the cyclopentenone ring. The quantitative conversion of the terpene umbellulone (129) to thymol (131)[68] serves as an example. Similarly, a mixture of (129) and its isomer (132) was converted to thymol (131) and the isomeric phenol (133).[69]

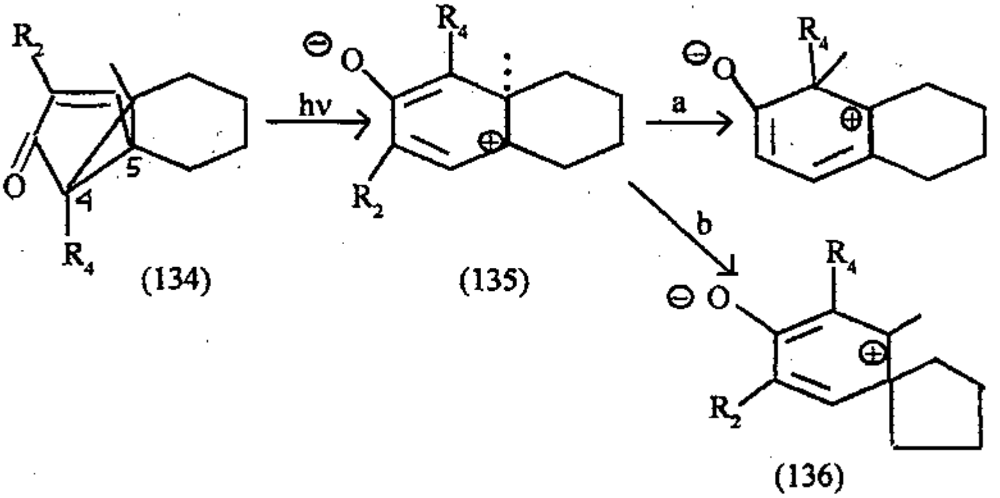


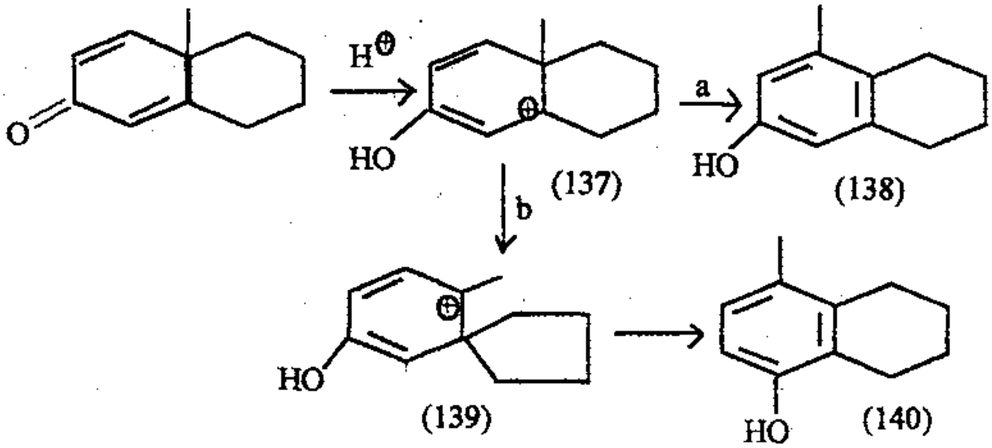
(129) (130) (131)



(129) + (132) (131) + (133)

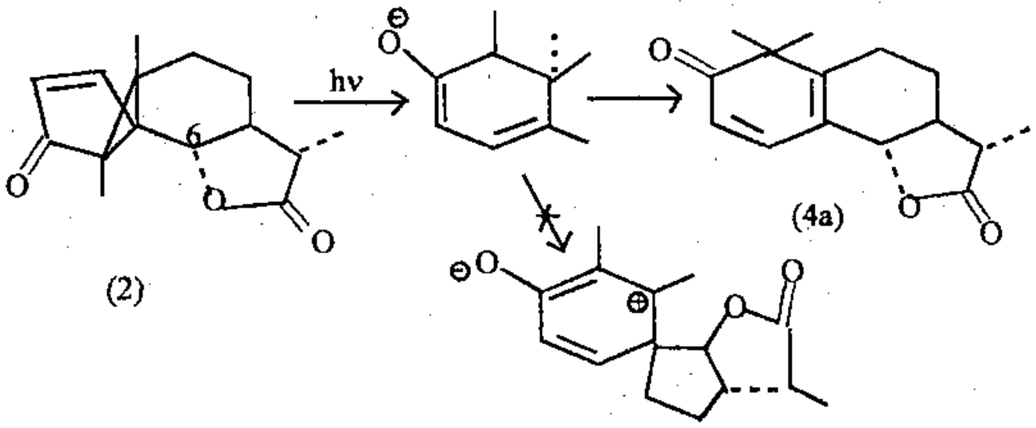
Intermediates of the type similar to (135) formed by cleavage of the 4-5 bond of cyclopropyl ketone of type (134) [cf. 137] are also encountered in the well-known acid - catalysed dienone - phenol rearrangements. In dienone-phenol rearrangement there is a delicate balance between two pathways of rearrangement : (a) 1,2 migration of the angular methyl substituent [cf. (138)] and (b) rearrangement through a spiro intermediate (139)[70] to afford (140) . The photochemical intermediate (135) also exhibits both types of rearrangement. However, in contrast to the acid-catalysed rearrangement , two pathways of photorearrangement have seldom been observed to occur simultaneously. Rearrangement through the spiro intermediate (136) has, in most cases, been found to be preferred except for several cases discussed below.





Rearrangements not involving spiro intermediates :

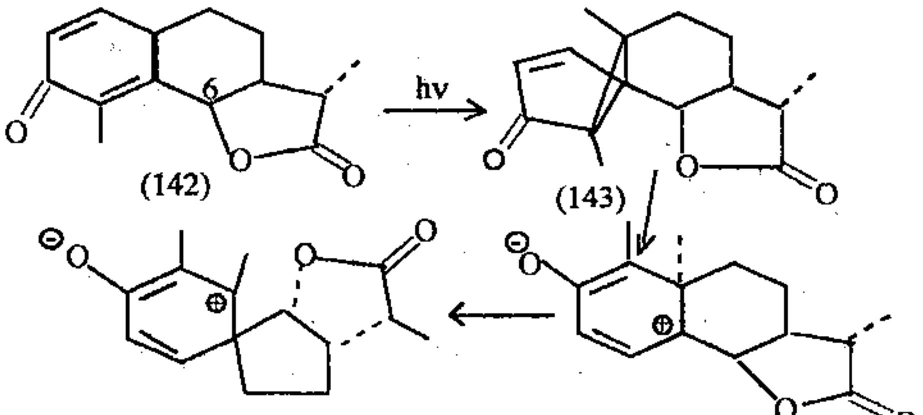
Lumisantonin (2) does not undergo photorearrangement through spiro intermediate but involves 1,2 methyl shift to give linearly conjugated cyclohexadienone(4a). Failure of the rearrangement via spiro intermediate has been attributed to highly strained trans fusion of two five membered rings[71,72] in spiro intermediate (141). Owing to the presence of cis fused γ-lactone ring formation of spiro intermediate (145) would be more favoured in 6-epi- α santonin (142) and therefore, considerable phenolic product is obtained[73] .



(2)

(4a)

(141)



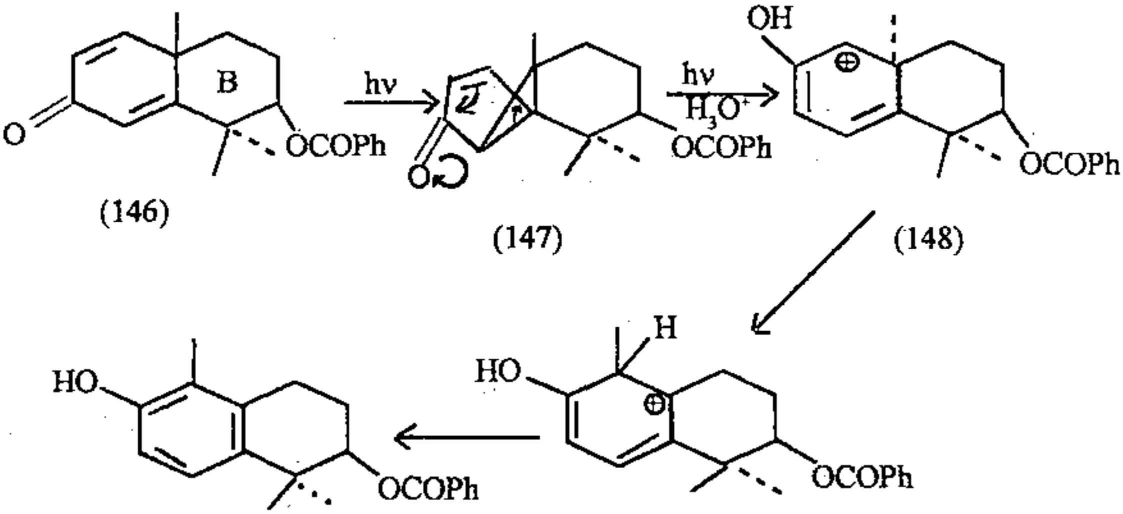
(142)

(143)

(144)

(145)

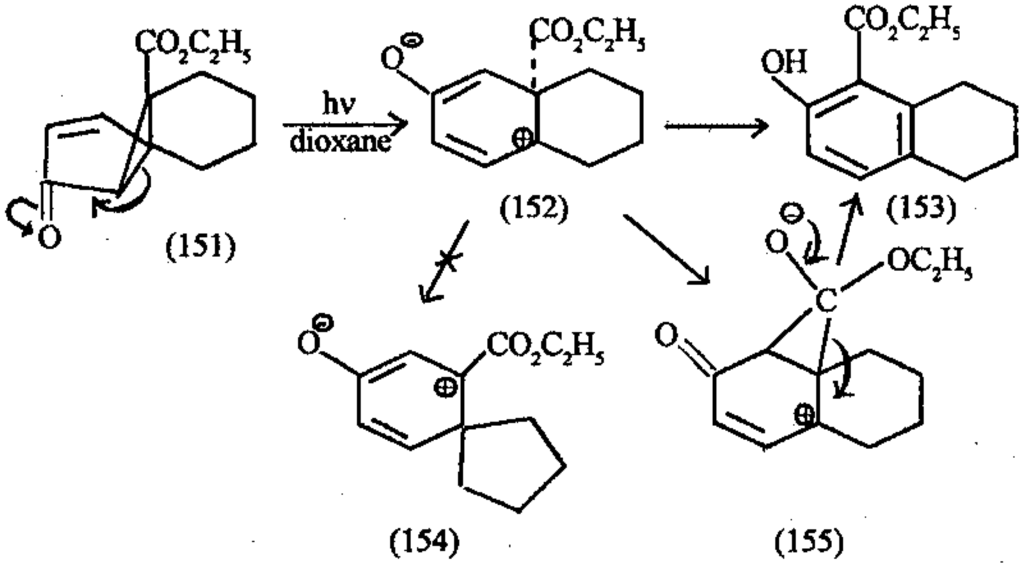
A second system is represented by the dienone (146) in which rearrangement through a spiro intermediate did not occur. Upon photolysis bicyclic 2,5-cyclohexadienone (146) in aqueous acidic media gave the phenol (149), besides several ketonic products. Here, also, 1,2-methyl shift has been proposed for the formation of the intermediate (150) which eventually yielded the phenol (149). The failure of this system to rearrange through a spiro intermediate has been attributed to a combination of steric interactions involving the ring-B substituents[72].



(146) (147) (148)

(149) (150)

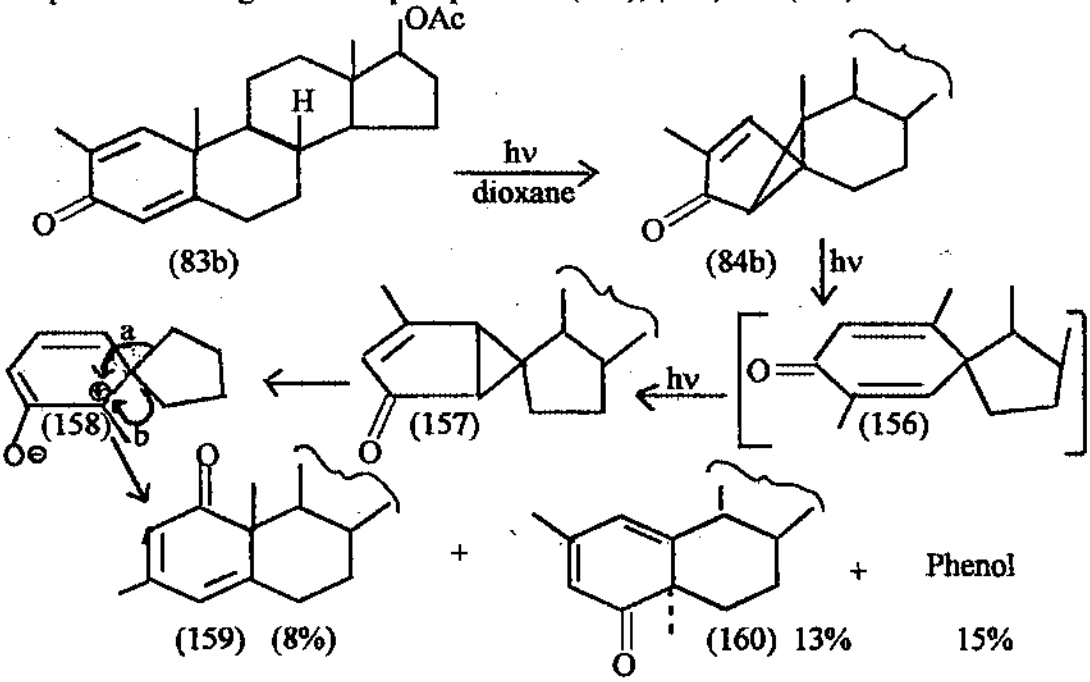
An interesting case has been registered, in which electronic, rather than steric, factors are attributed for the failure of rearrangement via a spiro intermediate. Irradiation of the carbethoxy lumiproduct (151) gave the phenol (153) in high yield. The presence of the electron-withdrawing carboethoxy substituents on the ring A which is already electron-deficient, gives rise to destabilisation of the spiro intermediate (154), or it could be due to greater migratory aptitude of the carbethoxy group. The migration might be assisted as depicted in (155).



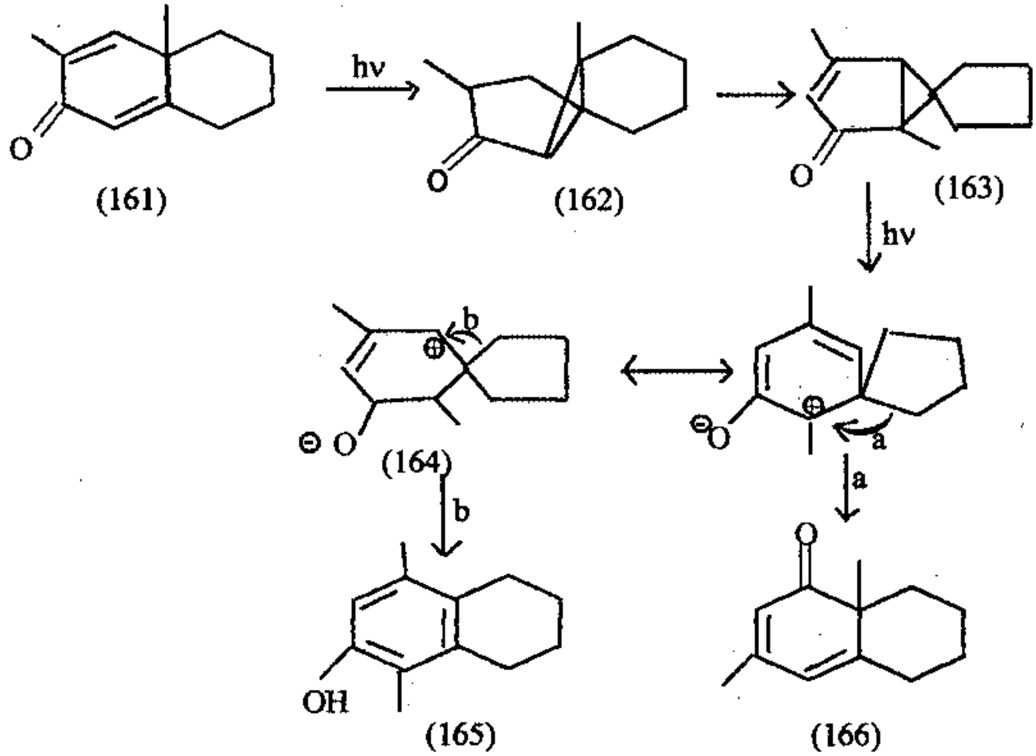
Rearrangements via spiro intermediates : solvent effects :

Numerous studies have been reported in the literature on the phototransformation of lumiproducts to phenols. In several cases marked solvent effects have been observed. Some of them are discussed below :

Ganter and coworkers[74] observed that upon irradiation, the lumiporuduct ((84b) from the 2-methyl steroid (83b) furnished ultimately two linearly conjugated hexadienones (159) and (160) and unidentified phenol in about 15% yield. The reaction proceeds through several spiro products (156), (157) and (158).

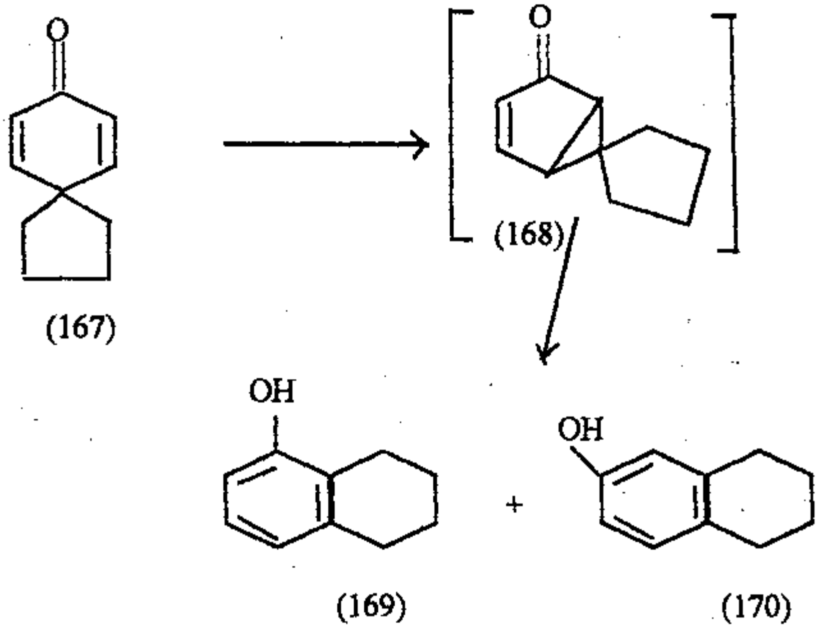


Kropp[75, 76] photolysed the lumicompound (162) obtained from the bicyclic 2,5-hexadienone (161) which is structurally related to the steroid derivative (83b). Through several spiro intermediates such as (163) the linearly conjugated cyclohexadienone (166) and the phenolic product (165) were obtained. This photoreaction is markedly effected by solvent. In nonacidic media, the dienone (166) is the principal product accompanied by only trace of phenolic product (165) while in acidic media the two products (166) and (165) are obtained in approximately equal yield.



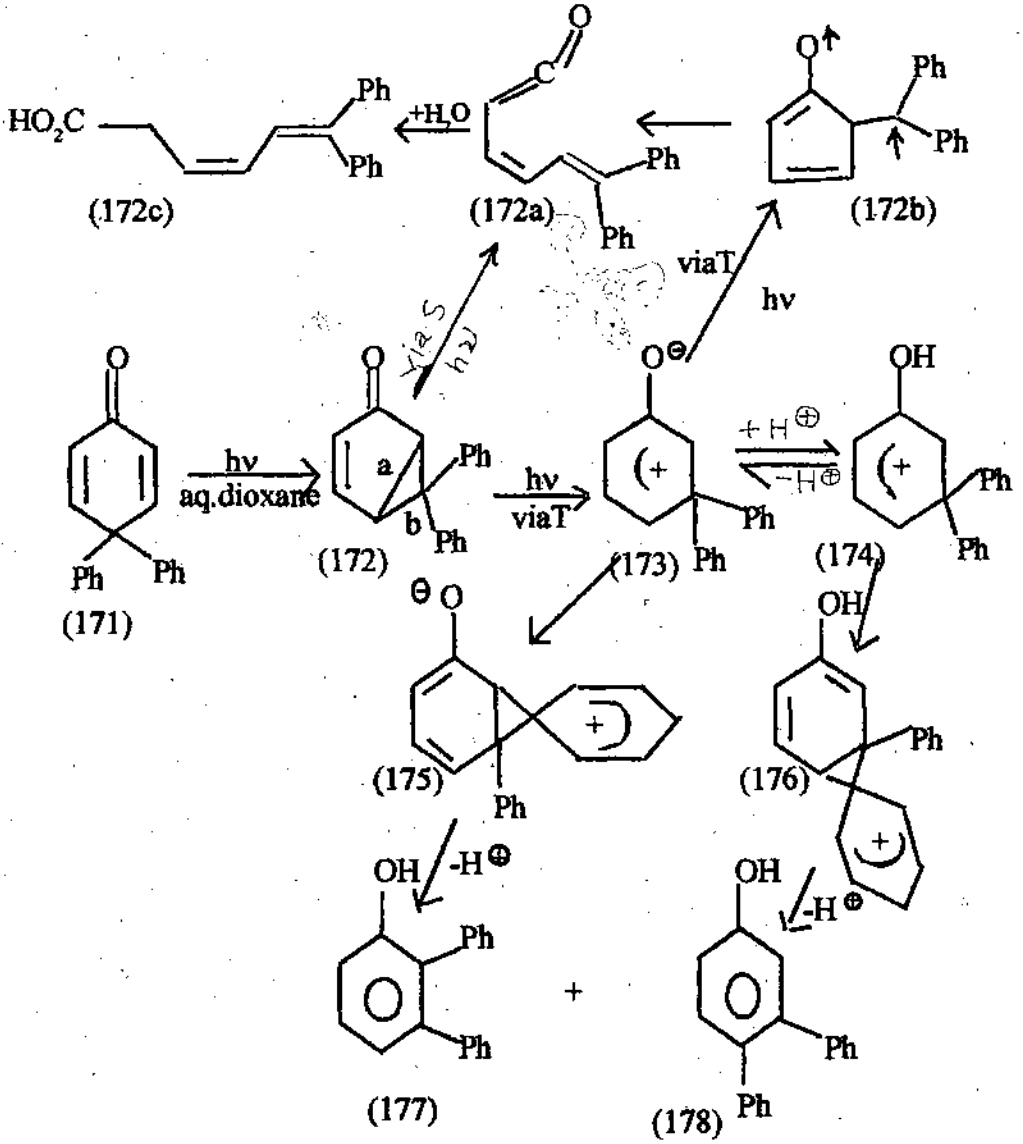
		(165)	(166)
From (161)	CH_3OH	trace	50%
(163)	CH_3OH	trace	57%
(163)	45% HOAc	33%	47%
(162)	CH_3OH	trace	62%
(162)	45% HOAc	28%	33%

Photolysis of the spiro dienone (167) afforded a mixture of the α- and β-tetrahydronapthols (169) and (170). Though not isolated, this phototransformation undoubtedly involved the cyclopropyl ketone (168). The ratio of the two phenolic products (169) and (170) was found to be considerably dependent upon the solvent used, the latter product being favoured in acidic media.



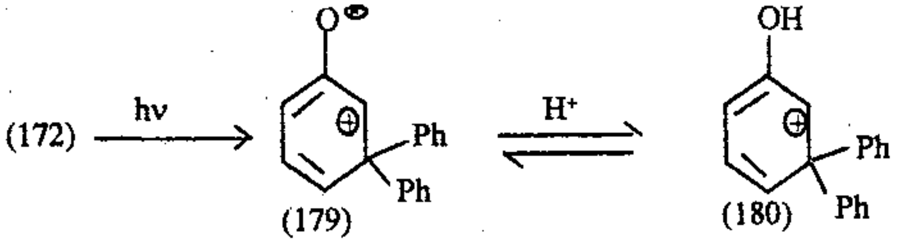
	(169)		(170)
ether	2	:	1
t-BuOH	1	:	1
HOAc	1	:	2

Formation of phenols from the irradiation of the cyclopropyl ketone (172) which is obtained from the photolysis of the cyclohedadienone (171) as the primary product, also exhibited noticeable solvent effects[30]. Aqueous dioxane yielded 2,3-diphenyl-phenol (177) as principal product with trace of its isomer 3,4-diphenylphenol (178), while in 50% acetic acid gave the two diphenyl isomers in approximately 1:1 ratio.



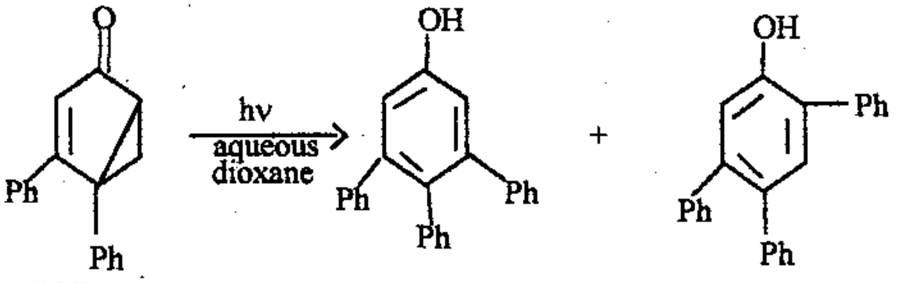
	(177)	(178)
Aq.dioxane	22.32%	trace
50% AcOH	1	1

In excited state of these cyclopropyl ketones in acidic media, a proton becomes available which greatly controls the photochemical behaviour. It has been demonstrated by Zimmerman that in a series of buffered aqueous dioxane solutions the ratio of the phenolic products (177) and (178) from (171) follows the acidity dependence that would be predicted for equilibrating dipolar (179) or cationic intermediates (180)[79].



The reactions of (172) on direct irradiation were considerably less efficient than the lumiproduct (172) formation from the dienone(171). The former reaction shows $\phi = 0.16$ against the later $\phi = 0.85$. It has been proposed that the difference could be attributed to the reversible fission(s) of either cyclopropane bond(s) in triplet (173).

On the other hand, a concerted breakage of both bonds (internal and external cyclopropane bonds) and direct collapse of singlet excited (172) to the diene ketene (172a) which when trapped with nucleophile gives unsaturated acid /ester (172c). Alternatively, the breaking of the external cyclopropane bond in triplet (173) gives rise to 1,4 biradical (172b) which subsequently affords (172a) by spin inversion and central bond cleavage. This scheme of photoreaction is particularly well documented at low temperature irradiation[82] and several cases have been reported.[83,84]

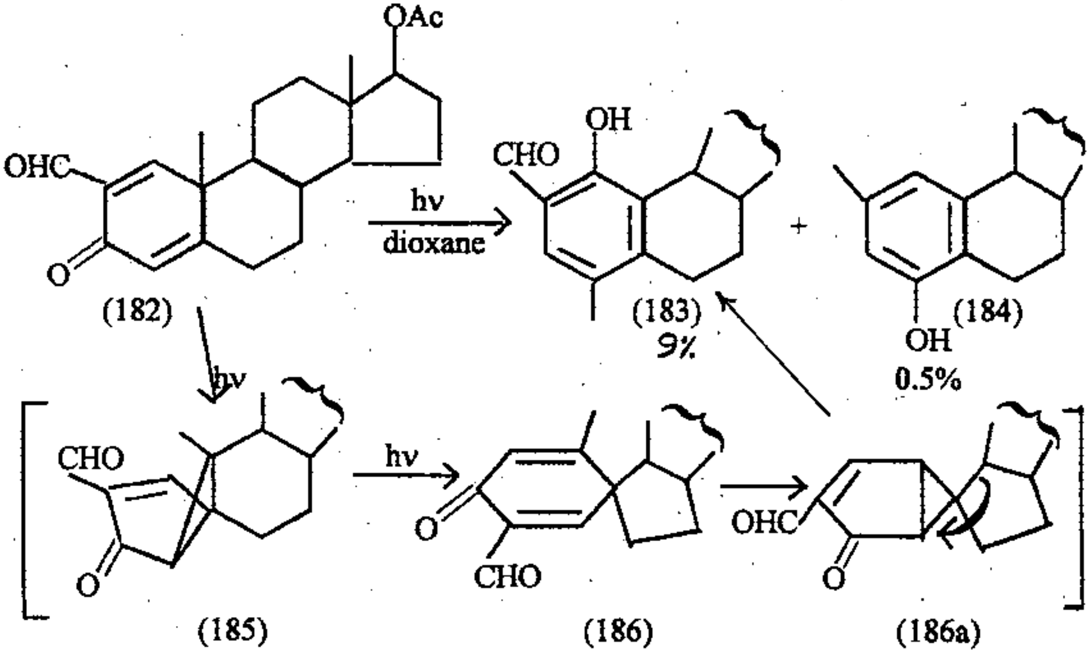


(181)

The influence of solvent acidity on phenol formation as mentioned earlier [29] is as would be predicted for equilibrating zwitterion (173) and cationic species (174), consideration based on maximisation of resonance stabilization[79] and on minimization of charge separation[80] in the dipolar half-migrated species favour intermediate (175) while migration in the protonated form (174) would be expected to predominate via (176) toward the more positive C- 4 in accordance with molecular orbital calculations [79].

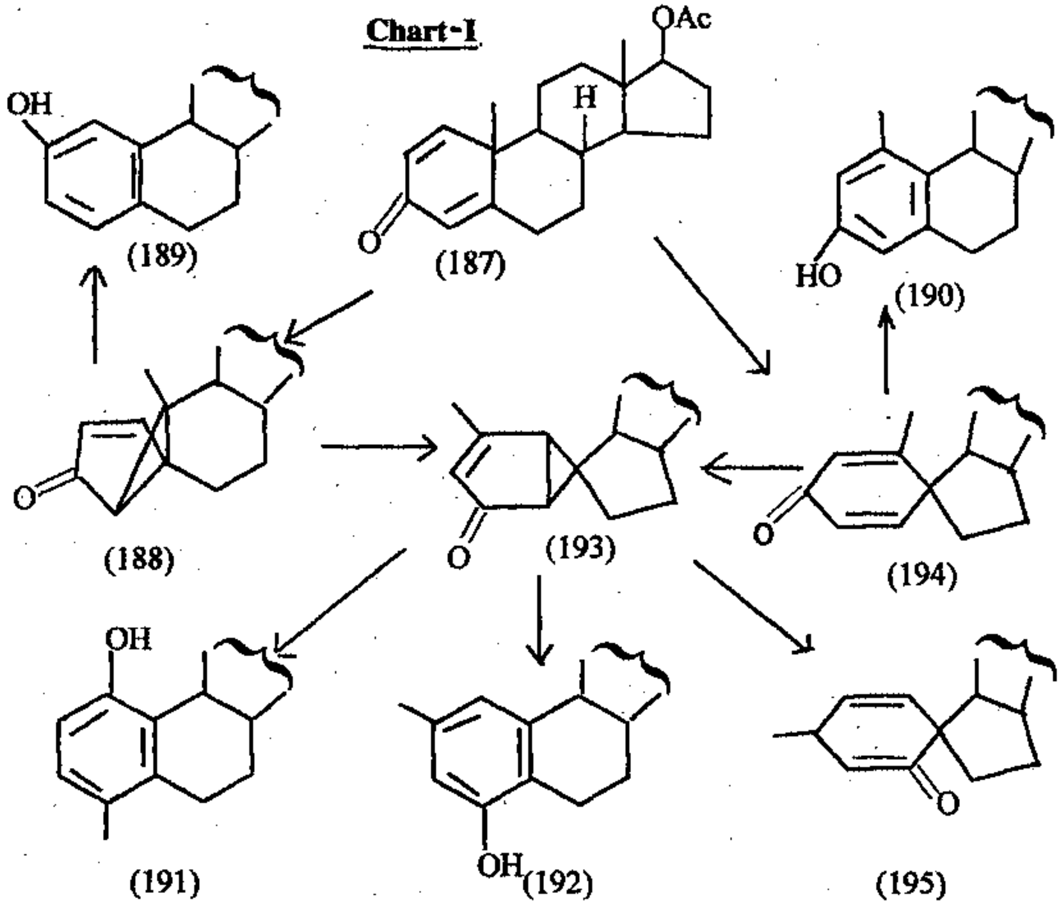
Several other cases of lumiproducts ⟶ phenols conversion were reported. Small[81] observed that photolysis of the cyclopropyl ketone (181) in aqueous dioxane also afforded two phenols as shown above :

Similarly, it was observed that irradiation of the 2-formyl dienone (182) in dioxane yielded a complex mixture of products, from which the phenol (183) was isolated and characterised[85]. Trace amount of (184) was also obtained. The formation of (183) was accounted for by the intervention of the ketones (185) to (186a) as intermediates.

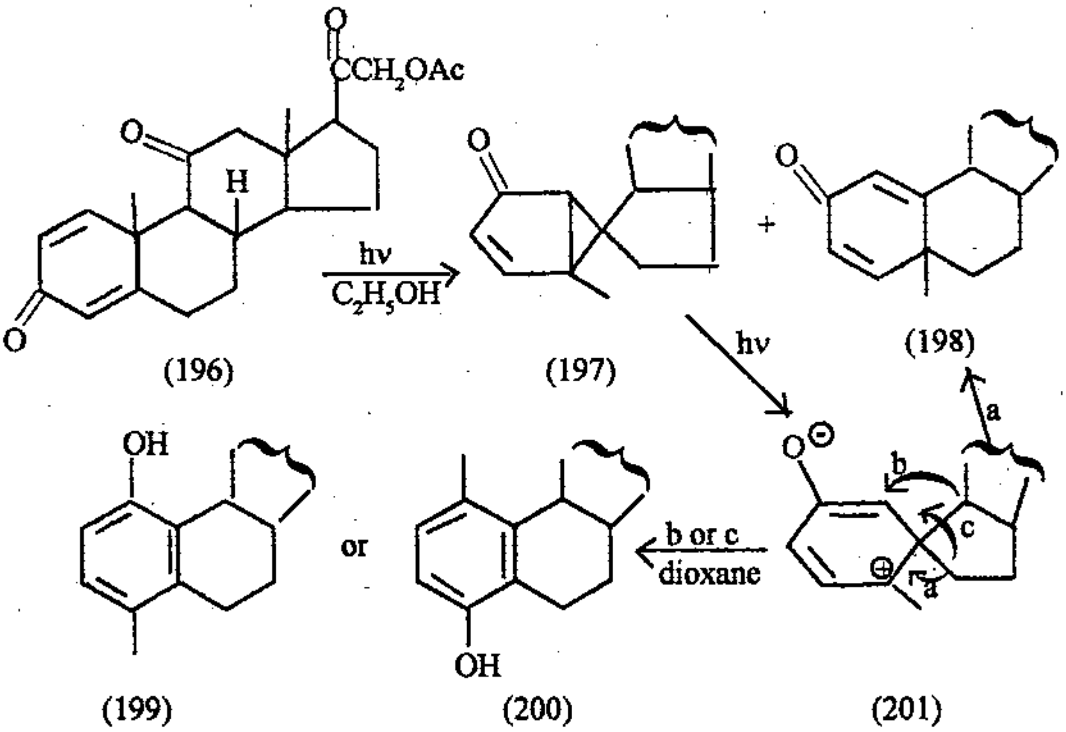


Jeger et al.[86,71,87] made an extensive analysis of the photo reaction of steroids having substituents in ring A and also without substituents in ring A. Jeger et al.[86] observed that photochemical hehaviour of dienones having no A-ring substituents such as the androste -1, 4-dien-3-one (187) type A is much more complex than that of their 2- and 4- methyl analogue. A complex mixture of products usually results, since there are no substituents present to stabilize preferentially some of the reaction pathways that are available. As a consequence , irradiation of (87) in dioxane gives a mixture of photoproducts from which four phenolic (189 - 192) and five ketonic products including (188), (193)-(195) have been isolated.[86] Interestingly, the relative amounts of ketonic and phenolic products vary with the extent of irradiation. Phenolic components are favoured on prolonged irradiation. Chart I shows the pattern of interconversions suggested by them.[86] Upon irradiation in glacial acetic acid the same four phenols [189 - 192] were obtained in yields of 1 to 20 per cent .[87] In some occasions,it has been noticed that choice of the appropriate solvents considerably reduce the complexity of photoproducts e.g., photolysis of (187) in refluxing aqueous acetic acid affords predominantly the phenol (189) accompanied by the expected hydroxy ketone photoproducts[71,87], while irradiation in methanol a 2 : 1 mixture of the two phenols (190) and (192) is formed in good yield[87].

Chart-I



Prednisone acetate (196) in ethanol, on photolysis, afforded lumiprednisone acetate (197) and isomeric dienone (198). When the latter was irradiated in dioxane a phenolic product was obtained (199) or (200)[88,89]. All these three products (198), (199) and (200) would be expected products arising out of the further rearrangement of (197). Interestingly, the phenolic product was not formed in ethanol and hence it appears that the intermediate (201) exhibits a solvent effect analogous to those described above for similar species.



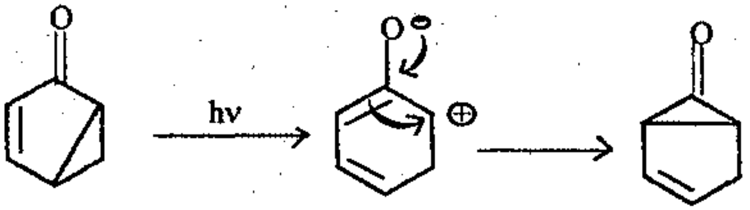
Photoconversion of lumiproduct to phenol at low temperature :

Photoreaction of lumiproduct carried out at low temperature [91] enabled photochemists to make extensive refinements of the reactive intermediates involved. The mechanistic path for the formation of cyclohexadienone and phenolic product, discussed earlier, by the cleavage of the internal cyclopropyl bond of lumiproduct may be operative at the ambient temperature and above. At low temperature around -190°C products may result via the formation of very transient ketene carbene and cyclopropanone intermediates as originally proposed for the formation of photosantonic acid from lumisantonium.

Schemes (I and II) depicted below describes the genesis of carbene ketene and cyclopropanone species starting from a model bicyclo [3.1.0] hexenone (212). Irradiation of (212) at temperature of -190°C leads to the formation of the unrearranged ketene (215) as shown in the scheme-I. The process occurs by breaking the external rather than the internal cyclopropyl bond [(213)→(214)]. The reaction may also be described as concerted electrocyclic reaction of [4+2] type[92].

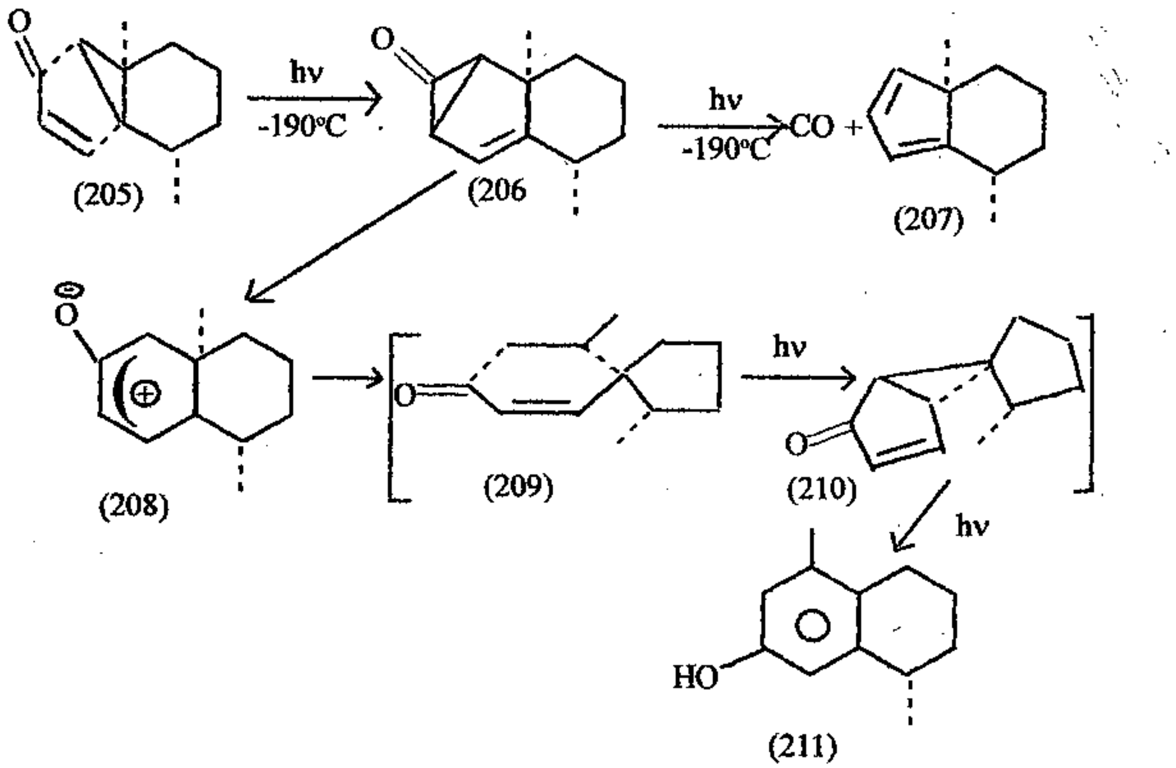
The thermal closure of ketene (215) to linearly conjugated 2,4-cyclohexadienone (216), the precursor to phenols in C-6 un - or monosubstituted cases is a general reaction. In several instances, ketene carbene (218) formed via (217), gives rise to ketene diene (219) produced with rearrangement of C-6 substituent.

It was postulated that the excited state (221) is produced (Scheme-II) that can lead to a ring opened zwitterion (222) which is the ring opened form of the cyclopropanone (223). The observation that cyclopropanone (204), the closed form of the zwitterion (203), is formed upon photolysis of (202) and matrix - isolated lends further evidence to the zwitterion hypothesis[93,94]. This rearrangement to cyclopropanone (223)[99] can be viewed as an allowed suprafacial [1, 3] sigmatropic[92] shift. Thermal σ-symmetric heterolysis can then give rise to the zwitterions (224) and (225) which ultimately produce phenol (s). Formation of the zwitterion (224) has been indicated by nucleophillic trapping to the product (226) by methanol.

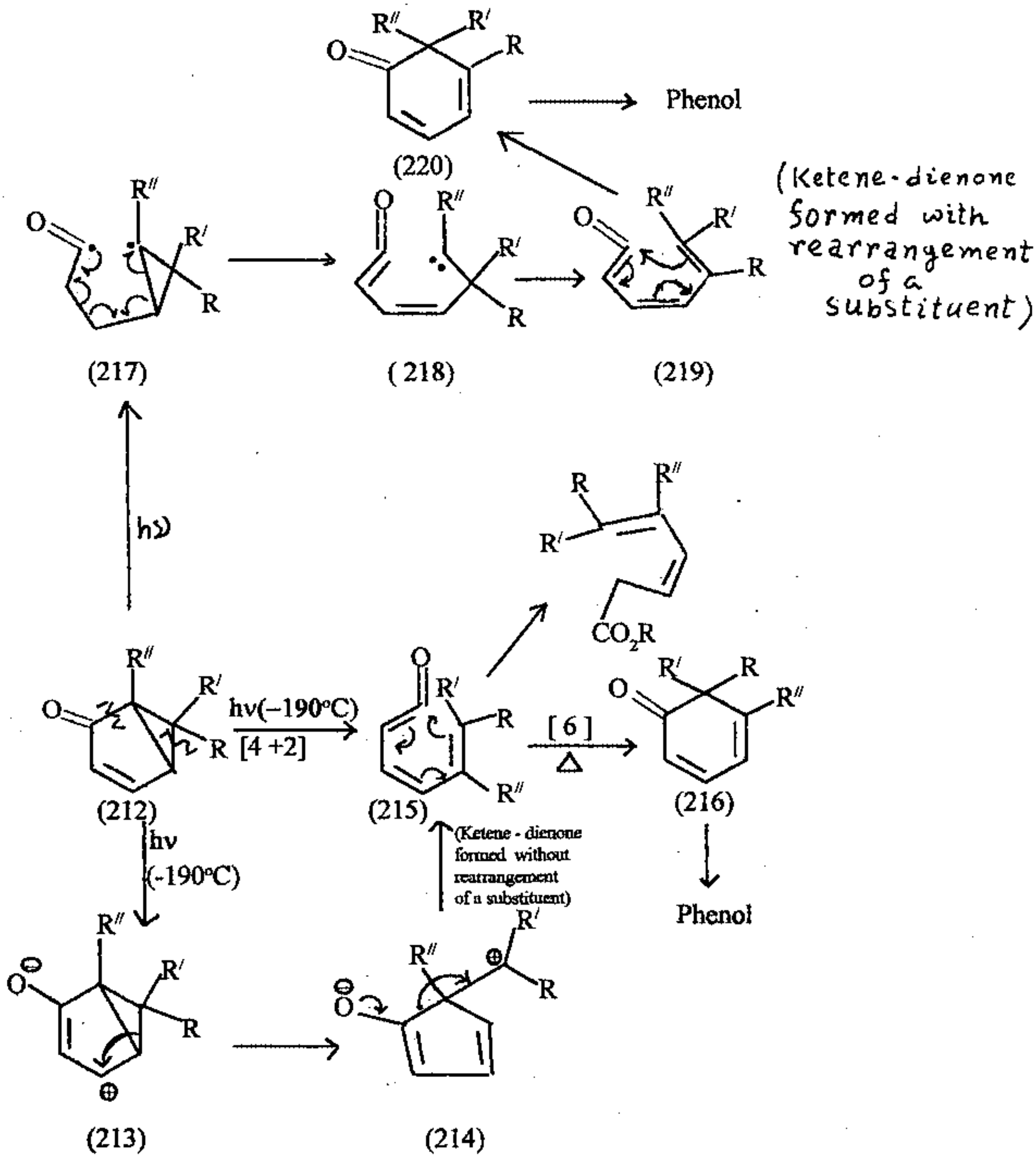


(202) (203) (204)

Chapman and coworkers[94] noticed that the lumiproduct (205) on irradiation at -190°C afforded the cyclopropanone (206) in the first photochemical step[99]. Further irradiation at low temperature resusited in decarbonylation to diene (207). On the other hand, warming of (206) in the presence of furan gave a 2 + 4 adduct which is characteristic of a three-membered ketone. Phenol (211) obtained at room temperature is likely to involve heterolysis of (206) to zwitterion (208), rearrangement to spirodienone (209), and a subsequent two-step photochemical sequence via the spirobicyclohexenone (210).


O
hν
-190°C
(205)
O
(206
hν
-190°C
CO +
(207)
O
(208)
O
(209)
hν
O
(210)
hν
HO
(211)

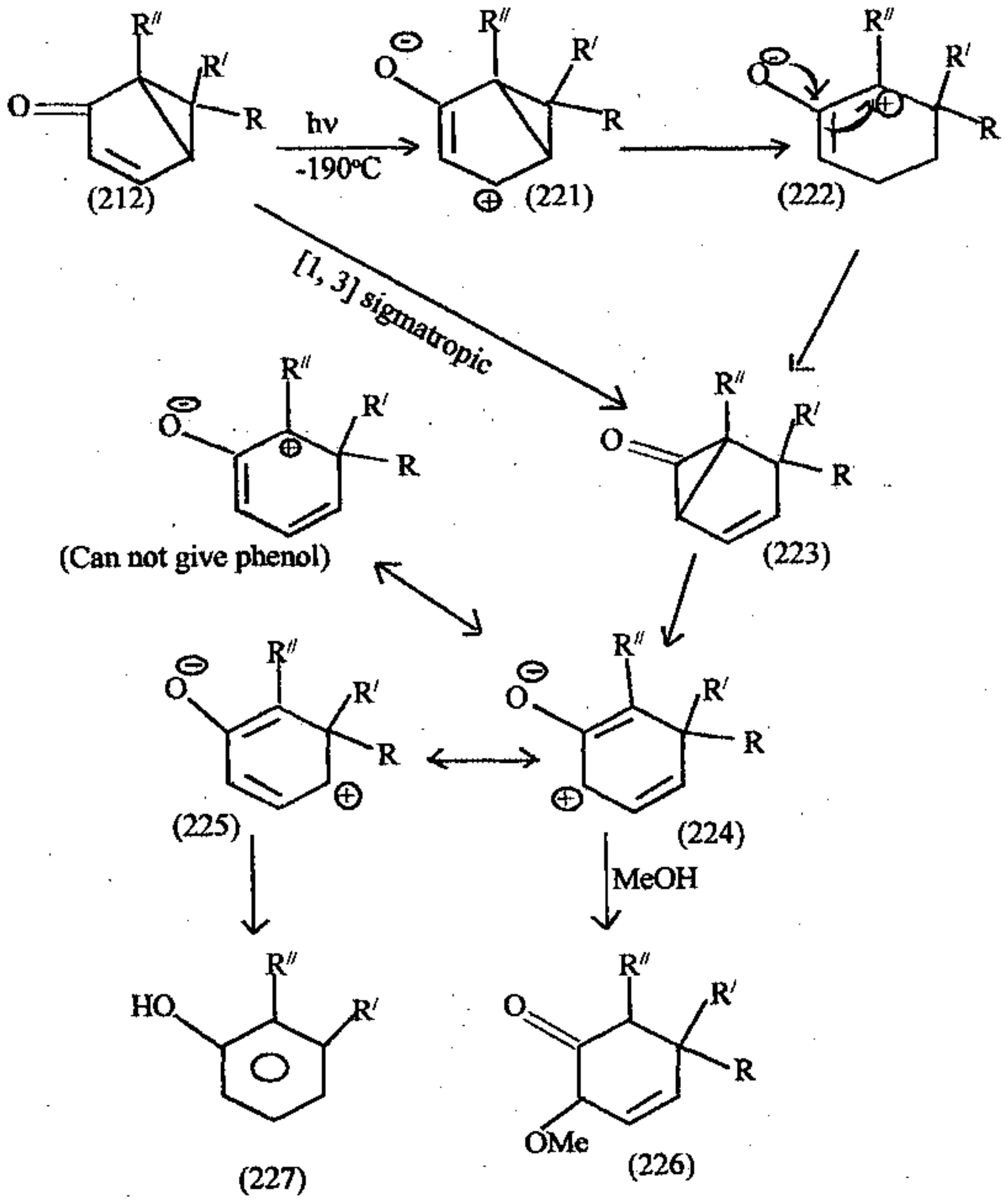
Scheme - I



(Ketene-dienone formed with rearrangement of a substituent)

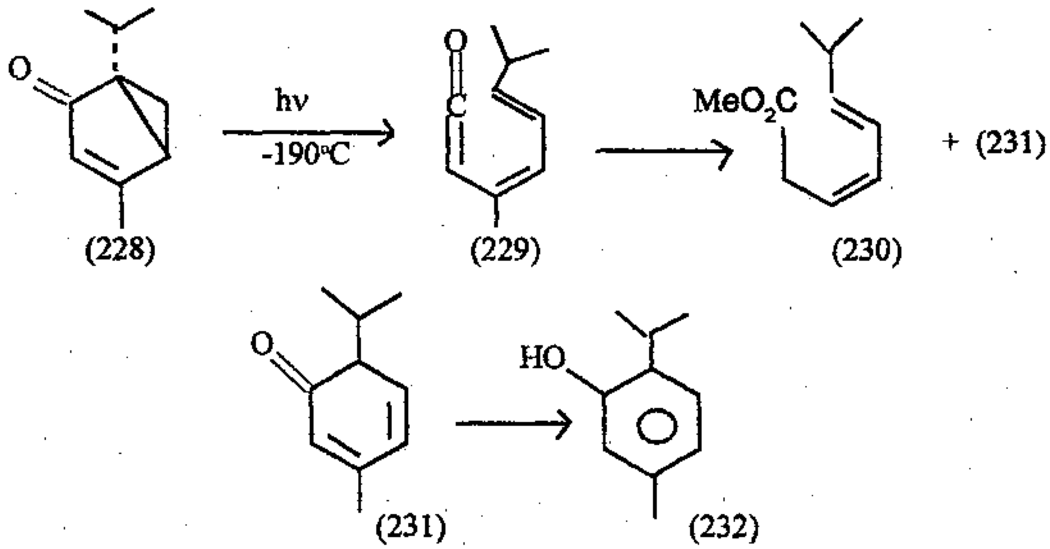
(Ketene - dienone formed without rearrangement of a substituent)

Scheme - II


(212)
hν
-190°C
(221)
(222)
[1, 3] sigmatropic
(Can not give phenol)
(223)
(225)
(224)
MeOH
(227)
(226)
HO
OMe

Now, we wish to discuss typical three photorearrangements of lumiproduct conducted at low temperature. It is to be observed that in one instant (a), a phenol will be formed via unrearranged ketene hexadiene, in another (b), phenol results from rearranged ketene hexadiene while in the third case(c) phenol is not formed, instead linearly conjugated cyclohexadiene is generated, which ultimately gives either acid or ester depending on the presence of the nucleophile water or alcohol.

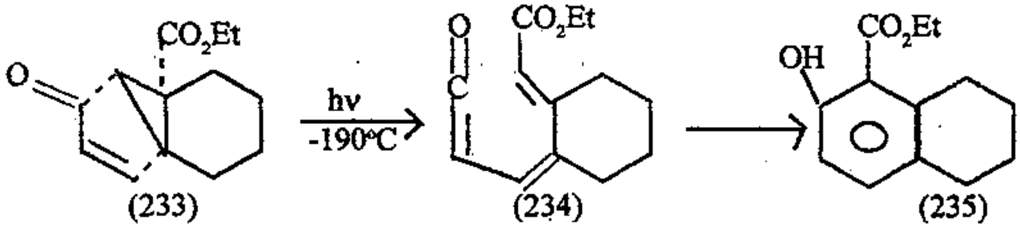
(a) Umbellulone (228) undergoes smooth aromatisation to thymol (232)[95-98] in methanol at room temperature, proceeds at -190°C via (229), which on warming cyclised to dienone (231) as is characteristic for such dien ketenes. It has been demonstrated that nucleophilic trapping by added methanol to give (230) can compete with the cyclization only below -80°C.



(228) (229) (230)

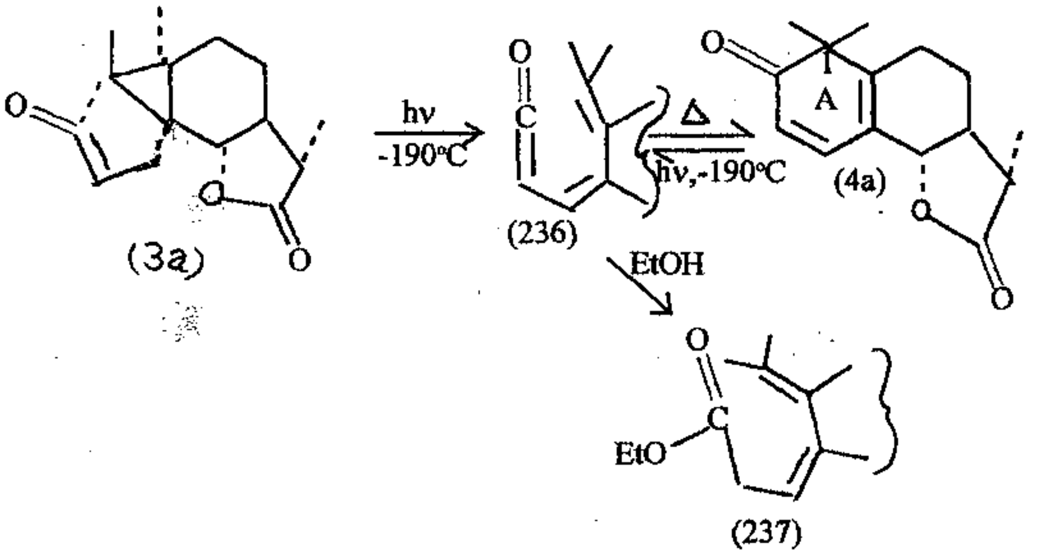
(231) (232)

(b) The bicyclic cyclopropyl ketoester (233) rearranges at room temperature to the phenol (235). The reaction is mediated through the rearmaged ketene diene (234) established at -190°C.[91]



(233) (234) (235)

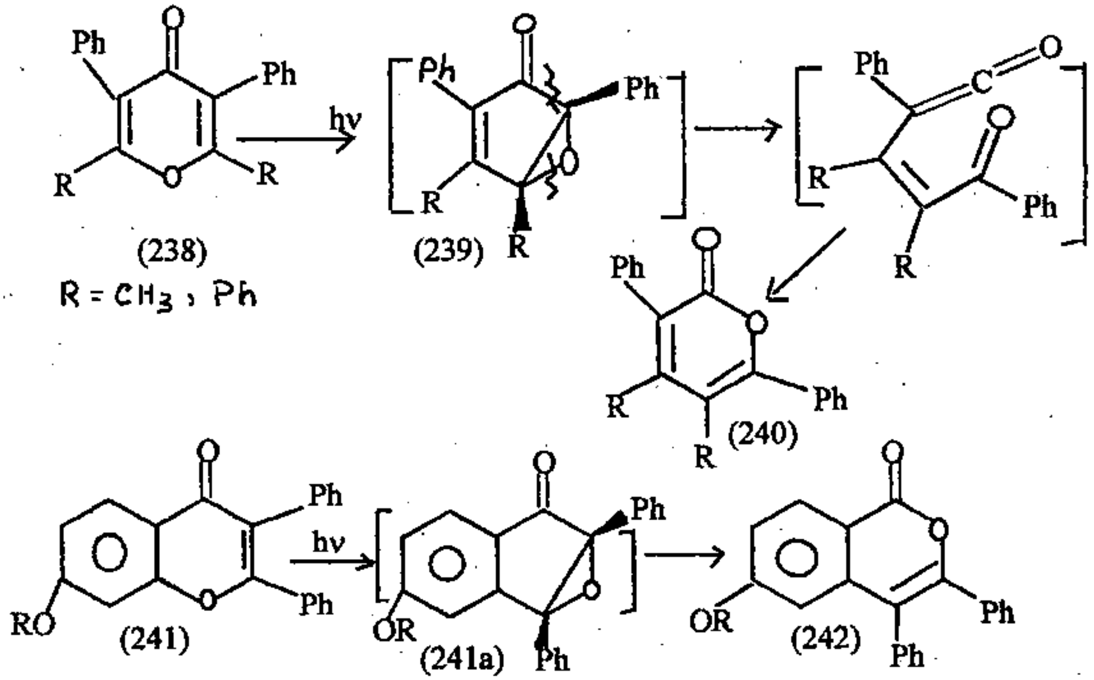
(c) Lamisantonin (3a) gave on irradiation at -190°C the ketene (236) which thermally gave mazda santonin (4a). Interestingly, (4a) on irradiation gave the same ketene (236). The cyclisation to (4a) is slower in comparison to the cyclisation of (229) →(231) and on warming in the presence of ethanol the ketene was quantitatively converted to photosantonin (237). Due to the presence of dimethyl substituents at C - 1 in (4a) further conversion to phenolic product by aromatisation of ring A is prevented.

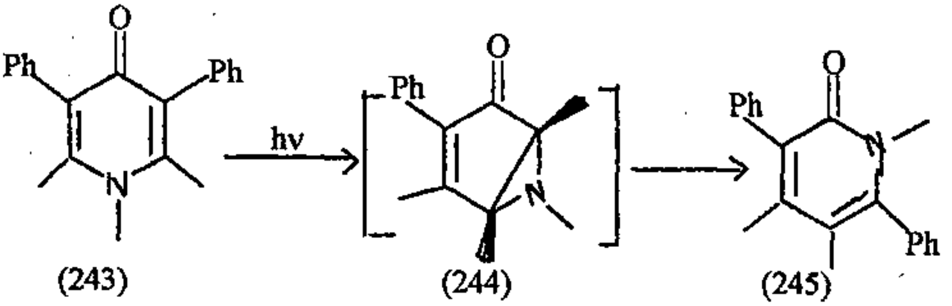


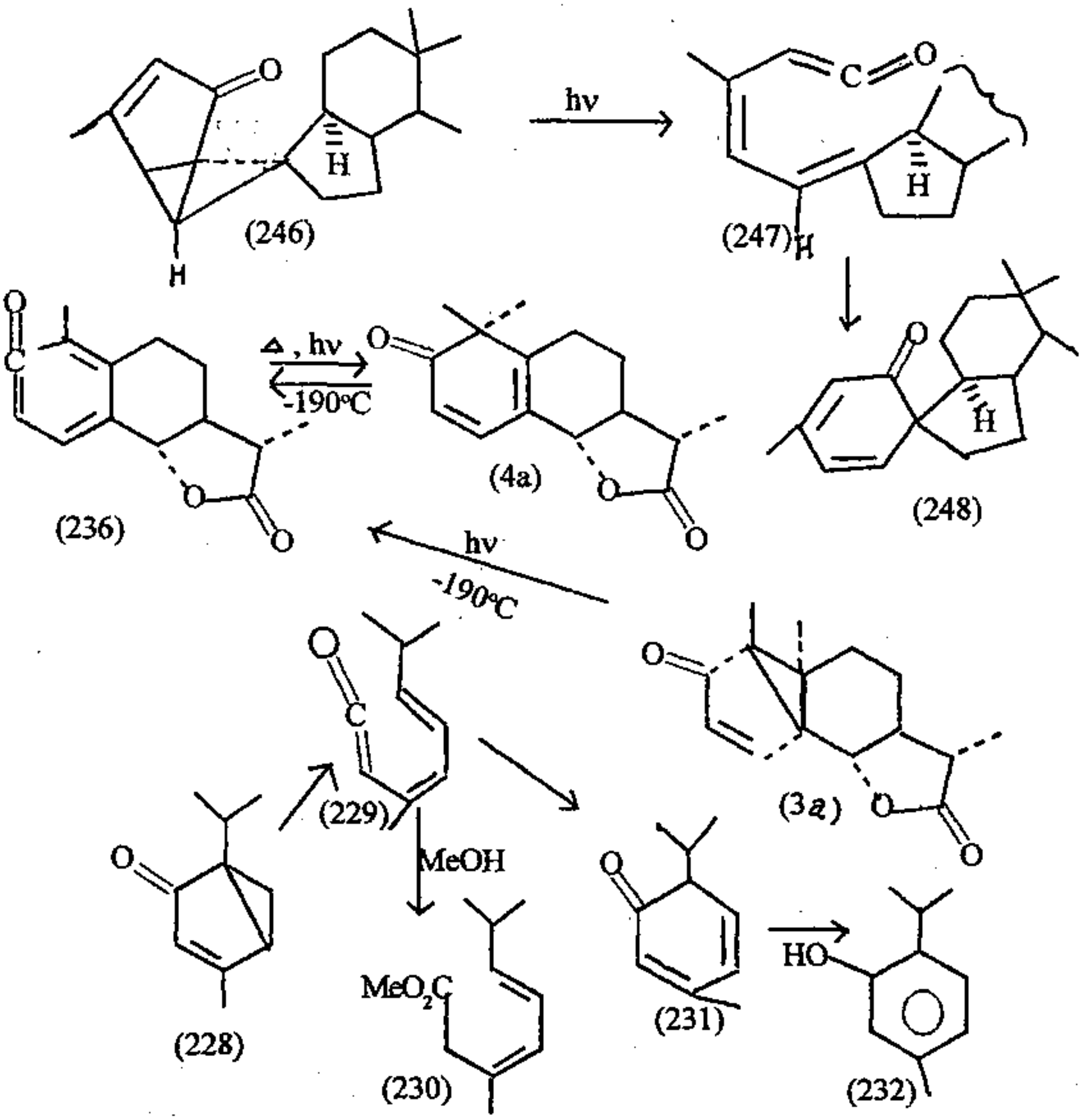
Section - F

(Hetero 2,5-Cyclohexadienones Photorearrangement)

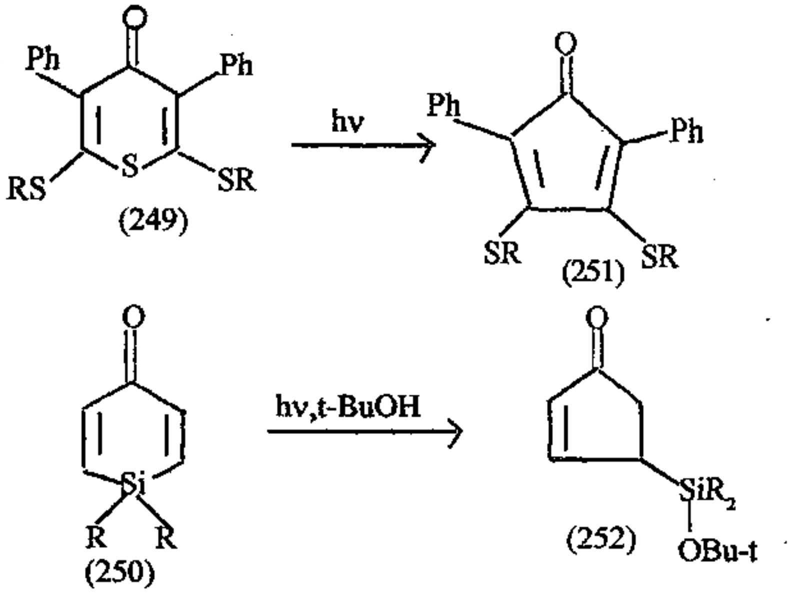
Phototransformation of 2,5-cyclohexadienones containing heteroatoms such as O, N, S and Si produced quite interesting result. End products have been obtained via the intermediate lumiproducts which being unstable could not be isolated in most cases. Heterocyclic cross-conjugated cyclohedadienones e.g. pyrone (238) isoflavones (241) and 4-pyridone (243) yielded 2H-pyran-2-one (240),[100, 101] isocoumarin (242)[103] and 2-pyridone (245)[102] via the unstable lumiproducts (239), (241a) and (244) respectively. It has been postulated that the final products were formed by a double fragmentation - thermal reclosure process from the lumiproduct as shown in case of pyrone (238). This diene ketene mechanicm has also been put forward for the photorearrangement of spiro bicyclohexenone[64] (246) to linearly conjugated cyclohexadienone (248) through the intermediate dienketene (247). The formation of this intermediate has been supported by low temp. photoreaction of lumi-santonin(3a)and unbellulone (228)[68,69] to mazdasantonin(4a) and thymol (232) respectively. Formation of some amount of ring-opened ester (230) from (229) in the presence of nucleophile methanol provided additional evidence for the ketene mechanism.




Ph
O
Ph
N
(243)
hν
Ph
O
N
(244)
Ph
O
N
Ph
(245)


O
H
H
(246)
hν
C
O
H
H
(247)
O
C
(236)
Δ, hν
-190°C
O
O
O
(4a)
O
H
(248)
hν
-190°C
O
C
(229)
MeOH
O
O
O
(3a)
O
(228)
MeO2C
(230)
O
(231)
HO
(232)

In contrast, β–β′ bonded intermediates formed from the irradiation of thiopyranones (249) and silyl compounds (250) did not give rise to lumporoducts but produced decomposition products (251)[104,105] or nucleophile captured cyclopentenone[106] products (252).

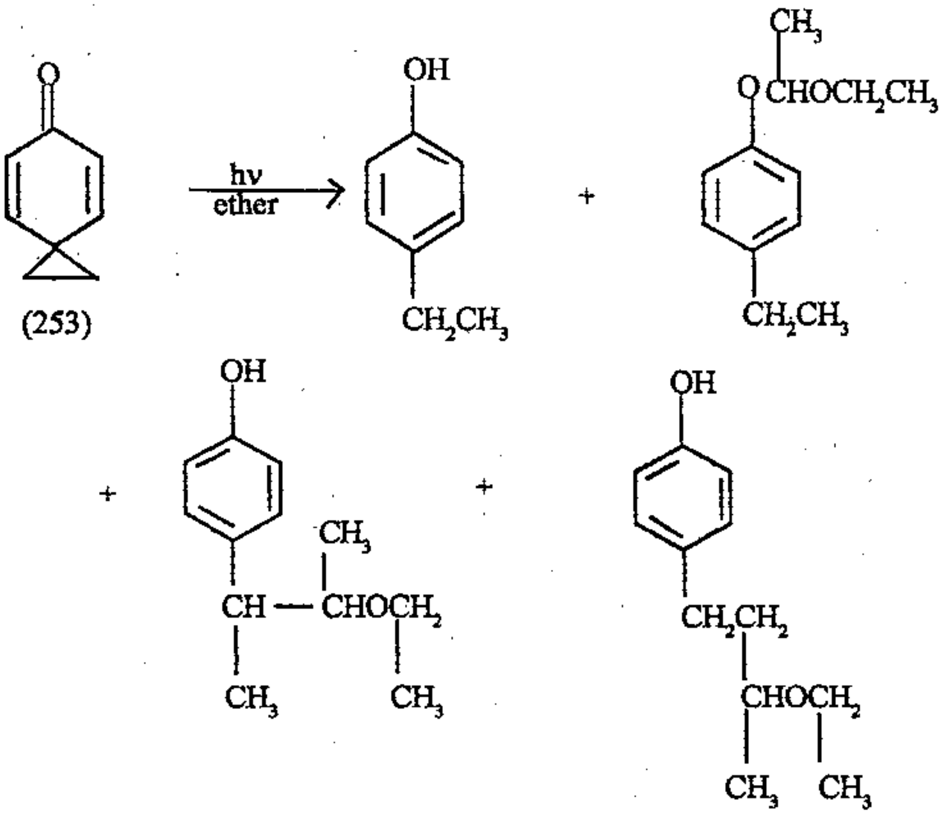


SECTION - G

(Anomalous Photorearrangement of 2,5-Cyclohexadienones)

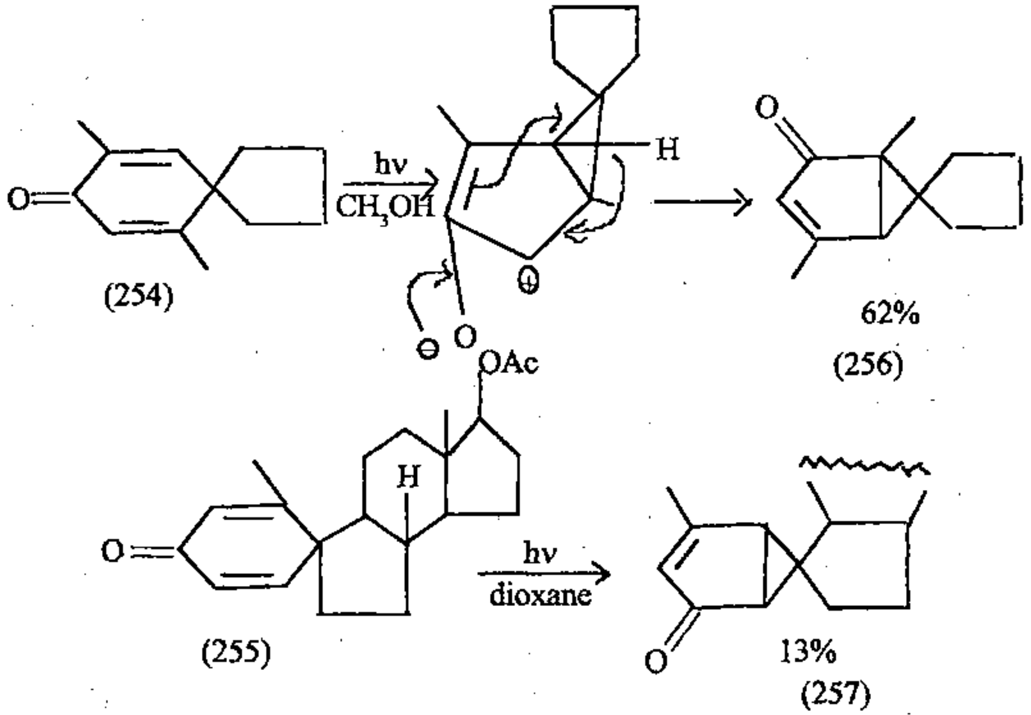
Although the formation of lumiproduct is fairly general, the presence of certain structural features in cross-conjugated cyclohexadienones (e.g. strain involved in ring skeleton or presence of certain polar substituents) lead to abnormal products. These either inhibit the formation of usual cyclopropyl intermediate or induce it to rearrange in an unusual way.

The spiro-cyclo propan containing cyclohexadienone moiety (253) is highly strained and did not produce the expected cyclopropyl ketone but gave rise to several phenolic derivatives.[107]



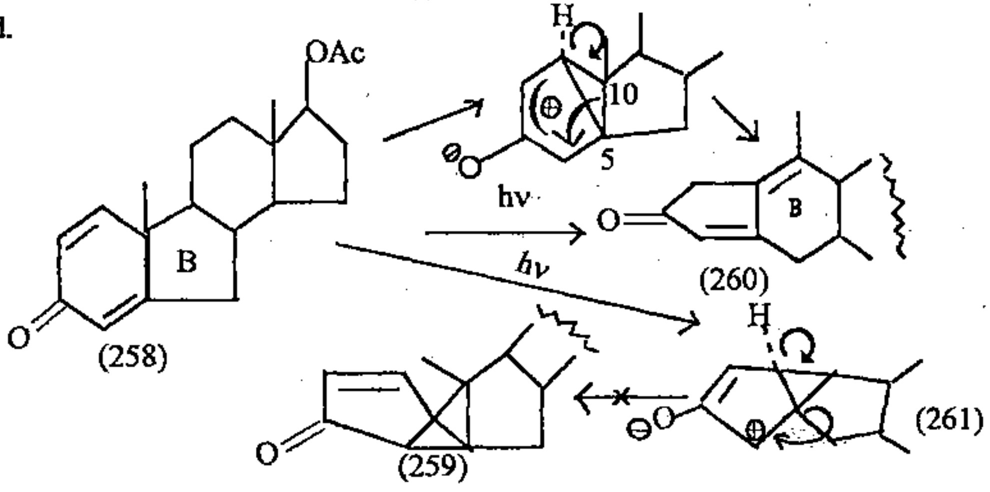
(253)

Usual cyclopropyl intermediate which would be highly strained in this case, is not formed. In contrast, the cyclohexadienones containing spiro-cyclopentane ring e.g. (254) and (255) are not so strained and underwent facile rearrangement to give the normal lumiproducts (256) and (257) respectively.[76]



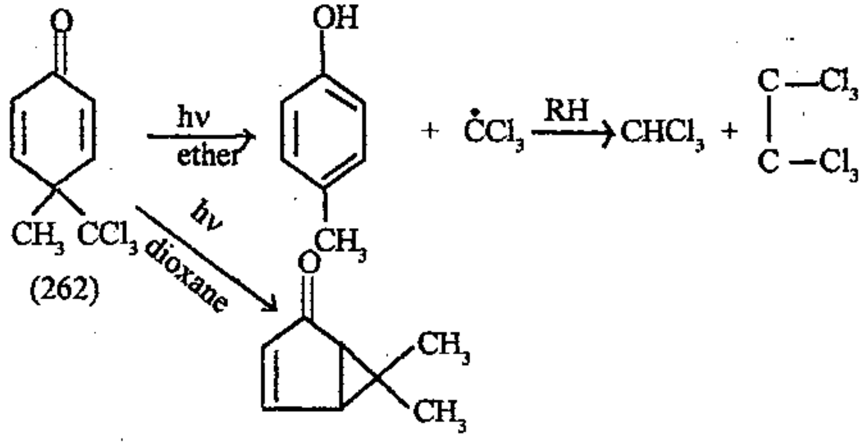
(254) (255) (256) (257)

Instead of the expected lumiproduct (259), irradiation of the steroidal B-nordienone(258) in dioxane yielded the abnormal product (260).[60] This transformation presumably involves rearrangement of the cyclopropyl intermediate (261) via rupture of the 5-10 bond with concomitant expansion of the five-membered B-ring. This process should be a bit more facile than the rearrangement to (259) which is somewhat strained.



(258) (259) (260) (261)

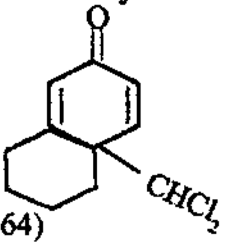
The anomalous products not only arise from cyclohexadienone compounds having strained rings, but also from substrates having substituents such as trichloromethyl, acetoxy or hydroxy at the para (C-4) position with respect to cyclohexadienone keto chromophore, when heterocyclic cleavage leads to a highly stable free radical expulsion of C- 4 substituent. Thus, irradiation of dienone (262) (containing - CCl_3substituent) in ethereal or hydrocarbon solvents gives p-cresol as a major product together with $CHCl_3$ and Cl_3CCCl_3[108]. On the other hand, irradiation in aqueous dioxane gives the normal lumiproduct (263).[109]



(262)

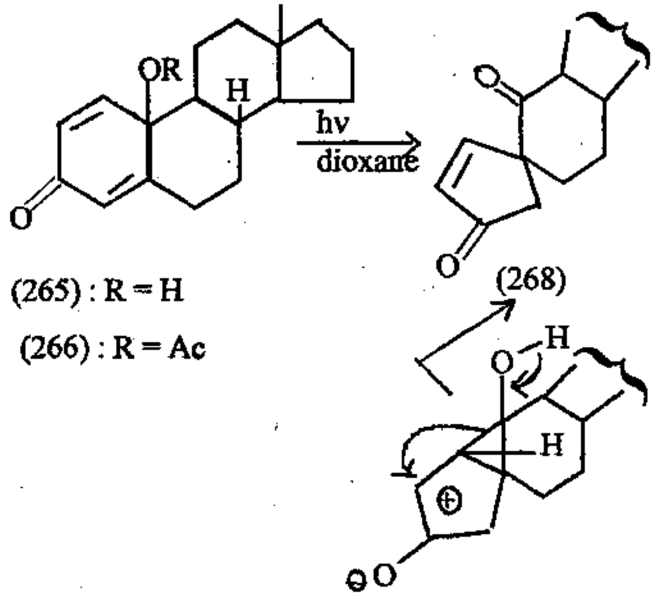
(263)

In contrast, the bicyclic dienone containing -$CHCl_2$ substituent (264) is inert under similar condition of irradiation.[110] The failure of (264) to undergo expulsion of the angular -$CHCl_2$ group may probably be due to the lesser stability of the dichloromethyl radical. Failure to produce usual lumiproduct can be attriabuted to the destabilizing electronn - withdrawing effect of the -$CHCl_2$ group in the usual β, β'- bonded intermediate which has an electron-deficient π - system.



(264)

Expulsion of an acetoxy group from the para-position has also been observed. Irradiation of (266) produced estradiol-17-acetate (267) in significant yield.[111] The presence of a hydroxyl group at para position also modifies the course of the photo reaction. Photolysis of (265) gave both the spiro-ketone (268) and estradiol-17-acetate (267).[112] Rearrangement to (268) is an expected fate of the cyclopropyl intermediate (269).



(265) : R = H

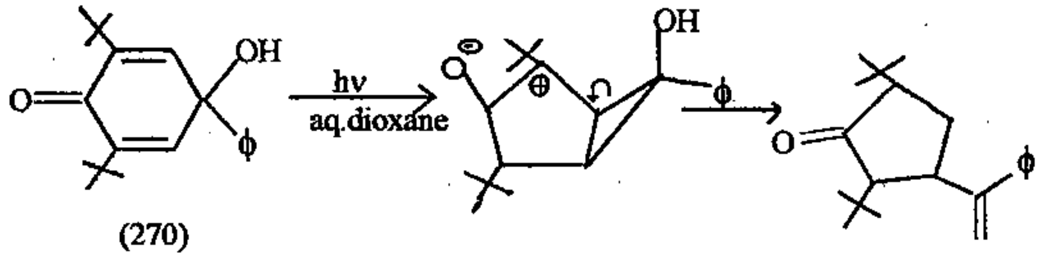
(266) : R = Ac

(268)

(267)

(269)

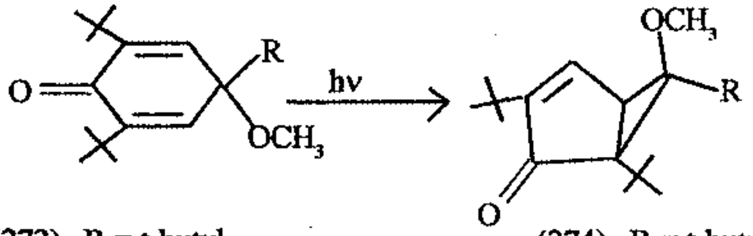
Collapse to a ketonic photoproduct (271) was also noticed in the case of the hydroxydienone (270).[113]



(270)

(271)

In the case of methoxy substituent at para position normal cyclopropyl ketone products were formed[114] e.g. (272) and (273) on photolysis afforded (274) and (275).



(272) R = t-butyl

(273) R = methyl

(274) R = t-butyl

(275) R = methyl