PART - I

ACTION OF HYDROGEN PEROXIDE IN PRESENCE OF SELENIUM DIOXIDE ON OXIME DERIVATIVES OF FRIEDELIN; LUPANONE AND TARAXERONE

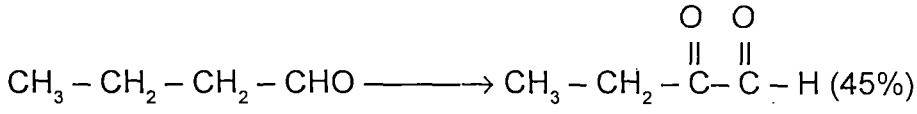
CHAPTER - I

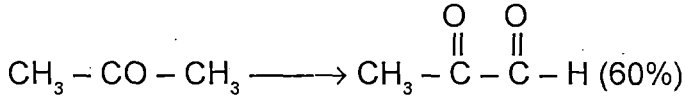
A CONCISE REVIEW OF SELECTIVE OXIDATIONS WITH SELENIUM-DIOXIDE

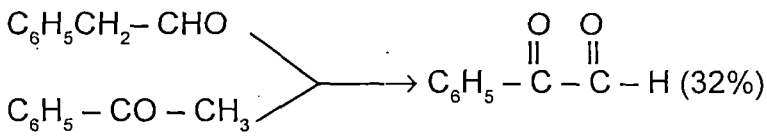
Selenium dioxide as a selective reagent in organic synthesis is in use since Riley's[1] pioneering research work in which he reported conversion of monocarbonyl compound having an adjacent methylene-group to an α-dicarbonyl compound by using selenium-dioxide. The transformation of a ketone or an aldehyde to an α-dione, allylic oxidation and the conversion of a monoketone or a 1, 4-diketone to an α, β-unasturated ketone or to an ene-dione are some of the key areas in which selenium dioxide has been widely used as selective reagent. Some of the oxidative reactions of selenium-dioxide under different conditions are as follows.

Formation of α - Dione

Methylene-groups adjacent to the carbonyl group of aldehydes and ketones would react with stoichimetric quantities of selenium dioxide to produce α-diketones and keto-aldehydes in good yield as shown below :

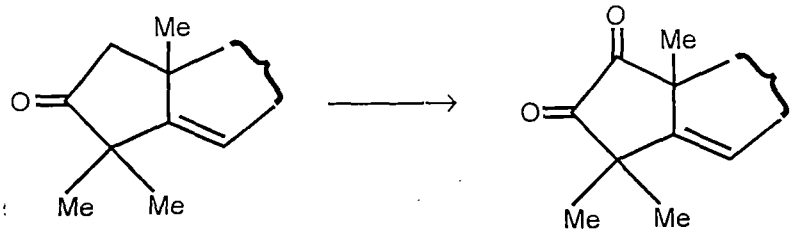






If the side or competing reaction is prevented then the yield of the product can be more. To get the better yield the carbonyl compounds to be oxidised should contain such structural arrangement which reduces or prevents side

or competing reaction from taking place. Thus, A-nor-allobetulone-3 and A-nor-4, 4-dimethyl cholest 5-ene-3-one both of which have the monoketone unit whose partial structure **(1)** are oxidised to the diketone **(2)** in 87% and 92% yield[2].



(1) **(2)**

Mechanism

The elaborate interpretation of the reaction was given by Corey and Schaefer[3] who studied acid catalysed oxidation of desoxybenzoin in 70% acetic acid at 89.2^0. They found the over-all reaction to be second order; first order in ketone and frist order in selenium (IV) reagent. The order of the acid catalysed reaction is as follows.

$$C_6H_5 - \overset{\overset{O}{\|}}{C} - CH_2 - C_6H_5 + SeO_2 \longrightarrow C_6H_5 - \overset{\overset{O}{\|}}{C} - \overset{\overset{O}{\|}}{C} - C_6H_5$$

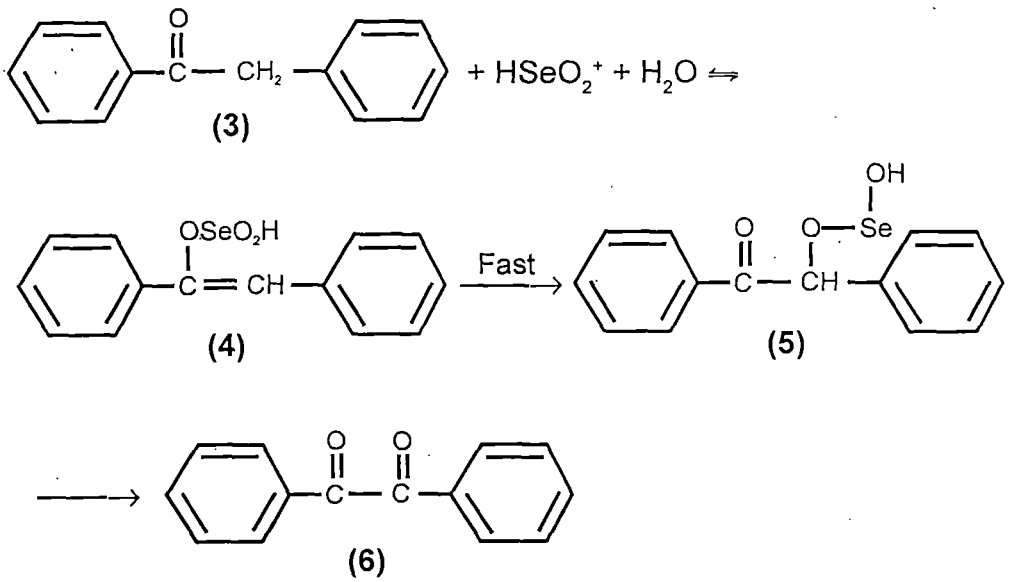
DESOXYBENZOIN BENZIL

$$\frac{-\,d\,(SeO_2)}{dt} = K\,[SeO_2]\,[Ph - COCH_2Ph]\,[H^+]$$

The two ortho-substituents on the ring adjacent to the carbonyl-group's presence did not depress the rate of acid catalysed oxidation which eliminated the possibility that carbonyl-addition was involved. Replacement of the α-hydrogen of desoxybenzoin (3) by deuterium resulted in a several-fold decrease in rate in the acid catalysed process. On the basis of these and other data it was proposed that the rate determining step in the oxidation of desoxybenzoin(3) was the formation of enol selenite ester (4) directly from

the ketone by a process mechanistically related to enolisation in which the electrophile - nucleophile pairs were $HSeO_2^+$ or $H_3SeO_3^+$ and H_2O. The enol selenite ester (4) rearranges in a series of first steps to an α-selenite (II) keto-ester (5) and finally to benzil (6).

SCHEME - I



Allylic Oxidation

Guillemonat[4-8] studied several oxidation reactions of olefins and then he reported that the course of selenium dioxide oxidation of alkenes could be ascertained from the rules mentioned below :

(i) The oxidation always occurred to alpha to the most substituted end of the double bond.

(ii) When the double bond was in a ring, whenever possible, oxidation occurred within the ring.

(iii) The order of preference for oxidation was $CH_2 > CH_3 > CH$.

(iv) When the double-bond was terminal rather than the expected secondary alcohol or derivatives thereof, the primary alcohol was formed with the migration of the double bond.

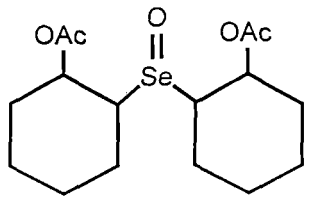
Guillemonat's[9-11] proposal was inadequate but his comprehensive studies of the behaviour of SeO_2 in acetic acid, acetic anhydride led to the formation of many useful and valid generalisation with respect to the site of attack in many cases. Yet another suggestion made by Waters[20] without any experimental evidence that the reaction involved neutral radical species.

Schaefer, Horvath and Kelvin[13] had shown that the reaction was not affected by inhibitors and therefore, could not be radical chain.

Trachtenberg et al[14] pointed out that no free radical was generated in the system, as the system was incapable of initiating polymerisation of acrylonitrile under the condition of temperature and concentration, where acrylonitrile is rapidly polymerised if a source of free radical is present.

Wiberg[15] established the seleoxides (7) involved in the oxidation of cyclohexene in acetic acid-acetic-anhydride reaction. Schaefer et. al.[13], however, showed that analogous compound (8) isolated from selenium dioxide oxidation of 1, 3-diphenyl propene (9) to 1,3-diphenyl-1,2-propen -1-ol acetate (10) at a slow rate to account for the main course of oxidation. The main pathway must involve solvolysis of an allylic selenite ester, although the structure of the latter has not been completely established. Schaefer et al[13] suggested the mechanism as shown in Scheme-II.

SCHEME - II



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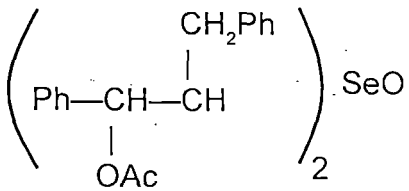

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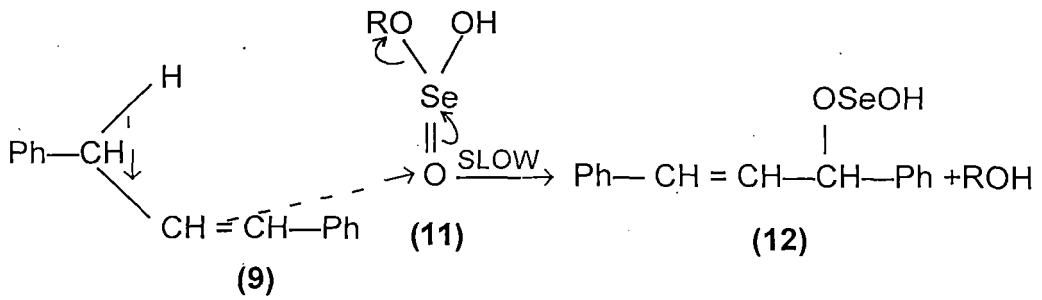
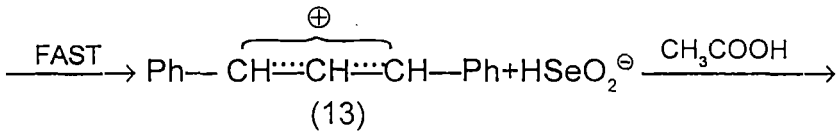


(9) **(11)** **(12)**



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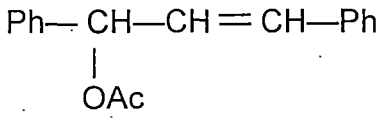
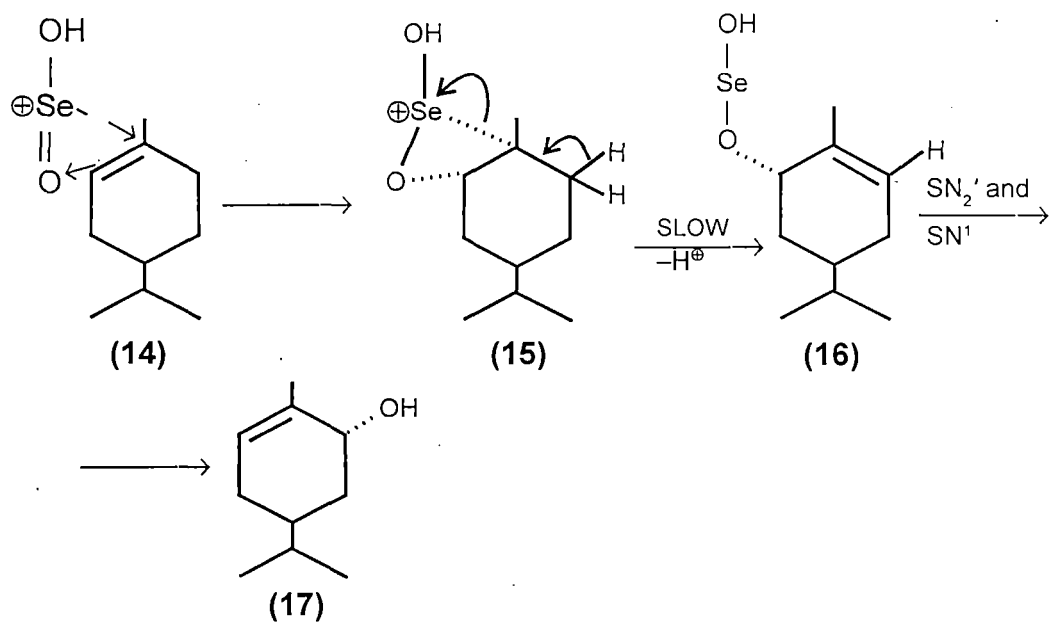


(10)

The rapid SN-1 reaction of (12) was in agreement with the observation that 3-deuterium labelled at C-3 showed equilibration of C-1 and C-3. Furthermore, the presence of a final solvolytic step was in agreement with observation on many systems. Thus, one obtained alcohols, acetates and ether when the selenium dioxide oxidation was performed in water, acetic acid and alcohol respectively.

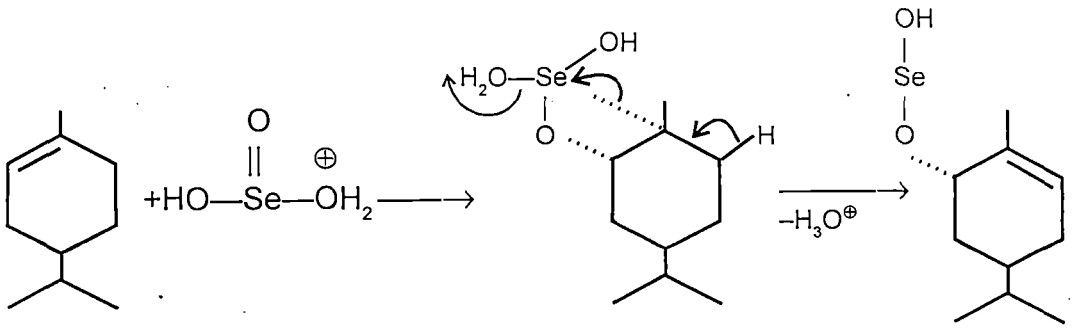
Schaefer et al's[13] mechanism did not explain the stereochemical results of the reaction. In order to explain the stereochemical results obtained by oxidation of a number of cyclohexenyl system. With D(+)-1-p-menthene as the substrate, Trachtenberg et. al.[14] suggested the following mechanism as shown in Scheme - III.

SCHEME -III



(14) **(15)** **(16)**

(17)

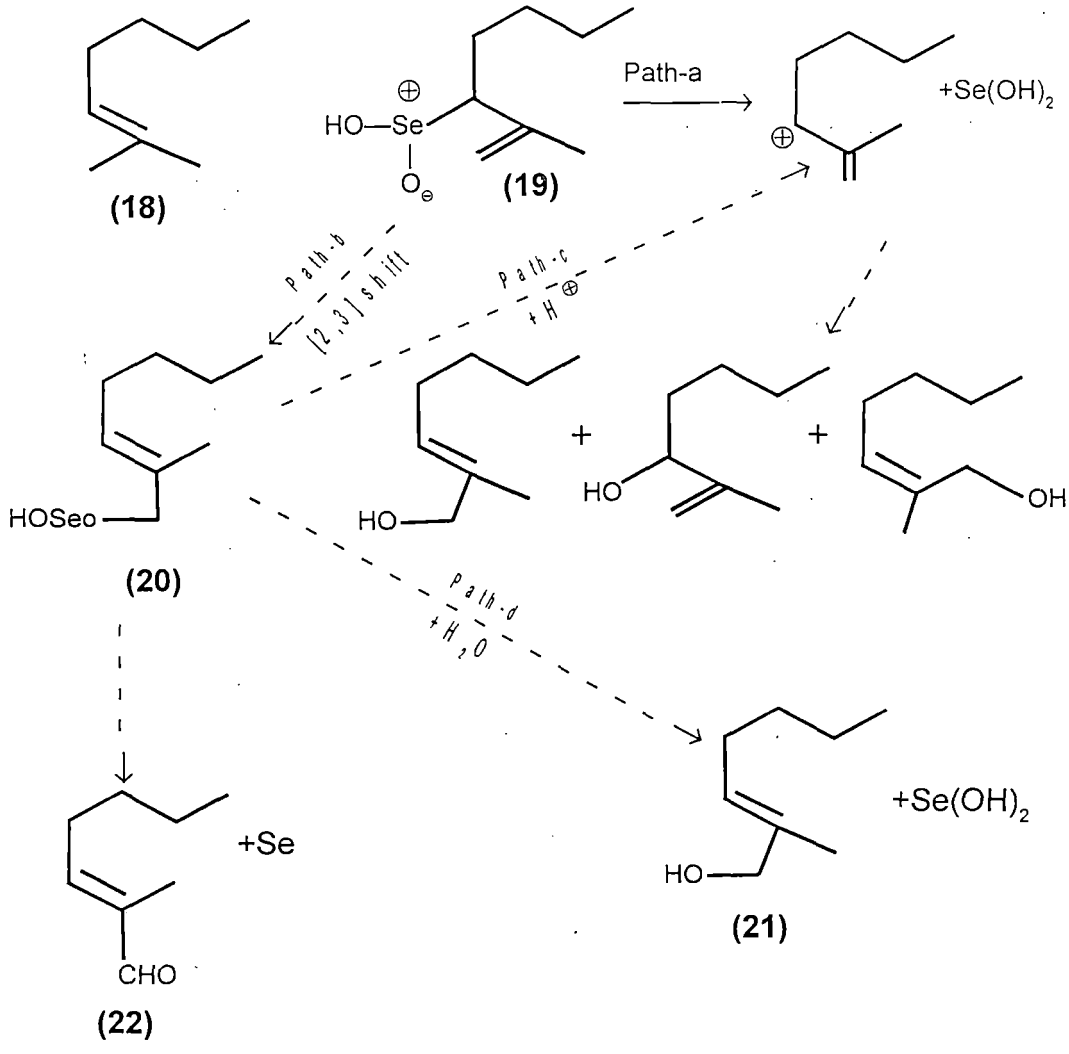


(14)

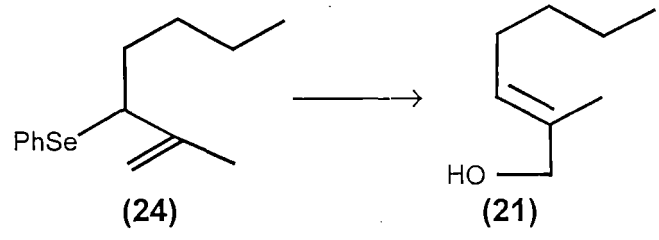
The first step does not signify a concerted 2+2 cyclo-addition but rather a typical Markownikoff type electrophilic addition with attack occuring through oxygen to produce positive character at the tertiary carbon followed by cyclization.

Sharpless and Lauer[16] have put forward different mechanism for allylic oxidation of olefins by selenium-dioxide. Schaefer[13] and Trachtenberg[14] have argued against the involvement of alylic selenic-acid (19), because of the known inertness of benzyl-selenic acid to solvolysis. However, a [2,3] sigmatropic rearrangement (Path-b) of **Scheme-IV** of allylic selenic acid (19) to a selenium (II) ester (20) occurred to Sharpless et. al[16] as a likely alternative to the solvolysis pathway-a. Sharpless and Lauer proposed that the [2,3] sigmatropic shift indicated in the path-b is a high yielding process (Scheme-IV).

SCHEME-IV

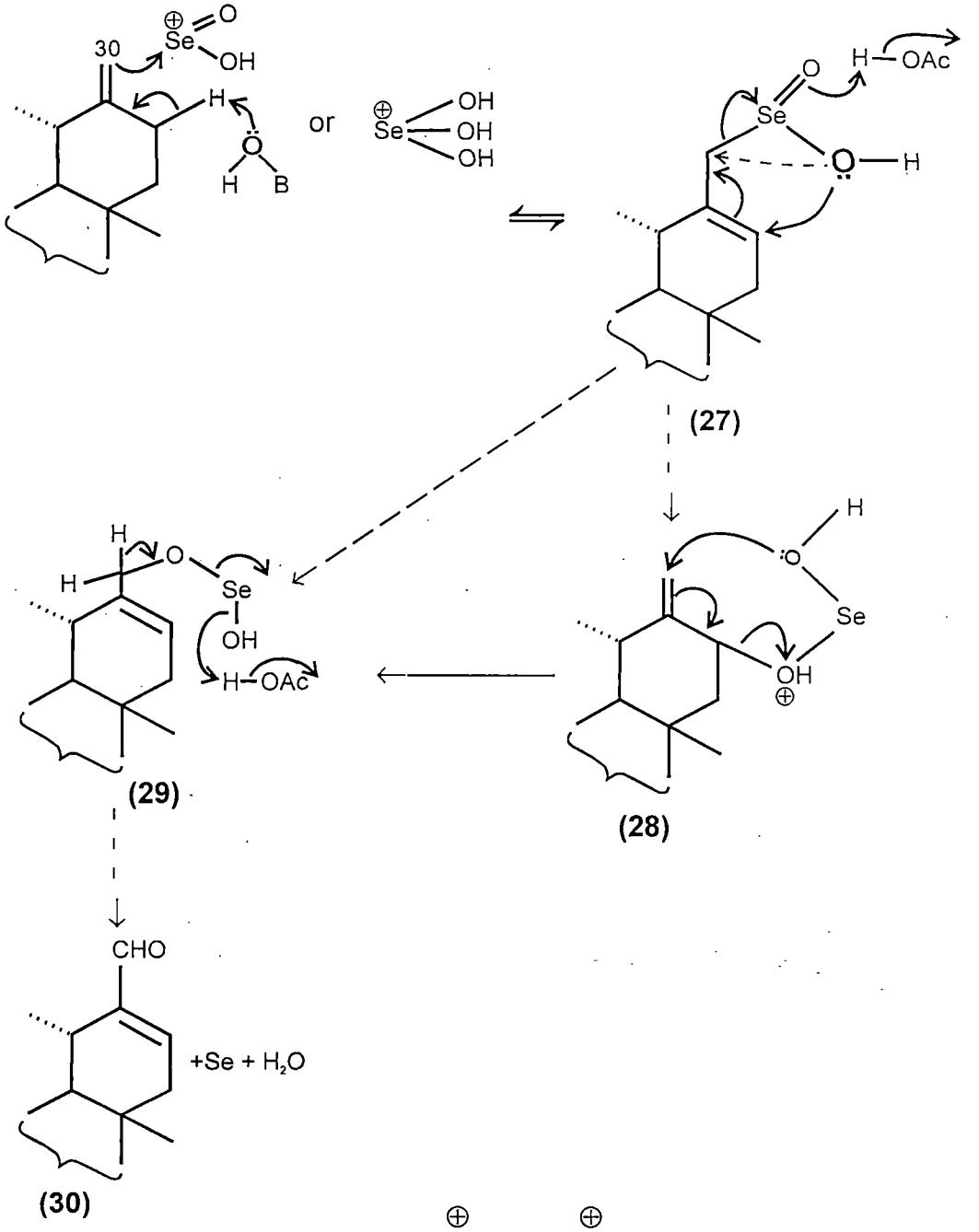


Buchi and Wuest[17] studied and established that selenium-dioxide selectively attacks trisubstituted olefins such as (18) to give only the (E)-alcohol(21). The allyl selenic acid, (19) must lead stereoselectively to the (E)-ester of (20) if the rearrangement proposed is correct. The mechanism was proved from the conversion of alkyl phenyl selenide (24) to (21).



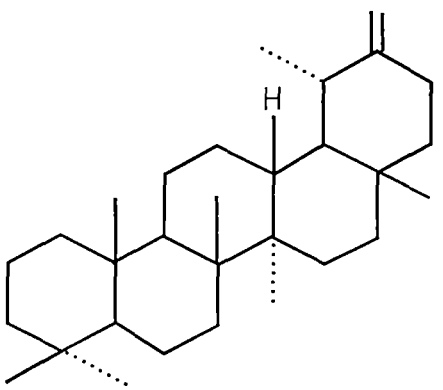
The oxidation of taraxastene **(25)** and Ψ-taraxastene **(26)** was studied by Talapatra et. al.[18] and gave the mechanism for the formation of the corresponding aldehyde as shown in the **Scheme - V.**

SCHEME - V



The electrophilic attack of $H\overset{\oplus}{S}eO_2$ or $H_3\overset{\oplus}{S}eO_3$ on the olefinic C-30 with simultaneous or subsequent nucleophilic attack on the allylic C-21-hydrogen leads to the formation of an unstable Selenium (IV) complex **(27)** having the

more stable double bond parallel to the trans D/E ring juncture. The complex (27) undergoes successive rearrangements as shown in **Scheme V** to form the unstable selenium (II) complex intermediate (28) and (29) involving 5 and 6-membered cyclic transition states respectively requiring low activation energies. The intermediate complex (29) could arise directly from (27) involving a 3-membered transition-state as shown in the **Scheme V.** The intermediate (29) then collapses to form the product (30) by the loss of an allylic proton with the deposition of metallic selenium as shown in **Scheme V.**



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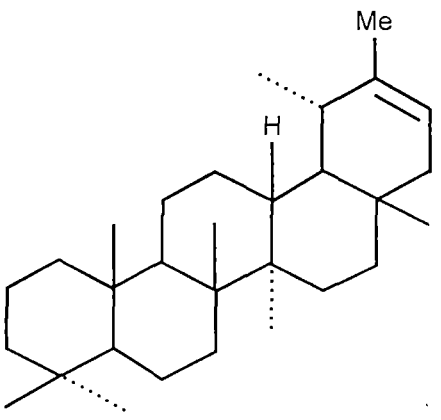
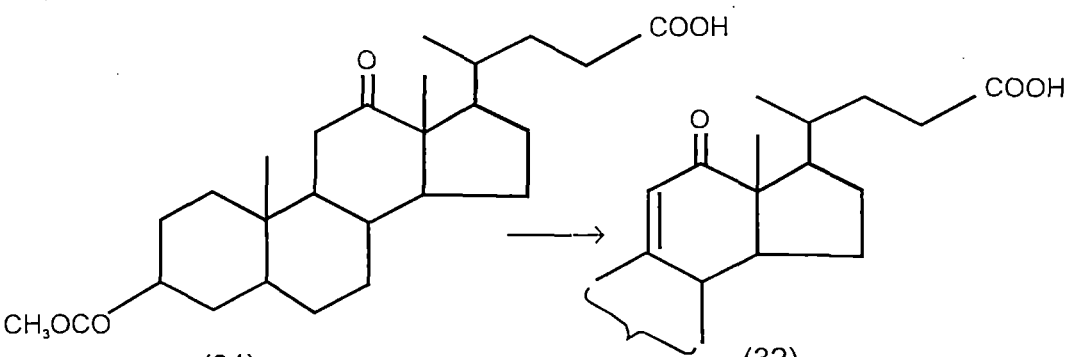


(26)

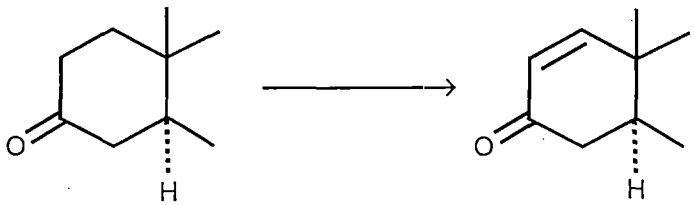
α, β - Dehydrogenation of Carbonyl Compounds

Dehydrogenation of diethyl-succinate to a mixture of the di and half ester of maleic acid was reported by Riley[19]. Schwenk and Stahl reported in the year 1947 that selenium dioxide oxidation of a 12-keto steroid (31) produced[9-11] the Δ–12 ketone of partial structure (32), rather than the 11, 12-diketone.[20-22]



(31) **(32)**

Selenium dioxide introduces a double bond at the 1, 2-position in either a 5α-3-keto steriod or Δ-3-keto steroid,[23,24] partial structure being **(33)** and **(34)**.



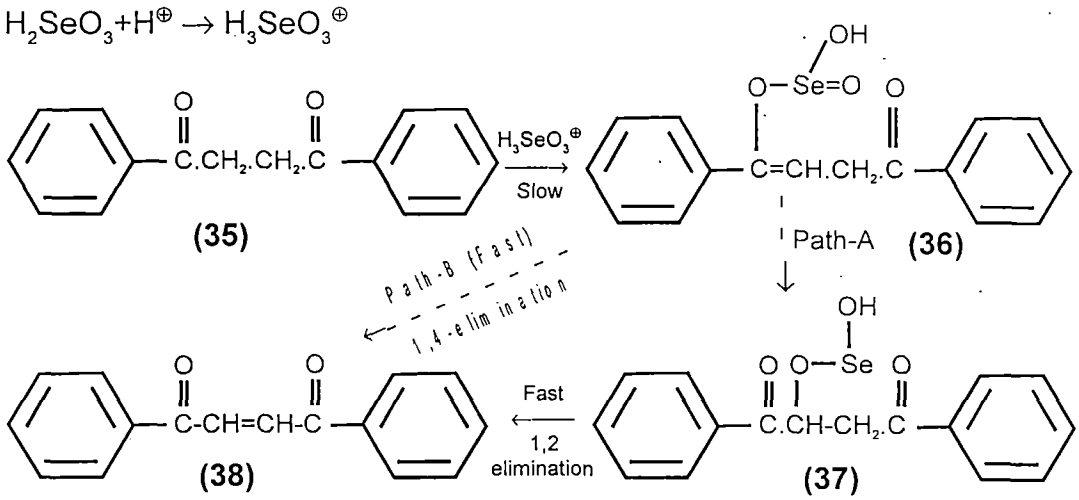
(33) **(34)**

Mechanism of α, β-dehydrogenation

A. 1, 4-diketones

Little detailed mechanistic information regarding the oxidation of organic compounds by selenium dioxide was available.[25] Schaefer et.al.[26] had carried out a study of the oxidation of 1,2-dibenzoyl ethane **(35)** to trans-1,2-dibenzoyl ethylene **(38)** in order to clarify the mechanism of oxidation of 1, 4-diketones to 1, 4-ene diones. In 80% acetic acid-20% water as solvent, **(38)** was obtained in 80-85% yield, no 1,4-diphenyl 1,2,4-butanetrione **(36)** could be detected. A kinetic study of the reaction was complicated by the fact that **(38)** also reacted with selenious acid, however, the rate of oxidation of **(38)** was 30 times slower than that of **(35)**. The mechanism for the oxidation of 1,2-dibenzoyl ethane **(35)** to trans-1,2-dibenzoyl ethylene **(38)** was proposed by Schaefer et. al.[26] The mechanism is as shown in **Scheme VI.**

SCHEME - VI



The mechanism shown in **Scheme VI** involved the following steps.

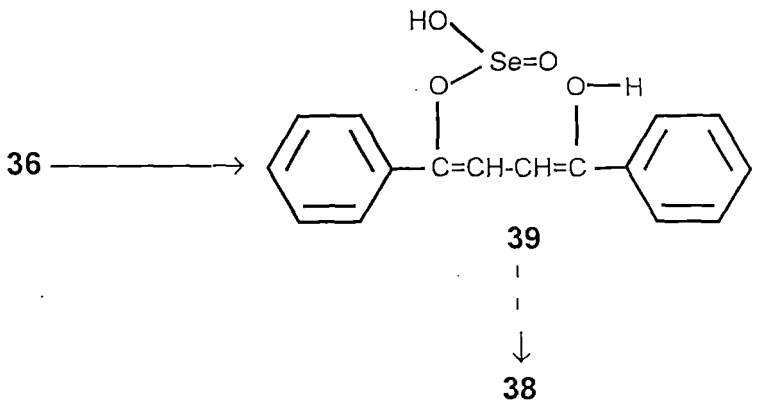
(i) production of oxidising selenium species, $H_3SeO_3^{\oplus}$, by protonation of selenious acid, H_2SeO_3.

(ii) the rate determining attack of the oxidising selenium species, $H_3SeO_3^{\oplus}$ on the substrate **(35)** to give an enol selenite ester **(36)** and

(iii) decomposition of **(36)** to the product via one of the two pathways.

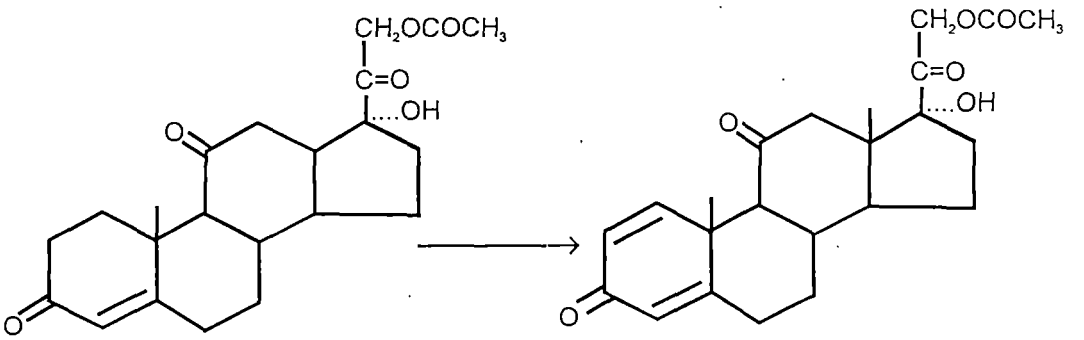
Path-A involved rearrangement of **(36)** to the product α-selenium (II) keto ester **(37)** and then to the product **(38)** by a rapid 1, 2-elimination of H_2SeO_2.

In Path-B, **(36)** was directly converted to **(38)** by a rapid 1,4-elimination of the element of H_2SeO_2. Path-A is essentially the same mechanism and intermediate already proposed for α-dione formation (Scheme-I)[27] of the two possibilities the 1,4-elimination from enol-selenite ester **(36)** was likely since this intermediate contained a doubly activated methylene unit. The latter simply required an enolisation to give the half-ester of the dienol **(39)**, which then decomposes to the product **(38)** via bond migration, the driving force being the reduction of selenium. The possibility of 1, 2-elimination of H_2SeO_2 appeared less likely in view of the fact that the alternative product of its decomposition 1,4-diphenyl 1, 2, 3-trioxobutane could not be detected. Either a direct 1,4-elimination from **(36)** or a rearrangement of **(36)** to **(37)** followed by a rapid elimination of the element of H_2SeO_2 would account for the formation of trans-1, 2-dibenzoyl ethylene **(38)**.



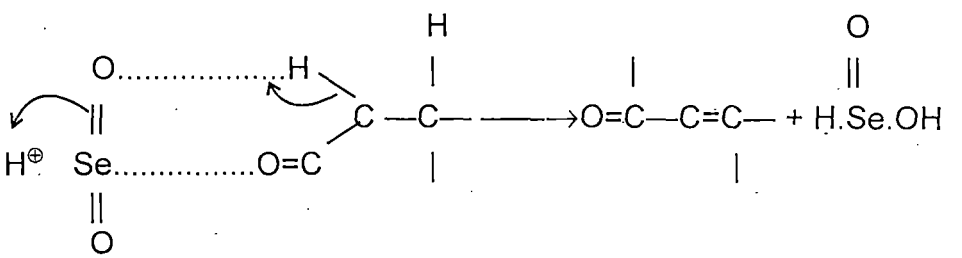
B. Mono-Ketone

The kinetics of dehydrogenation of an α, β-unsaturated ketones was investigated by Langbein.[28] He obtained a second-order rate constant for the Δ-dehydrogenation of cortisone acetate **(40)** to **(41)** from a plot which contained the concentration of ketone and selenium dioxide. Langbein[28] put forward a common intermediate similar to **(37)**, formed by direct attack of the oxidant on the ketone, which decomposed to form all the possible oxidation products.



(40) **(41)**

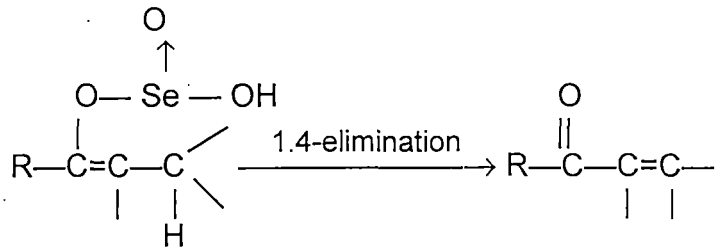
However, for α,β-dehydrogenation, Langbein[28] considered the more pausible-path as one that did not involve carbon-oxygen bond formation as **(42)**.



(42) **(43)**

The mechanism for this dehydrogenation may involve either concerted 1, 4-elimination from the enol ester **(44)** or concerted 1,2-elimination from Se(II) ester **(45)**. These intermediates were similar to **(36)** and **(37)** but without a

second carbonyl-group to activate the β-position and therefore should be less prone to undergo elimination.



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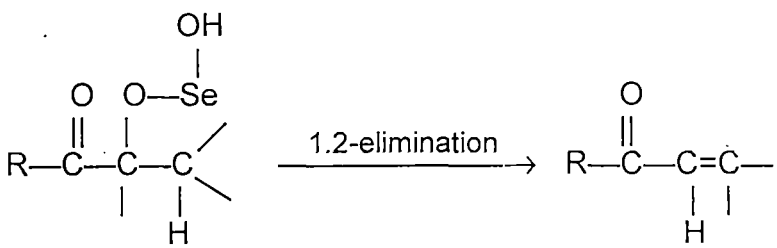

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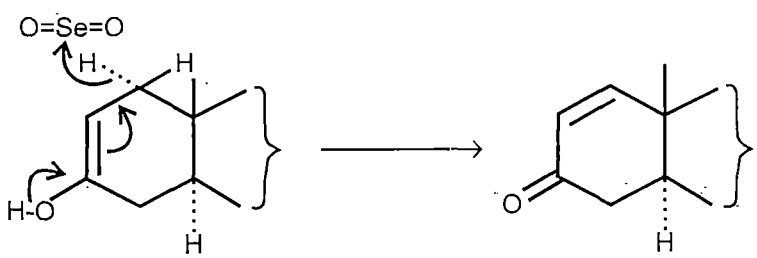
Another path, which circumvented the difficulty inherent in (44), would be direct attack of the selenium-dioxide on the allylic position in the enol to remove hydride ion.



(46)

Why do some mono-ketones give α-diones and others give α,β-unsaturated ketones remains unanswered. This is assumed to be partially due to solvent effect. Tertiary alcohols are normally used to carry out dehydrogenation reaction,[29] but the reaction can be effected in acetic acid[30] or in aromatic solvents.[31] α-diones are generally obtained by using ethyl-alcohol or dioxan.[32] Again shielding of α-CH_2 (methylene) group by nearby bulky substituents

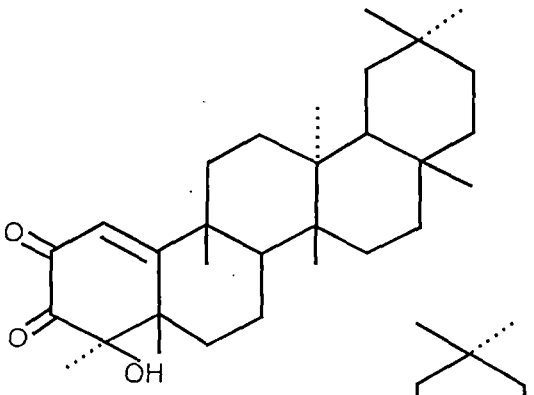
often favours the formation of α, β-unsaturated ketone. Both regio-chemical and stereo-chemical aspects of the allylic hydroxylation reactions of selenium dioxide was investigated by Stephenson et. al.[33] The important findings are as stated below :

(i) In tert-butyl alcohol the mechanism is more complex than predicted by using the ene-(2,3) sigmatropic shift scheme proposed by Sharpless et.al.[16]

(ii) The stereo-chemical complexities appear to derive from ionic intermediates and can be suppressed in more basic media, e.g. tert-butyl alcohol or pyridine.

(iii) The strong preference for trans allylic alcohol products in the reaction is due to steric preference in the [2, 3] sigmatropic migration. The ene step is non-selective.

The oxidation of friedelin **(47)** with selenium dioxide in tertiary butanol was carried out by Pradhan et. al.[34] and obtained two products to which they assigned the structure of friedel-1(10)-en-4β-ol-2, 3-dione **(49)** and 3α-acetyl-4-nor-friedel-1(10)-en-3β-ol-2-ene **(48)**.



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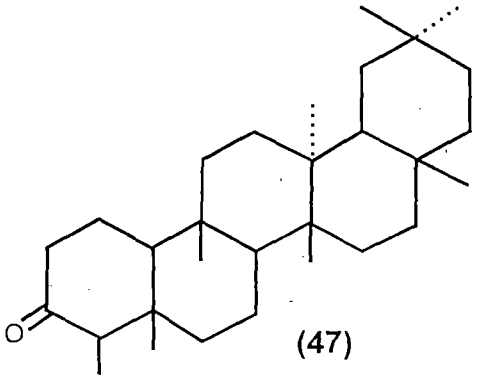

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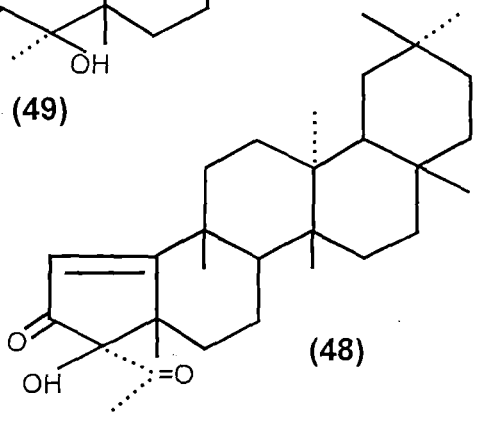
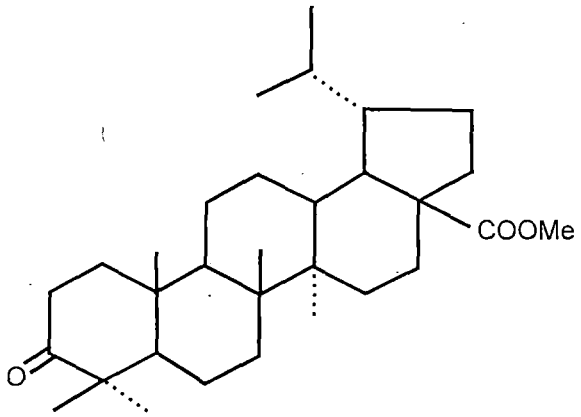


(48)

Pradhan et. al.[35] also reported that the 4-gem dimethyl-3-keto triterpenoid, methyl dihydrobetulonate (50) on prolonged heating with selenium-dioxide in tertiary-butanol gave lup-28-carbomethoxy-1(2)-ene-3-one-2-selenide(51) and A-nor-lup-28-carbomethoxy-2-carb→1-olide-3α-ol (52) and put forward the mechanism for their formation as depicted in **Scheme-VII.**



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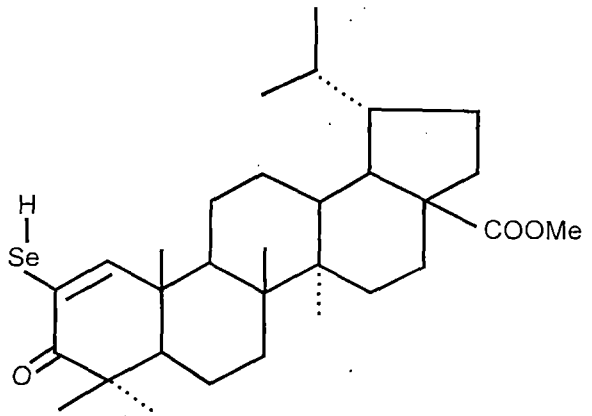

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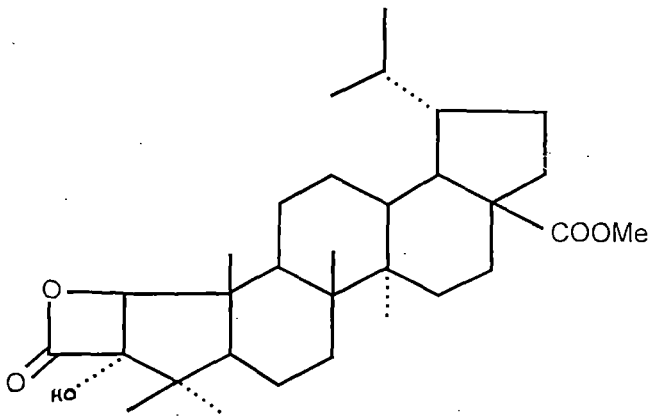
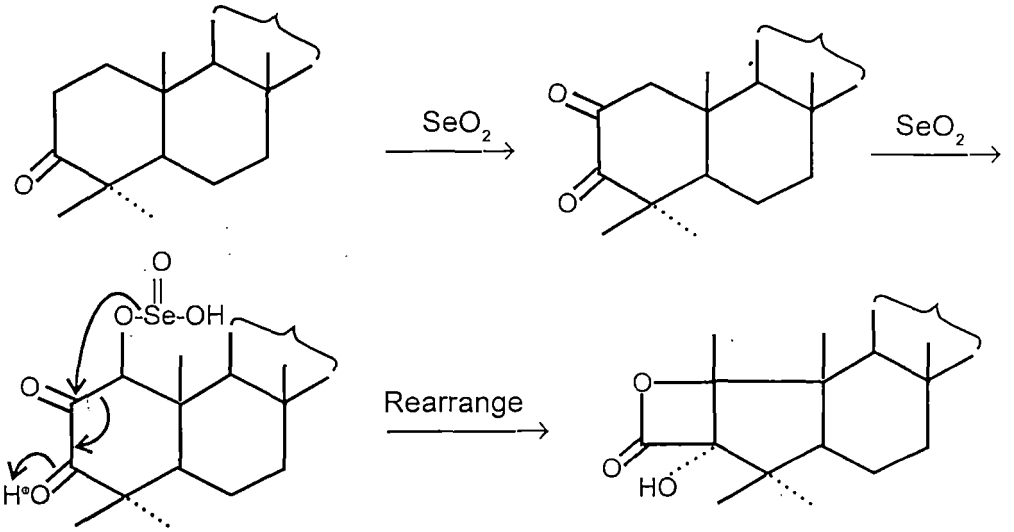


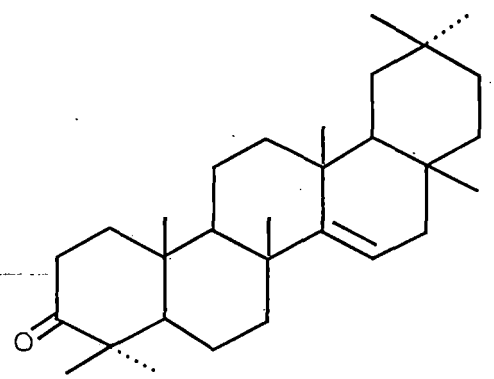
(52)

SCHEME-VII

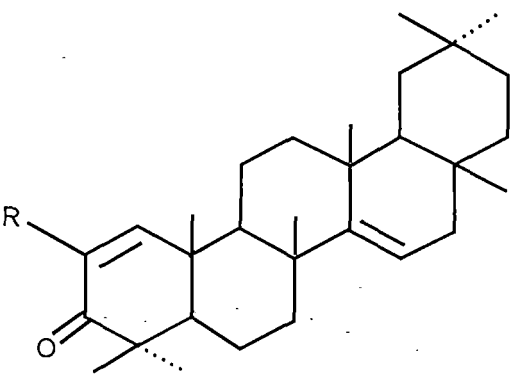


(52)

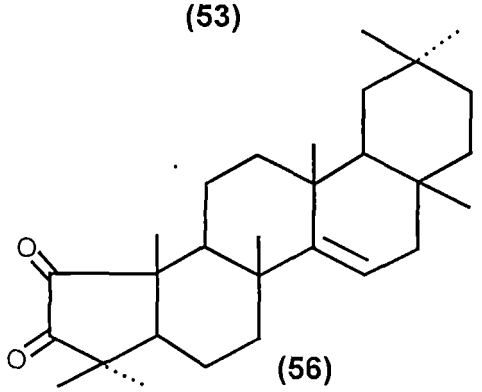
Pradhan et. al.[36] also carried out the same reaction on taraxerone **(53)** which resulted in the formation of five products, viz. 1(2)-dehydro-taraxerone **(54)**; 1(2)-dehydro taraxerone-2-selenide **(55)**; 2-nor-taraxer-1, 3-dione(56); 1(2)-dehydrotaraxerone-2, 2′-seleno-taraxer-1′, 3′-dione **(57)**; and 1β, 3α-dihydroxy-3-carboxy-A-nor-taraxerone **(58)**.



(53)



(54);R=H
(55);R=SeH



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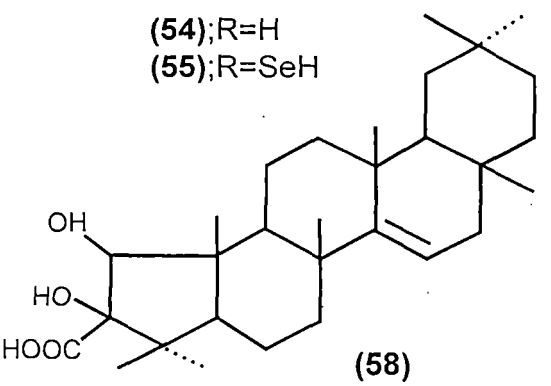
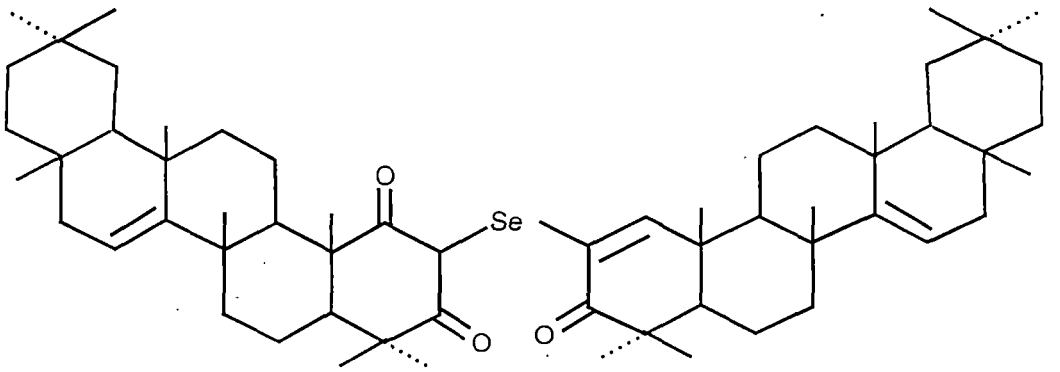
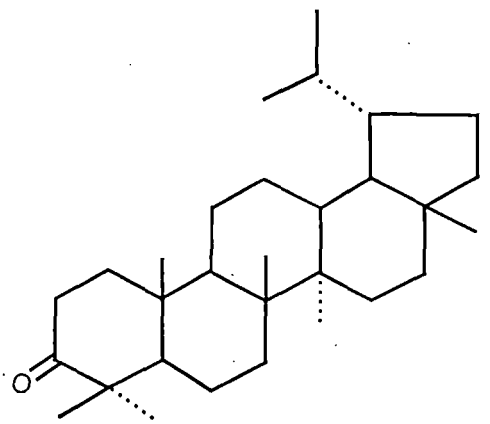


(58)



(57)

Lupanone **(59)** on similar treatment with selenium-dioxide in tertiary butanol afforded seven products[37] designated as Lup-1-en-3-one **(59a)**; Lup-1(2)-en-3-one-2-selenide **(59b)**; Lup-1-(2)-ene-3-one-2-bis selenide **(59c)**; 1β, 3α-dihydroxy-3 β-carboxy-A-nor-lupane **(59d)**; A-nor-lupan anhydride **(59e)**; 1-hydroxy-lupan anhydride **(59f)** and 1-hydroxy-A-nor lup-2-carb→4 olide **(59g)**.



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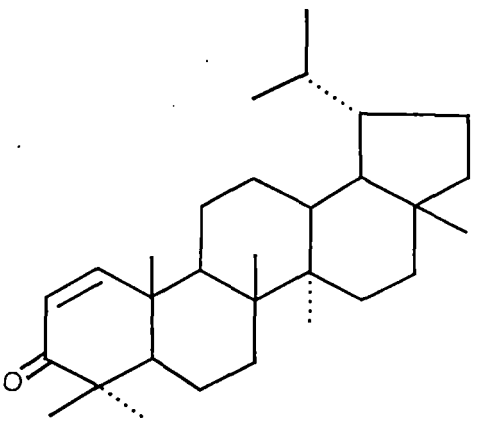
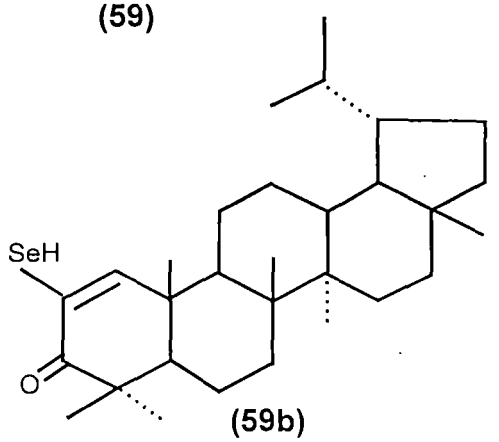
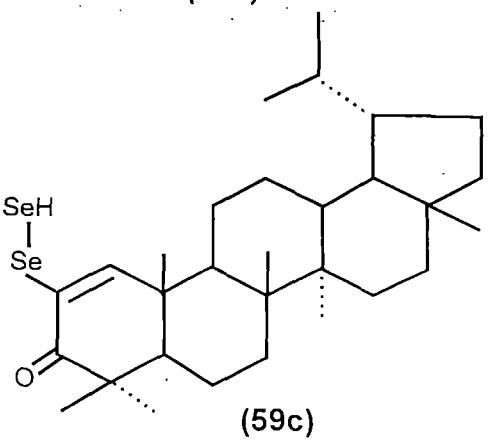


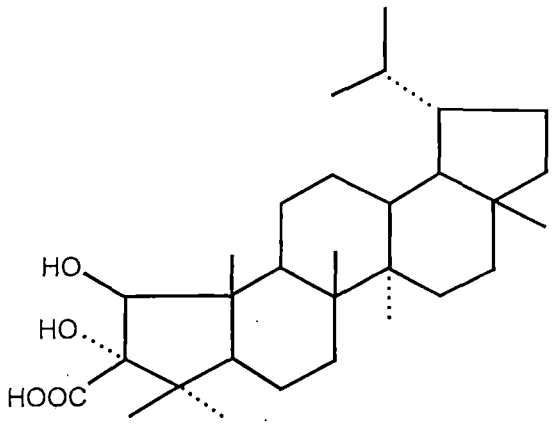
(59a)



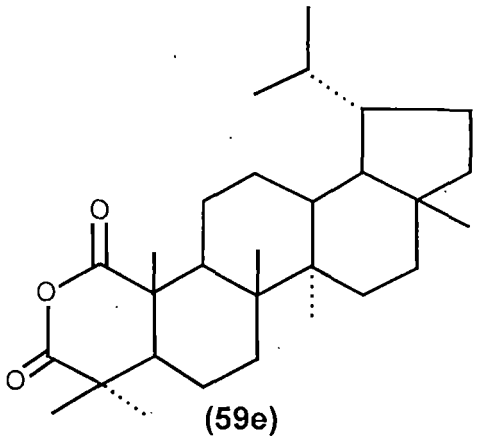
(59b)



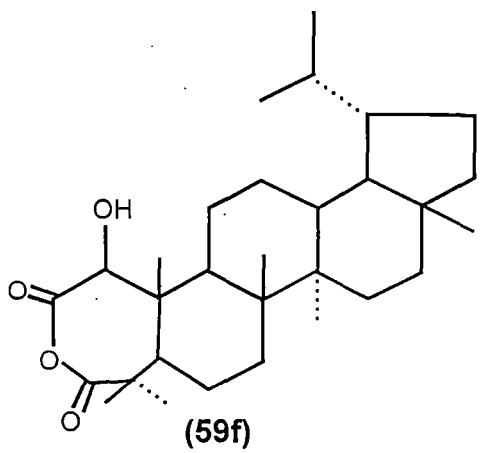
(59c)



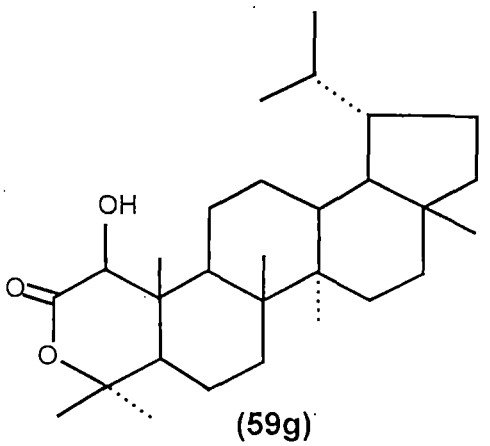
(59d)



(59e)



(59f)



(59g)

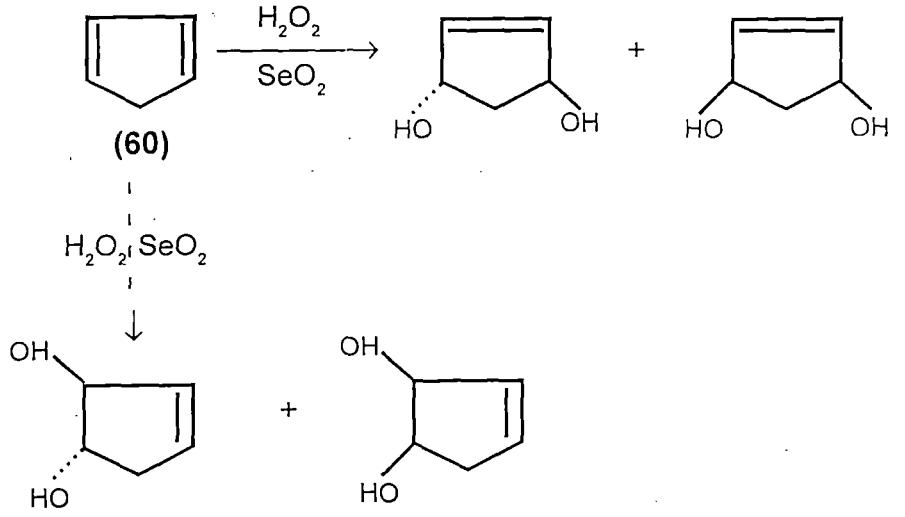
The structures of the above compounds have been established on the basis of analytical and spectral data.

2. A Concise Review on Reactions of Hydrogen Peroxide in Presence of Selenium Dioxide

The reactions of hydrogen peroxide in presence of selenium-dioxide was performed in many oxidative transformations. This section of the chapter deals with the short review on the products obtained by the reactions of hydrogen peroxide in presence of selenium dioxide.

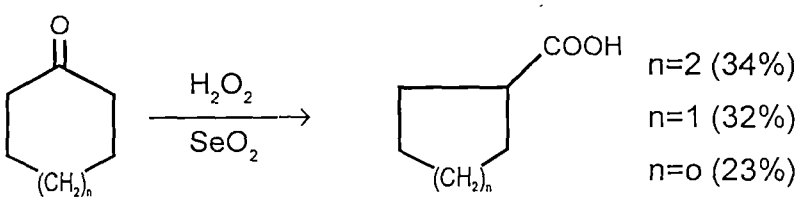
Seguin et. al.[38] prepared trans-cyclohexane-diol free from cis-compound from cyclohexene using hydrogen peroxide in presence of selenium dioxide and had also prepared 1, 2-diols of cyclopentadiene from cyclopentandiene. Selenium dioxide was used as catalyst by Curtuis et. al.[39] in presence of hydrogen peroxide to oxidise acrolein and metacrylic to monomeric acrylic

and metacrylic acids and suggested that at first selenious acid oxidised to selenic acid with hydrogen peroxide then that seleninic acid reacted with acrolein to give acrylic acid and selenious acid. In another case,[40] the reagents have been used for hydroxylation of cyclopentene and cyclopentadiene **(60)**, Per-selenic acid is probably the catalyst in this case.



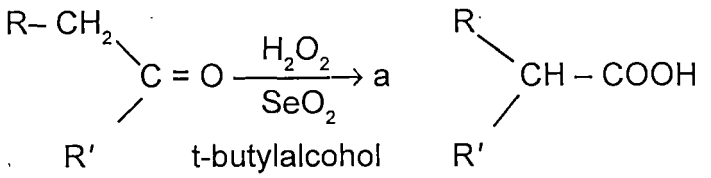
Oxidation of methylene groups adjacent to carbonyl groups with stoichimetric quantity of selenium dioxide to produce α-diketones or keto-aldehydes are well known.

Payne et. al.[41] conducted the oxidation of cycloheptanone, cyclohexanone and cyclopentanone with selenium dioxide in presence of hydrogen peroxide and considered that cyclic ketones might undergo the well-known reaction with selenium dioxide in presence of hydrogen peroxide to give α-diketone, serving to some extent to oxidise selenium metal back to the dioxide. Payne et. al.[41] observed that, all the three ketones underwent oxidative ring contraction to cyclohexane, cyclopentane and cyclobutane carboxylic acids in 34%, 32% and 23% yields respectively.



(61)

The oxidation of aliphatic ketones, RCH_2COR^1 with hydrogen peroxide in presence of selenium dioxide was investigated by Sonoda et. al.[42] and got carboxylic acids, RR'.CH.COOH accompanied by rearrangement of alkyl groups.



(62) where; $R \Rightarrow H$, $R' \Rightarrow$ alkyl group } R = R' = alkyl groups

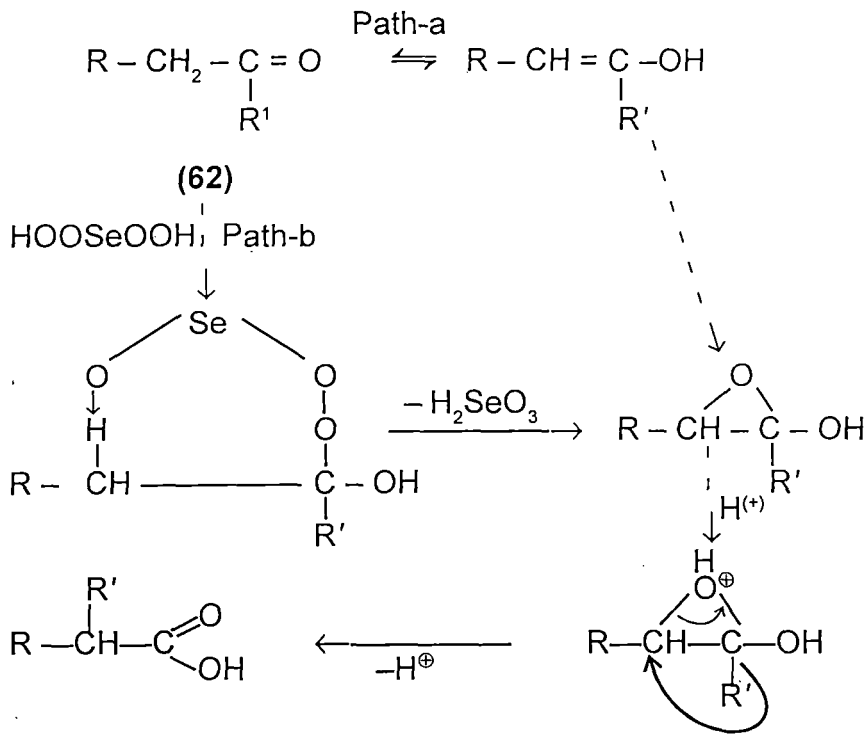
Sonoda et. al.[42] selected acetone, methyl ethyl ketone, methyl n-propyl ketone and diethyl ketone as the starting materials. They[42] proposed that the main rearrangement observed was due to migration of the alkyl-group having a small number of carbon-atoms to the α-carbon-atom of the larger alkyl-group. The migration of the alkyl-groups with a larger number of carbon-atoms to the smaller one also occurred in some degree. These workers shared the views of Hughes and Martin[43] who suggested the formation of peroxy selenious acid (63) from selenium dioxide in presence of hydrogen-peroxide.

$$SeO_2 + H_2O_2 \rightleftharpoons HOOSeO_2H$$

(63)

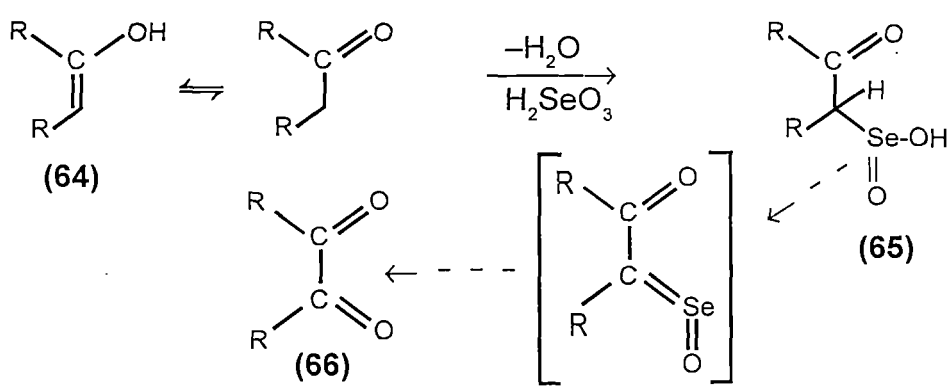
The mechanism of the reaction is shown in Scheme VIII.

SCHEME - VIII

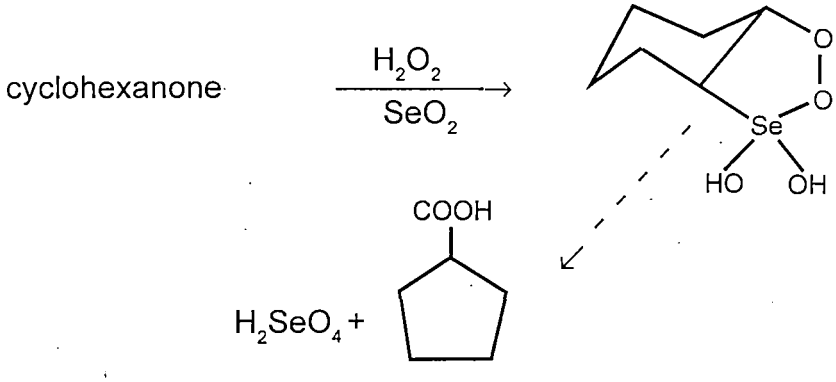


Sharpless et. al.[44] put forward the selenium dioxide oxidation of ketones and aldehydes to α-diketone and glycols involved an organo-selenium species. They proposed that the key intermediate in this sequence was the β-keto seleninic acid **(65)** formed by the electrophilic attack of selenous acid on the enol **(64)** which after rearrangement[45] produced **(66)**. (Scheme IX). They[44] also proposed that this β-keto seleninic acid intermediate was responsible for the unusual oxidative rearrangement, observed during selenium dioxide oxidation of ketones in the presence of hydrogen-peroxide (Scheme-X).

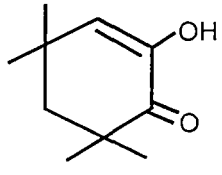
SCHEME - IX



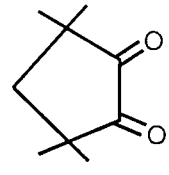
SCHEME - X



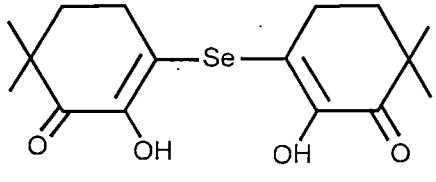
The isolation and structure determination of two new organo-selenium compounds **(69)** and **(70)** has been reported by T. Laitalainen and co-workers[46]. Diosphenol **(67)** on treatment with an equimolar amount of selenium dioxide in boiling dioxane for 1 hr. 30 min. gave a compound, which was assigned the structure **(69)**, bis (2-hydroxy-4, 4, 6, 6-tetramethyl-1-cyclohexene-3-one) selenide, on the basis of the analytical and spectroscopic evidence, whereas the same reaction with longer reaction times (4 to 6 hrs) gave **(70)** together with the diketone **(68)** and traces of **(69)**.



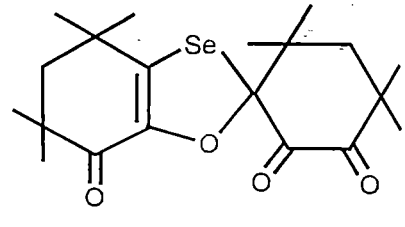
(67)



(68)



(69)



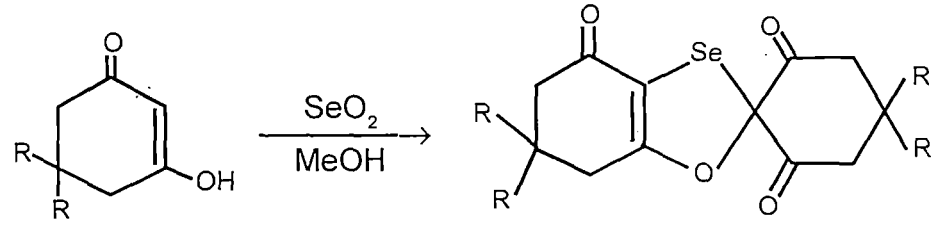
(70)

T. Laitalainen and T. Simonen have also reported the selenium dioxide oxidations of 1, 2 and 1, 3-diketones. They prepared 1, 3-oxaselenoles **(73)** and **(74)** by the reactions of cyclohexane 1,3-dione derivatives **(71)** and **(72)**

with selenium-dioxide. The reaction of the trione **(75)** with 0.5 mol. equivalent of selenium-dioxide in methanol obtained a new member of this series to which the structure **(76)** was assigned (SCHEME-XI) when the same reaction was carried out in boiling acetic-acid with 2.5 mol. equivalent of selenium-dioxide, 3,3,5,5-tetramethyl cyclopentane-1,2,4-trione was formed along with **(76)**. They[47] also isolated the bis-selenide **(78)** and the 1,3-oxaselenole **(79)** along with the ring contraction products **(80)** and **(81)** (SCHEME-XII) by oxidising the diketone **(77)** with an equimolecular-amount of selenium dioxide in 1, 4-dioxan, conducted in methanol with 0.5mol equivalent of selenium dioxide, the reaction yielded **(78); (79); (80); (81)** and **(82)**.

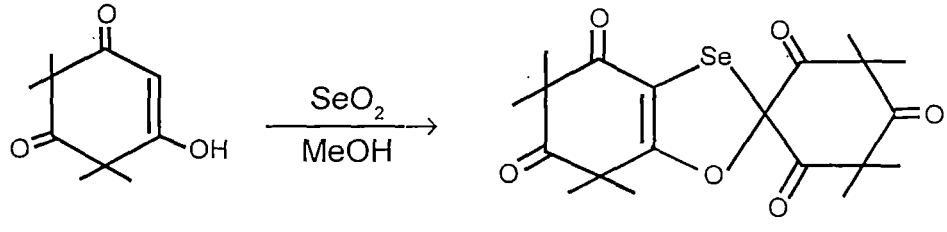
T. Laitalainen and T. Simonen[47] also carried out the oxidation of 3,5,5-trimethyl cyclohexane-1, 2-dione **(83)** in dioxan and reported the formation of bridge-selenide **(84)**[48] together with the elimination product **(85)**. They suggested the mechanism as shown in SCHEME-XIII with a probable intermediate **(19)**. The intervention of the intermediate **(88)** was further supported by metaperiodate oxidation of **(90)** to **(74)**.

SCHEME - XI



(71) : R=H
(72) : R=Me

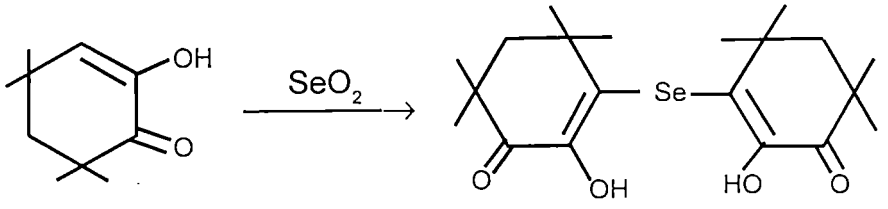
(73) : R=H
(74) : R=Me



(75)

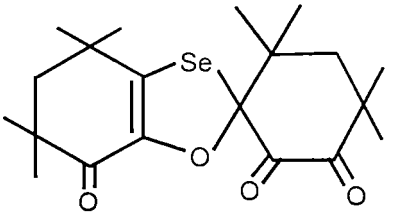
(76)

SCHEME - XII



(77) (78)

+



(79)

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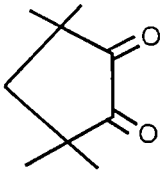

(80)

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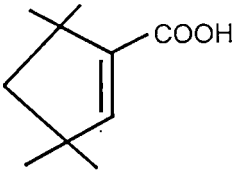

(81)

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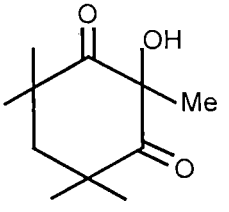
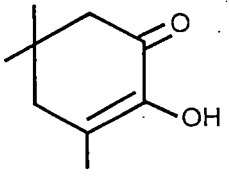
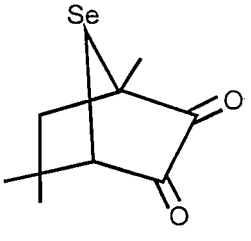


(82)



SeO_2



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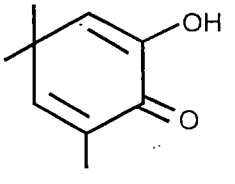
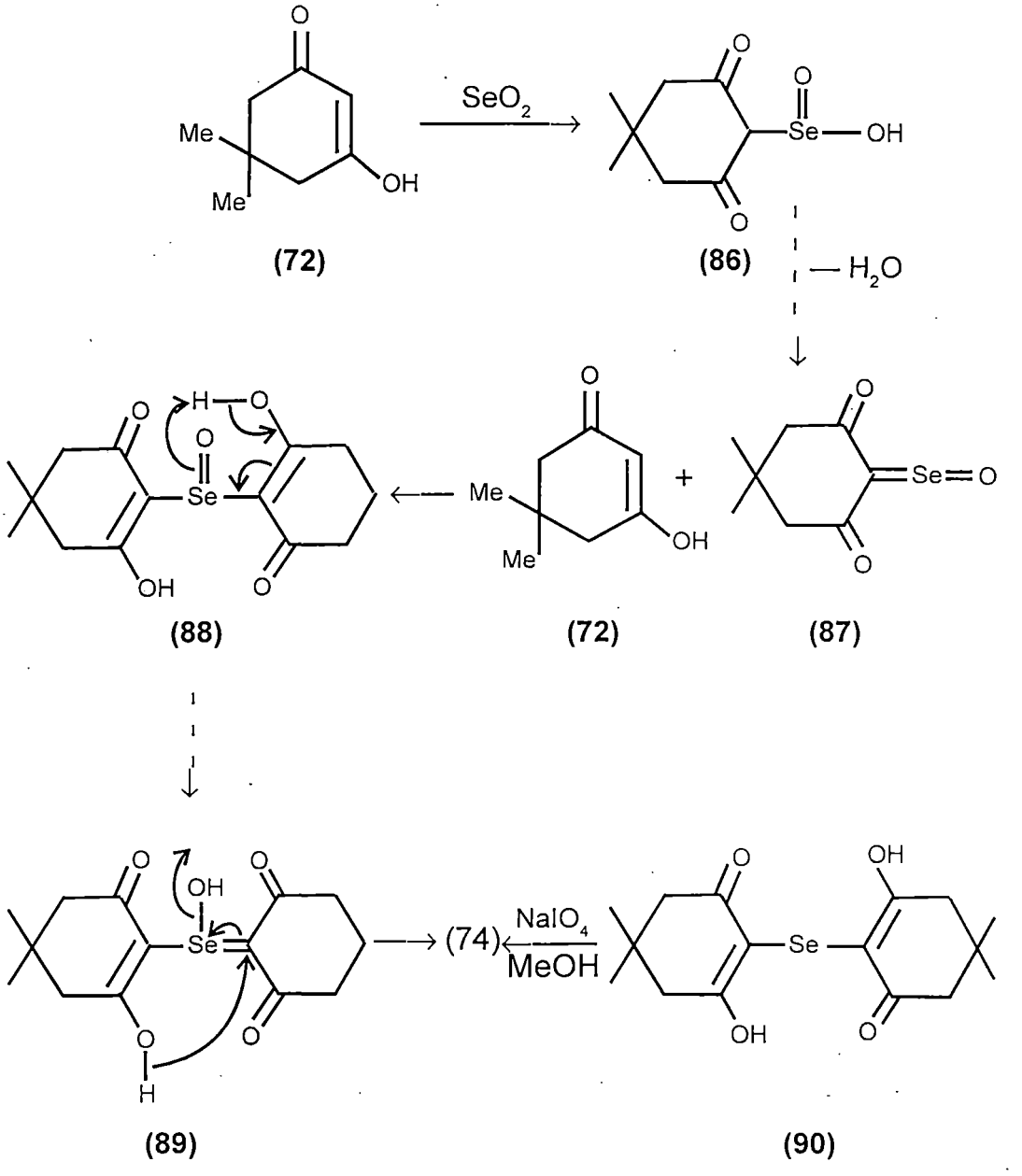


(83) (84) (85)

SCHEME - XIII

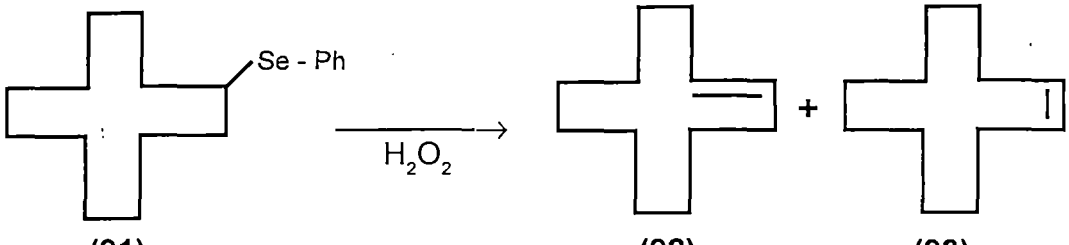


Uemura et. al.[49]. studied the treatment of secondary-alkyl phenyl selenides with various oxidants i.e. (H_2O_2; m-chloroperbenzoic acid, $NaIO_4$) producing the corresponding trans-alkene highly selective irrespective of the amount of oxidant.

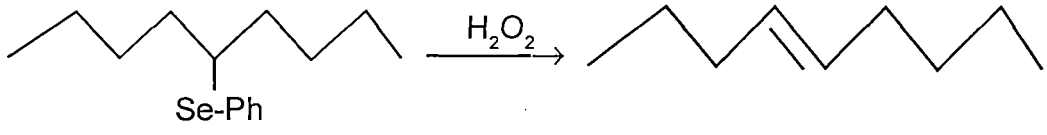
Uemura et. al.[49] re-examined the experiment conducted by Sharpless et. al.[50] on the oxidation of **(91)** with hydrogen-peroxide (70%) and isolated

(92) as main product together with a small amount of (93) in a sharp contrast to their[49] result of a quantitative yield of a 1:1 mixture of (92) and (93).

The oxidation of 5-nonyl phenyl selenide (94) was carried out with hydrogen-peroxide when the corresponding trans-alkene (trans-non-4-ene) was isolated (95).

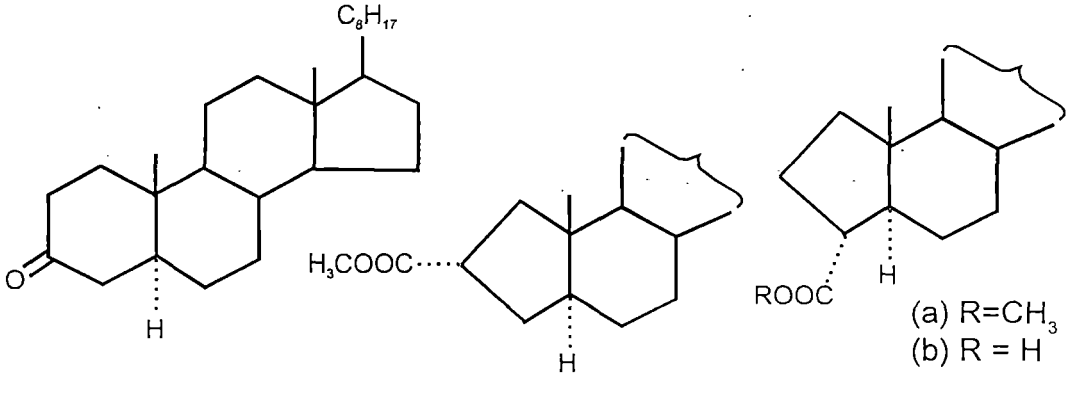


(91) **(92)** **(93)**



(94) **(95)**

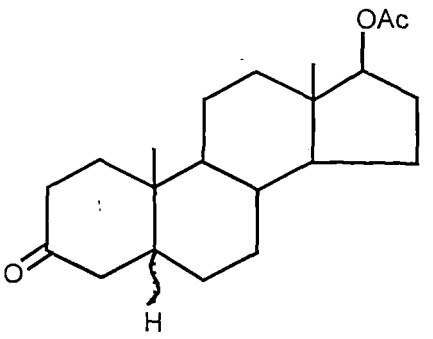
The above oxidation reaction was carried out with many keto-steroids. With 5α -cholestan-3-one **(96)** a mixture of acids was obtained[51]. The acids so obtained after esterification were separated and characterised as **(97)** and **(98)**. The yields were 25% and 19.5% respectively.



(96) **(97)** **(98)**

The reaction for steroidal 3-ketones of 5α-and 5β-series was studied by Caspi et. al[52] and found that the major reaction was not ring contraction but Baeyer. Villiger Oxidation.

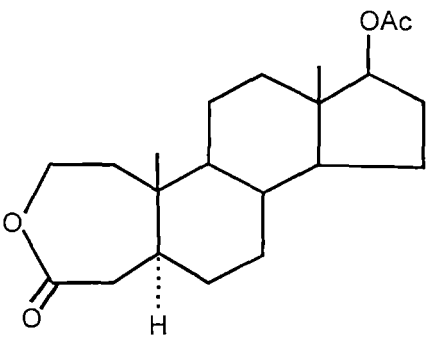
The compound with A/B trans juncture, 17 β-acetoxy-5α-androstran-3-one, **(99a)**, gave a lactone **(100)** and carboxylic acids, **(101)** and **(102)**. The oxidation of 17β-acetoxy-5β-androstran-3-one (99b) gave the lactone (103) as the single product.



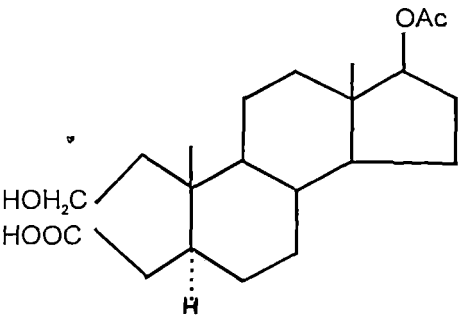
(99)

a = 5α–H

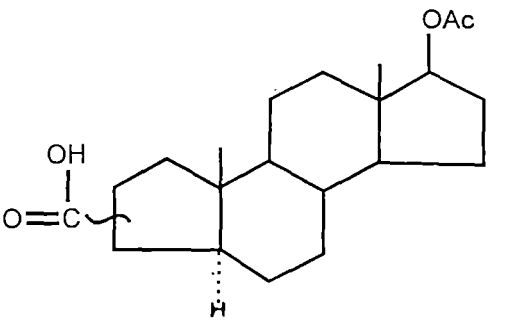
b = 5β–H



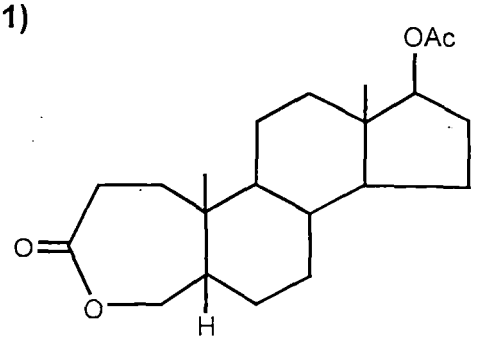
(100)



(101)



(102)

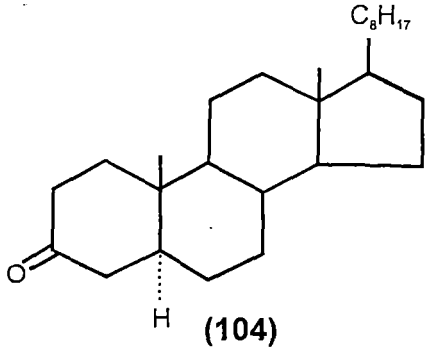


(103)

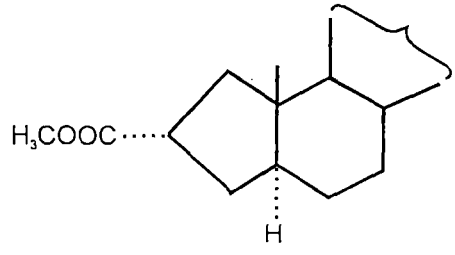
Hara et. al.[53] carried out the oxidation of 5α-and 5β-3 ketones in perbenzoic acid which yielded a mixture of lactones with an oxygen-atom inserted in either side of the 3-oxo group. With the commonly used peracids

it was seen that the reactions proceeds in a rather indiscriminate way.[54] Capsi et. al.[52] used neutral condition and concluded that the direction of attack was more substrate dependent and hence led to the formation of single compound. For example, for A/B trans-junction the 2, 3-bond and for A/B cis-junction the 3, 4-bonds are cleaved. Capsi et. al.[52] further observed that no directional influence of ring A/B junction on the course of the reaction occurs. However, the similar reaction on 17β-acetoxy-5-α-chlolestan-3-one **(61)**, **(62)** gave products which were different from those previously published.

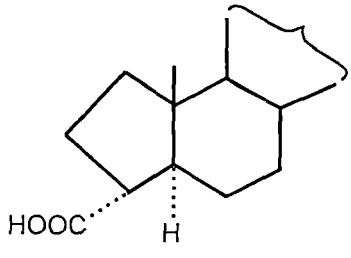
Jerussi et. al.[55] studied the reaction of **(104)**, with selenic acid and 30% H_2O_2 in tert-butyl alcohol and the reaction yielded a complex mixture of acids. Esterification of the crude product with diazomethane followed by chromatography and several times crystallisation yielded 2α-carbomethoxy-A-nor-5α-cholestane **(105)** and 2, 3-seco-5α-cholestane, 2, 3-dioate **(108a)** and **(107a)**, compound **(106)** was, however, not found.



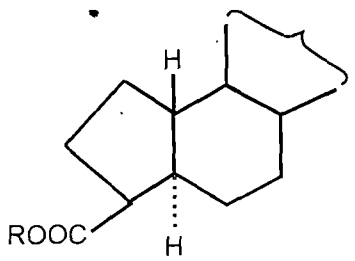
(104)



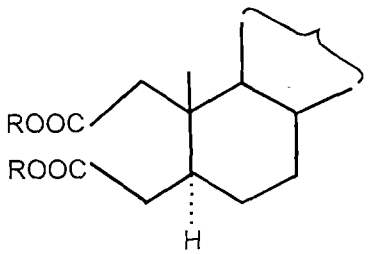
(105)



(106)



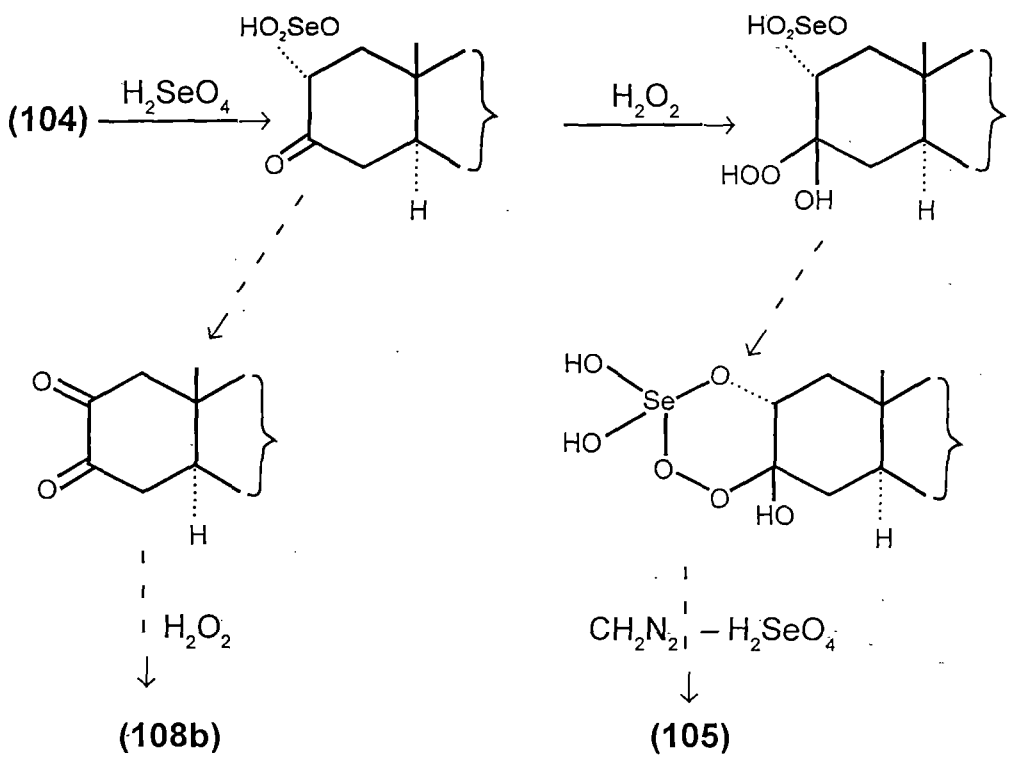
(107a) R = CH_3
(107b) R = H



(108a) R = CH_3
(108b) R = H

The mechanism given by Jerussi et. al.[55] is shown in Scheme XIV.

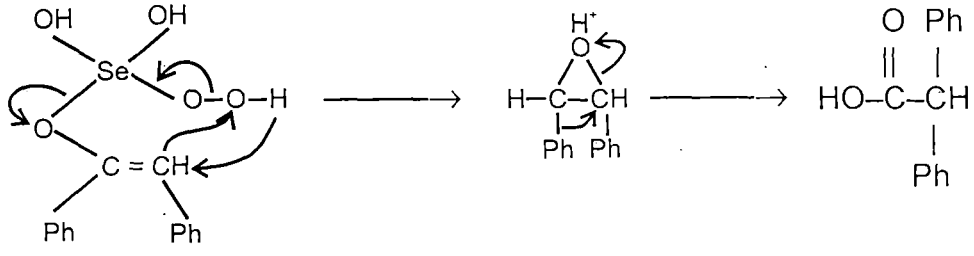
SCHEME - XIV



(108b) **(105)**

The mechanism given by Sonoda and Tsutsumi[56] for the rearrangement of desoxybenzoin in which a peroxy-selenious enol ester **(109)** was postulated as an intermediate. This then undergoes intramolecular epoxidation to give the enol epoxide **(110)** which rearranges to give diphenyl acetic acid **(111)**. Opening of the epoxide **(110)** in the given mechanism appears unlikely in

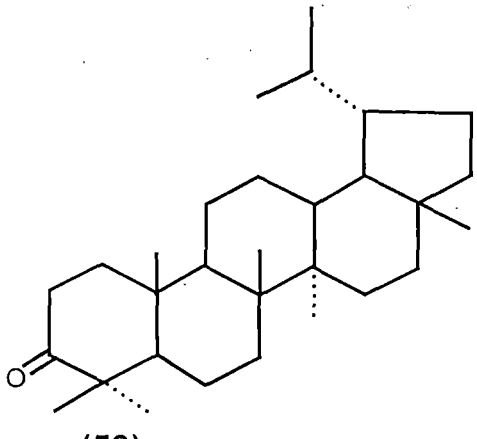
view of the course of the epoxide reactions in the acidic solution.[57]



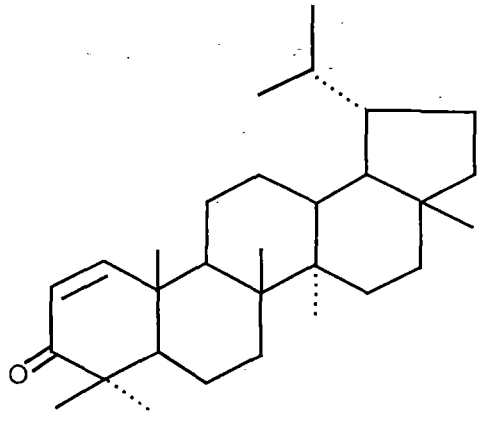
(109) **(110)** **(111)**

The oxidative rearrangements of ketones using H_2O_2 and selenic acid or SeO_2 have involved enolised ketone in almost all the examples. Non-enolisable ketones, even those having α-hydrogen atom fail to give the reaction.[58] Hence, it is pausible to assume that with steroid ketones also enolisation or enol ester formation is an essential step. An enol selenite ester, which rearranges to an α-keto selenium ester, has been proposed by Corey and Schaefer[27] as an intermediate in the selenious acid oxidation of desoxy benzoin.

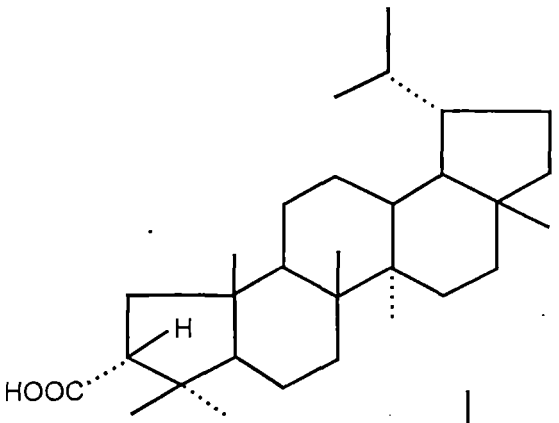
Pradhan et. al.[59] studied the selenium dioxide catalysed reaction of hydrogen peroxide on pentacyclic triterpene-3-ketone. They observed that lupanone **(59)** on oxidation with molar proportion of H_2O_2 and catalytic amount of SeO_2 in tertiary butanol afforded lup-1-ene-3-one[60] **(112)**, 2α-carboxyl-A-nor-lupane[61] **(113)** and 2,3-seco-lupane dicarboxylic acid **(114)**; with excess of H_2o_2, lupanone **(59)** furnished 4, 23, 24-tri-nor-lupane-3→5 olide, a δ-lactone **(115)** together with **(114)**.[62]



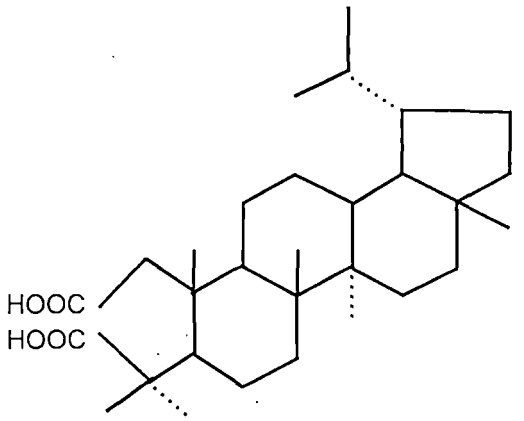
(59)



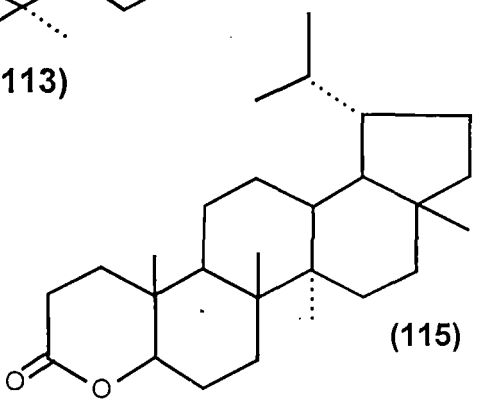
(112)



(113)



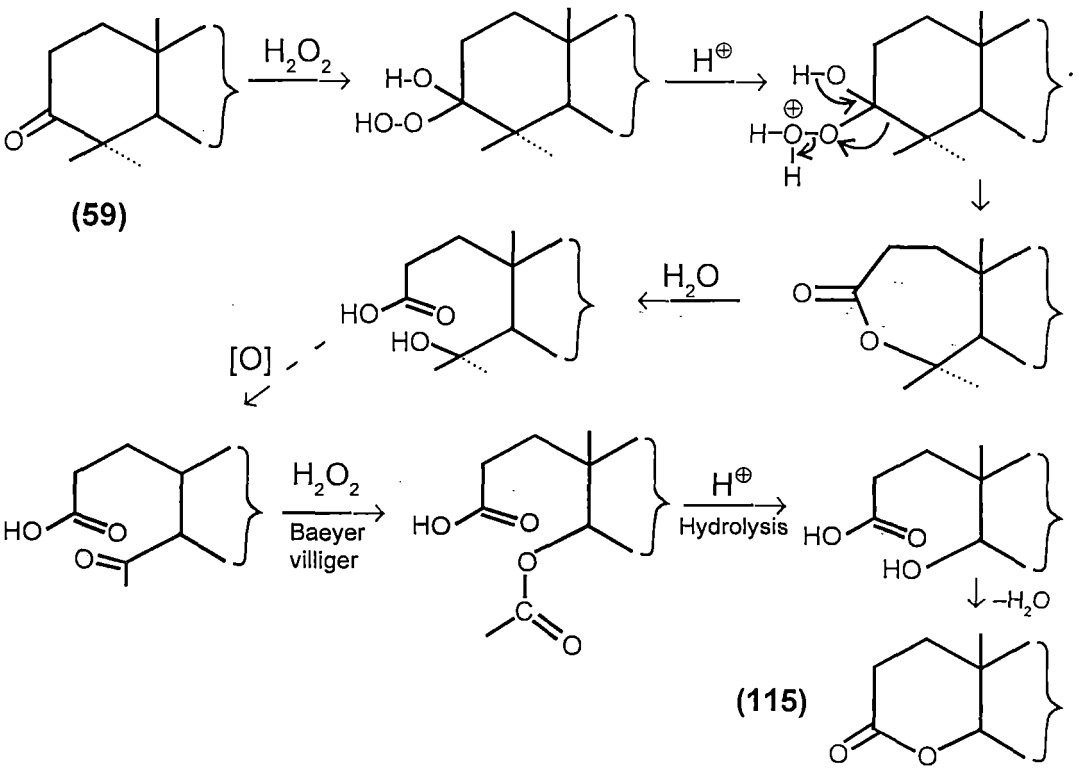
(114)



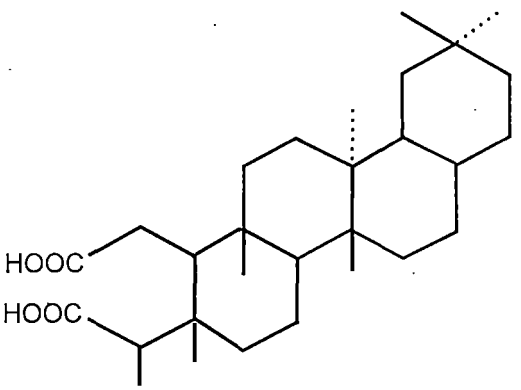
(115)

The mechanism for the formation of δ-lactone **(115)** is shown in **Scheme XV**.

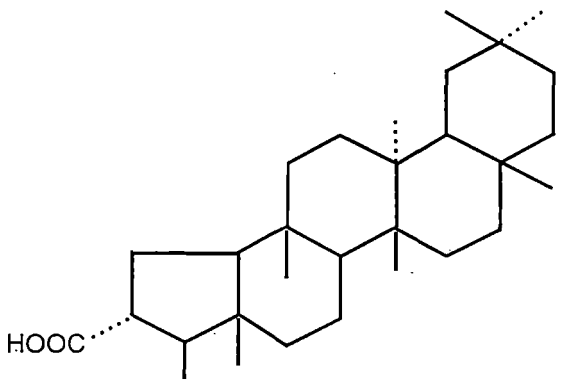
SCHEME XV



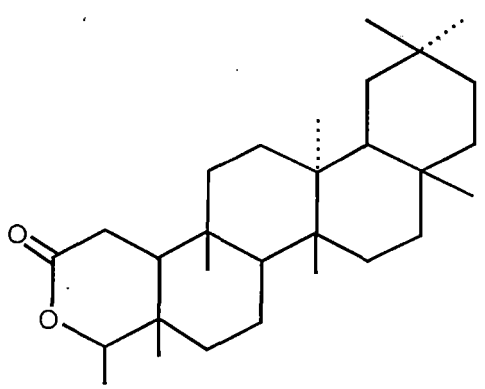
Pradhan et. al.[63] studied similar reaction of hydrogen peroxide-selenium dioxide in t-butanol on friedelin **(47)** and reported the isolation of 2,3-seco-friedelinic acid **(116)**; 2α-carboxy-A-nor-friedelin **(117)** and a δ-lactone **(118)**.



(116)



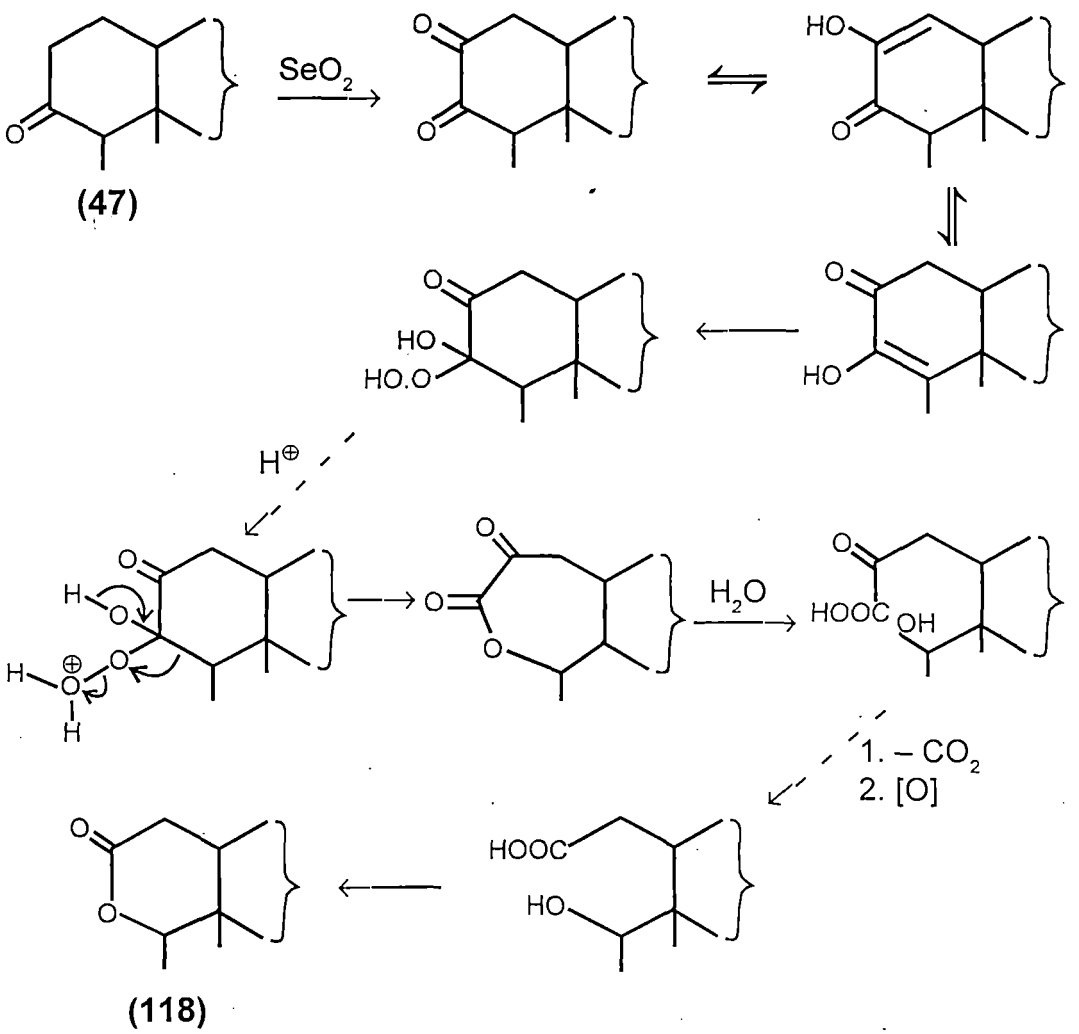
(117)



(118)

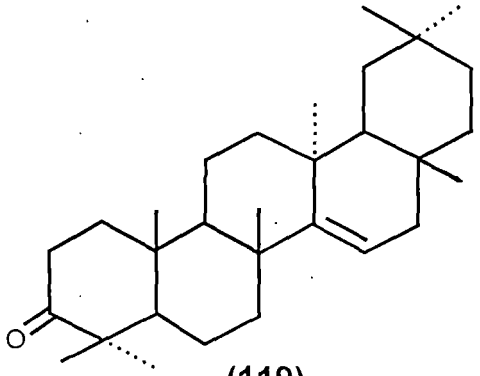
The mechanism for the formation of δ-lactone **(118)** from friedelin is shown in **Scheme XVI.**

SCHEME XVI

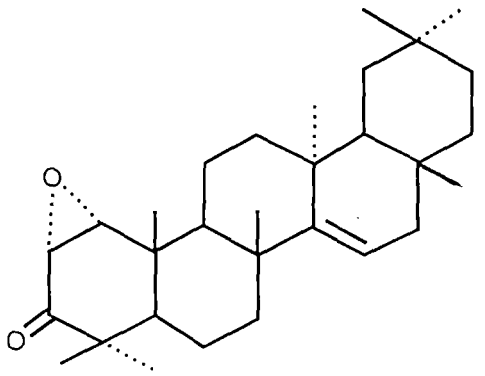


Pradhan et. al.[64] further studied the similar reaction on taraxerone **(119)** which is a 3-keto triterpenoid having a trisubstituted double bond. They observed that taraxerone on oxidation with H_2O_2 in presence of SeO_2 in t-butanol afforded 1α, 2α-epoxide **(120)**; 4, 23, 24-tri-nor-taraxerenes-3 → 5-olide, a δ-lactone **(121)** and taraxerene-ε-lactone **(122)** from neutral part and 2α-carboxy-A-nor-taraxerene **(123)** along with taraxerene-3, 4-seco-dicarboxylic acid **(124)** from the acid part. In the formation of the products

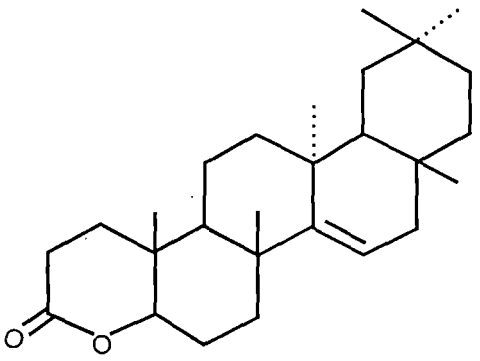
(120); (121), (122), (123) and **(124)** by the SeO_2 oxidation of taraxerone (119) no migration of 14-15 double bond took place. They[64] concluded from previous studies and present observations that the δ-lactones were formed irrespective of the presence of methyl group at C-4 position. The isolation of ε-lactone **(122)** supported the mechanism of the formation of δ-lactone via the ε-lactone. They[64] also reported that the formation of the epoxide **(120)** is via the unsaturated ketone.



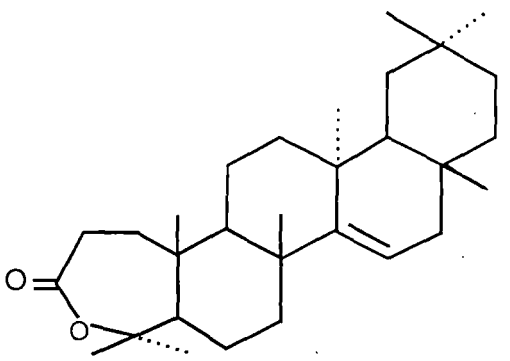
(119)



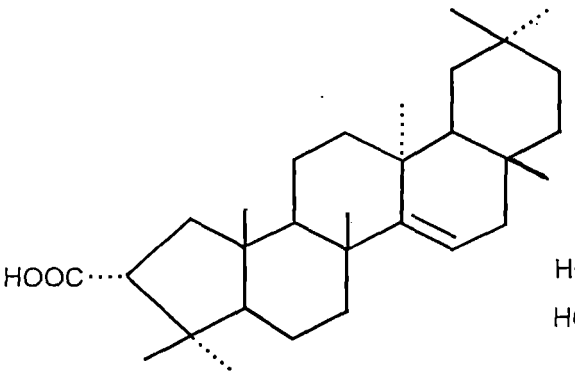
(120)



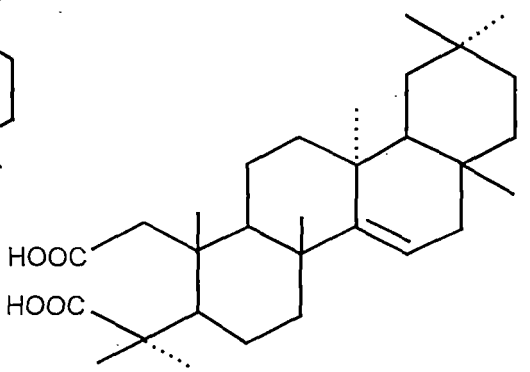
(121)



(122)



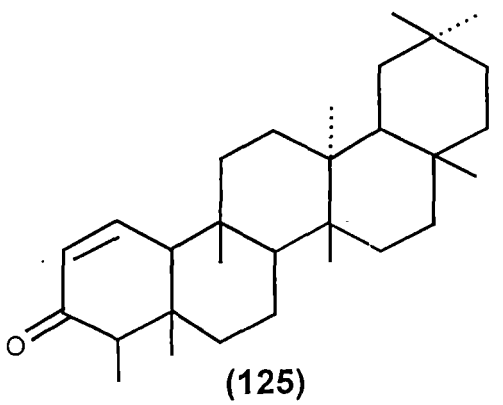
(123)



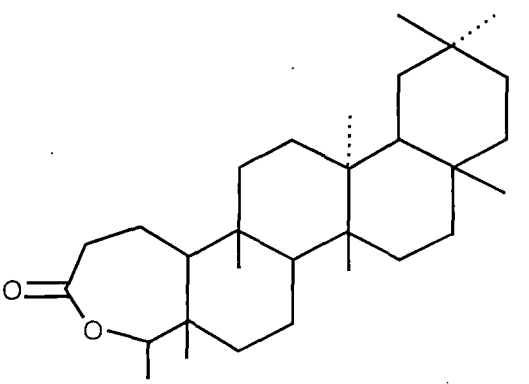
(124)

From the work of Pradhan et. al.[64] it was evident that the 3-keto triterpenoid can be transformed to tris-nor-triterpenoid lactone in a single pot reaction along with other products.

The oxidation of friedelin **(47)** with H_2O_2 in presence of SeO_2 in t-butanol was reinvestigated by Anjaneyulu et. al.[65] and reported the formation of friedel-1-ene-3-one **(125)** and friedelolactone **(126)** along with **(116)** and **(117)** which was already reported by Pradhan et. al.[63]



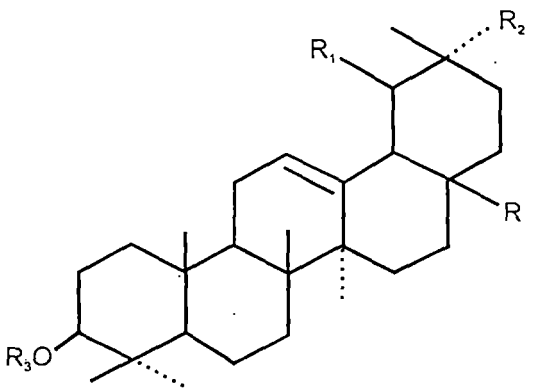
(125)

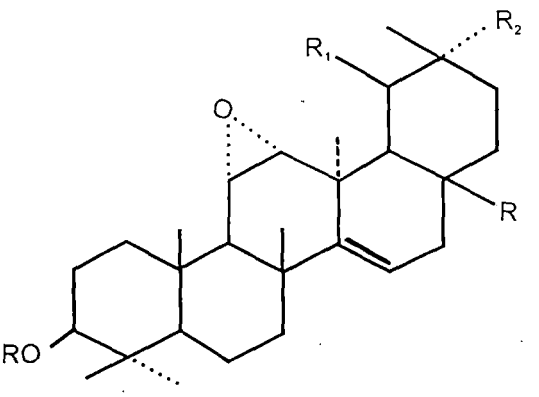


(126)

Pradhan et. al.[66] forwarded an interesting transformation of oleanane and Ursane skeletons to 11α, 12α-oxidotriterpenoids with H_2O_2 and SeO_2 in t-butanol. They reported the formation of **(128a)** and **(128b)** from β-amyrin acetate **(127a)** and **(129a)** and **(129b)** from β-amyrin acetate **(127b)** respectively.

The structure of these compounds were established on the basis of analytical and spectral data.





127a → $R_1 = R_3 = H$; $R = R_2 = Me$

127b → $R = R_1 = Me$; $R_2 = R_3 = H$

127c → $R_1 = R_3 = H$; $R_2 = Me$; $R = COOH$

127d → $R_1 = R_3 = H$; $R = CH_2OH$; $R_2 = Me$

127e → $R_2 = R_3 = H$; $R_1 = Me$; $R = CH_2OH$

127f → $R_3 = Ac$; $R_1 = H$; $R_2 = Me$; $R = COOMe$

127g → $R_3 = Ac$; $R_2 = H$; $R_1 = Me$; $R = COOMe$

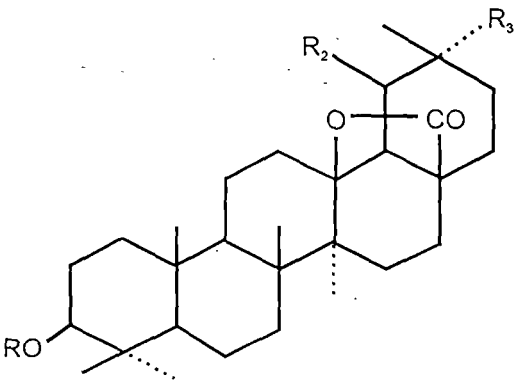
128a → $R = Ac$; $R_1 = H$; $R_2 = Me$

128b → $R = R_1 = H$; $R_2 = Me$

129a → $R = R_2 = H$; $R_1 = Me$

129b → $R = Ac$; $R_1 = Me$; $R_2 = H$

They[66] further carried out the similar reaction on acetyl oleanolic acid **(127e)** which gave a mixture of two compounds. The less polar one was isolated as 11α, 12α-epoxy oleanan 28→ 13 olide-3β-yl-acetate **(130a)** and more polar compound was identified as **(130b)**.



130a → $R = Ac$; $R_2 = H$; $R_3 = Me$

130b → $R = R_2 = R_3 = H$

130c → $R = R_2 = H$; $R_3 = Me$

130d → $R = R_3 = H$; $R_2 = Me$

130e → $R = Ac$; $R_2 = Me$; $R_3 = H$

The, same oxidation on the oleanane and ursane containing CH_2-OH or –COOMe group at the C–17 position afforded the corresponding epoxy-lactone[66] e.g. the formation of **(130c)** and **(130d)** from **(127d)** and **(127e)** respectively; **(130c)** and **(130a)** from **(127f)** and **(130e)** and **(130d)** from **(127g)** respectively.

From the above findings they concluded that

(i) the reaction is analogous to photochemical oxidation[67] in the formation of 11, 12-epoxide of oleanene and ursene skeleton.

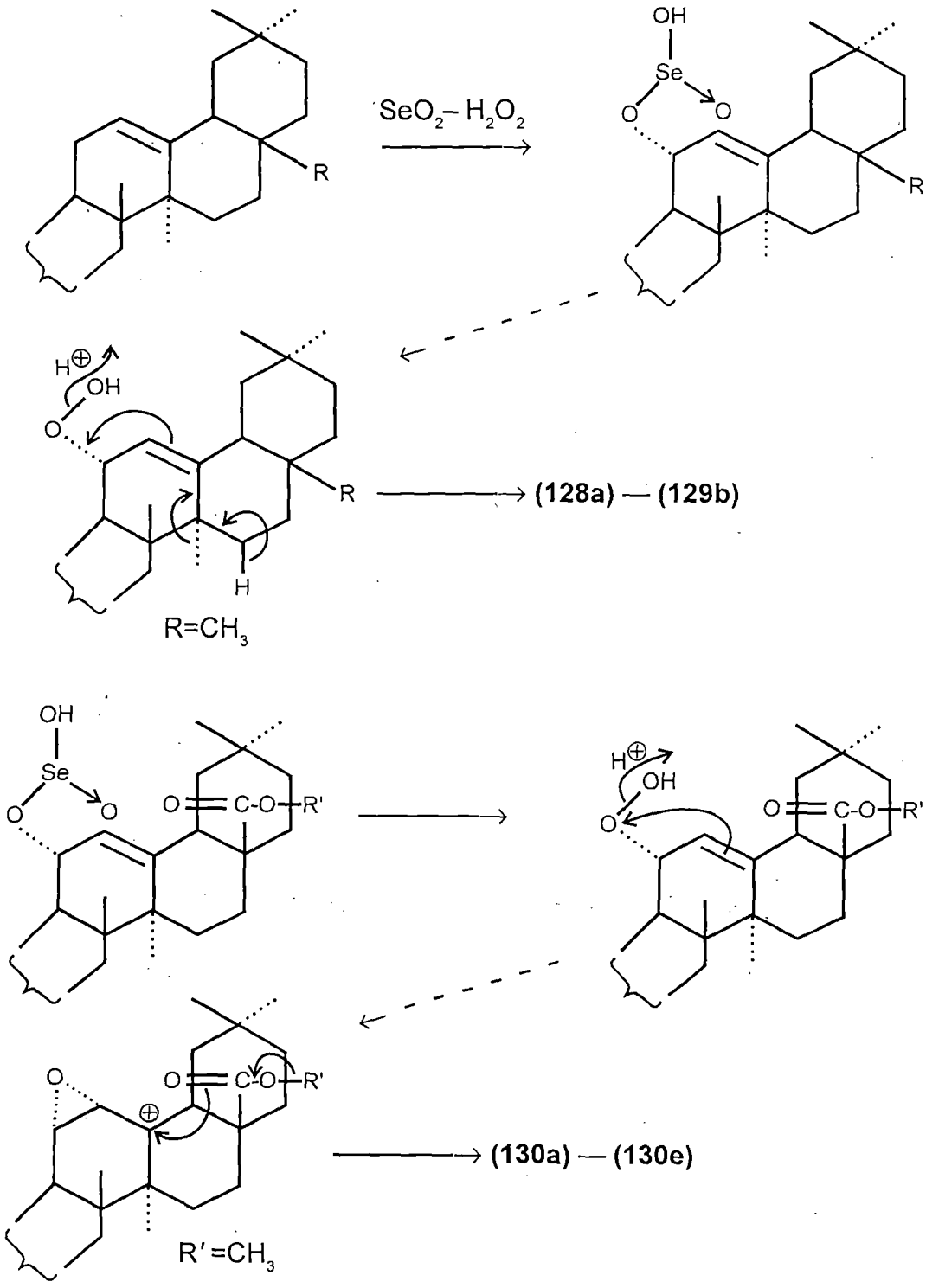
(ii) the C-17 methyl ester also generate lactone rings as well as the $-CH_2OH$ group.

(iii) the primary acetate at C-28 position remains intact whereas the secondary acetate at C-3 position undergoes hydrolysis during the reaction and

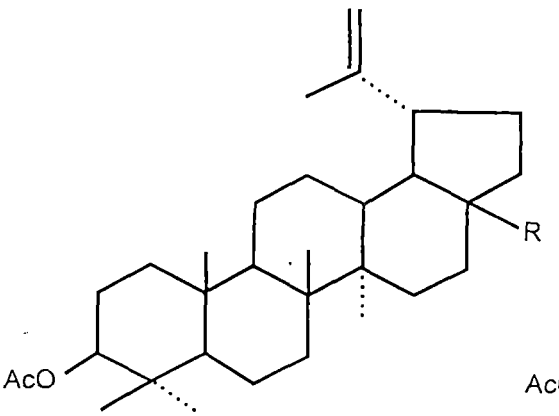
(iv) the acetate group allows smooth isomerization of the double bond from C-12(13) position.

The mechanism for the oxidation reaction as suggested by Pradhan et.al.[66] is shown in Scheme XVII.

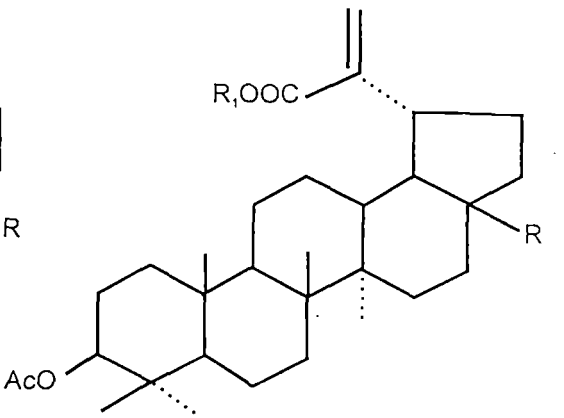
SCHEME XVII



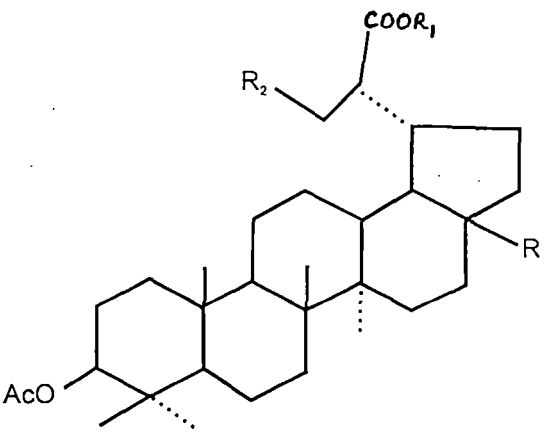
Pradhan et. al.[66] further reported the oxidative reaction of SeO_2 and H_2O_2 in t-butanol on triterpenoids containing isopropenyl side chain e.g. lupenyl acetate (131a) and methyl acetyl betulinate (131b). The products obtained were separated after esterification and acetylation. Three different oxidation products identified as 30-carbomethoxy-lupenyl acetate (132a); 30-carbomethoxy-lupan-3β 29-diyl acetate (132b) and 29-carbomethoxy-lupan-3 β-yl acetate (132c) were obtained from lupenyl acetate (131a) and two from compound (131b), designated as 28, 30-dicarbomethoxy lupenyl acetate (133a) and 28, 29-dicarbomethoxy-lupan-3β-yl acetate (133b).



131a → R = Me
131b → R = COOMe



132a → R = R_1= Me
133a → R = COOMe
R_1= Me



132b → R = R_1= Me
R_2= OAc
132c → R = R_1=Me
R_2= H