

MOLECULAR REARRANGEMENTS AND TRANSFORMATIONS IN TRITERPENES

**THESIS SUBMITTED FOR THE DEGREE OF DOCTOR
OF PHILOSOPHY (SCIENCE) OF THE
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SUMMARY

The work embodied in this thesis has been divided into two parts.

PART - I

This part deals with the preparation and photochemistry of cross-conjugated cyclohexadienone ring A of friedelane triterpene and has been divided into four chapters.

CHAPTER - I

This chapter gives a short review on the photochemistry of cross-conjugated cyclohexadienones. Herein mainly structural aspects have been reviewed in a few sections.

CHAPTER - II

In this chapter mechanistic aspects of the cross-conjugated cyclohexadienone photochemistry are reviewed in brief in a few sections.

CHAPTER - III

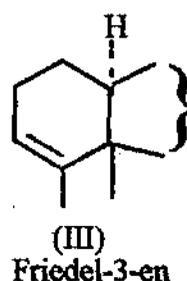
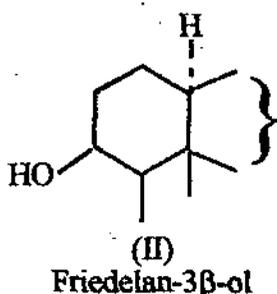
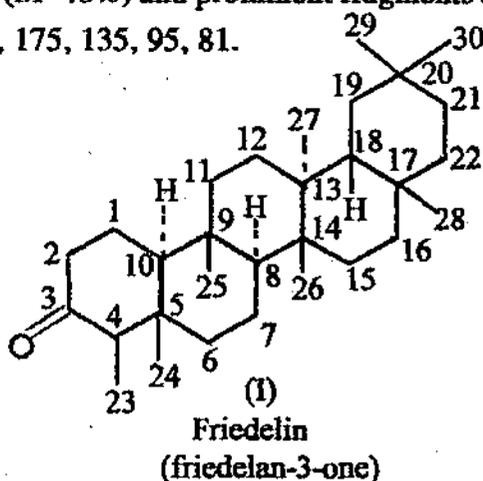
This chapter deals with the present work on the preparation and photochemistry of cross-conjugated cyclohexadienone ring A of friedelane triterpene and has been divided into three sections.

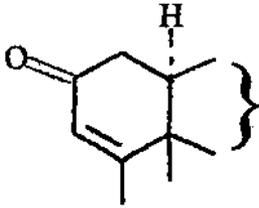
SECTION - A

This section describes the synthesis of the key compound, friedel-1(10), 3-dien-2-one (V), a cross conjugated cyclohexadienone system in ring A of friedelane, by a sequence of reactions using pentacyclic triterpene, friedelin (I) as the lead compound.

Friedelin (friedelan-3-one)_{C₃₀H₅₀O} (I) mp 260°-261°C obtained as the chief constituent from cork waste by extraction followed by purification by column chromatography, was reduced by sodium borohydride to afford friedelan-3β-ol (II), mp 282-284°C, IR(nujol) 3430 cm⁻¹ (OH), C₃₀H₅₂O. Dehydration of (II) with phosphoryl chloride in pyridine on steam-bath for 4 hr gave the olefin, friedel-3-ene(III), C₃₀H₅₀, mp 265-266°C. IR spectrum displayed bands at 780 and 750cm⁻¹ indicating the presence of a trisubstituted double bond. Compound (III) was subjected

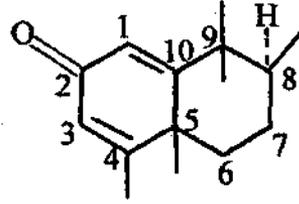
to two successive oxidations. The first oxidation with sodium dichromate in benzene- ACOH (1 : 1) at reflux temperature (4 hr) yielded (60%) the conjugated ketone, friedel-3-en-2-one (IV), $\text{C}_{30}\text{H}_{48}\text{O}$ (crystallised from ethyl acetate) mp 287-289°C. Its UV spectrum showed absorption maximum at 236 nm (ϵ 7600) (MeOH), IR (nujol) 1658, 1620, 850, 720 cm^{-1} (cyclohexenone chromophore). ^1H NMR (300 MHz, CDCl_3) gave signals for a vinyl proton at δ 5.65 (d, $J \sim 1\text{Hz}$, 1H), vinyl methyl 1.84(d, $J \sim 1\text{Hz}$, 3H) due to small splitting for allylic coupling, besides seven saturated tertiary methyls between 0.91 and 1.14, ^{13}C chemical shift values (75 MHz, CDCl_3) at 200.62 (C = O), two olefinic carbons at 172.06 and 125.32. In addition, signals for 27 saturated carbon atoms occurred between 55.60 and 17.62. (IV) on further oxidation with DDQ in dry dioxane under nitrogen blanket at reflux temperature for 3 hr afforded the key compound (V), mp 280-281°C (crystallised from EtOAc) $\text{C}_{30}\text{H}_{46}\text{O}$. Combination of spectral data enabled to deduce its cross-conjugated cyclohexadienone structure. It showed UV maximum at 246 nm (MeOH) (ϵ 17150), IR (nujol) bands at 1646, 1610, 1584 and 890 cm^{-1} . ^1H NMR spectrum exhibited resonances for 7 saturated methyl groups between δ 0.92 to 1.25, one vinyl methyl at 1.95(d, $J \sim 1\text{Hz}$, 3H) and two olefinic protons at 6.11 (d, $J \sim 1\text{Hz}$, 1H) and 6.02 (1H, s). ^{13}C NMR spectrum displayed peaks at δ 187.55 (C = O), four olefinic carbons at 177.50, 167.29, 125.68, 121.86 and 25 saturated carbons between 50.16 to 17.73. EIMS exhibited molecular ion peak at m/z 422 (M^+ 48%) and prominent fragments at 407 ($\text{M}^+ - \text{CH}_3$), 298, 286, 271, 229, 203, 182, 175, 135, 95, 81.





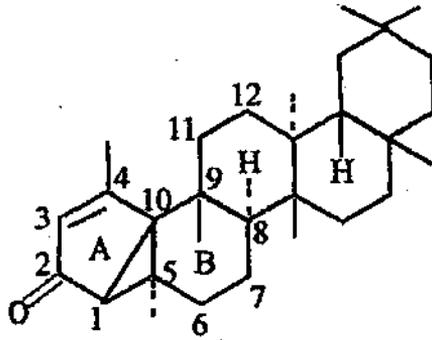
(IV)

Friedel-3-en-2-one



(V)

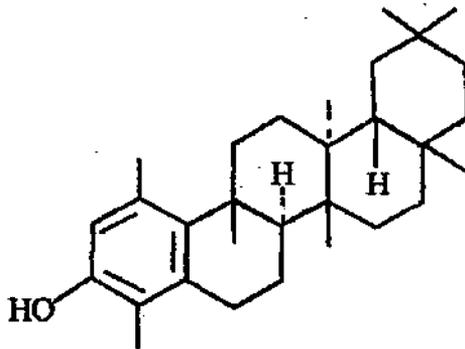
Friedel-1 (10), 3-dien-2-one



(VI)

Lumiketone

(Bicyclohex [3.1.0]enone type photoproduct)



(VII)

Phenolic product

SECTION - B

This section describes the photoirradiation of the synthesised key compound (V), isolation and elucidation of the structure of the major photoproduct, the bicyclo [3.1.0] hexenone (VI), also popularly known as the lumiproduct.

The photolysis of the cross-conjugated cyclohexadienone (V) at 254 nm (low-pressure mercury lamp) in dry dioxane at ambient temperature under nitrogen atmosphere for 15 min. was carried out. The progress of the photoreaction was monitored by TLC. Using pet ether-ethyl acetate (4:1) as eluent a colourless compound has been obtained, which on crystallisation from ethyl acetate afforded needles (VI), (62%), $C_{30}H_{46}O$, mp 305°C. Bicyclo [3.1.0] hexenone structure (also called popularly as lumiproduct) of (VI) was determined by combination of physical techniques. UV spectrum showed absorption maximum at 241 nm (MeOH) (ϵ 8200) (conjugated ketone), IR (nujol) at 1675, 1595 cm^{-1} (cyclopentenone). A detailed analysis of 1H NMR, ^{13}C NMR and EIMS enabled us to deduce the structure of (VI). 1H NMR showed resonances at δ 5.65 (d, J - 1Hz, 1H) for olefinic proton and at 2.14 (d, J - 1Hz, 3H) for vinyl methyl group and between 0.92 to 1.15 for seven tertiary methyls. ^{13}C NMR revealed resonances at δ 206 (C = O), two olefinic carbons at 175 and 133, besides 27 sp^3 carbons between 58.80 and 16.84. EIMS registered molecular ion peak at m/z 422 (M^+ , 73%) and other important fragmented ions at 407 ($M^+ - CH_3$), 298, 218, 204, 175, 161, 149, 136, 123, 109 and 95.

Since lumiproduct VI itself is photolabile, prolonged irradiation results in a complex reaction mixture.

Considerable attention has been directed to and works have been reported on the stereochemical aspect of cyclohexadienone photochemistry. This photoreaction appears to be stereospecific and proceed with inversion of configuration at the migrating carbon atom. Since conflicting and ambiguous results have occasionally been encountered, the problem of stereochemistry has to be resolved satisfactorily. In the light of currently accepted view the stereostructure of the lumiketone has been assigned to be (VI). The stereochemistry has also been discussed in the light of chiroptical measurements.

SECTION - C

This section describes the isolation and characterisation of the phenolic photoproduct (VII) obtained on irradiation of the key compound (V) for an extended period. Also it is formed as a secondary photoproduct upon irradiation of the lumiproduct (VI).

On carefully monitoring the photolysis by TLC it has been noticed that a second spot made its appearance on prolonged irradiation. The phenol (VII) was subsequently isolated as a white solid on silica gel chromatography. It was crystallised from ethyl acetate as needles mp 198°C. It exhibited absorption maximum at 281 nm (ϵ 2250) in UV spectrum and a strong IR band at 3320cm^{-1} indicative of phenolic OH group. Mass spectrum recorded a molecular ion peak at m/z 422 showing that (VII) is isomeric with (V) as well as (VI) and suggest to originate from an intramolecular photorearrangement. It was further substantiated by an accurate mass measurement in high resolution mass spectrum (HRMS, M^+ observed m/z 422.2501, calculated for $\text{C}_{30}\text{H}_{46}\text{O}$ m/z 422.2508) which supported the molecular formulation as $\text{C}_{30}\text{H}_{46}\text{O}$. Owing to the paucity of the material its NMR spectrum could not be recorded. Based on above-mentioned spectral observations coupled with currently accepted mechanistic considerations, we propose the structure (VII) for the phenolic product.

CHAPTER - IV

Experimental portion has been described in this chapter.

PART - II

This part deals with the preparation and molecular rearrangement of 2 α , 3 α -epoxy lupan-1-one catalysed by boron trifluoride and by ultraviolet irradiation and has been divided into three chapters.

CHAPTER - I

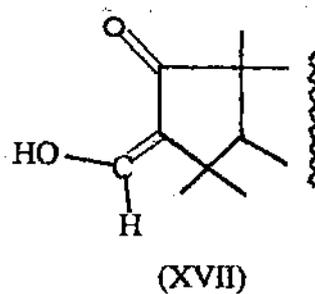
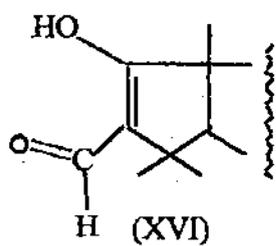
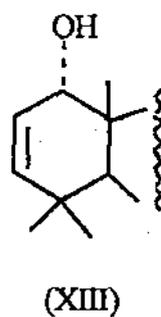
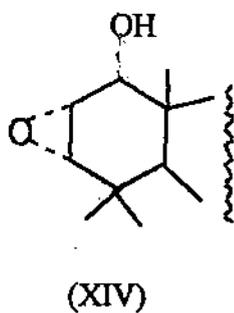
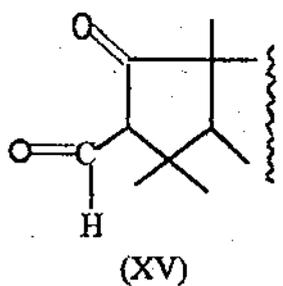
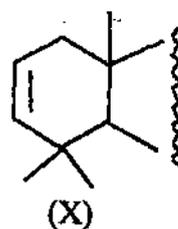
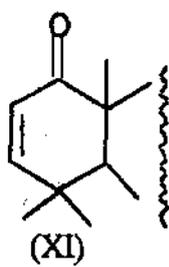
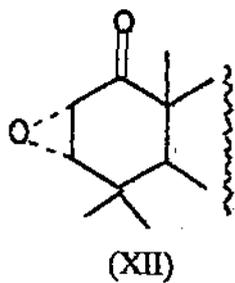
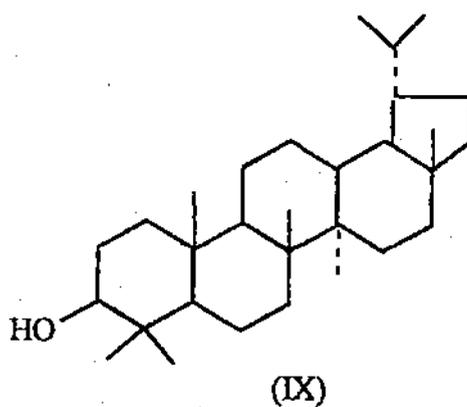
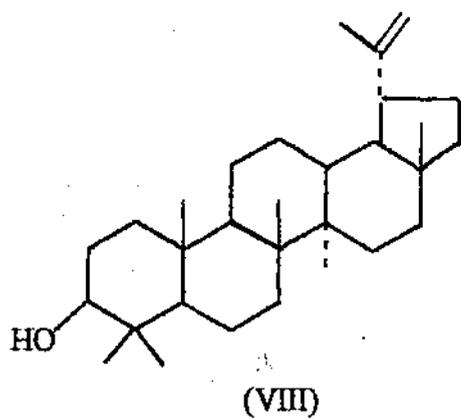
This chapter gives a short review on the molecular rearrangement of α,β -epoxy ketones, SECTION - A : induced by the Lewis acid, boron trifluoride-etherate and SECTION - B : induced by ultraviolet irradiation.

CHAPTER - II

This chapter describes the present work on preparation and molecular rearrangement of 2 α , 3 α - epoxy lupan-1-one (XII) catalysed by boron trifluoride and by ultraviolet irradiation and has been presented in three sections.

SECTION - A

This section describes the synthesis of 2 α , 3 α -epoxy lupan-1-one (XII) using lupeol (VIII), a pentacyclic triterpene of lupan series, as the lead compound, obtained abundantly from the plant *Zanthoxylum budrunga* growing in North Bengal. Compound (VIII) on catalytic reduction furnished lupanol (IX) which on dehydration with phosphorus oxychloride in pyridine afforded lup-2-en(X). Oxidation of (X) with sodium dichromate in benzene-acetic acid mixture (1:1) yielded the conjugated ketone, lup-2-en-1-one (XI), λ_{\max} 220nm, ν_{\max} 1667 cm^{-1} . Since the system 2-en-1-one of ring A in triterpenes is stable towards alkaline hydrogen peroxide, attempts to epoxidise the conjugated ketone (XI) with alkaline H_2O_2 had failed. Consequently, an alternative method had been adopted for the preparation of the epoxy ketone (XII). Lup-2-ene (X) on selenium dioxide oxidation in dioxane with a few drops of water added in it, gave the allylic alcohol, lup-2-ene-1 α -ol (XIII). Compound (XIII) was epoxidised with metachloro-perbenzoic acid in chloroform to yield the epoxy alcohol, 2 α , 3 α -epoxy lupan-1 α -ol(XIV). The key compound, 2 α , 3 α -epoxy lupan-1-one (XII) was then prepared by the chromium trioxide-pyridine oxidation of (XIV). In ^1H NMR spectrum, appearance of resonances at δ 3.1 (doublet, $J = 4\text{Hz}$) and δ 3.27 (doublet, $J = 4\text{Hz}$) enabled to assign 2 α , 3 α -epoxy ketone stereochemistry for (XII).



SECTION - B

This section deals with the molecular rearrangement of the synthesised α,β -epoxy ketone (XII) induced by the Lewis acid, $\text{BF}_3 \cdot \text{Et}_2\text{O}$.

Boron trifluoride catalysed rearrangement of (XII) in dry benzene at ambient temperature afforded the ring A contracted keto aldehyde, 2-formyl-A-nor-lupan-1-one (XV) in 60% yield. It practically exists in solution as the enolised form (XVI). The structure of the rearranged product was deduced by the physical techniques UV, IR, NMR and mass spectra. Of the two possible enolised forms (XVI) and (XVII), the former one (XVI) was supported by aldehydic proton singlet at δ 9.4 in the ^1H NMR analysis.

The attack by BF_3 upon (XII) opens the epoxide ring to generate electron-deficient centre which subsequently undergoes rearrangement to afford ring-A contracted keto aldehyde (XV).

SECTION - C

This section deals with the photolysis of the epoxy ketone (XII). Since α,β -epoxy ketones are much susceptible to photochemical alteration, it was felt pertinent to irradiate (XII) and make a comparison of the light-induced rearranged product with that of acid-catalysed rearranged one (XV).

Irradiation of (XII) in dioxane with medium pressure mercury lamp ($\lambda > 290$ nm) at ambient temperature under argon atmosphere for 0.5 hr. has been carried out. Isolation of the same keto aldehyde (XV) has been achieved in good yield (52%). The identity has been established by comparison of mp, mmp, UV, IR, ^1H NMR and mass determinations. Since the initial product (XV) is also photolabile, irradiation for an extended period results in a complex reaction mixture giving a low yield of (XV). The diradical generated from excited singlet manifold by homolysis of $\text{C}-\text{O}$ bond rearranges to the keto aldehyde (XV) by a process in which the bond-migration and carbonyl formation steps are considered to be concerted.

CHAPTER - III

This chapter gives the description of the experimental portion.

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(PREPARATION AND PHOTOCHEMISTRY OF CROSS- CONJUGATED CYCLOHEXADIENONE RING A OF FRIEDALANE TRITERPENE)

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PART – II

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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 century¹. The pioneering studies by Barton, Jeger, Vantamelen and their groups resolved the structure and stereochemistry of various photoproducts of α -santonin²⁻⁹. Subsequently, it was observed that photo transformations in cross-conjugated cyclohexadienones are fairly general and could be correlated with α -santonin photoproducts. Several detailed reviews¹¹⁻¹⁷ 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 principal product obtained is the bicyclo [3.1.0] hex-3-en-2-one, a cyclopropyl ketone (also called as lumiprodukt, analogous to lumisantonin 2). On prolonged irradiation secondary transformation of lumiketone gives rise to several spiro-ketones and eventually phenols. Interestingly, when irradiation is effected in acidic solution the lumiprodukt 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 aqueous dioxane where lumiprodukt and phenol are principal products, our review will involve the formation of lumiprodukts 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).

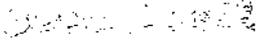
SECTION - A

(A short review on Santonin \rightarrow Lumisantonin Photorearrangement)

Barton and coworkers⁵ observed that irradiation of α -santonin(1) in neutral media gave an isomer lumisantonin(2). This compound was also obtained by Buchi, Jeger² and Cocker and their groups³. 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) λ_{max} 239 nm (ϵ 5860) indicating an α, β -unsaturated ketone. Three C-Me groups were determined both chemically and by quantitative IR measurements.

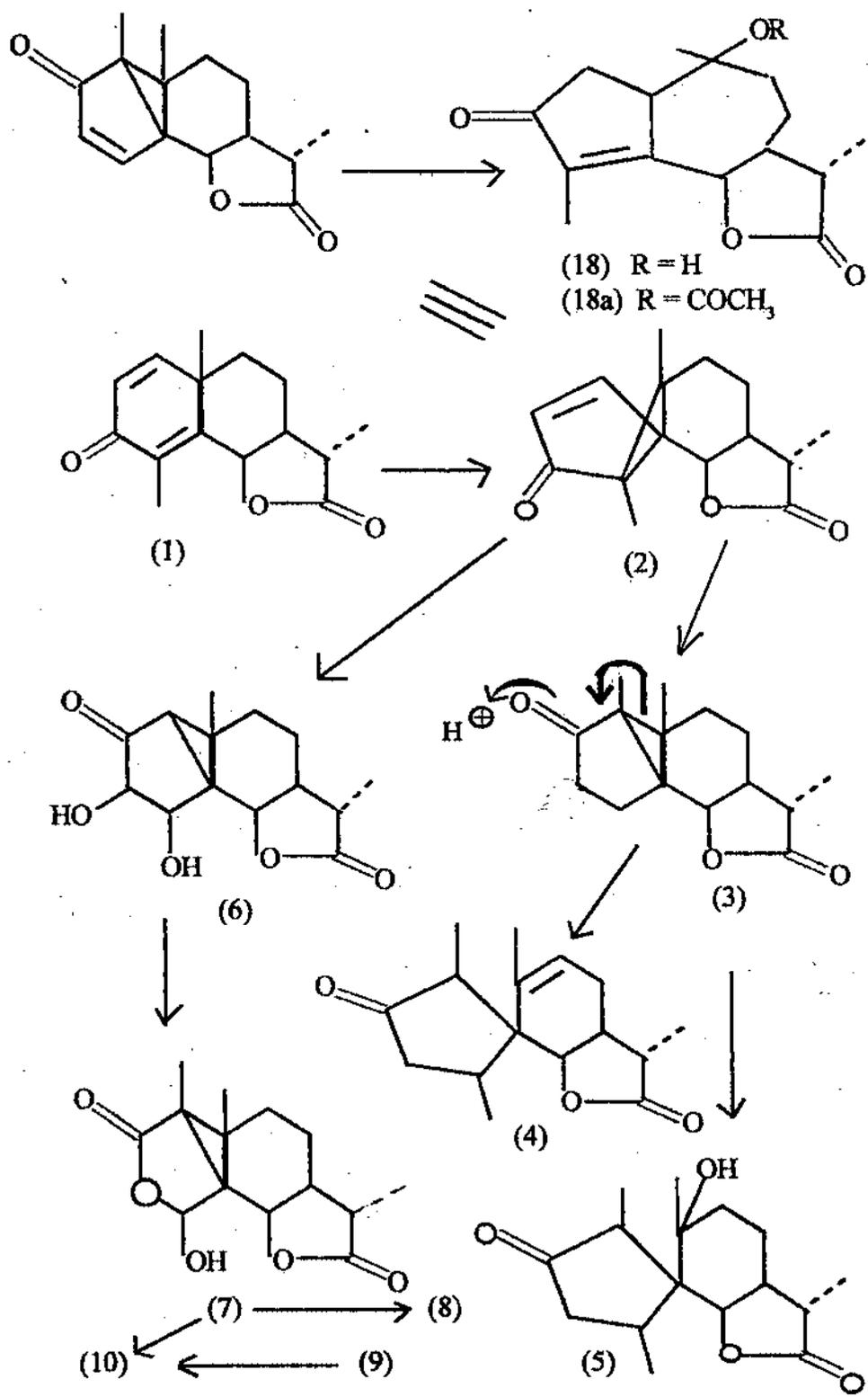
(2) was readily hydrogenated to a dihydroderivative (3) which showed IR bands at 1770 (γ -lactone) and 1703 cm^{-1} . The later frequency at 1703 cm^{-1} is indicative of a bicyclo [3.1.0] hexan-2-one system. On refluxing with aqueous AcOH (3) furnished an isomer (4) and the corresponding tertiary alcohol(5). 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).

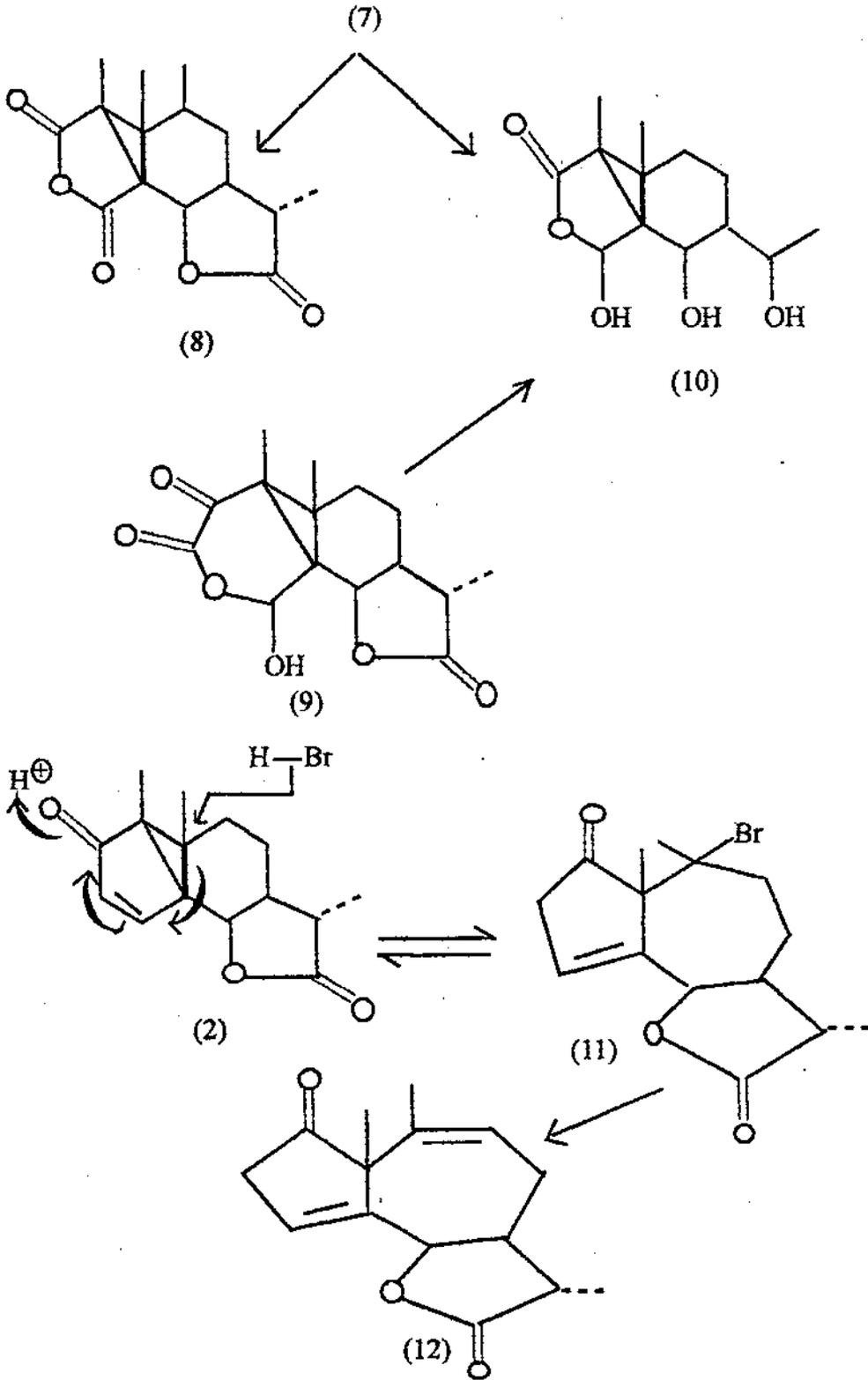
Treatment of (2) with OsO_4 gave a crystalline glycol (6) having IR bands at 3360(OH), 1770 (γ -lactone) and 1726 cm^{-1} (cyclopentanone) and UV absorption same as dihydrolumisantonin (5). It consumed 2 mole of periodic acid to afford a C-14 aldehydic acid which is regarded as existing in the lactol 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 ($-\text{C}-\text{CH}=\text{CH}-$) 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

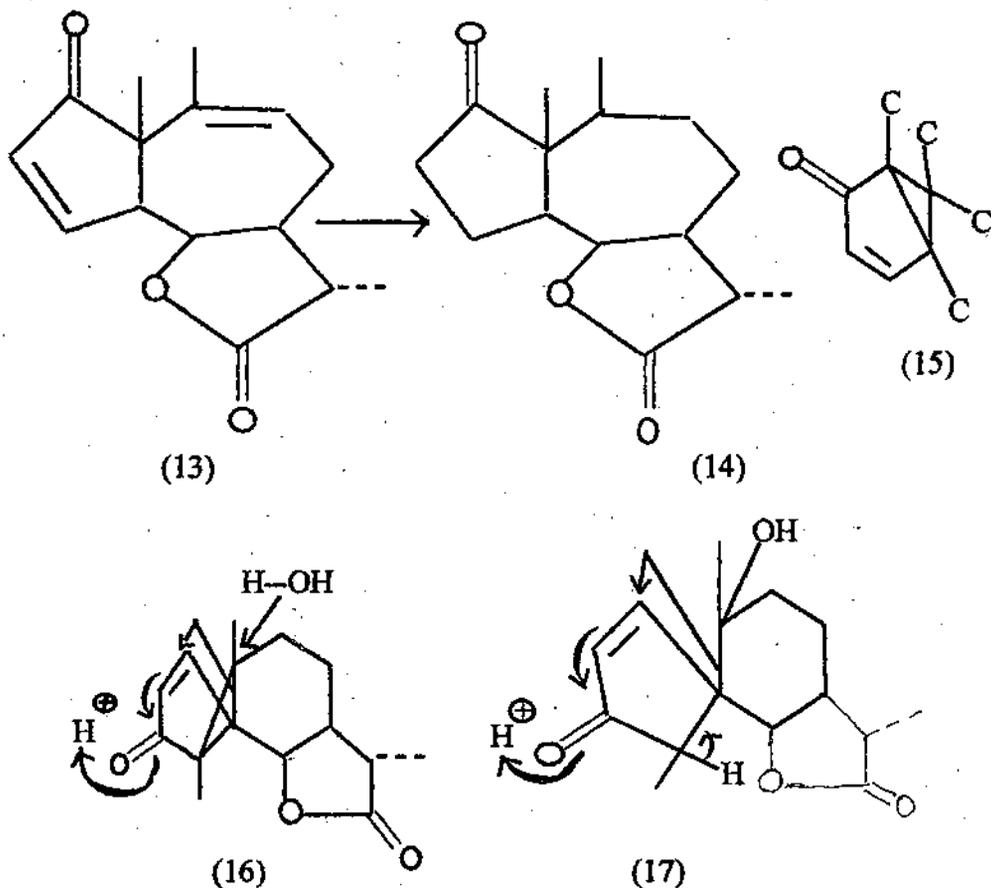
cleaved the compound (9) to afford  (10), the constitution of which followed when it was obtained also by opening the lactone-ring of lactol (7) with alkali.

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 perchloric 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.







The Stereochemistry of Lumisantonin :

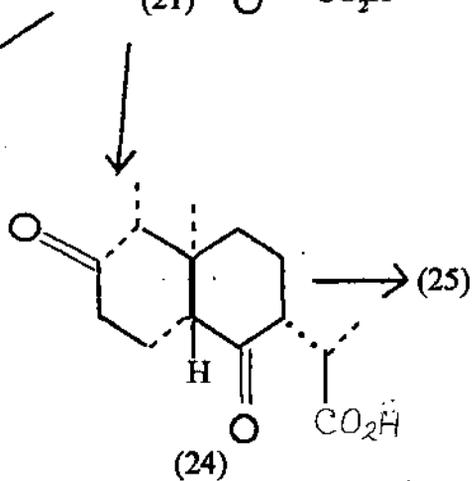
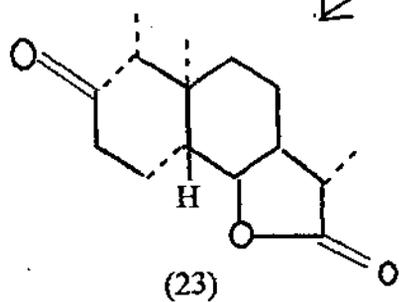
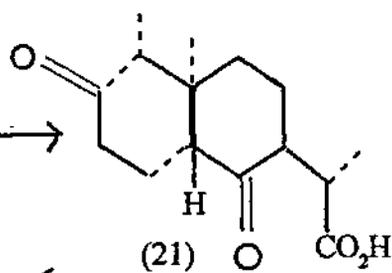
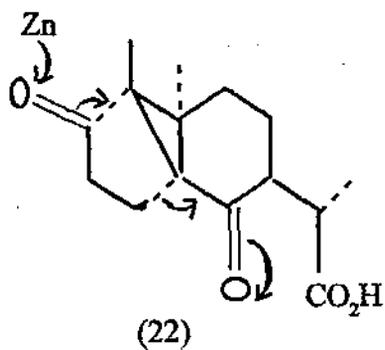
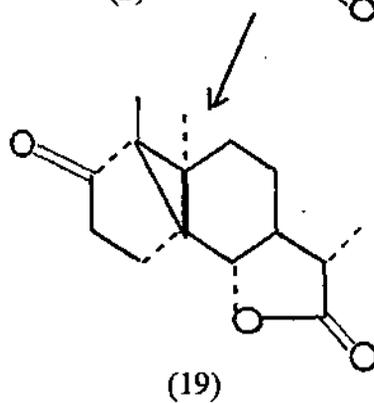
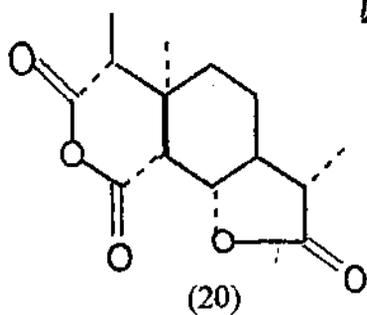
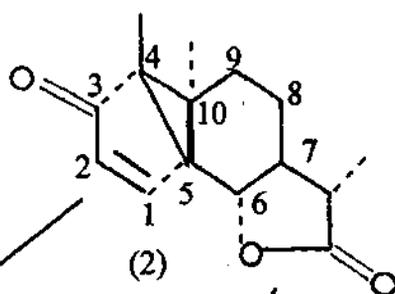
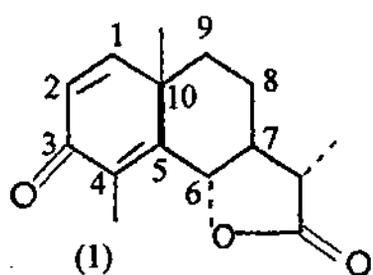
Barton and Gilham⁶ carried out a detailed degradative study to deduce the stereochemistry of lumisantonin(2). Its stereochemistry has been evaluated at every centre of asymmetry. It has been shown that the cyclopropane ring is fused *cis* to its attached five and six-membered rings. The photorearrangement is stereospecific with inversion of configuration at the angular methyl group.

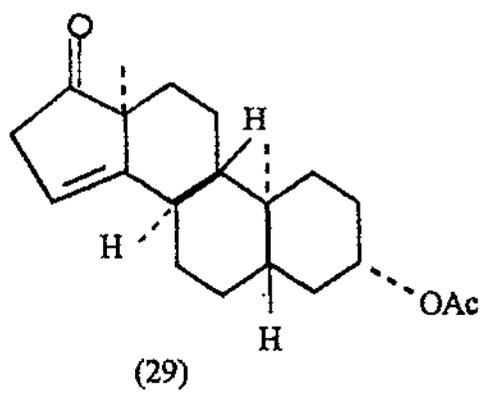
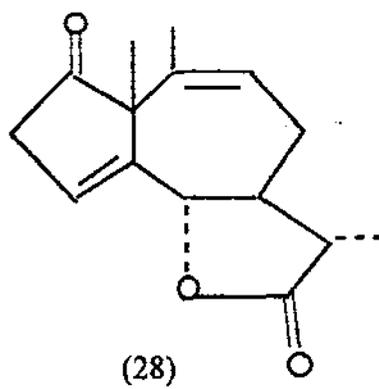
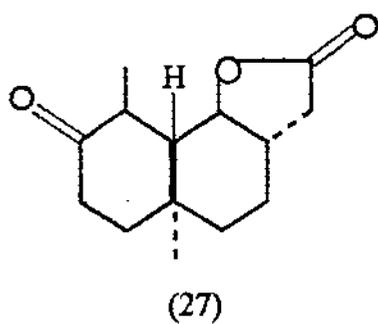
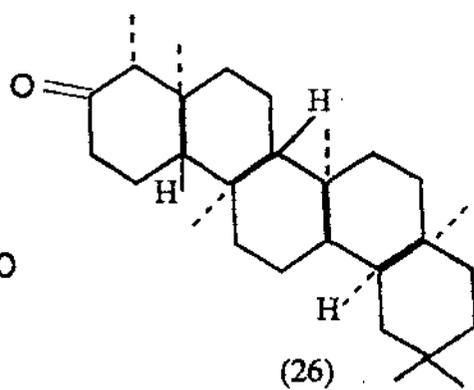
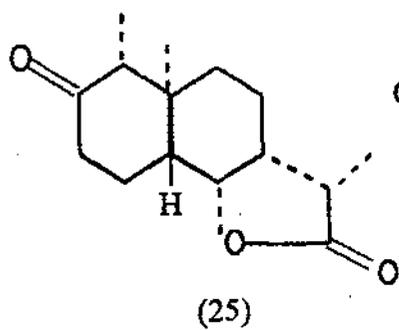
The centres of asymmetry at position 6,7 and 11 are not altered in the photoisomerisation. Since these centres do not have bonds permitting the UV absorption needed for this reaction and since all four possible santonins epimeric at C-6 and C-11 have been irradiated and shown to furnish four different transformation products³⁰, a fact best explained if C-6, C-7 and C-11 are not altered in any way on irradiation.

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 ($[M] -5700^\circ$) of enantiomeric type of that of a comparable model steroid (29). The latter had a single Cotton Effect with a peak near 330 nm ($[M] + 4800^\circ$). 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 Arigoni² et al. and Cocker³ et al. .

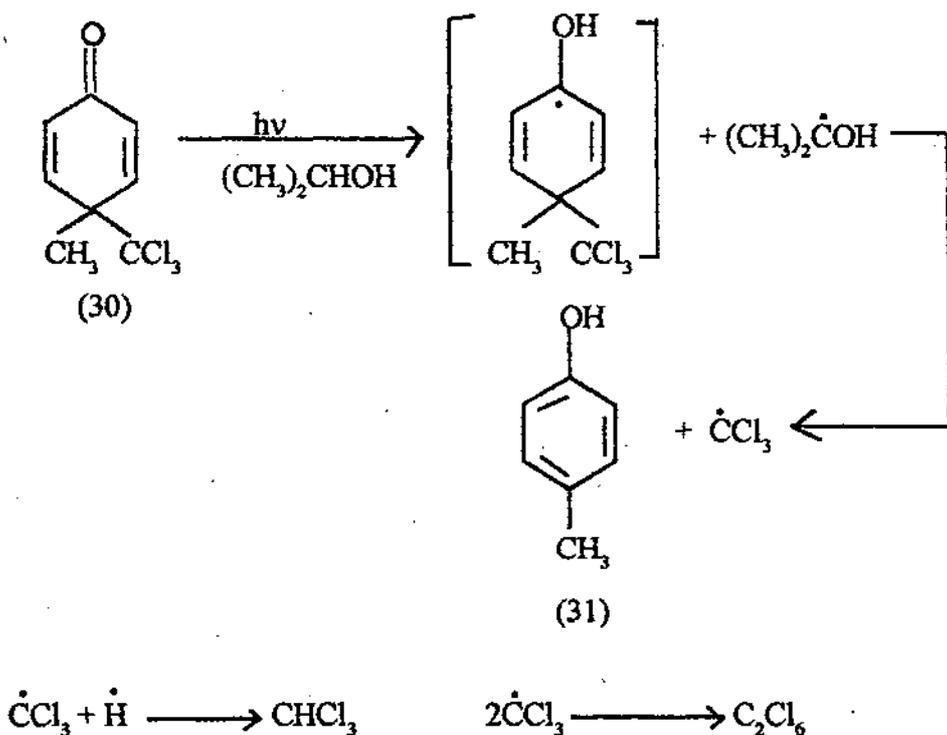
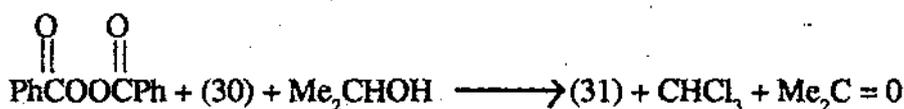




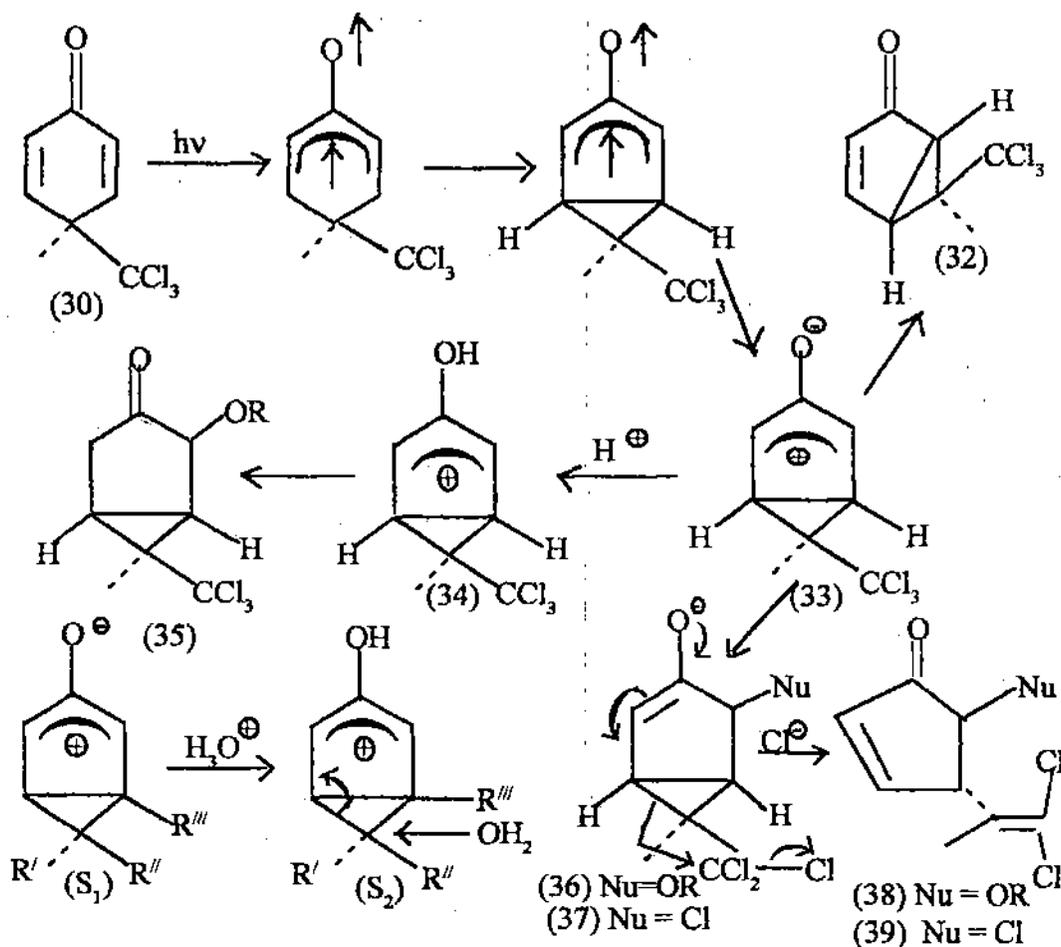
SECTION - B

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

For extensive study Schuster and co-workers¹⁸ 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 $80^\circ C$ in isopropanol in which (30) was added. P-cresol (31) was obtained along with $CHCl_3$ in good amount.

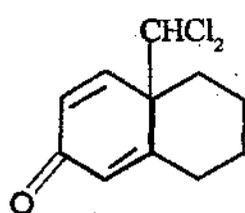


On the other hand, irradiation in benzene yielded the lumiproduct (32). Schuster et al. also utilized this compound for providing unequivocal proof for the intermediacy of zwitterion at the later stage of this deep-seated rearrangement. A close look at the structure of (30) shows that due to the presence 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

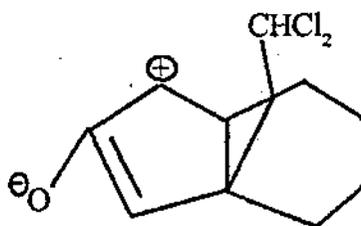


anionic Grob-type process. On increasing LiCl concentration in methanol and trifluoroethanol the ratio (39)/(32) and (38)/(39) increase linearly and the quantum yield of the formation of the zwitterion (33) approaches to unity.

In contrast to (30) the closely related bicyclic dienone (40) is inert under similar condition of irradiation²². 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 lumiprduct formation can be accounted for by the destabilising electron-withdrawing effect of the dichloromethyl group on the usual intermediate (41) possessing an electron deficient π -system.

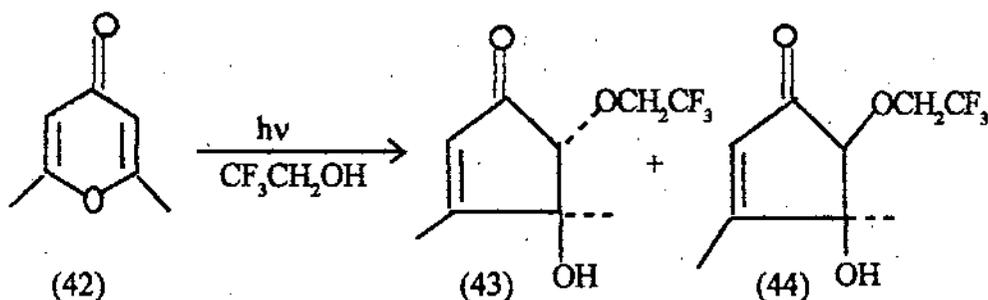


(40)



(41)

Pavlik et al.²³⁻²⁴ irradiated 2,6 - dimethyl-4H-pyran-4-one (42) in 2,2,2-trifluoroethanol 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.

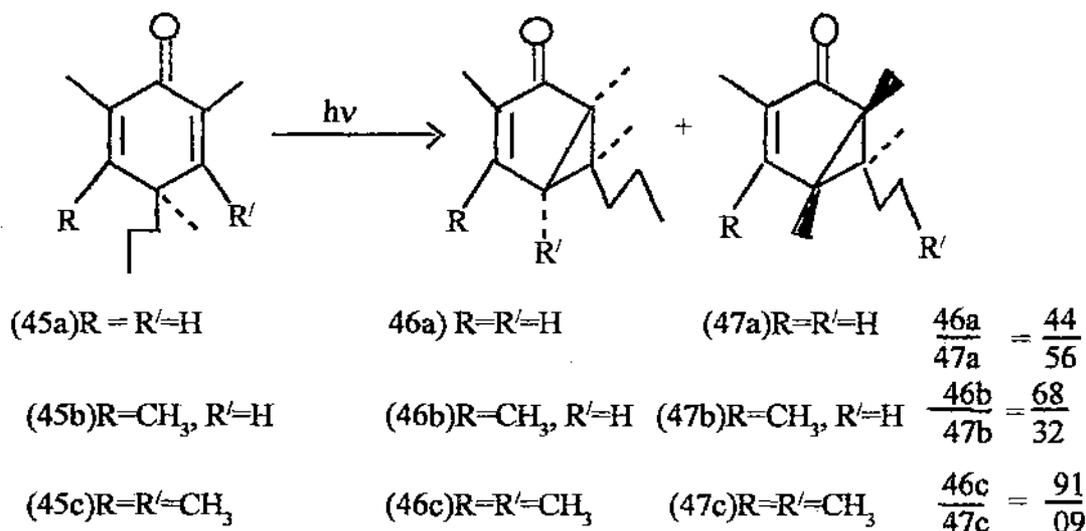


(42)

(43)

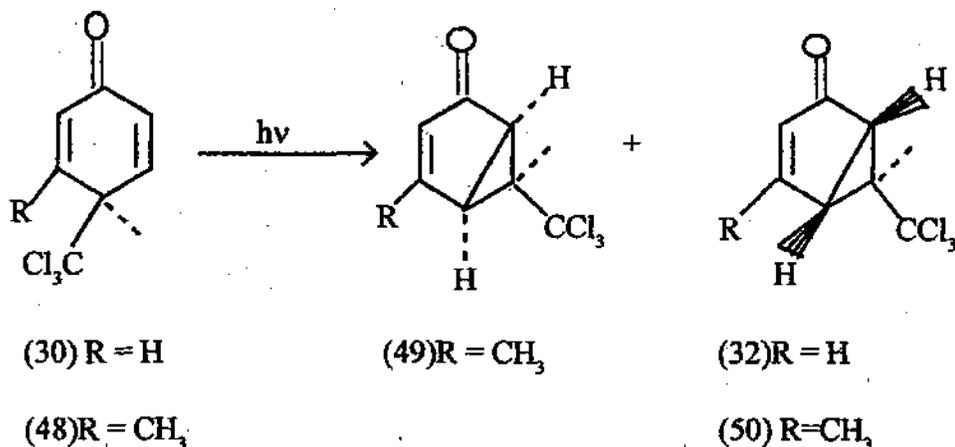
(44)

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-by-cyclohexenone 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 Heart²⁵ 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) they²⁵ demonstrated that the ratio of the products $\frac{(46a-c)}{(47a-c)}$, as shown below, support their proposition, provided the inversion of configuration on the [1,4] shift is assumed.



In order to examine the relative contribution of electronic and steric effects, Schuster and coworkers¹⁸⁻¹⁹ 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 $-\text{CCl}_3$ 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

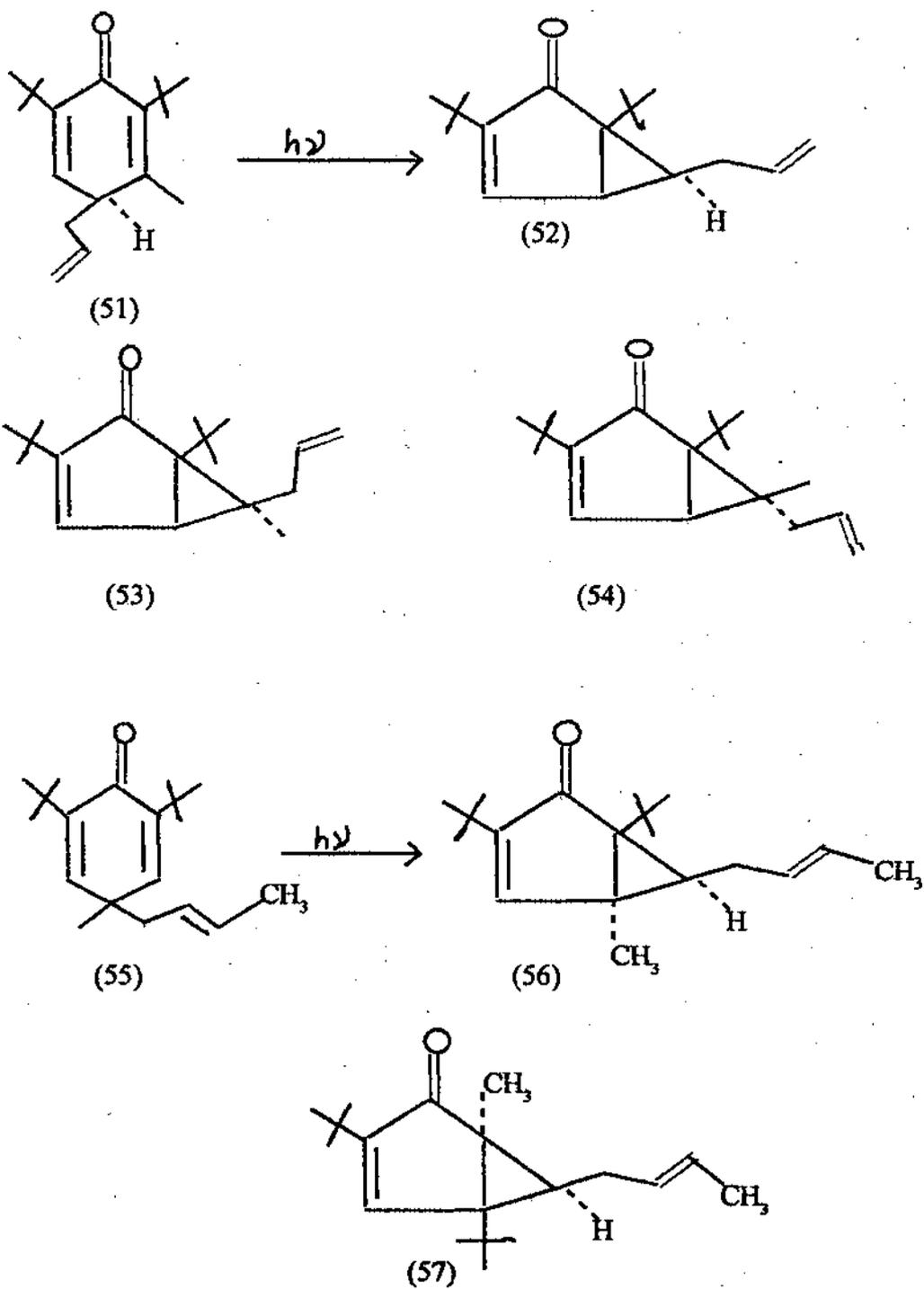


electron-rich group. In these systems, it is clear that electronic effects dominate in the reaction course.

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 bi-cyclohexenone products seem to exert a selective influence in the direction in which migration proceeds. The product formation reflects a preference for α , β -di or β -monosubstituted double bond.²⁵⁻²⁷

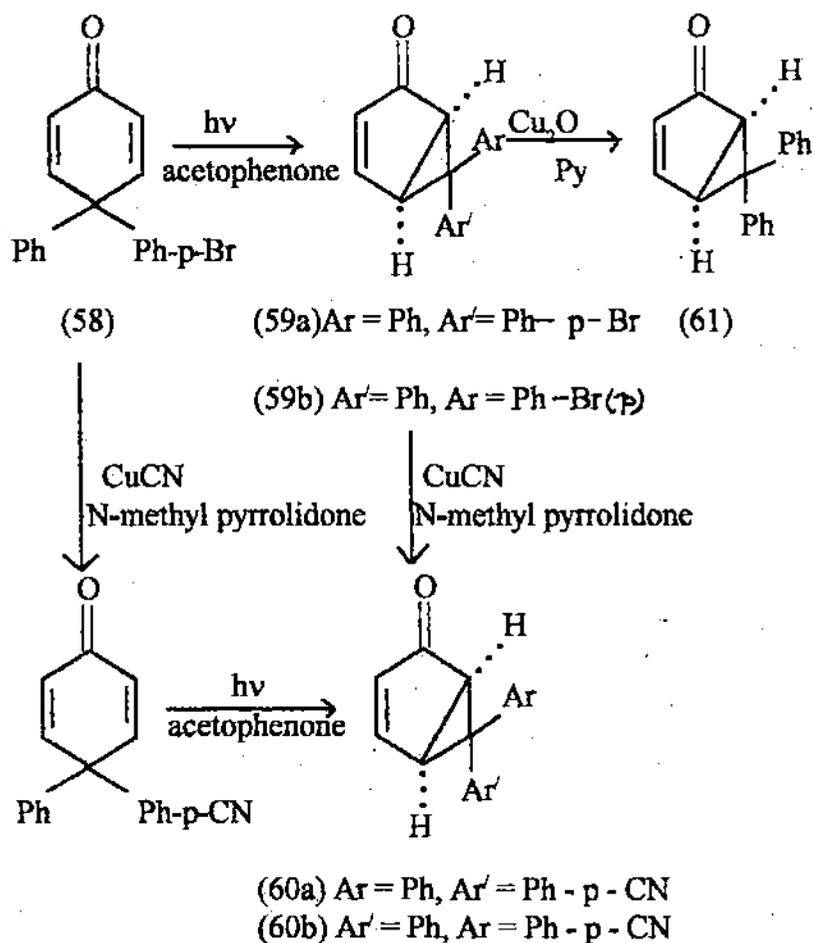
Miller²⁸ observed that irradiation of (51) containing allyl group at C - 4 gave (52). NMR analysis of the product showed that the cyclopropyl proton and the allyl group are on the same carbon which can only be C - 6. The geometry of C - 6 was deduced from the unusually high field absorption (τ 7.96) 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.

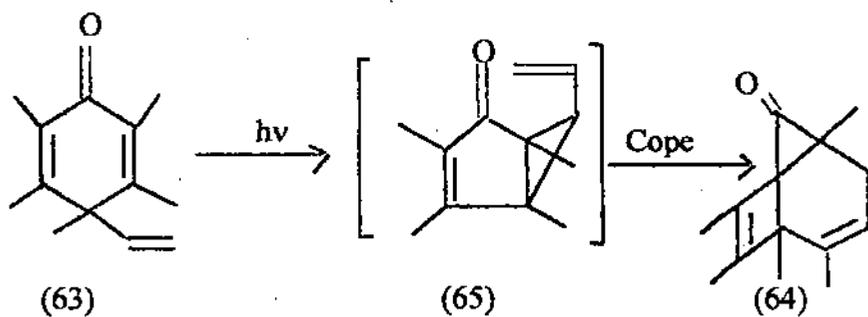


The selective rearrangement of (55) to (56) combines preferential *endo* puckering with a [1,4] shift toward the product with an α -monosubstituted double bond. This reversion of the [1,4] shift trend could be due to less severe steric compression between methyl and t-butyl groups in (56) than in the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

On irradiation of 4-p-bromophenyl-4-phenyl-2,5-cyclohexadienone (58) Zimmerman and Grunewald²⁹ obtained two isomeric *cis* and *trans* 6-p-bromophenyl-6-phenyl-bicyclo-[3.2.0]-hex-3-en-2-ones (59a) and (59b). That they were the stereoisomeric product^s 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 \rightarrow C- 3 aryl migration.

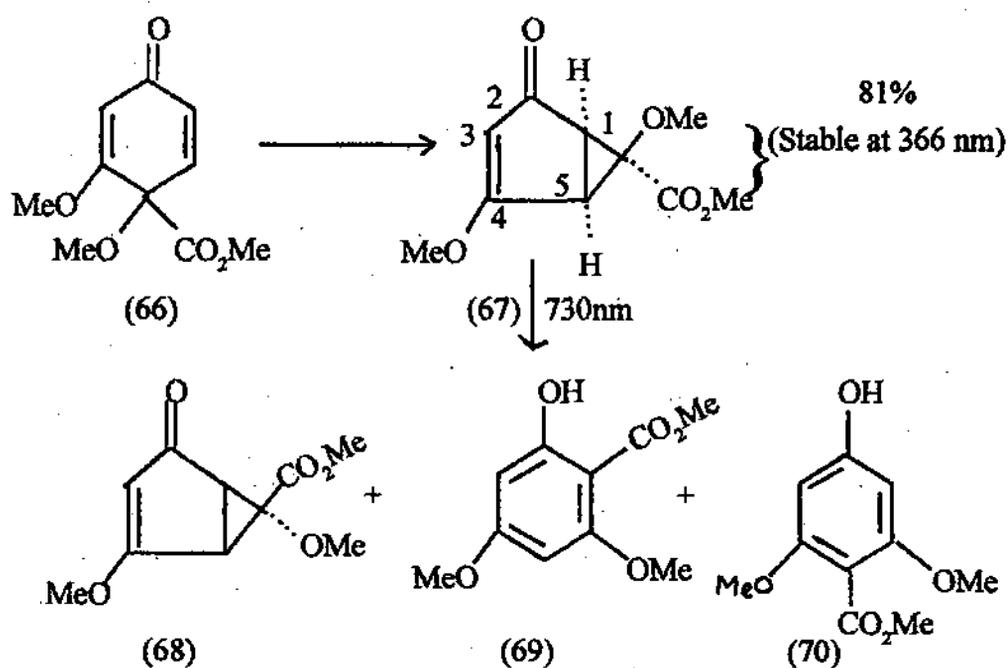


The first example of photochemistry of 2,5-cyclohexadienones with a 4-vinyl substituent was reported by Hart and Nitta.³¹ The initially formed luniprodut resulted in an unusual skeleton rearrangement.

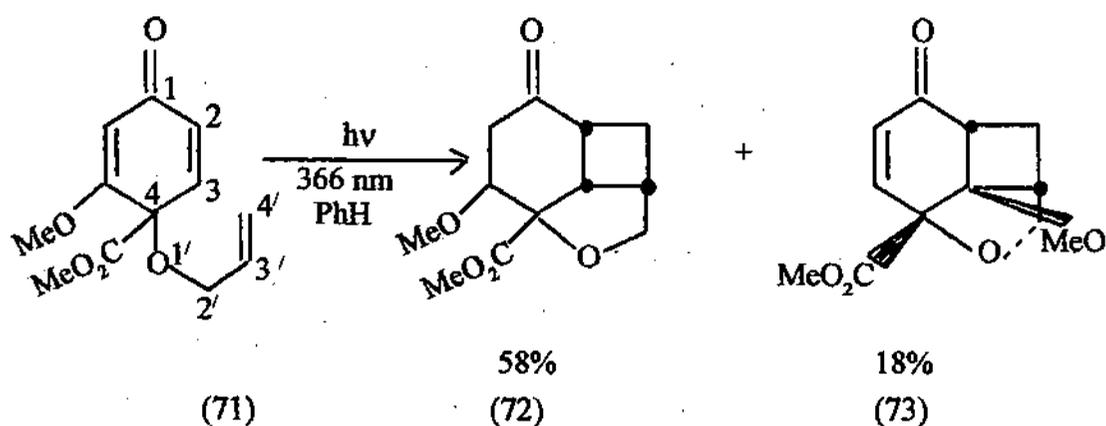


The structure of the product (64) was deduced from its spectral data and method of synthesis. Elemental analysis and the mass spectrum showed that (64) was an isomer of (63). The carbonyl absorption $\nu_{c=O}$ 1753 cm^{-1} and uv λ_{max} (280 nm) (ϵ 24), end absorption of spectrum at 220 nm (ϵ 7149) 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 lumiprodukt which being a cis-divinylcyclopropane spontaneously undergoes Cope rearrangement to (64).

In 1991 A.G.Schultz and R.E. Hazrington³² 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.



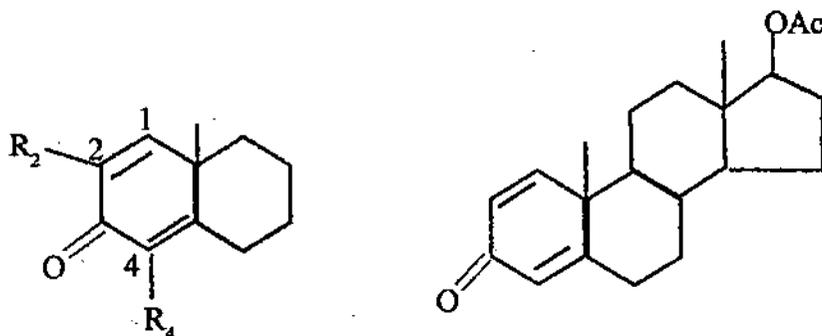
It is proposed that ground state conformational effects control the type A photochemistry of (66) and that rearrangement to (67) occurs in accordance with the principle of least motion in the transition state for rearrangement to diastereomerically related zwitterions of (66). Irradiation of (71) in 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 photo-rearrangement.



SECTION - C

(A short review on Bicyclic Cross-conjugated Cyclohexadienones)

Like photochemistry of monocyclic cyclohexadienones, bicyclic ones also have been studied intensely. Formation of lumiprodukt is fairly general. It has been observed earlier that a good amount of lumiprodukt 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 lumiprodukts. Initially, this difference of lumiprodukt formation has been attributed to a basic difference in reaction pathway and various explanations have been afforded³⁷⁻⁴⁰. 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 photoprodukts which are derived via the lumiprodukt. Hence, the difference between unsubstituted and 4-methyl substituted systems actually stems from the basic difference in the rate of conversion of dienone to lumiprodukt and the rate of destruction of lumiprodukt to other secondary photoprodukts and is not a fundamental difference in reaction pathway.

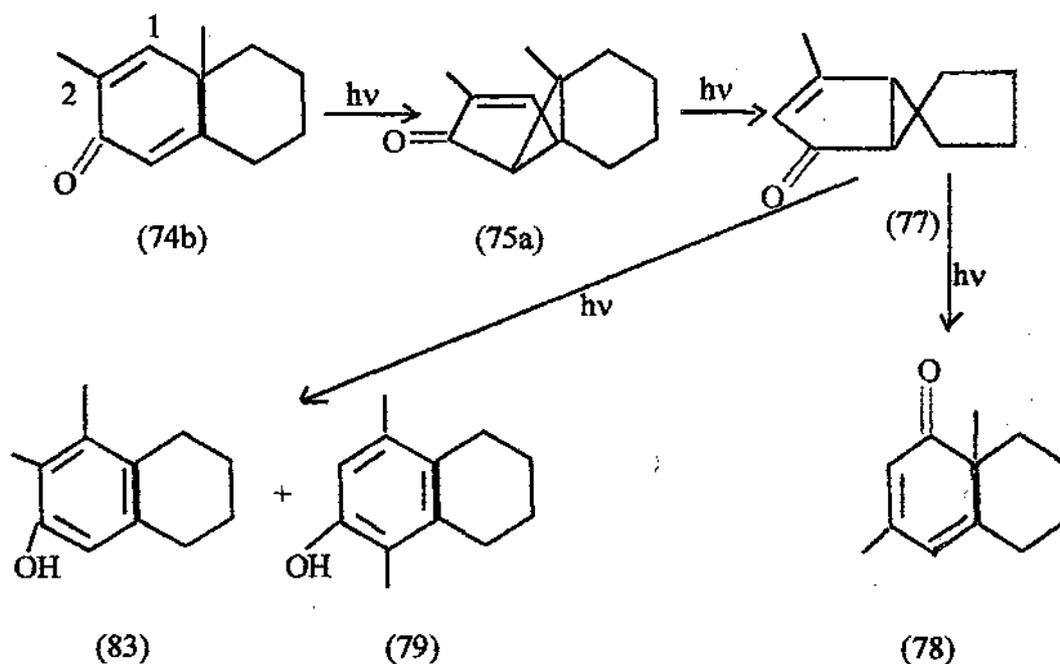


- (74a), $R_2 = R_4 = H$
 (74b), $R_2 = Me, R_4 = H$
 (74c), $R_2 = H, R_4 = CH_3$

(75)

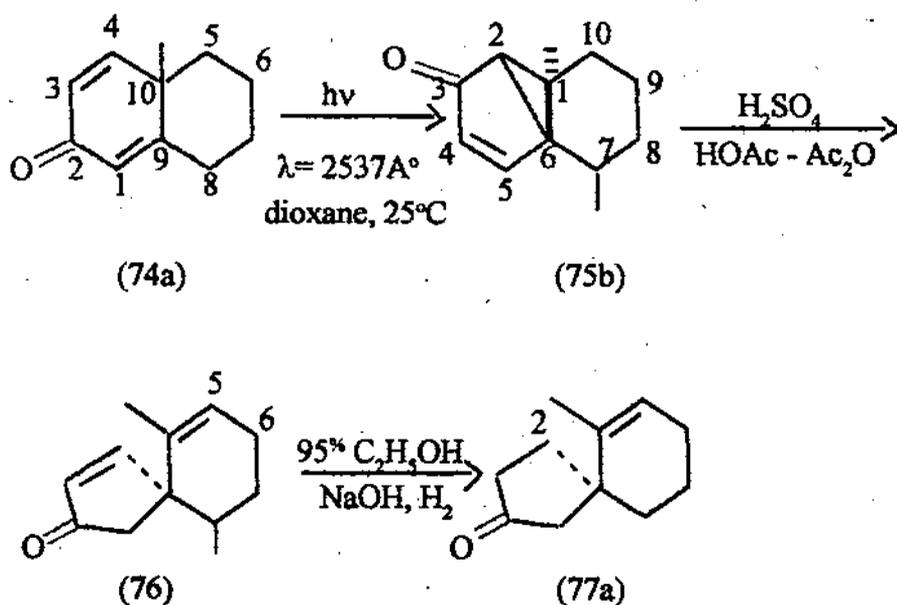
Although the photostationary concentration of the lumiproducs from many unsubstituted (74a) or 2-methyl substituted dienones (74b) are quite low in the presence of the broad spectrum of high-pressure mercury lamp, this difficulty often can be overcome by the use of monochromatic light source of 253.7 nm available from low-pressure mercury lamp^{40,41}. At this particular wavelength, the absorption by the lumiproducs is usually only about a sixth of the starting dienone and hence the rate of lumiproducs formation significantly exceeds the rate of further conversion of lumiproducs to secondary photoproducts. Consequently, interruption of irradiation at the appropriate time afforded lumiproducs in good yields. This technique also improved further the yield of lumiproducs 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, Kropp³³ 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) (lumiproducs) and (77) as intermediates.



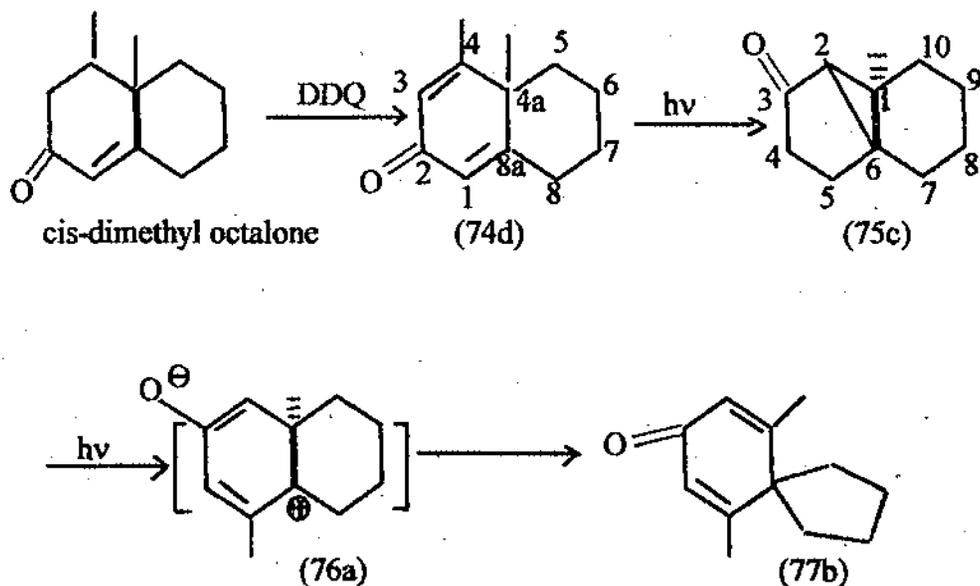
Two minor products formed in neutral as well as acidic media had been characterised as phenols (79) and (83). He also commented upon the significant role of the 2-methyl substituent in the photochemical properties of (74b).

Utilizing photochemical technique as a synthetic tool, Caine and co-workers³⁴ 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 $^1\text{H NMR}$ signals at δ 0.96 (s, $J = 6.7\text{ Hz}$, 3H, 7- CH_3), 1.18 (s, 3H, 1- CH_3), 5.82 (q, $J_{\text{AB}} = 5.5$, $J_{\text{BX}} = 1.1\text{ Hz}$; 1H, 4-H) and 7.19 (q, $J_{\text{AB}} = 5.5$, $J_{\text{AX}} = 0.8\text{ Hz}$, 1H, 5-H). Mass spectrum registered molecular ion peak at m/z 176 (M^+).

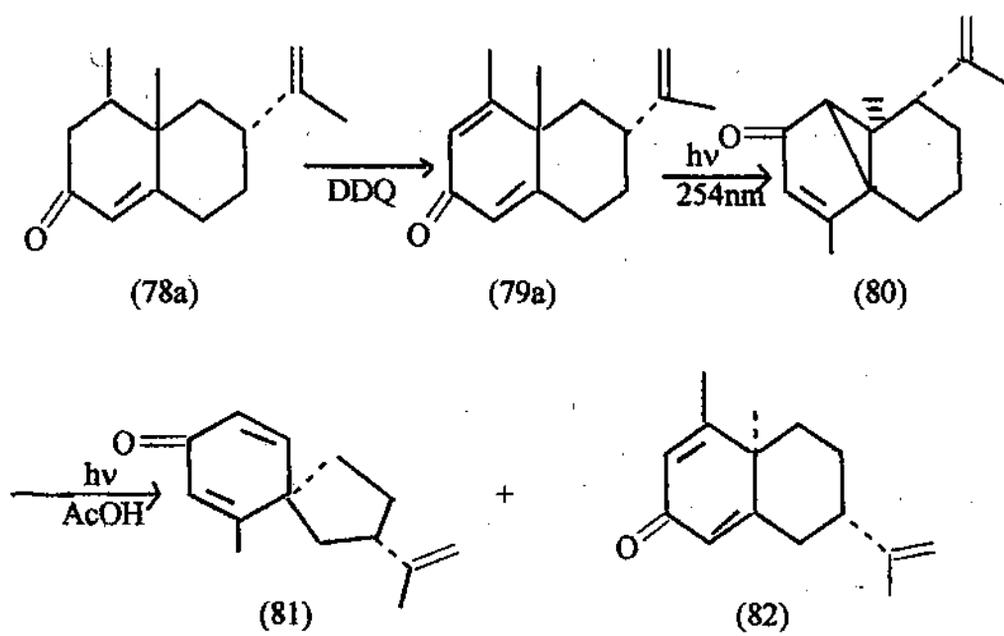


The key compound (75b) was first treated with $\text{HOAc} - \text{Ac}_2\text{O}$ in H_2SO_4 to afford the spirodienone (76) which ultimately gave rise to the spiroenone (77a) a precursor of spirovetivone, on catalytic reduction in alcoholic alkali.

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 octalone³⁶ and irradiated in anhydrous dioxane at 254 nm to produce the lumiprodukt, 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).



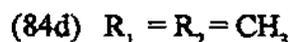
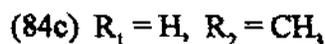
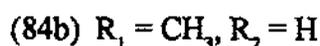
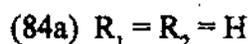
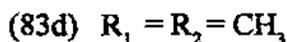
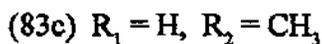
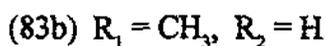
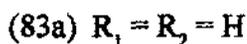
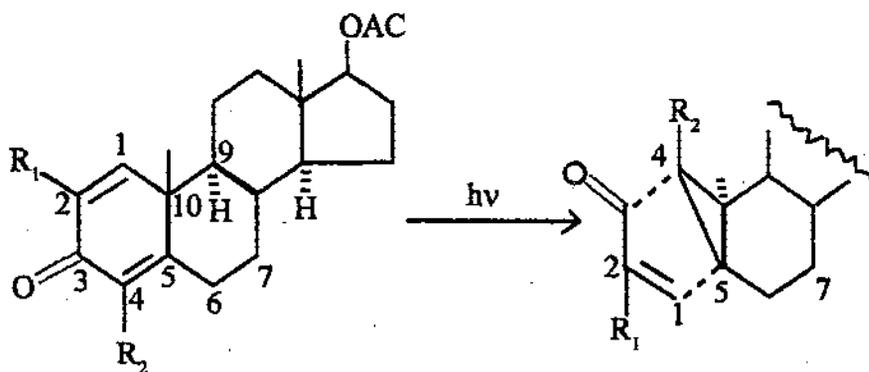
They³⁵ also studied the photochemical behaviour of various bicyclic dienone with sesquiterpene carbon skeleton. 3,4-dehydronootketone (79a) which was prepared by DDQ oxidation of nootkatone (78a), on irradiation at 254nm in anhydrous dioxane afforded the lumiprodukt, the tricyclodecanone (80) which on further irradiation in 45% aqueous acetic acid for 30 min using pyrex-filtered UV light yielded the spirotrienone (81), the bicyclic trienone (82) and dehydronootketone (79a) in 46, 37 and 12% yield, respectively.



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 coworkers⁴² first carried out photoreaction of O-acetyl-1-dehydrotestosterone (83a) with broad spectrum high-pressure mercury lamp in dioxane and recorded the formation of the corresponding lumiprodukt (84a) in low yield (11%). Later, in same solvent but using a low pressure lamp (2537A^o) 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 lumiprodukt (84a) were isolated. Spectral data, NMR and rotatory dispersion data were advanced in support of lumiketone structure (84a).

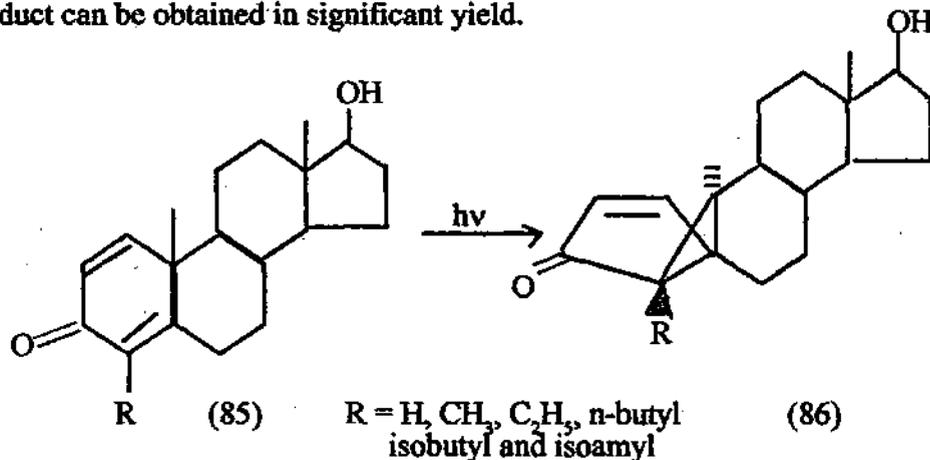


This photoreaction has been successfully utilised to achieve the selective inversion of configuration at C-10 and the accomplished the γ synthesis of 10 α -testosterone with unnatural angular configuration starting from (83a) in seven steps.⁴⁴

Arigoni, Jeger⁴⁵ and their group studied the effect of methyl substituent at C-4 testosterone derivative (83c) on lumiprodect formation. Upon irradiation with high pressure lamp in dioxane 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 lumiprodect (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 that⁴⁵ the photochemical isomerisation of cross-conjugated steroid dienones is profoundly influenced by the presence of a methyl substituent at C - 4.

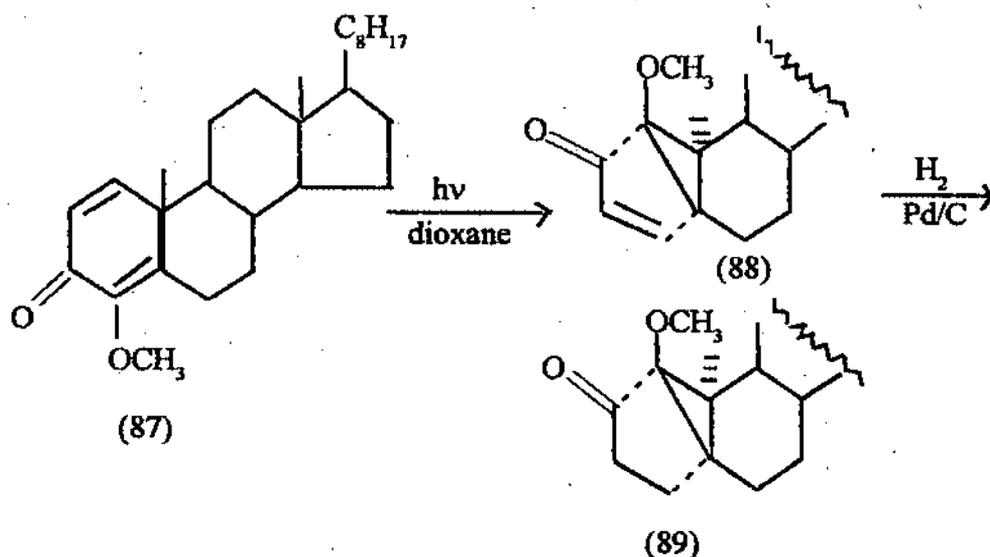
Schaffner, Jeger and coworkers⁴⁶ also noticed that on irradiation 2-methyl substituted testosterone derivative (83b) in dioxane with broad spectrum high pressure lamp afforded the corresponding lumiprodect (84b) as one of the products. Furthermore, the close relationship between the sequence of rearrangement 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 lumiprodect, 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 2537Å. At this particular wavelength, the absorption of the lumiprodect is about one sixth of the starting dienone. Consequently, the rate of lumiprodect formation considerably exceeds the rate of further conversion of the lumiprodect to secondary photoproducts. Thus, by arresting the photoreaction at an appropriate time the lumiprodect can be obtained in significant yield.

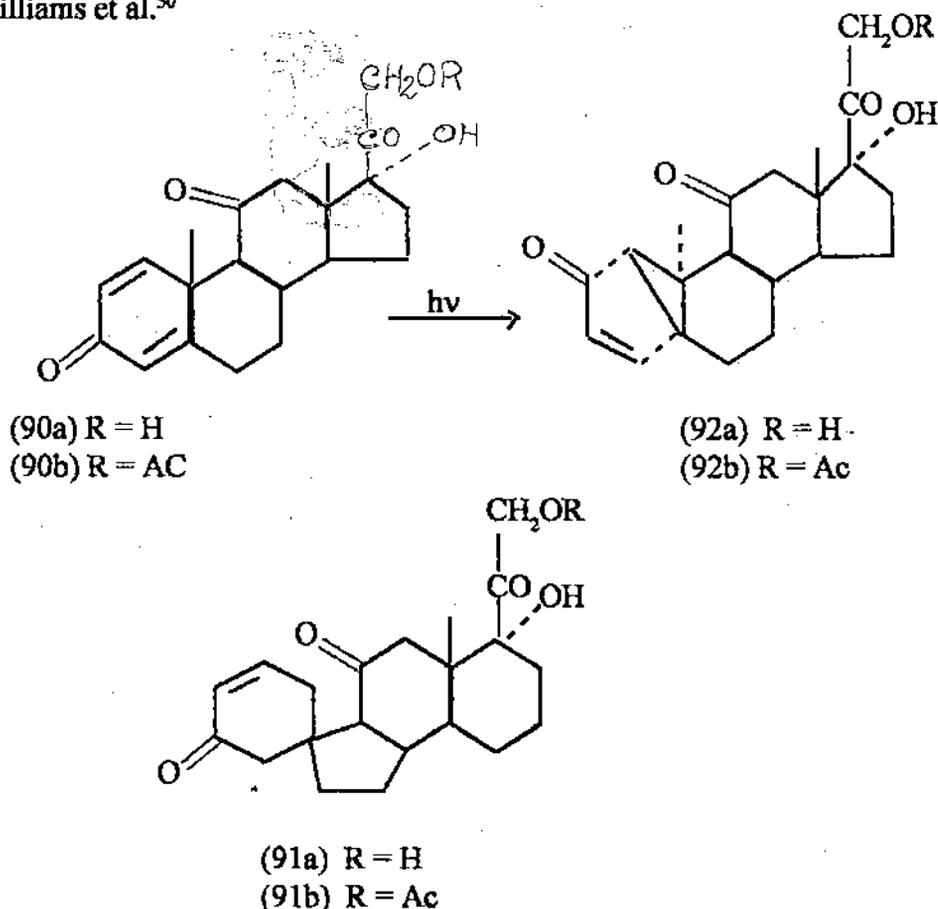


Schuster and Barringer⁴⁷ synthesised several 4-alkylated dehydrotestosterones (3) ($R = H, CH_3, C_2H_5, n\text{-butyl, isobutyl and isoamyl}$) and conducted their photolysis at 2537\AA in dioxane. The corresponding lumiketones (86) were obtained with variable quantum efficiency. The photoreaction is quenched 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 T_n, π^* and $T\pi, n^*$ 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 ($E_t = \sim 70 \text{ kcal mol}^{-1}$) to a triplet ($E_t = 60 \text{ kcal/mol}$) 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.

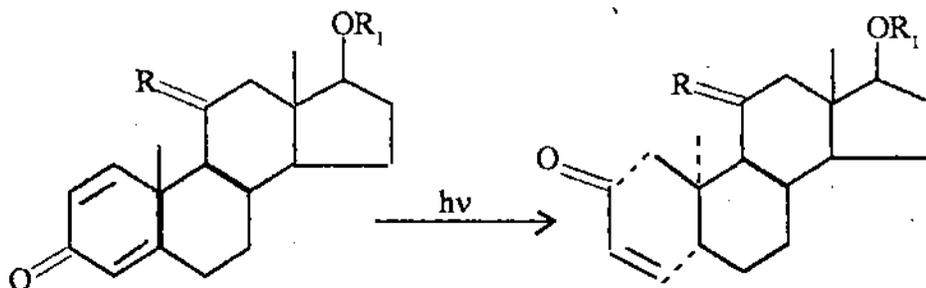
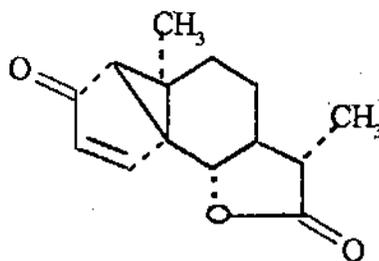
Pete and Wolfhugel⁴⁸ irradiated 4-methoxy-cholesta - 1,4-dien-3-one(87) in dioxane at 360 nm and got the lumiprotect (88). The structure of the photoproduct was deduced by spectroscopic methods coupled with hydrogenation to a saturated ketone (89). The uv spectrum of (88) in hexane exhibited absorption at 242 (4500) and 285(1360) nm and IR bands at 1740, 1660 and 1575 cm^{-1} . NMR spectrum showed resonances at 83.41 (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. 900 cm^{-1} and an NMR resonance at 83.41 (s, 3H) besides other resonances.



Barton and Taylor⁴⁹ first carried out the photolysis of prednisone (90a) and its acetate (90b) and assigned the structure (91a) and (91b) for the corresponding lumiproducs. Since their assigned structure differed from that expected (92a) and (92b), based on the new generally accepted mechanism for photoisomerisation of cross-conjugated dienones, reinvestigations of the photochemistry were undertaken by Williams et al.⁵⁰



The assignment of the structure and stereochemistry of (92a) and (92b) was by comparison of their spectral data with those of lumiproducs (94a) and (94b), derived by photoisomerisation of 17 β -acetoxy-1-dehydrotestosterones (93a)⁵¹ and (93b)⁵² in dioxane with 254 nm light. The structure of the lumiproduc (94a) was proven by chemical degradation⁵² and by CD measurement.⁵⁴ The UV of the lumiproduc (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 lumiproducs (92a) and (92b) show a very characteristic coupling pattern similar to that described for (94a)⁵². Namely, in the

(93a) R = 2H, R₁ = Ac(93b) R = O, R₁ = Ac(94a) R = 2H, R₁ = Ac(94b) R = O, R₁ = Ac

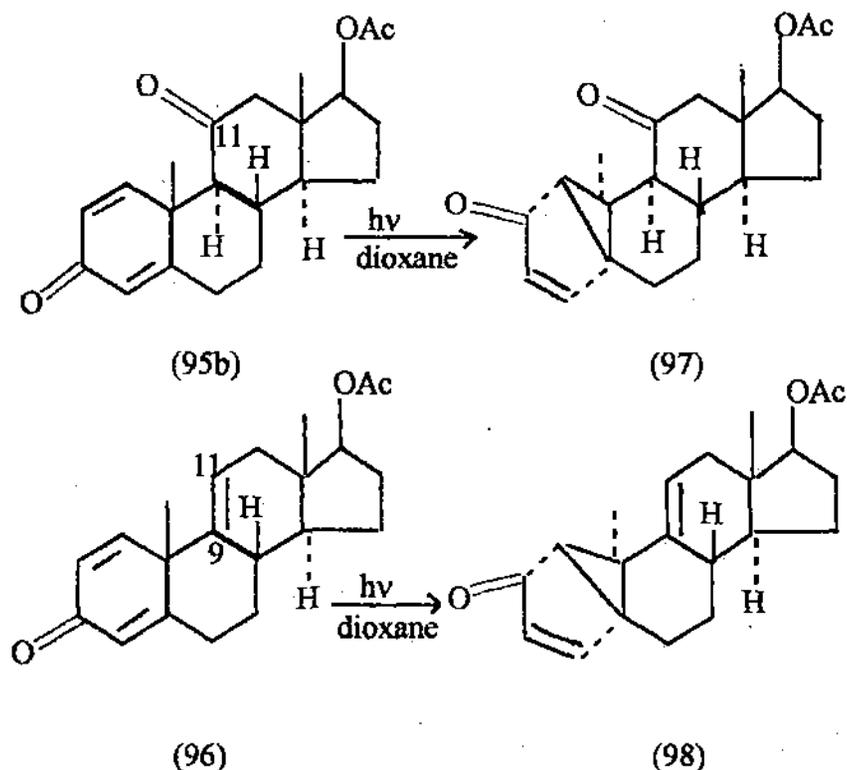
(95a)

NMR spectra of (92a), (92b) there are two doublets centred at 87.26 (7.20) and 5.87(5.86) with $J = 6.0\text{Hz}$, 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 ¹³C NMR spectra for (92a), the chemical shift assignments for the carbon atoms in rings A and B of (92a) are based on those of lumisanotone (95a) and bicyclo [3.1.0] hex-3-en-2-one and C and D rings of cortisone acetate⁵⁵. A significantly different ¹³C 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 10.3⁵⁴. Thus, CD supports very strongly structure (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).

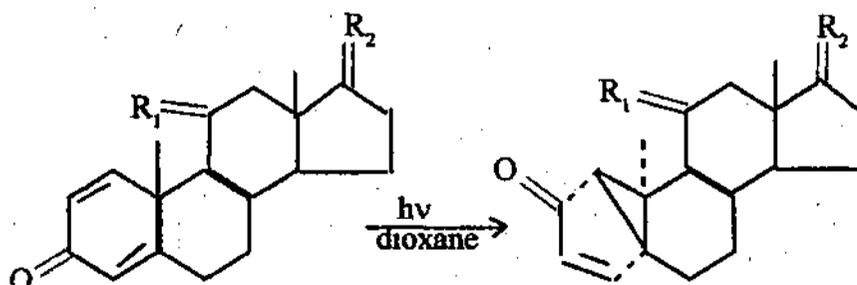
Finally, a comparison of lumiproductone acetate with that prepared by Barton and Taylor⁴⁹ showed them to be identical and hence, their structure for lumiprednisone acetate should be (92b).

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 coworkers⁵⁶ 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 cyclohexadienone under neutral condition. This also revealed that a keto group at 11 or a double bond at 9(11) position did not exert any noticeable influence on the course of this phototransformation.



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

(100) in neutral condition and got the expected lumiproducs (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) $R_1 = \alpha\text{-H}, \beta\text{-OH}, R_2 = \alpha\text{-OH}, \beta\text{-COCH}_2\text{OAc}$; (101) $R_1 = \alpha\text{-H}, \beta\text{-OH}$

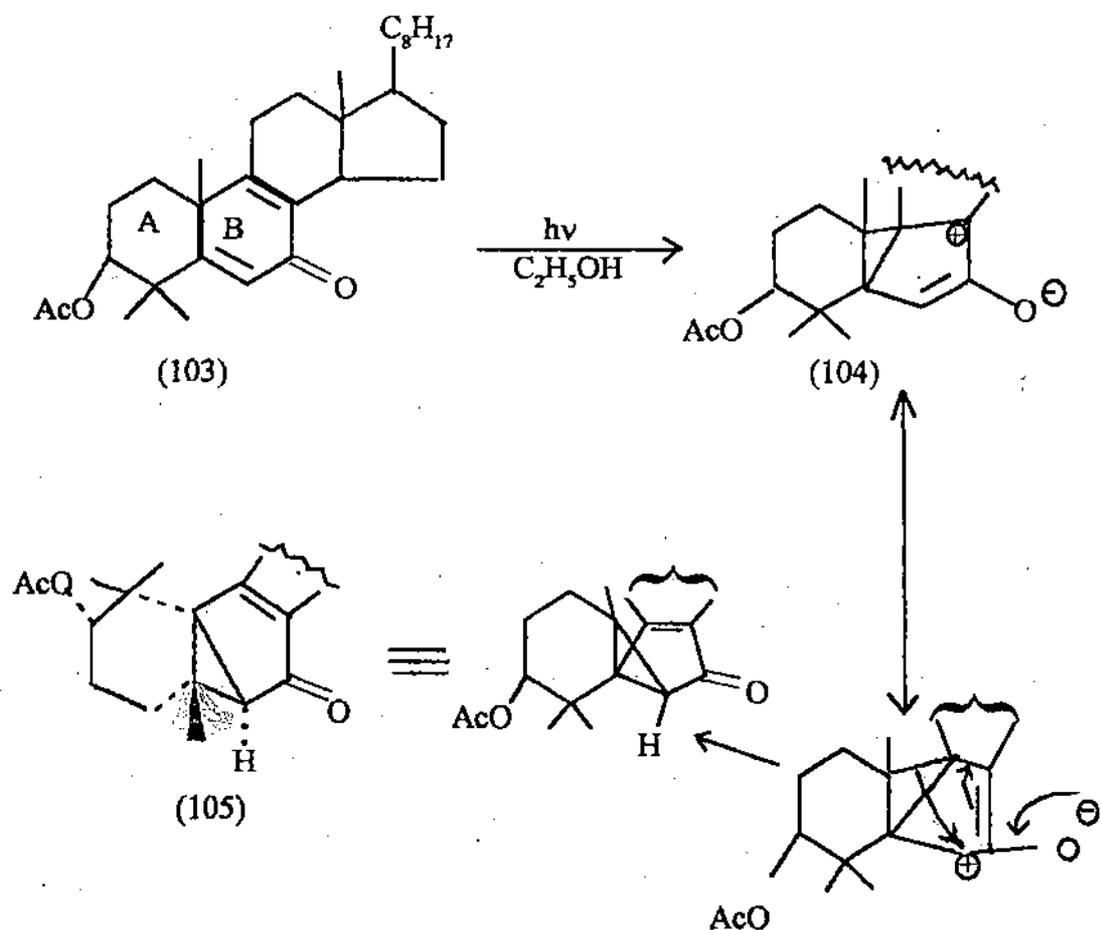
(100) $R_1 = \alpha\text{-OH}, \beta\text{-H}, R_2 = \alpha\text{-H}, \beta\text{-COCH}_3$; $R_2 = \alpha\text{-OH}, \beta\text{-COCH}_2\text{OAc}$

(102) $R_1 = \alpha\text{-OH}, \beta\text{-H}$

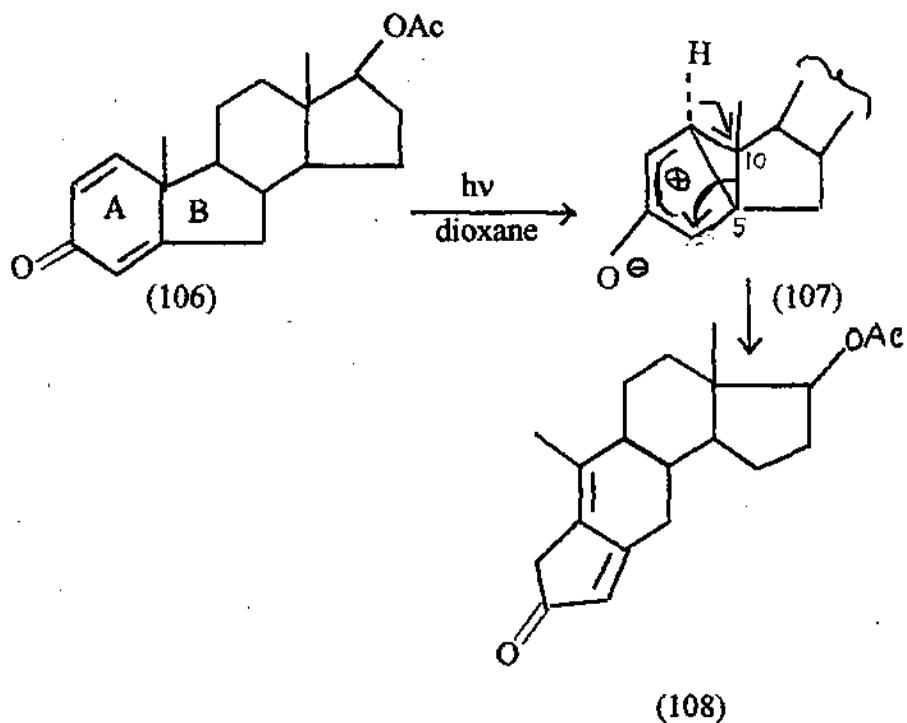
$R_2 = \alpha\text{-OH}, \beta\text{-COCH}_3$

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.

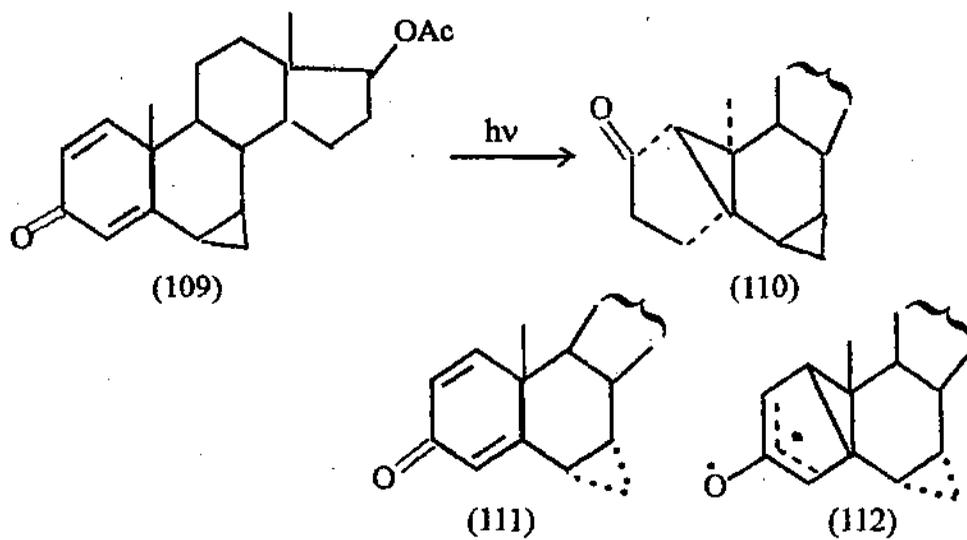
Cyclopropyl ketone (lumiprodukt) formation is fairly general for 2,5-cyclohexadienone (cross-conjugated) and is not limited to those having the hexadienone chromophore in ring A only. Irradiation of a B-ring containing this chromophore in steroid, 3 β -acetylanosta-5,8-dien-7-one (103), gave a product 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.



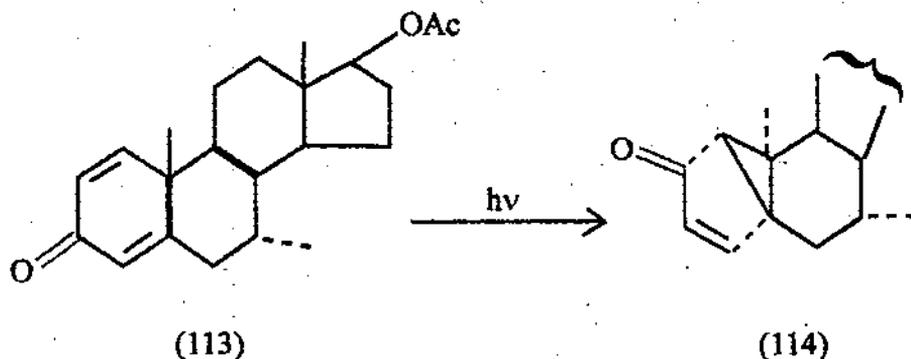
In dioxane solution, the B-nor dienone (106) is converted exclusively to the linear dienone (108). The preference for ¹⁵ fission of the 5, 10 bond in the proposed intermediate (107) has been attributed to the relief of enhanced ring strain which is introduced by the five-membered B-ring as compared to the structurally analogous intermediate having a six-membered B-ring.



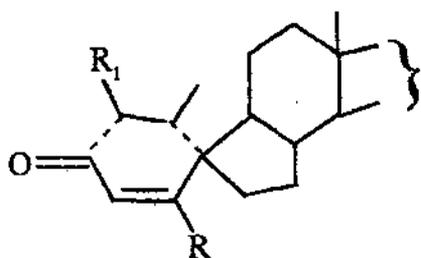
The 6β , 7β methano homolog of steroid (109), upon irradiation in dioxane isomerises readily to the bicyclohexenone (110) while the 6α , 7α - isomer (111) is extraordinarily stable toward irradiation⁶¹.



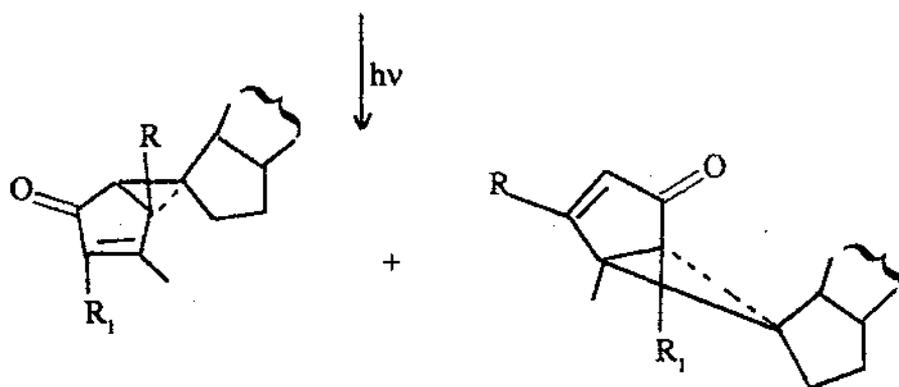
The apparent failure of (111) to react may be due to the high steric strain which would be introduced by the two adjacent three-membered rings on ring B upon 1,5-bridging. This could cause reversal of primary diradical formation (112) and corresponding zwitterion might not be formed. In contrast, a steric 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 7 α -methyl homolog of (83a), isomerizes to (114) smoothly⁶². In this case, the steric interaction in the primary product structure can be expected to be less severe than in (112).



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' bonding, (ii) the configurational fate of the migrating carbon in the subsequent [1, 4] shift and (iii) the direction in which this migration proceeds.



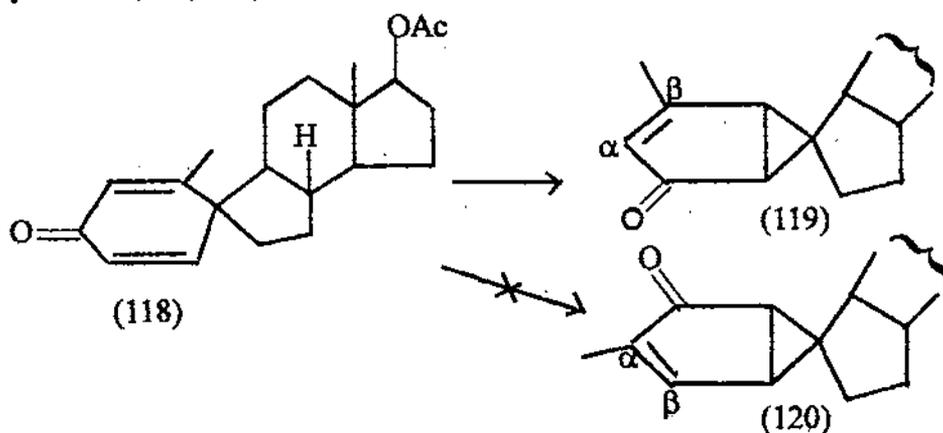
- (115a) $R = R_1 = H$
 (115b) $R = CH_3, R_1 = H$
 (115c) $R = H, R_1 = CH_3$



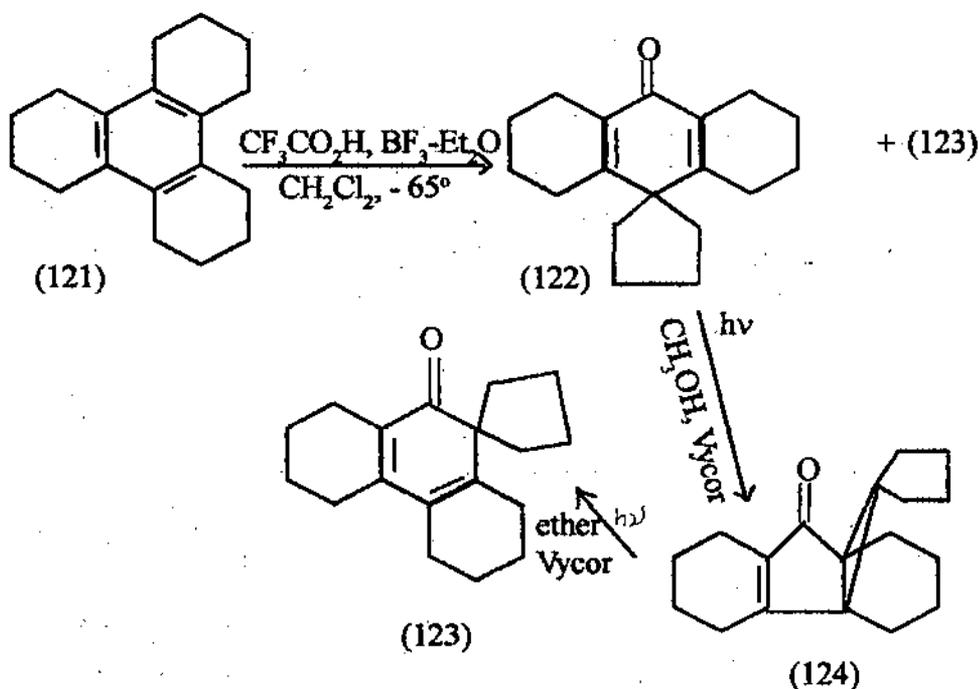
- (116a) $R = R_1 = H$
 (116b) $R = CH_3, R_1 = H$
 (116c) $R = H, R_1 = CH_3$

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

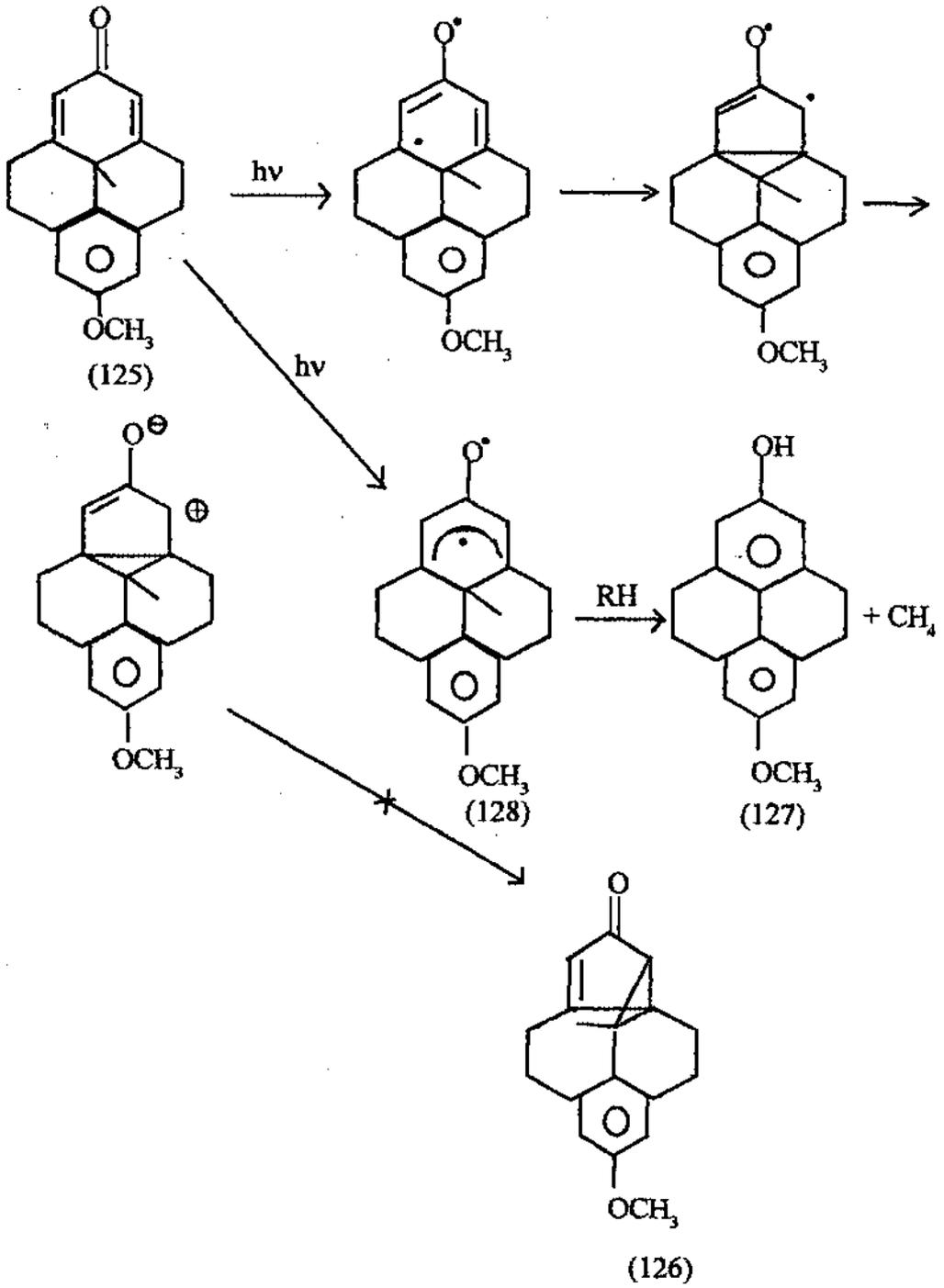
It is interesting to note that photolysis of (118) gives rise to the photoproduct (119) in preference to the alternative possibility (120). This selectivity is perhaps attributable to a preferred formation of the more stable β -methyl-substituted-enone system of (119)⁶⁵.



Hart and Lankin⁶⁶ observed that symmetrical dodecahydrotriphenylene (121) on oxidation with $\text{CF}_3\text{CO}_2\text{H}$ 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.



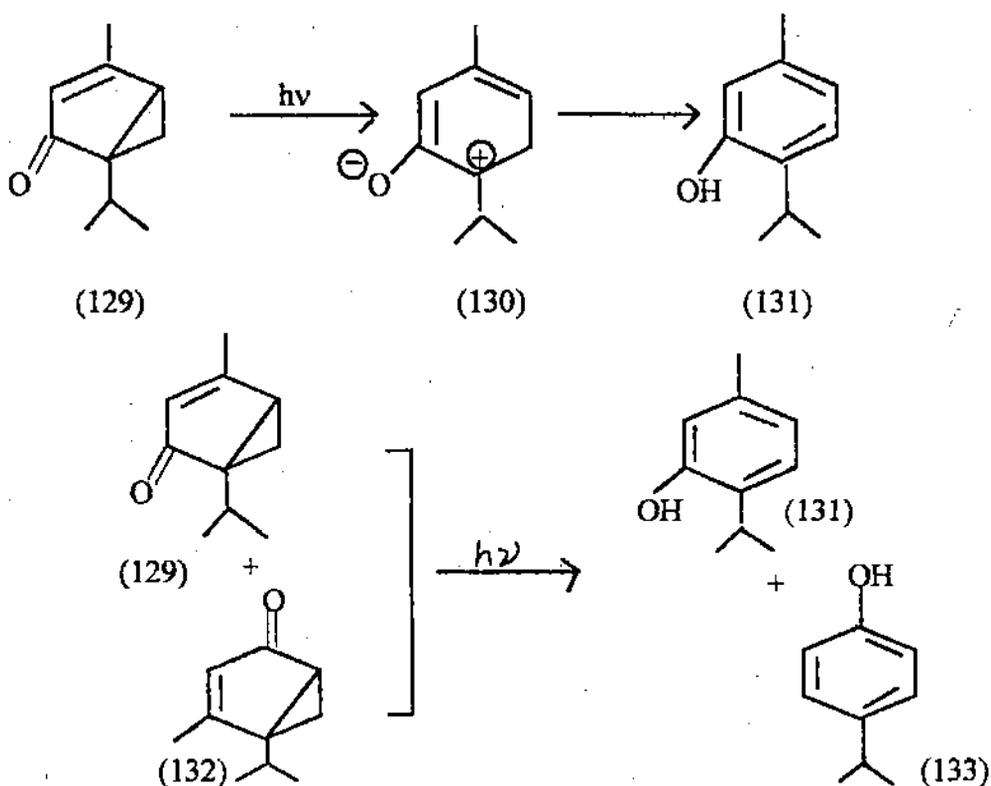
An interesting case of polycyclic cyclohexadienone (125) has been reported by Zimmerman⁶⁷. (125) can not rearrange photochemically to afford the type A rearrangement product (126) owing to the constrain imposed by the geometry of the molecule. Here, $\beta - \beta'$ bonding should not be inhibited, but 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 abstraction of hydrogen from hydrogen donating solvent at the excited dienone triplet state (128).



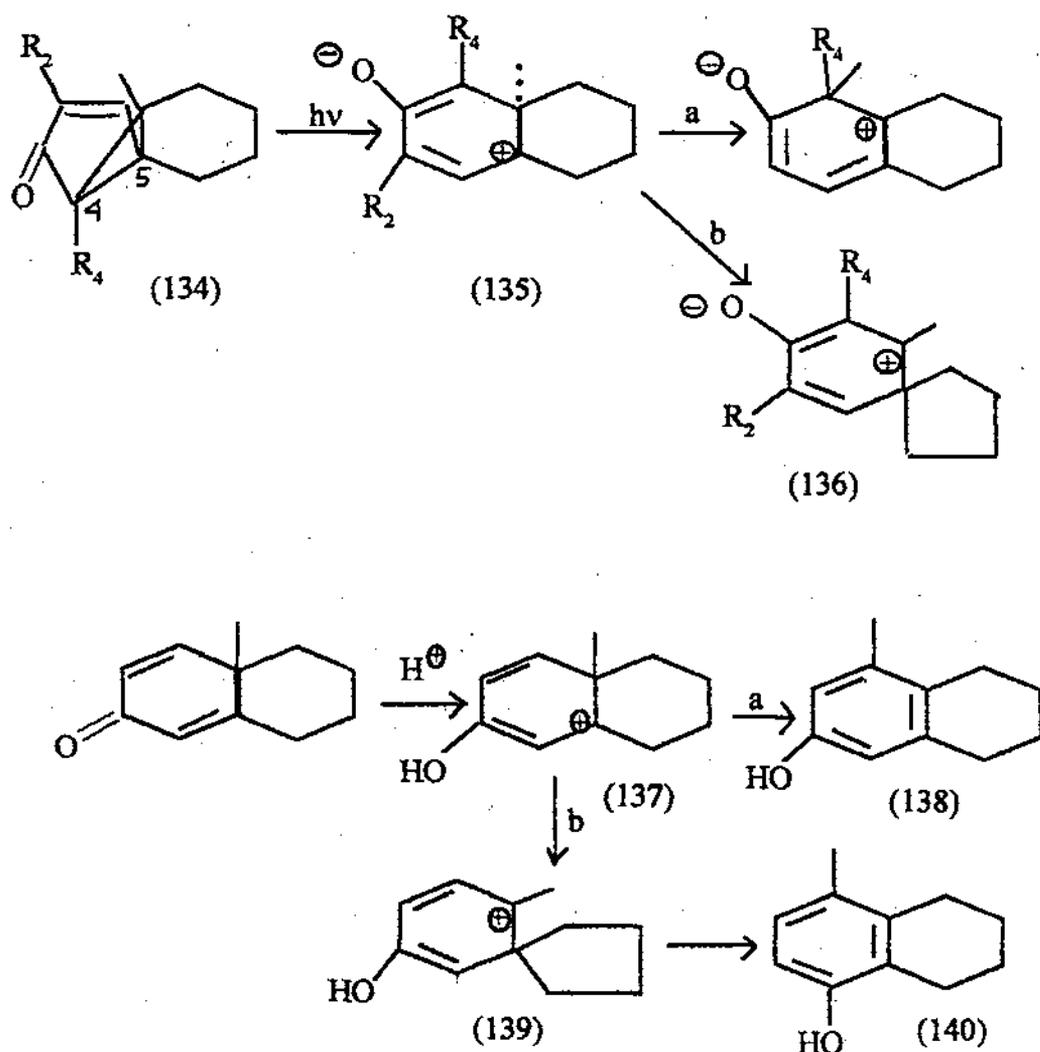
SECTION - E

(Formation of Phenolic Photoproducts)

Since the primary photoproducts i.e. lumiproduces (also called cyclopropyl ketones) possess bicyclo [3.1.0] hex-3-en-2-one skeleton, can themselves be considered as dienone in which one of the double bonds has been replaced by a cyclopropane ring. This renders the lumiproduces photolabile and this is one of the reasons for complexity of the 2,5-cyclohexadienone phototransformations. These lumiproduces on further irradiation or 2,5-cyclohexadienones 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

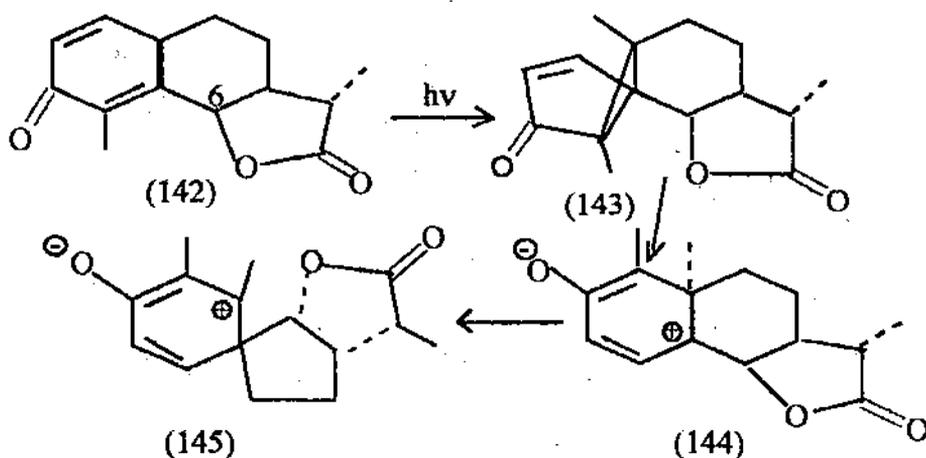
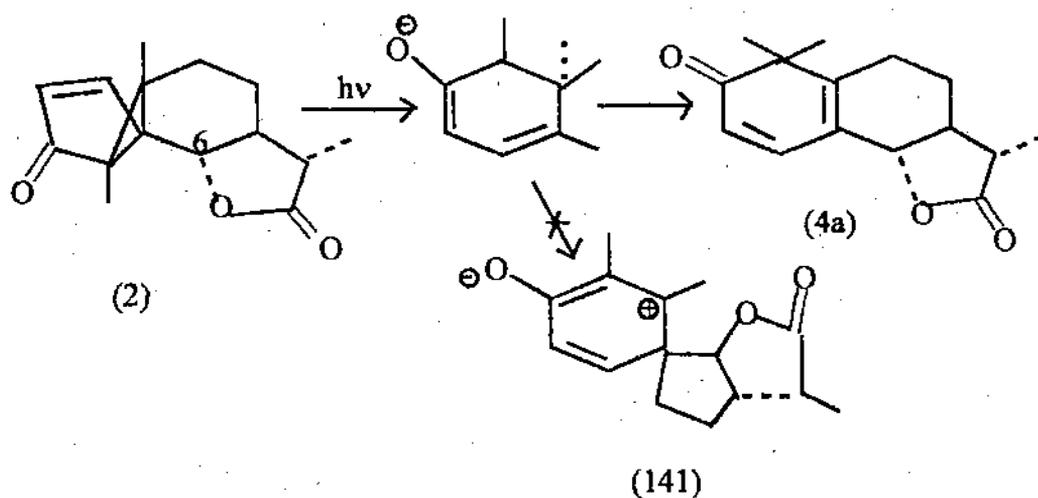


Intermediates of the type similar to (135) formed by cleavage of the 4-5 bond of cyclopropyl ketone of type (134) [cf. 137] are also encountered in the well-known acid-catalysed dienone-phenol rearrangements. In dienone-phenol rearrangement there is a delicate balance between two pathways of rearrangement : (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.

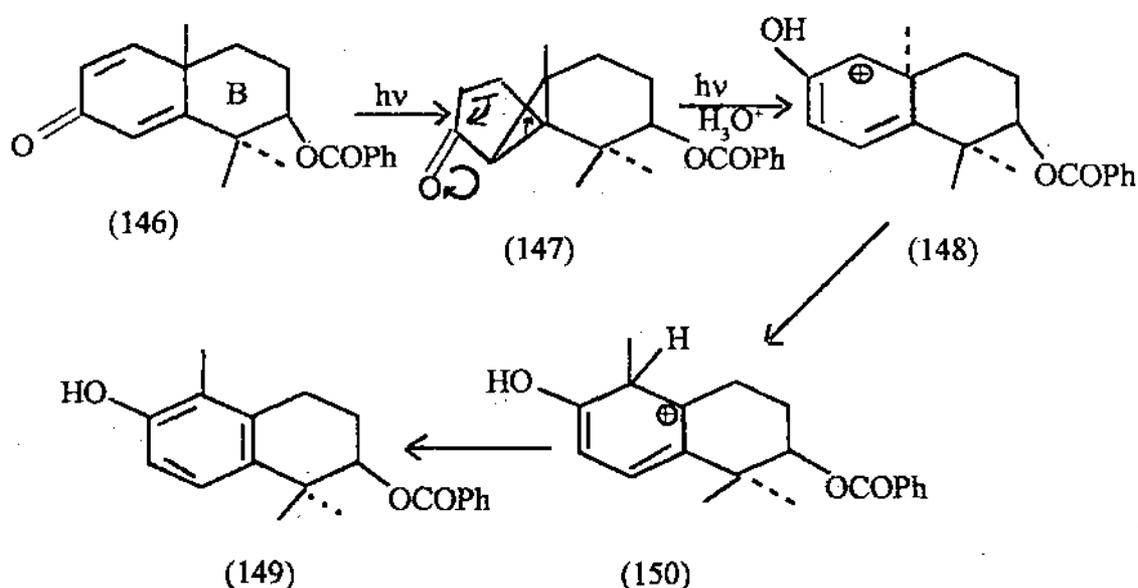


Rearrangements not involving spiro intermediates :

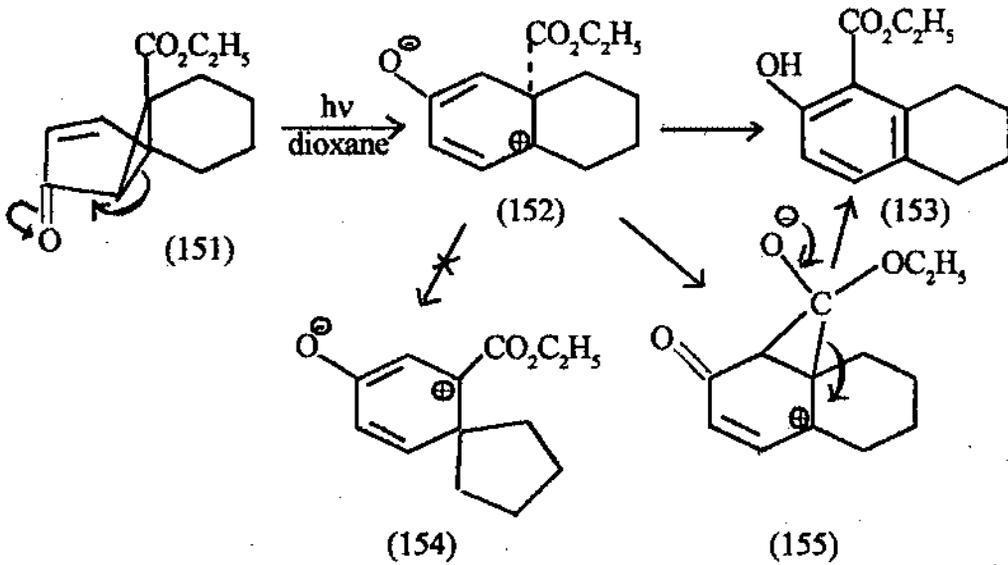
Lumisantonin (2) does not undergo photorearrangement through spiro intermediate but involves 1,2 methyl shift to give linearly conjugated cyclohexadienone(4a). Failure of the rearrangement via spiro intermediate has been attributed to highly strained trans fusion of two five membered rings^{71,72} in 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 obtained⁷³.



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 substituents⁷².



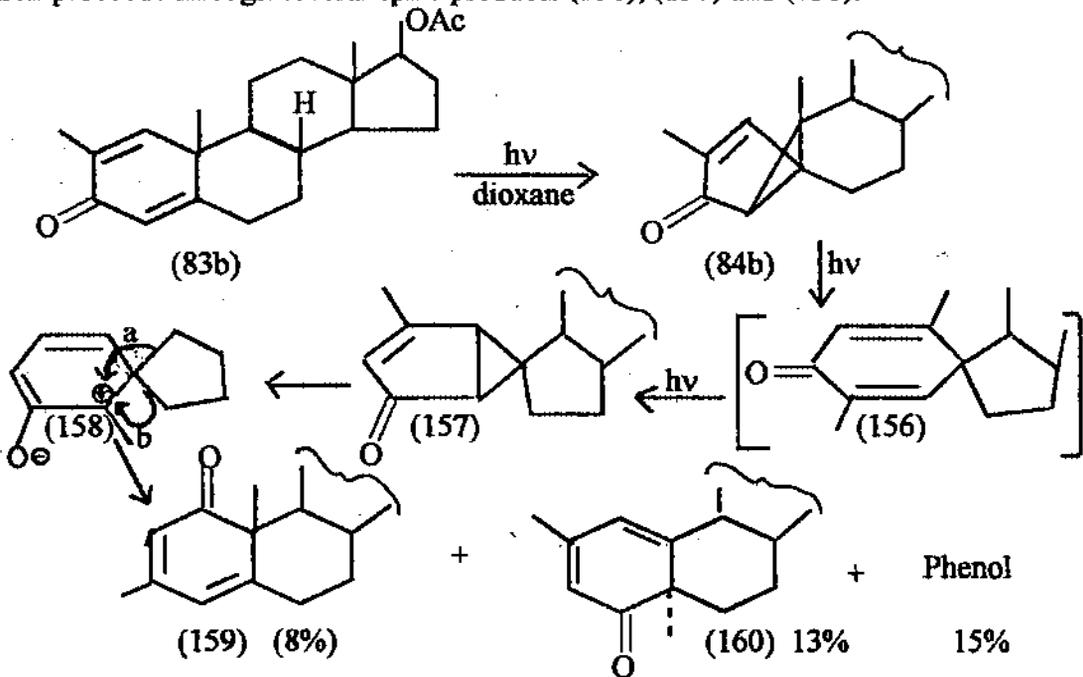
An interesting case has been registered, in which electronic, rather than steric, factors are attributed for the failure of rearrangement via a spiro intermediate. Irradiation of the carbethoxy lumiprodukt (151) gave the phenol (153) in high yield. The presence of the electron-withdrawing carboethoxy 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).



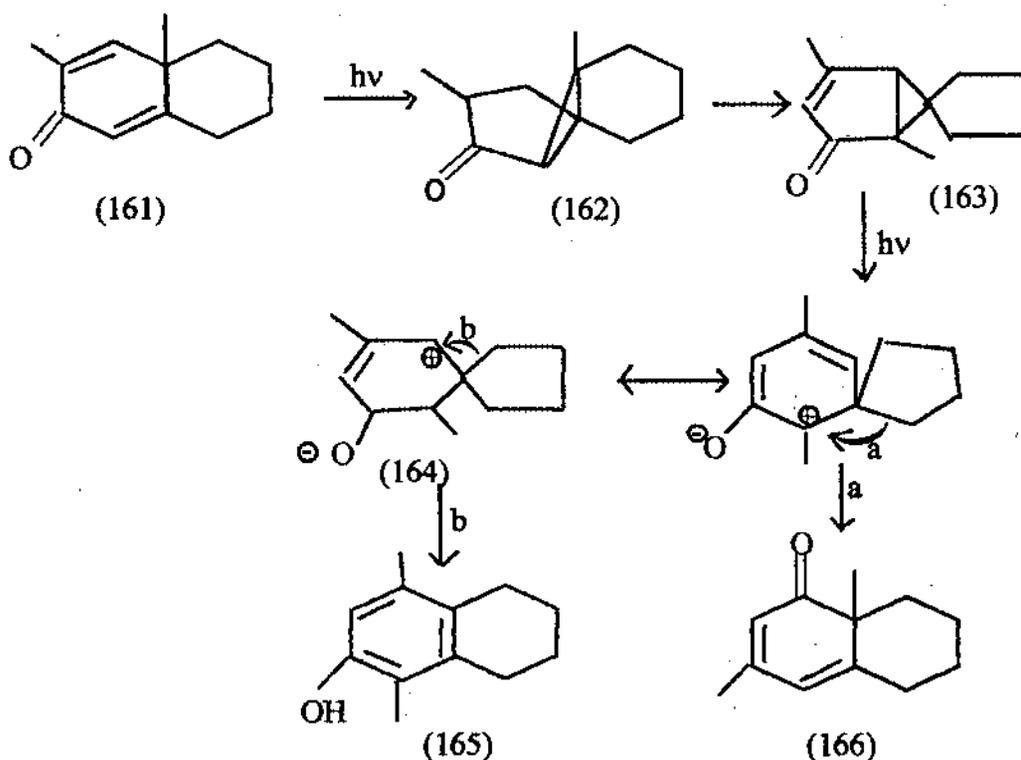
Rearrangements via spiro intermediates : solvent effects :

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 coworkers⁷⁴ observed that upon irradiation, the lumiporoduct ((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).

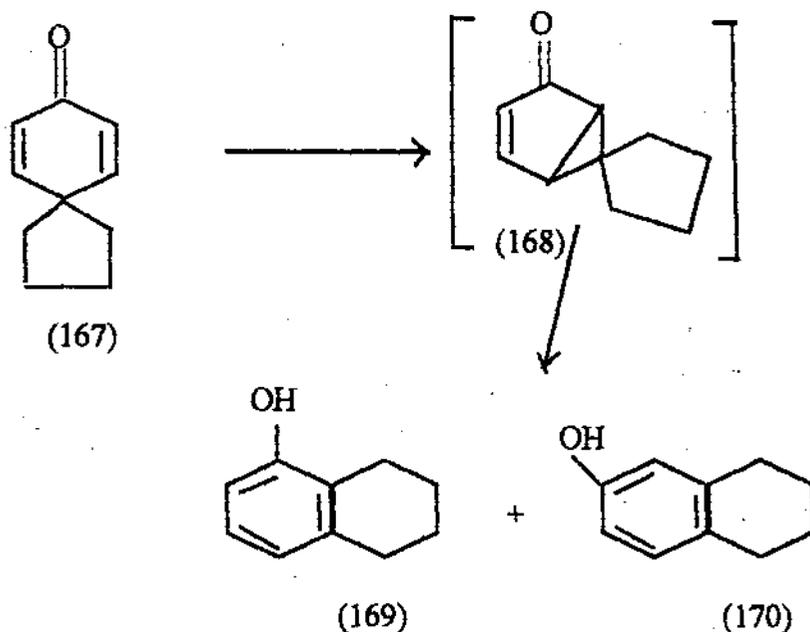


Kropp^{75, 76} photolysed the lumicompound (162) obtained from the bicyclic 2,5-hexadienone (161) which is structurally related to the steroid derivative (83b). Through several spiro intermediates such as (163) the linearly conjugated cyclohexadienone (166) and the phenolic product (165) were obtained. 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.



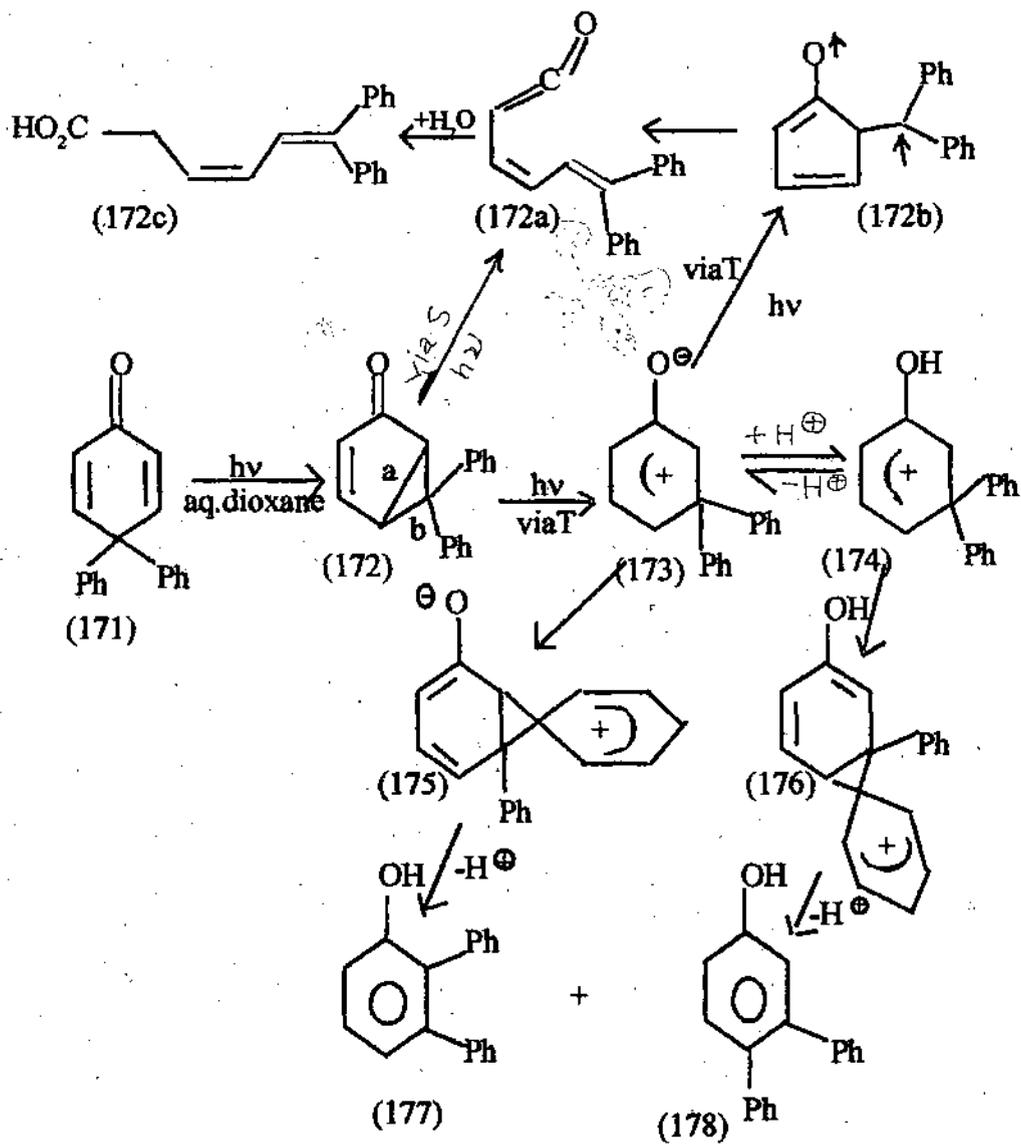
		(165)	(166)
From (161)	CH ₃ OH	trace	50%
(163)	CH ₃ OH	trace	57%
(163)	45% HOAc	33%	47%
(162)	CH ₃ OH	trace	62%
(162)	45% HOAc	28%	33%

Photolysis of the spiro dienone (167) afforded a mixture of the α - and β -tetrahydronaphthols (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

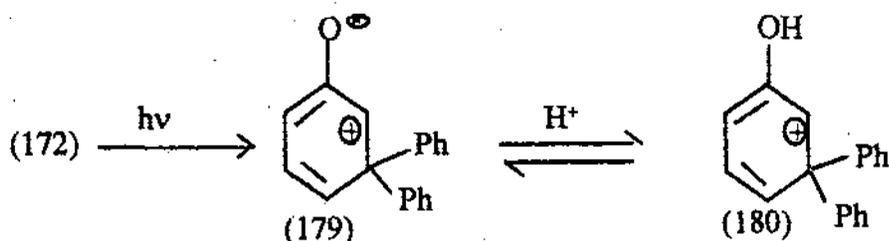
Formation of phenols from the irradiation of the cyclopropyl ketone (172) which is obtained from the photolysis of the cyclohexadienone (171) as the primary product, also exhibited noticeable solvent effects³⁰. Aqueous dioxane yielded 2,3-diphenyl-phenol (177) as principal product with trace of its isomer 3,4-diphenylphenol (178), while in 50% acetic acid gave the two diphenyl isomers in approximately 1:1 ratio.



Aq. dioxane 22.32%
 50% AcOH 1

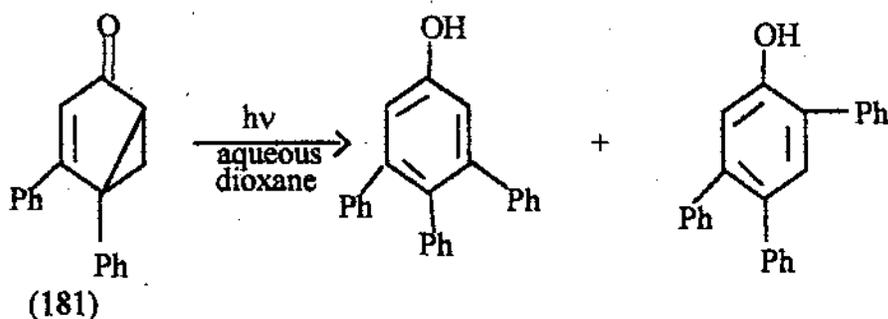
trace
 1

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 lumiproduet (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).

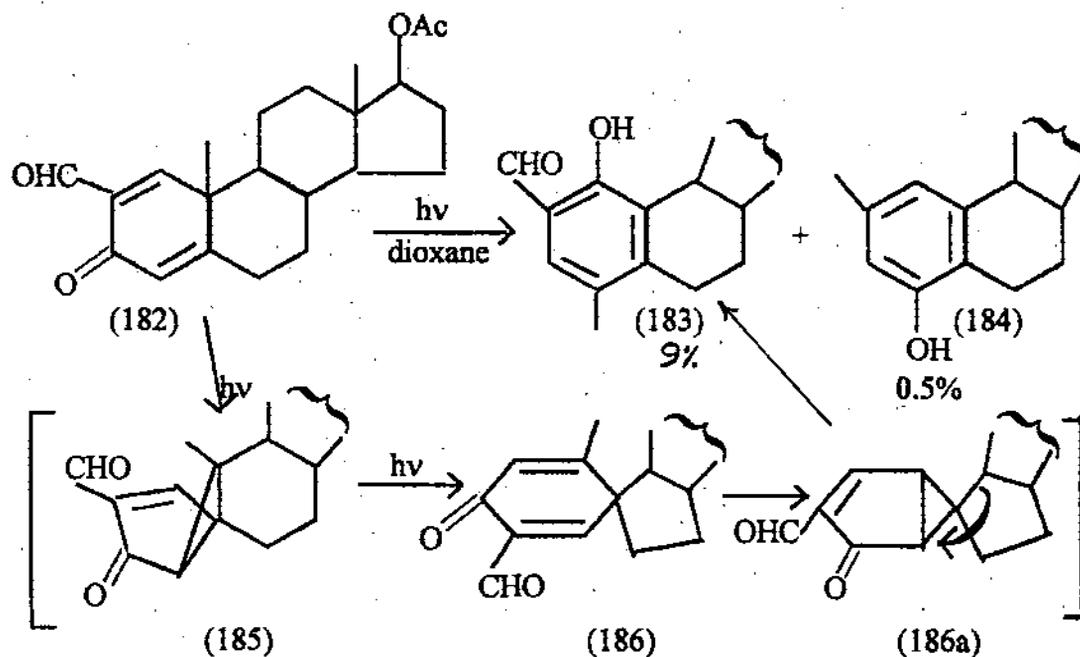
On the other hand, a concerted breakage of both bonds (internal and external cyclopropane bonds) and direct collapse of singlet excited (172) to the diene ketene (172a) which when trapped with nucleophile gives unsaturated acid /ester (172c). Alternatively, the breaking of the external cyclopropane bond 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 irradiation⁸² and several cases have been reported.^{83,84}



The influence of solvent acidity on phenol formation as mentioned earlier²⁹ is as would be predicted for equilibrating zwitterion⁽¹⁷³⁾ and cationic species (174), consideration based on maximisation of resonance stabilization⁷⁹ and on minimization of charge separation⁸⁰ 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 calculations⁷⁹.

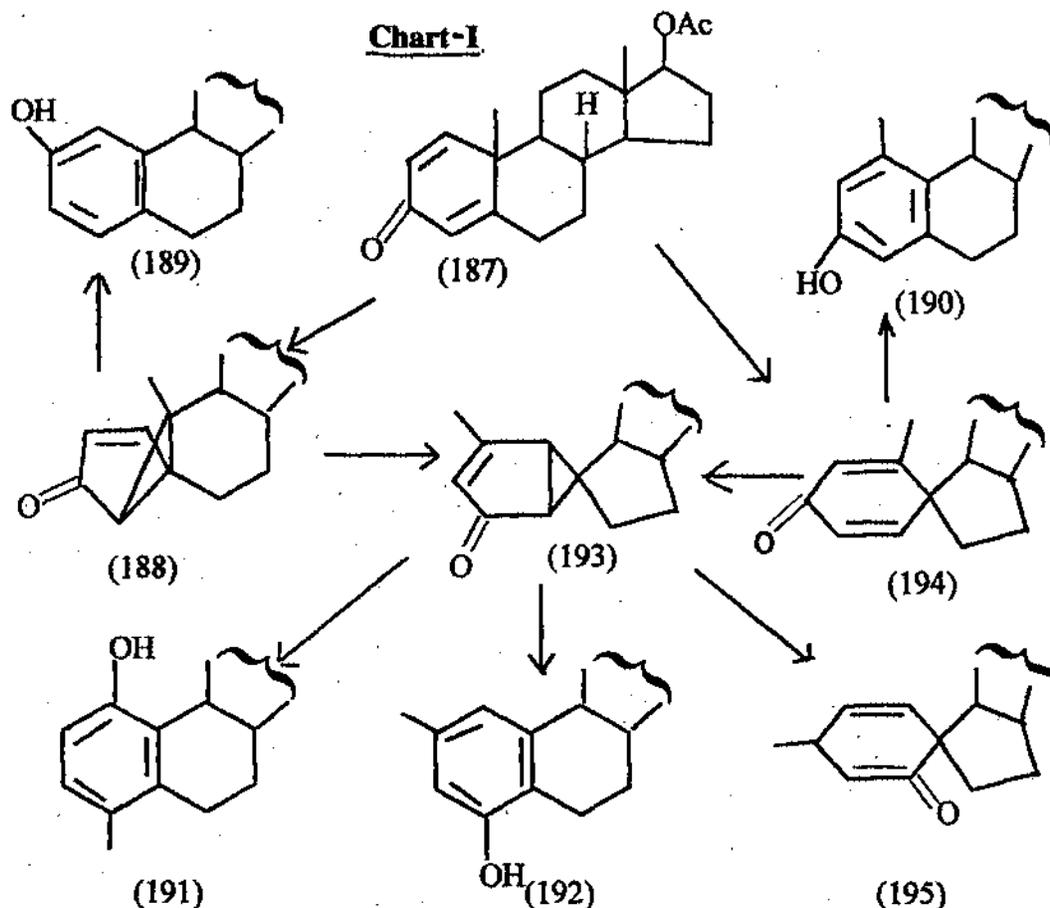
Several other cases of lumiproduets \rightarrow phenols conversion were reported.⁸¹ Small observed that photolysis of the cyclopropyl ketone (181) in aqueous dioxane also afforded two phenols as shown above :

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 characterised⁸⁵. 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.

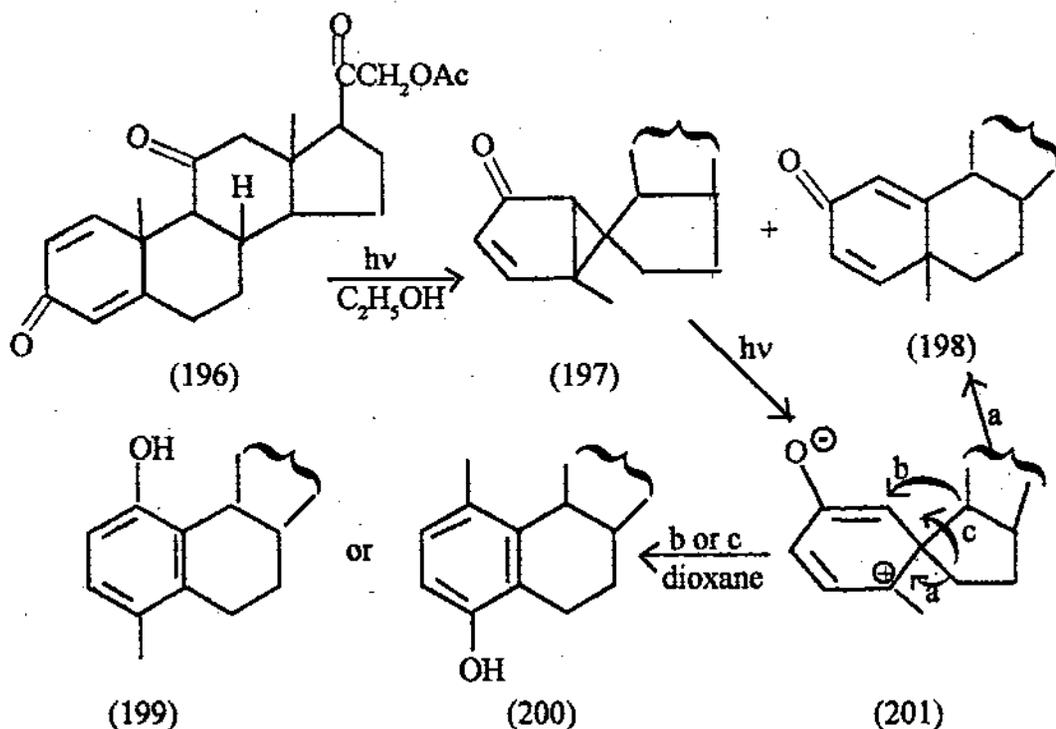


Jeger et al.^{86,71,87} made an extensive analysis of the photo reaction of steroids having substituents in ring A and also without substituents in ring A. Jeger et al.⁸⁶ observed that photochemical behaviour of dienones having no A-ring substituents such as the androste -1, 4-dien-3-one ^{(187) type} _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 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 yield⁸⁷.



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.



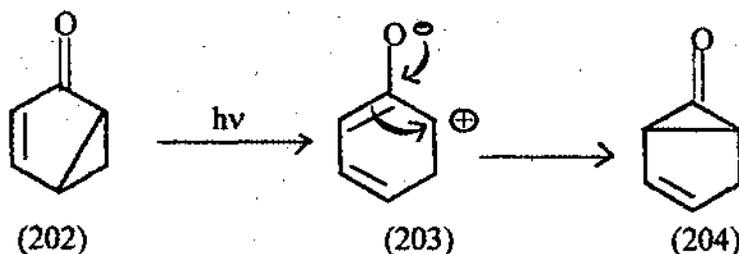
Photoconversion of lumiprodukt to phenol at low temperature :

Photoreaction of lumiprodukt carried out at low temperature⁹¹ 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 lumiprodukt may be operative at the ambient temperature and above. At low temperature around $-190^\circ C$ products may result via the formation of very transient ketene carbene and cyclopropanone intermediates as originally proposed for the formation of photosantonin acid from lumisantonium.

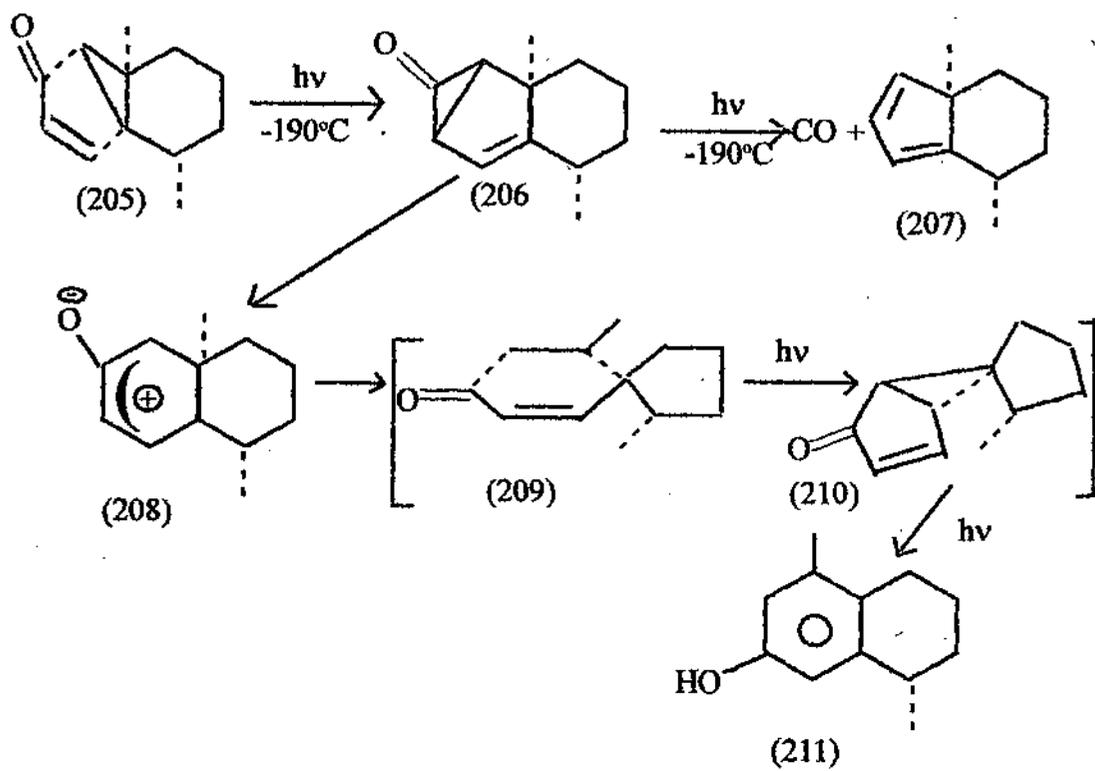
Schemes ^(I and II) depicted below describes the genesis of carbene ketene and cyclopropanone species starting from a model bicyclo [3.1.0] hexenone ⁽²¹²⁾. Irradiation of (212) at temperature of $-190^\circ C$ leads to the formation of the unrearranged ketene (215) as shown in the scheme-I. The process occurs by breaking the external rather than the internal cyclopropyl bond [(213) \rightarrow (214)]. The reaction may also be described as concerted electrocyclic reaction of [4+2] type⁹².

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.

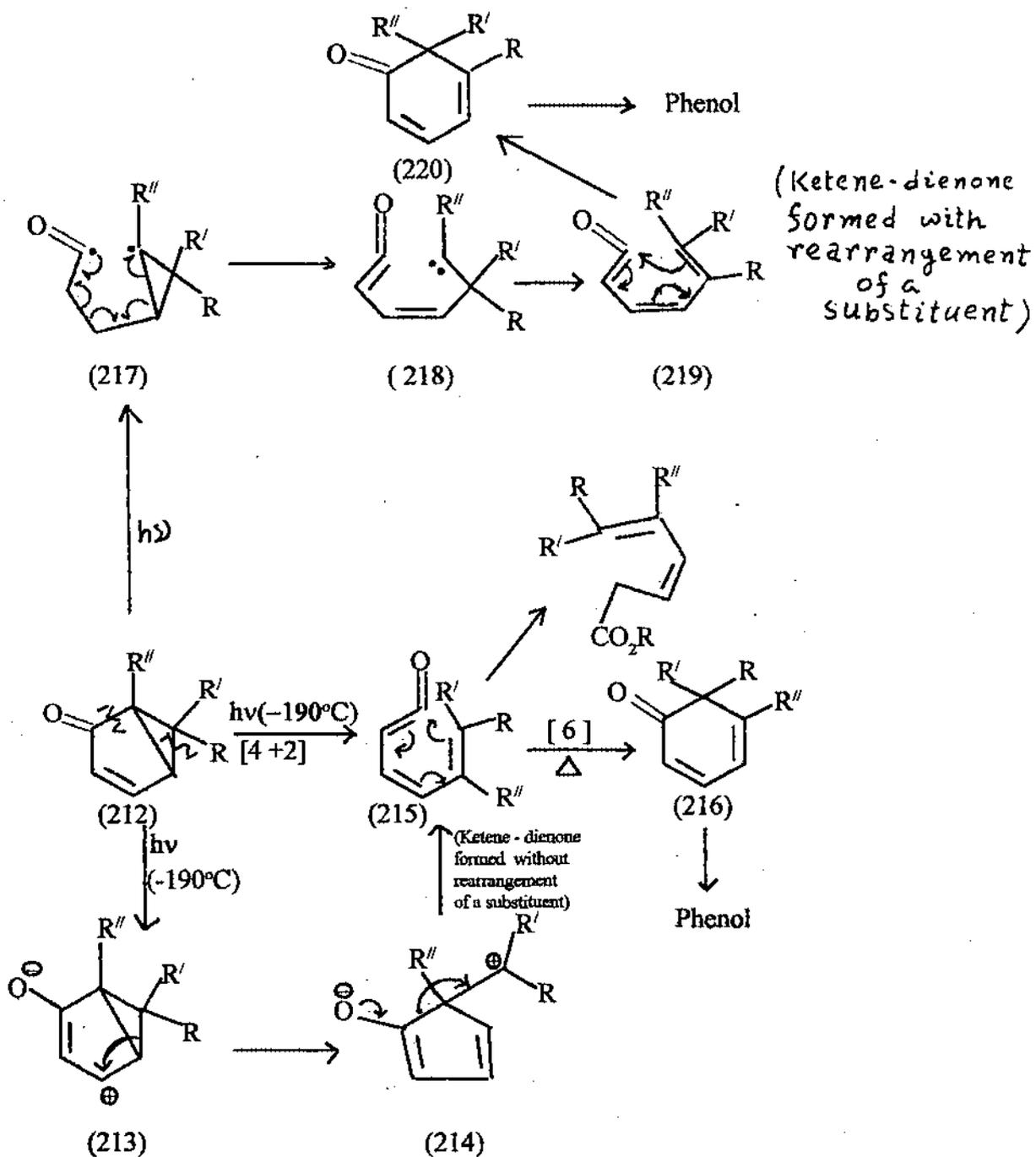
It was postulated that the excited state (221) is produced (Scheme-II) that can lead to a ring opened zwitterion (222) which is the ring opened form of the cyclopropanone (223). The observation that cyclopropanone (204), the closed form of the zwitterion (203), is formed upon photolysis of (202) and 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] sigmatropic⁹² 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 nucleophilic trapping to the product (226) by methanol.

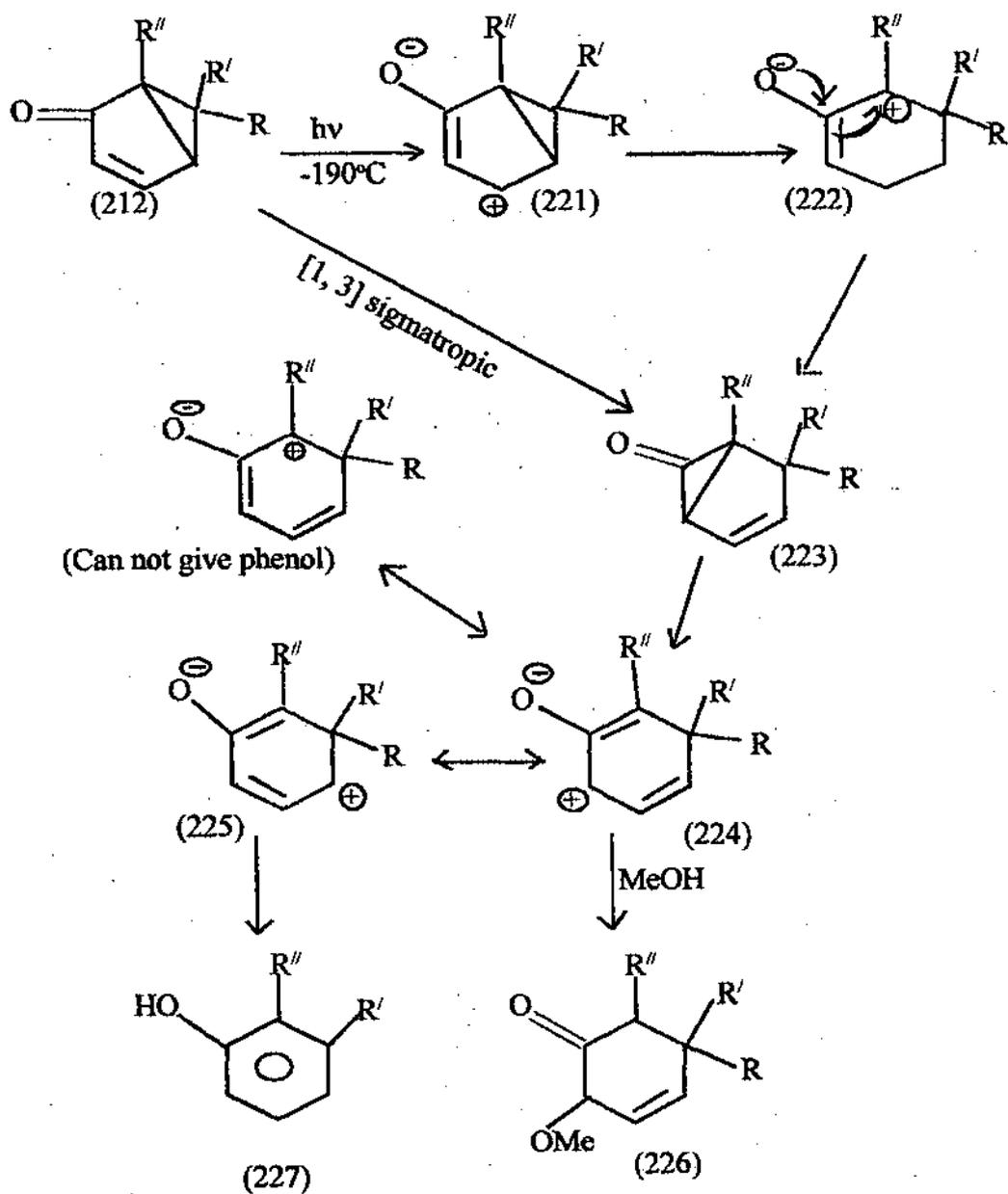


Chapman and coworkers⁹⁴ noticed that the lumiprodukt (205) on irradiation at -190°C afforded the cyclopropanone (206) in the first photochemical step⁹⁹. Further irradiation at low temperature resulted in decarbonylation to diene (207). On the other hand, warming of (206) in the presence of furan gave 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).



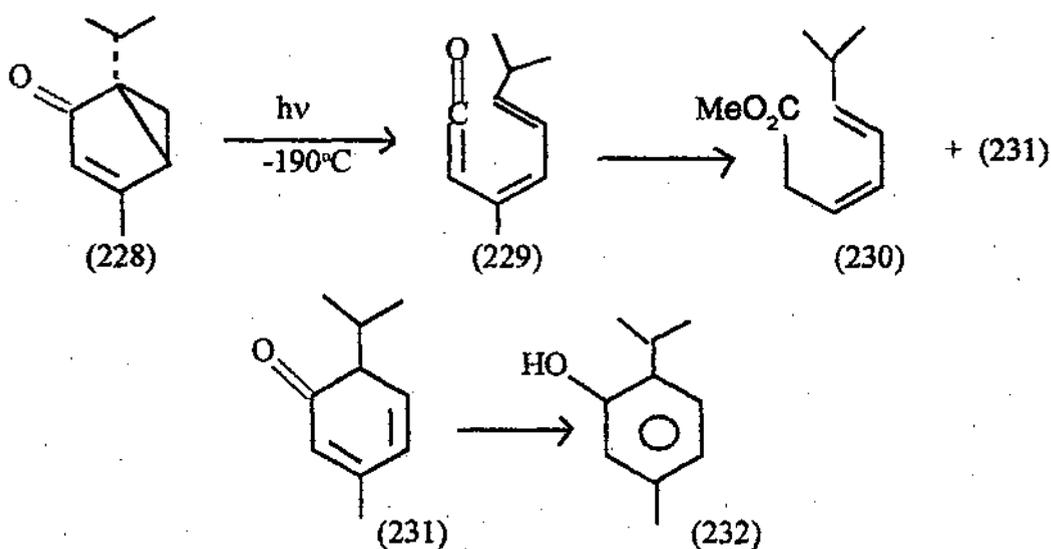
Scheme - I



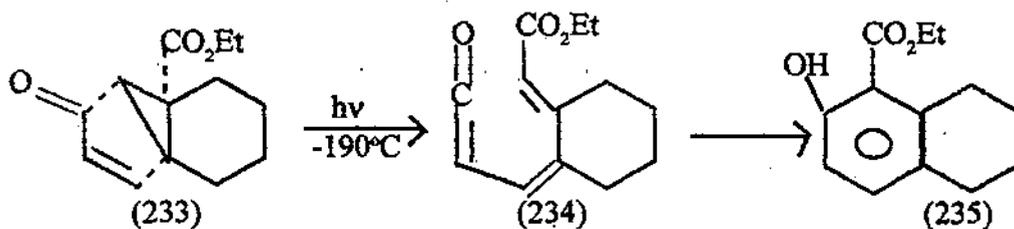
Scheme - II

Now, we wish to discuss typical three photorearrangements of lumiprodukt 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.

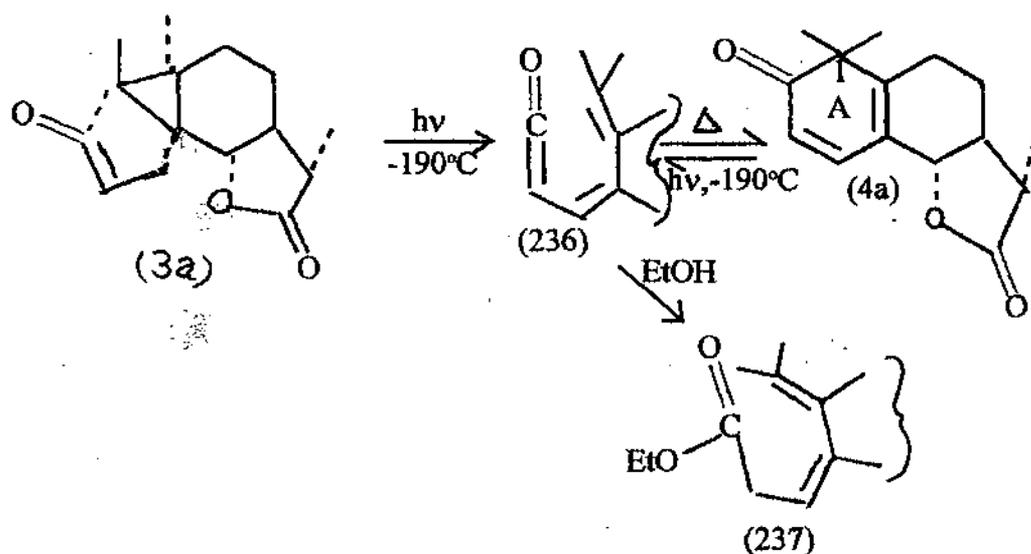
(a) Umbellulone (228) undergoes smooth arom^{TH} atisation to thymol (232)⁹⁵⁻⁹⁸ in methanol at room temperature, proceeds at -190°C via (229), which on warming cyclised to dienone (231) as is characteristic for such dien ketenes. It has been demonstrated that nucleophilic trapping by added methanol to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



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



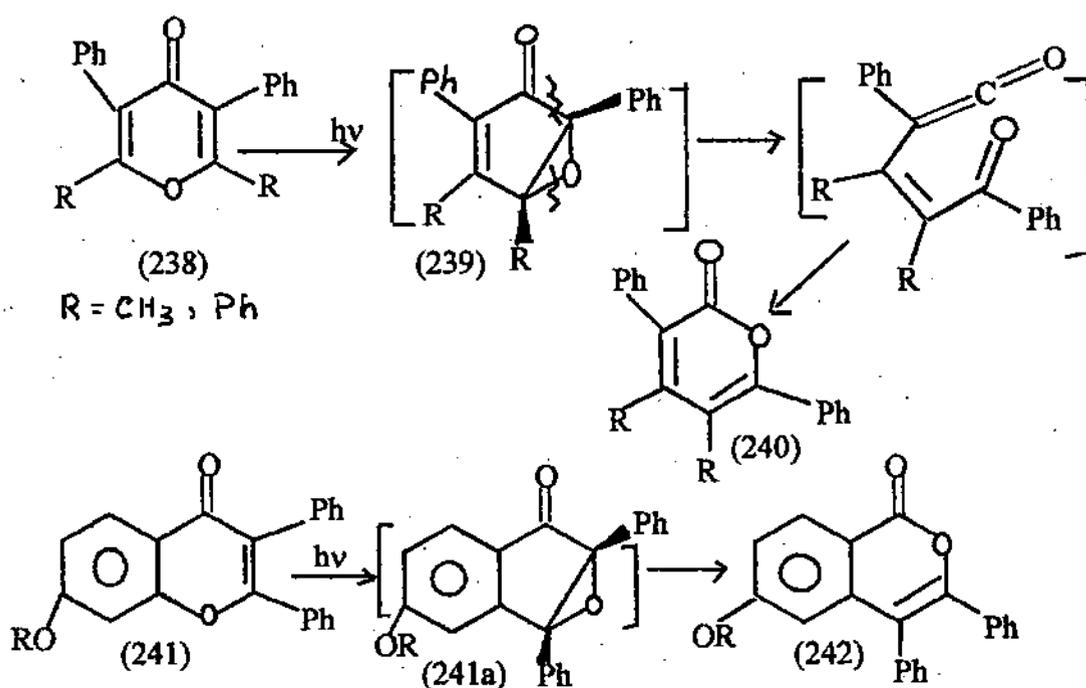
(c) Lamisantoinin (3a) gave on irradiation at -190°C the ketene (236) which thermally gave mazda santoinin (4a). Interestingly, (4a) on irradiation gave the same ketene (236). The cyclisation to (4a) is slower in comparison to the cyclisation of (229) \rightarrow (231) and on warming in the presence of ethanol the ketene was quantitatively converted to photosantoinin (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.

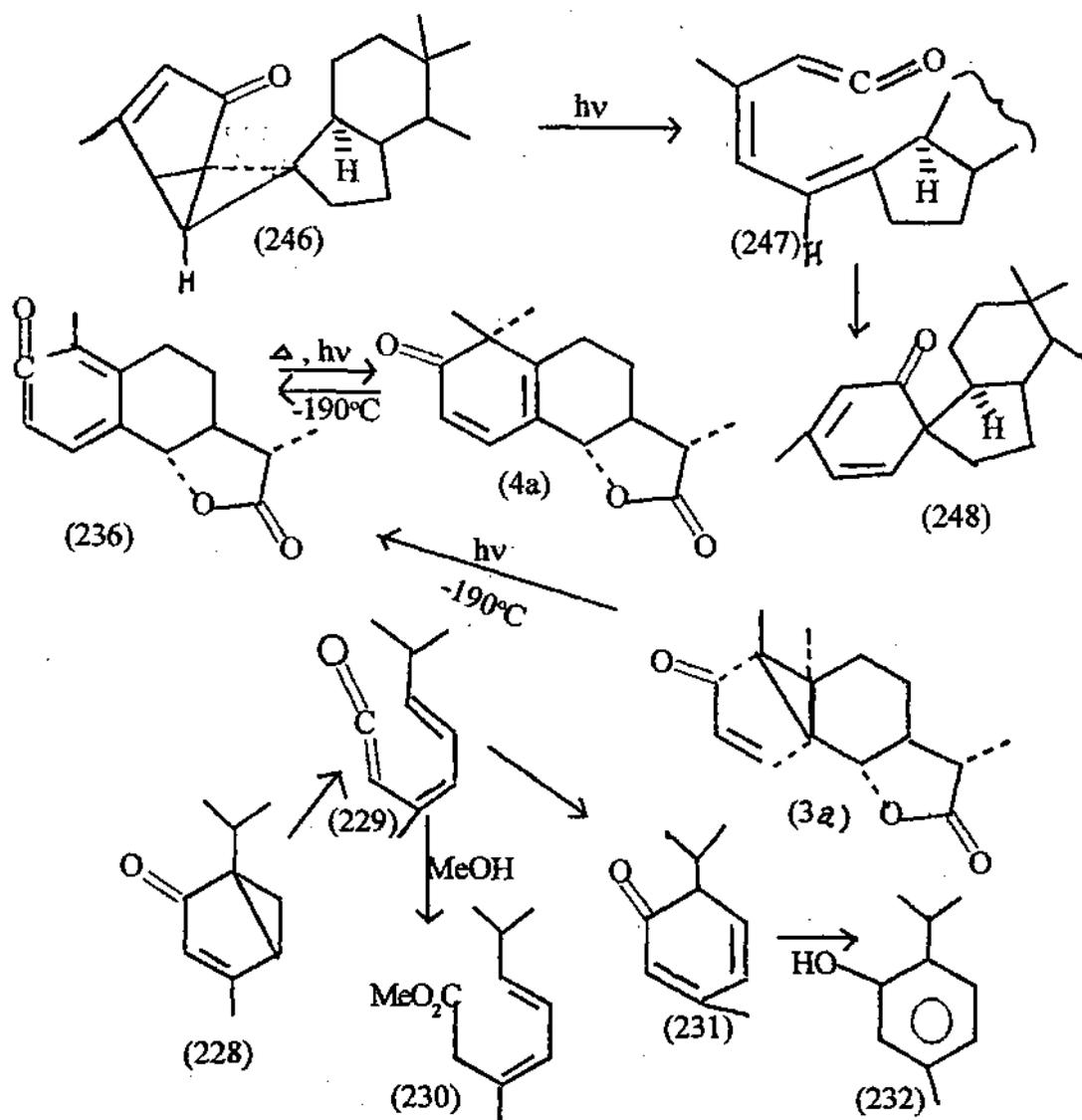
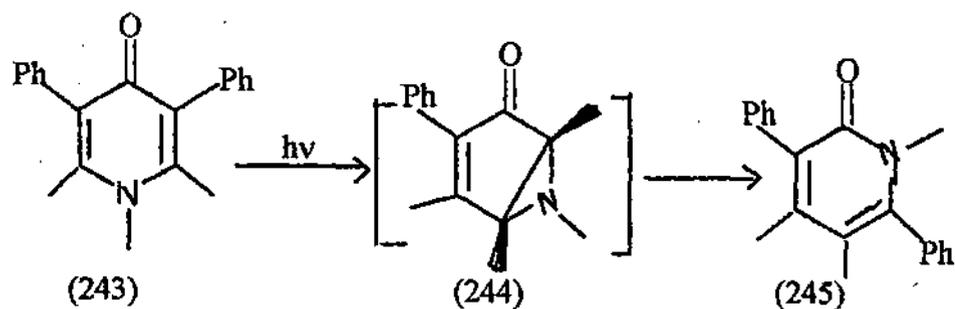


Section - F

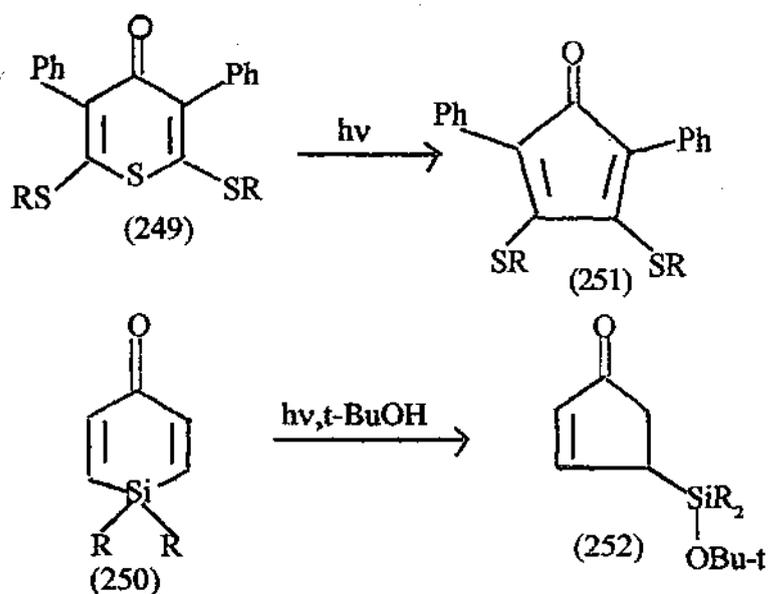
(Hetero 2,5-Cyclohexadienones Photorearrangement)

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 lumiproducs which being unstable could not be isolated in most cases. Heterocyclic cross-conjugated cyclohexadienones 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 lumiproducs (239), (241a) and (244) respectively. It has been postulated that the final products were formed by a double fragmentation - thermal reclosure process from the lumiproducs as shown in case of pyrone (238). This diene ketene mechanism has also been put forward for the photorearrangement of spiro bicyclohexenone⁶⁴ (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-*Sax* tonin(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.





In contrast, β - β' bonded intermediates formed from the irradiation of thiopyranones (249) and silyl compounds (250) did not give rise to lumporproducts but produced decomposition products (251)^{104,105} or nucleophile captured cyclopentenone¹⁰⁶ products (252).

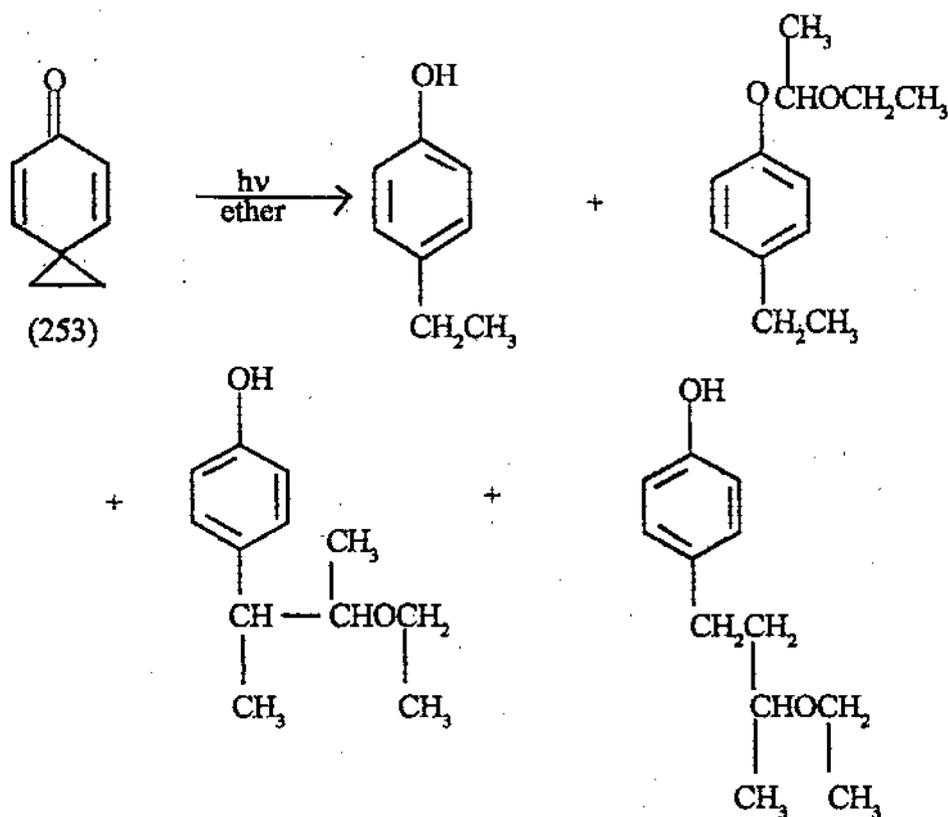


SECTION - G

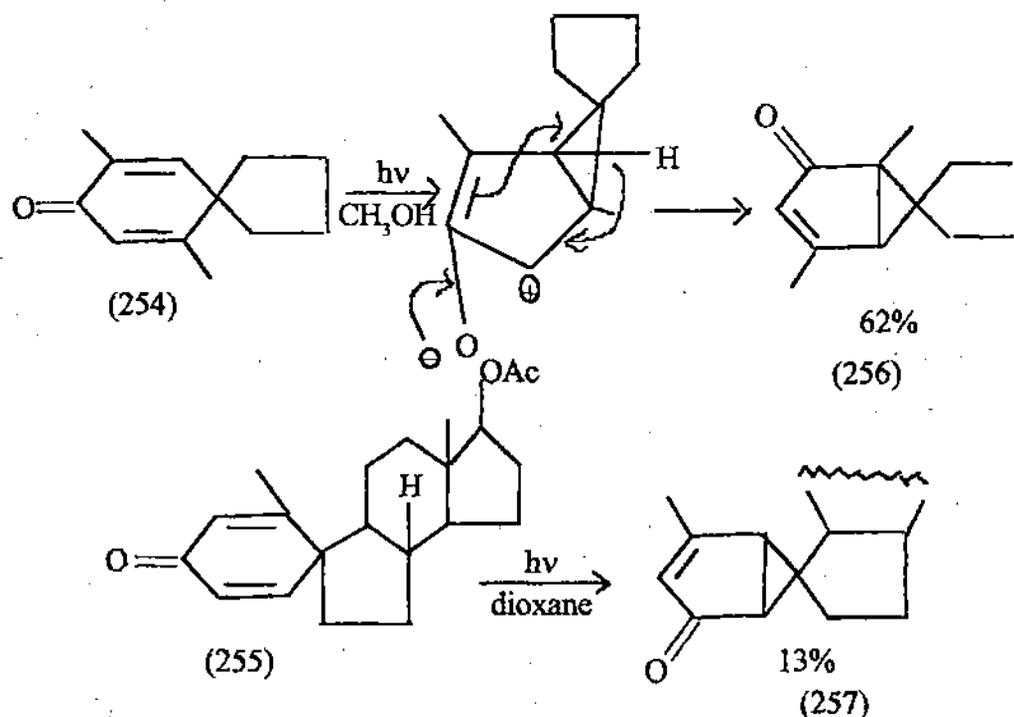
(Anomalous Photorearrangement of 2,5-Cyclohexadienones)

Although the formation of lumiprodukt 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.

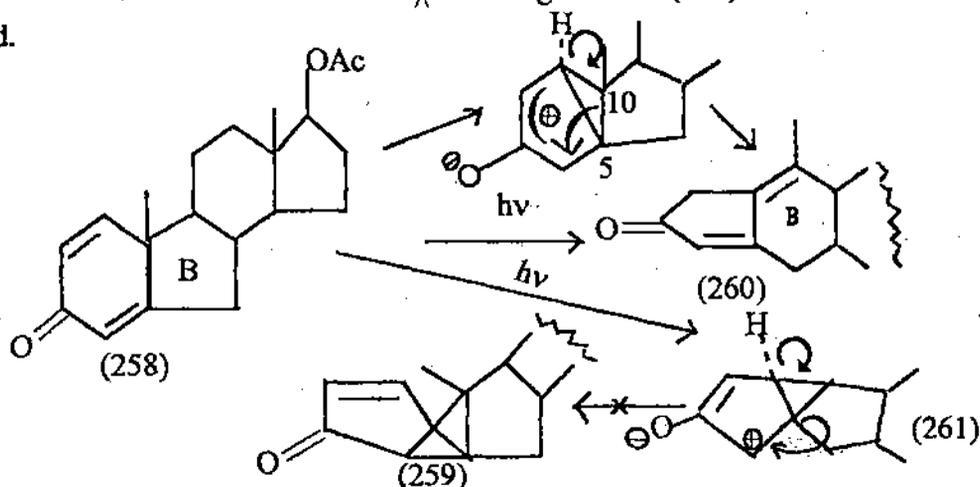
The spiro-cyclopropan containing cyclohexadienone moiety (253) is highly strained and did not produce the expected cyclopropyl ketone but gave rise to several phenolic derivatives.¹⁰⁷



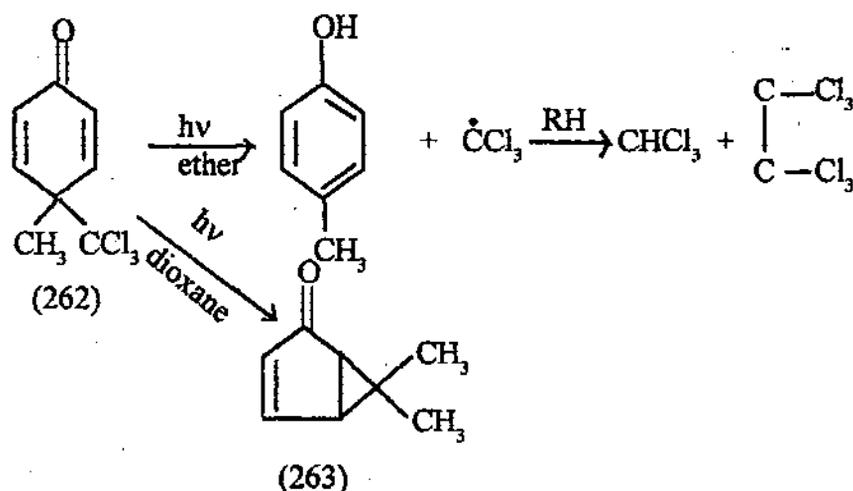
Usual cyclopropyl intermediate which would be highly strained in this case, is not formed. In contrast, the cyclohexadienones containing spiro-cyclopentane ring e.g. (254) and (255) are not so strained and underwent facile rearrangement to give the normal lumiproducs (256) and (257) respectively.⁷⁶



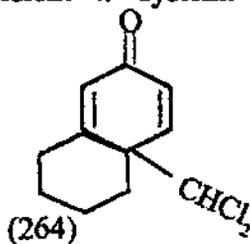
Instead of the expected lumiproducs (259), irradiation of the steroidal B-nordienone (258) in dioxane yielded the abnormal product (260).⁶⁰ This transformation presumably involves rearrangement of the cyclopropyl intermediate (261) via rupture of the 5-10 bond with concomitant expansion of the five-membered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



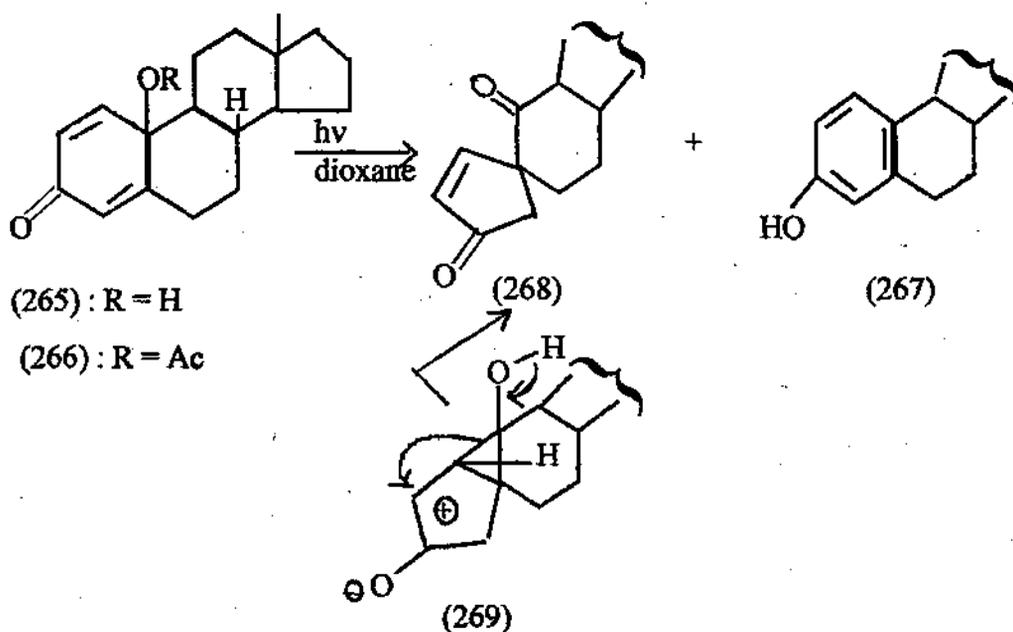
The anomalous products not only arise from cyclohexadienone compounds having strained rings, but also from substrates having substituents such as trichloromethyl, acetoxy or hydroxy at the para (C-4) position with respect to cyclohexadienone keto chromophore, when heterocyclic cleavage leads to a highly stable free radical expulsion of C-4 substituent. Thus, irradiation of dienone (262) (containing -CCl₃ substituent) in ethereal or hydrocarbon solvents gives p-cresol as a major product together with CHCl₃ and Cl₃CCCl₃¹⁰⁸. On the other hand, irradiation in aqueous dioxane gives the normal lumiprodut (263).¹⁰⁹



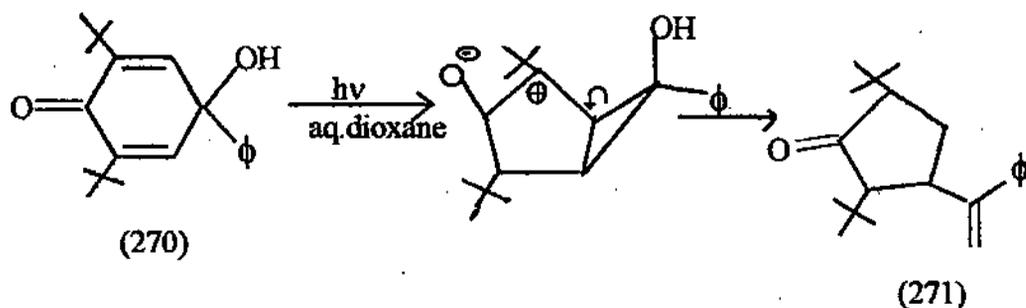
In contrast, the bicyclic dienone containing -CHCl₂ substituent (264) is inert under similar condition of irradiation.¹¹⁰ The failure of (264) to undergo expulsion of the angular -CHCl₂ group may probably be due to the lesser stability of the dichloromethyl radical. Failure to produce usual lumiprodut can be attributed to the destabilizing electronn - withdrawing effect of the -CHCl₂ group in the usual β, β'-bonded intermediate which has an electron-deficient π - system.



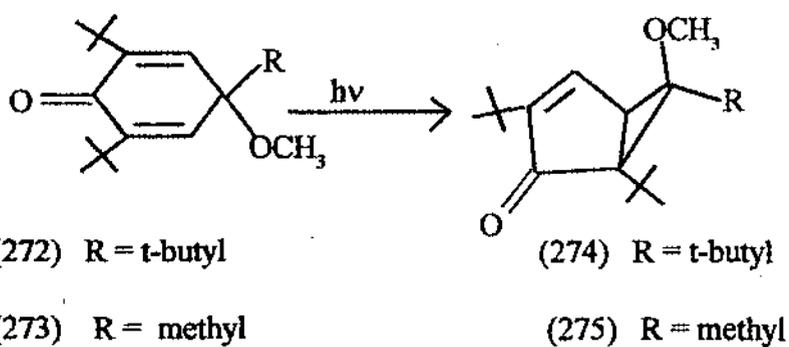
Expulsion of an acetoxy group from the para-position has also been observed. Irradiation of (266) produced estradiol-17-acetate (267) in significant yield.¹¹¹ The presence of a hydroxyl group at para position also modifies the course of the photo reaction. Photolysis of (265) gave both the spiro-ketone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



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



In the case of methoxy substituent at para position normal cyclopropyl ketone products were formed¹⁴ e.g. (272) and (273) on photolysis afforded (274) and (275).



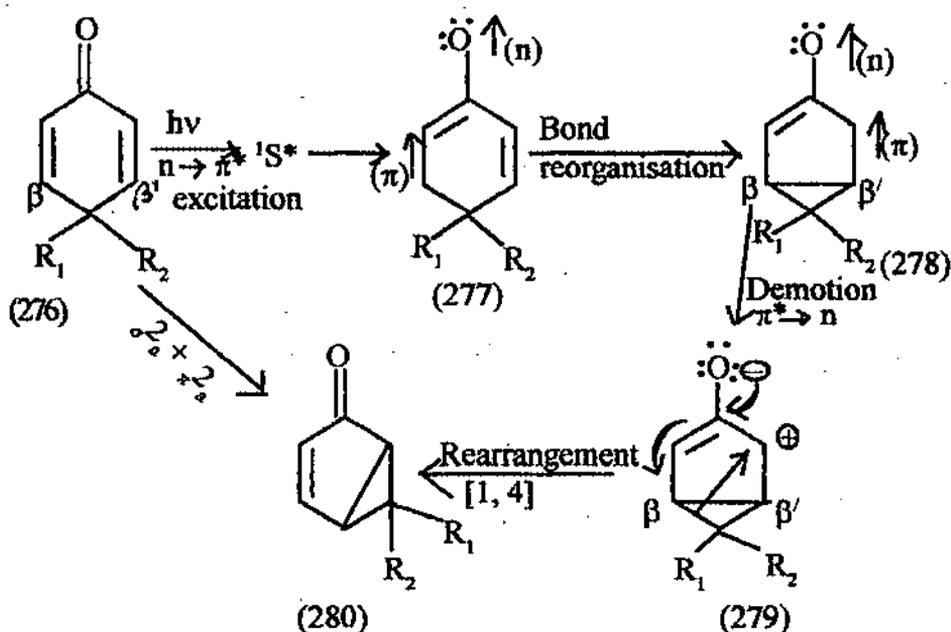
CHAPTER - II

(A short review on Mechanistic Aspect of Cyclohexadienone Photochemistry)

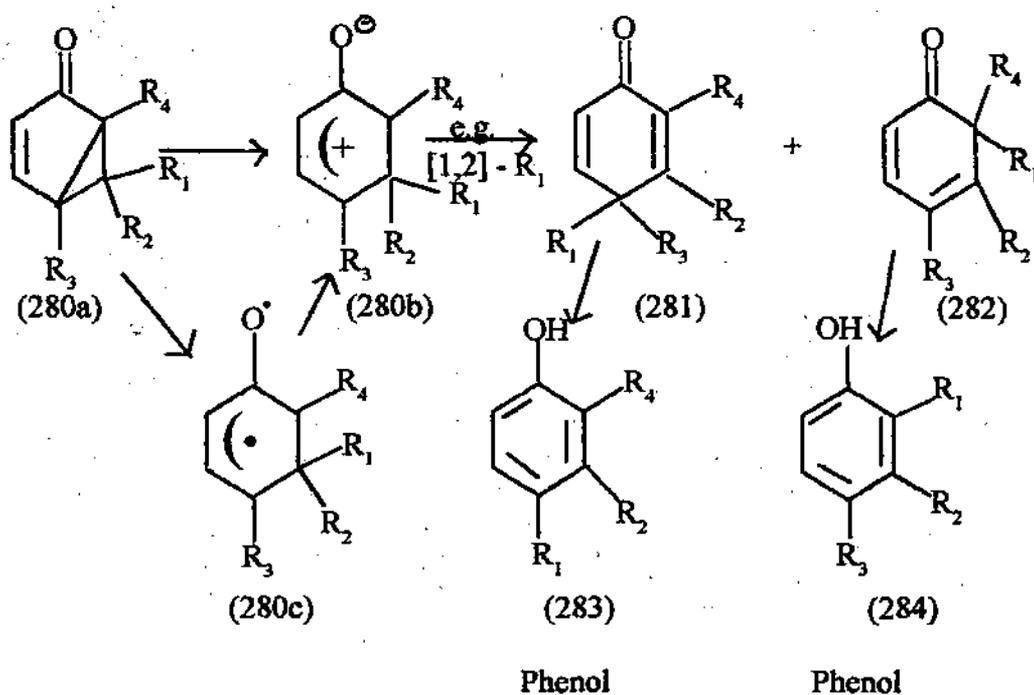
Introduction :

Because of facile, fascinating but complicated nature of deep-seated molecular rearrangements of cross-conjugated cyclohexadienones initiated by UV-irradiation between 250 to 360 nm their mechanisms have attracted a good deal of work over last three decades. Eventually, a deep-insight into the various aspects of the mechanisms^{16,17} has been achieved. A unifying concept has been arrived at encompassing the polar state proposition put forward by Chapman¹² and non polar radical type species developed during initial stages of electron excitation and demotion as postulated by Zimmerman and Schuster.⁷⁸

Scheme - III



Formation of bicyclo [3, 1, 0] hexenone(230) from photo-reaction of a model 2,5-cyclohexadienone (276) has been considered to proceed through a series of steps involving n, π^* singlet excited state (276), inter system crossing to the triplet n, π^* state (277), β, β' bridging (rebonding) to furnish (278) which is still an electronically excited molecule of the n, π^* type and results in ground state zwitterion (279) which rearranges finally to the lumiketone (280). The cyclohexadienone \rightarrow bicyclohexenone transformation can be viewed in a formal manner as a concerted $\sigma^2_a + \pi^2_a$ cyclo addition in terms of conservation of orbital symmetry principles formulated by Woodward-Hoffman. The process can also be dissected into the initial formation of a new bond between β, β' carbon atom (279) followed by [1, 4] - sigmatropic shift across 2-oxybutenyl frame with inversion of configuration at the migrating carbon atom. In



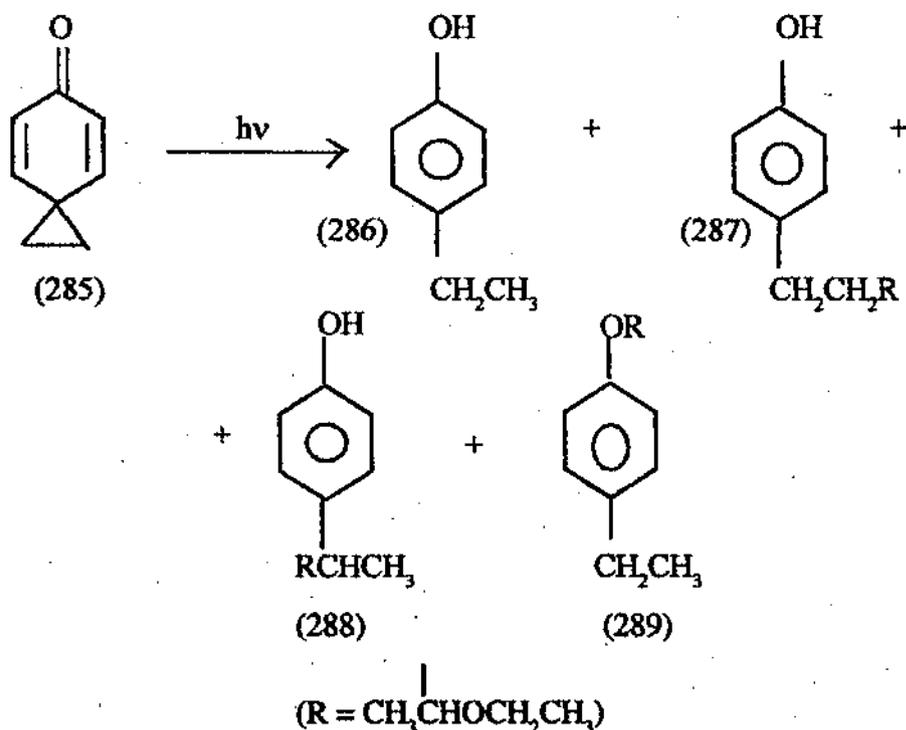
lumiprotect (280a) prolonged irradiation eventually gives rise to secondary photoproducts e.g. phenols (283) and (284) and ketones (281) and (282) as indicated above depending upon the nature of substitution. In the beginning we shall consider evidence in support of radical species generated during initial electron excitation

(SECTION-A) and subsequently involvement of Zwitterionic polar species following electron demotion (SECTION - B). Finally, we shall discuss on the spin multiplicity of excitation i.e. singlet vs. triplet (SECTION - C) and evidence on the electronic configuration i.e. n, π^* vs. π, π^* of the reactive excited state (SECTION-D).

SECTION - A

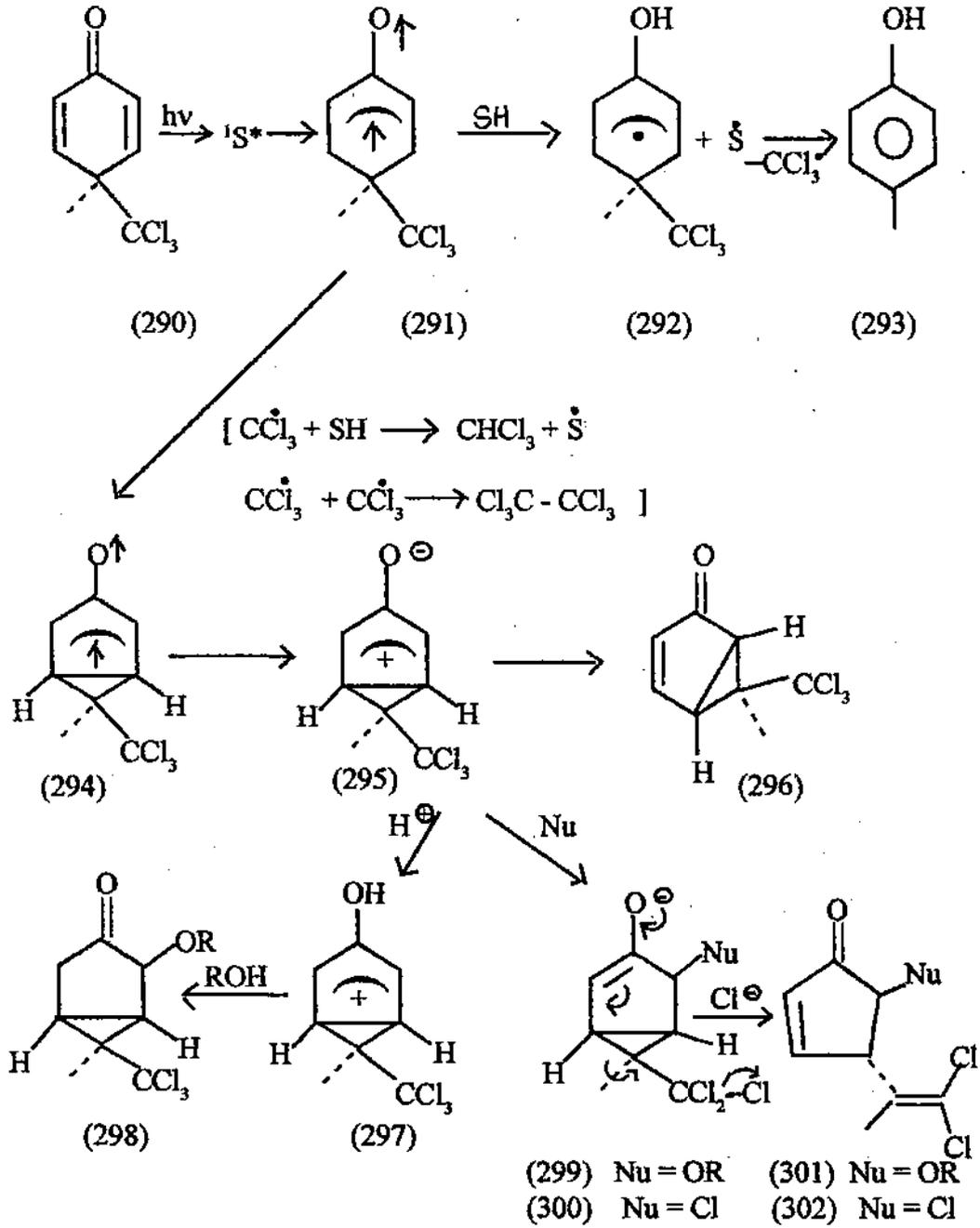
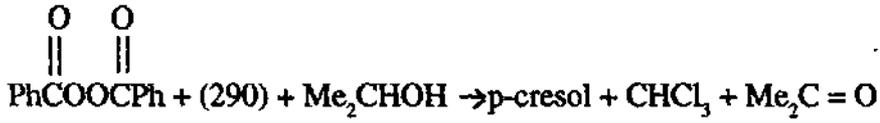
(Involvement of Free Radical Intermediates)

Convincing evidence was sought by Schuster group^{107,115} for involvement of free-radical intermediate using spiro-dienone (285). Photolysis of (285) in ether yielded four principal products (286), (287), (288) and (289). Formation of these products clearly demonstrated the involvement of free - radical intermediates and hence strongly disfavours the idea of polar state description of the excited state.

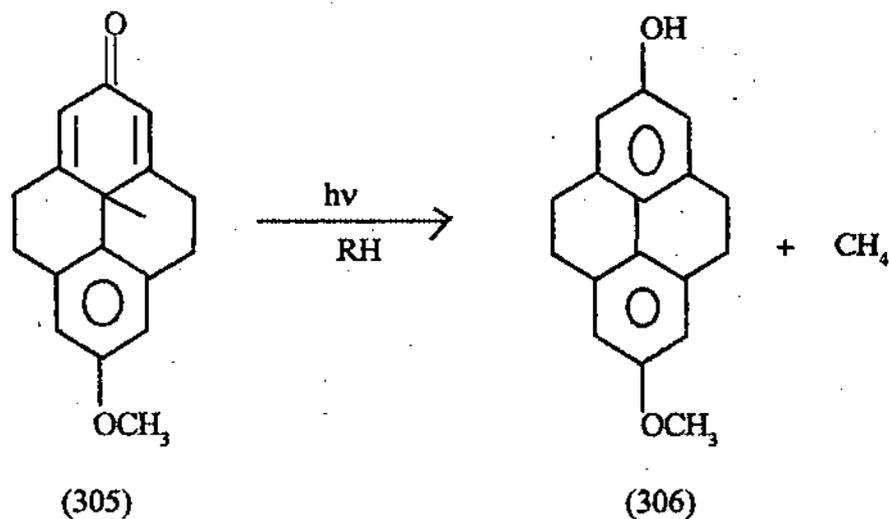


Further in-depth study was carried on better model compound trichloromethyl dienone (290) which is practically strainless as compared to highly strained spiro dienone (285) and contains a trichloromethyl substituent at C_4 which is easily expellable as radical. On irradiation (290) afforded chloroform, hexachloroethane and p-cresol as depicted in the scheme below. This reaction has been found to occur efficiently in solvents e.g. 2-propanol, diethyl ether and cyclohexane which are known as good hydrogen donors toward free radicals. A ketyl radical (291) is first generated by

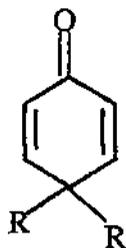
abstraction of hydrogen by triplet excited dienone(290) and then elimination of the substituent as radical occurs from the radical (291). This reaction could be quenched by triplet quenchers and sensitized by triplet sensitizers¹⁸. Rate constant for H-abstraction derived from Stern - Volmer plot was $3.9 \times 10^8 \text{ M}^{-1} \text{ S}^{-1}$. This value is considerably higher than H-abstraction by standard n, π^* triplet such as benzophenone ($K_{\text{obs}} \sim 10^6 \text{ M}^{-1} \text{ S}^{-1}$) but close to value derived for intramolecular H abstraction in the Norrish type II reaction ($K_{\text{obs}} \sim 10^8 \text{ M}^{-1} \text{ S}^{-1}$). When flash photolysis was carried out on (290) in degassed isopropyl ether, ethyl ether or cyclohexane, but not in benzene, CCl_4 or t-BuOH, a long-lived transient which decayed by first order kinetics with a lifetime of $\sim 200 \mu\text{s}$ was observed.¹¹⁷ This transient exhibited maxima at 540 and 580 nm were assigned to ketyl radical (291) by comparison with the spectrum of the parent cyclohexadienyl radical (291) and precursors (presumably the dienone triplet) were intercepted by oxygen and ditertiary - butyl nitroxide but 1,5-cyclohexadiene only intercepts the precursor. P-cresol and CHCl_3 were also obtained in good yield when (290) was thermolyzed at 80° in presence of benzoyl peroxide in isopropyl alcohol. This affords a technique to generate Me_2COH radical from isopropanol by a non-photochemical path, which can initiate the radical chain reaction.



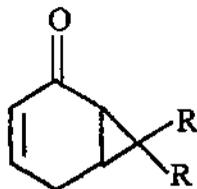
These studies unequivocally prove the free radical nature of the lowest dienone triplet state. In 2-propanol, hydrogen abstraction which leads to (293) competes with the ionic route to (301). The addition of lithium chloride selectively reduced the yield of only the later product. This demonstrates the sequential formation of dienone triplet state (291) and zwitterion (295) in accordance with the Zimmerman-Schuster mechanism. When irradiated in hydrogen-donating solvent cyclohexadienone (305) afforded phenol (306) and methane following the same mechanistic route as (290) \longrightarrow (293). The compound does not react in benzene and all attempts to trap a Zwitterion intermediate with nucleophile or 1,3-dipolarophiles was unsuccessful.⁶⁷



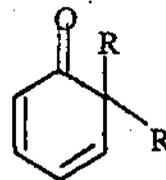
In order to examine the possibility of formation of bicyclohexenones at the bridged biradical state after $\beta - \beta'$ bonding, Swenton *et.al.*⁸³ conducted the photochemistry of 2,5-cyclohexadienones both in solution state and gas phase. At the photoenergies used in the ϵ excitation of the dienones (< 4 ev) in isolated molecules, it is unlikely that polar structures in which unit charges are separated by the distance of one C-C bond are attainable. In polar solvents, on the other hand, with high dielectric constant of medium as well as solvation can lower the energy with respect to the ground state of these structures to a point where they may be accessible to the electronically excited dienone molecules. Thus, involvement of the intermediacy of ionic species may be examined by the comparison of the photochemistry of a given compound in the gas phase at low pressure and in solution in a polar solvent. Irradiation of (276a) and (276b) in solution in cyclohexane at 300-370 nm gave two isomeric ketones (280c) and (280d) and (282a) and (282b). Irradiation of (276a) at the same wavelength in aqueous dioxane gave in addition to (280c) two phenols characterised as (283a) and (283b).



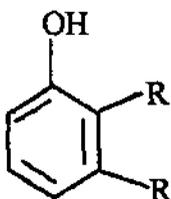
(276a) $R = \text{CH}_3$
 (276b) $R = \text{C}_6\text{H}_5$



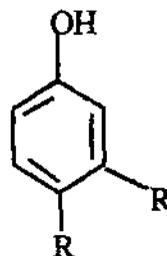
(280c) $R = \text{CH}_3$
 (280d) $R = \text{C}_6\text{H}_5$



(282a) $R = \text{CH}_3$
 (282b) $R = \text{C}_6\text{H}_5$

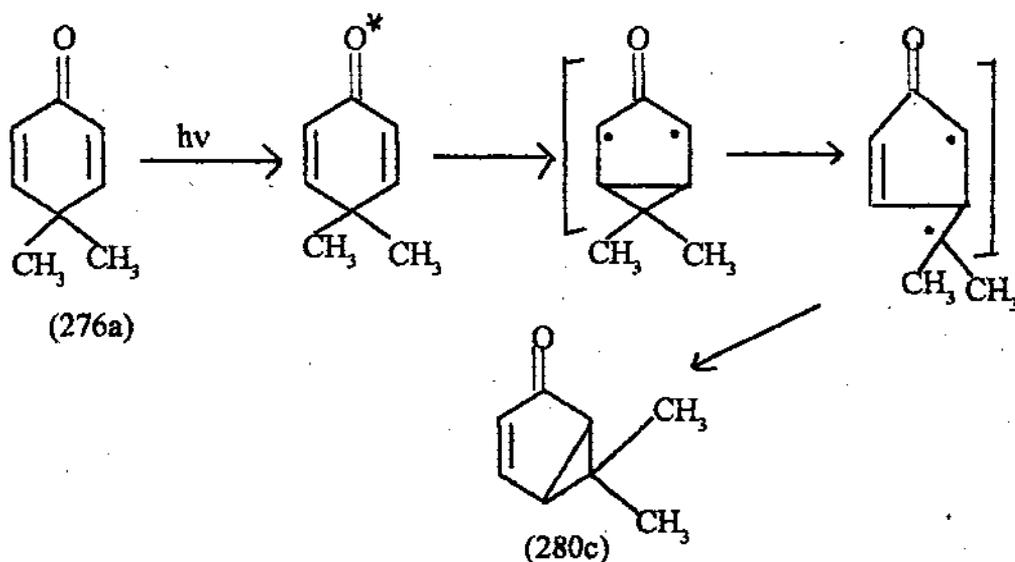


(283a)

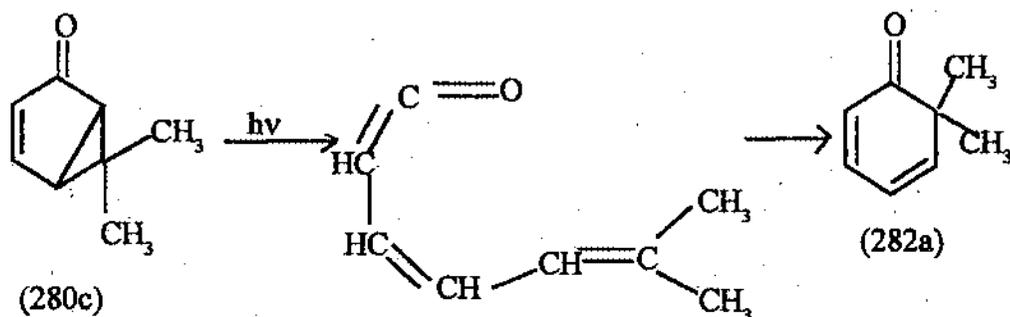


(283b)

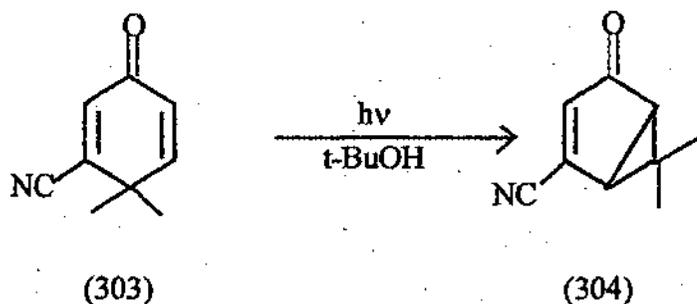
The gas phase irradiation of (276a) at 366 nm at 85°C and at pressure of 6 torr. gave at first (280c) but as soon as about 6% of (280c) had built up in the reaction system, (282a) began to appear. The mass balance was excellent upto about 15% conversion of (276a). There is no doubt that (276a) leads to (280c) which in turn gives (282a). In contrast to irradiation of aqueous dioxane where involvement of mesoionic intermediates has been proposed¹¹⁸ at least in this instance (276a) can be transformed to (280c) via nonionic intermediate. This conversion may be viewed as a specific example of the vinyl methane to vinyl cyclopropane rearrangement which is known to be a general photochemical process¹¹⁹. Based on this idea, the following mechanism has been advanced.



In the vapour phase the transformation of (280c) and (282a) should also involve a nonionic pathway, whereas the formation of the phenols (283a) and (283b) from (280c) probably involves zwitterionic intermediates since it is only observed in a polar medium. The formation of (282a) is reduced by the presence of methanol which supports the intermediacy of a ketone which ultimately can cyclize to yield (282a) as shown below :



The assumption that unit charge separation necessary for zwitterion formation is not possible in vapour state and hence the reaction proceeds from excited bridged biradical species, has been challenged by Schuster¹⁸ who argued that the available excited state energy of ca. 100 Kcal/mole might still be sufficient to accommodate the energy requirement for charge separation in the vapour state. The regioselective transformation (303) to (304) in *t*-butyl alcohol serves a better case in favour of rearrangement in the biradical stage¹²⁰. In a zwitterionic intermediate, [1,4] shift would have been expected to give the 5-cyano isomer rather than the product (304).

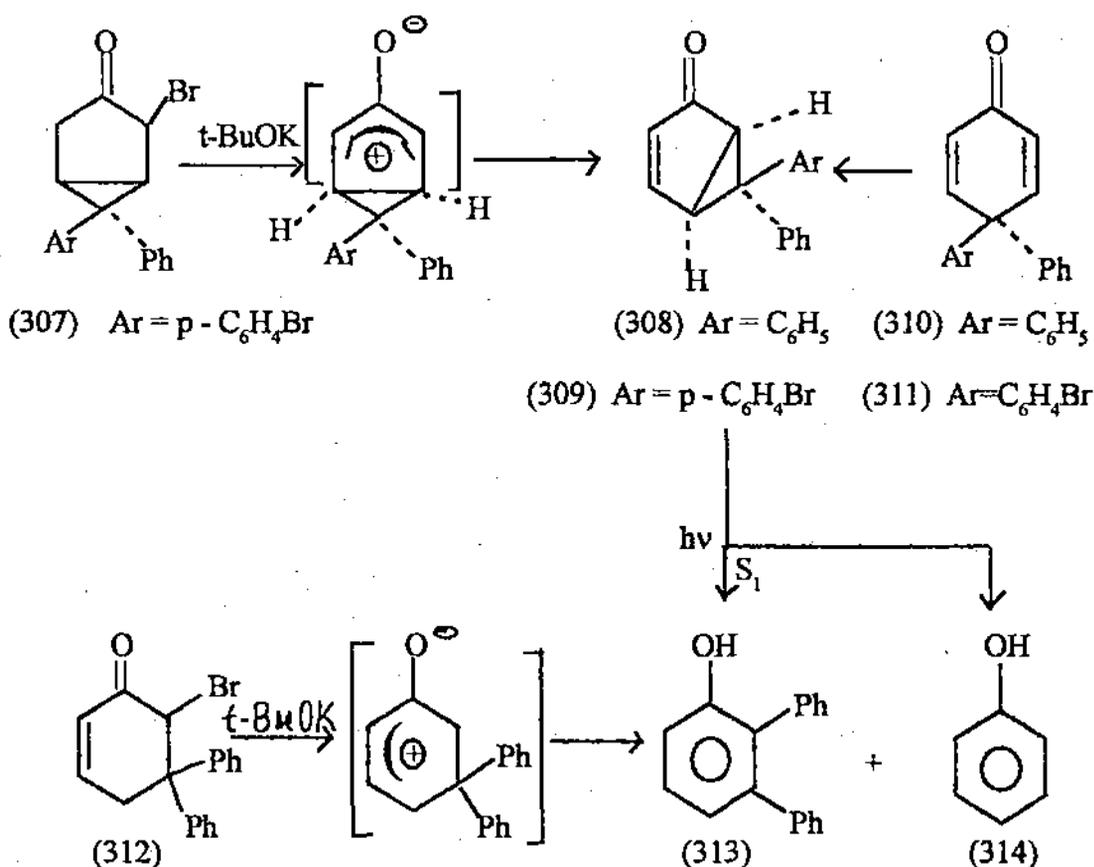


All the physicochemical studies described above supposes a description of the primary photochemical intermediate as a radical like species.

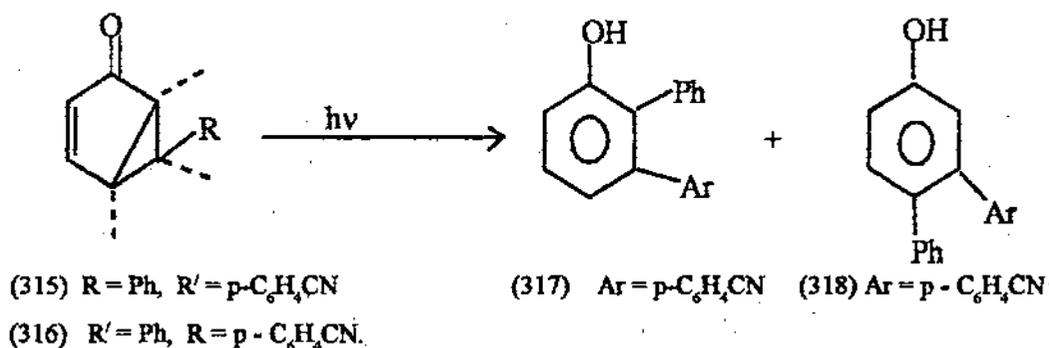
SECTION - B

(Involvement of Zwitterion Intermediates)

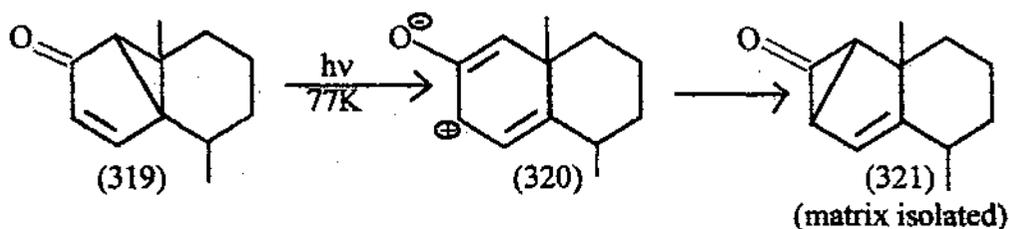
Formation of a vast multitude of products on photoexcitation of cyclohexadienones and bicyclohexenones has got strong resemblance to the products obtained from ground state electron deficient species, although the rearrangements do not completely rule out involvement of biradical species (278) and (280a). Nonetheless some type of products, for instance, formation of hydroxy ketone in acidic medium is really difficult to explain without participation of zwitterion intermediates (279) and (280b).



Zimmerman developed experiments¹²¹⁻¹²⁴ to generate zwitterion in ground state process of the type (279) and (280b) which undergo rearrangement to bicyclohexenones and phenols respectively. Favorskii-type rearrangement, as described above, of the bromoketone (307) furnished in high yield (309), one of the stereoisomeric photoketone of the corresponding dienone(311). The bromoketone (312) yielded the phenols (313) and (314) on treatment with *t*-BuOK in the same ratio as is obtained from the photolysis of (308). This result supports the proposition that generation of phenol from irradiation of bicyclohexenone proceeds through the intermediacy of zwitterion. Under both direct irradiation²⁹ and triplet-sensitized condition the stereo isomeric ketones (315) and (316) in aqueous *t*-butanol rearranges to similar ratios of phenols (317) and (318). No cyanophenyl migrated product was formed. Therefore, phenyl migration occurred to a positive centre rather than to a radical one and hence gave support that demotion to zwitterion must have preceded the rearrangement.

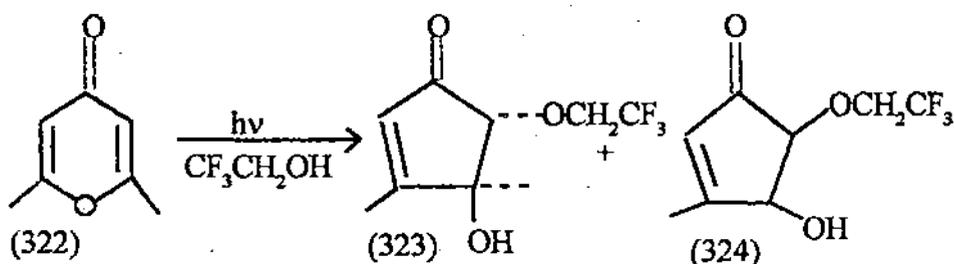


Formation of (321), a close form of zwitterion (320), which can be matrix isolated from the irradiation of (319) leads further support^{93,94} for zwitterion hypothesis.

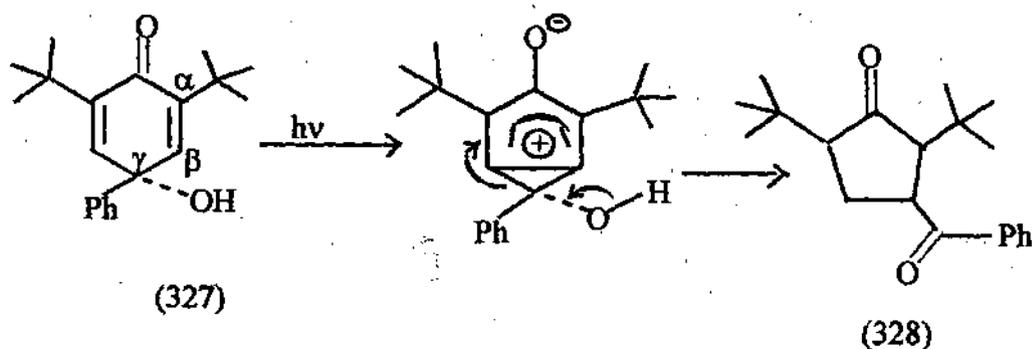
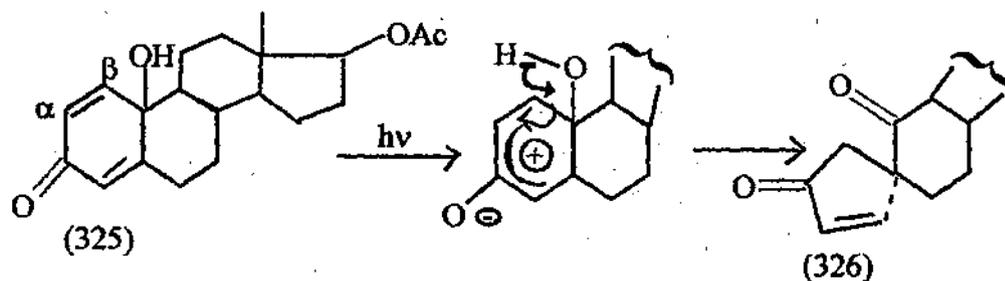


A direct evidence that leads to the definitive involvement of zwitterions in these types of photorearrangement in solution would require their capture, when formed photochemically from dienones by nucleophiles before further conversion occurs. The dienone (290) and related compounds have been found to be very suitable for this purpose and subjected to extensive studies¹⁸⁻²¹. The build up of positive charge at C-4 in (290) has greatly enhanced owing to the attachment of electron-withdrawing trichloromethyl substituent and hence making [1,4] rearrangement and cyclopropane cleavage in (279) less favourable. This also improved the susceptibility of these intermediates to capture by nucleophile and rendered the zwitterion (295) accessible for trapping and kinetic study. The species (332) has been found to be the common precursor of products (296), (298), (301) and (302). In alcohols (methanol, ethanol, propan-2-ol) acidified with hydrogen chloride protonation of (295) gives (297) which by capture of solvent affords (334). It is unique in the sense that these are examples of dienone photoproducts in which the skeleton of the proposed zwitterion is preserved. In absence of the appropriate electrophile (332) was captured by nucleophiles such as alcohol solvent and added halide ions to yield (299) and (300) respectively, which then undergo fragmentation in an anionic Grob-type process giving (301) and (302). In 2,2,2-trifluoro ethanol and methanol, the ratios (302)/(296) and (302)/(301) has been noted to increase linearly as the LiCl concentration in the solutions was increased and the quantum efficiency of formation of zwitterion (295) was nearly unity.

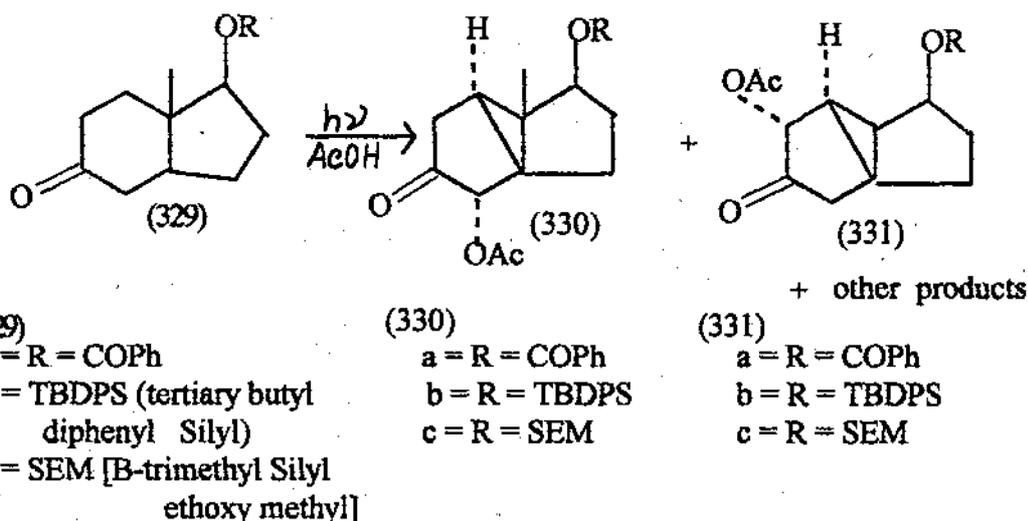
Just as the trichloromethyl compound (290) discussed above, zwitterion derived from 4H-pyran-4-ones e.g. (322) should also be susceptible to nucleophilic trapping and fragmentation. This expectation was borne out when it was recorded^{23,24} that irradiation of (322) in 2,2,2-trifluoro ethanol afforded the stereoisomer (323) (major isomer) and (324) (minor one) clearly resulting from trapping of zwitterion intermediate.



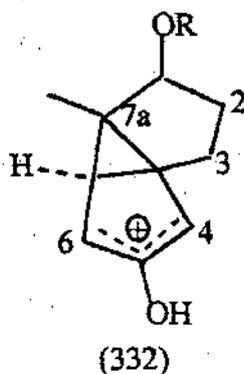
A few examples can be cited to demonstrate that nature of the photoproducts formed is explained by proposition of zwitterion intermediates.



4-hydroxycyclohexadienones (γ -substituted with respect to carbonyl group) (325) and (327) furnished ring contracted photoisomerised enediones, (326)¹¹² and (328)¹¹³ respectively on photolysis in anhydrous and aqueous dioxene. Many more cases¹²⁵⁻¹²⁸ of similar photoisomerization have since been reported. Recently Caine et al.¹²⁹ have demonstrated the formation of, amongst other products, tricyclic ketones of the type (330), (331) in polar solvent (acetic acid) on irradiation of bicyclic cross conjugated cyclohexadienones having 8-oxy substituents, (329a-c).



The tricyclic acetoxo-ketones (330a-c) and (331a-c) were derived from trapping of Zimmerman-Schuster cyclopropyl carbocation intermediate (332) by acetic acid. These products provided the first examples of solvent trapping of Zimmerman-Schuster intermediates during photolysis of fused-ring cross-conjugated cyclohexadienones.



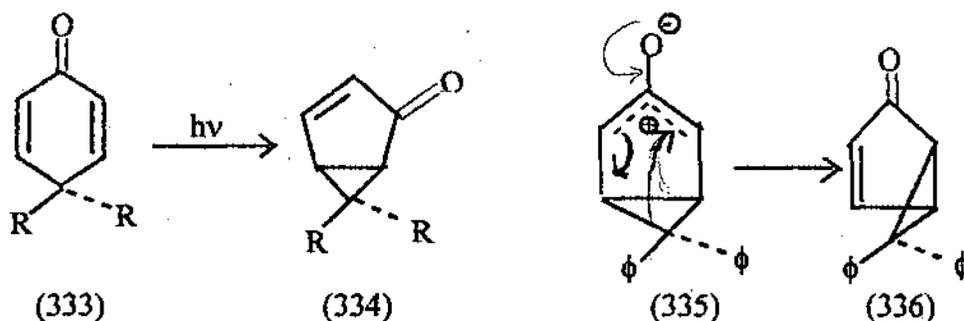
This type of reaction was reported by Schuster and coworkers¹¹⁷ in monocyclic dienone (290) discussed earlier. Interestingly product of the type (330) or (331) was not formed¹³⁰⁻¹³¹ when irradiation was carried out on the substrates 6/5 fused dienones without containing 8-oxygen substituents. Therefore, in dienones such as (329) it appears that the C-1 oxysubstituents reduce the rate of cleavage of the cyclopropane ring of the Zimmerman-Schuster intermediate (332) sufficiently to permit the trapping process occur. This effect may_A^{be} steric and/or electronic in origin.

Schuster and Liu²¹ observed that addition of LiCl had absolutely no effect on the efficiency of lumiketone formation on photolysis of santonin or dienone(310) in 2,2,2-trifluoro-ethanol and no new products were obtained. This shows that either (a) zwitterions are not reaction intermediates in these systems or (b) zwitterions are actually involved but their lifetimes are much shorter than that of (279). The authors favoured the explanation (b). Since lumiketone formation is the only primary reaction occurring on photolysis of santonin and (310), zwitterions in these cases have only two options, (i) decay to the ground state dienone and, (ii) [1,4] sigmatropic rearrangement. Since the lumiketone formation has high quantum efficiencies (~ 0.85), it is evident that lifetime of zwitterion is determined principally by rate of lumiketone formation.

Fisch and Richards^{132,133} observed the formation of a blue transient intermediates from the irradiation of santonin, lumisantoinin and some α -haloderivatives in glasses or polystyrene at 77°K. These intermediates are not paramagnetic and considered to be corresponding zwitterions. This assignment must be considered tentative as these species could not be trapped.

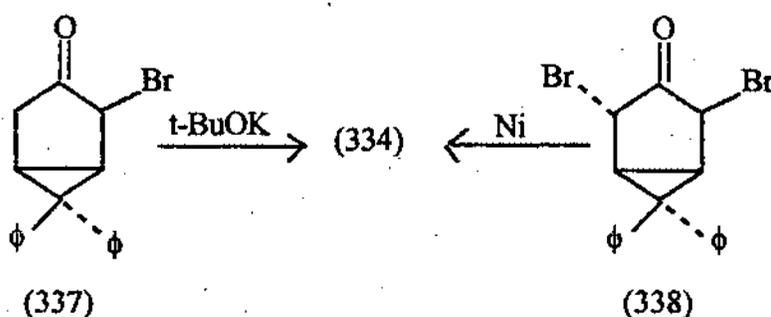
In summary, the discussion so far made clearly points to the involvement of diradical species during electronic excitation and demotion followed by zwitterion generation in the cross - conjugated cyclohexadienone and bicyclohexenone photorearrangement at ambient temperature as postulated in Zimmerman-Schuster mechanism.

Much work has been done to elucidate the mechanism¹³⁴ of the photochemical rearrangement of 4,4-disubstituted cyclohexadienones (333) to form 6,6-disubstituted bicyclo [3.1.0] hex-3-ene-2-ones (334), products which themselves suffer subsequently further rearrangements, ring opening and so on.



It was proposed at early stage⁷⁸ (e.g. when R = phenyl) that the initial cold product was a Zwitterion (335) which subsequently rearranged to (336).

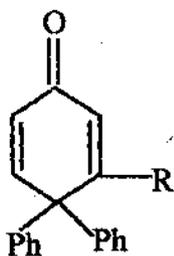
Strong evidence^{124,135} for such an intermediate is the fact that both the dehydrobromination of (337) with base and the debromination of (338) with sodium produce (334).



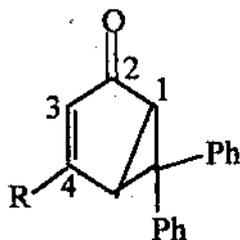
With a view to understanding regioselectivity in cyclohexadienone photochemistry, Zimmerman and Pasteris¹⁴⁵ studied the photochemistry of 3-cyano-4,4-diphenyl-2,5-cyclohexadienone (303a) and also the dark generation of the 1-cyano-6,6-diphenylbicyclo [3.1.0] type A zwitterion (351). Despite the possibility of the formation of both 4-cyano-6,6-diphenyl bicyclo [3.1.0] hex-3-en-2-one (304a) and its 5-cyano isomer (340) only the 4-cyano regioisomer was formed both in direct and methoxyacetophenone sensitized irradiations. The independent generation of the ground-state type A zwitterion was achieved by base treatment of 1-cyano-2-bromo-6,6-diphenyl bicyclo [3.1.0] hexan-3-one (347) and its 4-bromo isomer (348). Both

reactions led to the regioselective formation of the 4-cyano bicyclic photoproduct. In addition, the reaction of diiron nonacarbonyl with 1-cyano 2,4-dibromo-6,6-diphenyl bicyclo [3.1.0] hexan-3-one (349) led to the same bicyclic product. Hence, the type A zwitterion leads to complete regioselectivity to that isomer of bicyclic product (350) having the cyano group on the residual double bond and the photochemistry is consistent with a zwitterion pathway. It has also been observed that the regioselectivity did not depend on solvent polarity.

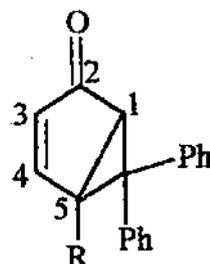
Zimmerman and Pasteris¹⁴⁶ also carried out the irradiation of 3-methoxy-4,4-diphenyl-2,5-cyclohexadienone (303b). Here, too, the product is regioselective with a preference for formation of 4-methoxy-6,6-diphenyl bicyclo [3.1.0] hex-3-en-2-one (304b) relative to 5-methoxy isomer (346a) formed (1.4:1) in benzene.



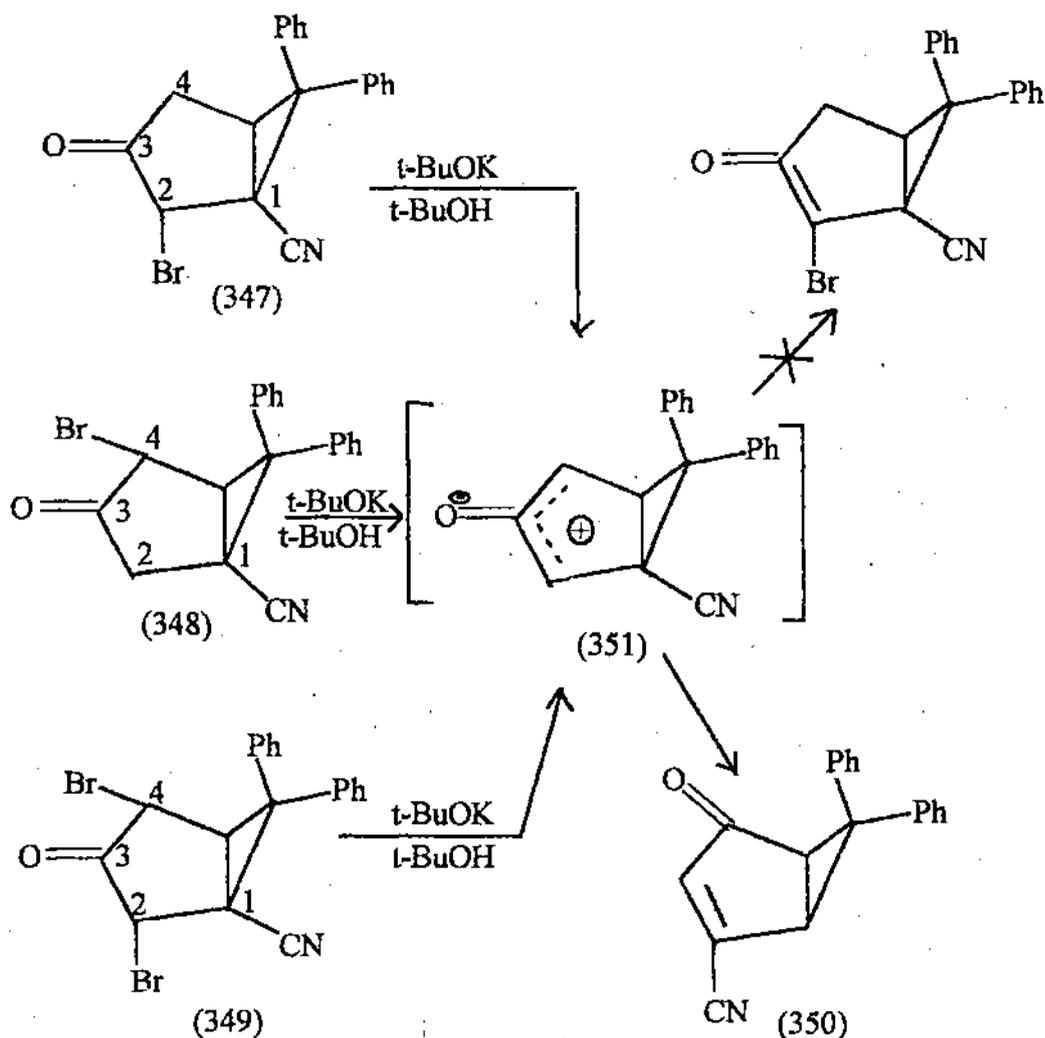
(303a), R = -CN
(303b), R = -OCH₃



(304a), R = -CN
(304b), R = -OCH₃



(346), R = -CN
(346a), R = -OCH₃



(Zwitterion Mechanism for the Dark type A Rearrangement)

Schuster and Liu¹⁴⁷ presented a detailed kinetic study which showed that a zwitterionic species is an obligatory intermediate in the photochemical conversion of 2,5-cyclohexadienone to lumiprodukt. Lithium chloride present in the reaction mixture successfully intercepts the zwitterionic intermediate. Their studies on the temperature dependence of the zwitterion-derived photoreactions also reveal that the main source of inefficiency in the system appears to be electrocyclic reversion of zwitterion to the cyclohexadienone by an orbital symmetry forbidden pathway that becomes increasingly important as the temperature is raised.

SECTION - C

(Multiplicity and Energy of the Reactive Excited State)

A good deal of efforts has been directed to study the nature of multiplicity, energy and electronic configuration of reactive excited state of cross conjugated cyclohexadienone photochemistry. Numerous mechanistic proposals that have piled up over last three decades, will now be considered in the light of available data.

Photoconversion of santonin and dienones (310) and (311) to lumiketone on direct irradiation has been favoured to be very efficient and the quantum yield almost approaches to unity. Same quantum efficiency has been recorded on sensitised reaction from triplet sensitizer such as benzophenone ($E_T = 68.5$ KCal/mole) or acetophenone ($E_T = 73.6$ KCal/mole). This gives some idea that the photoreaction occurs from triplet state and $S \rightarrow T$ intersystem crossing efficiency is nearly unity. This was further strengthened by the observation that the photoconversion is completely quenched if irradiation of α -santonin at 3660Å or (290) under a pyrex filter¹⁴⁸ is carried out in piperylene as a solvent, a triplet state quencher. Similar results were obtained with another triplet state quencher 1,3-cyclohexadiene.

Schaffner et al. made an interesting observation that γ -irradiation of toluene or benzene solutions of 1-dehydrotestosterone acetate induced isomerisation to the corresponding lumiprodut with a G-value of 1.9 to 3.0, which on further irradiation afforded the same mixture of ketonic and phenolic products as obtained by photolysis at $\lambda > 280$ nm. Since isomerization could not be induced in the absence of an aromatic sensitizer, triplet sensitization by aromatic solvents have been proposed¹³⁶.

Although the sensitization studies with triplet sensitizers and quenching studies with piperlin (1,3-pentadiene) and 1,3-cyclohexadiene indicate the involvement of a triplet path, the result from another triplet quencher naphthalene renders the quenching studies inconclusive as regards the precise nature, energy and identity of quenchable triplet. Low temperature phosphorescence measurements of α -santonin, (290) and (310) led to the determination of the lowest spectroscopic triplet state energy to be $E_i = 68$ KCal/mole. This values indicates that triplet energy transfer to naphthalene ($E_i = 61$ KCal/mole), 1,3-pentadiene ($E_i = 57 - 59$ KCal/mole) and 1,3-cyclohexadiene

($E_1 = 53$ KCal/mole) should take place at the same diffusion-controlled rate. Contrary to the expectation, naphthalene failed completely to quench (310) and the quenching ability of 1,3-pentadiene has been found to be considerably lower than 1,3-cyclohexadiene in case of santonin, (290) and (310). Two possible explanations have been advanced¹⁶. Firstly a triplet exiplex $^3(\text{DA})^*$ formation between the donar (D) and acceptor (A) has been proposed. It might diminish the rate constants for energy transfer by factors other than the difference in donor (D) and acceptor (A) triplet energies and it is different for different acceptors. Secondly, the quenching of the spectroscopic dienone triplet might not occur, since the relaxation to a lower-energy geometry might be sufficiently fast. Furthermore, this relaxed quenchable triplet was considered to adopt a geometry, interposed between (277) and (278), which has an out-of-plane twist of the dienyl radical moiety and possesses an energy about or lower than 60 KCal/mole.

SECTION - D

(Electronic Configuration of Reactive Excited State [n, π^* vs. π, π^*])

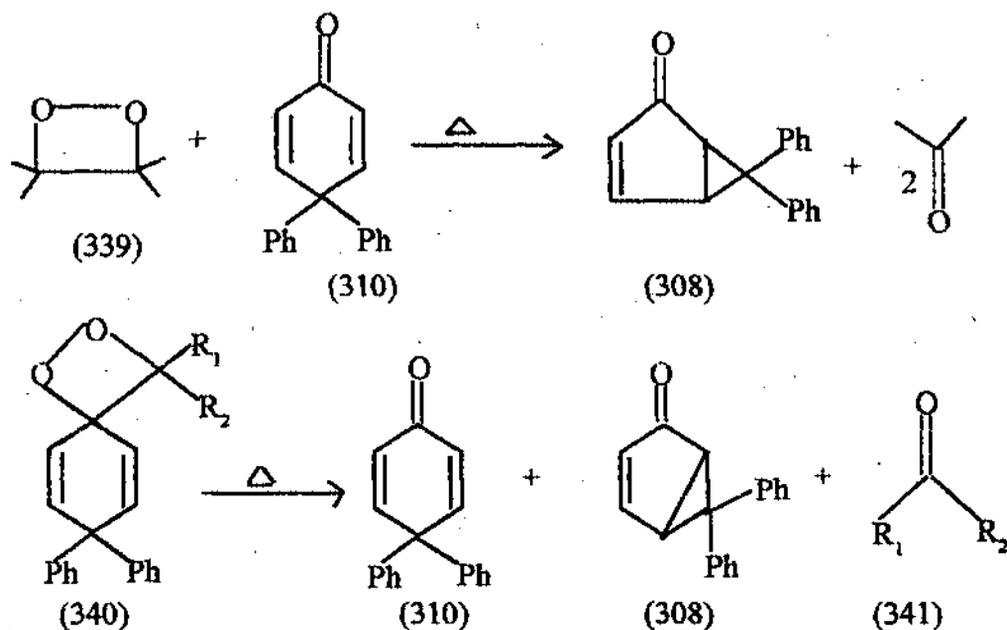
Cross-conjugated cyclohexadienones show an intense absorption band centred around 240 nm and another less intense band around 300 nm. The former band is associated with $\pi-\pi^*$ and the later to $n-\pi^*$ electronic transitions. All the usual photochemical rearrangements undergone by dienone systems can be effected by photolysis at either wavelength. Of course, the quantum efficiency and chemical yields of various products vary substantially. As because the initiation of the photoreaction can occur at wavelengths corresponding to low energy n, π^* transition, it is often assumed that reactive excited state is of n, π^* character. This has been the basis of Zimmerman-Schuster⁷⁸ mechanism of cyclohexadienone photorearrangement.

Since the photoreaction occurs from a triplet state, as discussed earlier, this could be $^3n, \pi^*$. This contention has been supported^{137,138} by low temperature phosphorescence measurements of (290) and some other monocyclic dienones in glasses. On the basis of short emission life time (about 0.5 msec.), direction of emission polarization, effect of solvent polarity on emission wavelength and the similarity of the vibrational pattern of the phosphorescence emission spectrum with that characteristic of n, π^* emission, support the $^3n, \pi^*$ configuration.

Phosphorescence was thought to originate from $^3n, \pi^*$ state. However, phosphorescence excitation measurement at 4.2 K and investigation of heavy atom effects on santonin and some analogues¹³⁹ led to the proposition that phosphorescence in later cases stems from $^3\pi, \pi^*$ state lying below the $^3n, \pi^*$ state. There is also strong vibronic interaction between the two states. Interestingly, Schuster has observed that (292a), 3-methyl analogue of (292) possesses a lowest $^3\pi, \pi^*$ state though (292) a $^3n, \pi^*$ state. It shows that slight change in geometry by introducing a substituent or conformational flexibility may switch over from one energy state to the other. The T_2 state can be thermally populated from an unreactive T_1 state, particularly when the two triplets are energetically proximate, at ambient temperature as observed¹⁴⁰ in case of certain aryl ketones. Therefore, reaction of the type e.g. β, β' bonding [(278) \rightarrow (279) Scheme -III] from an $^3n, \pi^*$ state (T_1 or T_2) is still a distinct possibility. To adduce further evidence in support of involvement of $^3n, \pi^*$ excited state, Zimmerman et al.¹⁴¹ generated triplet acetone

from thermolysis of dioxitane (339), which by triplet excitation converted (310) to (308). Then, an idea of effecting intramolecular electronic excitation by internal incorporation of a dioxitane moiety was envisaged by him in order to effect unimolecular rearrangement in excited state. These are examples of photochemistry without light, since in these cases excitation energy is not derived from irradiation but derived from thermolysis.

The lumiketone (308) was formed in considerable yield ($16.6 \pm 3.2\%$) on thermolysis of five different dioxitances (340a - e). In four cases, the alternative (341a-d) have higher triplet energies than (310), but in the fifth case (340c) the reaction course was not altered despite the product (341e) acetone has lower energy π, π^* triplet ($E_T = 59$ KCal/mole) than the n, π^* triplet of (310) ($E_T = 68.5$ KCal/mole). The argument has been advocated that the higher energy n, π^* triplet of (310) is formed preferentially to the lower energy π, π^* triplet of (341). This also supports the view that the n, π^* triplet of (310) is kinetically formed and rearranges prior to any equilibration with the π, π^* excited state.

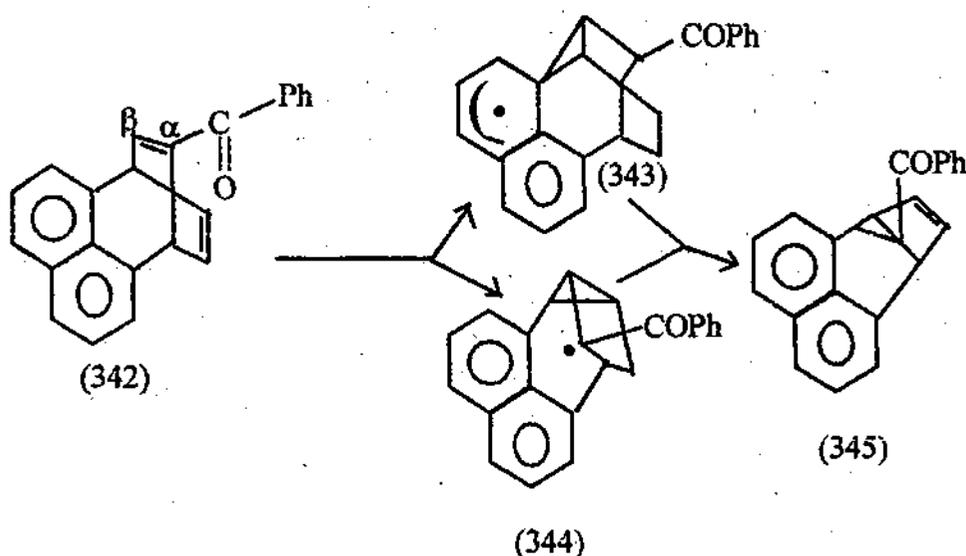


(340)

a= R_1 =Me, R_2 =Ph; b= R_1 =Me, R=*n*-MeOPh;c= R_1 =Bu, R_2 =Ph, d= R_1 = R_2 =Me;e = R_1 =Me, R_2 =2-naph.

Although this strengthens support for the involvement of the n, π^* excited state, proposed long ago, cannot rule out yet the possibility that n, π^* triplet of (310) is not reactive but thermally populates the higher-lying $^3\pi, \pi^*$ state after which the rearrangement occurs.

Schaffner and coworkers^{142,143} have carried out an interesting photoreaction of (342) giving further insight into this mechanistic aspect. This reaction is structurally related to the β, β' bonding process in (278) \longrightarrow (279) and afforded the photo product (345) which is formed via two competing rearrangement paths initiated by bridging from the olefinic β -carbon of the cross-conjugated ketone in (342) as depicted below



The phosphorescence spectrum of (342) is that of a 1,8-bridged naphthalene and possesses $E_p = 58.2$ KCal/mole. The quantum yield of the photorearrangement has been determined at different wave length as well as on sensitization with donors of different triplet energies between 61.9 to 68.9 KCal/mole. It has also been observed that all of these occurred at similar rates close to diffusion-limited in benzene $[(2.8-4.2) \times 10^9 \text{M}^{-1}\text{Sec}^{-1}]$. A nanosecond transient intermediate at room temperature has been demonstrated in laser flash experiments and *e s r* at 77K and IR spectroscopy in 77-294 K range exhibited two biradical intermediates (343) and (344). They have envisaged that the initial excitation leads to an upper singlet (S_2) π, π^* state which is followed by a highly efficient intersystem crossing to populate T_2 ($60 < E_p < 63$ KCal/mole) or by direct formation of biradicals with an efficiency similar to that from t_2 or

by both reaction pathways. Irradiation with 435 nm generates lowest-lying naphthalene triplet state. Reaction from this state or energy transfer from phenanthrene ($E_T=61.9$ KCal/mole) occurs with via thermal population of T_2 or separate inefficiency path. They also adduced evidence¹⁴⁴ to show that the rearrangement (342) \rightarrow (345) occurs also from ground state thermal process reversibly through competing stepwise and thermally allowed concerted processes.

CHAPTER - III

(Preparation and Photochemistry of Cross-Conjugated Cyclohexadienone Ring A of Friedalane Triterpene¹⁴⁹)

Introduction :

Light-induced molecular transformations of substrates possessing cyclohexadienone chromophore in general and 2,5-cyclohexadienone (also known as cross-conjugated cyclohexadienone) in particular, have been studied extensively. These photoreactions are facile and fascinating, but highly complex in nature. Often a plethora of products are obtained through a multistep process depending upon structural variations, substitution patterns, solvent polarities and different exciting wave lengths used. When a cross-conjugated cyclohexadienone is photolysed in nonpolar solvents such as dioxane or ether using exciting wave length of 254 nm, the principal product obtained is the bicyclo [3.1.0] hexen-3-one, a cyclopropyl ketone (also popularly known as a lumiprodukt). This lumiprodukt is itself photolabile and ultimately gives rise to several unsaturated ketones (2,4- and 2,5-cyclohexadienones) and phenols on prolonged irradiation. Lumiprodukt may not be obtained as the principal product if the exciting light used is of wave length ranging from 300 to 360 nm. Eventually, unsaturated ketones and phenols are main isolable photoproducts formed at the expense of the unstable lumiprodukt. The story does not end there. Interestingly, when irradiation is effected in acidic solution such as aqueous or glacial acetic acid lumiprodukt is not obtained, instead, the major photoproducts obtained are mixture of two hydroxy ketones, one 5/7 fused hydrazulene type and other spiro [4,5]decane type. Such extraordinary versatility, which is generally characteristic of compounds possessing the cyclohexadienone chromophore, renders the study of their photochemical behaviour attractive from the preparative as well as mechanistic view point.

When this versatile photoreaction is applied in the synthesis of natural products, the chemists are often confronted with a major problem. This is because most of the naturally occurring substances do not possess this inbuilt photoactive chromophore. This problem can be circumvented by introducing this photolabile moiety in a molecule by a sequence of reactions before a photoreaction is attempted. Following this strategy, therefore, the modern-day synthetic chemists have found a powerful tool in the adaptation of organic photochemistry for preparative purposes. Since this phototransformations have great synthetic potential, these have been intensely applied

for the partial and total synthesis of several fused-ring and spiro-cyclic naturally occurring sesquiterpenes^{149a,150} such as β -vetivone¹⁵¹, α' -vetispirene¹⁵², diterpene grayanotoxin II¹⁵³, unnatural 10α -steroid¹⁵⁴, 10α -testosterone acetate, aporphine alkaloid, boldine¹⁵⁵.

Since the application of this photoreaction in the triterpene natural product is scant, we have planned to apply this photoreaction for the synthesis of useful triterpene derivatives. A closer look at the structural feature present in triterpene reveals that because of the presence of 4,4,10-trimethyl ring A system (352) in triterpenes such as α -amyrin, β -amyrin and lupane series (Scheme-IV), the introduction of this chromophore in ring A is not feasible. In contrast, this can be introduced in ring A of friedelane triterpenes (353) having 4,5-dimethyl ring A system. Therefore, we, at first, have introduced this cross-conjugated cyclohexadienone moiety in friedelane by a sequence of reactions and applied phototransformation upon it. We have been motivated to undertake this work for several reasons : (1) some of the friedelene derivatives are biologically active¹⁵⁶, (2) no photoreaction has been reported on cross-conjugated cyclohexadienone ring A derivatives of friedelane triterpenes, (3) interesting and novel compounds obtained from this photolysis are difficult to prepare by conventional chemical methodology. Furthermore, the lead compound friedelin (354) can be easily obtained in good yield from cork waste, necessary for this type of multi step synthesis.

We have divided this work in three sections. First one describes the preparation of the photolabile key compound, the cross-conjugated cyclohexadienone ring A of friedelane, friedel 1(10), 3-dien-2-one (358) [SECTION - A] and the second one photolysis of the key compound (358) for preparation of lumiprodut (360) [SECTION-B] and the phenolic product (361) [SECTION-C].

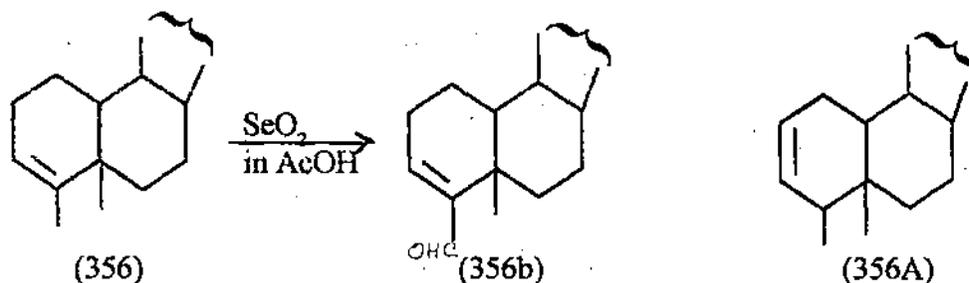
SECTION - A

(Preparation of the key compound (358) : Scheme - IV)

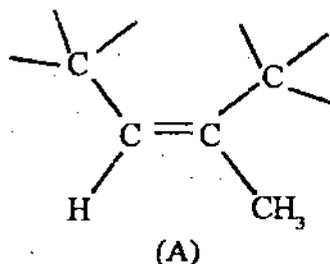
To achieve this preparation, we have used friedelin (354) as the lead compound. Cork waste provides a good number of substances of which the triterpene ketone friedelin is the chief constituent. Friedelane-3-one, friedelin (354), m.p. 260°-261°C (lit¹⁵⁷ m.p. 261-263°C) C₃₀H₅₀O, IR (nujol) 1705cm⁻¹ (C=O) (Fig.1) was abundantly obtained from the benzene extract of cork waste in a soxhlet apparatus for 20 hr. followed by purification through column chromatography (0.43% yield, based on dried cork waste). Sodium borohydride reduction of friedelin (354) in dioxane-methanol mixture at ambient temperature for 24 hr. afforded friedelan-3β-ol (Scheme-IV) (355) C₃₀H₅₂O, m.p. 282-284°C (lit¹⁵⁸ m.p. 283-285°C), IR (nujol) 3430cm⁻¹ (OH) (Fig. 2). Dehydration of this alcohol (355) with phosphoryl chloride in pyridine on steam-bath for 4 hr. gave an olefin⁴⁵⁹ C₃₀H₅₀, m.p. 265-266°C. IR spectrum displayed bands at 780 and 750 cm⁻¹ indicating the presence of a trisubstituted double bond (Fig. 3). Because of its low solubility ¹H NMR could not be recorded. Its mass spectrum (Fig.4) showed strong molecular ion peak at m/z 410(M⁺), but did not register a peak m/z 342 (M⁺-68). The latter peak has been ascribed to the retro Diels-Alder fragmentation of ring A of a Δ²-hydrocarbon¹⁷⁸. Thus, the absence of a peak at m/z 342 gave a strong evidence that the hydrocarbon was a Δ³-hydrocarbon(356) and not a Δ²-hydrocarbon (356A). In order to provide further evidence for the presence of Δ³- double bond, SeO₂ oxidation of the olefin was undertaken. SeO₂ oxidation of (356) in acetic acid afforded the compound friedel-3-en-23-al (356b) m.p. 265°C, UV (Fig.5) showed the λ_{max} at 227nm, 330 nm characteristic for α,β-unsaturated aldehyde. IR (Fig.6) showed the bands at 2720, 1680, 1640, 1420, 830 cm⁻¹ for α,β-unsaturated aldehyde. ¹H NMR (Fig. 7) spectrum of this derivative could be readily taken in CDCl₃ solution. Besides showing signals for 7 tertiary methyl groups at saturated carbons between δ 0.74 -1.14, it showed signals at

δ 6.52 (1H, m, $-\text{CH}=\underset{\text{C}}{\underset{|}{\text{C}}}-\text{CHO}$), δ 9.24 (1H, s, $-\text{CH}=\underset{\text{C}}{\underset{|}{\text{C}}}-\overset{\text{O}}{\parallel}{\text{C}}-\text{H}$). Thus, the Δ³

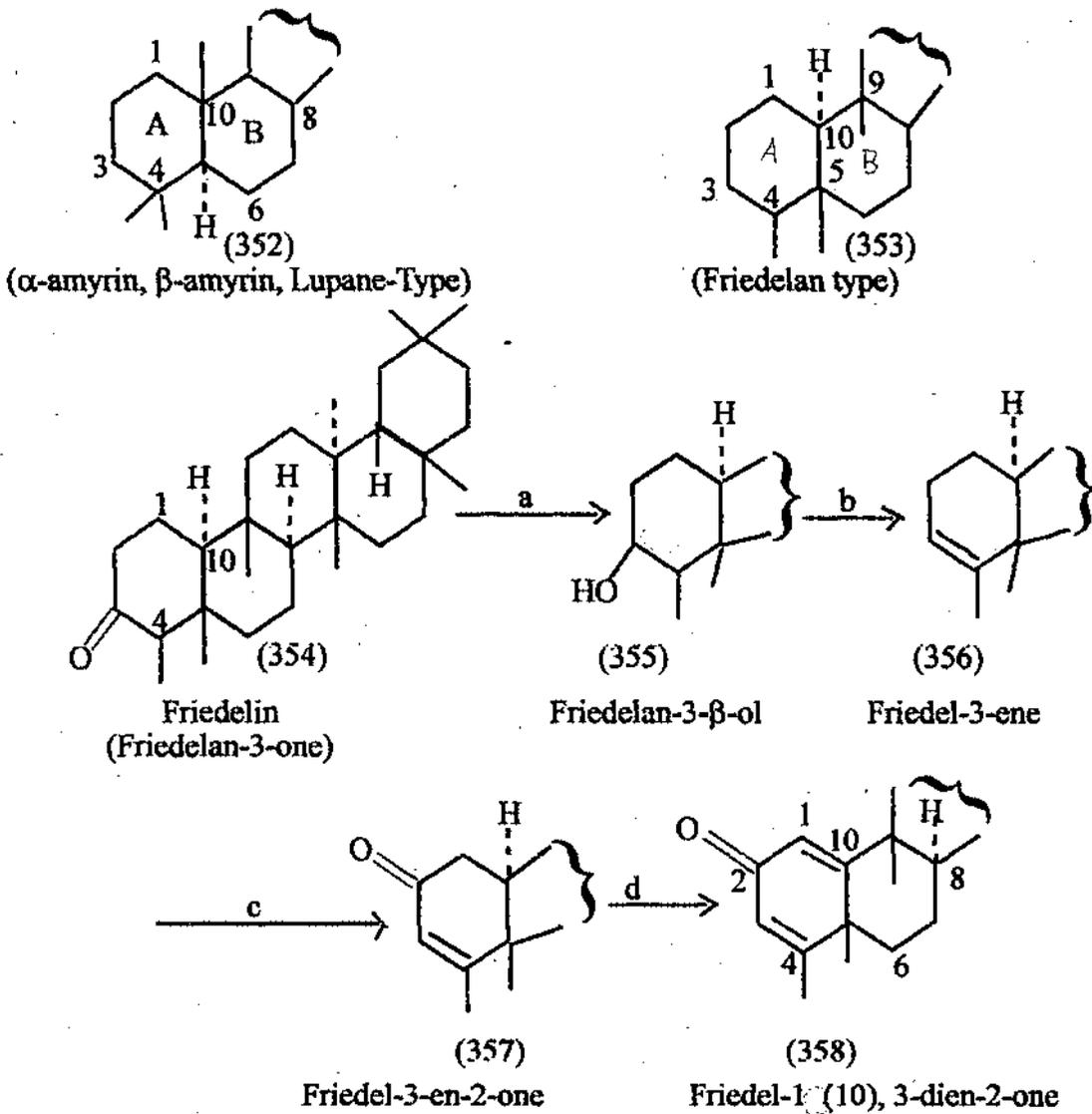
- structure of the olefin (356) was assigned on a firm basis.



The olefin (356) was then subjected to oxidation with sodium dichromate in benzene - acetic acid (1 : 1) at reflux temperature for 4 hr. to afford a substance (60% yield) which was crystallised from ethyl acetate. The spectral measurements enabled us to deduce its structure as the conjugated ketone, friedel-3-en-2-one (357), $C_{30}H_{48}O$, m.p. 287-289°C (lit¹⁵⁸ m.p. 291-292°C). Its UV spectrum (Fig. 8) showed absorption maximum at 238 nm (ϵ 7600) in methanol, IR (nujol) (Fig. 9) exhibited bands for cyclohexenone chromophore at 1658, 1620, 850, 720 cm^{-1} . Under closer examination of ¹H NMR (300 MHz $CDCl_3$) spectrum a splitting due to a small allylic coupling¹⁶⁰ indicates the presence of a system (A) in (357). The spectrum (Fig. 10) gave signals for a vinyl proton at δ 5.65 (d, $J \sim 1$ Hz, 1H), vinyl methyl at 1.84 (d, $J \sim 1$ Hz, 3H, CH_3), besides seven saturated tertiary methyls between 0.91 and 1.14. ¹³C NMR spectrum (75 MHz, $CDCl_3$) (Fig. 11) recorded peaks at δ 200.62 (C = O), two olefinic carbons at 172.06 and 125.32. In addition, signals for 27 saturated carbon atoms occurred between δ 55.60 and 17.62 [Fig. 11A, expanded (δ 16 to 57)].



After the introduction of enone chromophore system in (357) we envisaged the introduction of another double bond between C-1 and C-10 which would enable us to construct cross-conjugated chromophore system. For this purpose, we have used the mild oxidant dichlorodicyano benzoquinone (DDQ) in neutral medium, dioxane, under nitrogen blanket at reflux ^{temperature} for 2.5 hr. After purification through the column chromatography a white compound was obtained. It was crystallised from ethyl acetate to provide needle (358), $C_{30}H_{46}O$, m.p. 280-281°C. Combination of spectral data enabled us to deduce its cross-conjugated cyclohexadienone structure (358). It showed UV maximum (MeOH) (Fig. 12) at 246 nm (ϵ 17150) and IR (nujol) bands (Fig. 13) at 1646, 1610, 1584 and 890 cm^{-1} . 1H NMR (300 MHz, $CDCl_3$) (Fig. 14) exhibited resonances for 7 saturated tertiary methyl groups between δ 0.92 to 1.25, one vinyl methyl at 1.95 and two olefinic protons at 6.11 and 6.02. A closer look at the spectrum showed that the olefinic proton at δ 6.11 appeared as a doublet with small splitting ($J \sim 1$) due to allylic coupling with the vinyl methyl group at δ 1.95 ($J \sim 1$) and the other olefinic proton at δ 6.02 as singlet [Fig. 14A, expanded (δ 0.8 to 2.25)]. These spectral observations enabled us to assign singlet peak at 6.02 due to olefinic proton at C - 3 and the vinyl methyl at C - 4. Thus, the cross-conjugated chromophore system in (358) has been established and this key compound has been assigned structure, friedel - 1(10), 3-dien-2-one (358). This has been further substantiated by ^{13}C NMR spectrum (Fig. 15) which showed resonances at δ 206 (C = O), 177.50, 167.29, 125.68 and 121.86 (four olefinic carbons) and 25 - sp^3 carbons between 50.16 and 17.73 [Fig. 15 A, expanded (δ 15 to 55)]. EIMS (Fig. 16) registered molecular ion peak at m/z 422

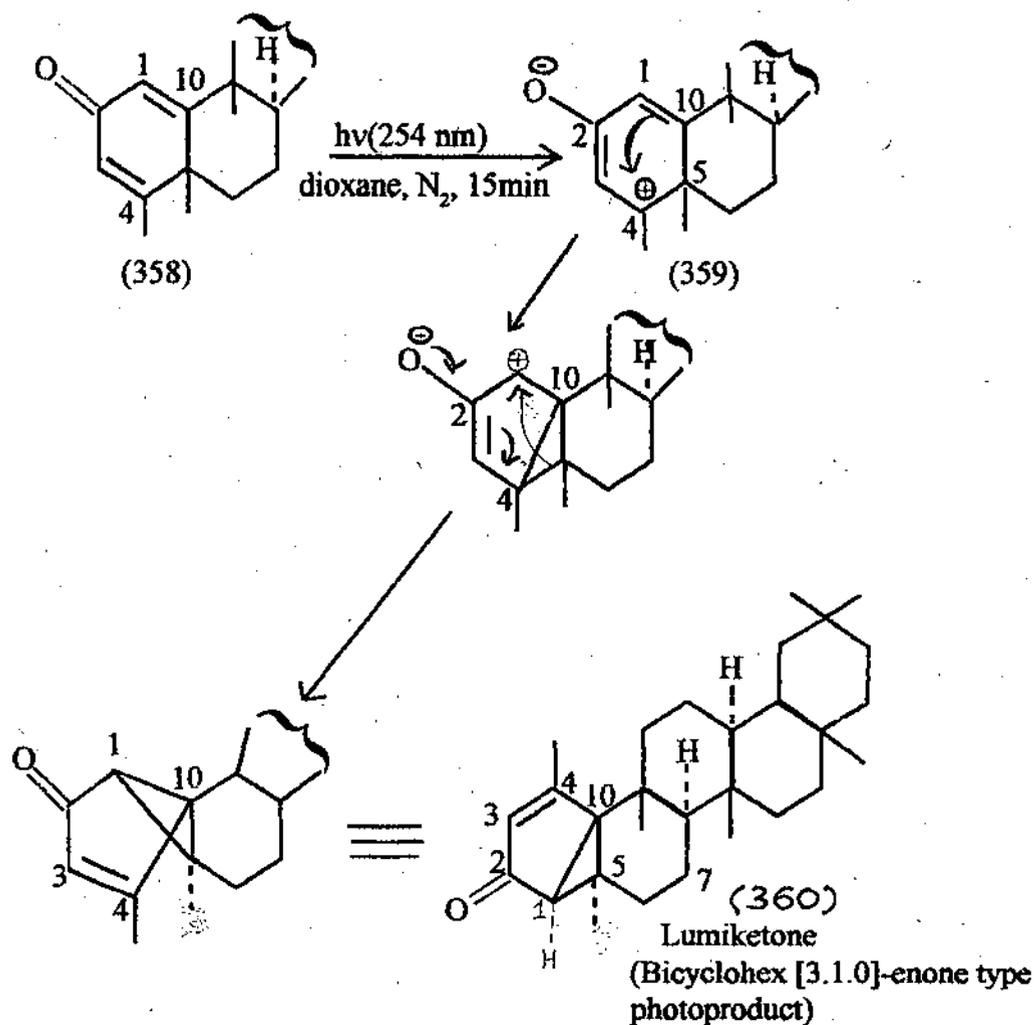
Scheme - IV

Reagents and Conditions : (a) NaBH_4 , dioxane-methanol (2:1), r.t., 24 hr; (b) POCl_3 , Pyridine, steam bath, 4 hr; (c) $\text{Na}_2\text{Cr}_2\text{O}_7$, AcOH-PhH (1:1), reflux, 4 hr; (d) DDQ, dioxane, N_2 , reflux, 2.5 hr.

[Synthesis of the key compound, friedel-1(10), 3-dien-2-one (358) from friedelin (354)]

(M^+ , 48%) and other important fragmented ions at 407 ($M^+ - CH_3$), 298, 286, 271, 229, 203, 182, 175, 135, 95 and 81. Circular dichroism (CD) spectrum in dioxane (Fig. 17) recorded maxima one positive at 260 nm ($\Delta\epsilon +10.4$) and other negative at 239 nm ($\Delta\epsilon - 7.7$). This too, provides additional information regarding the proposed structure of (358).

Scheme - V



[Conversion of the key intermediate (358) to the lumiketone photoproduct (360)]

Section - B

(Formation and characterisation of the Lumiprodukt (360)) : Scheme - V)

The cross-conjugated cyclohexadienone (358) that synthesised by a sequence of reactions, was photolysed with low pressure mercury lamp (more than 95% of emitted wavelengths 254 nm) in dry dioxane at ambient temperature under nitrogen blanket (Scheme-V). Initially, we carried out irradiation for 15 min. Experience gathered over the past several years by different groups inferred that irradiation for a short time in nonnucleophilic neutral solvent in an inert atmosphere is the most appropriate condition for lumiprodukt formation. Its yield considerably increases by using irradiation at 254 nm. This is due to much lower UV absorption of lumiprodukt at this wavelength in comparison with the starting dienone and hence possibility of further conversion of primary photolabile lumiprodukt to secondary photoprodukt(s) is considerably reduced. The progress of the photoreaction was monitored by TLC and we noticed that short irradiation for approximately 15 min. gave almost single product, lumiketone (360). From column chromatography of the reaction mixture, using pet ether-ethyl acetate (4:1) as eluent a colourless compound was obtained which on crystallisation from ethyl acetate afforded fine needles in 74% yield (360) $C_{30}H_{46}O$ m.p. 305°C. Bicyclo [3.1.0]-hexenone structure of the lumiketone (360) was deduced by a combination of physical techniques.

UV spectrum (Fig. 18) (MeOH) showed absorption maximum at 241 nm (ϵ 8100) for conjugated ketone, IR (nujol) (Fig. 19) at 1675, 1595 cm^{-1} for cyclopentenone system. A detailed analysis of 1H NMR (300 MHz, $CDCl_3$) (Fig. 20) showed resonances at δ 5.65 (d, $J \sim 1$, 1H) for olefinic proton and at 2.14 (d, $J \sim 1$, 3H) for vinyl methyl group and between 0.92 to 1.15 for seven saturated tertiary methyls [Fig. 20A, expanded (δ 0.6 to 2.4)]. Thus, here also we have noted a small splitting due to allylic methyl coupling indicating the maintenance of the structural feature (A) as in (357) and (358). ^{13}C NMR (75 MHz, $CHCl_3$) (Fig. 21) revealed resonances at δ 206 (C = O), two olefinic carbons at 175 and 133, besides 27 sp^3 carbons between 58.80 and 16.84 [Fig. 21A, expanded (δ 25 to 60)]. EIMS (Fig. 22) registered molecular ion peak at m/z 422 (M^+ , 73%) and other important fragmented ions at 407 ($M^+ - CH_3$), 298, 218, 204, 175, 161, 149, 136, 123, 109 and 95.

Elemental composition coupled with mass spectral measurement shows that it is isomeric with the starting dienone and must therefore result from an intramolecular photorearrangement.

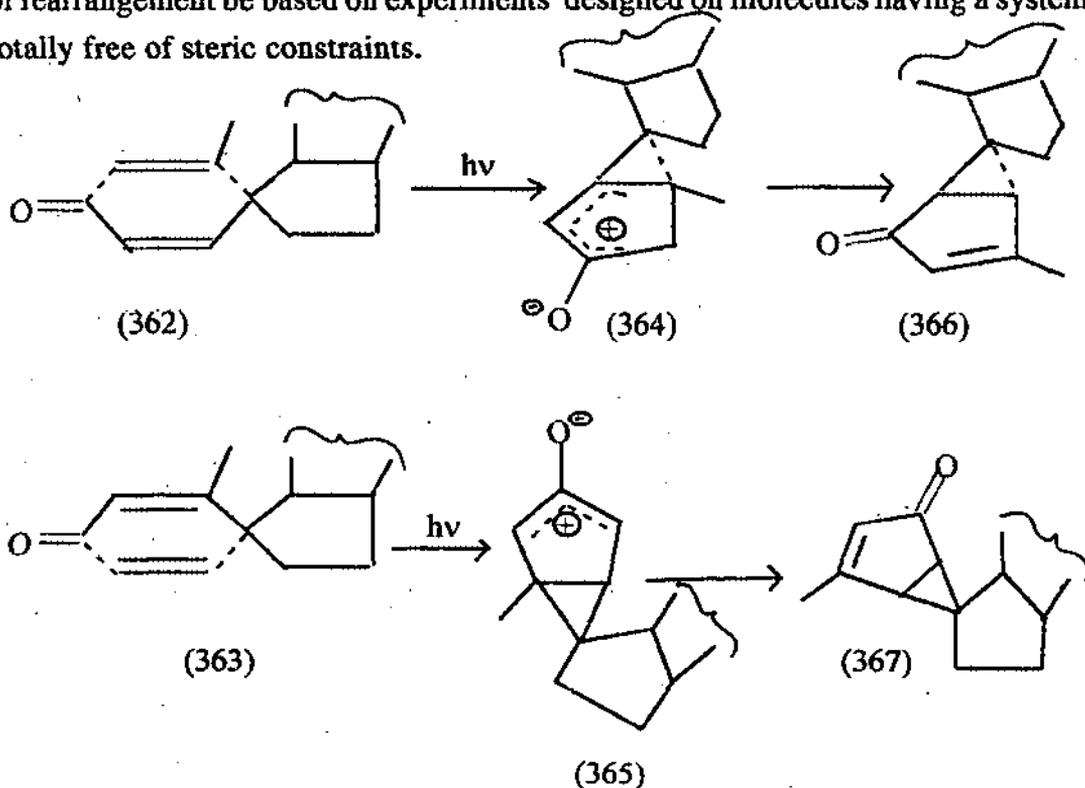
It has long been worked out by several groups that 2,5-cyclohexadienone \longrightarrow bicyclohexenone photorearrangement occurs from an excited triplet state. We have also observed that this photoreaction has been sensitized by the triplet state sensitizer benzophenone and quenched by the triplet state quencher naphthalene. We have noted it carefully that this phototransformation is efficiently quenched even by a small concentration of the quencher naphthalene. This led us also to infer that this photoreaction occurs from excited triplet manifold. In line with observation previously made, we too noticed that it is a very efficient photoreaction. The quantum efficiency for lumiprotectin formation was measured by using standard procedure of ferri-oxalate actinometry and showed $\phi = 0.77$.

Stereochemistry of Lumiketone (360) :

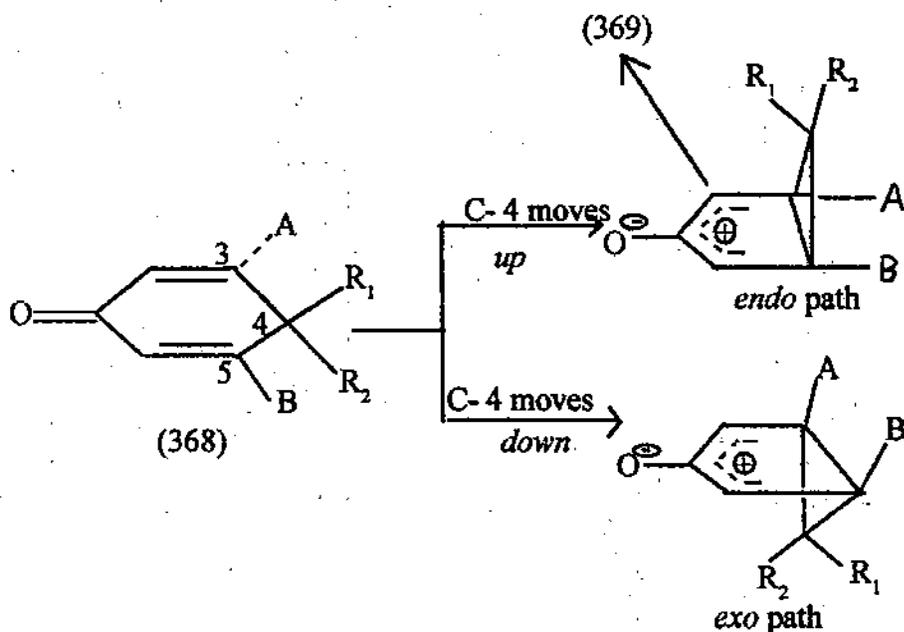
Since we have not yet touched upon the stereochemistry of lumiketone formation, here we wish to give first a brief review of lumiketone stereochemistry and then to extend it for discussion of our lumiketone (360) stereochemistry. Chronological events that have been postulated for the photochemical conversion of 2,5-cyclohexadienone to bicyclohexenone (lumiketone) make the determination of stereochemical course of this unique rearrangement quite complicated. β , β' -bonding (3,5 bonding) occurring after the initial excitation leading to substantial puckering of the cyclohexadienone ring system, the configurational fate of the migrating carbon in the subsequent [1,4] sigmatropic shift and the direction in which this migration proceeds are all to be taken into consideration before a clear picture concerning the stereochemistry emerges.

Schaffner, Jeger and coworkers^{64,162} carried out an extensive study on the steroid 2,5-cyclohexadienones \longrightarrow lumiketone photorearrangement and proposed an inversion of configuration when both modes were *a priori* possible. Two spirodienones (362) and (363) gave lumiketones (366) and (367), respectively and the proposition was made that the reaction occurs via intermediates (364) and (365). If the absolute configuration of the dienones and lumiketones as depicted here are correct, the rearrangement must have occurred with inversion of configuration i.e. *endo* group in the zwitterion intermediate remains *endo* in the final product. They have advanced complex arguments based in part on the chemical relationship

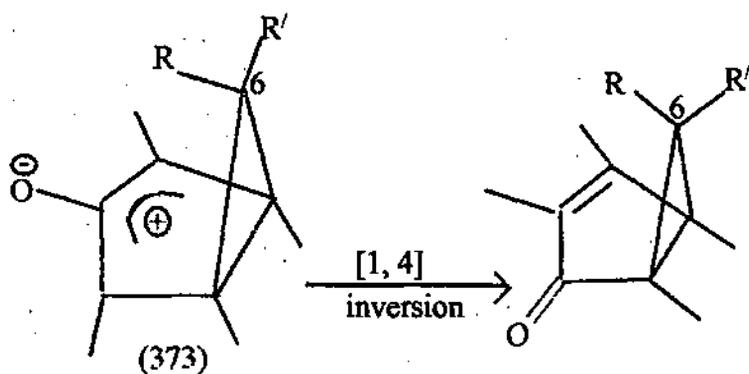
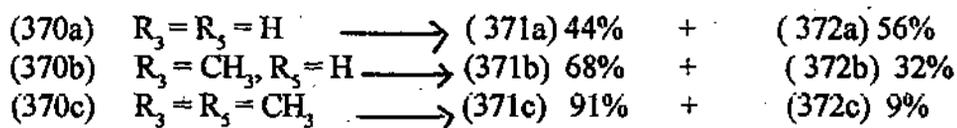
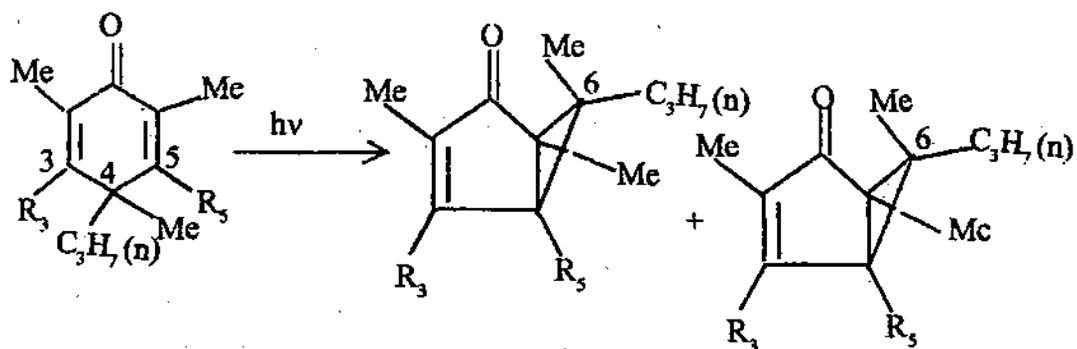
of these molecules to others of known absolute configuration. Since these molecules are rigid and constrained, the determination of absolute configuration of this type of rearrangement be based on experiments designed on molecules having a system totally free of steric constraints.



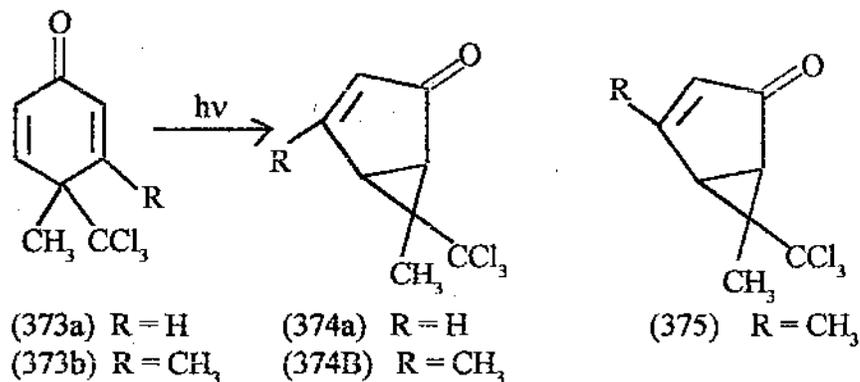
Rodgers and Hart¹⁶³ observed that irradiation of monocyclic, nonrigid (strain-free) dienones of the type (368) with different alkyl groups at C-4 invariably leads to predominant formation of lumiketones with bulkier alkyl groups in the *endo* orientation (369). This tendency becomes more pronounced as the steric requirements of the substituents at C-3 and C-5 in (368) increase. This has been explained in the following way. The conversion of 2,5-cyclohexadienone to dipolar ion proceeds from a nearly planar geometry to that of fused bicyclo [3.1.0] ring system. In this conversion, C-4 can move either *up* or *down*. If it moves *up*, placing R_1 *endo*, then at some stage R_2 must pass by groups A and B on C-3 and C-5. The situation becomes opposite of C-4 moves *down*. When repulsions between R_1 and/or R_2 on C-4 and A and/or B are significant, prediction may be made that if R_1 is larger than R_2 , the product with R_1 *endo* will predominate.



To test their proposal Rodgers¹⁶³ and Hart carried out irradiation of 4-propyl-4-methyl-2,5-cyclohexadienones in methanol with 2537A° lamp. The bicyclic ketones were separated by VPC and identified by spectroscopic techniques UV, IR and NMR. The increase in yield of the product with larger (propyl) group *endo* as hydrogens at C-3 and C-5 in (370) are successively replaced by methyls is consistent with their postulate that the stereochemistry can be controlled by steric factors. Thus, the direction of ring puckering, induced at the outset of 3,5-bonding, seems to be predominantly steric in the absence of other perturbations in the dienone system and increased steric requirements of the substituents at C-3 and C-5 directs the bulkier C-4 substituent in the *endo* orientation. This rationalisation, however, is based on the assumption that the position of substituents at C-6 (C-4 of the starting dienone) is unchanged in the subsequent [1,4] sigmatropic shift leading to the lumiketone. This means that the product stereochemistry is determined in the first stage of the reaction. In the ground state rearrangement of the dipolar ion (373)¹⁶⁴, the [1,4] sigmatropic shift is predicted to occur with inversion of configuration at C-6,^{165,166} maintaining the *exo-endo* orientation of the substituents at C-6 on proceeding from the intermediate (373) to the lumiketone, but direct experimental evidence providing unequivocally that the light-induced rearrangement proceeds in the same manner, has not yet been obtained. However, circumstantial evidence to this effect is available¹⁶⁷.

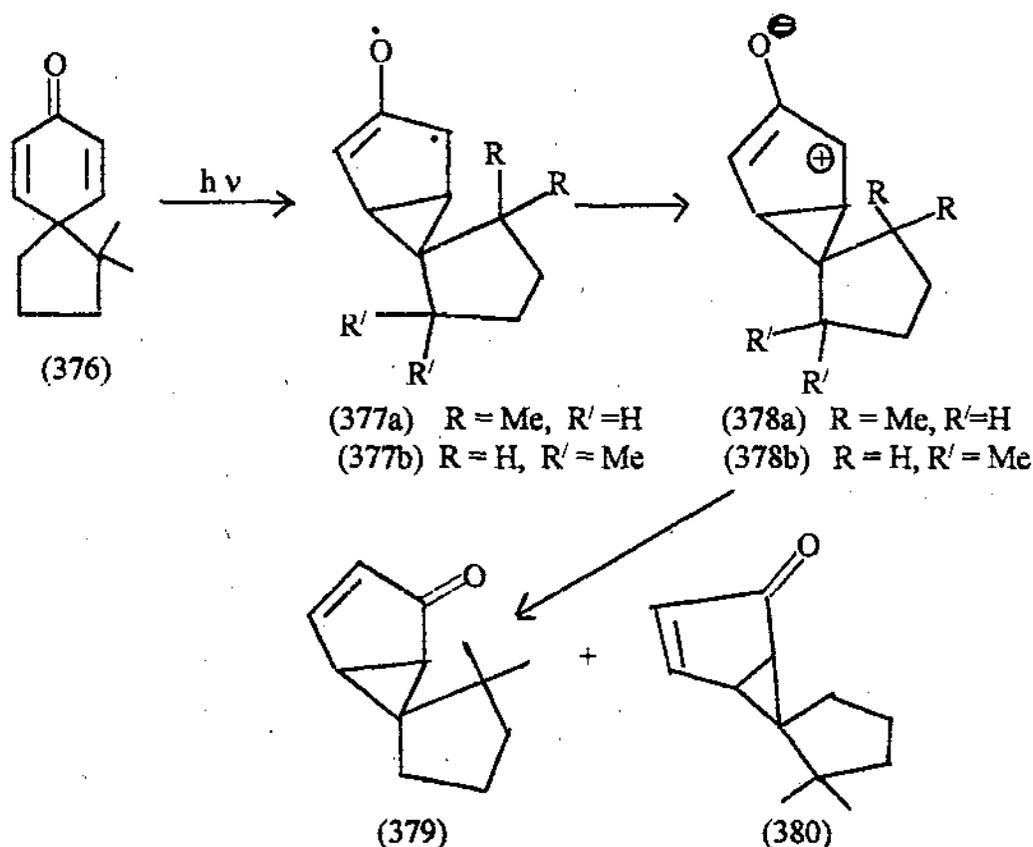


In order to examine the electronic effect on the stereochemical course of this phototransformation, Schuster and Patel¹⁶⁸ have initially conducted irradiation of a strain-free monocyclic system with a strong electron-withdrawing CCl_3 group at C-4, 4-methyl-4-trichloromethyl-2,5-cyclohexadien-1-one (373a). The sole lumiketone formed was (374a) having the CCl_3 group in the *exo* orientation. Schuster and Prabhu¹⁶⁹ later photolysed 3,4-dimethyl-4-trichloromethyl-2,5-cyclohexadien-1-one (373b), a C-3 methyl homologue of (373a), in a number of solvents. The effects on the photochemistry produced by introduction of the additional group are varied and pronounced. In *t*-butyl alcohol, both epimeric lumiketones (374b) and (375) were formed in a ratio of about 5 : 1. Structure and stereochemistry have been deduced from spectral data, hydrogenation experiments and an X-ray crystal analysis and was shown that the major product (374b) has the CCl_3 group in *exo* orientation.



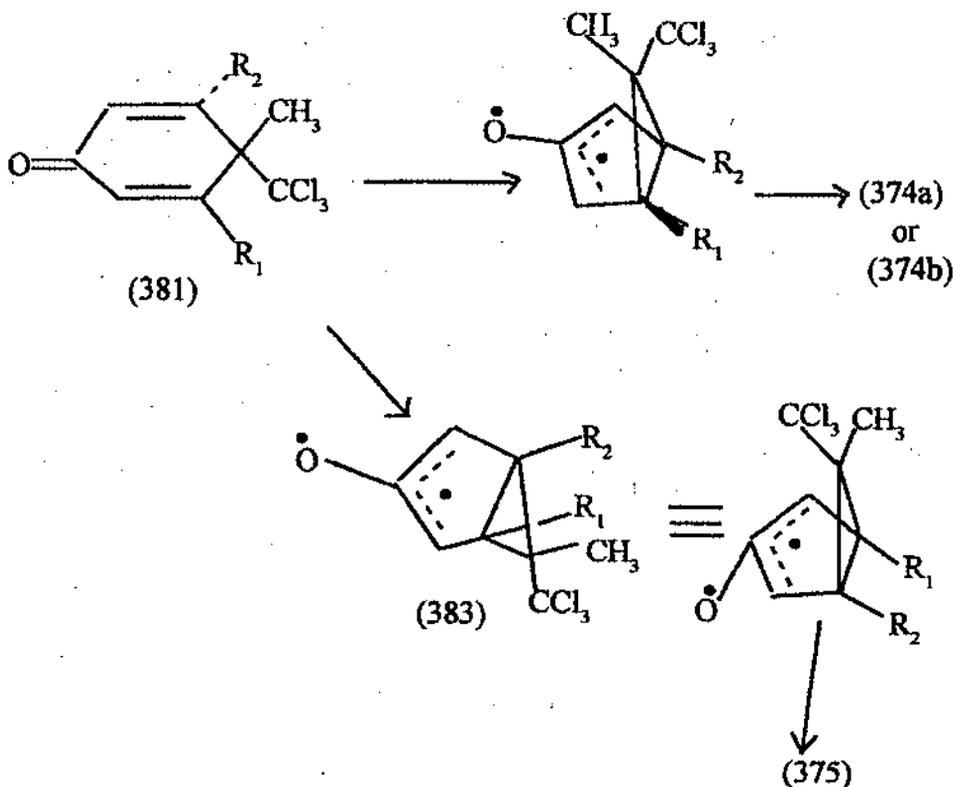
Schuster and Currah¹⁷⁰ have also conducted irradiation of Spirodienone (376) without having strain or unusual electronic effects to complicate interpretation. Isomeric spiro lumiketones (379) and (380) have been obtained. Interestingly, stereoisomeric 3,5-bonded intermediates (377a and 377b) and dipolar ions (378a and 378b) are possible in the generation of lumiketones. The final step in the lumiketone generation is a sigmatropic change of order [1,4] which could occur in two distinct stereochemical modes. The intermediate (378b) could rearrange concertedly to lumiketone (379) by a pivot mechanism with retention of configuration at the migrating spiro carbon atom. Bond formation, on the other hand, could occur with inversion of configuration at the

spiro carbon atom leading (378b) to (380). The latter stereochemical mode is predicted for concerted rearrangement of the ground state zwitterion¹⁷¹ and inversion of configuration has indeed been noted in several thermal [1,4] sigmatropic rearrangement of systems analogous to (378)¹⁷²⁻¹⁷⁴. Mention may be made in this context that rearrangement by two successive 1,2-alkyl shifts¹⁷¹ can also lead to same stereochemical result.



With a view to investigating the effect of electron-rich group, Schuster and Pravu¹⁶⁹ conducted irradiation of generalised model cyclohexadienone (381) containing CCl_3 substituent at C-4. The intermediate (382) (CCl_3 , *exo*) or (383) (CCl_3 , *endo*) results by either *upward* or *downward* movement respectively, of C-4 by disrotatory ring closure with formation of 3,5-bond. The *downward* motion to give (383) is favoured by steric factors because this avoids interaction of flanking substituents at C-3 and C-5 with bulky CCl_3 group. However, this same motion brings the electron-rich CCl_3 ,

group close to the dienone π system introducing coulombic charge repulsion. In the extreme situation when (383) is fully formed, an extensive repulsion between the nearly parallel CCl_3 , and $>\text{C}=\text{O}$ dipoles occurs. Thus, the formation of (383) is electronically unfavourable although sterically favoured, compared with the formation of (382). The formation of exclusive *exo* isomer (374a) from dienone (373a) indicates only one mode of disrotatory ring closure takes place, as suggested by Rodgers and Hart¹⁶³. Hence the electronic effects dominate the reaction in this system. In case of (373b) where only one methyl group has been introduced, electronic effects are hardly unchanged from those in (373a), but the steric effects operate against the formation of (382). Here, competitive formation of both intermediates (382) and (383) with (382) still in excess takes place. Thus, it seems that there is a subtle balance of steric and electronic effect. Products resulting from (383) appears to occur in substantial amount in polar solvents where steric effect can exert a more prominent role as Coulombic interactions can be reduced to some extent due to solvation. Other electron-withdrawing groups such as CF_3 , CN , CO_2R can exert the same electronic effects¹⁶⁹.



Thus, it appears that stereochemical course of this photoreaction is quite complicated and depends, particularly in a strain-free nonrigid system such as monocyclic or of similar type, upon steric and electronic effects. Besides, polarity of a solvent which exerts its influence by solvation, is also a factor of considerable importance.

Ours is a system which is pentacyclic triterpenoid friedelane, and is, consequently, much constrained and rigid in nature comparable to tetracyclic steroid system. Although it has not yet been proved conclusively¹⁷⁵ that cyclohexadienone \longrightarrow lumiketone rearrangement occurs mandatorily by inversion of configuration at the migrating carbon atom, Schaffner and coworkers¹⁷⁵ have produced extensive data including circular dichroism spectroscopic measurements¹⁷⁷ to establish that in rigid system such as steroid inversion of configuration takes place.

CD Study of the Lumiproduct (360) :

Circular dichroism (CD) arising from differential absorption of left and right circularly polarised radiation, is an important technique for the study of chiral geometries and chirally discriminating interactions in asymmetric substances and biomolecules. This CD technique has been applied by Schaffner and Snaatzke to study stereochemistry of lumiproduct formation in steroids. In order to learn more about stereo-chemistry, we have measured CD spectra of the cross-conjugated dienone (358) and its lumiproduct (360). (358) (Fig. 17) showed in dioxane +ve *Cotton Effect* at 260 nm ($\Delta\epsilon +10.4$) and a -ve *Cotton Effect* at 239 nm ($\Delta\epsilon -7.7$), while (360) in dioxane (Fig. 23) exhibited +ve *Cotton Effect* at 353 nm ($\Delta\epsilon +3.8$), negative one at 271 nm ($\Delta\epsilon -10.4$) and a positive one at 237 nm ($\Delta\epsilon +11.5$).

CD spectral change associated with conversion of steroid cross-conjugated dienones to lumiketone photoproducts bears a resemblance with that of triterpenoid friedelan dienone (358) to the lumiketone (360) photoconversion. This observation coupled with general mechanistic considerations established on a firm basis, led us to propose the stereostructure (360) for the lumiproduct as depicted in the scheme-(V) with inversion of configuration at the migrating carbon atom.

Further confirmation of the stereostructure rests on X-ray crystal structure determination. Despite our best effort to develop suitable crystals, necessary for crystallographic study, from a number of single as well as mixed solvents, we have been unsuccessful. Hence, further study of the stereostructure of (360) could not be undertaken.

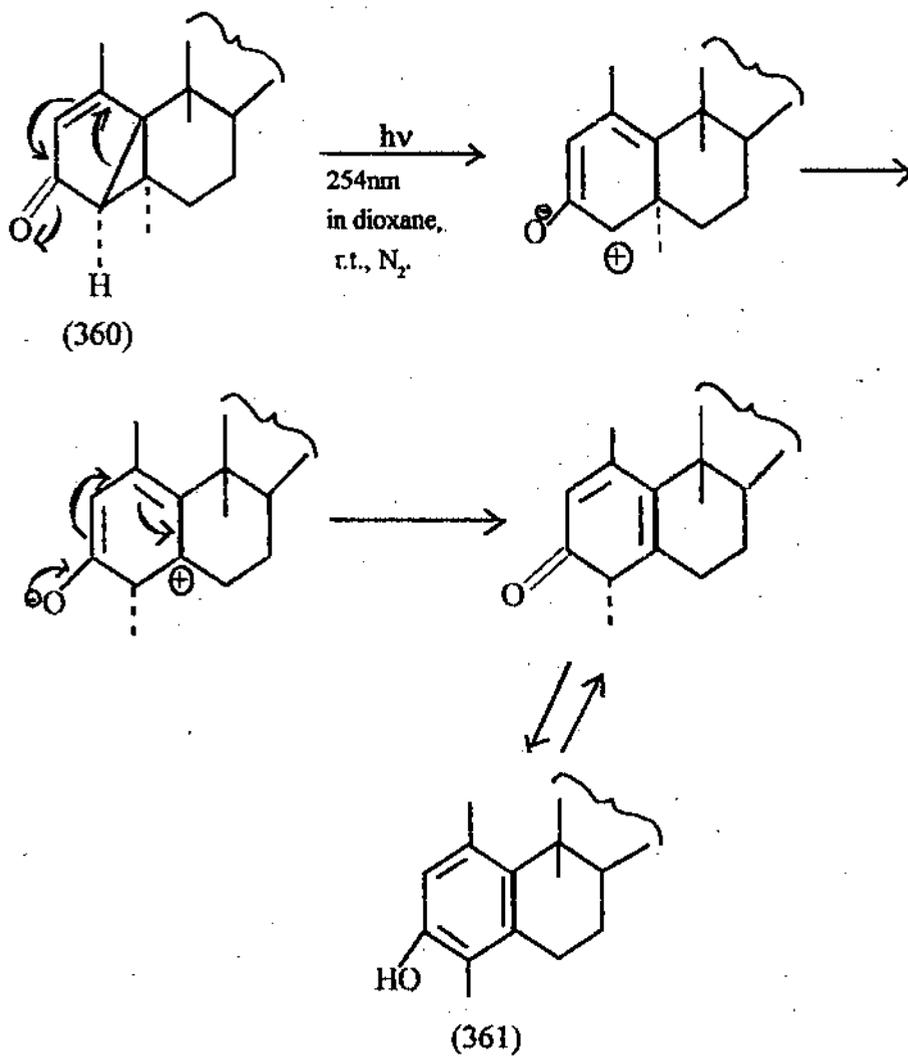
Section - C

(Isolation and Characterisation of the Phenolic Product (361) : Scheme-VI)

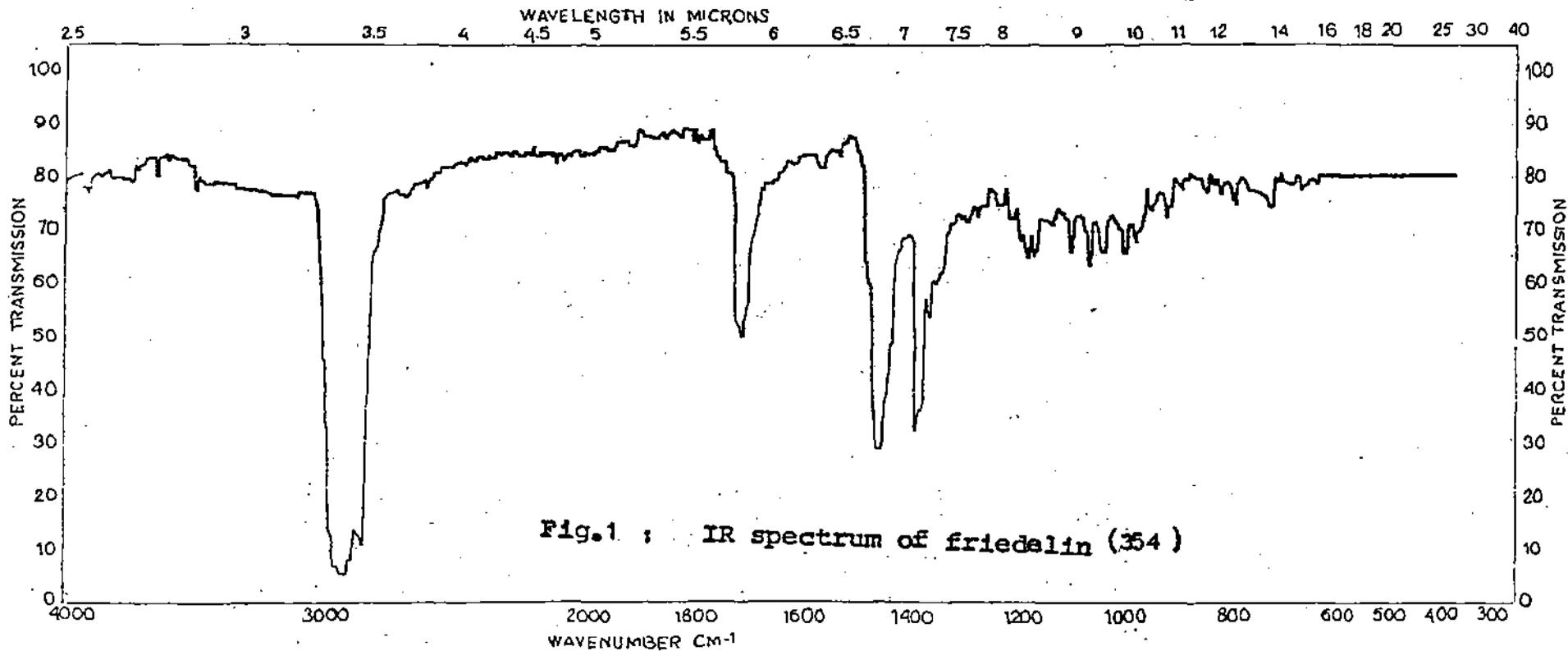
When this photoreaction was carefully monitored by thin layer chromatography it was noticed that during the first phase of reaction (less than 15 min.) only single spot of lumiprodut (360) [$R_f = 0.63$, EtOAc : $C_6H_6(1:9)$] described above, appeared; but on prolonged irradiation (more than 15 min.) a second spot [$R_f = 0.80$, EtOAc : $C_6H_6(1:9)$] made its appearance, which we have identified as phenol (361) described below. It has also been observed that the spot of phenol (361) became more intense at the expense of the lumiprodut (360) which is eventually reduced in intensity. Besides, several other low intensity spots were also detected making the whole reaction more complicated.

Since it is well known that in many cases phenol is the ultimate product of cross-conjugated cyclohexadienone photochemistry formed via lumiprodut, it occurred to us that our phenol (361) could be formed as a stable secondary product via the primary lumiprodut (360). This proposition was proved correct when we found that the isolated lumiketone (360) on photolysis under the same irradiation conditions afforded the phenol (361). Consequently, we have advanced the mechanism of its formation as shown in the Scheme - VI.

The irradiated material was subjected to silica gel column chromatography. After a forerun of tarry material pet. ether- ethyl acetate (4:1) eluted a white solid which on crystallisation from ethyl acetate yielded needles m.p. 198°C. It showed absorption maximum at 282 nm (ϵ 2250) (Fig. 24) and a strong IR (Fig. 25) band at 3320 cm^{-1} indicative of OH group. The mass spectrum (Fig. 26) recorded the molecular ion M^+ at 422 m/z showing that (361) is isomeric with the lumiprodut (360) and results from intramolecular photorearrangement. Further support for molecular formulation as $C_{30}H_{46}O$ came from an accurate mass measurement in the high-resolution mass spectrum (HRMS, M^+ observed m/z 422.2501, calculated for $C_{30}H_{46}O$ m/z 422.2508). Based on already established mechanistic path of lumiketone \longrightarrow phenol rearrangement coupled with spectral measurements we have assigned most plausible structure (361) to the phenol. Because of paucity of the material we were unable to record its NMR spectrum. Consequently, the structure could not be ascertained on a firm basis.

Scheme -VI

[Formation of Phenol (361) from Lumiprodukt (360)]



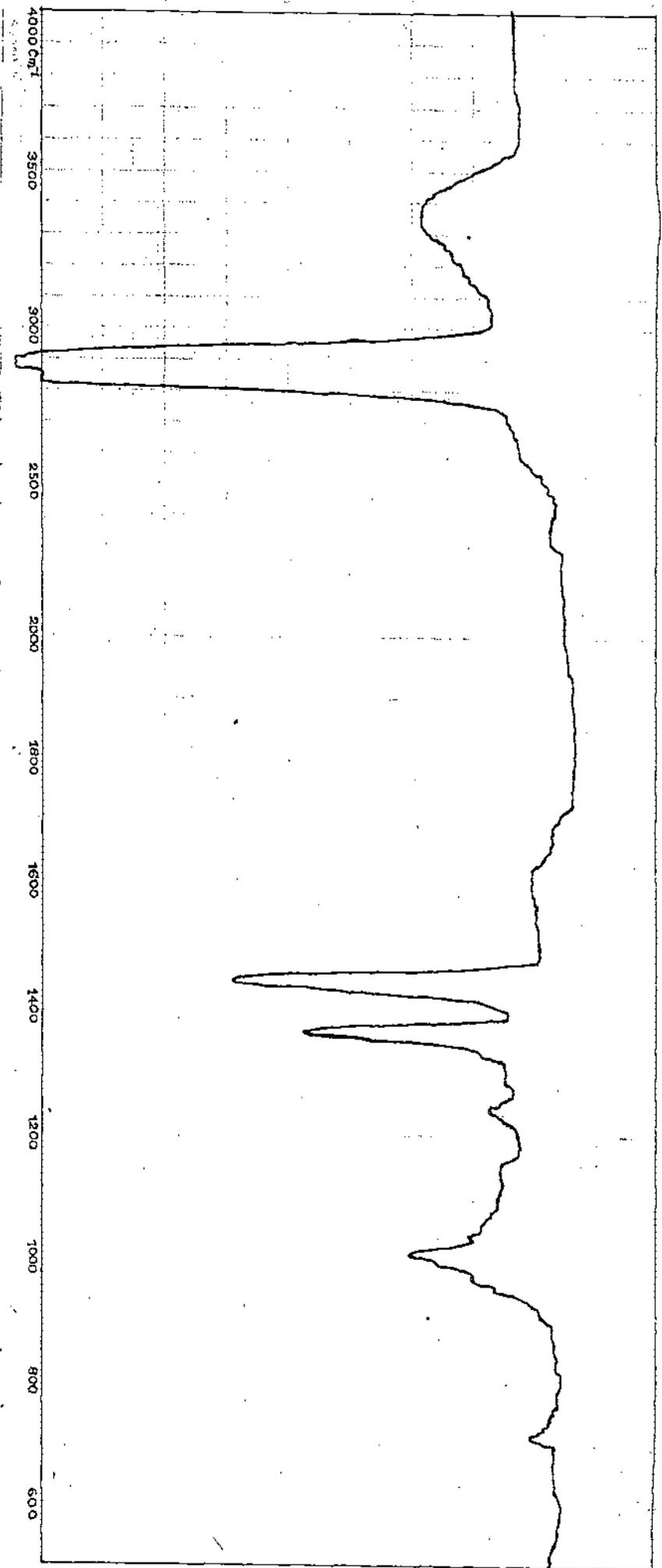


Fig.2 : IR spectrum of Friedel-Crafts alkylation product - 3/3 - 01 (355)

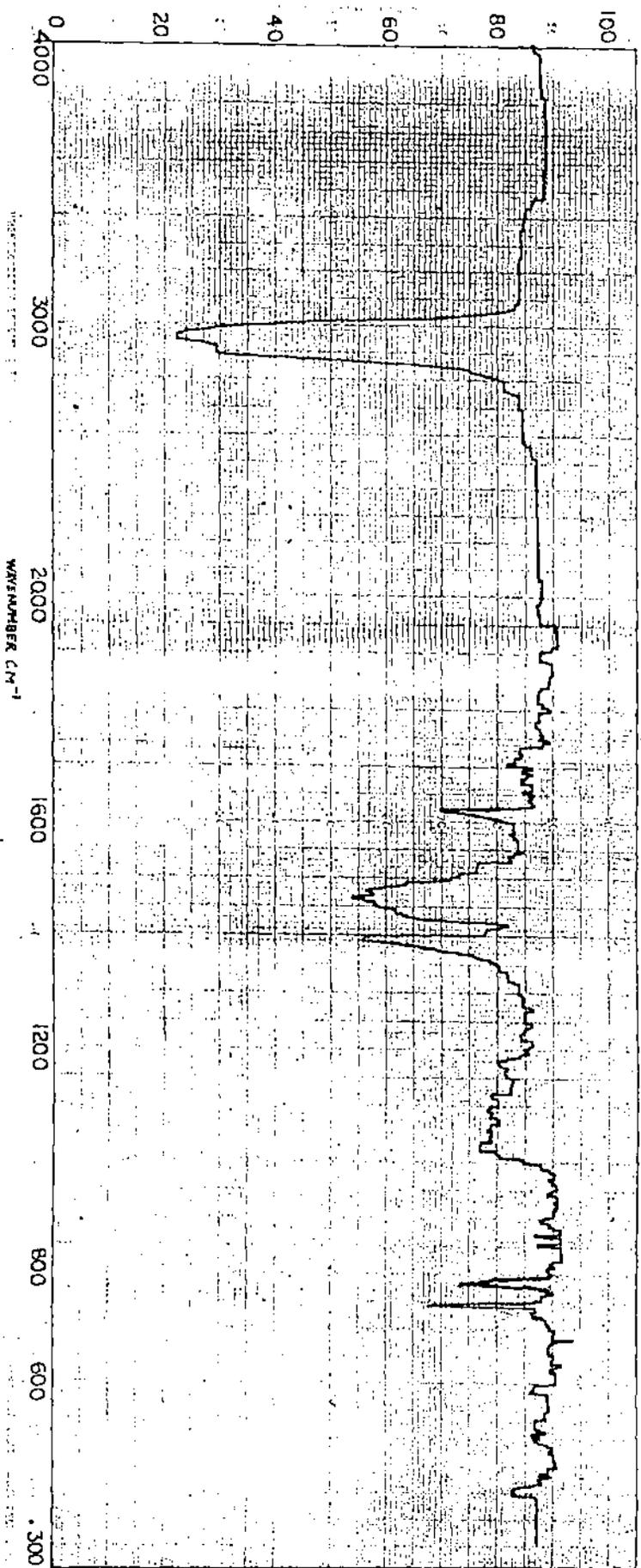


Fig. 3 : IR spectrum of Friedel-Crafts catalyst (356)

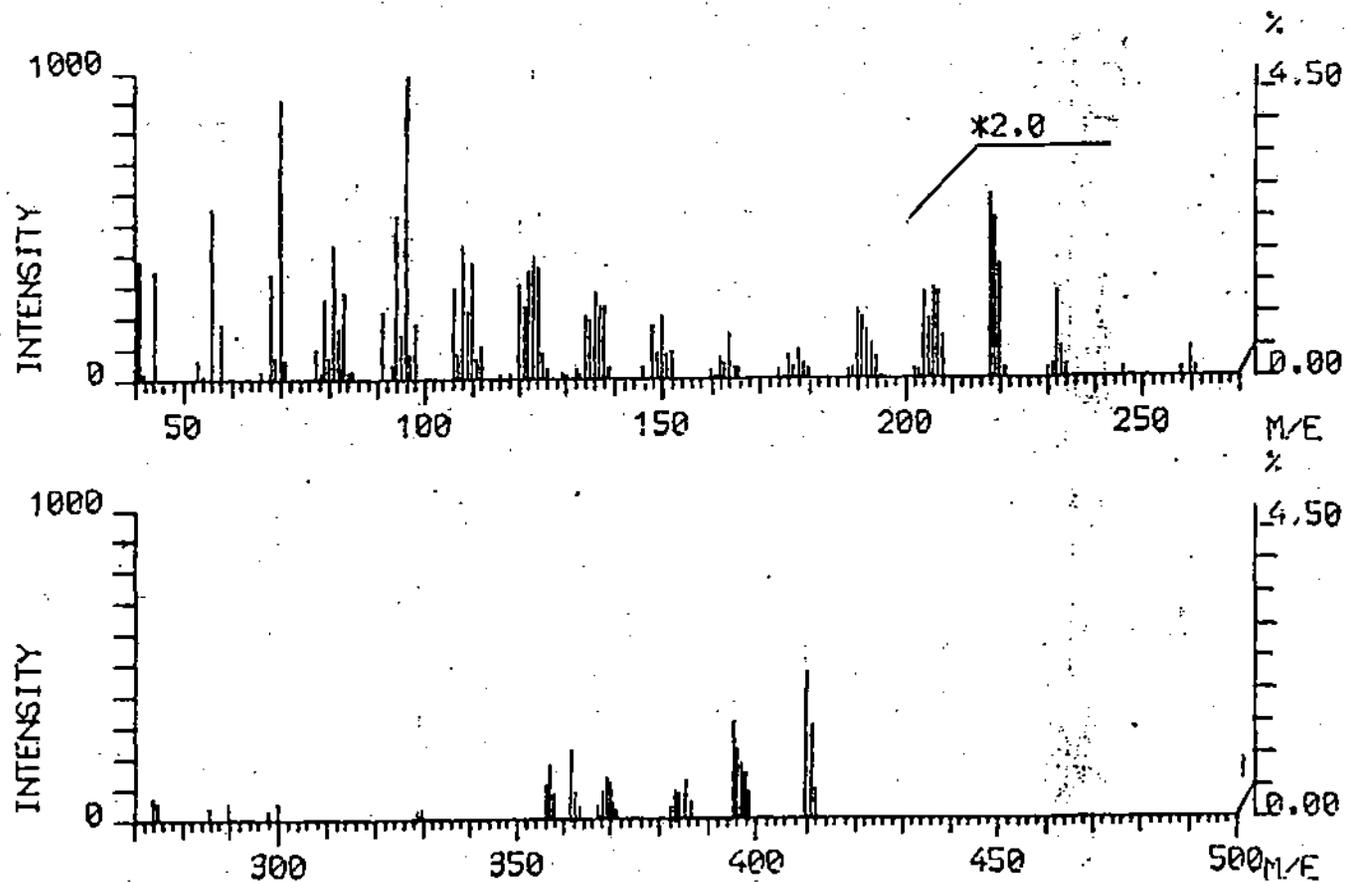


Fig.4 : Mass spectrum of Friedel-3-ene (356)

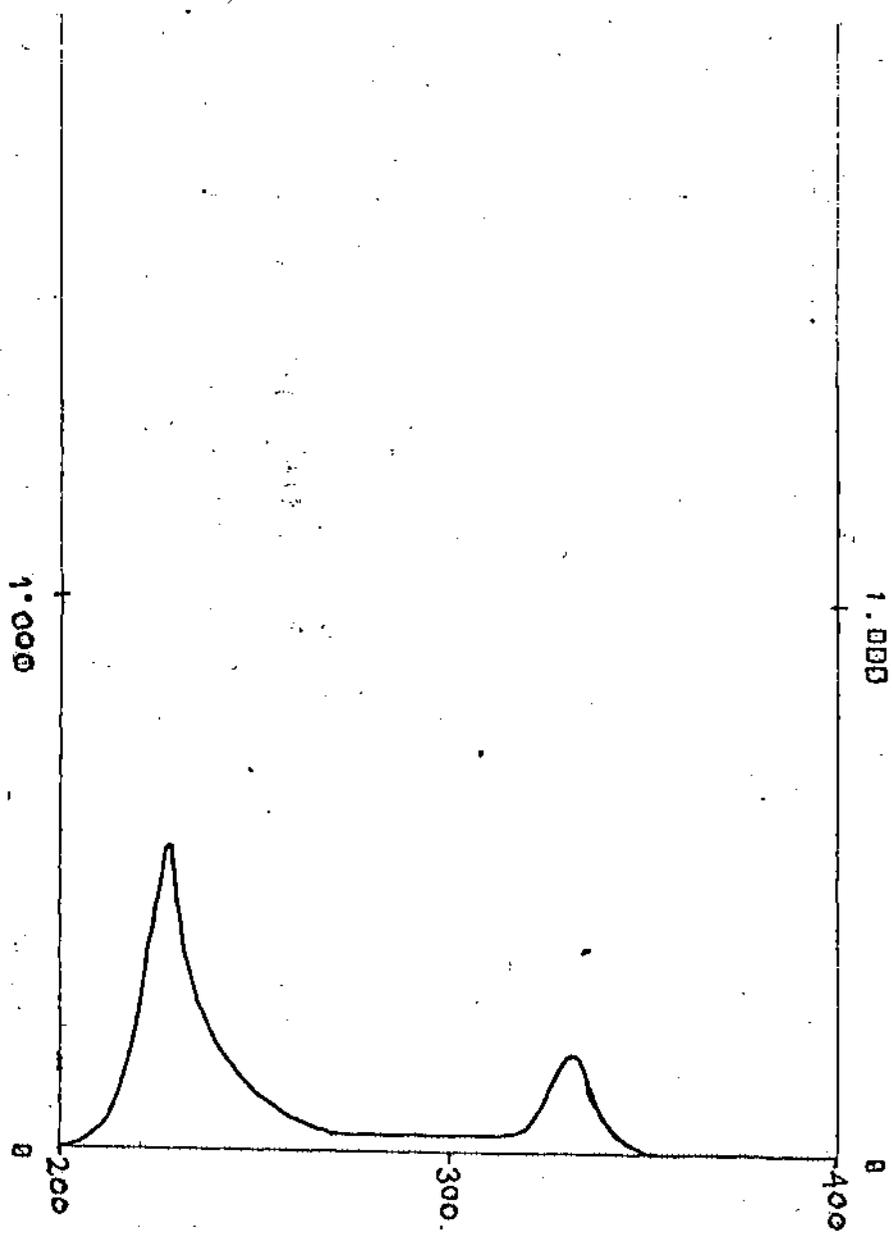


Fig. 5 : UV spectrum of Friedel-Crafts alkylation product (356 B)

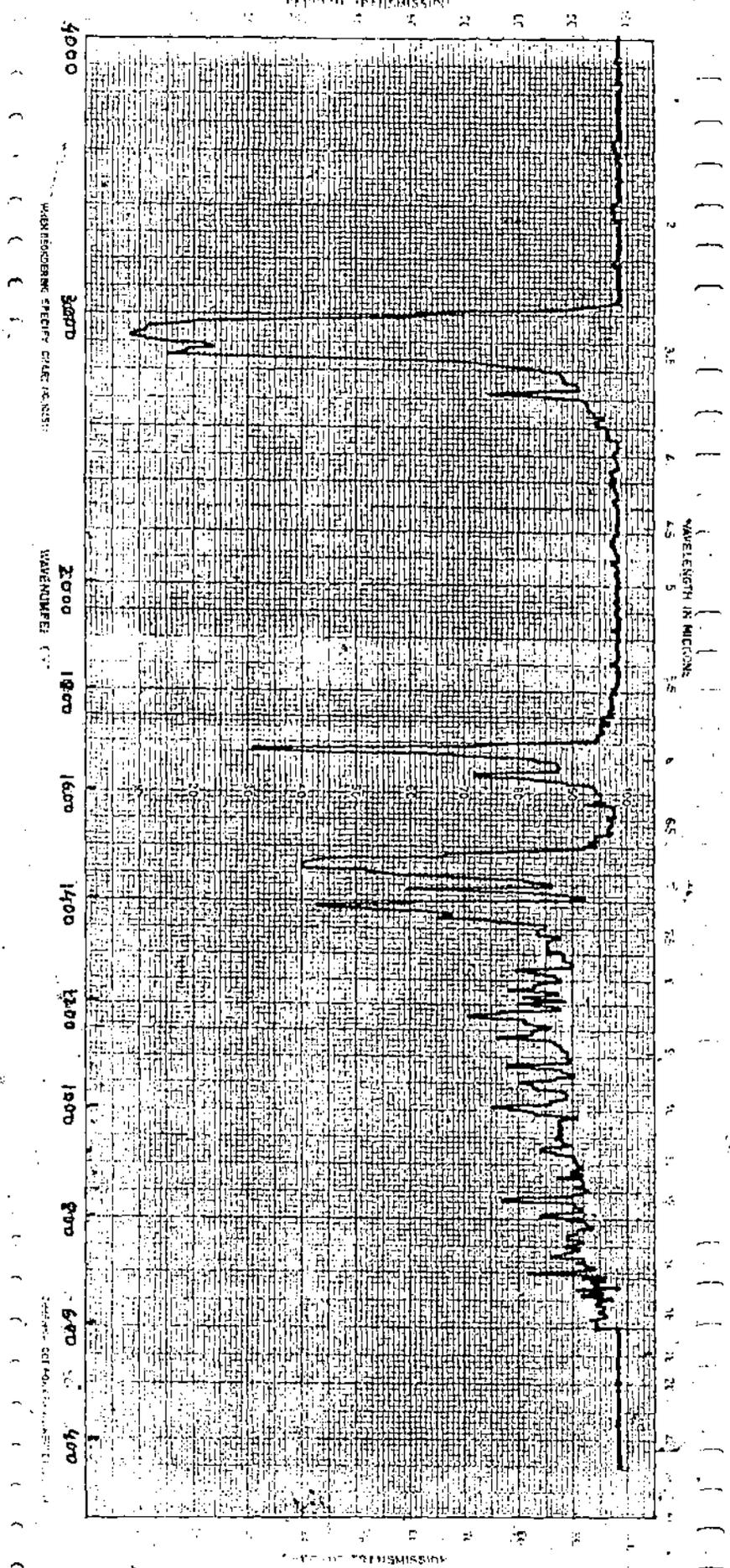


Fig. 6 : IR spectrum of Friedel-3-en-23-al (336 B)

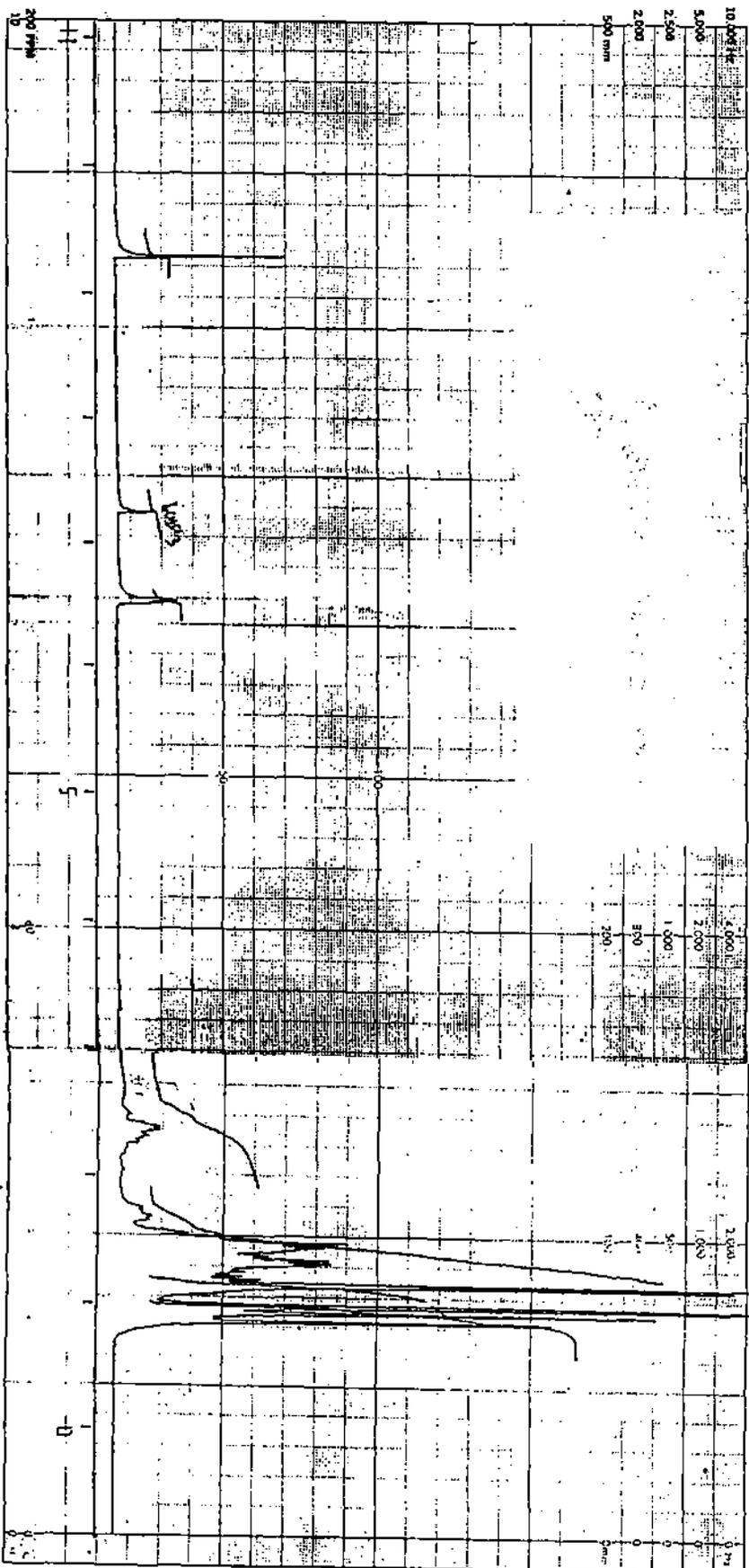


Fig. 7 : ^1H NMR spectrum of Friedel-3-en-23-al (356 B)

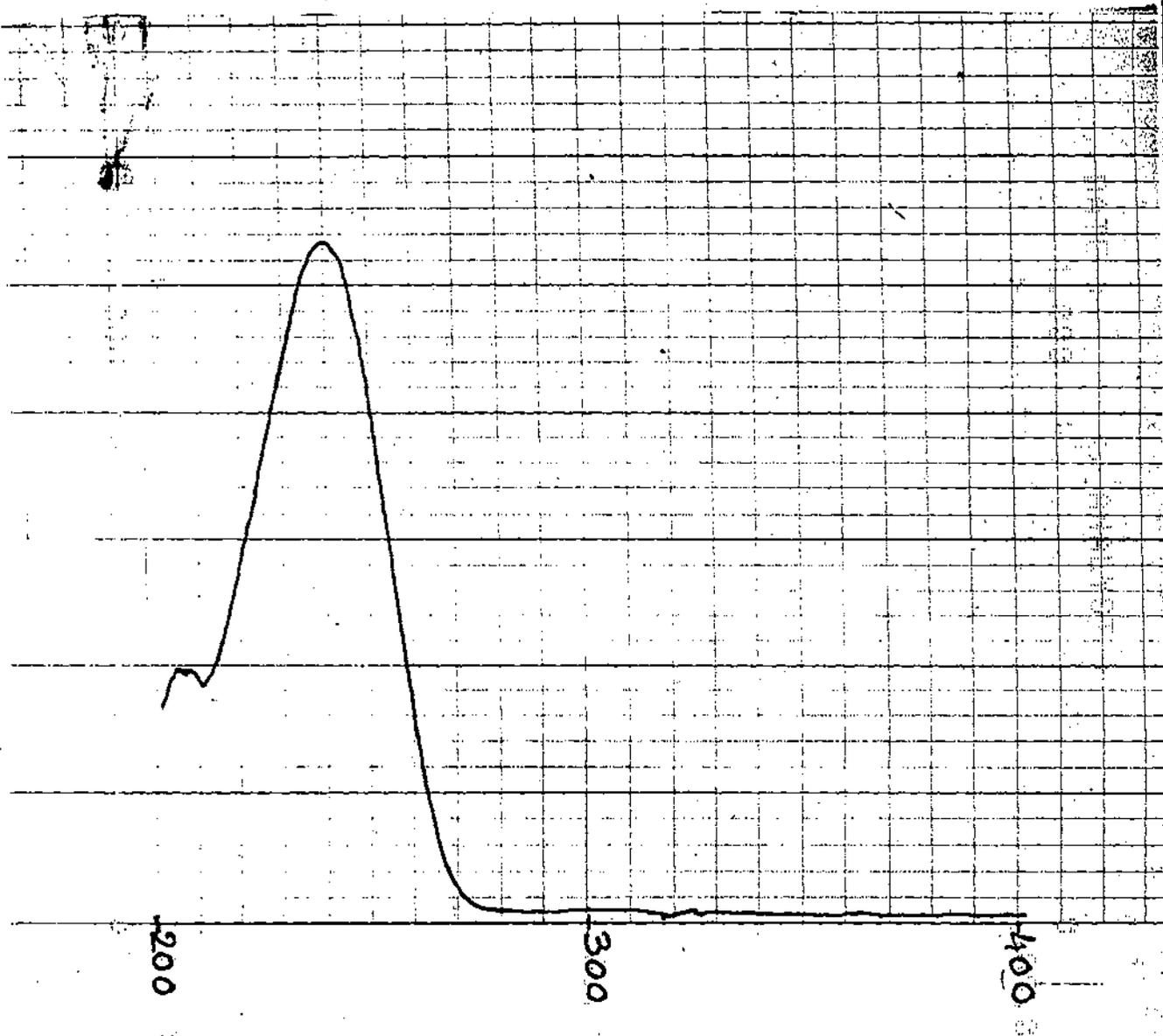
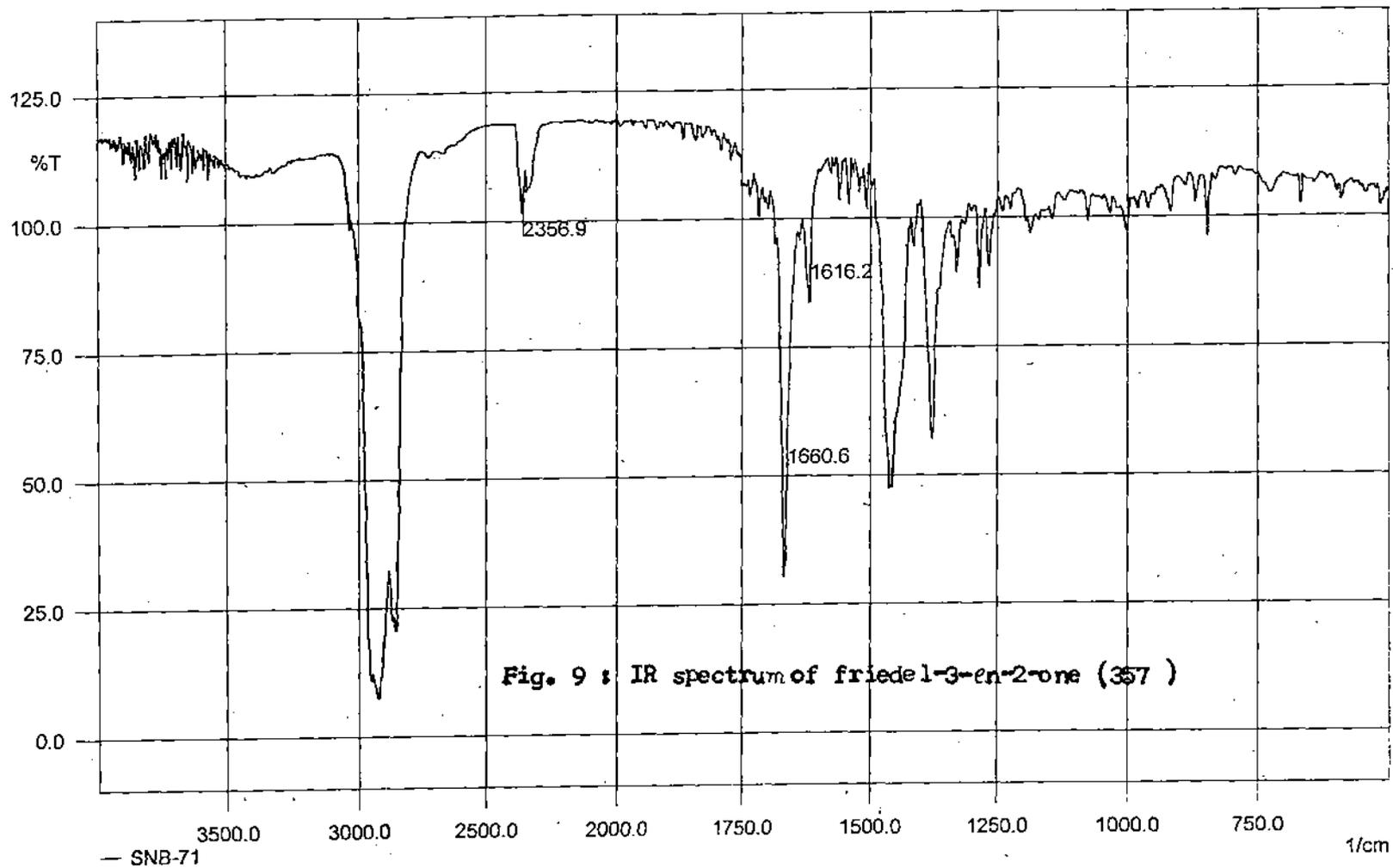


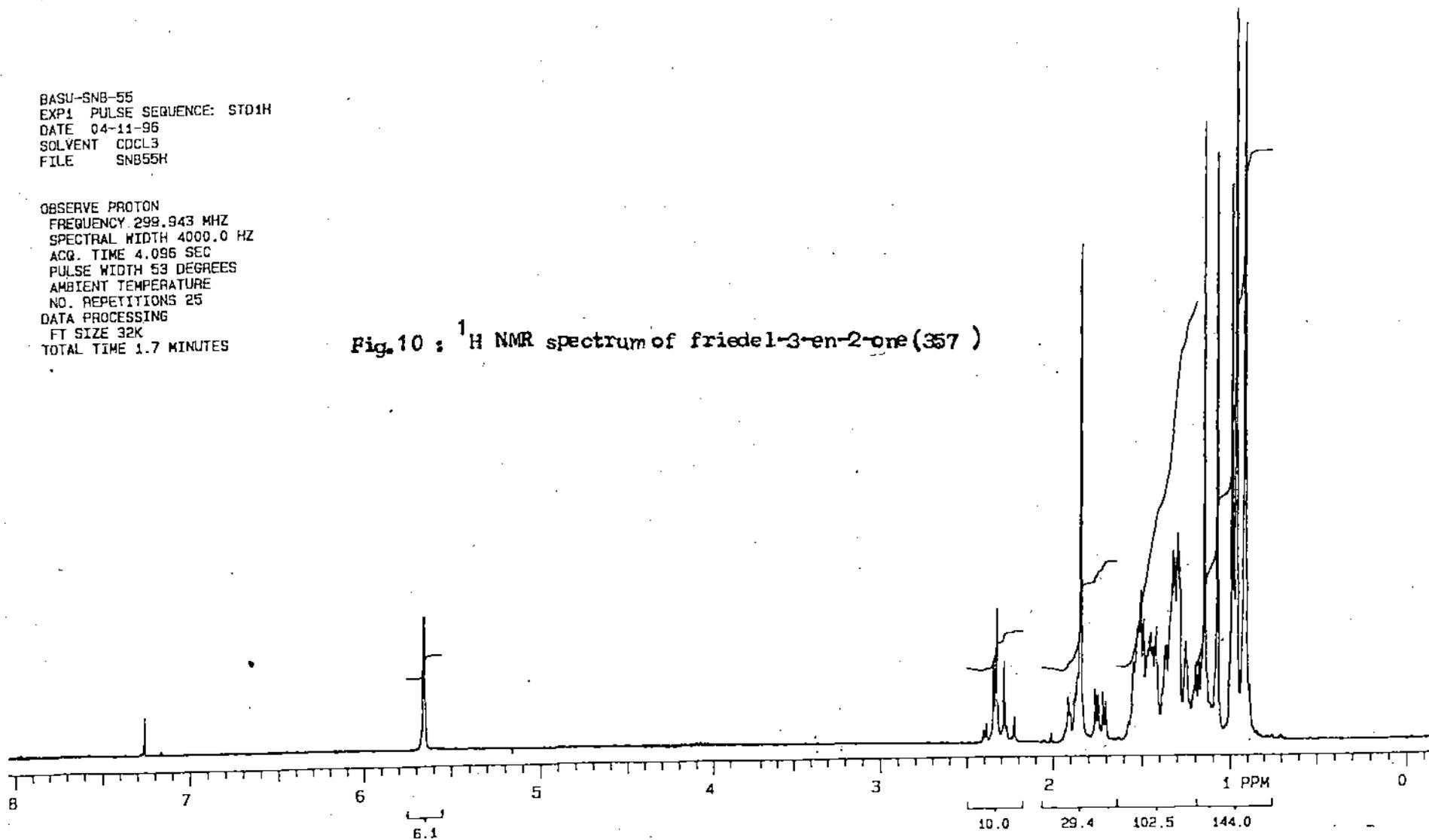
Fig.8 : UV spectrum of Friedel-Crafts alkylation product (357)



BASU-SNB-55
EXP1 PULSE SEQUENCE: STD1H
DATE 04-11-96
SOLVENT CDCL3
FILE SNB55H

OBSERVE PROTON
FREQUENCY 299.943 MHZ
SPECTRAL WIDTH 4000.0 HZ
ACQ. TIME 4.096 SEC
PULSE WIDTH 53 DEGREES
AMBIENT TEMPERATURE
NO. REPETITIONS 25
DATA PROCESSING
FT SIZE 32K
TOTAL TIME 1.7 MINUTES

Fig. 10 : ^1H NMR spectrum of friedel-3-en-2-one (357)



BASU-SNB-55
EXP1 PULSE SEQUENCE: STD13C
DATE 04-11-96
SOLVENT CDCL3
FILE SNB55C

OBSERVE CARBON
FREQUENCY 75.429 MHZ
SPECTRAL WIDTH 20000.0 HZ
ACQ. TIME 0.992 SEC
RELAXATION DELAY 0.5 SEC
PULSE WIDTH 31 DEGREES
AMBIENT TEMPERATURE
NO. REPETITIONS 240
DECOUPLE PROTON
LOW POWER 2 DB
WALTZ-16 MODULATED
CONTINUOUS DECOUPLING
DATA PROCESSING
LINE BROADENING 1.0 HZ
FT SIZE 64K
TOTAL TIME 6.0 MINUTES

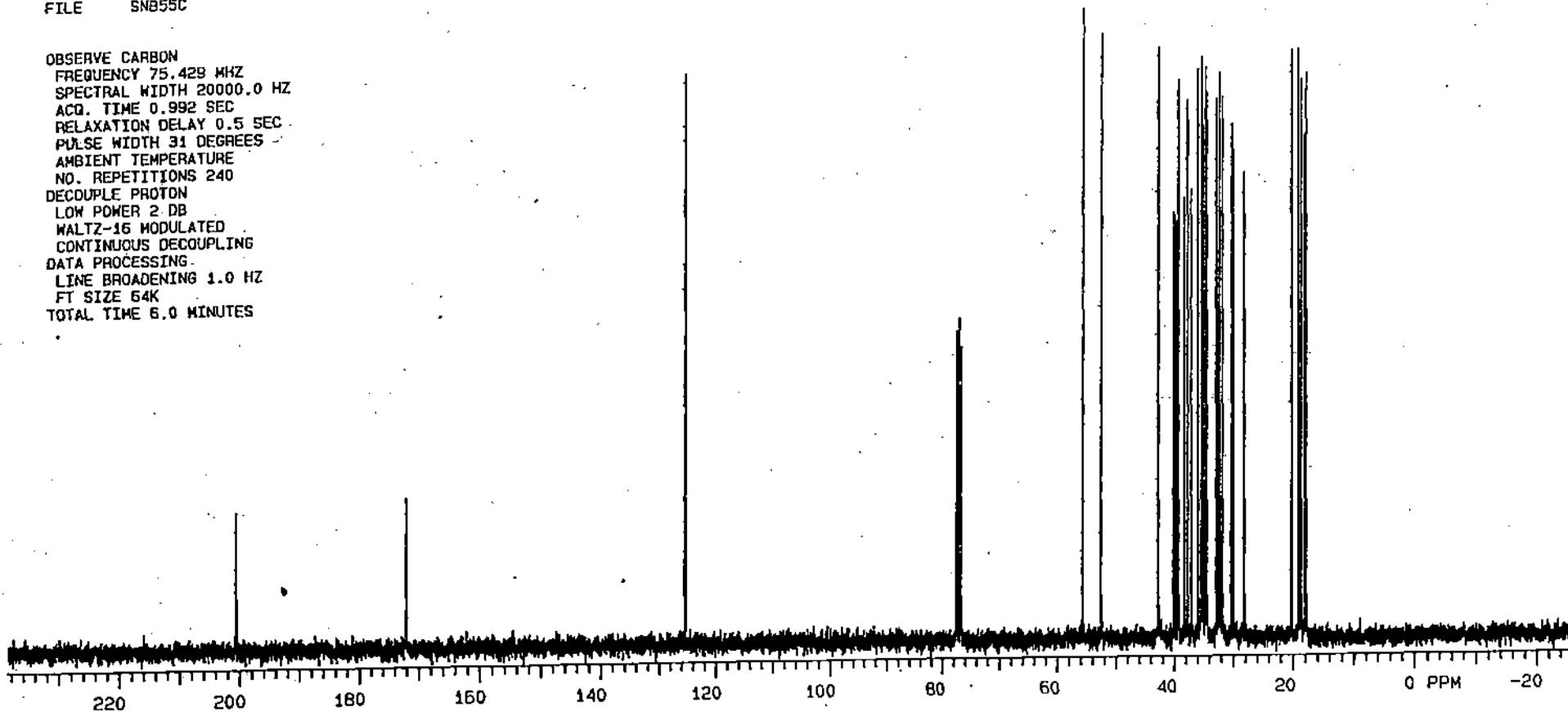
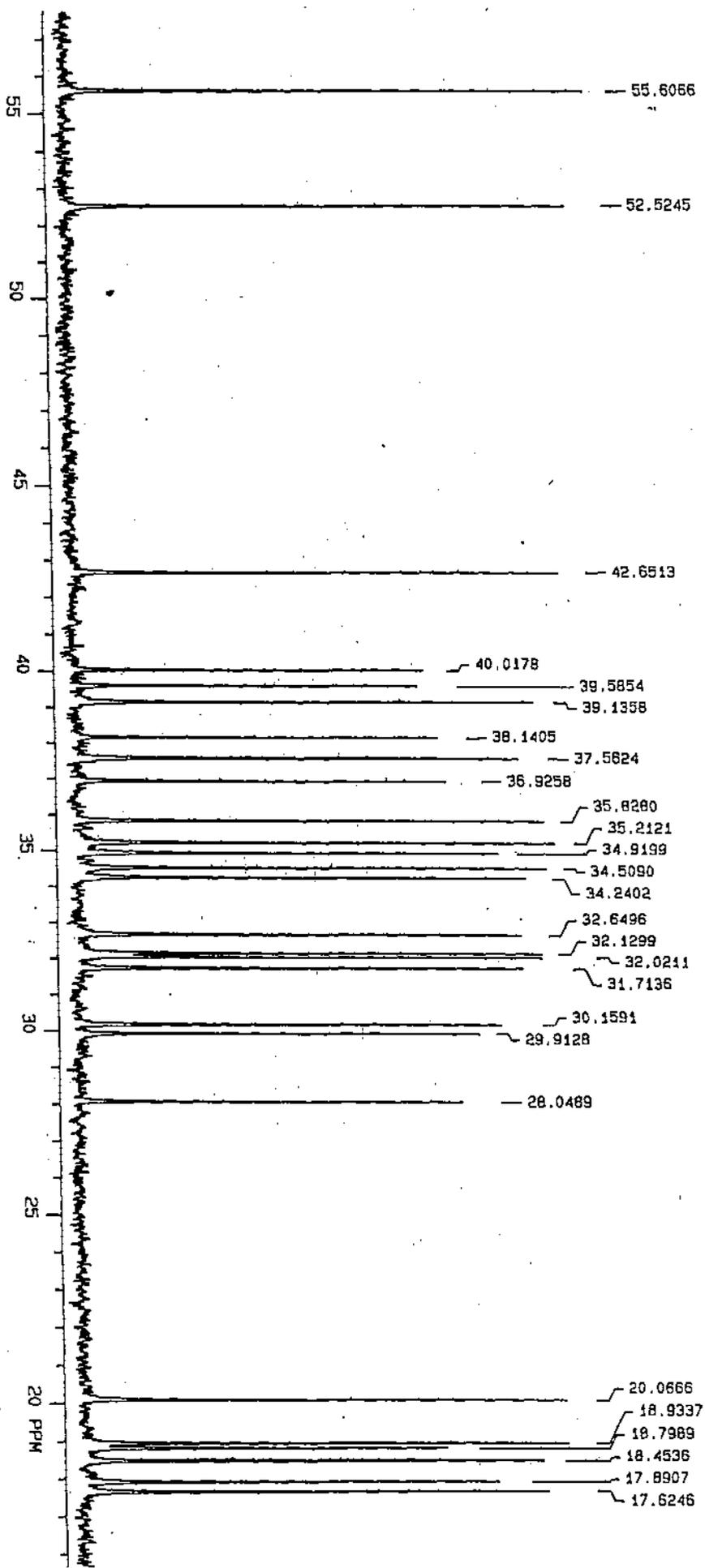
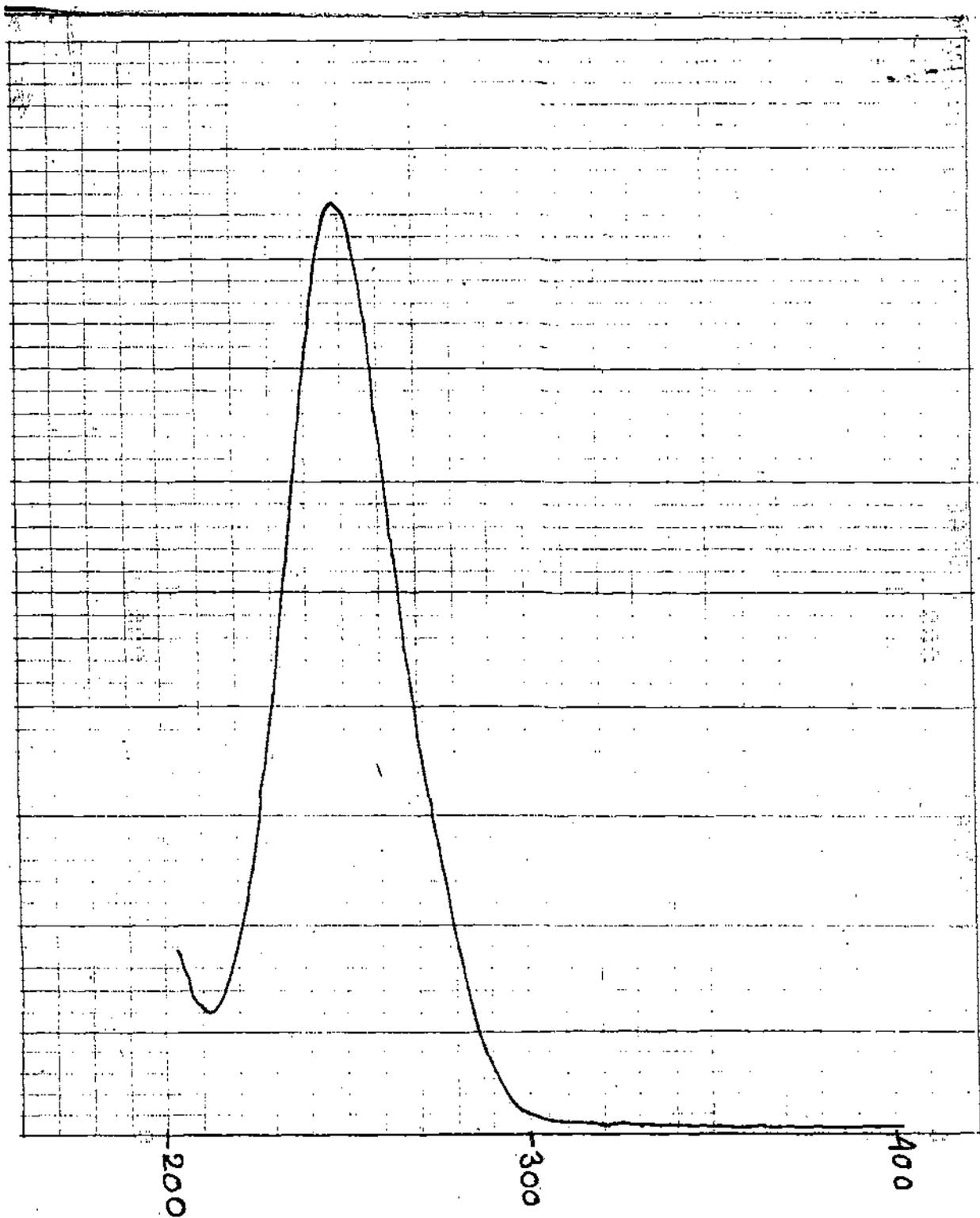


Fig. 11 : ¹³C NMR spectrum of friedel-3-en-2-one (357)

Fig. 11A : Expanded ^{13}C NMR spectrum of Friedel-3-en-2-one (357)





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Fig.12 : UV spectrum of friedel -1 (10),3-dien-2-one (358)

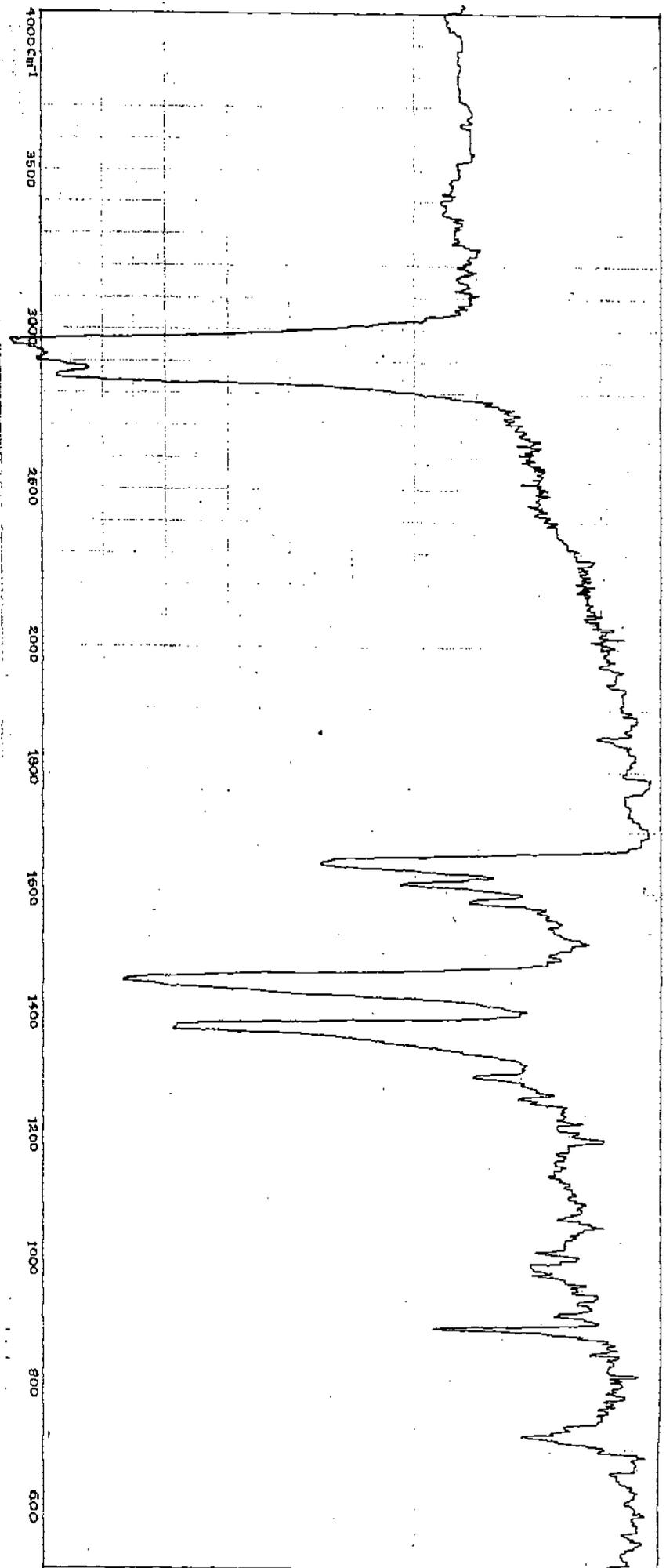
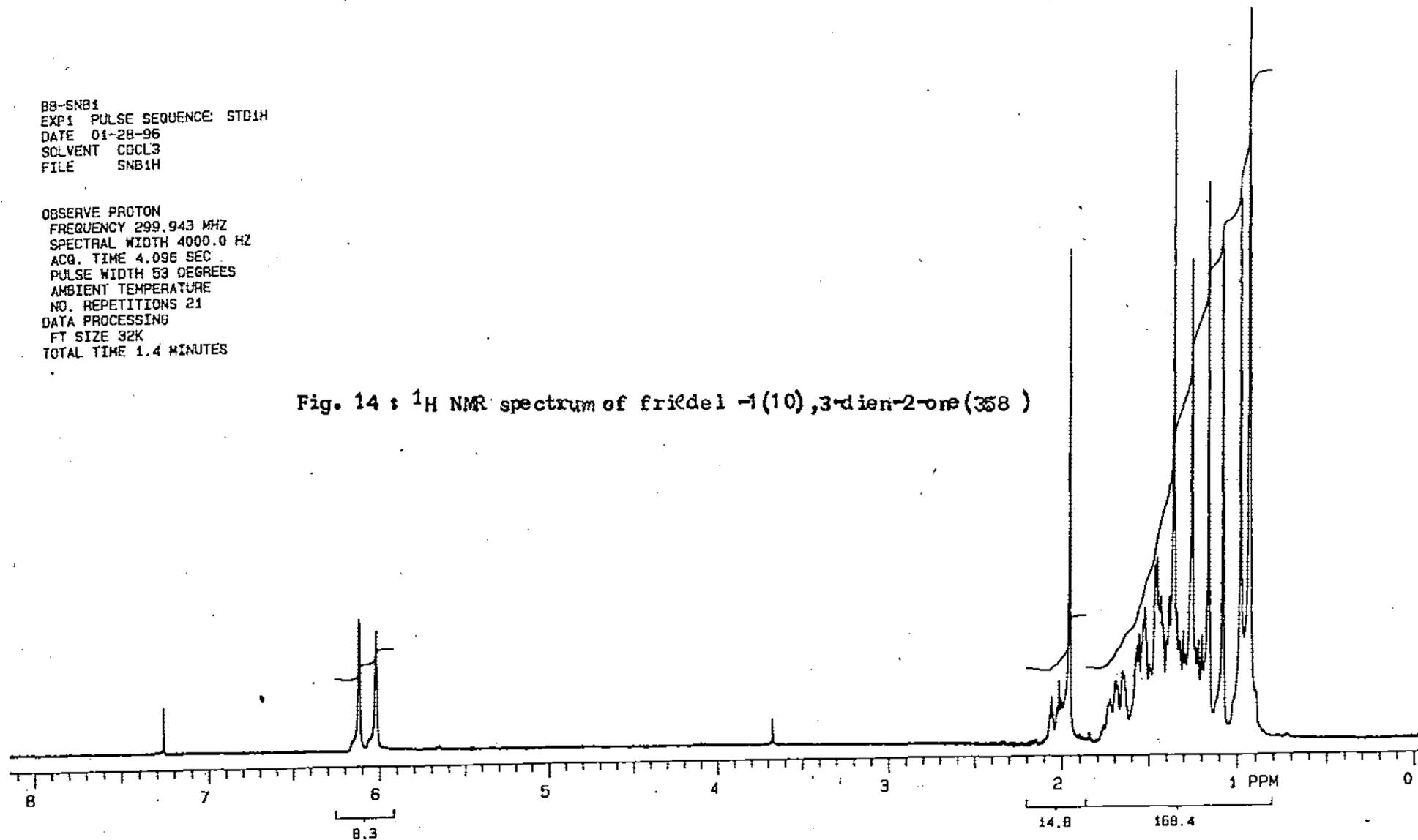


Fig. 13 : IR spectrum of Friedel-Crafts alkylation product (358)

BB-SNB1
EXP1 PULSE SEQUENCE: STD1H
DATE 01-28-96
SOLVENT CDCL3
FILE SNB1H

OBSERVE PROTON
FREQUENCY 299.943 MHZ
SPECTRAL WIDTH 4000.0 HZ
ACQ. TIME 4.096 SEC
PULSE WIDTH 53 DEGREES
AMBIENT TEMPERATURE
NO. REPETITIONS 21
DATA PROCESSING
FT SIZE 32K
TOTAL TIME 1.4 MINUTES

Fig. 14 : ^1H NMR spectrum of frideal -1(10),3-dien-2-one(358)



BB-SNB1
EXP1 PULSE SEQUENCE: STD1H
DATE 01-28-96
SOLVENT CDCL3
FILE SNB1H

OBSERVE PROTON
FREQUENCY 299.943 MHZ
SPECTRAL WIDTH 4000.0 HZ
ACQ. TIME 4.096 SEC
PULSE WIDTH 53 DEGREES
AMBIENT TEMPERATURE
NO. REPETITIONS 21
DATA PROCESSING
FT SIZE 32K
TOTAL TIME 1.4 MINUTES

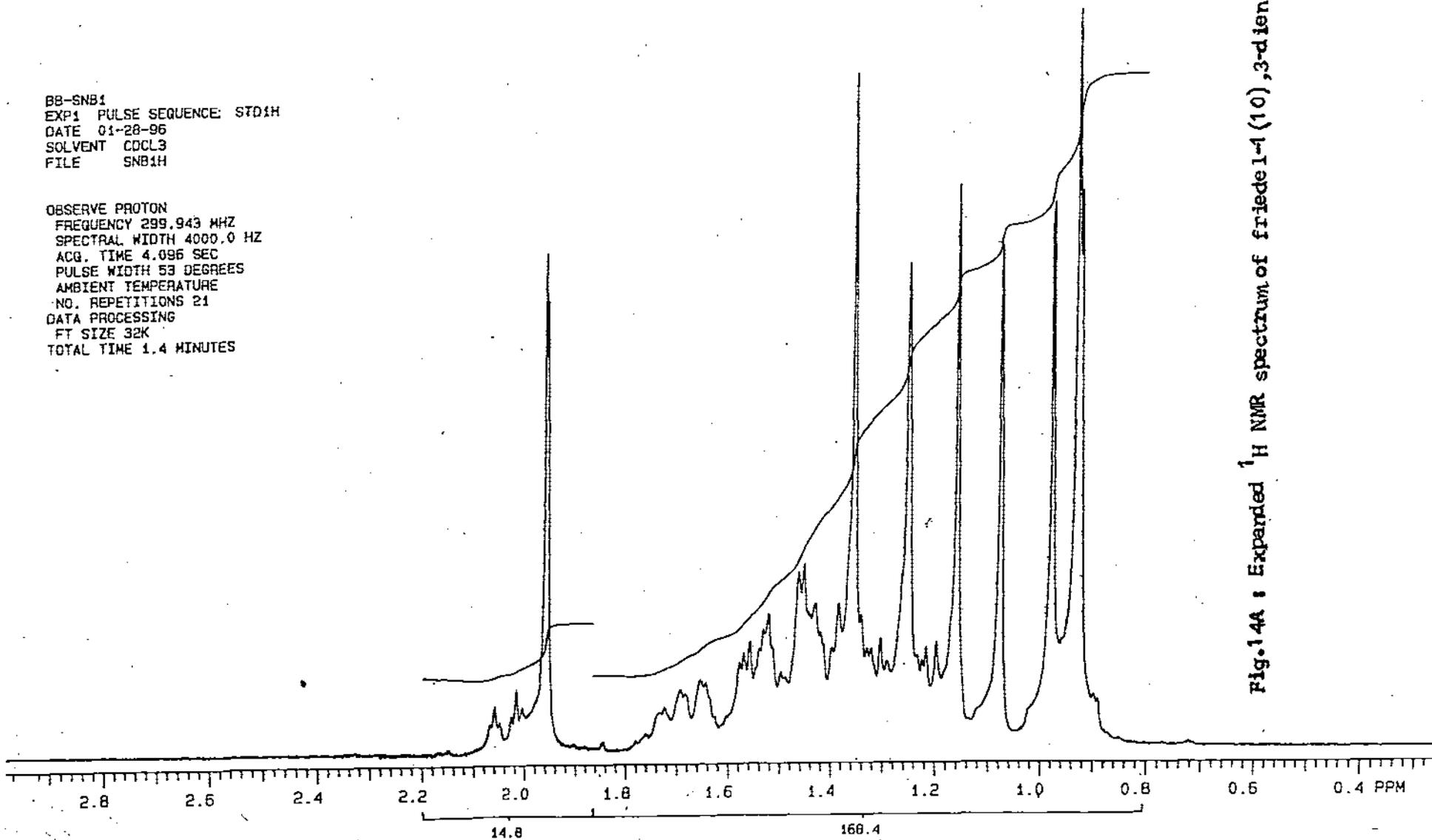


Fig. 14A : Expanded ¹H NMR spectrum of Friedel-Crafts alkylation product (358)

BB-SNB-1
EXP1 PULSE SEQUENCE: STD13C
DATE 01-28-95
SOLVENT CDCL3
FILE SNB1C

OBSERVE CARBON
FREQUENCY 75.429 MHZ
SPECTRAL WIDTH 20000.0 HZ
ACQ. TIME 0.992 SEC
RELAXATION DELAY 0.5 SEC
PULSE WIDTH 31 DEGREES
AMBIENT TEMPERATURE
NO. REPETITIONS 273
DECOUPLE PROTON
LOW POWER 2 DB
WALTZ-16 MODULATED
CONTINUOUS DECOUPLING
DATA PROCESSING
LINE BROADENING 1.0 HZ
FT SIZE 64K
TOTAL TIME 6.8 MINUTES

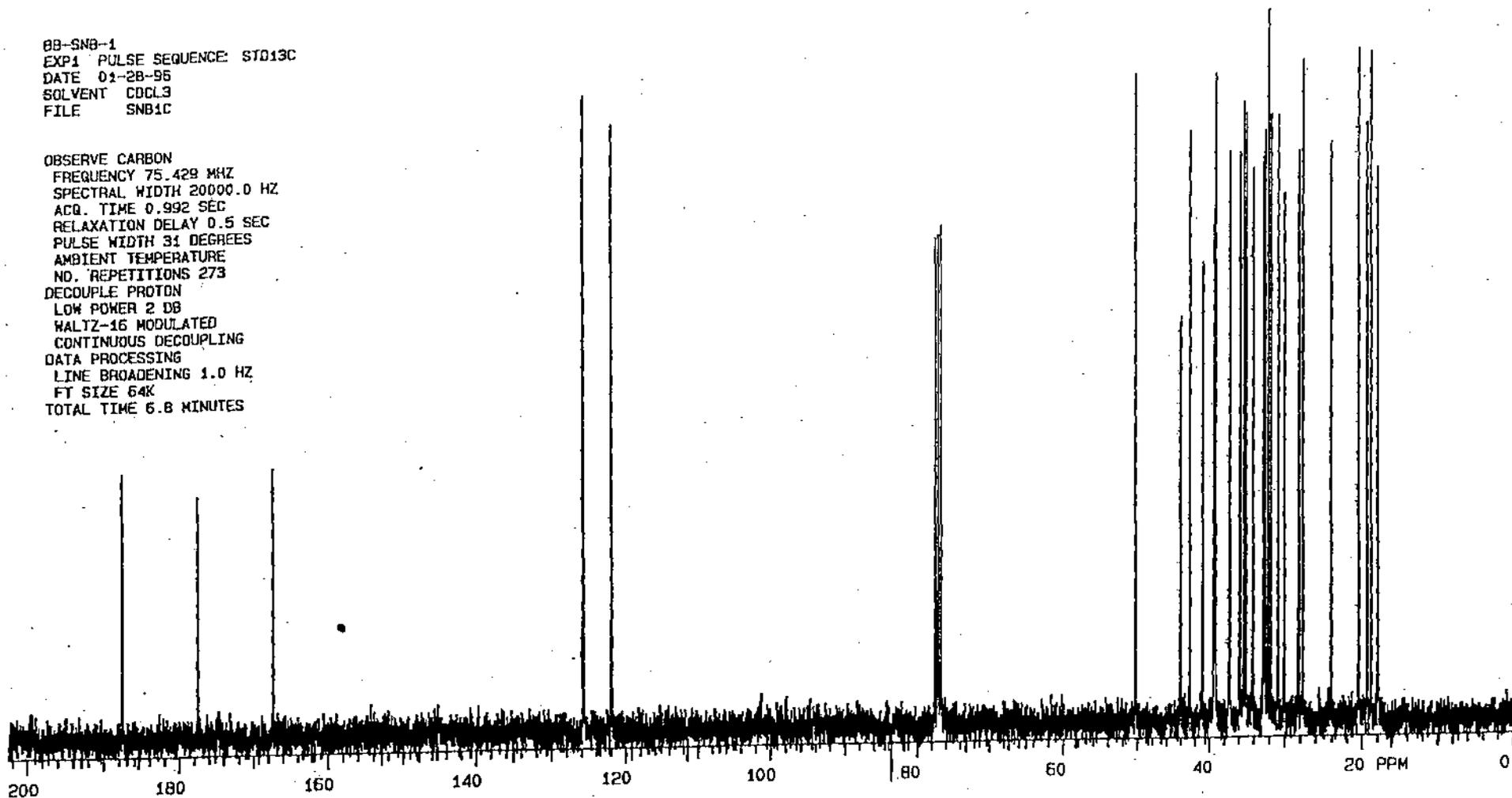
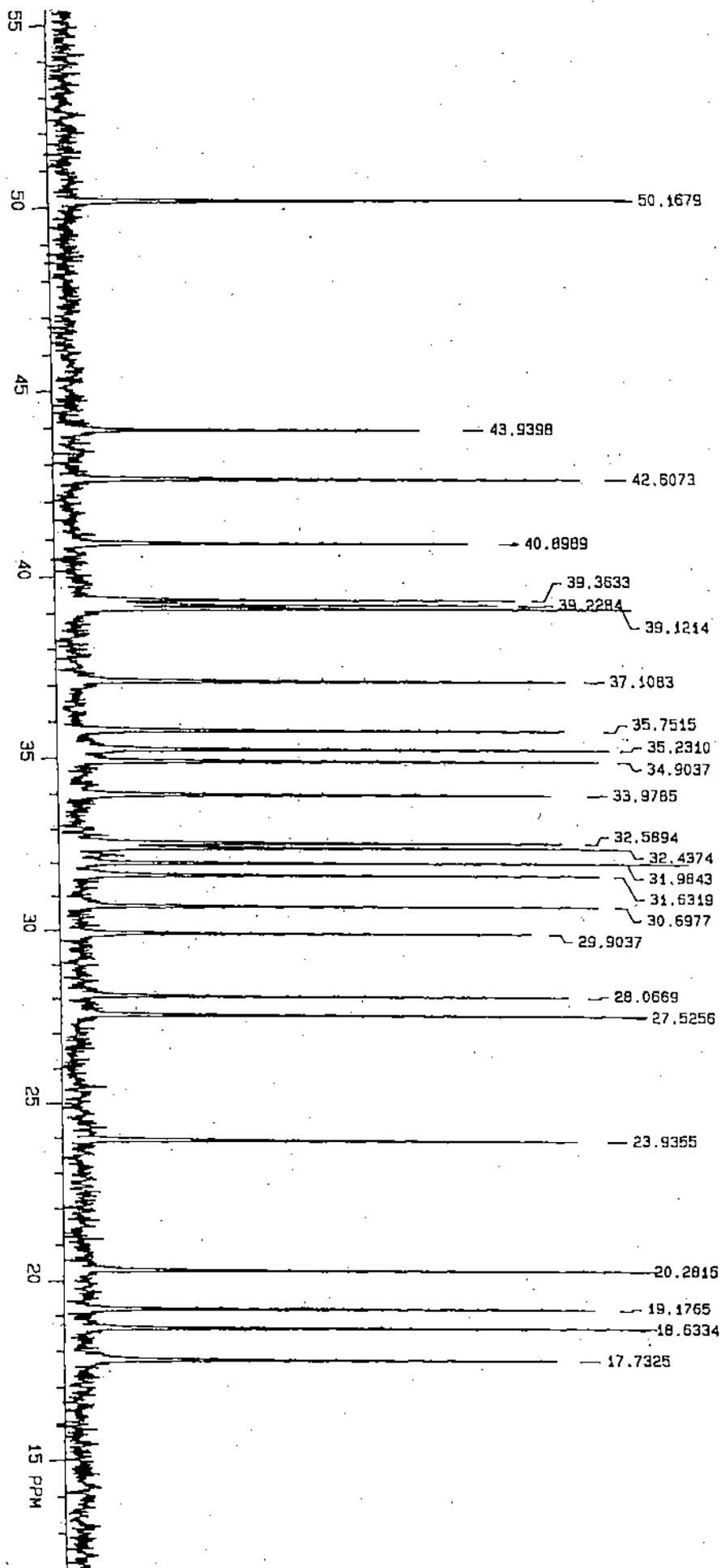


Fig.15 : ^{13}C NMR spectrum of friedel-1(10), 3-dien-2-one (358.)

Fig. 15A : Expanded ^{13}C NMR spectrum of Friedel-1-(10), 3-dien-2-one (358)



File : SahaSCI57, Vers. 1, of Fr, 14.06.1996, 10:26 h

Spectrum 5

Comment : EI-MS/70eV/T=. 200°C

Commission : SUBSTANZBEZEICHNUNG : SCI 57

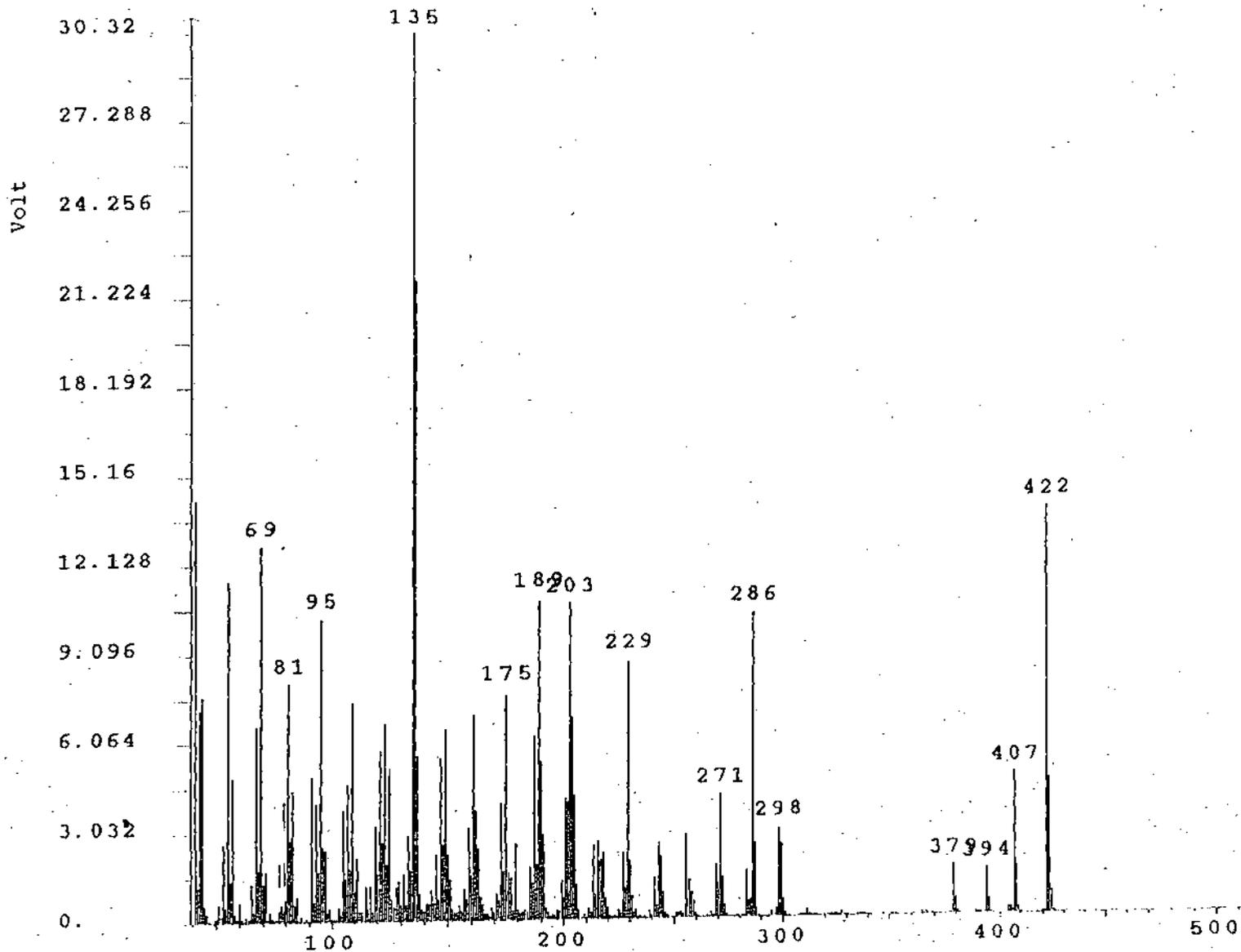
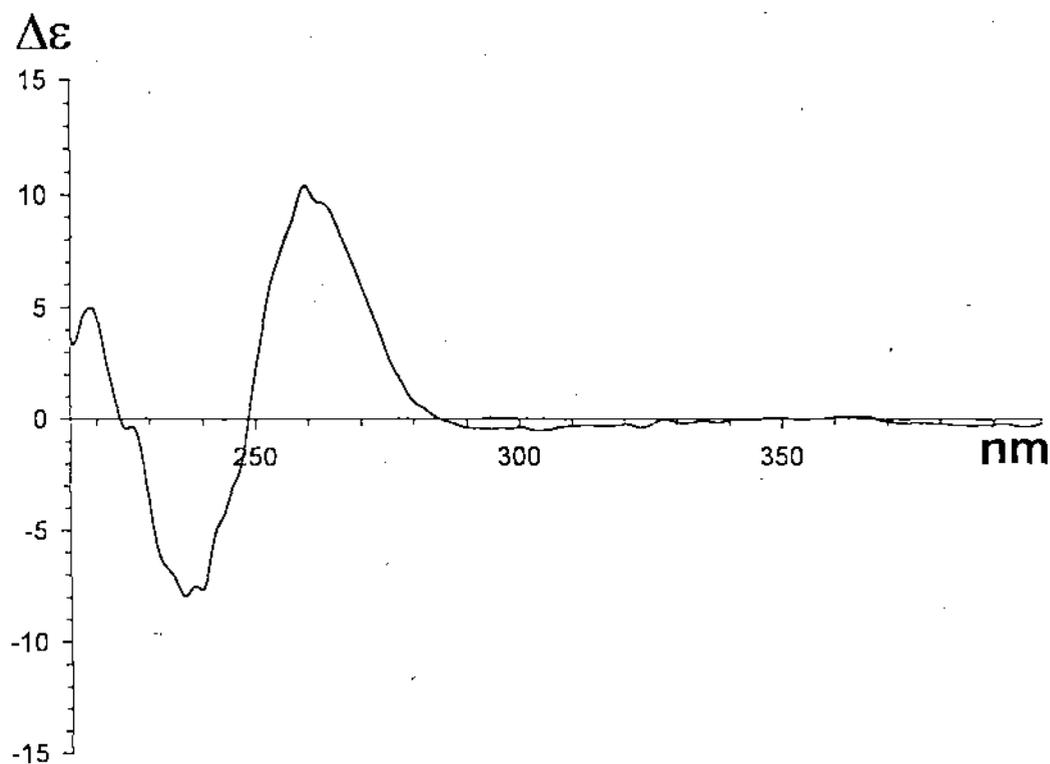


Fig.16 : Mass spectrum (EIMS) of friedel-(10),3-dien-2-one (358)

SNB-57



CD_{max.} (in dioxane)

$\Delta\epsilon$ + 10.4 (260 nm)
- 7.7 (239 nm) (UV_{max.} 241 nm)

Fig. 17 : CD spectrum of friedel - 1(10), 3-dien-2-one (358)

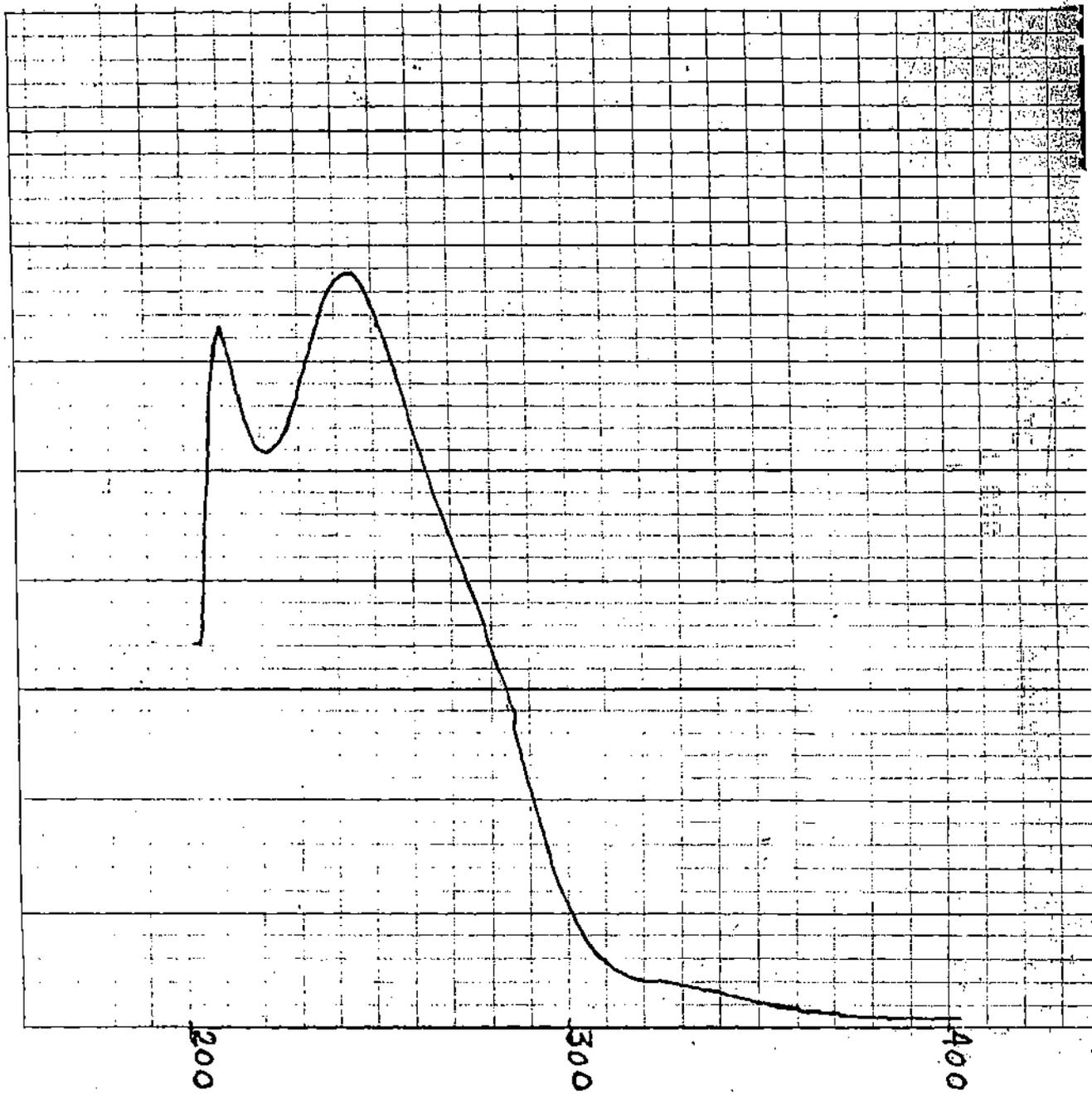


Fig. 18 : UV spectrum of the lumiprodukt (360)

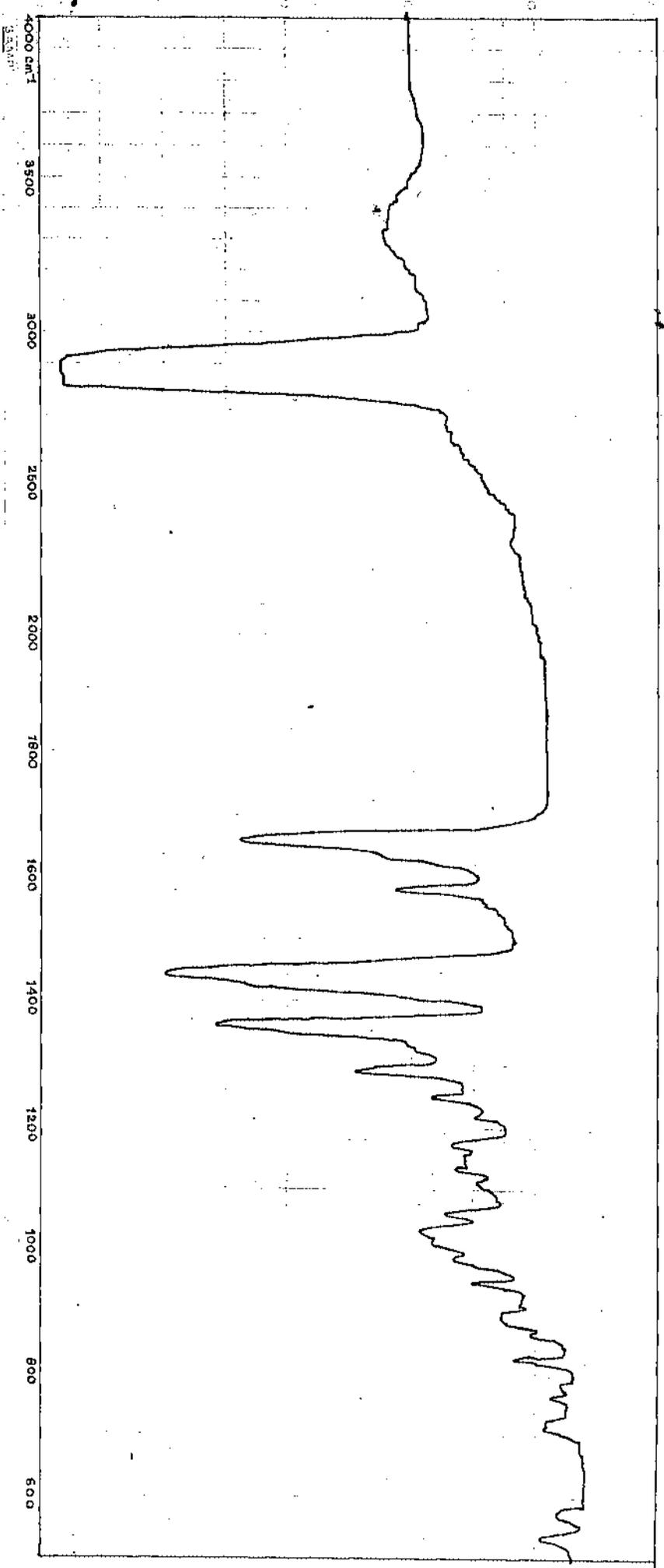


Fig.19 : IR spectrum of the Junipproduct (360)

BB-SNB-II
EXP1 PULSE SEQUENCE: STD1H
DATE 01-28-96
SOLVENT CDCL3
FILE SNB2H

OBSERVE PROTON
FREQUENCY 299.943 MHZ
SPECTRAL WIDTH 4000.0 HZ
ACQ. TIME 4.096 SEC
PULSE WIDTH 53 DEGREES
AMBIENT TEMPERATURE
NO. REPETITIONS 20
DATA PROCESSING
FT SIZE 32K
TOTAL TIME 1.4 MINUTES

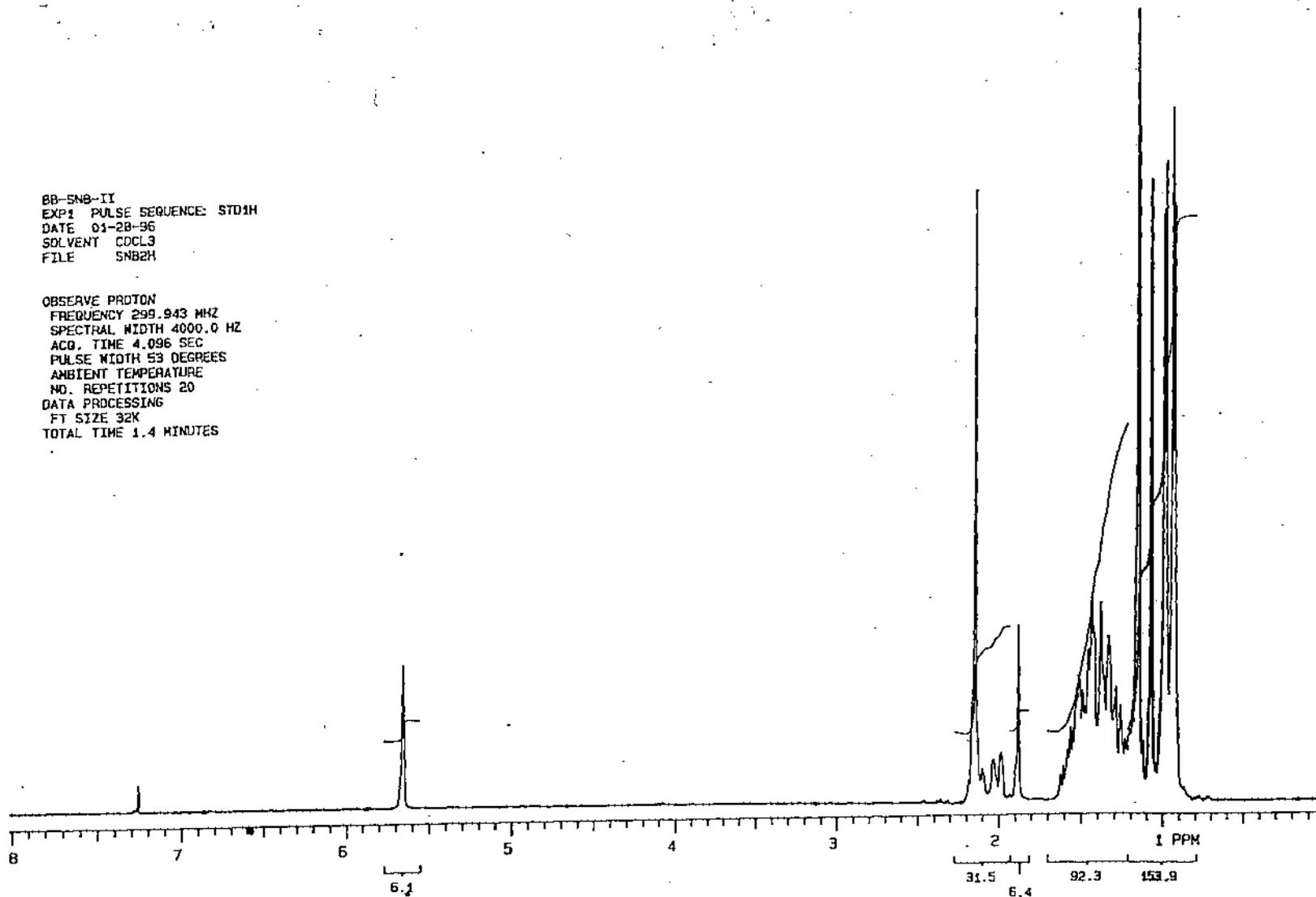


Fig.20 : ¹H NMR spectrum of the lumiproduet (360)

BB-SNB-II
EXP1 PULSE SEQUENCE: STD1H
DATE 01-28-95
SOLVENT CDCL3
FILE SNB2H

OBSERVE PROTON
FREQUENCY 299.943 MHZ
SPECTRAL WIDTH 4000.0 HZ
ACQ. TIME 4.096 SEC
PULSE WIDTH 53 DEGREES
AMBIENT TEMPERATURE
NO. REPETITIONS 20
DATA PROCESSING
FT SIZE 32K
TOTAL TIME 1.4 MINUTES

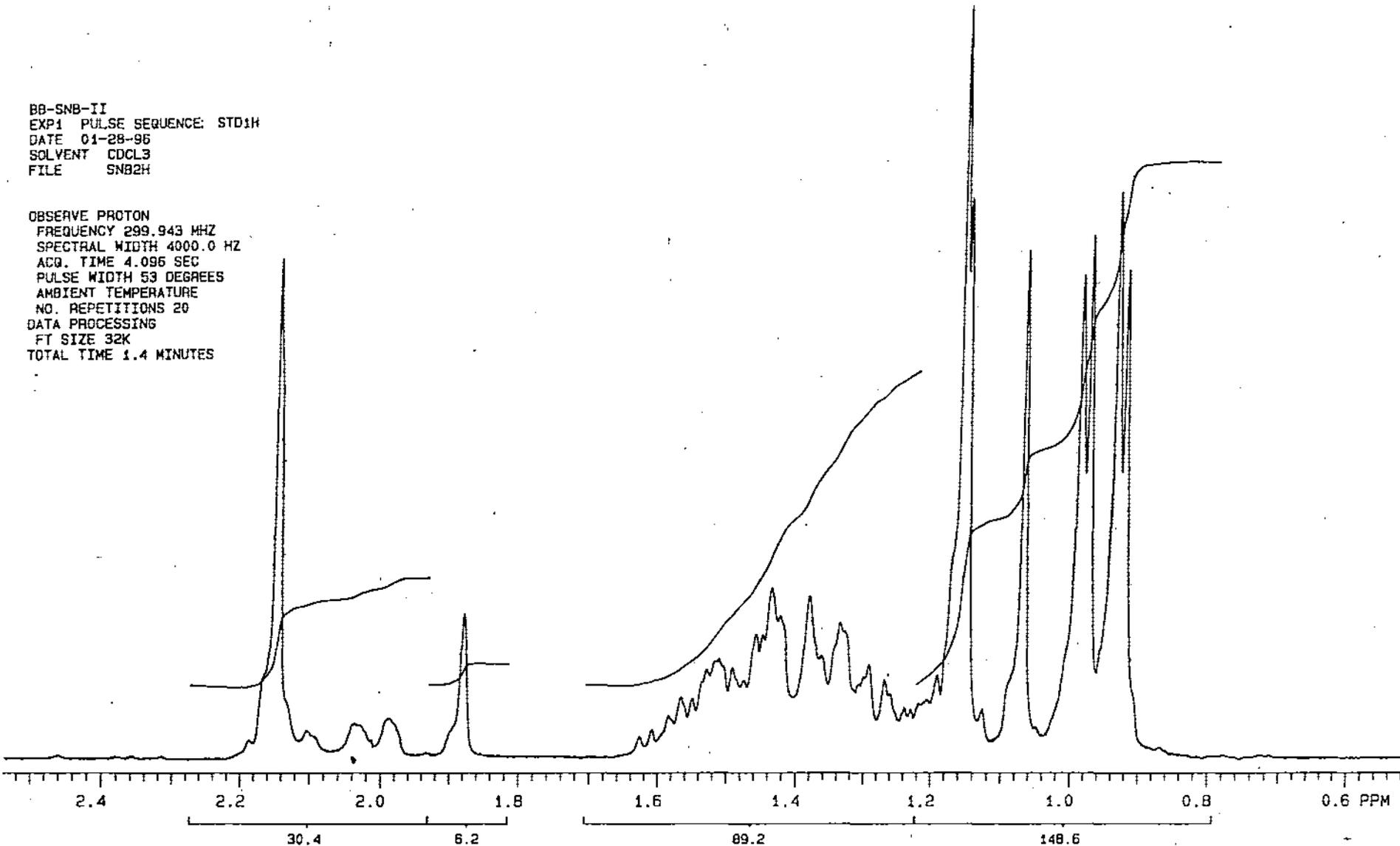


Fig. 20A ; Expanded ^1H NMR spectrum of the lundproduct (360)

BB-SNB-II
EXP1 PULSE SEQUENCE: STD13C
DATE 01-28-96
SOLVENT CDCL3
FILE SNB2C

OBSERVE CARBON
FREQUENCY 75.429 MHZ
SPECTRAL WIDTH 16501.7 HZ
ACQ. TIME 0.993 SEC
RELAXATION DELAY 0.5 SEC
PULSE WIDTH 31 DEGREES
AMBIENT TEMPERATURE
NO. REPETITIONS 339
DECOUPLE PROTON
LOW POWER 2 DB
WALTZ-16 MODULATED
CONTINUOUS DECOUPLING
DATA PROCESSING
LINE BROADENING 1.0 HZ
FT SIZE 32K
TOTAL TIME 8.5 MINUTES

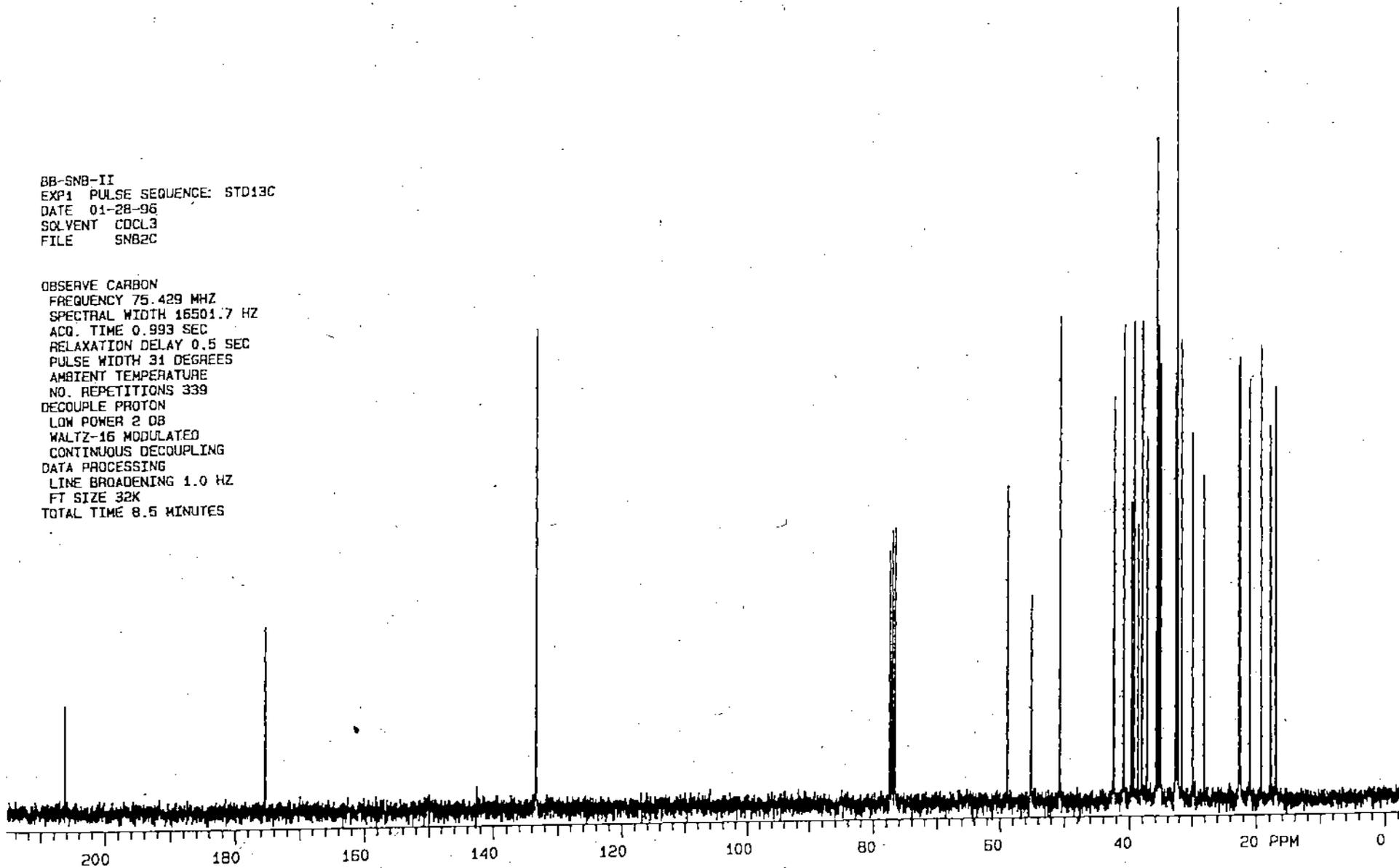
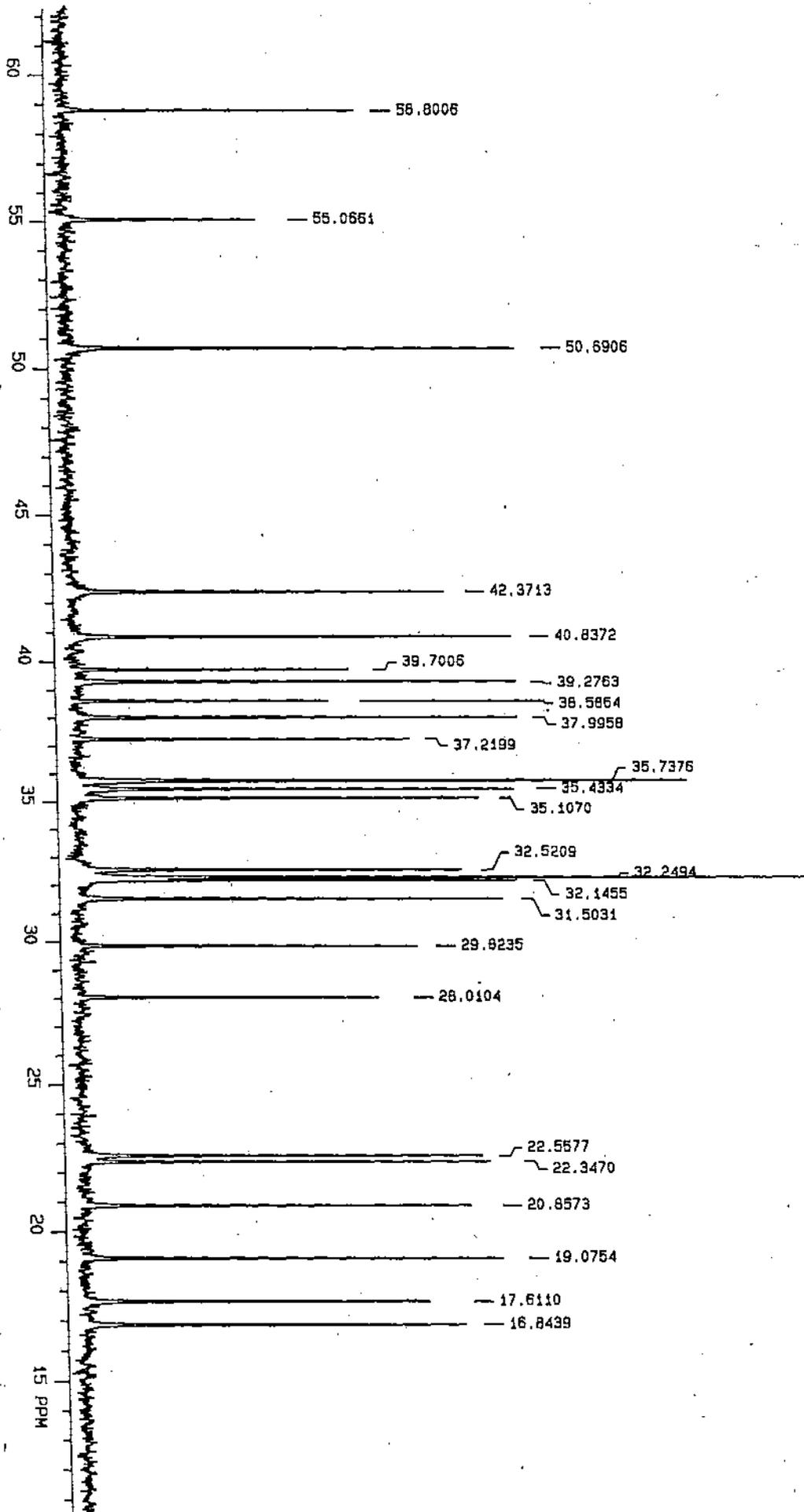


Fig.21 : ¹³C NMR spectrum of the lumipproduct (360)

Fig. 21 A : Expanded ^{13}C NMR spectrum of the lundiproduct (360) .



File : Saha64-II, Vers. 1, of Do, 13.06.1996, 11:55 h

Spectrum 6

Comment : EI-MS/70eV/T=170°C

Commission : SUBSTANZBEZEICHNUNG : Sci 64II

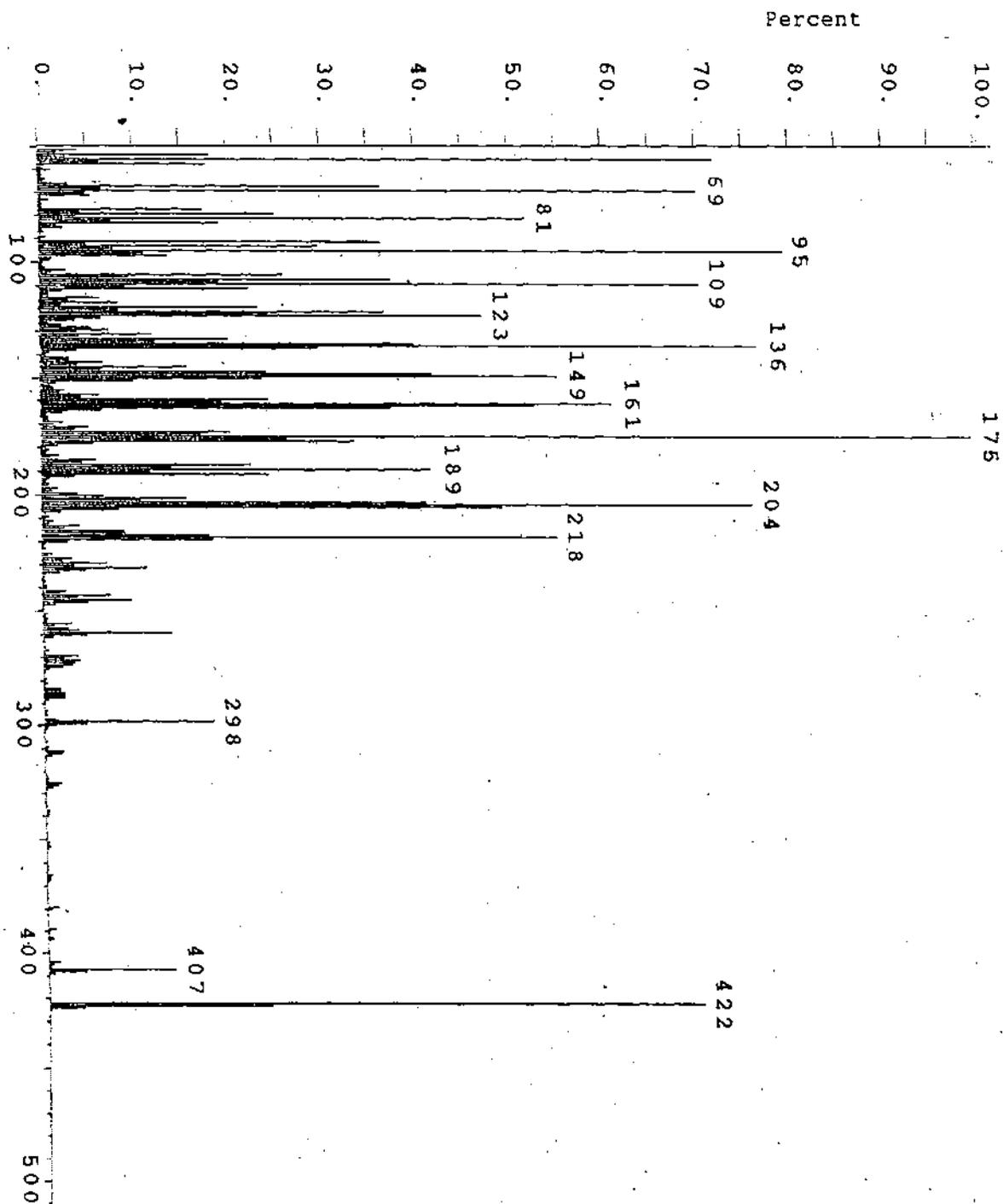


Fig.22 : Mass spectrum (EIMS) of the lumiprodukt(360)

SNB-64

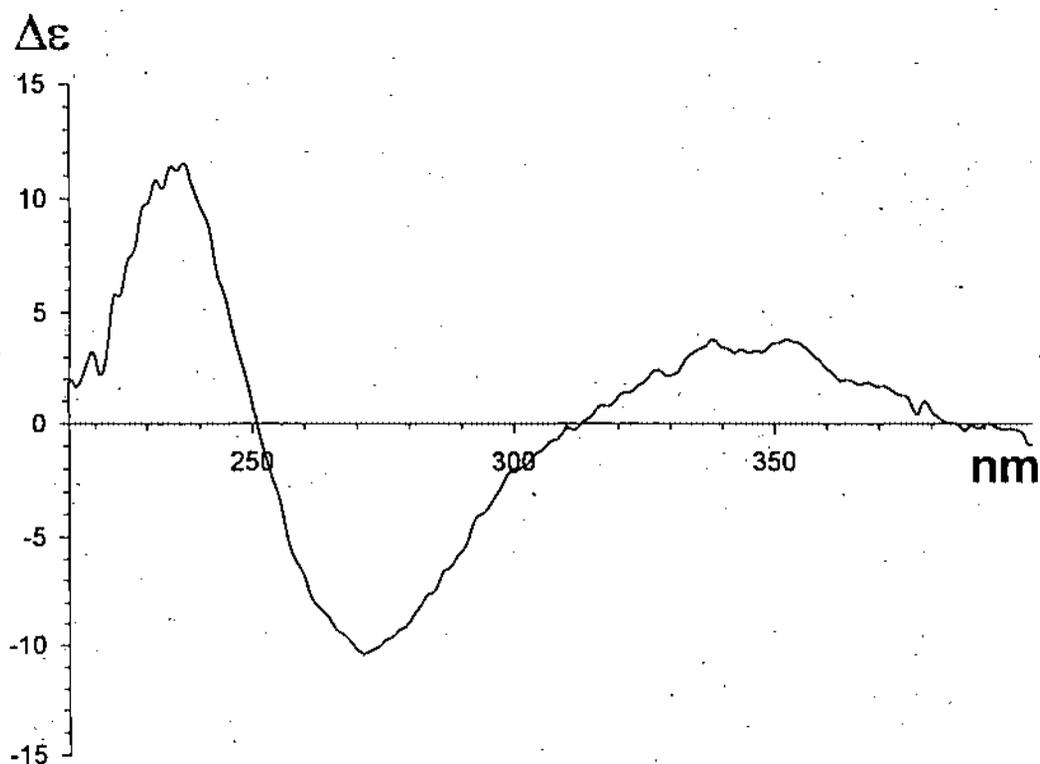


Fig.23 : CD spectrum of the lumipproduct (360)

CD_{max.} (in dioxane)

$\Delta\epsilon$ +3.8 (353 nm)

-10.4 (271 nm)

+11.5 (237 nm) (UV_{max} 234 nm)

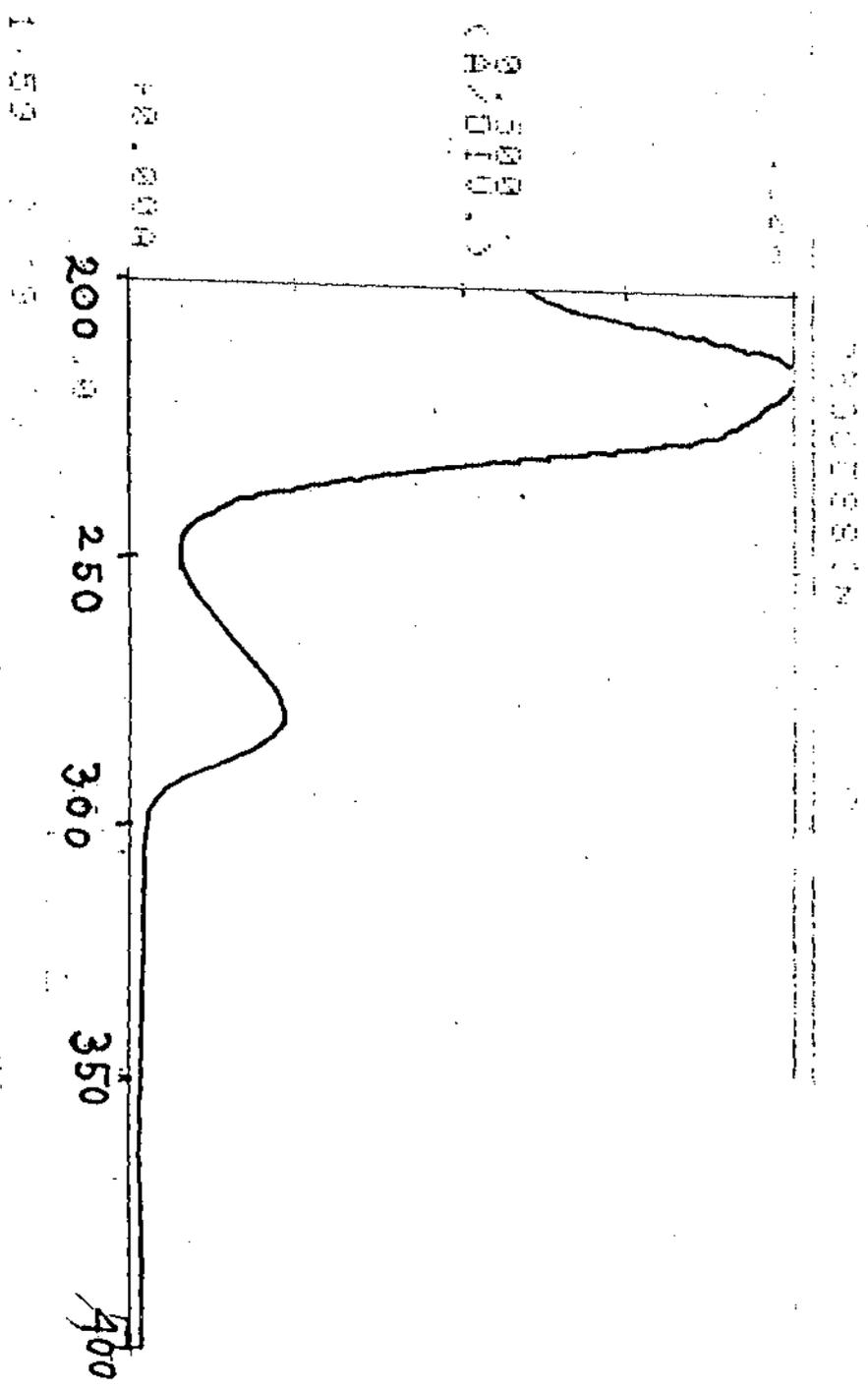


Fig. 24 : U V spectrum of the Phenolic product (36d)

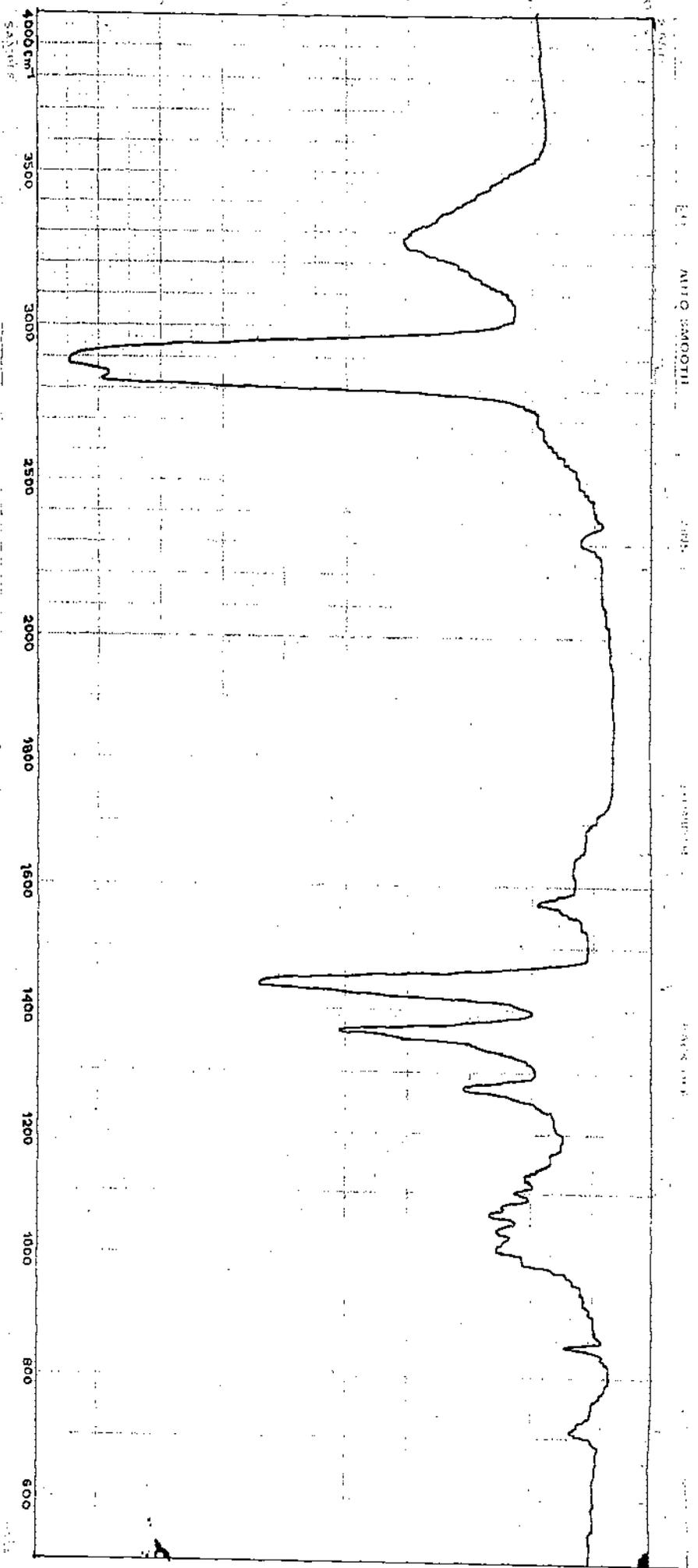


Fig. 25 : I R spectrum of the phenolic product (361)

Spectrum 9

Comment : EI-MS/70eV/T=.210°C

Commission : SUBSTANZBEZEICHNUNG : Sci 64I

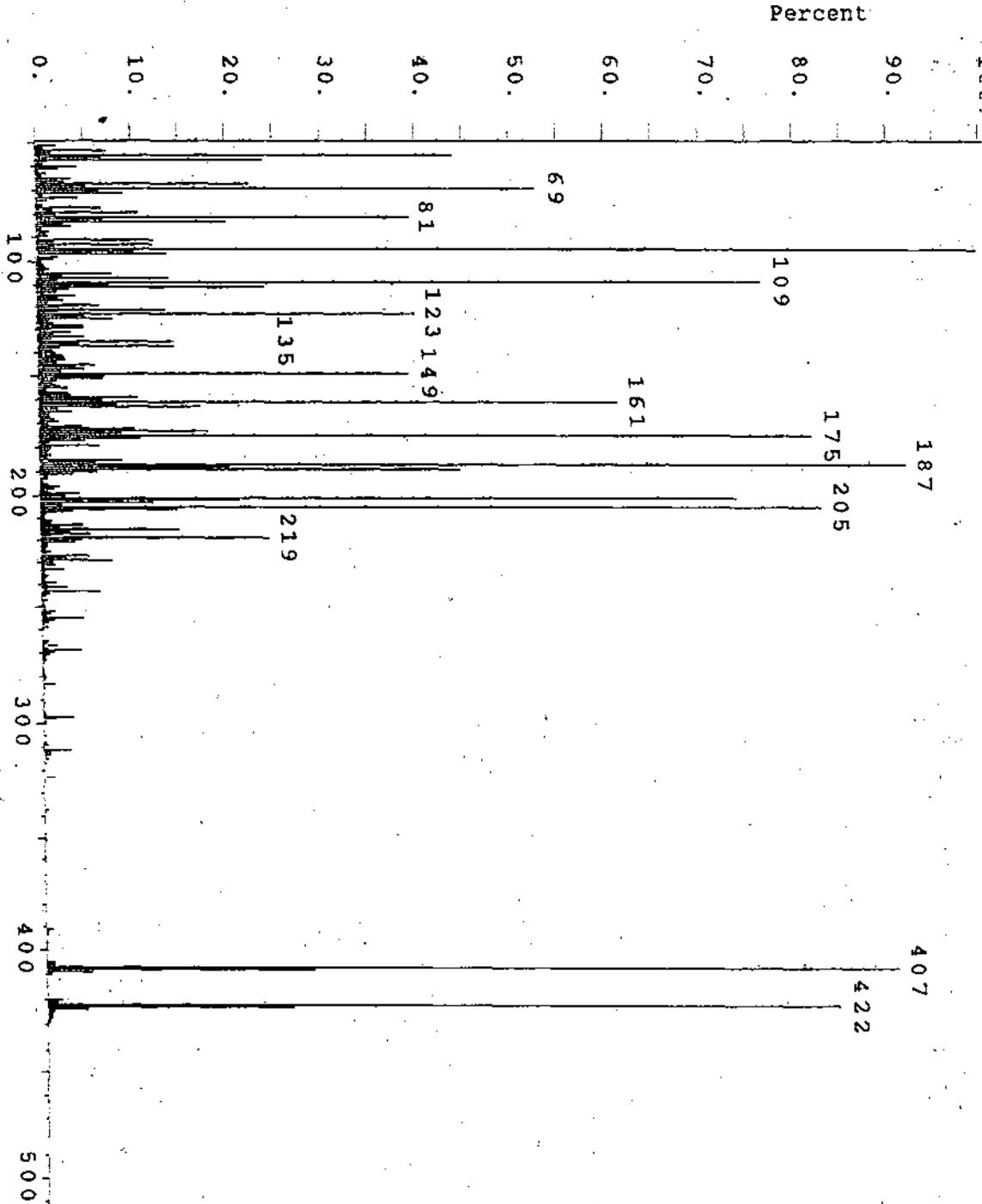


Fig. 26 : Mass spectrum (EIMS) of the phenolic product (361)

CHAPTER - IV

(Experimental Section)

General :

Melting points are uncorrected. The pet ether used throughout the investigation had b.p. 60 - 80°. NMR spectra were determined on a Varian AMX 300 spectrophotometer using chloroform-*d* solution containing tetramethylsilane as reference. This instrument operates at 300 MHz for ^1H and 75 MHz ^{for} ^{13}C . The IR spectra were recorded in Pye Unicam-SP-300S and Shimadzu FTIR- 8300 spectrophotometers. the mass spectra were determined with Jeol JMS-D300 mass spectrophotometer using direct sample introduction in the ion source. UV absorption spectra were taken in Shimad-Zu UV-240 spectrophotometer in 95% ethanol solution unless stated otherwise. CD-spectra were determined with Jobin Yvon-III spectrophotometer in dioxane solution unless stated otherwise. TLC was done on chromatoplate of silica gel G (E.Merck) and spots were visualized by exposing to iodine vapour in iodine chamber. In case of UV absorbing components, TLC was carried out on precoated Merck silica gel 60 F₂₅₄ aluminium sheets and spots were visualised by UV light. Column chromatography was performed on silica gel (60-120 mesh).

Photoirradiation was carried out with a low-pressure UV lamp (16 W), > 95% of irradiation at 254 nm. Sample solution for irradiation was degassed with nitrogen for 15 min before irradiation and passage of nitrogen continued for entire irradiation period.

Extraction of cork wastge : Isolation of Friedelin(354)

Dried and powdered cork waste (2 kg) was extracted with pet ether in soxhlet apparatus for 20 hr. Pet ether was distilled off and the gummy residue(11g) was purified by column chromatography over silica gel. Elution with pet ether as eluent gave a white solid (9 g) which on crystallization from chloroform-methanol afforded 7.2 g of pure friedelin (354), m.p. 260° - 261°C (lit. m.p. 262°-263°C), $[\alpha]_D - 39.7^\circ$ which was identical with an authentic sample of friedelin (TLC comparison done).

% Analysis for $C_{30}H_{50}O$

Found : C = 84.35 H = 11.91

Calculated : C = 84.44 H = 11.81

IR (nujol) : 1705 cm^{-1} (C = O)

Fig. 1

NaBH₄ reduction of Friedelin (354) in dioxane-methanol mixture : Preparation of Friedelan-3 β -ol (355)

6g Friedelin(354) was dissolved in 350 ml distilled dioxane by little warming. After cooling down at room temperature 90 ml MeOH and 6g NaBH₄ were added to it and the mixture was kept for 72 hours at room temperature (1g NaBH₄ was added additionally after 24 hours and another 1g NaBH₄ was added additionally after 48 hours). After 72 hours dil. HCl was added into the mixture until acidic and the mixture was taken up in CHCl₃ and the CHCl₃ layer was washed with repeatedly until neutral. The CHCl₃ layer was dried with anhydrous Na₂SO₄ and evaporated to dryness. A crude mass (5.8g) of friedelan-3 β -ol(355) containing a little amount of Friedelin (354) was obtained (TLC comparison done). The crude mass was subjected to column chromatography on silica gel. Pet ether:ethyl acetate (4:1) eluted a white solid which on crystallisation from CHCl₃ - MeOH afforded pure Friedelan-3 β -ol(355), crystalline white solid, 4.8g, m.p. 282°-284°C (lit. m.p. 283° - 285°C).

% Analysis for $C_{30}H_{52}O$

Found : C = 83.81 H = 11.90

Calculated : C = 84.11 H = 12.15

IR (nujol) : 3430 cm^{-1} (OH)

Fig. 2

Dehydration of Friedelan-3 β -ol(355) with phosphoryl chloride in pyridine : Preparation of Friedel-3-ene (356)

4.7g of Friedelan-3 β -ol(355) was dissolved in 180ml dry pyridine (little warming). 25ml POCl₃ was added and the mixture was heated gently over steambath for 2.5 hrs. The mixture was cooled, poured into crushed ice and the precipitated brown mass was filtered, dried and chromatographed on silica gel. Elution with pet ether gave a white solid (4.1g) which on crystallization from a large volume of chloroform afforded pure friedel-3-ene (356) m.p. 266°-267°C (lit. m.p. 268°-269°C).

% Analysis for C₃₀H₅₀

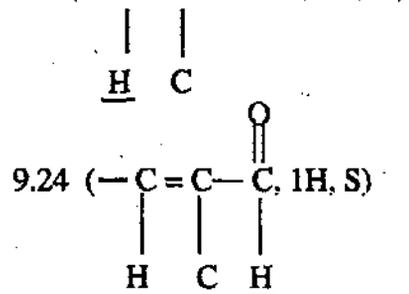
Found	:	C = 86.2	H = 11.9
Calculated	:	C = 87.8	H = 12.2
IR (nujol)	:	C = 780 cm ⁻¹ , 750 cm ⁻¹ (trisubstituted double bond) Fig. 3	
Mass (70 ev)	:	m/z 410 (M ⁺), 395, 361, 219, 190 Fig. 4	

Selenium dioxide oxidation of Δ^3 -Friedelene (356) : Preparation of Friedel-3-en-23-al (356B)

Δ^3 -friedelene (356) (0.5g) was dissolved in 1 litre acetic acid; 0.8g selenium dioxide was added and refluxed for 4 hr. The hot solution was filtered, cooled and poured into water. The mixture was extracted with ether, washed with water until neutral and dried (Na₂SO₄). The solid was chromatographed over silica gel. Elution with pet ether - ethyl acetate (9:1) gave a white solid which on crystallisation from chloroform-methanol furnished the crystalline compound friedel-3-en-23-al (356B).

% analysis of $C_{30}H_{48}O$

Found	: C = 84.73	H = 11.5
Calculated	: C = 84.78	H = 11.41
UV (ethanol)	: 227 nm, 330 nm (α,β -unsaturated aldehyde). (Fig.5)	
IR (Nujol)	: 2720, 1680, 1640, 1420, 830 cm^{-1} (signals for α,β -unsaturated aldehyde). (Fig. 6)	
1H NMR (200 MHz)	: δ 0.74 - 1.14 (7 methyls)	
	6.52 ($-C=C-CHO$, 1H, m)	



(Fig. 7)

Oxidation of Friedel-3-ene(356) with $Na_2Cr_2O_7$ in benzene - AcOH : Preparation of Friedel-3-en-2-one (357)

A mixture of Friedel-3-ene(356) (3.5g), $Na_2Cr_2O_7$ (6g), benzene (350 ml) and glacial AcOH (350 ml) was refluxed for four hours. After cooling water was added and the organic material was taken up in $CHCl_3$. $NaHCO_3$ was added and made neutral by repeated washing with water. The $CHCl_3$ solution was dried by anhydrous Na_2SO_4 and then evaporated to dryness. The solid (3.0g) thus obtained was chromatographed over silica gel.

Fractions eluted with pet ether-ethyl acetate (4:1) were combined and crystallisation from ethyl acetate to afford pure friedel-3-en-2-one(357), a crystalline white compound (2.2g), m.p. 287°-289°C (lit. m.p. 291°-292°C).

% Analysis of $C_{30}H_{48}O$

Found : C = 84.22 H = 10.89
 Calculated : C = 84.9 H = 11.32
 IR (nujol) : 1658, 1620, 850, 720 cm^{-1} (Cyclohexenone chromophore). **Fig. 9**
 UV (MeOH) : 236 nm (ϵ 14500) **Fig. 8**

1H NMR (300 MHz, $CDCl_3$) : δ 5.65 (vinyl proton, d, $J \sim 1$ Hz, 1H)
 δ 1.84 (vinyl methyl, d, $J \sim 1$ Hz, 3H)
 δ 0.91 to δ 1.14 (seven saturated t-methyl). **Fig. 10**

^{13}C NMR (75 MHz, $CDCl_3$) : 200.62 (C = O)
 172.06 and 125.32 (two olefinic carbons)
 55.60 to 17.62 (27 saturated carbon atom). **Fig. 11**

^{13}C NMR : δ 17.62, 17.89, 18.45, 18.79, 18.93, 20.06,
 [Expanded (δ 16 to 57)] 28.04, 29.91, 30.15, 31.71, 32.02, 32.12,
 32.64, 34.24, 34.50, 34.91, 35.21, 35.82,
 36.92, 37.56, 38.14, 39.13, 39.58, 40.01,
 42.65, 52.52, 55.60. **Fig. 11A**

DDQ oxidation of Friedel-3-en-2-one (357) : Preparation of Friedel-1(10), 3-dien-2-one (358)

2g of friedel-3-en-2-one (357) was dissolved in 200 ml of dry distilled dioxane. To it 2.5g of DDQ was added and the mixture was refluxed for 3 hours under nitrogen blanket. The mixture was kept for 48 hrs at room temperature and then filtered through neutral Al_2O_3 . The filtrate, diluted with water, extracted with $CHCl_3$, washed with Na_2CO_3 and then with water until neutral. The liquid was dried with anhydrous Na_2SO_4 and then evaporated to dryness to afford a solid (1.7 g), TLC (EtOAc : ϕ H = 1:9) of which revealed the presence of two spots. One spot (R_f 0.73) was due to presence of unreacted starting material (357) and the other of the oxidised product (358) (R_f 0.55). The crude reaction mixture was chromatographed over silica gel. Elution with pet ether-ethyl acetate (4:1) yielded a white solid which on crystallisation from ethyl acetate afforded fine needles of (358) (35% yield), m.p. 279° - 280°C.

% Analysis of C₃₀H₄₆O

Found	: C = 84.9	H = 10.2	
Calculated	: C = 85.3	H = 10.9	
IR (nujol)	: 1646, 1610, 1584 and 890 cm ⁻¹		Fig. 13
UV (MeOH)	: 246 nm		Fig. 12
¹ H NMR	: δ 0.92 to 1.25 (seven saturated methyl group)		
	δ 1.95 (one vinyl methyl, d, J ~ 1 Hz, 3H)		
	δ 6.11 (d, J ~ 1 Hz, 1H), δ 6.02 (1H, S) (two olefinic protons)		Fig. 14
¹ H NMR	:		
[Expanded (δ 0.8 to 2.25)]			Fig. 14A
¹³ C NMR	: δ 187.55 (C = O)		
	δ 177.50, 167.29, 125.68, 121.86 (four olefinic carbons)		
	δ 50.16 to 17.73 (25 saturated carbons)		Fig. 15
¹³ C NMR	:		
[Expanded (δ 15 to 55)]			
	δ 17.73, 18.63, 19.17, 20.28, 23.93, 27.52, 28.06, 29.90, 30.69,		
	31.63, 31.98, 32.43, 32.58, 33.97, 34.90, 35.23, 35.75, 37.10,		
	39.12, 39.22, 39.36, 40.89, 42.60, 43.93, 50.16.		Fig. 15A
EIMS (70eV)	: M ⁺ 422 (48%), 407 (M ⁺ - CH ₃),		
	298, 286, 271, 229, 203, 182,		
	175, 135, 95, 81 m/z.		Fig. 16
CD (dioxane):	Δε +10.4 (260 nm)		
	-7.7 (238 nm)		Fig. 17

Photolysis of Friedel-1(10), 3-dien-2-one (358) : Formation of Phenolic Product (361) and Lumiprodukt (360)

300 mg of friedel-1(10), 3-dien-2-one(358) was dissolved in 110 ml dry and distilled dioxane, the solution was degassed by passing nitrogen for 15 min and was irradiated at ambient temperature with 254 nm low pressure mercury lamp in nitrogen atmosphere for 15, 30 and 65 minutes (each time the progress of the reaction was monitored in TLC (precoated plates). The photoreaction was almost complete in 45 minutes (only a trace of starting material could be observed). Dioxane was removed

at 40°C under rotary vacuum evaporator and the mass obtained was washed with water in CHCl_3 solution. It was evaporated to dryness and the solid obtained (280 mg, was subjected to TLC.

TLC revealed three spots. One was due to unreacted starting material (R_f 0.55) and other two were of photo products (R_f 0.63 and 0.80). the crude photolysed material was chromatographed on silice gel. The first photoproduct (phenolic) (361) eluted in pet ether-ethyl acetate (8:1) was crystallised from ethyl acetate to give fine needles (yield < 1.5%) (R_f 0.80), m.p. 198°C.

UV (MeOH)	: λ_{max} 280 (log ϵ 3.42) (tetrasubstituted phenol)	Fig. 24
IR (nujol)	: ν_{max} 3281(OH) 1574 cm^{-1} (aromatic)	Fig. 25
EIMS (70 eV)	: M^+ 422(85%), 407 ($M^+ - \text{CH}_3$) (92%), 205, 187, 175, 161, 149, 109, 95 m/z.	Fig. 26
Accurate mass measurement in high resolution mass spectrum (HRMS)	: Found m/z 422.2501 Calculated for $\text{C}_{30}\text{H}_{46}\text{O}$ m/z 422.2508	

Fractions eluted with pet ether : ethyl acetate (6 : 1) were combined and on crystallisation from ethyl acetate afforded needles of lumiprodukt (360) (R_f 0.63) (yield 53%).

% Analysis of $\text{C}_{30}\text{H}_{46}\text{O}$

Found	: C = 84.81	H = 10.4	
Calculated	: C = 85.3	H = 10.9	
IR (nujol)	: 1675, 1595 cm^{-1} (Cyclopentenone)		Fig. 19
UV (MeOH)	: 241nm (conjugated ketone)		Fig. 18
^1H NMR	: δ 5.65 (Olefinic proton, d, $J \sim 1\text{Hz}$, 1H) δ 2.14 (Vinyl methyl group), d, $J \sim 1\text{Hz}$, 3H) δ 0.92 to 1.15 (seven tertiary methyl)		Fig. 20
^1H NMR	: [Expanded (δ 0.06 to 2.4)]		Fig. 20A
^{13}C NMR	: δ 206 (C = O) δ 175 and 133 (two olefinic carbons) δ 58.80 to 16.84 (27 sp 3 carbons)		Fig. 21

¹³C NMR :[Expanded (δ 15 to 60)]

δ 16.84, 17.61, 19.07, 20.85, 22.34, 22.55, 28.01, 29.82,
 31.50, 32.14, 32.24 (2 Cs), 32.52, 35.10, 35.43, 35.73
 (2 Cs), 37.21, 37.99, 38.58, 39.27, 39.70, 40.83, 42.37,
 50.69, 55.06, 58.80.

Fig. 21A

EIMS (70 eV)

: M⁺ 422 (73%), 407 (M⁺ — CH₃), 298, 218,

204, 175, 161, 149, 136, 123, 109 and 95.

Fig. 22

C. D. (Dioxane)

: 253nm ($\Delta\epsilon = + 3.8$)271 nm ($\Delta\epsilon = -10.4$)237 nm ($\Delta\epsilon = + 11.5$)

Fig. 23

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PART – II

**(Preparation and Molecular Rearrangement of
2 α , 3 α -Epoxy Lupan-1-one Catalysed by Boron
Trifluoride and by Ultraviolet Irradiation)**

CHAPTER - I

(A Short Review on the Molecular Rearrangement of α,β -Epoxy ketones Induced by (1) the Lewis Acid, Boron Trifluoride and (2) by Ultra-violet Irradiation)

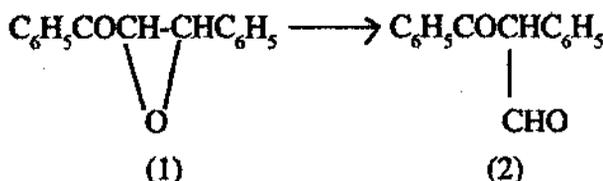
Introduction :

For several decades, ring contracted reactions involving molecular rearrangements have attracted the attention of organic chemists. These provide convenient and expedient methods for the preparation of many naturally occurring and novel synthetic compounds. Of several techniques adopted for ring contraction, molecular rearrangement of α,β -epoxy ketones induced by the Lewis acid, borontrifluoride - etherate is a unique one and has successfully been utilised by many groups. This is because of easy availability and pronounced reactivity of boron trifluoride. Interestingly, this same molecular rearrangement, in many cases, of α,β -epoxy ketones has also been effected by ultraviolet irradiation. Consequently, we have divided this review into two sections, SECTION - A, induced by BF_3 -etherate and SECTION-B, induced by ultra-violet irradiation.

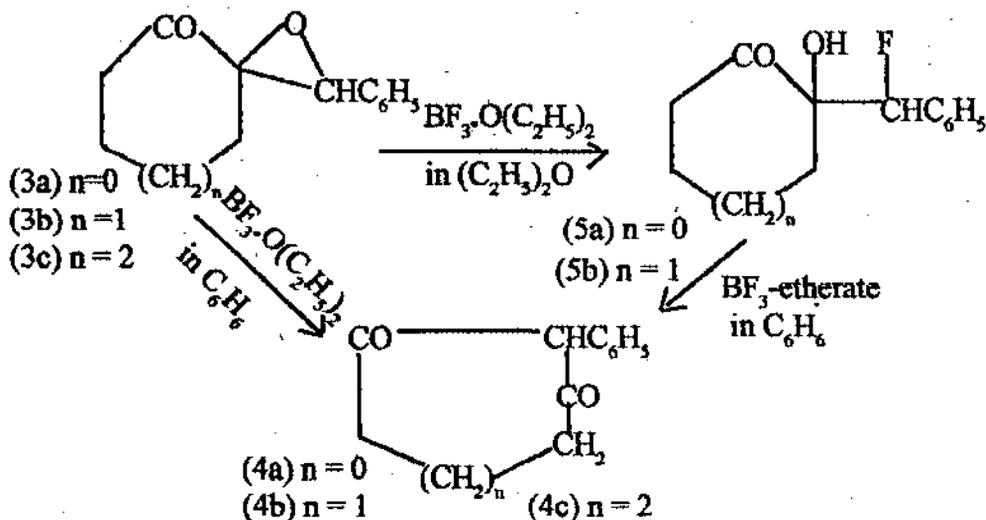
SECTION A

(Induced by BF_3 -Etherate)

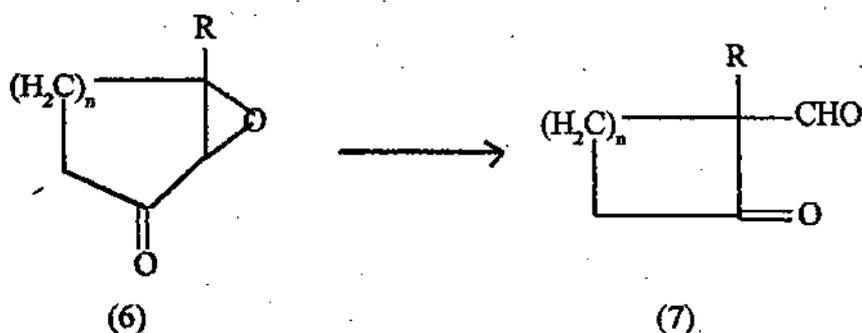
House¹ initially noticed that acid-catalysed isomerisation of *trans*-benzalacetophenone oxide (1) yielded α -formyldeoxybenzoin (2) involving a intramolecular migration of the benzoyl group.



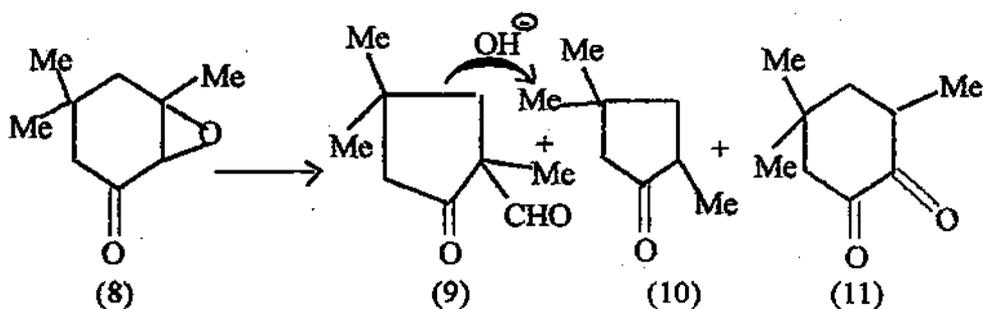
House and Wasson² then observed that 2-benzalicyclopentanone oxide (3a), 2-benzalicyclohexanone oxide (3b) and 2-benzalicycloheptanone oxide (3c) have undergone isomerisation to 2-phenyl-1,3-cyclohexanedione (4a), 2-phenyl-1,3-cycloheptanedione (4b) and 2-phenyl-1,3-cyclooctanedione (4c) respectively, on treatment with $\text{BF}_3 \cdot \text{Et}_2\text{O}$ in benzene solution. When the same cyclohexanone and cycloheptanone derivatives were treated with BF_3 in ether solvent, the products were fluorohydrins (5a-b) which ultimately produced (4a-b) on treatment with benzene. The products in these cases resulted from ring expansion.



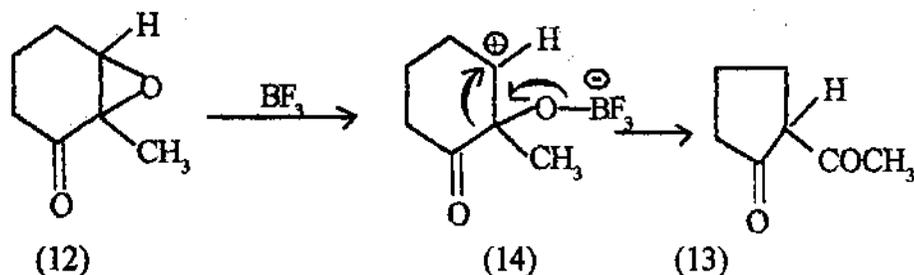
House and Wasson³ have further extended their study and have observed that cyclic epoxy ketones of the type (6, $n > 1$) in the presence of BF_3 -etherate undergo molecular rearrangement with reduction in ring size of ketones to produce the ketoaldehyde (7). This reaction is fairly general and provides a convenient method for the conversion of α,β -epoxy cyclohexanone derivatives to the corresponding ring contracted α -formyl or α -acyl cyclopentanone accompanied in certain instances by 1,2-cyclohexane diones.



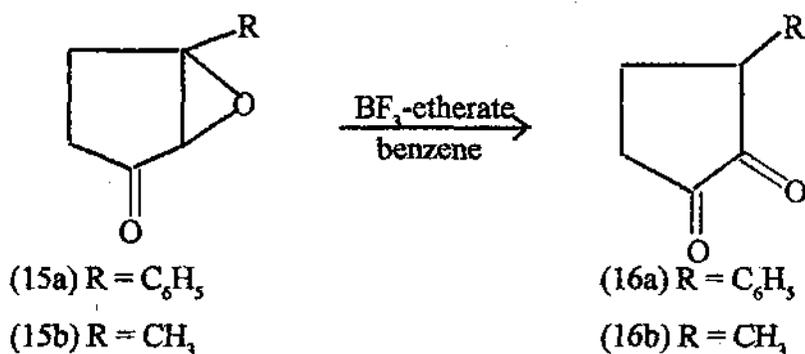
Isophorone oxide (8) gave the ring contracted ketoaldehyde (9) as the major product along with some deformed product (10) and 1,2-diketone (11). Amount of (10) increased considerably on alkali treatment of (9).



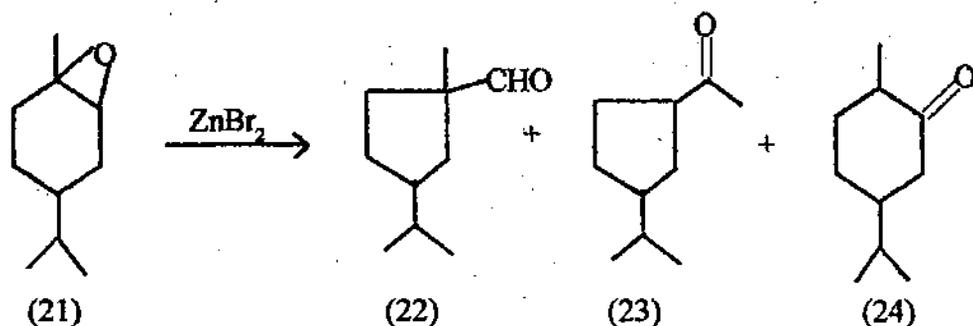
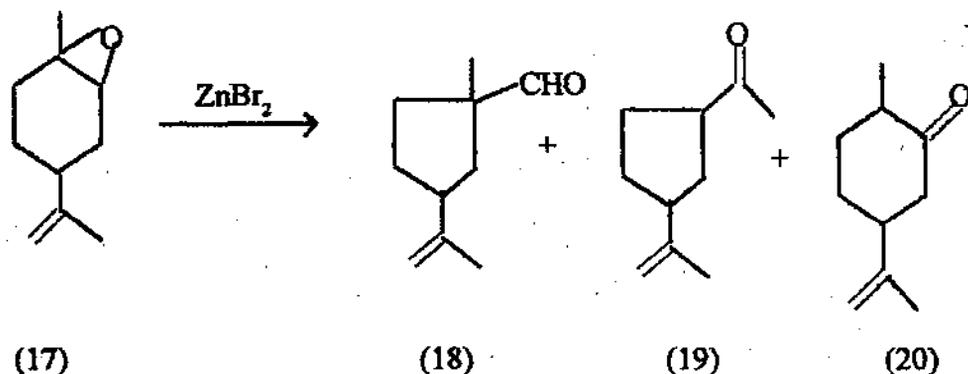
On the other hand, 2,3-epoxy-2-methyl cyclohexanone (12) afforded the ring-contracted β -diketone (13) as the sole product. They invoked the intermediate (14) which subsequently on ring contraction formed (13).



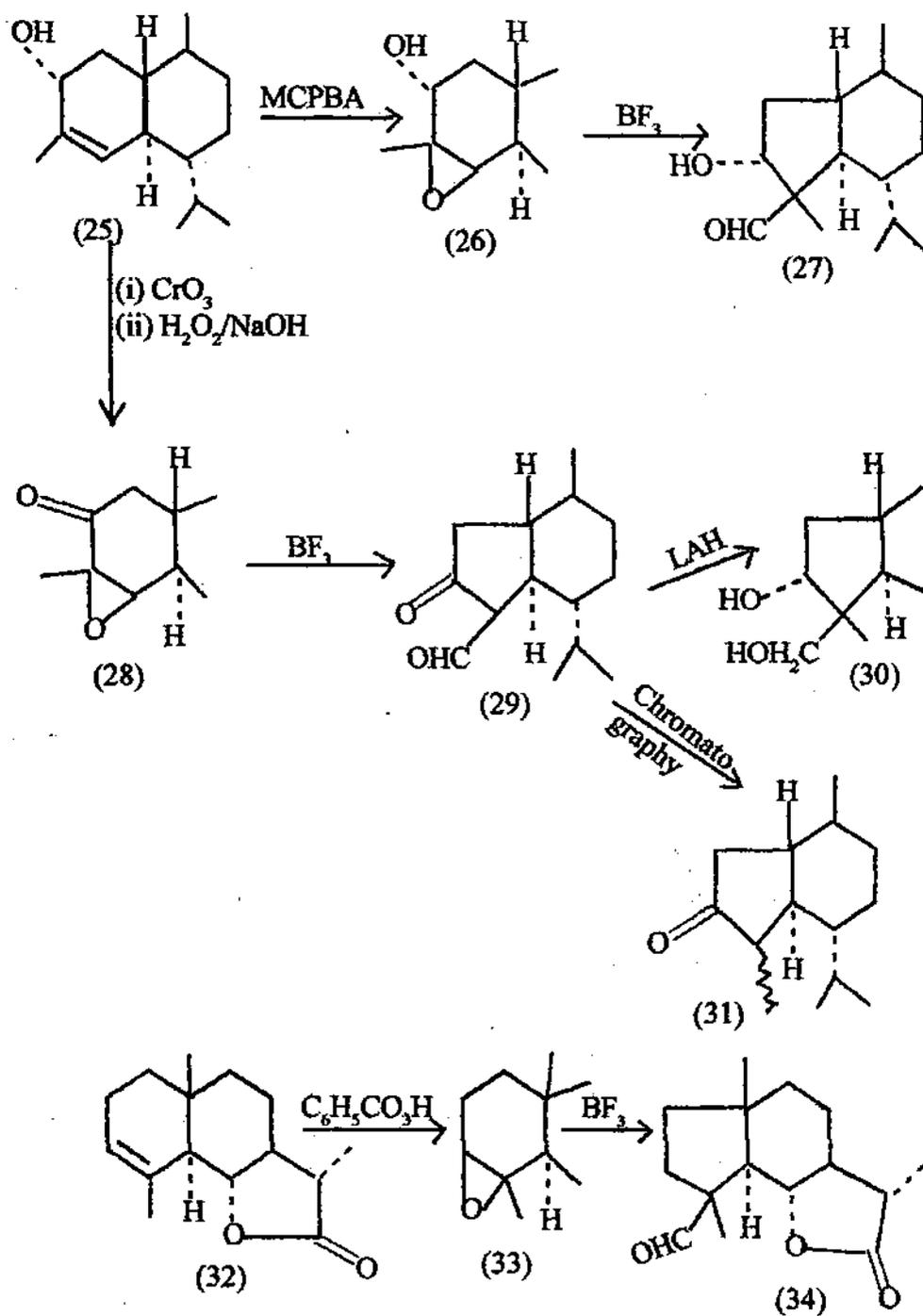
This reaction did not produce ring-contracted cyclobutanone derivatives from corresponding cyclopentanone e.g. from the rearrangement of (15a, b), (16a, b) were the only products isolated as the enol form of α -diketone.



This rearrangement is not monopoly of epoxyketones. Suitable epoxides also can undergo this reaction. Setting and coworkers⁴ carried out molecular rearrangement of monoterpenoid, limonene oxide (17) induced by ZnBr_2 and obtained a ring contracted aldehyde (18), a ring-contracted ketone (19) and a uncontracted ketone, dihydrocarvone (20) in 30%, 10% and 59% yield, respectively. They also applied this reaction on carvomentheneoxide (21) and obtained similar type of products (22), (23) and (24).

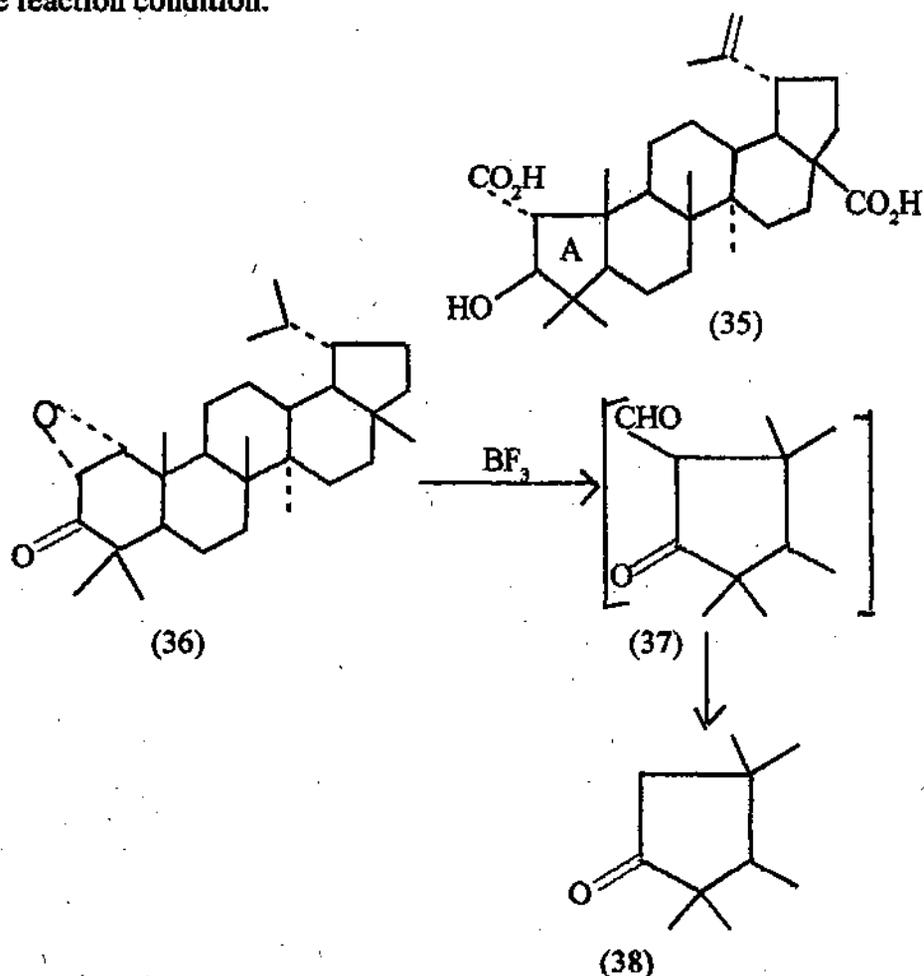


Kartha and Chakrabarti³ studied the action of BF_3 -etherate on epoxides and epoxy-ketones. They noted that BF_3 not only induced molecular rearrangement of epoxyketones but also of epoxides. The success depends on the nature and position of the double bond from which epoxides are prepared. Several cadinenic and selenic epoxides derived from sesquiterpenoids, on treatment with BF_3 have been found to undergo ring-contraction resulting in the formation of fully substituted aldehydes. The epoxide (26) derived from dihydrokhusinol (25) by MCPBA on BF_3 treatment afforded ring-contracted crystalline hydroxy aldehyde (27) possessing characteristic IR bands at 2703 and 1712 cm^{-1} . The epoxyketone (28) derived from (25) by CrO_3 oxidation followed by epoxidation by alkaline H_2O_2 , on BF_3 treatment gave the ring-contracted ketoaldehyde (29) showing IR bands at 2725, 1709 (CHO) and 1742 (cyclopentanone). The ketoaldehyde (29) on LAH treatment afforded the crystalline diol (30), and chromatography through slightly alkaline alumina gave the deformylated product, the cyclopentanone (31), the structure of which was supported by NMR analysis which displayed a peak at τ 7.8 (3H) due to three protons α to the carbonyl group.

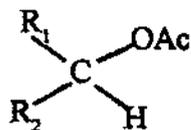


The epoxide (33) derived from α -santenolide (32) on BF_3 -etherate treatment gave fully substituted ring-contracted aldehyde (34) which exhibited IR bands at 2703, 1724 (aldehyde), 1767 cm^{-1} (γ -lactone). The NMR spectrum is in conformity with its assigned structure.

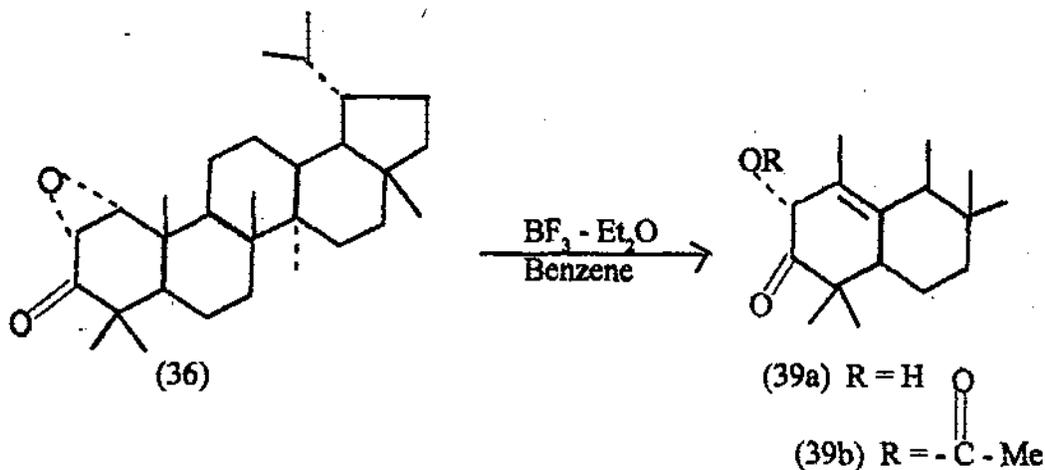
With a view to developing a method for partial synthesis of the A-ring-contracted triterpene acid, cianothic acid (35), Chatterjee and colleagues⁶ took up the study of BF_3 -etherate catalysed rearrangement of the model triterpene, $1\alpha, 2\alpha$ -epoxylupan-3-one (36) following the same procedure prescribed by House et al.⁵. However, in this reaction, they could not isolate the ketoaldehyde (37), but obtained only the ketone, A-norlupan-2-one (38) in good yield. Most probably, the intermediate ketoaldehyde (37) that was formed initially underwent easy loss of the formyl group under the reaction condition.



Ganguly et al.⁷ carried out BF_3 -catalysed rearrangement of $1\alpha, 2\alpha$ -epoxy lupan-3-one (36) and obtained a crystalline unsaturated α ketol which showed ν_{max} 3500(OH), 1712 (cyclohexanone) cm^{-1} , λ_{max} end absorption at 208 nm; on acetylation it gave a crystalline acetate ν_{max} 1740, 1220 (acetate), 1725 cm^{-1} (cyclohexanone). The NMR spectrum of the acetate showed signals at δ 2.21 ($-\text{COCH}_3$) and a sharp singlet at 85.45



which prior to acetylation appeared at δ 4.5. Finally, olefinic Me signal of the rearrangement product appeared as a singlet at δ 1.3. Based on the above observation, the rearrangement product was assigned structure 1-methyl-2 α -hydroxylup-1(10) α -3-one (39a) and the corresponding acetate (39b). Here, most probably due to the presence of a neopentyl system adjacent to the epoxy ketone system, methyl migration occurred instead of ring contraction.

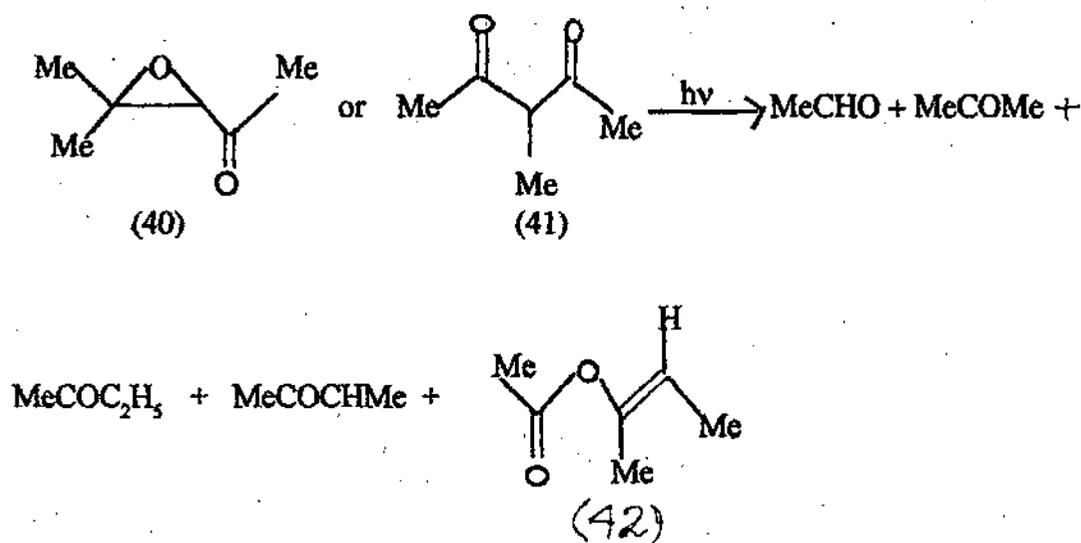


SECTION - B

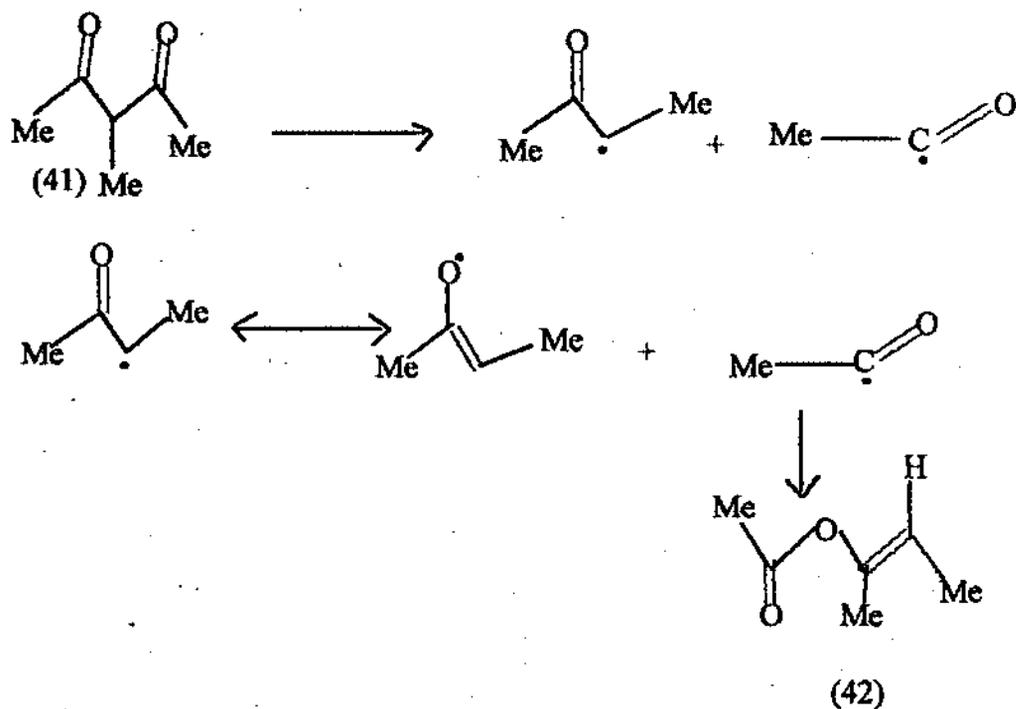
(Induced by UV Irradiation)

When atoms with π -bonding electrons such as carbonyl group, are attached to the carbon atom of adjacent three membered cyclopropyl or α,β -epoxyketone group having bent bondings, some overlapping and interaction between the bent bonds and the π -orbitals occur giving rise to delocalisation. This delocalisation has been studied by UV,^{8,9} IR⁸, NMR¹⁰ and theoretical^{11,12} considerations. The interaction becomes maximum when the three-membered ring lie parallel to the π orbital of the carbonyl group. The delocalised orbitals of the three-membered ring in this geometric position overlap with the non bonding π electrons of the carbonyl oxygen. This small amount of admixed π character makes the n,π^* somewhat comparable to the allowed π,π^* transition. As a result, the electric-dipole-transition moment of the n,π^* transition which is symmetry-forbidden in simple ketones, is no longer forbidden in these systems^{13,14}.

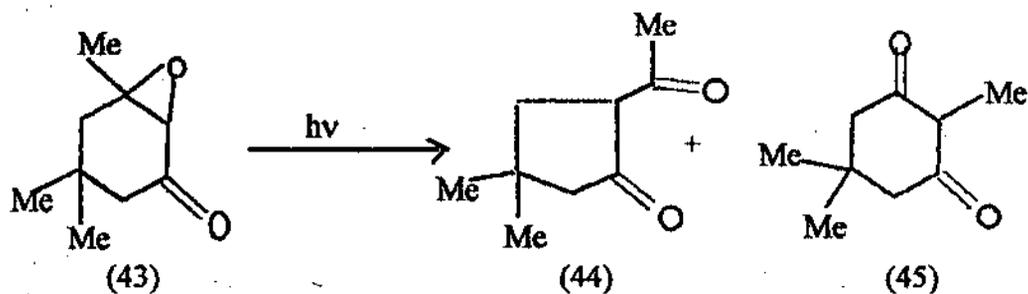
Simple acyclic α,β -epoxyketones e.g. 3,4-epoxy-4-methyl-2-pentanone (40) on photolysis using wavelength above 250 nm gave 3-methyl-pentane-2,4-dione (41) in yields of 2 to 12 per cent¹⁵. Since the photoproduct 1,3-diketone (41) is also photolabile, its yield is low and on further irradiation (40) and (41) gave acetaldehyde, acetone, methyl ethyl ketone, methyl isopropyl ketone, 2-butenyl acetate (42) and other high-boiling components. These host of products are obtained as secondary processes particularly in the absence of any radical or ion-stabilizing groups.



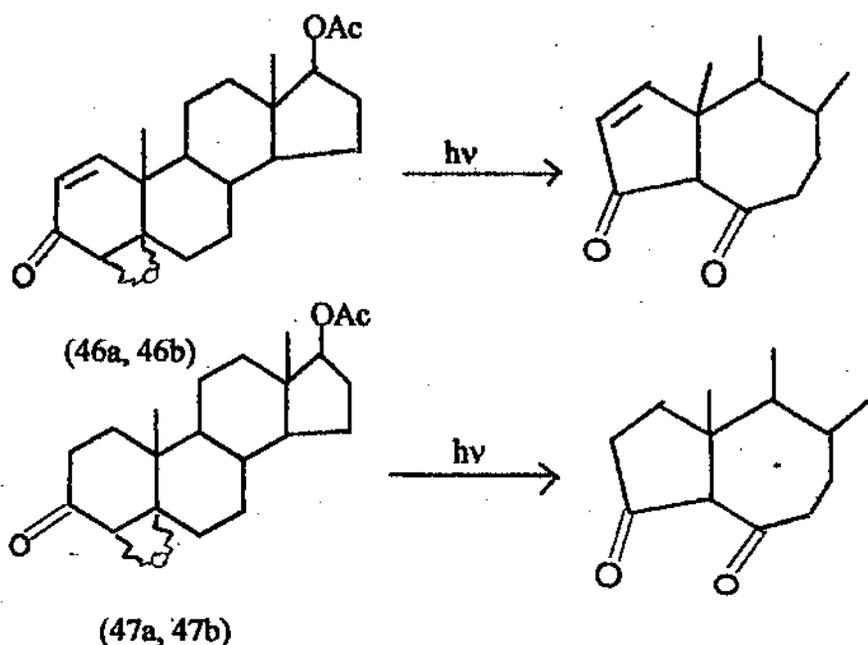
Formation of (42) is accounted for in the following way :



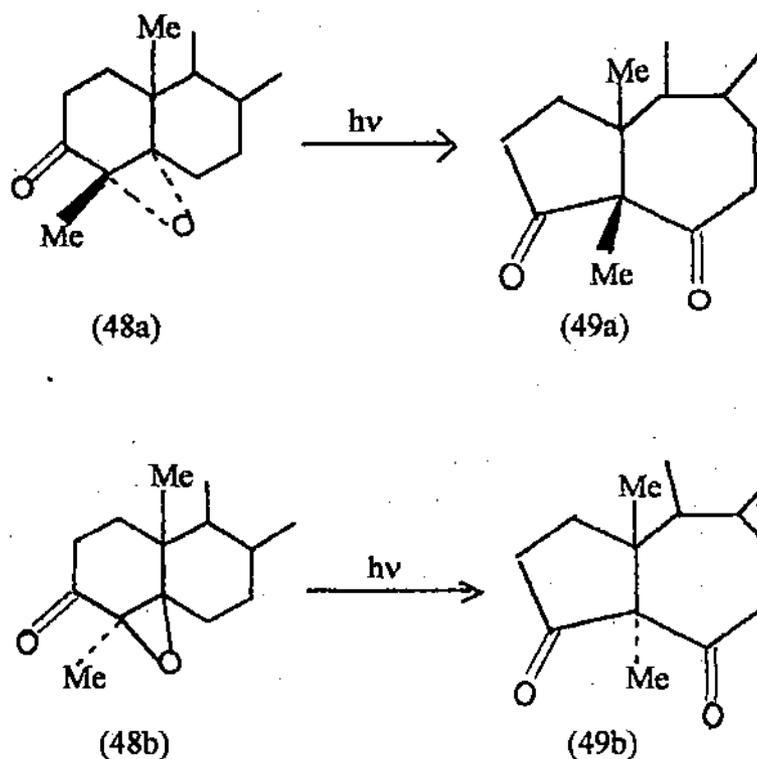
The photolysis of monocyclic isophorone oxide (43) in a variety of solvents gave a mixture of 1,3 diketones 2-acetyl-4,4-dimethylcyclohexanone (44) and 2,5,5-trimethylcyclohexanone - 1,3-dione (45) in 9 : 1 ratio.



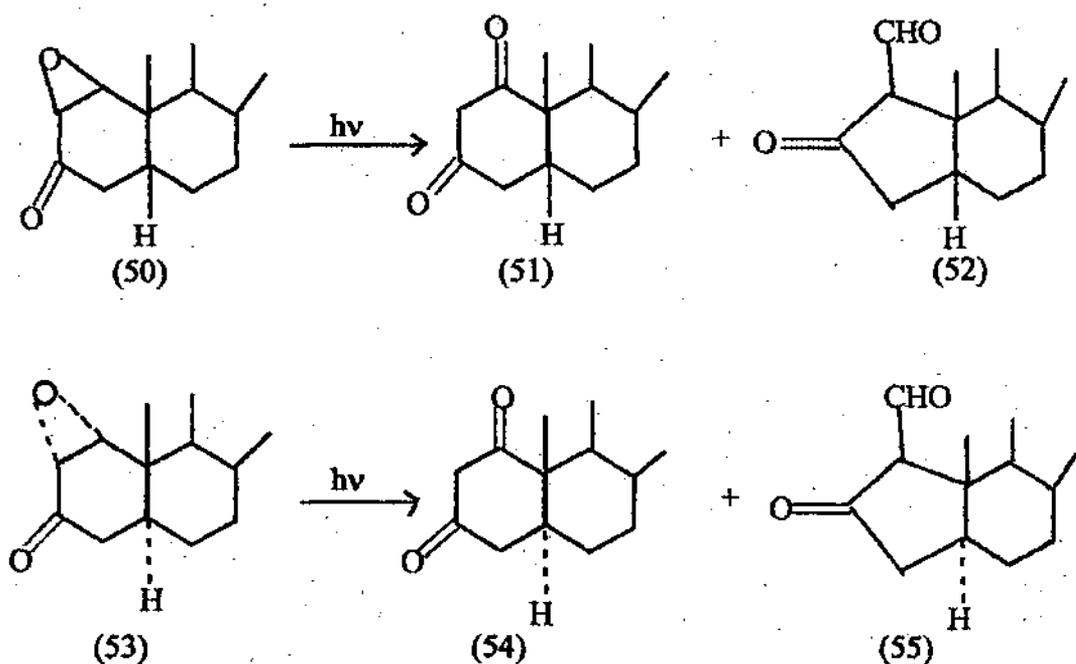
An analogous finding was reported in the polycyclic α,β -epoxy ketone derivative of steroid¹⁶. On irradiation, the oxides (46) and (47) produced the β -diketones as a result of an alkyl group shift from the β to the α carbon. Irrespective of the relative configuration of the oxide ring, two stereoisomeric pairs (46a, 46b) and (47a, 47b) yielded a single 1,3-diketone. It has been demonstrated by Wehrli and coworkers¹⁷ that the photochemical transformations occurring in the 3-oxo-4,5-oxidosteroids systems are stereospecific.



Photolysis of stereoisomeric 4-methyltestosterone oxides (48a, 48b) afforded the β -diketones (49a) and (49b) which are stereospecific, differing only in their configuration at C-4. The stereospecificity has been accounted for by assuming that the cyclodecane system of the transition state retains the relative spatial arrangements of the reaction centres in the starting epoxy ketone which makes the observed stereospecificity of this rearrangement possible.

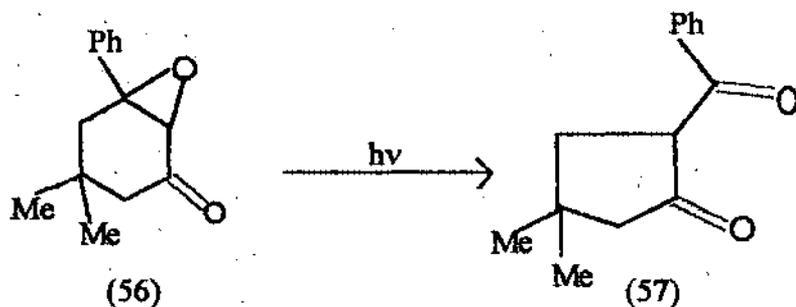


Jeger et al.¹⁸ carried out studies on the stereochemical requirement of the β -alkyl-group migration in some detail. From irradiation of a dioxane solution of 1 β , 2 β -oxido-17 β -acetoxy-5 β -androstan-3-one(50) a mixture of the 1,3-diketone(51) and ketoaldehyde (52) were obtained. Similarly, the 5 α -isomer (53) gave the related 1,3-diketone (54) and keto aldehyde (55).

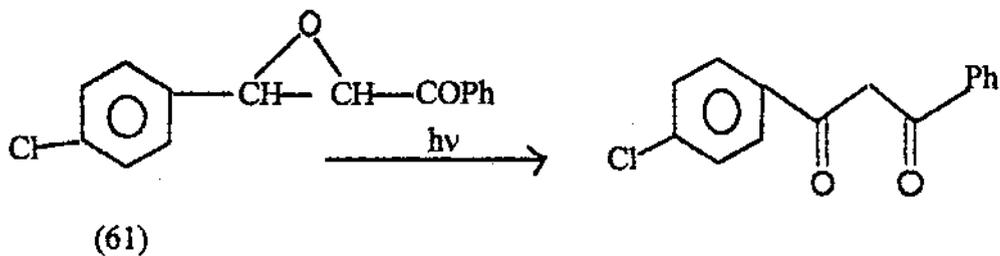
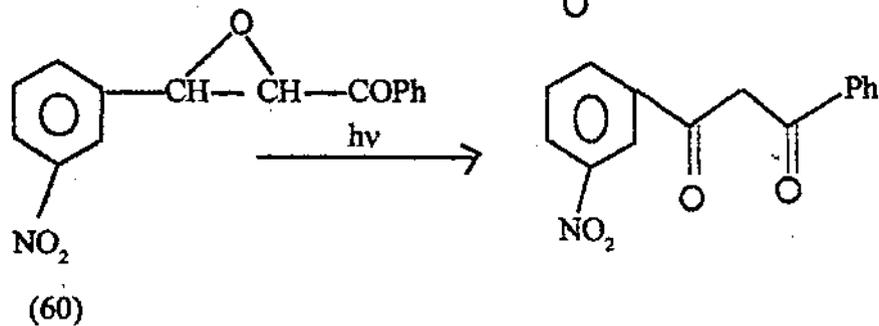
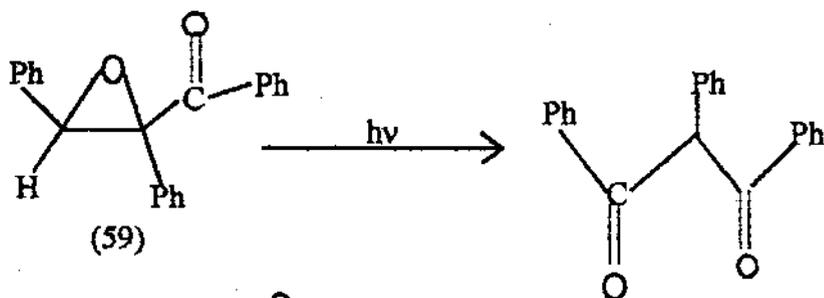
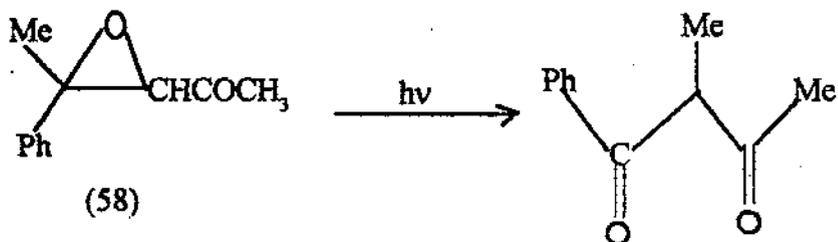


It has been envisaged that these products are formed as a result of migration of carbon atom 10 and of a competing 1,2 hydrogen shift. In order to explain the observed stereospecificity Jeger¹⁸ has proposed that the hydrogen shift or the 1,10-bond migration is concerted with the formation of carbonyl at C-1.

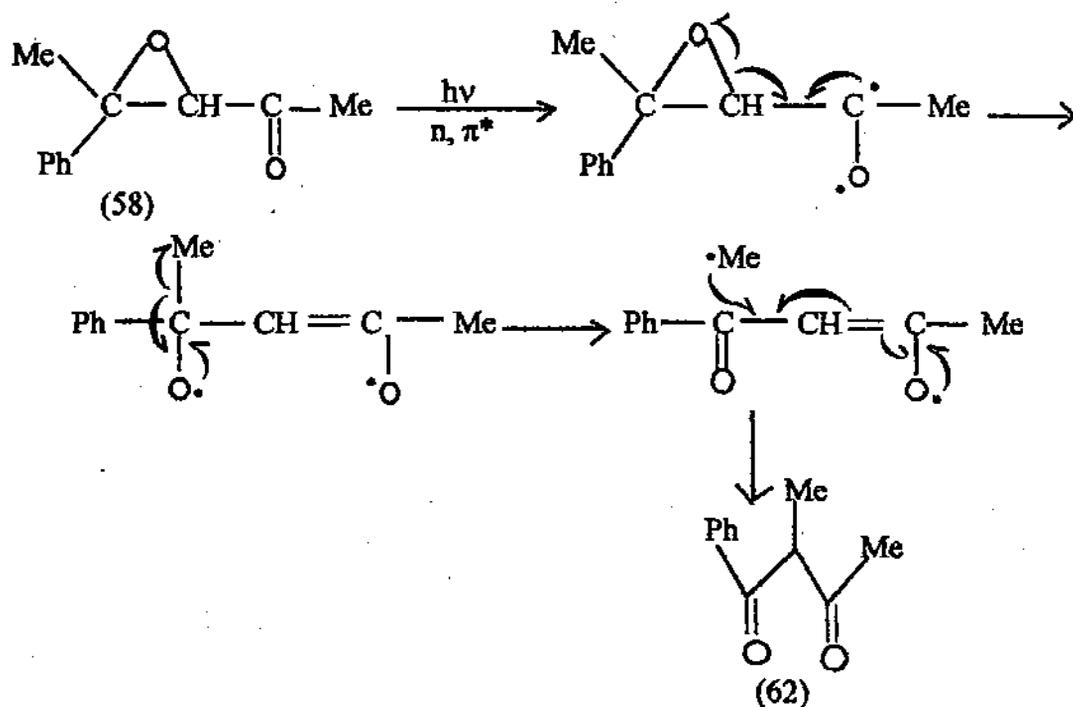
Johnson and coworkers¹⁵ carried out irradiation of 3-phenyl-5,5-dimethyl-2,3-epoxycyclohexanone (56) and obtained 2-benzoyl-4,4-dimethylcyclopentanone (57) and surprisingly, no detectable quantity of the isomeric cyclohexadienone. This preferential shift of alkyl rather than aryl group - an unusual order of migratory aptitude for the photochemical rearrangement of α,β -epoxyketones to β -diketones seems to be a fundamental characteristic of the reaction.



The absence of phenyl migration and the same preferential order of migration has been observed too in many open-chain epoxyketones (58)¹⁹, (59)²⁰ and (61)²¹. This appears to be not due to steric factors but rather suggestive of considerable bond-breaking in the transition state of this phototransformation.

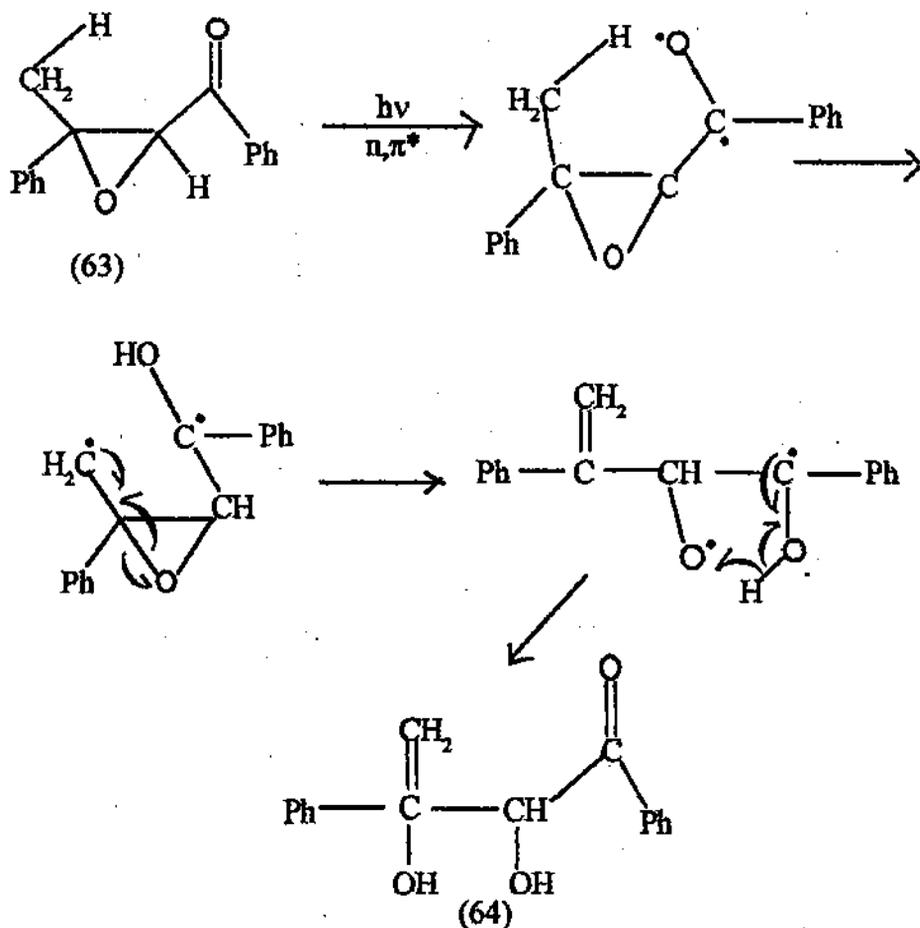


Zimmerman et al.²² proposed a mechanism for the photochemical conversion of α,β -epoxyketones to β -di-ketone. This reaction occurs from n,π^* excited state in which the electron density at the carbonyl carbon is enhanced relative to that in the ground state. Substituents alpha to the carbonyl group would readily be expelled by elimination either as anion or as odd electron species from the n,π^* excited manifold. Whether the excited state expels an anion or a radical is related to the ability of the environment to stabilize the ionic species by solvation. The unusual migratory aptitude behaviour in this system has been explained by Zimmerman by homolytic carbon oxygen fission as shown in the scheme :



The preferred expulsion of the methyl radical as opposed to the phenyl radical in the case of epoxyketone is analogous to the direction of radical fragmentation noticed in the decomposition of cumyl peroxide¹⁸ and phenyldimethylcarbinyl hypochlorite²³. Upon direct irradiation in solution (63) undergoes n,π^* excitation to form an excited state which rearranges and produces 1,3-diphenyl-3-buten-2-ol-1-one (64). After the n,π^* promotion one remaining $2p$ electron is still localised on oxygen which shows behaviour characteristic of reactive alkoxy radicals, one property of which is hydrogen abstraction. Abstraction of the γ -hydrogen gives rise to a species in which the odd electron is conjugated with the oxirane group. Homolytic

ring cleavage followed by intramolecular disproportionation rationalises nicely the observed product as depicted below :

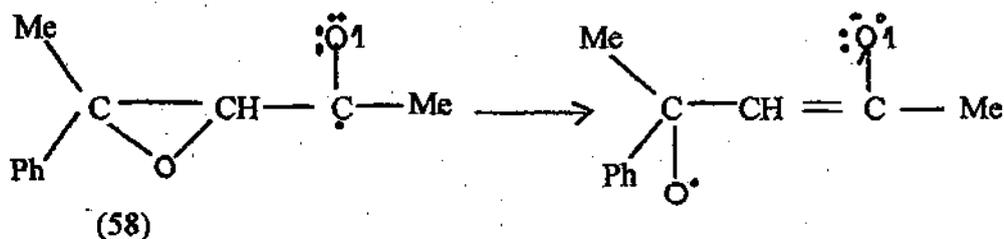


This mechanism requires proximity of the benzoyl and methyl groups for effective hydrogen transfer to occur. That *cis*-dypnone oxide fails to give this reaction supports this proposition²².

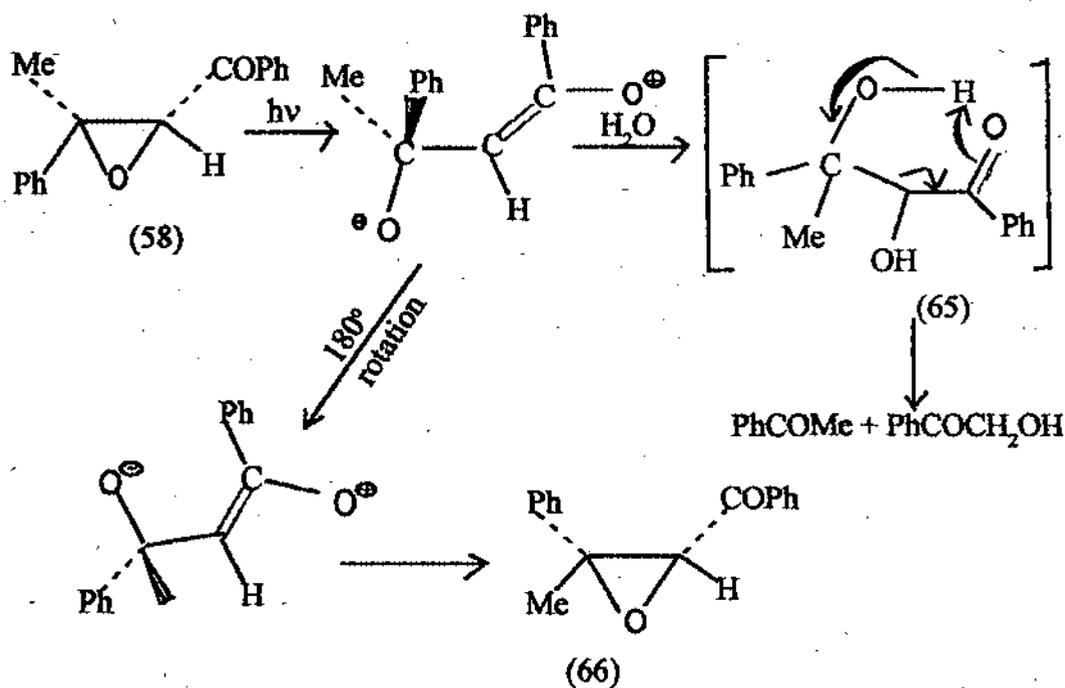
Markos and Reusch²⁴ observed that epoxy ketone photorearrangements are not sensitive to the presence of oxygen or changes in the solvents. Furthermore, the known triplet quenchers such as piperylene and 2,5-dimethyl-2,4-hexadiene used in concentration ranging from 0.1 to 9.0 M, did not affect the rate and course of rearrangement, led to the proposition that this phototransformation is derived from singlet manifold. Besides, acetophenone (0.5 M), a triplet state sensitizer, did not function as a sensitizer for the rearrangement in acetonitrile solution. The low quantum

yield observed for some of these rearrangements has been attributed to poor efficiency for the $[S_1]$ \rightarrow 1,3 diradical formation or an unfavourable competition between rearrangement and oxirane ring formation from the diradical. A report²⁵ concerning the thermal decomposition of β -methyl- β -phenyl- β -peroxypropiolactone noted a fivefold preference for methyl migration vs. phenyl and suggested a 1,3-diradical intermediate similar to the photoreaction. This unusual migrational aptitudes suggest that migrating group must have radical character.

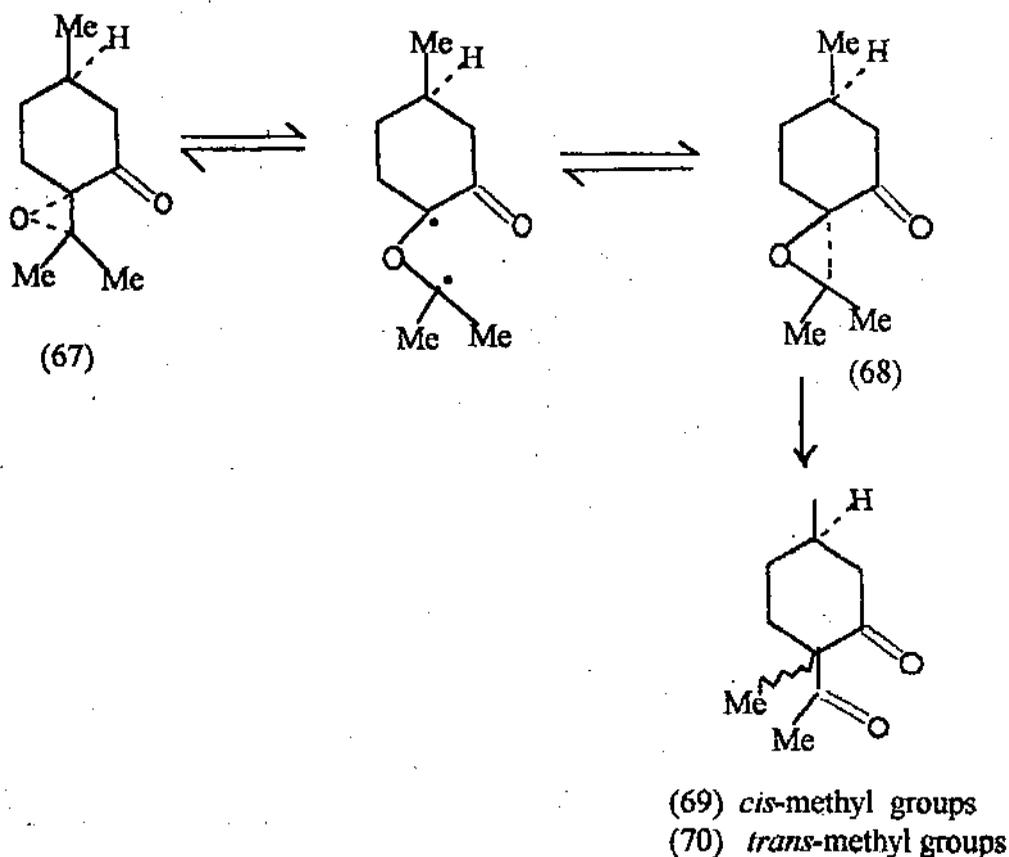
An interesting case of photo-reaction of α,β -epoxy ketone on the nature of the carbonyl group has been noted. In contrast to 3,4-epoxy-4-phenyl-2-pentanone (58) which rearranges to β -diketone (62), the structurally related *trans*-dypnone oxide (63) exhibits an entirely different photochemical sequence²². The striking difference in the photochemical behaviour of (63) and (58) is due to the greater delocalisation of the electron in the benzoyl group which decreases the possibility of ring scission in (63). On the other hand, the excited acetyl group in (58) has the electron in the π^* orbital localised on the carbon and consequently, more available for β -elimination.



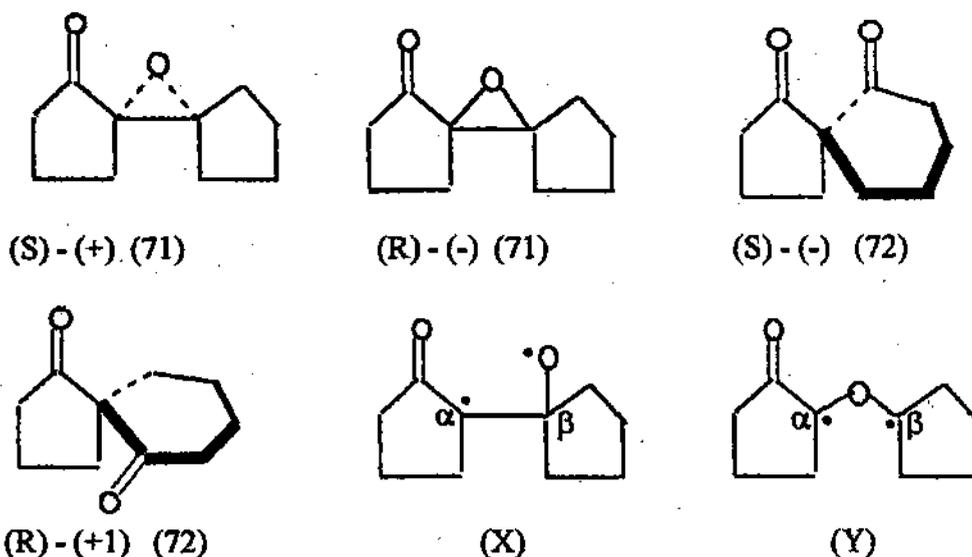
Irradiation of *trans*-dypnone oxide (58) in aqueous ethanol is interesting²⁰. Under this condition (58) isomerised to the diastereoisomer *cis* isomer (66). In addition, acetophenone and α -hydroxyacetophenone were obtained. Formation of these products has been explained by zwitterion type of intermediate. It has been postulated that the zwitterionic species can rotate about the central C-C single bond, resulting in the formation of the diastereoisomer after collapse. It can also react with a molecule of water to form an intermediate glycol (65), which subsequently undergoes photochemical dealdolisation to furnish acetophenone and α -hydroxyacetophenone.



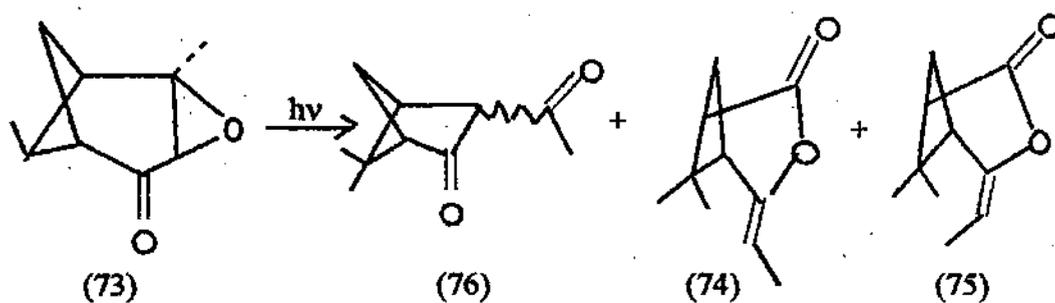
α,β -epoxy ketones in several cases undergo *cis-trans* isomerisation under photolytic conditions. It would imply the reversible formation of a reactive intermediate. Homolytic C—C bond fission and rotation prior to collapse would also account for this *cis-trans* isomerisation. When an ether solution of α - and β -pulegone oxides (67) and (68) were irradiated¹⁵ rearrangement to the stereoisomeric 2-acetyl-2,5-dimethylcyclohexanones (69) and (70) as well as isomerisation to (67) and (68) were both observed. The rate of isomerisation appears to be slightly greater than the rate of rearrangement. The steady state concentration of (69) and (70) is roughly 7% with (69) predominating.



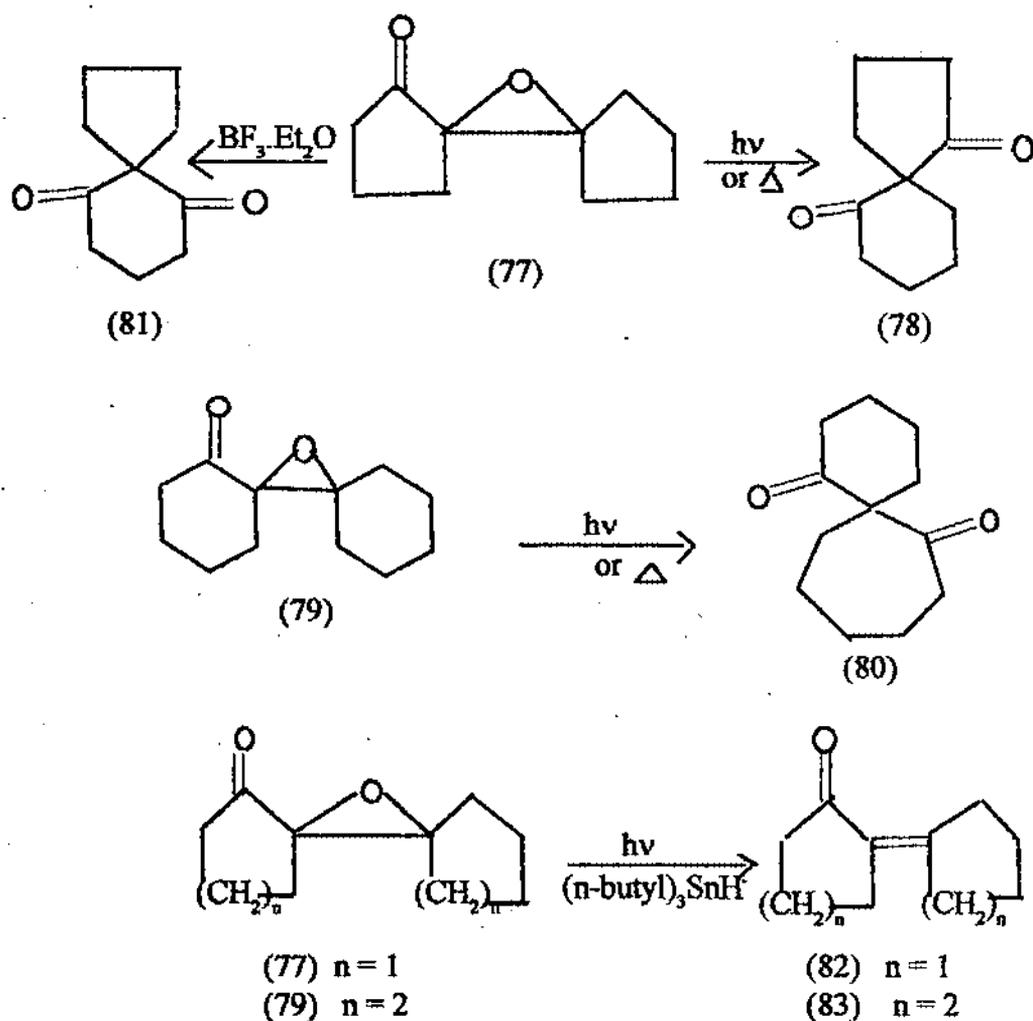
Wuthrich and coworkers²⁶ carried out studies on rearrangement and racemisation of spirocyclic α,β -epoxy ketones induced by direct UV irradiation as well as triplet sensitized by acetophenone. Spirocyclic α,β -epoxy ketone (R)-(-)(71) has undergone racemisation and rearrangement to the enantiomeric spiro- β -di ketones (R)-(+)(72) and (S)-(-)(72). They have applied spectral techniques including ORD/CD measurement for structure elucidation as well as racemisation studies. They have postulated the intermediate diradical type (X), produced by C_α -O epoxide cleavage, for rearrangement requires that the rate of rearrangement is greater than the rate of rotation around the $C_\alpha - C_\beta$ in (X) and the rate difference is greater in singlet-generated (X) than in the triplet analogue. The reclosure of diradical (X) and/or photolytic $C_\alpha - C_\beta$ cleavage to diradical (Y) and reclosure can account for the racemisation of (71).



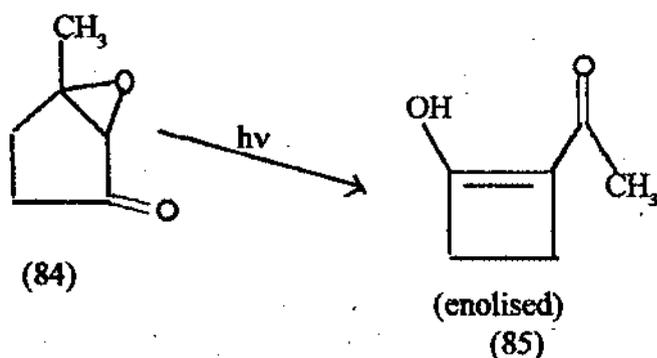
Gibson²⁷ conducted photolysis of the epoxide (73) derived from epoxidation of (-) trans-vervenone. Upon irradiation with a medium-pressure mercury arc lamp for 12 hr pentane or benzene solution of (73) produced a complex reaction mixture analysis of which by gas chromatography showed that starting material (73) comprised 56% of the mixture. Isolation of the products by preparative GLC and analysis by spectroscopic methods allowed the identification of the enol lactone (74) (30%), its isomer (75) (2%) and an inseparable 3:1 mixture of the ring-contracted diketone (76) (12%). When irradiation was performed with lamps emitting at 300 nm, only the ring-contracted diketone (76) was formed although at a slow rate.



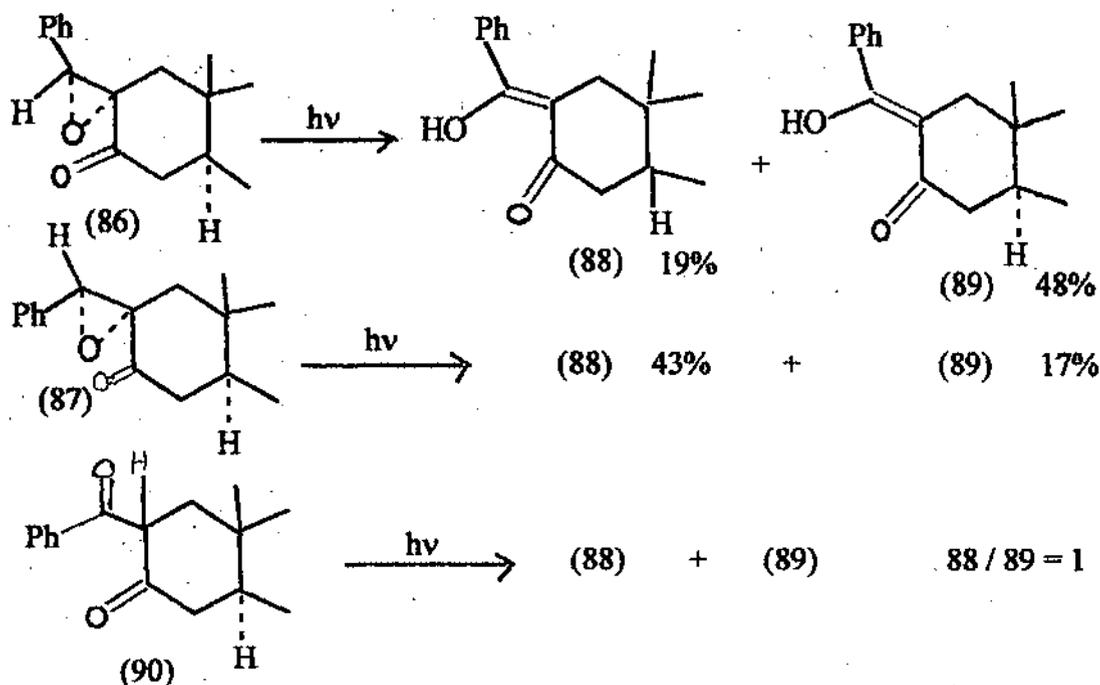
In order to synthesise spiro β -diketones, Williams et al.²⁸ subjected α,β -epoxy ketones to photochemical, thermal and acid-catalysed rearrangements. 2-cyclopentenyldene-cyclopentan-1-one oxide (77) and 2-cyclohexyldene-cyclohexan-1-one oxide (79) have been isomerised photochemically and thermally via 1,2-alkyl shift to spiro [4.5] decane - 1,6-dione (78) and spiro [5.6] dodecane - 1,7-dione (80), respectively. On the other hand, acid-catalysed isomerisation of (77) occurs via 1,2-acyl shift to yield spiro [4.5] decane - 6,10-dione (81). Interestingly, in the presence of tri-*n*-butyl stannane isomerisation does not take place and the reaction provides conjugated ketone with the elimination of epoxy oxygen, 2-cyclopentenyldene-cyclopentan-1-one (82) and 2-cyclohexyldene-cyclohexan-1-one (83) were formed respectively from the epoxy ketones (77) and (79).



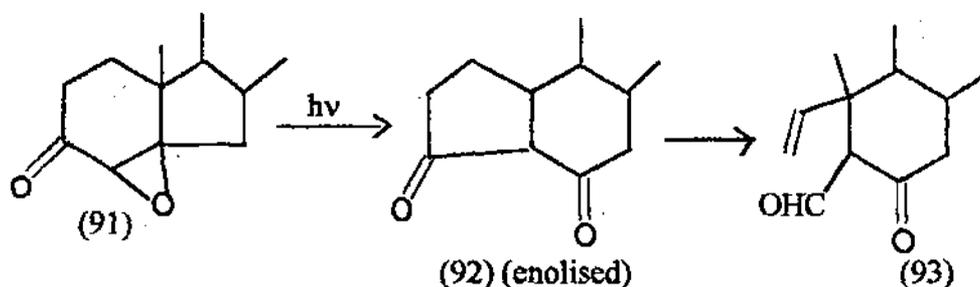
Wehrli et al.²⁹ reported the formation of a strained four-membered ring (85) from the photolysis of (84) a cyclopentane epoxy ketone. This constitutes the first example of rearrangement to a cyclobutanone derivative. The formation of this strained four-membered ring led them to prefer a single step or synchronous route for rearrangement from 1,3-diradical.



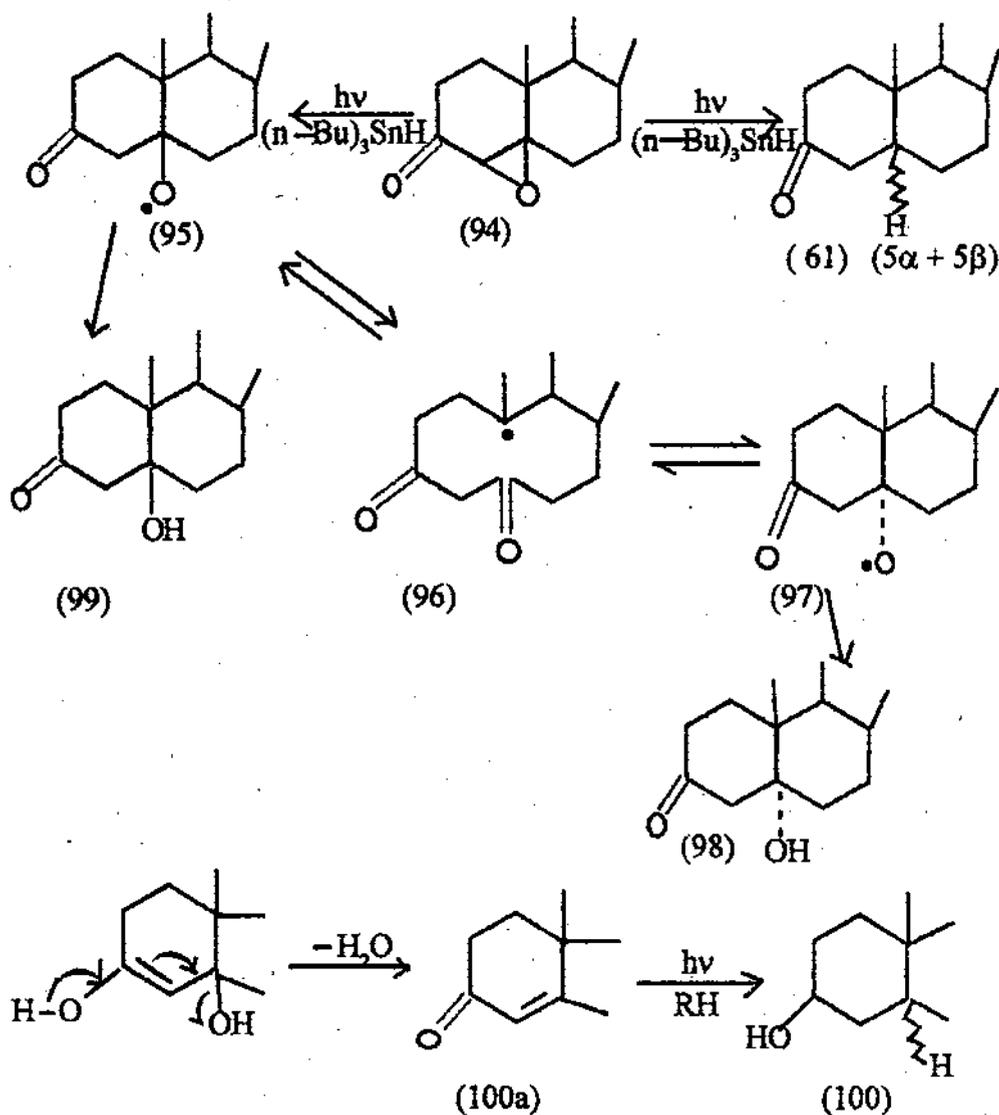
Muzart and Pete³⁰ prepared epoxides derived from 2-benzylidene-5 α -cholestan-3-one. The photochemical behaviour of these compounds depends considerably on stereochemistry. No photoepimerisation has been noticed. Expected β -diketones are formed. A δ hydrogen abstraction by the benzoyl group is involved in the photolysis of these diketones.



The initially formed β -dicarbonyl compounds are themselves photolabile and prolonged irradiation lead to further phototransformation, for example, the epoxy ketone (91) first gives rise to β -diketone (92) which undergoes partly α -cleavage and acyl-alkyl diradical disproportionation to the enolised unsaturated aldehyde-ketone (93)³¹.

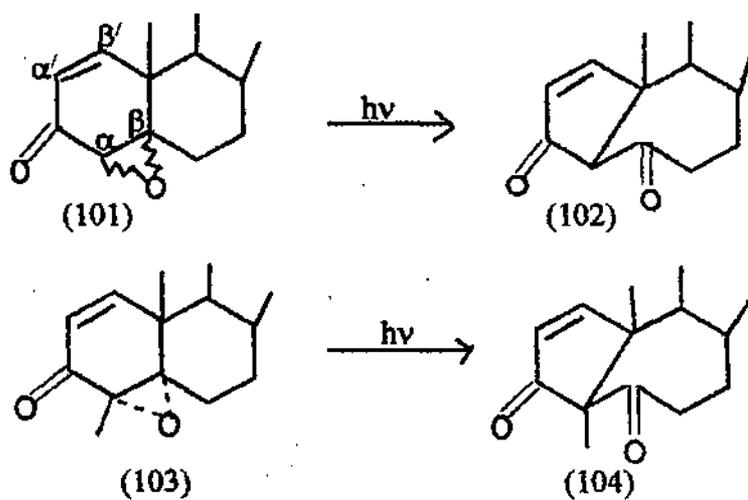


In the presence of tri-*n*-butylstannane, a very good hydrogen donor, the photolytic reaction of epoxy ketones takes a different course^{32,33}. The steroidal epoxy ketone (94) on irradiation at > 310 nm in benzene solution is rapidly converted to a mixture of compounds (98) and (99) (74%, combined yield) and (100) (26%). It is proposed that the intermediate keto-oxy radical (95) which is in equilibrium with the isomer (97) through the diketo-alkyl radical (96) on addition of a stannane hydrogen produce (99) and (98), respectively. The formation of saturated ketones (100, 5α and 5β) has been postulated to involve the intermediacy of testosterone acetate (100a) resulting from the addition of a second hydrogen to the enol forms of (95) and (97) and subsequent elimination of water.



A discussion on the photochemistry of steroid with Δ^1 -4,5-epoxy-3-ketone system (101) is of much interest³⁴. The corresponding rearranged 3,5-diketone (102) is obtained in excellent yield upon excitation with light of wavelength 2537\AA to its π, π^* absorption band. This photolytic rearrangement does not occur on excitation with light of wavelength 3300\AA to its n, π^* absorption band. This wavelength dependence photoreaction of α', β' -unsaturated α, β -epoxy ketones has been attributed to the π^* -assisted cleavage and occurs selectively in the presence of additional nonconjugated keto groups which absorb in the longer wavelength only.

Here too, the rearrangement is stereospecific indicated by the reaction of the 4 β -methyl homologue (103) which give the 4 β -methyl diketone (104).



CHAPTER - II

(Preparation and Molecular Rearrangement of 2 α , 3 α -Epoxy Lupan-1-one(109) Catalysed by Boron Trifluoride and by Ultraviolet Irradiation*)

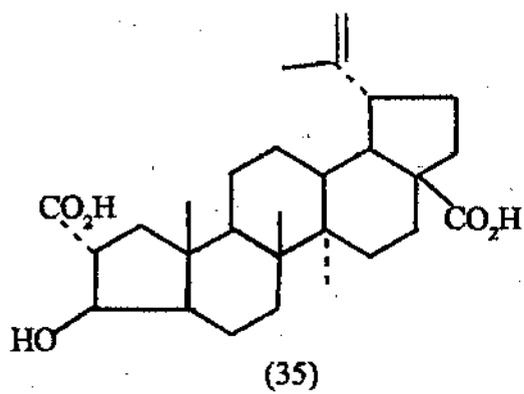
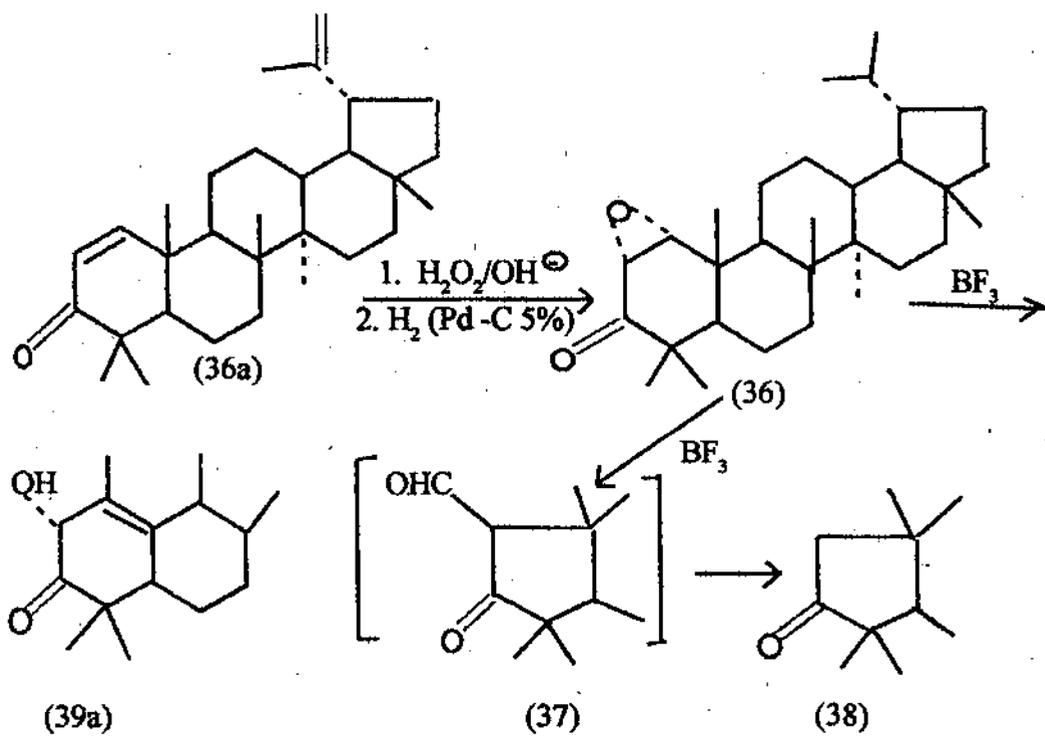
Introduction :

Over the past several decades molecular rearrangement of α,β -epoxy ketones induced by Lewis acids has been studied extensively. A large number of substances including steroid and terpenoid^{4-6,7a} epoxy ketones have been investigated and yielded compounds of synthetic importance. Equally interesting studies have been conducted on molecular rearrangement of these substrates by photolytic reactions.

An α,β -unsaturated ketone, glochidone (36a), a pentacyclic triterpene of lupane series, obtained from *Glochidion hohenackeri* by Ganguly and coworkers,^{7a} on treatment with alkaline hydrogen peroxide followed by hydrogenation afforded 1 α , 2 α -epoxy lupan-3-one (36). They carried out⁷ BF₃-catalysed rearrangement of (36) and obtained the product 1-methyl-2 α -hydroxy-lup-1(10)en-3-one (39a). Here, most probably due to the presence of a neopentyl system adjacent to the epoxy ketone system, methyl migration occurred instead of ring contraction.

With a view to synthesising the naturally occurring ceanothic acid (35), a ring contracted triterpene hydroxy acid of lupane series, Chatterjee et al.⁶ also studied initially the same rearrangement on the same substrate (36) which they used as a model compound. They did not report the same product (39a), but reported the formation of the ring-contracted nor-ketone (38), presumably formed by the elimination of formyl group from the initial product, 2-formyl cyclopentanone (37). It is surprising to note that two groups of workers reported the formation of two different types of products i.e. methyl group migrated product (39a) by Ganguly et al.⁷ and ring-contracted product (38) by Chatterjee et al.⁶ from the same molecular rearrangement on the same substrate (36).

*S.N.Bose and S.K.Chanda, *Ind. J. Chem.*, **40B**, 510-514 (2001) [reprint attached at the end of the thesis]



A close look at the structure of lupeol (105) revealed that an epoxy ketone, 2 α , 3 α -epoxy lupan-1-one (109) could be constructed synthetically in ring A of lupane, which would be isomeric with 1 α , 2 α -epoxy lupan-3-one (36) and which also possesses a neopentyl system adjacent to epoxy ketone grouping. In view of the interesting studies conducted by Ganguly et al.⁷ and Chatterjee et al.⁶ on epoxy lupanone (36) the study of this isomeric epoxy lupanone (109) would be interesting too. Our objective, therefore, has been to synthesise the desired epoxy ketone (109) by a multistep synthesis starting from the lead compound lupeol (105), obtained abundantly from the plant *Zanthoxylum budrunga* growing in North Bengal. Then, we have planned to carry out molecular rearrangement on the synthesised compound (109) induced by the Lewis acid, BF₃-etherate. Since the photorearrangement of cyclic epoxy ketone also gives interesting rearranged product, it was felt worthwhile to conduct photoreaction of this compound (109) induced by UV-irradiation. The purpose has been to see whether Lewis acid induced rearrangement and UV-induced rearrangement would furnish the same product or not.

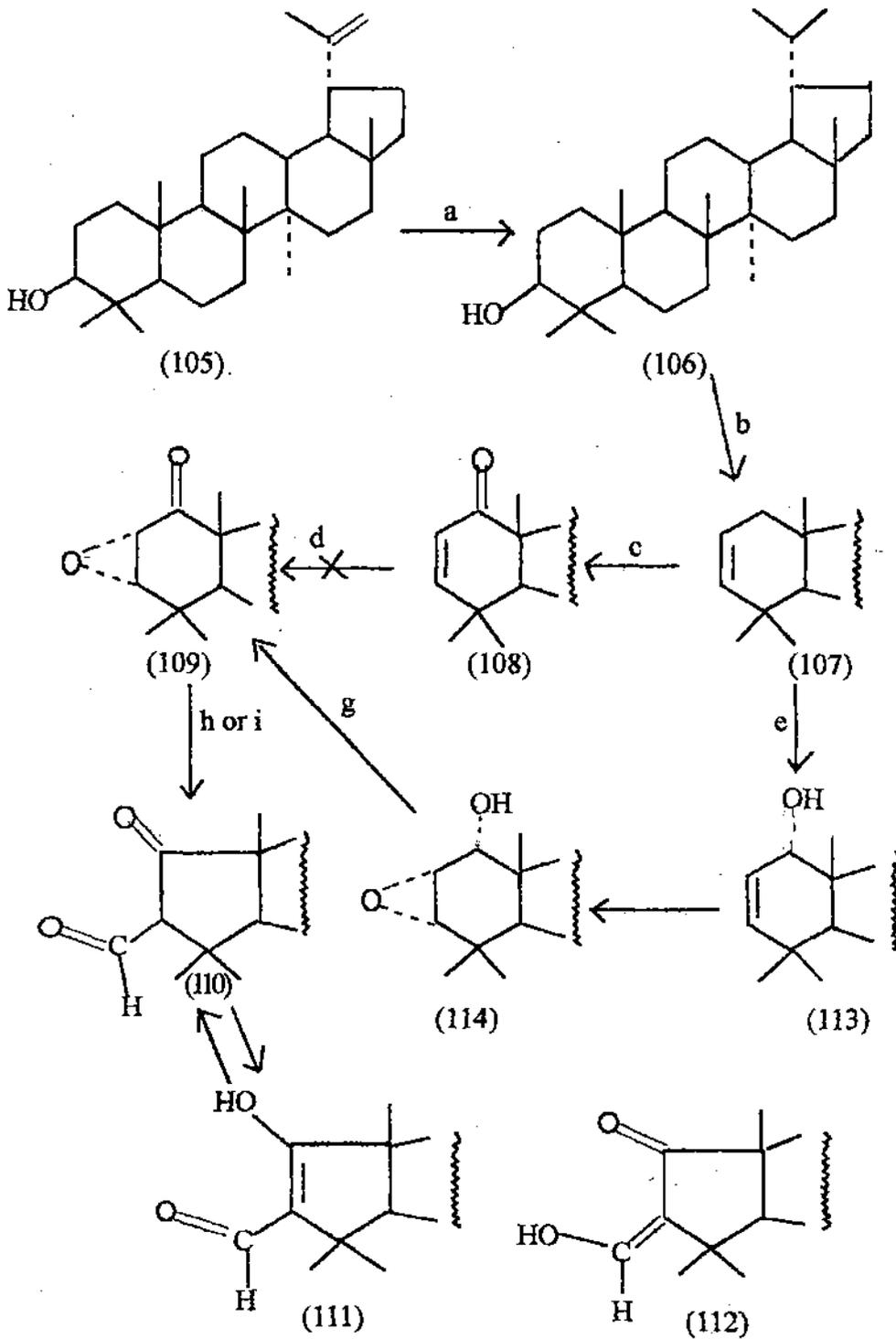
Thus, we have divided our presentation into three sections. Firstly, the synthesis of the key compound 2 α , 3 α -epoxy lupan-1-one (109) from the starting material lupeol (105) [SECTION- A], secondly, the molecular rearrangement of the epoxy ketone (109) induced by BF₃-etherate to give 2-formyl-A-nor-lupan-1-one (110) [SECTION - B] and thirdly or finally the molecular rearrangement of the epoxy ketone (109) induced by UV irradiation to give the same product (110) with a conclusion on the whole process [SECTION - C].

SECTION -A

Synthesis of the Key Compound 2 α , 3 α -epoxy lupan-1- one (109) from lupeol (105) : (Scheme-1)

The lead compound for this synthetic sequence, lupeol (105), was obtained abundantly from the plant *Zanthoxylum budrunga* growing in North Bengal. Extraction was carried out with either pet ether or benzene in a soxhlet apparatus for 20 hr. The extract was concentrated and purified by column chromatography over silica gel. Elution with pet ether : ethyl acetate (9 :1) as eluent afforded lupeol (105) as white solid, crystallised from chloroform-methanol as needles, mp 224-215°C (lit.³⁹ mp 215-216°C). It showed (Fig.1) IR bands at 3420 for OH group and 1630, 890cm⁻¹ for = CH₂. Compound (105) on catalytic reduction with Pd/C in ethyl acetate furnished lupanol (106) mp 202-203°C (lit.⁴⁰ mp 201-202°C). IR spectrum showed a band at 3390 cm⁻¹ for OH group but did not register bands for = CH₂ (Fig.2). Lupanol (106) on phosphorous oxychloride dehydration in dry pyridine yielded lup-2-ene (107), mp 190-192°C (lit.⁴¹ mp 192-193°C). It showed IR band at 1630, 850 cm⁻¹ for C = C. Oxidation of (107) with sodium dichromate in benzene-acetic acid mixture (1:1) afforded the conjugated ketone lup-2-en-1-one (108) in 65% yield. It exhibited (Fig. 3A) UV absorption at 220 nm (ϵ 15200) and IR (Fig. 3) bands at 1667, 1625 cm⁻¹ showing the presence of cyclohexenone system in (108).

Next, we attempted epoxydation of the conjugated ketone(108) with alkaline hydrogen peroxide which is an usual reaction, but our repeated attempts failed to obtain the desired epoxy ketone (109). At this juncture a literature survey revealed that the system 2-en-1-one of ring-A in triterpenoids is stable towards alkaline hydrogen peroxide epoxydation as noted by Barton and coworkers³⁵. Consequently, we adopted an alternative method for the preparation of the epoxy ketone (109). The olefin, lup-2-ene(107) on selenium dioxide oxidation in dioxane with a few drops of water added in it gave the allylic alcohol, lup-2-ene-1 α -ol (113) following the reaction conditions prescribed by Vystreil et al.³⁶. The crude reaction mixture was chromatographed over silica gel. Elution with pet ether-ethyl acetate (3:1) gave a white solid which on crystallisation from chloroform - methanol gave needles of lup-2-en-1 α -ol (113) in moderate yield (48%). It showed IR bands at 3424 (OH) and 1625, 862 cm⁻¹ (C = C). Its ¹H NMR spectrum (Fig. 4) showed resonances at δ 3.6 (m, 1H) for -CHOH, 5.5 (d, 1H, $J = 12$ Hz) for C₃-H and 5.7 (q, 1H, for C₂-H) besides 8 saturated methyls between 0.7 to 1.1.

Scheme - 1

Reagents and conditions : (a) $H_2/Pd-C$, ETOAc, rt, 4hr (b) $POCl_3$, Py, 4hr, water-bath (c) $Na_2Cr_2O_7$, C_6H_5-AcOH (1:1), 3 hr, reflux (d) H_2O_2 , NaOH, rt (e) SeO_2 , dioxane, traces of water, 6 hr, reflux (f) *m*-CPBA, $CHCl_3$, $5^\circ C$, 72hr (g) CrO_3 , Py, $5^\circ C$, 48h (h) BF_3 -etherate, C_6H_6 , 1hr, rt (i) $hv > 290\text{ nm}$, dioxane, 0.5 hr, rt.

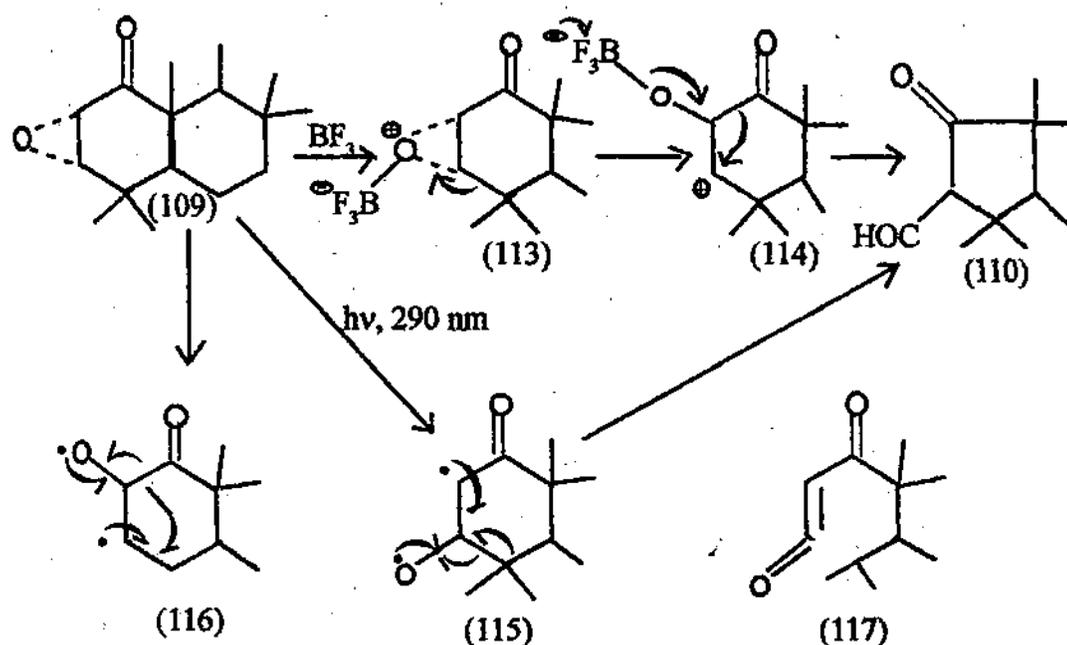
The compound (113) was epoxidised³⁶ with metachloro-perbenzoic acid in chloroform to yield the epoxy alcohol 2 α , 3 α -epoxy lupan-1 α -ol (114). We have prepared the key compound, 2 α , 3 α - epoxy lupan-1-one (109) by the chromium trioxide-pyridine oxidation of (114) in 48% yield. The key compound (109) exhibited IR band (Fig. 5) at 1695 cm⁻¹ for carbonyl of epoxy ketone. In ¹H NMR spectrum (Fig. 6) appearance of resonances at δ 3.1 (doublet, $J = 4$ Hz) and δ 3.27 (doublet, $J = 4$ Hz) enabled us to assign 2 α , 3 α -epoxy ketone stereochemistry for (109). Vystrcil and coworkers³⁶ settled the stereochemistry for (114), the precursor of (109), as 2 α , 3 α -epoxy lupan-1 α -ol by carrying out its conversion with LAH to 1 α , 3 α -dihydroxy lupane of known structure. This conversion was achieved by them in connection with conformational analysis of the ring-A of 1,3-dihydroxy derivatives of pentacyclic triterpenoids³⁶. EIMS mass spectrum of (109) (Fig. 7) also supported its formulation as epoxy ketone structure. Besides showing other ion peaks, the mass spectrum recorded molecular ion peak 440 m/z and a peak at 397 (M⁺-isopropyl).

SECTION - B

**Molecular Rearrangement of the Key Compound, Epoxy Ketone (109)
Induced by Borontrifluoride -Etherate : (Chart-2) and (Scheme-1)**

The epoxy ketone (109) was then subjected to molecular rearrangement induced by the Lewis acid, boron trifluoride-etherate in dry benzene at ambient temperature for 1 hr. Chromatography of the crude reaction mixture afforded the ring-A contracted keto aldehyde, 2-formyl-A-nor-lupan-1-one (110) in 60% yield. It practically exists in solution as the enolized form (111). The structure of the rearranged product was deduced by the combination of physical techniques. UV spectrum (Fig. 8) showed maximum absorption at 227 nm in methanol, which shifted to 292 nm in 0.1 M NaOH. IR recorded bands at 3450 (OH), 1710 (unsaturated aldehyde) and 1595 cm^{-1} ($\text{C} = \text{C}$). $^1\text{H NMR}$ exhibited (Fig. 9) resonances at δ 0.7 - 1.2 (8 CH_3 s), and 9.4 (S, 1H, -CHO). EIMS spectrum (Fig. 10) showed molecular ion peak at 440 (M^+), 397 ($\text{M}^+ - \text{isopropyl}$) m/z besides several other prominent peaks. Elemental analysis coupled with mass spectral data established that the molecular rearrangement is intramolecular. Of the two possible enolized forms (111) and (112), the former one (111) was supported by an aldehydic proton singlet at δ 9.4 in the $^1\text{H NMR}$ analysis.

Chart - 2



The mechanistic aspects of this ring - contracted reaction have been thoroughly investigated^{1,2}. Most possibly the ion (113) (Chart - 2) generated by the attack of BF_3 on (109) gives rise to carbocation (114) which eventually rearranges to the ring-contracted product (110). The whole process might be synchronous.

SECTION - C

Molecular Rearrangement of the Key Compound, Epoxy Ketone (109) Induced by Ultraviolet Irradiation : (Chart - 2) and (Scheme - 1)

The photorearrangement of cyclic epoxy ketones is well documented^{26c,34,37}. Upon photolysis, they afford 1,3-diketones or keto-aldehydes. We have carried out irradiation of (109) in dioxane at $\lambda > 290$ nm at ambient temperature under argon-atmosphere for 0.5 hr. We have been able to isolate the same keto-aldehyde (110) in good yield (52%). Identity was established by m.p. and m.m.p. determination and by comparison of spectral data (UV, IR, ¹H NMR and mass). Since the initial product (110) is also photolabile, irradiation for an extended period results in a complex reaction mixture giving a low yield of (110).

This photoreaction occurs from excited singlet manifold^{34,37,38} via diradical generated by homolysis of C_α - O bond, the retention of configuration³⁴ in the resulting 1,2-diketones obtained from the stereoisomeric steroidal epoxy ketones supports the proposition of a predominantly concerted rearrangement maintaining close orbital overlap throughout the entire radical migration³⁴. Accordingly, the mechanistic pathway of the photorearrangement of (109) studied by us can be depicted as in Chart- 2. The diradical (115) or (116) generated initially on photoexcitation rearranges to the keto-aldehyde (110) by a process in which the bond-migration and carbonyl formation steps are concerted.

During publication of this paper, one reviewer very pertinantly commented that the keto ketene (117) could be an attractive intermediate in this reaction pathway (Chart - 2), but no product corresponding to this intermediate has been isolated.

In conclusion, the molecular rearrangement conducted by us on isomeric epoxy ketone (109) induced by either BF₃-etherate at ambient temperature or under photolytic condition, enabled us to obtain the ring contracted keto-aldehyde (110) in line with the finding of the original workers³. Though Chatterjee et al.⁶ did not obtain the rearranged ring contracted keto-aldehyde (37), but obtained a ring contracted ketone (38), presumably formed by deformylation of the intermediate keto-aldehyde (37). Incidentally, we did not observe the formation of methyl migrated product of type (39a) isolated by Ganguly et al.⁷

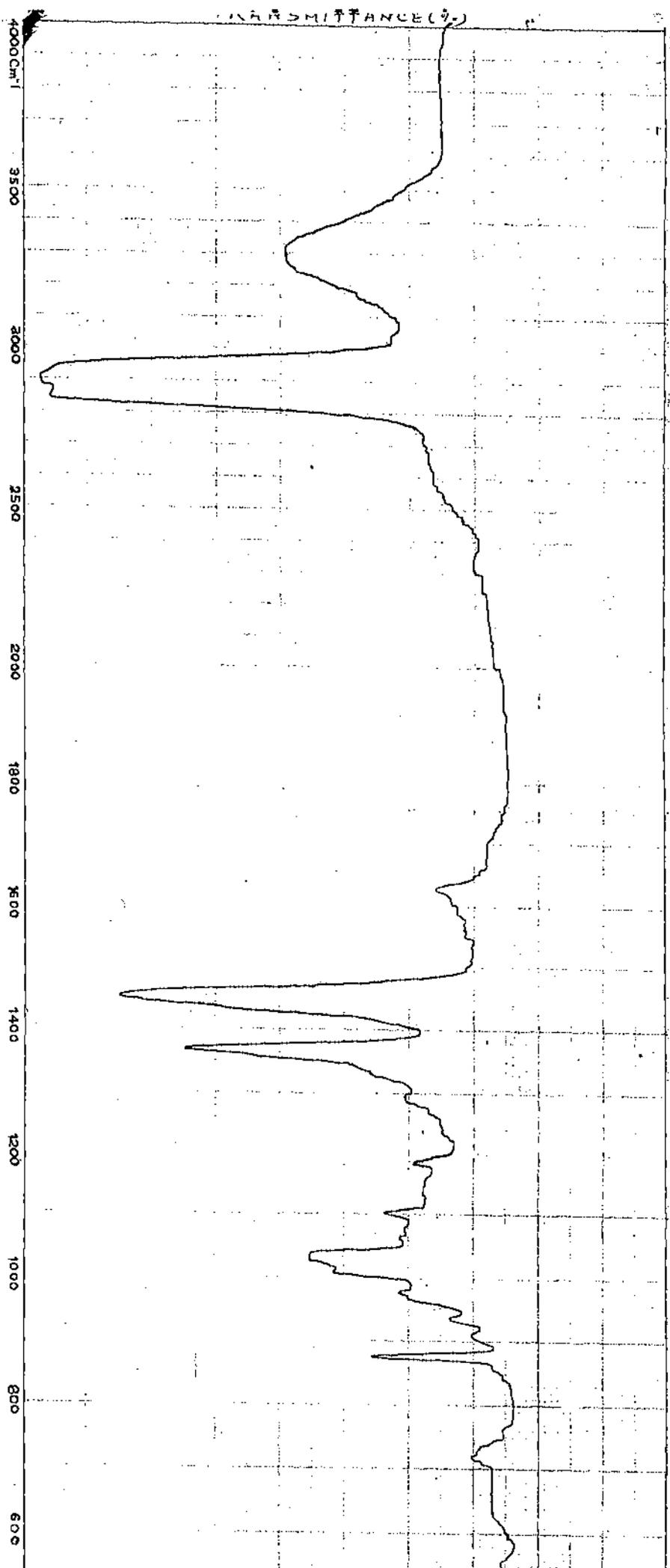


Fig. 1 : I R spectrum of Lupcol (405)

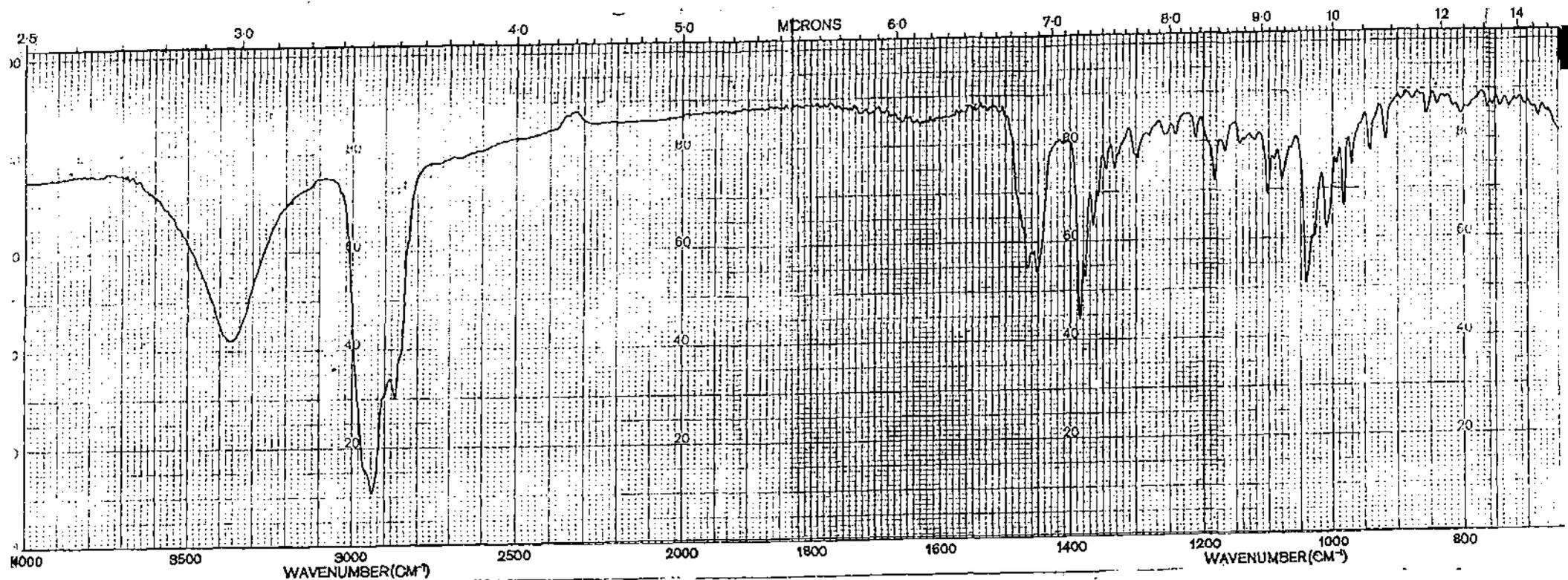


Fig. 2 : I R spectrum of luparol (106)

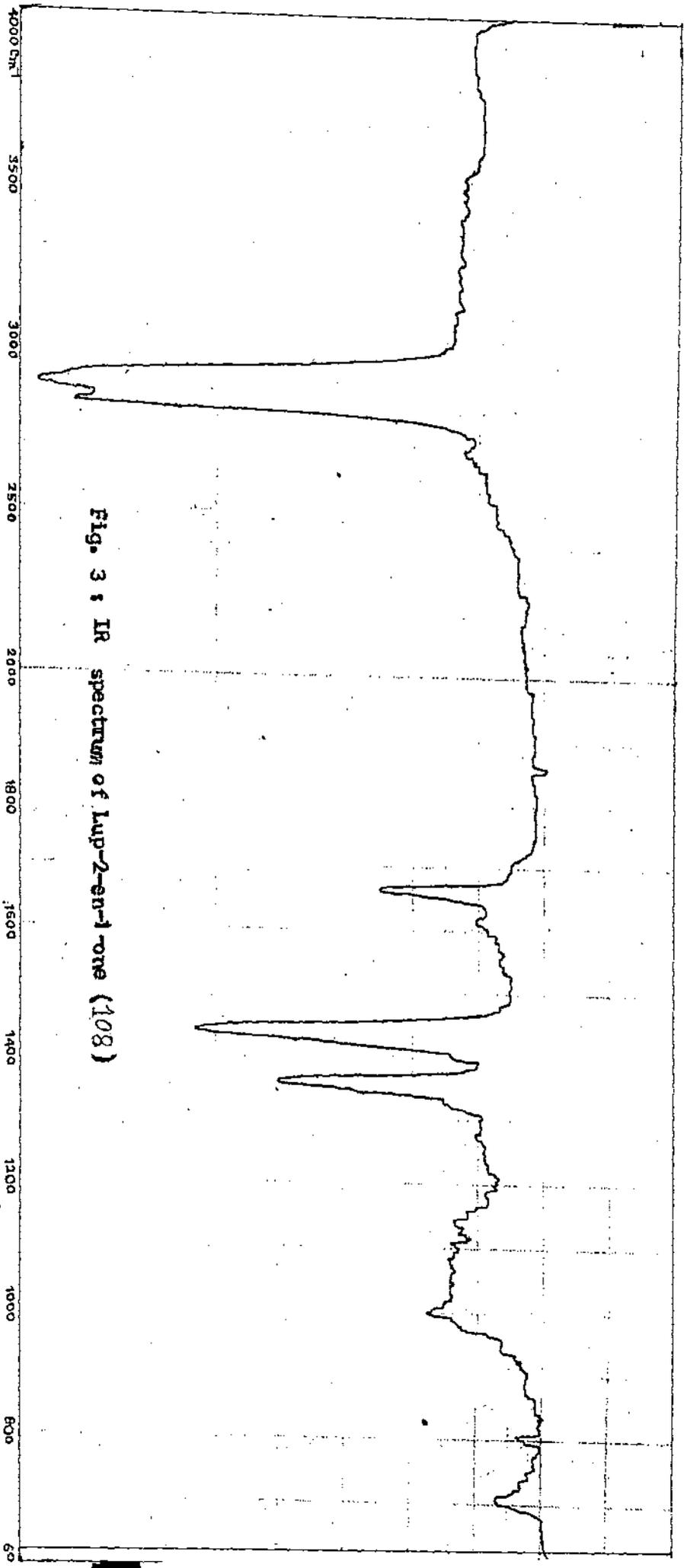


Fig. 3 : IR spectrum of Lup-2-en-1-one (108)

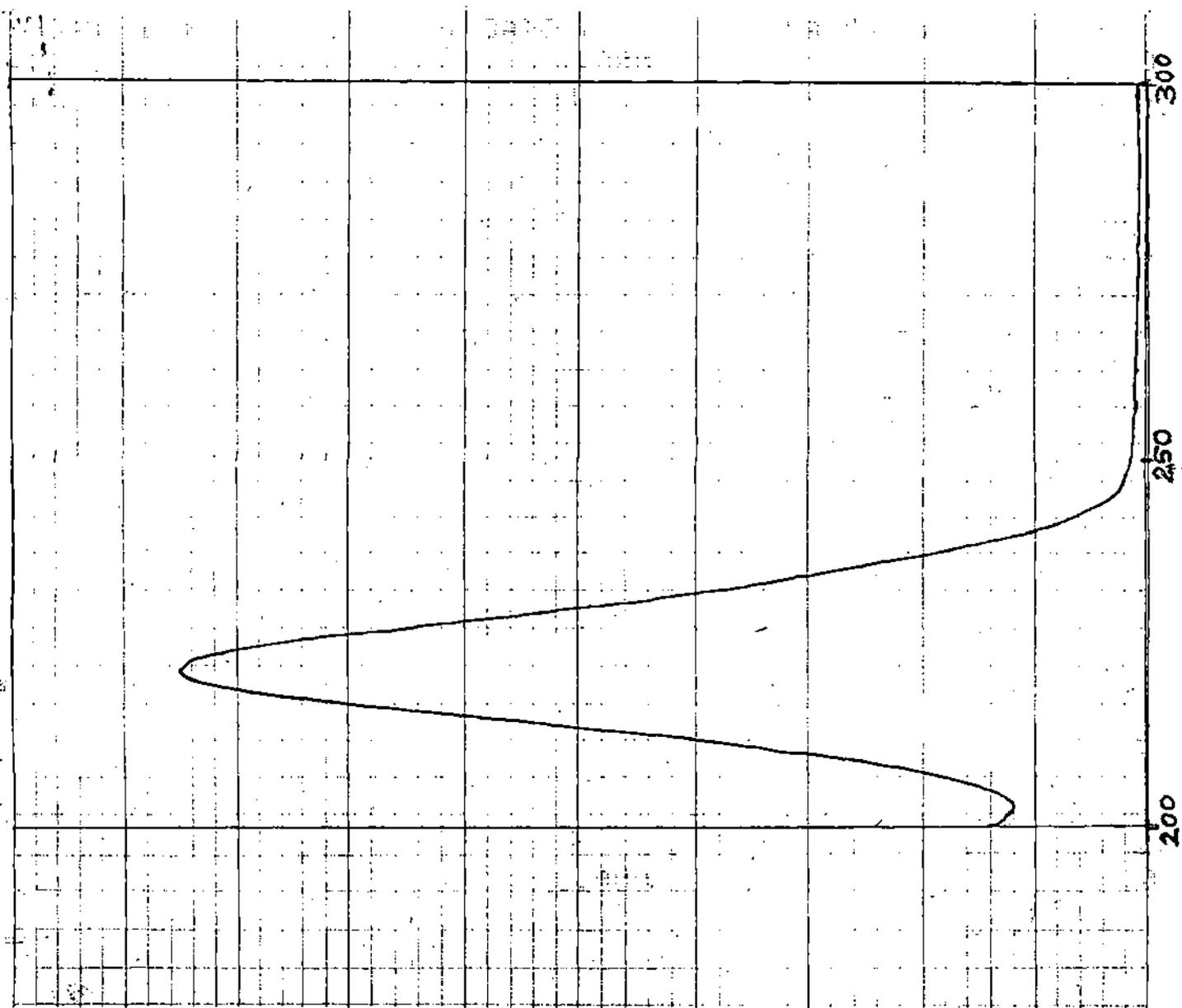
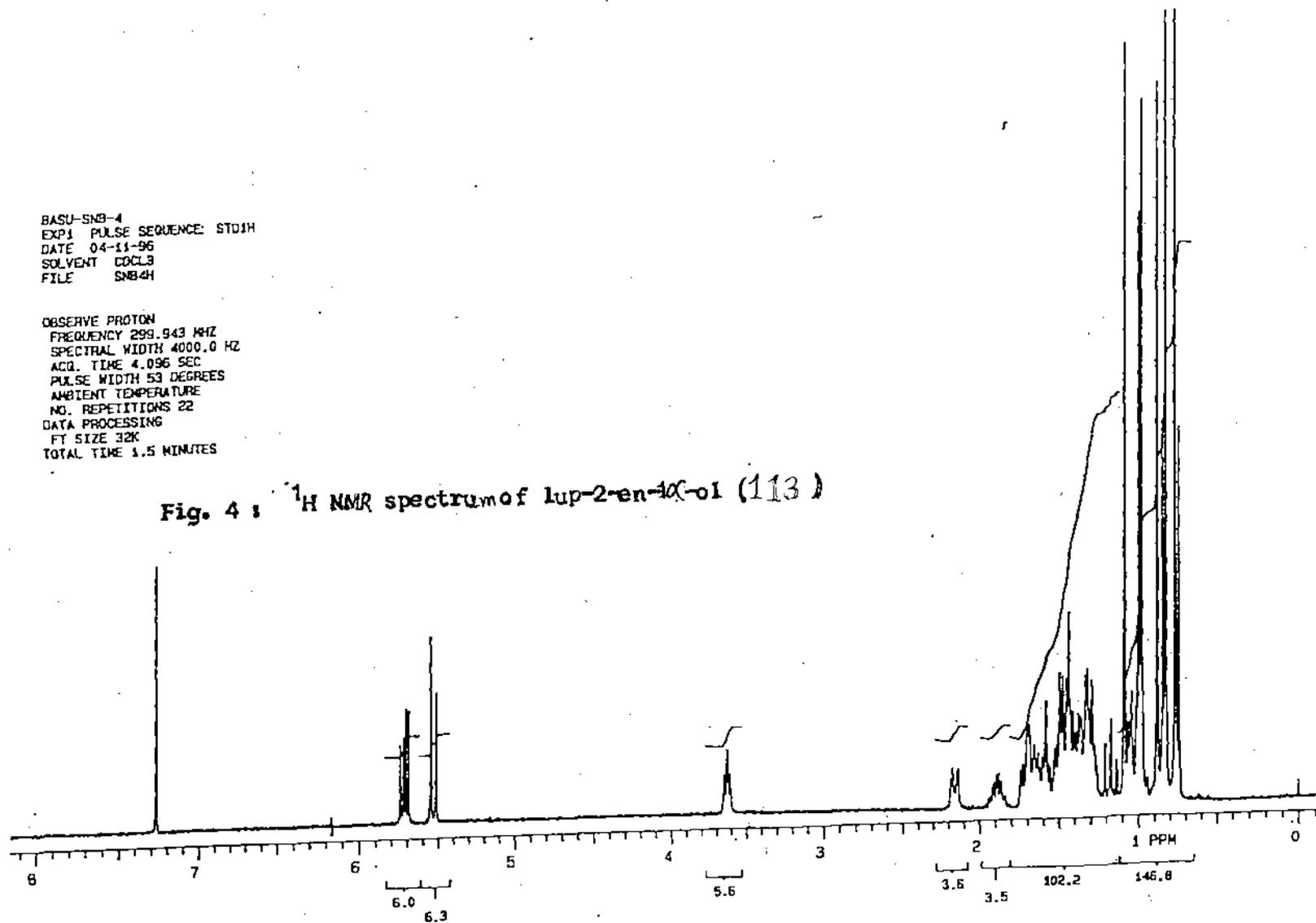


Fig.3A : UV spectrum of lup-2-en-1-one(108)

BASU-SNB-4
EXP1 PULSE SEQUENCE: STD1H
DATE 04-11-96
SOLVENT CCL3
FILE SNB4H

OBSERVE PROTON
FREQUENCY 299.943 MHZ
SPECTRAL WIDTH 4000.0 HZ
ACQ. TIME 4.096 SEC
PULSE WIDTH 53 DEGREES
AMBIENT TEMPERATURE
NO. REPETITIONS 22
DATA PROCESSING
FT SIZE 32K
TOTAL TIME 1.5 MINUTES

Fig. 4 : ^1H NMR spectrum of lup-2-en-10-ol (113)



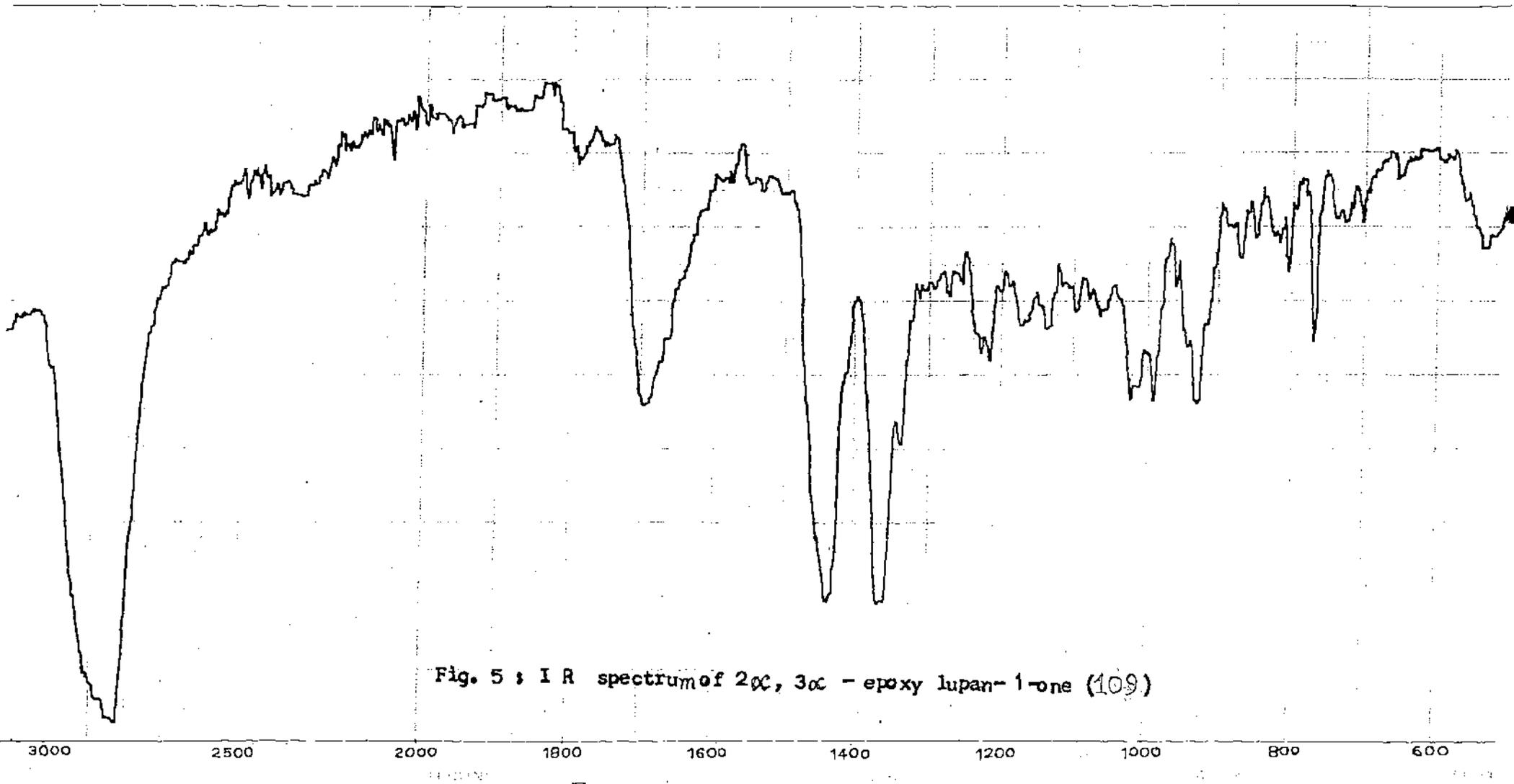


Fig. 5 : I R spectrum of 2,3 - epoxy lupan-1-one (109)

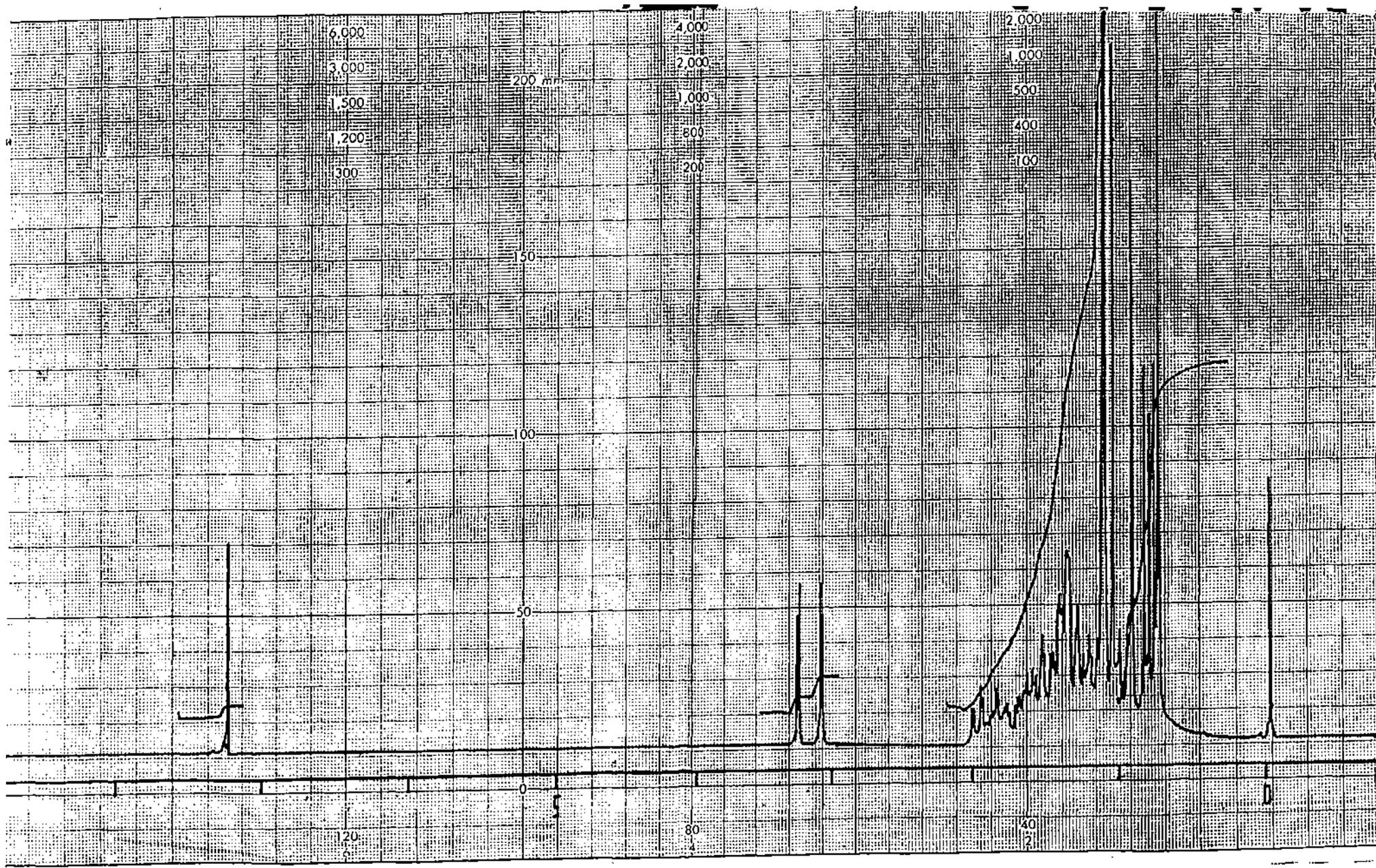


Fig. 6 : ^1H NMR spectrum of 2 α , 3 α -epoxy lupan-1-one (109)

CENTRAL DRUG RESEARCH INSTITUTE
06-11-1992

JN1129X.LRP SCI 49(3) DR S.N.BOSE W BENGAL
Date run : 06-11-1992 Operator : MADHU

Scan : 5 RT= 0:40 No.ions= 126 Base= 66.4%F TIC=191655

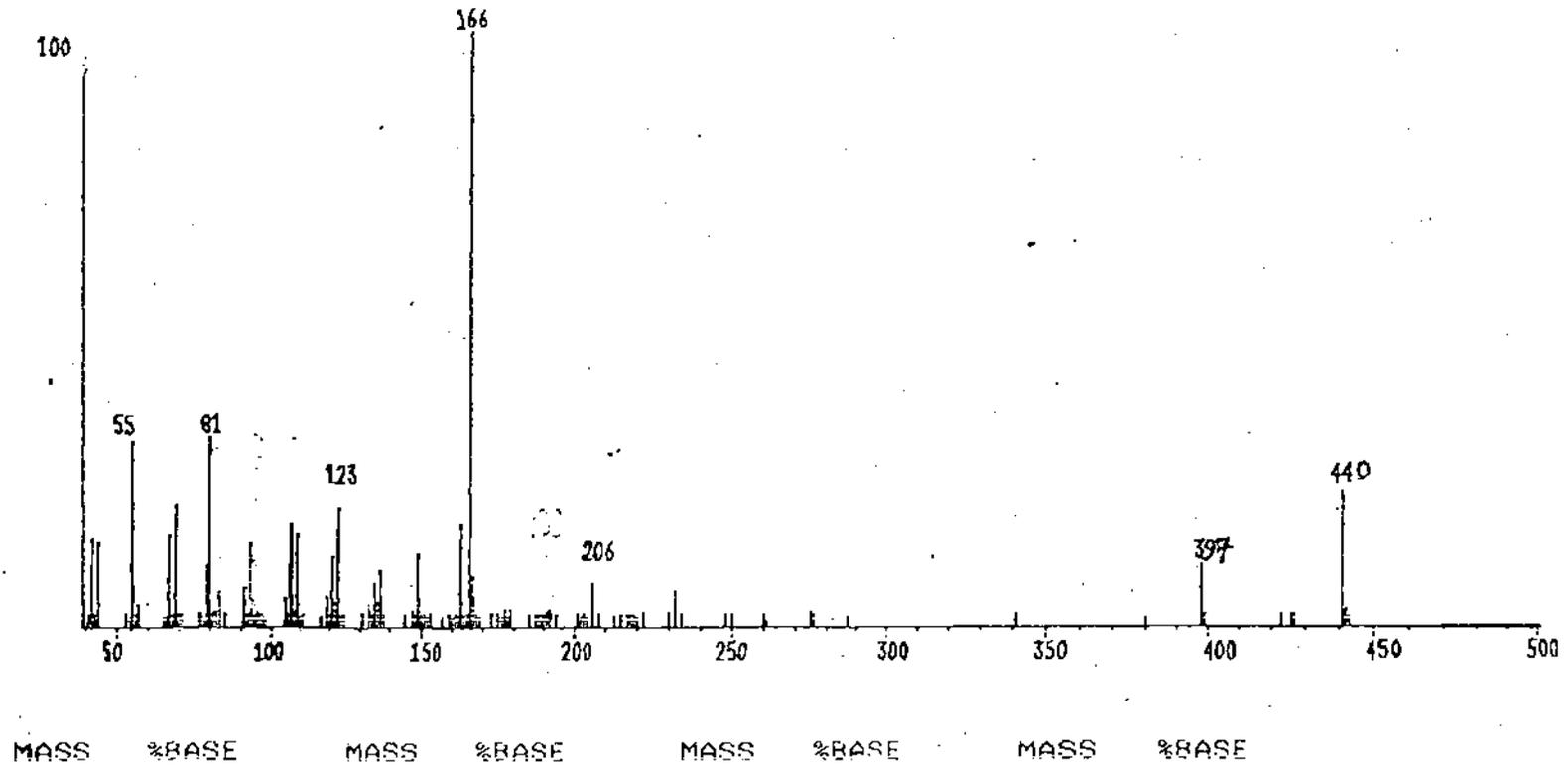
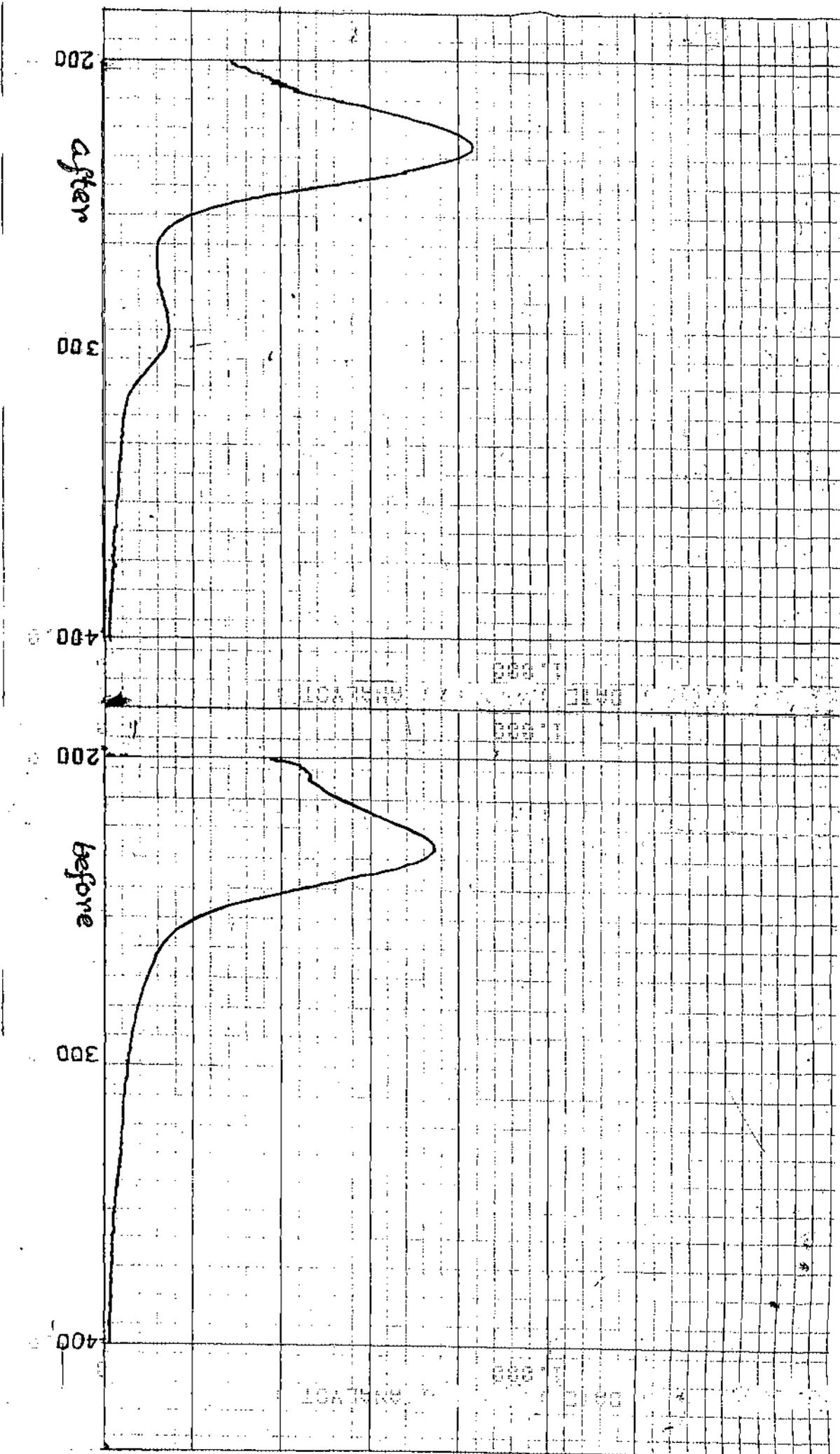


Fig. 7: mass spectrum of 2 α , 3 α -epoxy lupan-1-one (109)

Fig. 8 : UV spectrum of 2-formyl-L-tryptophan (110) before and after alkali addition .



BASU-SNB-50
EXPT1 PULSE SEQUENCE: STD1H
DATE 04-11-96
SOLVENT CDCL3
FILE SNB50H

OBSERVE PROTON
FREQUENCY 299.943 MHZ
SPECTRAL WIDTH 4000.0 HZ
ACQ. TIME 4.096 SEC
PULSE WIDTH 53 DEGREES
AMBIENT TEMPERATURE
NO. REPETITIONS 32
DATA PROCESSING
FT SIZE 32K
TOTAL TIME 2.2 MINUTES

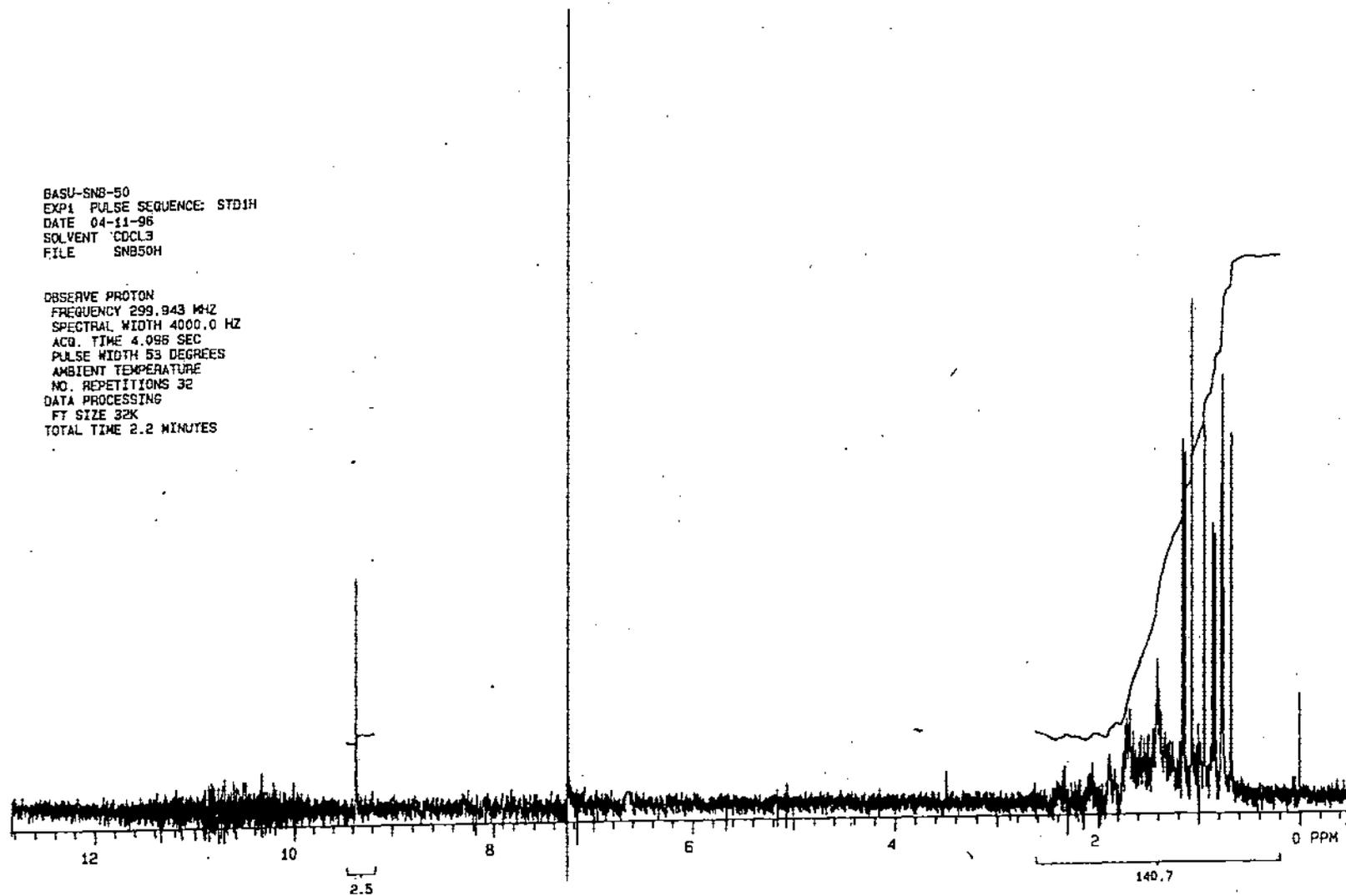
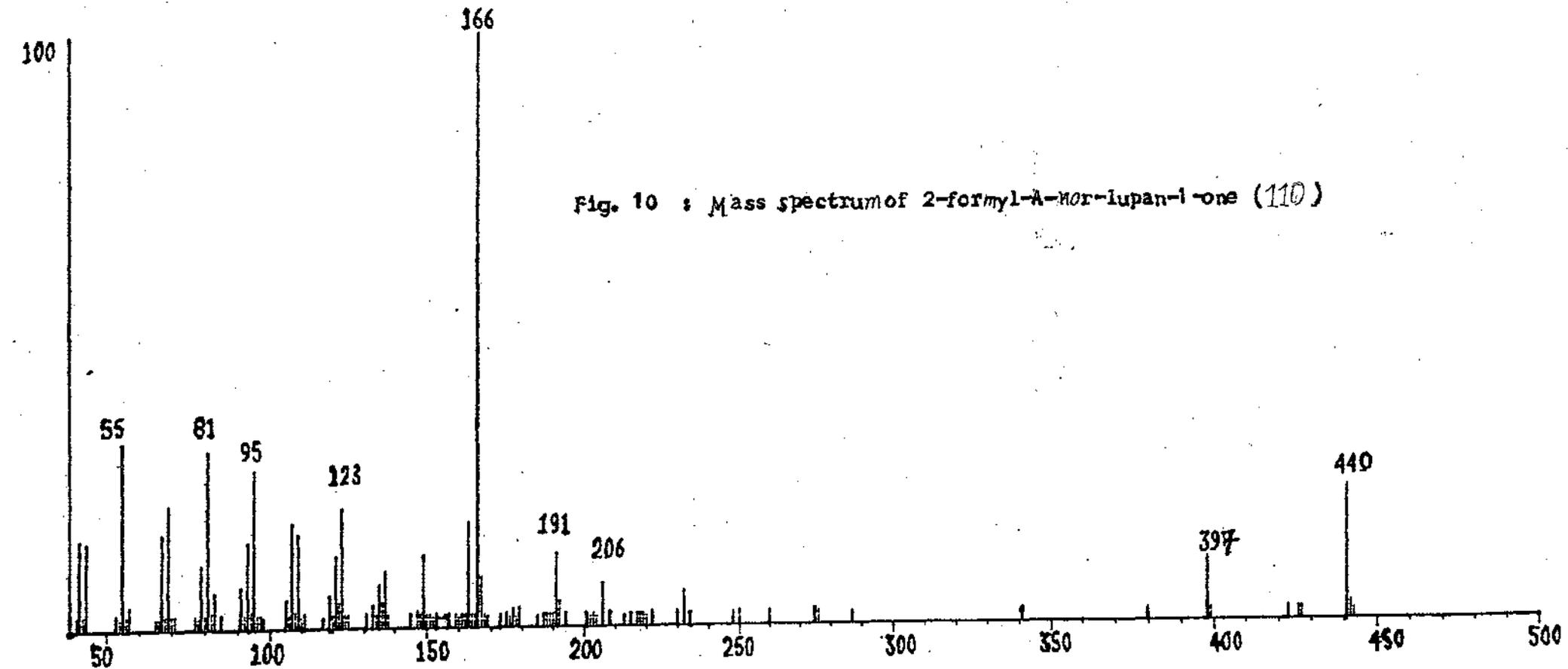


Fig. 9 : ^1H NMR spectrum of 2-formyl-A-nor-lupan-1-one (110).

JN1129X.LRP SCI 49(2) DR S.N. BOSE W BENGAL
Date run : 06-11-1992 Operator : MADHU

Scan : 5 RT= 0:40 No. ions= 126 Base= 66.4%F TIC=191655



MASS %BASE MASS %BASE MASS %BASE MASS %BASE

CHAPTER - III

(Experimental Section)

General :

Melting points were determined in a sulphuric acid bath and are uncorrected. The pet ether used throughout the investigation had b.p. 60-80°C. ¹H NMR spectra were recorded on a VNXL-200 spectrophotometer in CDCl₃ solution using TMS as internal reference; IR spectra on a Pye Unicam-Sp-300S and UV on a Shimad-Zu UV-240 spectrophotometers; and mass spectra (EIMS) on a Jeol JMS-D300 mass spectrophotometer, using direct sample introduction into the ion source at 70 eV. TLC was done on chromatoplate of silica gel G (E.Merck) and spots were visualised by exposing the plates in iodine vapour.

Isolation of Lupeol (105)

Stem-bark of *Zanthoxylum budrunga*⁴² was extracted in a soxhlet apparatus for 20 hr. with benzene. the extract was concentrated and purified by column chromatography over silica gel. Elution with pet ether : ethyl acetate (9:1) as eluent gave lupeol (105) as white solid, crystallised from chloroform-methanol as needles, m.p. 2314-215°C (lit³⁹ m.p. 215-216°C), which was identical in all respect with authentic sample of lupeol.

% Analysis of C₃₀H₅₀O

Found	: C = 84.41	H = 11.61
Calculated	: C = 84.50	H = 11.73
IR (nujol)	: 3420 (OH), 1630, 890 (= CH ₂) cm ⁻¹ ,	

Fig. 1.

Preparation of Lupanol (106) from Lupeol (105)

To a solution of lupeol (105) (21 mmoles) in ethyl acetate (450 ml) was added Pd-C (5%, 1g) and hydrogenated for 5 hr. Pd-C was removed by filtration and the filtrate on concentration afforded fine white needles of lupanol (106), m.p. 202-203°C (lit⁴⁰ m.p. 201-202°C).

% Analysis of C₃₀H₅₂O

Found : C = 83.92 H = 12.11

Calculated : C = 84.11 H = 12.15

IR (nujol) : 3390 cm⁻¹ (OH)

Fig.2

Mass : M⁺ 428 m/z, 385 (M⁺ - isopropyl), 367 (M⁺ - isopropyl -H₂O) and several other peaks.

Preparation of Lup-2-ene (107) from Lupanol (106)

To a solution of lupanol (106) (16 mmoles) in dry pyridine (200 ml) was added phosphorus oxychloride (25 ml). The reaction mixture was kept on a water-bath for 4 hr. and then overnight at room temperature. It was poured on ice-water. The precipitated brown solid obtained on filtration was chromatographed on silica gel. Elution with pet ether gave lup-2-ene (107) (yield 65%) as white solid, m.p. 190-192°C (lit⁴¹ m.p. 192-193°C).

% Analysis of C₃₀H₅₀

Found : C = 87.91 H = 12.11

Calculated : C = 87.80 H = 12.19

IR (nujol) : 1630, 850 cm⁻¹ (C = C)

Preparation of Lup-2-en-1-one (108) from Lup-2-ene (107)

To a solution of lup-2-ene (107) (11 mmoles) in benzene : acetic acid (1 : 1, 300 ml) sodium dichromate (15 mmoles) was added and the mixture refluxed for 3 hr. The excess oxidant was destroyed by addition of methanol (20 ml). The reaction mixture was extracted with ether (500 ml), washed with Na₂CO₃ and then with water until neutral. The brown mass obtained on evaporation was chromatographed over silica gel. Elution with pet ether : ethyl acetate (4:1) as eluent gave (108) as white solid (yield 55 %), m.p. 194-195°C.

% Analysis of $C_{30}H_{48}O$

Found : C = 87.13 H = 11.19

Calculated : C = 87.26 H = 11.32

UV (MeOH) : 220 nm

Fig. 3A

IR (nujol) : 1667, 1625 cm^{-1} (conjugated ketone)

Fig. 3

Alkaline Hydrogen Peroxide treatment of Lup-2-ene-1-one (108)

To a solution of (108) (2.5 mmoles) in dioxane (50 ml) was added aqueous hydrogen peroxide (30%, 8 ml) and aqueous NaOH (6N, 10 ml) and stirred over a period of 2 hr. After usual work-up unchanged starting material (108) was recovered in almost quantitative yield (mp and mmp).

Preparation of Lup-2-en-1 α -ol (113) from Lup-2-ene (107)

To a solution of (107) (5.2 mmoles) in dioxane (200 ml) SeO_2 (6.7 mmole) was added. After addition of traces of water (4 drops) the mixture was refluxed for 8 hr. The warm filtrate obtained on removal of Se was poured into aqueous KOH solution (2.5%, 1.2 L). The precipitated solid was chromatographed over silica gel. Elution with pet ether : ethyl acetate (3:1) gave a white solid which on crystallisation from chloroform-methanol gave needles of lup-2-en-1 α -ol (113), m.p. 201-202°C (lit³⁶ m.p. 203-204°C).

% Analysis of $C_{30}H_{50}O$

Found : C = 84.12 H = 11.61

Calculated : C = 84.44 H = 11.81

IR (nujol) : 3424 (OH), 1625, 862 cm^{-1} (C = C) 1H NMR : δ 0.7 - 1.1 (8 CH_3 s),3.6 (m, 1H, $CHOH$),5.5 (d, 1H, $J = 12$ Hz, $C_3 - H$),5.7 (q, 1H, $C_2 - H$)

Fig.4

Mass : M^+ 426 m/z, 383 (M^+ - isopropyl), 366 (M^+ - isopropyl -OH) and several other peaks.

Preparation of 1 α -hydroxy-2 α , 3 α -epoxy Lupane (114) from Lup-2-en-1 α -ol (113)

To a solution of (113) (10.5 mmoles) in chloroform (55 ml) was added *m*-CPBA (14.6 mmoles). The reaction mixture was kept at 5°C for 72 hr., extracted with ether (250 ml), washed with Na₂CO₃ solution and then with water until neutral. The white solid obtained on evaporation of solvent, was crystallised from chloroform - methanol to furnish pure (114) (yield 72%), m.p. 233-234°C (lit³⁶ m.p. 232°C).

% Analysis of C₃₀H₅₀O₂

Found : C = 81.47 H = 11.09

Calculated : C = 81.33 H = 11.35

Mass : M⁺ 442 m/z

Preparation of 2 α , 3 α -epoxy Lupan-1-one (109) from 1 α -hydroxy-2 α , 3 α -epoxy Lupane (114)

To a solution of (114) (2.5 mmoles) in pyridine (20 ml) was added a slurry of CrO₃ (3.6 mmoles) in pyridine (15 ml) at 5°C and kept at this temperature for 48 hr. The reaction mixture was diluted with ethyl acetate (200 ml). The precipitate was filtered off. The clear brown filtrate was treated with aqueous HCl (10%), washed with water until neutral. Evaporation of the solvent left a brown mass which was chromatographed over silica gel. Elution with pet ether : ethyl acetate (4:1) yielded a white solid which on crystallisation from chloroform-methanol afforded fine needles of (109) (yield 48%), m.p. 191°C.

% Analysis of C₃₀H₅₀O₂

Found : C = 81.45 H = 10.68

Calculated : C = 81.81 H = 10.91

IR (nujol) : 1695 cm⁻¹ (C = O)

Fig. 5

¹H NMR : δ 0.72 - 1.1 (8CH₃s),
3.11 (d, 1H, J = 4 Hz, C₃-H),
3.27 (d, 1H, J = 4Hz, C₂-H)

Fig. 6

Mass (EIMS) : 440 (M⁺),

397 m/z (M⁺-isopropyl), several other peaks. Fig 7

BF₃- etherate rearrangement of 2 α , 3 α -epoxy Lupan-1-one (109) : preparation of 2-formyl-A-nor-Lupan-1-one (110)

The epoxy ketone (109) (1.2 mmoles) in dry benzene (25 ml) was treated with freshly distilled BF₃-etherate (5ml) at room temperature for 1 hr. The reaction mixture was diluted with water, extracted with ether and washed with water. On evaporation a thick gum was obtained which was purified by chromatography over silica gel. Pet ether : ethyl acetate (7:3) eluted a white solid (110) (yield 60%), m.p. 93-94°C.

% Analysis of C₃₀H₄₈O₂

Found : C = 81.55 H = 11.02

Calculated : C = 81.78 H = 10.91

UV (MeOH) : 227 nm, shifted to 292 nm in 0.1 M NaOH Fig. 8

IR (nujol) : 3450 (OH), 1710 (unsaturated aldehyde),
1595 (C = C) cm⁻¹ (enol form).

¹H NMR : δ 0.7 - 1.2 (8 CH₃s),
9.4 (s, 1H, -CHO) Fig. 9

Mass (EIMS) : 440 (M⁺),
397 m/z (M⁺ -isopropyl), several other peaks. Fig. 10

Photolysis of 2 α , 3 α -epoxy Lupan-1-one (109) : Formation of 2-formyl-A-nor-Lupan-1-one (110).

A solution of (109) (1.1 mmole) in dry dioxane (100 ml) was irradiated for 0.5 hr. with medium pressure mercury lamp placed in a central water-cooled pyrex immersion well under argon atmosphere at ambient temperature. Evaporation of the solvent in a rotary vacuum evaporator followed by chromatography of the crude product on silica gel using pet ether : ethyl acetate (7:3) as eluent gave a white solid (yield 52%) which was found to be identical with (110) (previously prepared) by mp and nmp determinations and by comparison of spectral data (UV, IR, ¹H NMR and mass) .

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62 Proc. 87th Ind. Sc. Cong. Part III (Advance Abstracts)

99. Preparation and Photochemistry of Cross-Conjugated Cyclohexadienone Ring A of Friedelane Triterpene

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Key words : *Cross-conjugated cyclohexadienone, Friedelin, Photochemistry, Lumiprodukt*

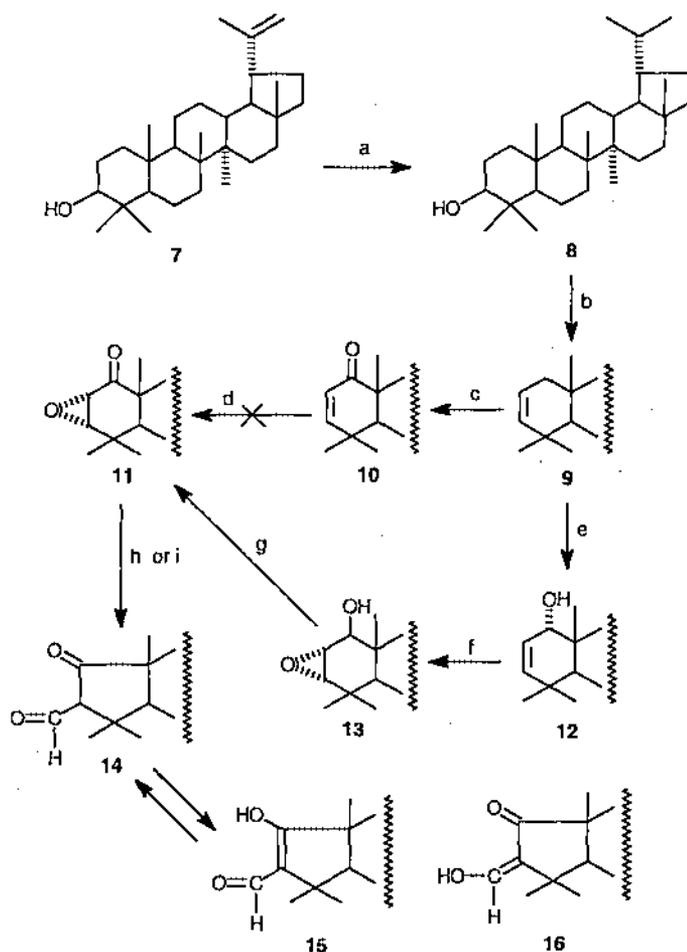
Because of the presence of 4,4,10-trimethyl ring A system in triterpenes α -amyrin, β -amyrin and lupane series, the introduction of photolabile cross-conjugated cyclohexadienone chromophore in ring A is not feasible. In contrast, in friedelane triterpene having 4,5-dimethyl ring A system this can be introduced. Thus, by a sequence of reactions starting from friedelane the key compound friedel-1(10), 3-dien-2-one, a cross-conjugated cyclohexadienone system in ring A, was synthesised. This upon UV irradiation at 254 nm in neutral and non-nucleophilic solvent, dioxane, in nitrogen atmosphere at ambient temperature yielded the bicyclo (3.1.0) hex-3-en-2-one derivative (lumiprodukt) in good yield (62%). Its structure has been elucidated by the combination of UV, IR, PMR, CMR and EI mass spectral analysis. The stereochemistry has been studied by chiroptical (CD) measurements. Prolonged irradiation results in a complex reaction mixture.

100. Synthesis of Some New Arylamides as Biologically Active Agents

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Key words : *Arylamides, Antimicrobial Activity*

The study of arylamides has revealed valuable drugs for the diseases like Cancer, Malaria, Tuberculosis, Fungal, Viral and



Scheme I

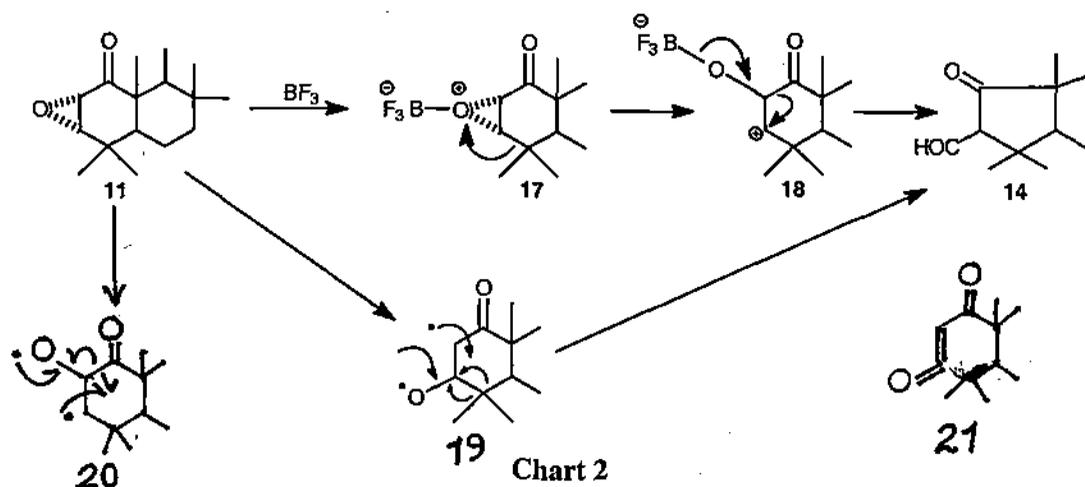
Reagents and conditions. (a) $\text{H}_2/\text{Pd-C}$, ETOAc, rt, 4hr (b) POCl_3 , Py, 4hr, water-bath (c) $\text{Na}_2\text{Cr}_2\text{O}_7$, C_6H_6 -AcOH (1:1), 3hr, reflux (d) H_2O_2 , NaOH, rt (e) SeO_2 , dioxane, traces of water, 6hr, reflux (f) *m*-CPBA, CHCl_3 , 5°C , 72hr (g) CrO_3 , Py, 5°C , 48h (h) BF_3 -etherate, C_6H_6 , 1hr, rt (i) $h\nu > 290\text{ nm}$, dioxane, 0.5hr, rt.

prescribed by Vystreil *et. al.*⁷. Compound 12 was epoxidised⁷ with metachloro-perbenzoic acid in chloroform to yield the epoxy alcohol, 2 α , 3 α -epoxy lupan-1 α -ol 13. We have prepared the key compound, 2 α , 3 α -epoxy lupan-1-one 11 by the chromium trioxide-pyridine oxidation of 13. In ¹H NMR spectrum, appearance of resonances at δ 3.1 (doublet, $J = 4\text{Hz}$) and δ 3.27 (doublet, $J = 4\text{Hz}$) enabled us to assign 2 α , 3 α -epoxy ketone stereochemistry for 11. Vystreil and coworkers⁷ settled the stereochemistry of 13, the precursor of 11, as 2 α , 3 α -epoxy lupan-1 α -ol by carrying out its conversion with LAH to 2 α , 3 α -dihydroxy lupane of known structure. Boron trifluoride catalysed rearrangement of 11 in dry benzene at ambient temperature afforded the ring A contracted keto aldehyde, 2-formyl-A-nor-lupan-1-one 14 in 60% yield. It practically exists in solution as the enolized form 15. The structure of the rearranged

product was deduced by the physical techniques UV, IR, NMR and mass spectra (see Experimental). Of the two possible enolized forms 15 and 16, the former one 15 was supported by aldehydic proton singlet at δ 9.4 in the ¹H NMR analysis.

The mechanistic aspects of the ring contraction reaction have been thoroughly investigated^{1,2}. Most possibly the ion 17 (Chart 2) generated by the attack of BF_3 on 11 gives rise to carbocation 18 which eventually rearranges to the ring contracted product 14. The whole process might be synchronous.

The photorearrangement of cyclic epoxy ketones is well documented^{8,9}. Upon photolysis, they afford 1,3-diketones or keto-aldehydes. We have carried out irradiation of 11 in dioxane at $\lambda > 290\text{ nm}$ at ambient temperature under argon-atmosphere for 0.5 hr. We have been able to isolate the same keto-aldehyde 14 in good yield (52%). Since the initial product 14 is also



photolabile, irradiation for an extended period results in a complex reaction mixture giving a low yield of **14**.

This photoreaction occurs from excited singlet manifold^{8,9} via a diradical generated by homolysis of $\text{C}_\alpha\text{-O}$ bond, the retention of configuration⁹ α in the resulting β -diketones obtained from the stereoisomeric steroidal epoxy ketones supports the proposition of a predominantly concerted rearrangement maintaining close orbital overlap throughout the entire radical migration⁹. Accordingly, the mechanistic pathway of the photorearrangement of **11** studied by us can be depicted as in Chart 2. The diradical **19** or **20** generated initially on photoexcitation rearranges to the keto-aldehyde **14** by a process in which the bond-migration and carbonyl-formation steps are concerted.

Though the ketoketene **21** could be an attractive intermediate, no product corresponding to this intermediate has been isolated.

In conclusion, the molecular rearrangement conducted by us on isomeric epoxy ketone **11**, induced by either BF_3 -etherate at ambient temperature or under photolytic condition, enabled us to obtain the ring contracted keto-aldehyde **14** in line with the finding of the original workers¹. Though Chatterjee *et al.*⁴ did not obtain the rearranged ring contracted keto-aldehyde **6**, but obtained a ring contracted ketone **5**, presumably formed by deformylation of the intermediate keto-aldehyde **6**. Incidentally, we did not observe the formation of methyl-migrated product of the type **4** isolated by Ganguly *et al.*³.

Experimental Section

General. Melting points were determined in a

sulphuric acid bath and are uncorrected. The pet. ether used throughout the investigation had B.P. 60-80°C. ¹H NMR spectra were recorded on a VNXL-200 spectrophotometer in CDCl_3 solution using TMS as internal reference; IR spectra on a Pye Unicam-Sp-300S and UV on a Shimadzu UV-240 spectrophotometers; and mass spectra (EIMS) on a Jeol JMS-D300 mass spectrophotometer, using direct sample introduction into the ion source at 70 eV. TLC was done on chromatoplate of silica gel G (E. Merck) and spots were visualised by exposing the plates in iodine vapour.

Isolation of lupeol 7. Stem-bark of *Zanthoxylum budrunga*⁵ was extracted in a Soxhlet apparatus for 20 hr. with benzene. The extract was concentrated and purified by column chromatography over silica gel. Elution with pet-ether-ethyl acetate (9:1) as eluent gave lupeol **7** as white solid, crystallised from chloroform-methanol as needles mp 214-15°C (lit.¹⁰ mp 215-16°C); IR (nujol): 3420 (OH), 1630, 890 cm^{-1} ($=\text{CH}_2$).

Lupanol 8. To a solution of lupeol **7** (21 mmol) in ethyl acetate (450 mL) was added Pd-C (5%, 1g) and hydrogenated for 5 hr. Pd-C was removed by filtration and the filtrate on concentration afforded fine white needles of lupanol **8**, mp 202-03°C (lit.¹¹ mp 201-02°C), IR (nujol): 3390 cm^{-1} (OH), $\text{C}_{30}\text{H}_{52}\text{O}$ (M^+ 428 m/z).

Preparation of lup-2-ene 9. To a solution of lupanol **8** (16 mmol) in dry pyridine (200 mL) was added phosphorus oxychloride (25 mL). The reaction mixture was refluxed on a water-bath for 4 hr and then overnight at room temperature. It was poured on ice-water. The precipitated brown solid obtained on filtration was chromatographed on silica gel. Elution

with pet. ether gave lup-2-ene **9** (65%) as, white solid mp 190-192°C (lit.¹² mp 192-93°C); IR (nujol) :1630, 850 cm^{-1} (C = C).

Preparation of lup-2-en-1-one 10. To a solution of lup-2-ene **9** (11 mmoles) in benzene-acetic acid (1:1, 300 mL) sodium dichromate (15 mmoles) was added and the mixture refluxed for 3 hr. The excess oxidant was destroyed by addition of methanol (20 mL). The reaction mixture was extracted with ether (500 mL), washed with Na_2CO_3 and then with water until neutral. The brown mass obtained on evaporation was chromatographed over silica gel. Elution with pet. ether—ethyl acetate (4:1) as eluent gave **10** as white solid (55%), mp 194-95°C, UV (CH_3OH): λ_{max} 220 nm, IR (nujol): 1667, 1625 cm^{-1} (conjugated ketone).

Alkaline hydrogen peroxide treatment of lup-2-en-1-one 10. To a solution of **10** (2.5 mmoles) in dioxane (50 mL) was added aqueous hydrogen peroxide (30%, 8 mL) and aqueous NaOH (6*N*, 10 mL) and stirred over a period of 2 hr. After usual work-up unchanged starting material **10** was recovered in almost quantitative yield (mp and mmp).

Preparation of lup-2-en-1-ol⁷ 12. To a solution of **9** (5.2 mmoles) in dioxane (200 mL) SeO_2 (6.7 mmole) was added. After addition of traces of water (4 drops) the reaction was refluxed for 8 hr. The warm filtrate obtained on removal of Se was poured into aqueous KOH solution (2.5%, 1.2L). The precipitated solid was chromatographed over silica gel. Elution with pet. ether-ethyl acetate (3:1) gave a white solid which on crystallisation from chloroform-methanol gave needles of lup-2-en-1-ol **12**, mp 201-02°C (lit.⁷ mp 203-04°C), $\text{C}_{30}\text{H}_{50}\text{O}$ (M^+ 426 m/z), IR (nujol) : 3424 (OH), 1625, 862 cm^{-1} (C=C), $^1\text{H NMR}$: δ 0.7 - 1.1 (8 CH_3S), 3.6 (m, 1H, CHOH), 5.5 (d, 1H, $J=12$ Hz C_3 -H) and 5.7 (q, 1H, C_2 -H). Anal. Calcd for $\text{C}_{30}\text{H}_{50}\text{O}$: C, 84.44; H, 11.81. Found: C, 84.12; H, 11.61%.

Preparation of 1 α -hydroxy-2 α , 3 α -epoxy lupane 13. To a solution of **12** (10.5 mmoles) in chloroform (55 mL) was added *m*-CPBA (14.6 mmoles). The reaction mixture was kept at 5°C for 72 hr, extracted with ether (250 mL), washed with Na_2CO_3 solution and then with water until neutral. The white solid obtained on evaporation of solvent, was crystallised from chloroform-methanol to furnish pure **13** (72%), mp 233-34°C (lit.⁷ mp 232°C); $\text{C}_{30}\text{H}_{50}\text{O}_2$ (M^+ 442 m/z), Anal. Calcd for $\text{C}_{30}\text{H}_{50}\text{O}_2$; C, 81.33, H, 11.35. Found: C, 81.47; H, 11.09%.

Preparation of 2 α , 3 α -epoxy lupan-1-one 11. To a solution of **13** (2.5 mmoles) in pyridine (20 mL) was added a slurry of CrO_3 (3.6 mmoles) in pyridine (15 mL) at 5°C and kept at this temperature for 48 hr. The reaction mixture was diluted with ethyl acetate (200 mL). The precipitate was filtered off. The clear brown filtrate was treated with aqueous HCl (10%), washed with water until neutral. Evaporation of the solvent left a brown mass which was chromatographed over silica gel. Elution with pet. ether-ethyl acetate (4:1) yielded a white solid which on crystallisation from chloroform-methanol afforded fine needles of **11** (48%) mp 191°C; IR (nujol): 1695 cm^{-1} (C = O); $^1\text{H NMR}$: δ 0.72 - 1.1 (8 CH_3S), 3.11 (d, 1H, $J = 4$ Hz, C_3 -H) and 3.27 (d, 1H, $J = 4$ Hz, C_2 -H); Mass : 440 (M^+), 397 m/z (M^+ -isopropyl). Anal. Calcd. for $\text{C}_{30}\text{H}_{50}\text{O}_2$: C, 81.81; H, 10.91. Found: C, 81.45; H 10.68%.

BF_3 -etherate rearrangement of 11. Preparation of 2-formyl-A-nor-lupan-1-one 14. The epoxy ketone **11** (1.2 mmoles) in dry benzene (25 mL) was treated with freshly distilled BF_3 -etherate (5 mL) at room temperature for 1 hr. The reaction mixture was diluted with water, extracted with ether and washed with water. On evaporation a thick gum was obtained which was purified by chromatography over silica gel. Pet. ether-ethyl acetate (7:3) eluted a white solid (60%), mp 93-94°C, UV (MeOH); λ_{max} 227 nm, shifted to 292 nm in 0.1*M* NaOH, IR (nujol): 3450(OH), 1710 (unsaturated aldehyde), 1595 (C=C) cm^{-1} , $^1\text{H NMR}$: δ 0.7-1.2 (8 CH_3S), 3.11 (d, 1H, $J = 4$ Hz, C_3 -H), 3.27 (d, 1H, $J = 4$ Hz, C_2 -H) and 9.4 (s, 1H, -CHO); Mass : 440 (M^+), 397 m/z (M^+ -isopropyl). Anal. Calcd for $\text{C}_{30}\text{H}_{48}\text{O}_2$: C, 81.81; H, 10.91. Found: C, 81.55; H, 16.72%.

Photolysis of 11 : Formation of 2-formyl-A-nor-lupan-1-one 14. A solution of **11** (1.1 mmole) in dry dioxane (100 mL) was irradiated for 0.5 hr with medium pressure mercury lamp placed in a central water-cooled pyrex immersion well under argon atmosphere at ambient temperature. Evaporation of the solvent in a rotary vacuum evaporator followed by chromatography of the crude product on silica gel using pet. ether-ethyl acetate (7 : 3) as eluent gave a white solid (52%) which was found to be identical with **14** by mp and mmp determinations and by comparison of spectral (UV, IR, $^1\text{H NMR}$ and mass) data .

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