PART-III

OXIDATION OF PENTACYCLIC TRITERPENOID KETONE, LACTONE AND ESTER WITH META CHLOROPERBENZOIC ACID IN CHLOROFORM.

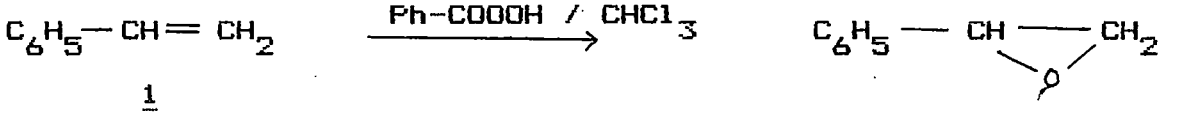
CHAPTER-I

A BRIEF REVIEW OF OXIDATIVE REACTIONS BY PER-ACIDS AND PEROXIDES.

Peracids have been used most extensively for the selective oxidations of carbon-carbon double bonds,conversion of ketones to esters and recently functionalisation of unactivated carbon atoms. Among the peracids, commonly used are performic acid, perchloric acid, per-acetic acid,hydrogen peroxide, perbenzoic acid, benzoyl peroxide,meta-chloro perbenzoic acid (mCPBA), trifluoro per acetic acid and mono perphthalic acid. A few of them are prepared by the actions of hydrogen peroxide on their corresponding acid and the resulting reaction mixture is used as peracid. A short discussion is given below:

OXIDATION OF CARBON-CARBON DOUBLE BOND.

Olefins[1,2]. 1, 2 are converted to epoxides by peracids in good yield.



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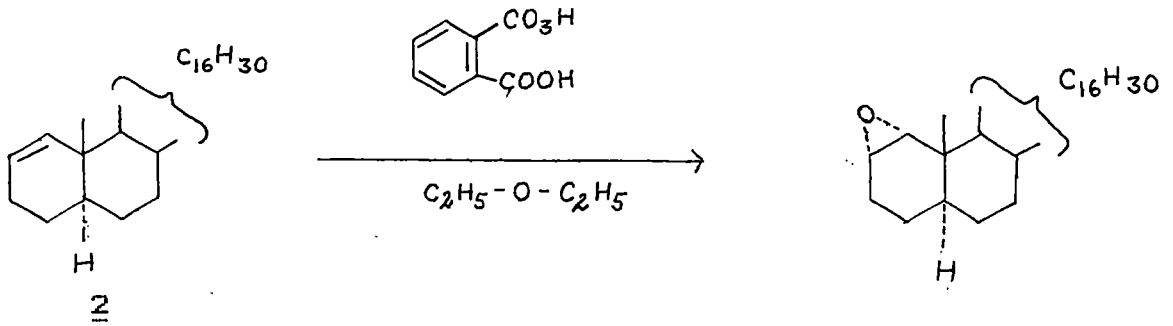
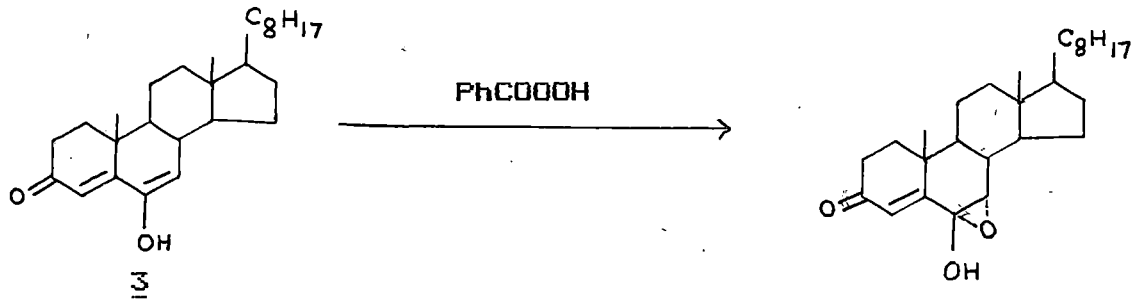


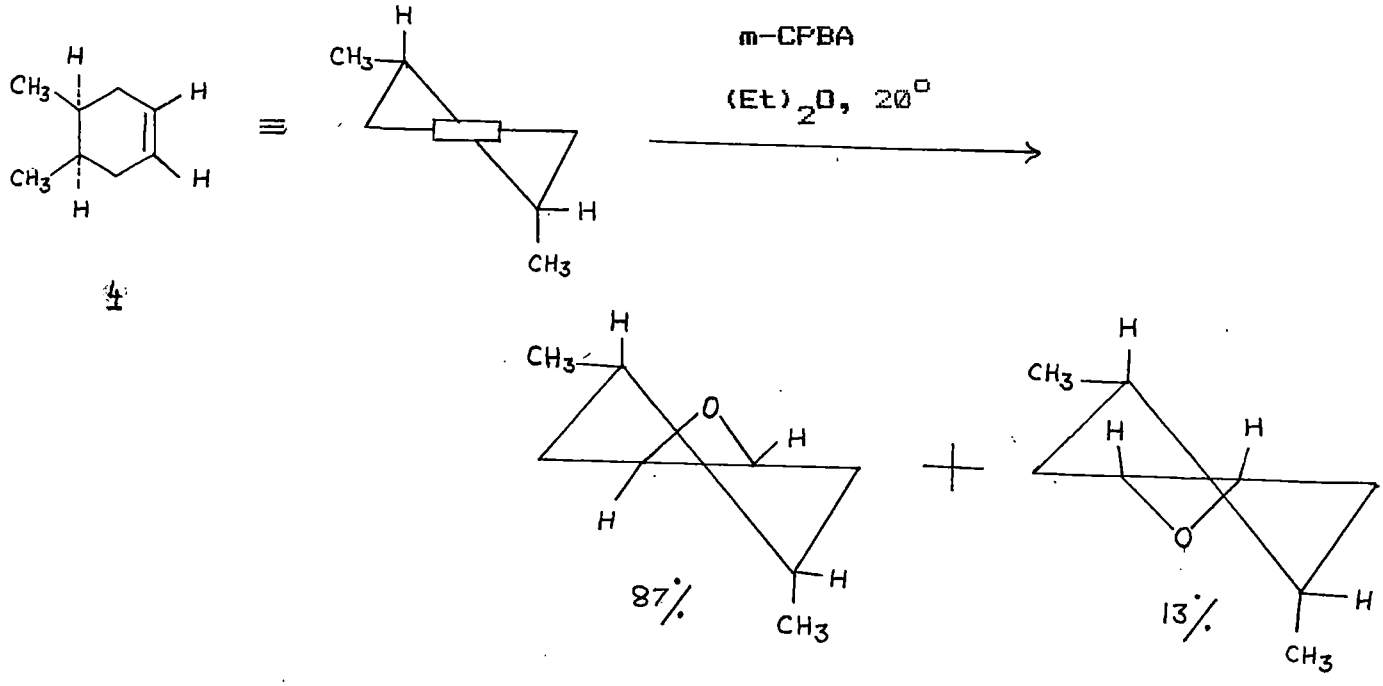
2

Carbon-Carbon double bond is selectively oxidised[3] (eg.3) in presence of hydroxyl or carbonyl functions.



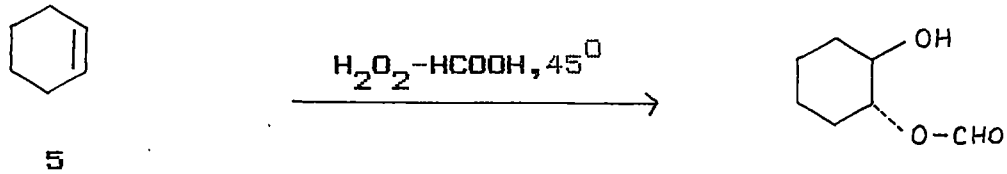
3

Rickborn et al[4] reported two different epoxide of compound 4 by action of mCPBA in diethyl ether



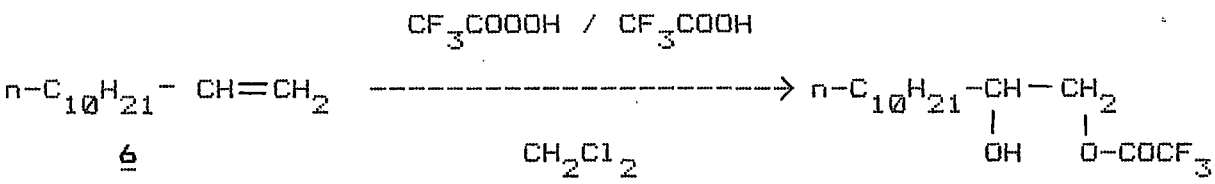
4

The use of perbenzoic acid or mCPBA in chloroform or methylene chloride has an advantage of isolating the epoxide formed while epoxidation reactions with olefin 5 run with peracids in presence of an excess of the corresponding carboxylic acid frequently yield the hydroxy esters[5] derived from the initially formed epoxide.

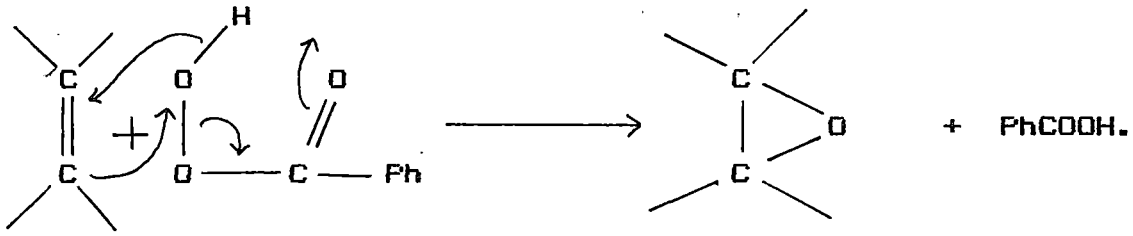


5

Reactions run either with monopermaleic acid in methylene chloride[6] or with mixtures of peroxytrifluoroacetic acid and the strongly acidic trifluoroacetic acid(P_{ka}-Ø.3) in methylene chloride[7] usually produce 1,2 diol derivatives as shown compound **6**



The epoxidation of olefins is believed to proceed by an electrophilic attack [8,9] as indicated in the accompanying equation:

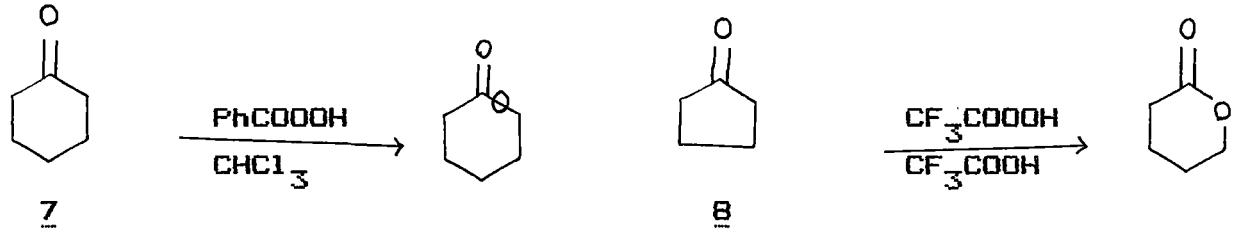


where the per acids usually attacks the olefin from the less hindered side to produce the less hindered epoxide as the major product.But the stereospecificity may be influenced by changes in the reaction solvent.[4]

OXIDATION OF CARBONYL COMPOUNDS.

The rate of oxidation of ketones with per acids is usually much slower than the epoxidation of olefins. But relatively long reaction times, strong acids as catalyst or very reactive per acids permit the conversion of carbonyl compounds, known as Baeyer-Villiger reactions[10,11,12] to corresponding esters in good yield.

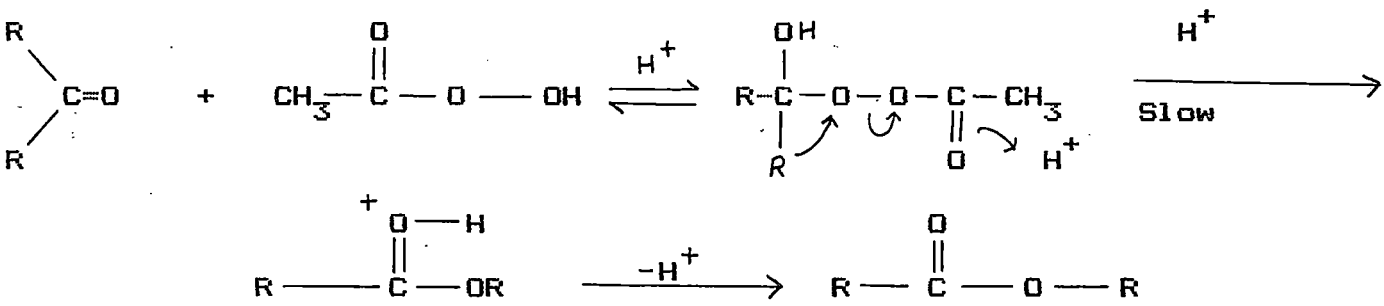
The oxidation of cyclic ketones 7 and 8, with per acids, serves as a useful route to lactones.[13,14]



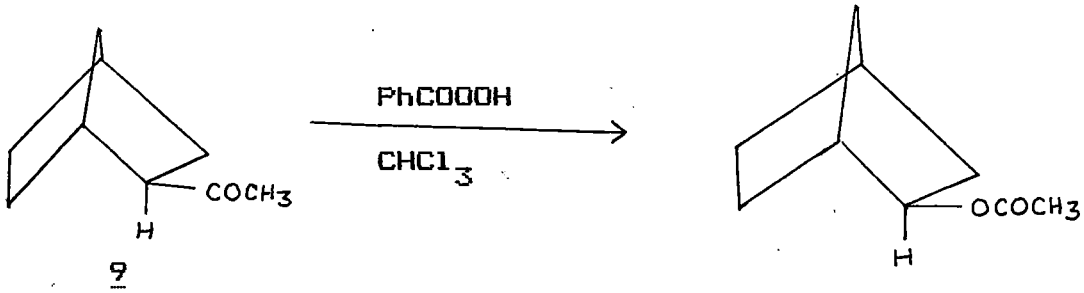
7 8

The conversion is catalysed by acids and the rate of oxidation is accelerated by electron donating groups in the ketone and electron withdrawing groups in the per acids.

After a variety of studies[12,13,15,16] of the Baeyer-Villiger reaction indicate that the mechanism is as follows:-



The reaction has been shown to occur with retention of configuration[17] as shown in the reaction of 9.



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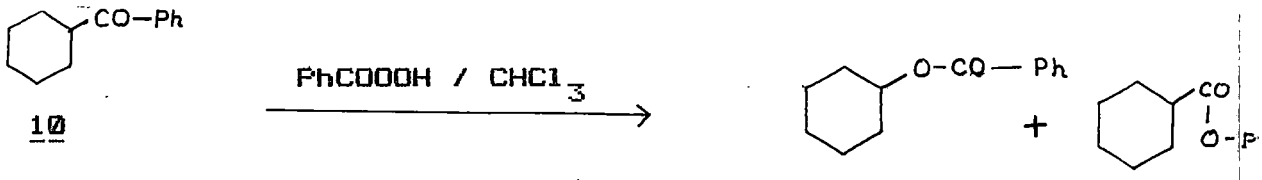
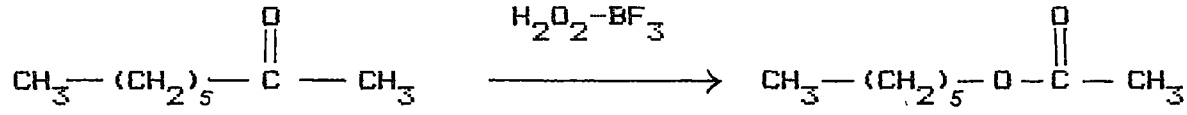
Oxidation of unsymmetrical ketone (eg. 10) can lead to two isomeric esters[16b]



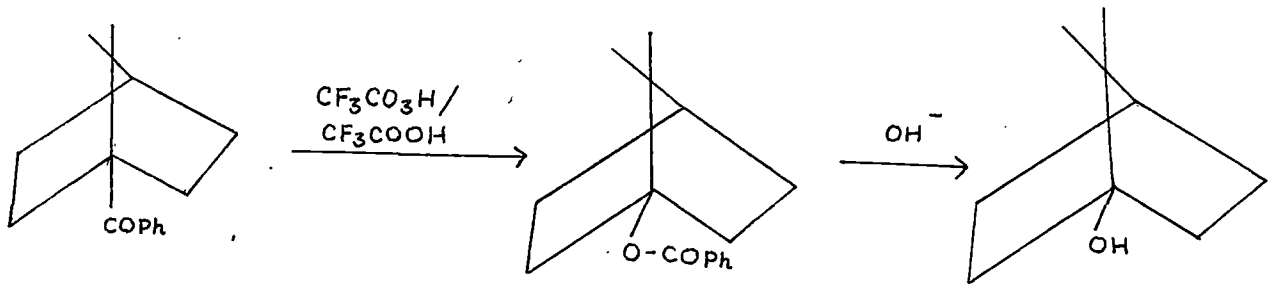
10

Mcclure et al[17e] reported B.V.oxidation by a complex of hydrogen peroxide-Boron trifluoride etherate complex.



From a series of study of various unsymmetrical ketones,[12,15,16] the migratory aptitude of various groups in the Baeyer-Villiger reaction has been found to be:-

t-alkyl > cyclohexyl ~ sec.alkyl ~ benzyl ~ phenyl > primary alkyl cyclo propyl > methyl. Even a bridgehead t-alkyl group (11) & (12) migrates readily,providing a useful synthetic route to bridgehead alcohols[15a,18]



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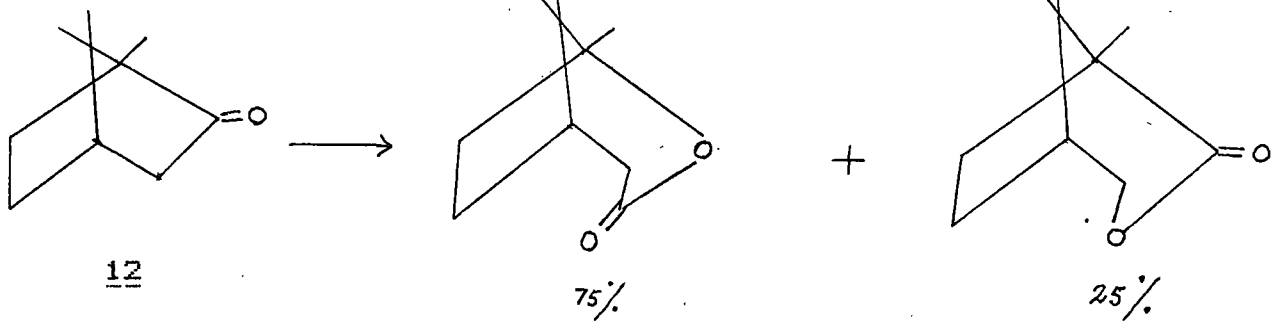


12

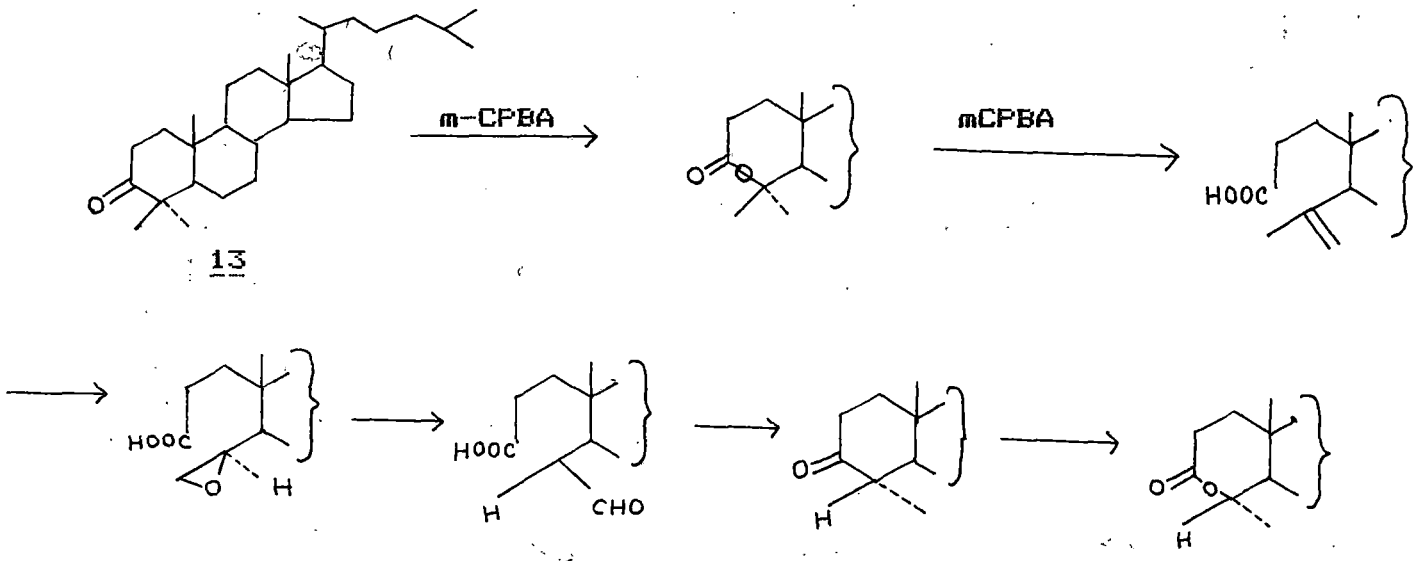
Fumio Toda et al[19] reported that some Baeyer-Villiger oxidations of ketones with mCPBA proceed much faster in the solid state than in solution.

Hara et al[20] had shown that perbenzoic acid oxidation of 5α and 5β 3-ketones yielded mixture of lactones with an oxygen atom inserted in either side of the 3-oxo group of triterpenoids with commonly used per

acids it would seen that the reaction proceeded in a rather indiscriminate manner[21].

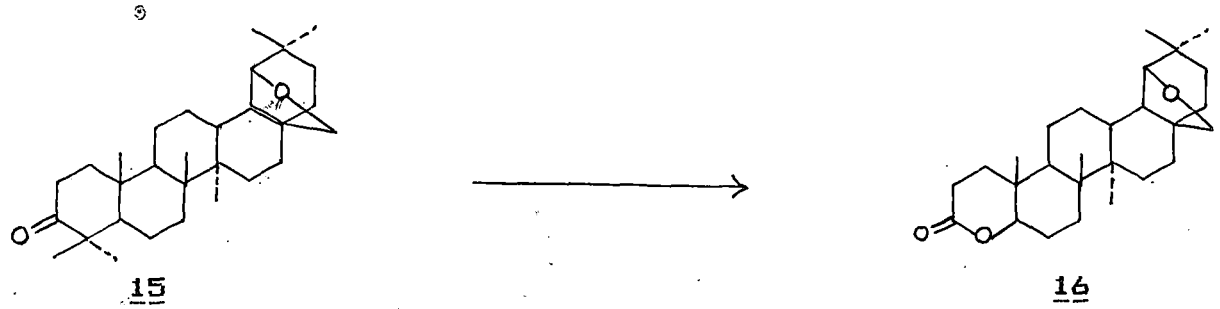
Whittam[22] found that 4,4-dimethyl cholestan 3-one **13** on treatment with mCPBA or perbenzoic acid in presence of mineral acid gave 4α methyl 4-oxa-A-homo-cholestan 3-one **14**. This apparently unique loss of a methyl group in a Baeyer-Villiger oxidation merited a careful investigation of the reaction. After careful investigation the mechanism was proposed as shown in the following scheme:-

SCHEME-I



13 **14**

Hase et al[23] reported a case of exhaustive Baeyer-Villiger oxidation of pentacyclic triterpenoid,allobetulone **15**, giving **16** in 50% yield on treatment with peracetic acid and boron trifluoride-etherate. Hase et al established that the reaction was general for condensed cyclic α,α-dimethyl substituted ketone.

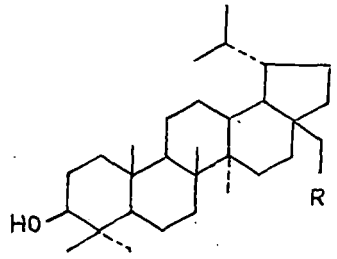


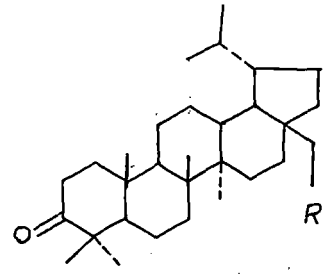
15 **16**

FUNCTIONALIZATION OF UNACTIVATED CARBON ATOM.:-

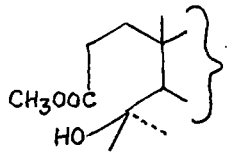
Motoo Tori et al[24] reported functionalization of unactivated carbon atoms by action of mCPBA on a number of triterpene derivatives in chloroform under reflux. They reported Lupan 3β,28 diol **17** on refluxing with mCPBA in chloroform for 6 hours afforded three compounds which were identified as 28 hydroxy lupan 3-one,**18**, methyl 4,28 dihydroxy 3,4 seco lupan 3-oate,**19** and methyl 28 hydroxy 3,4 seco lup 4(23)-en-3-oate,**20** from spectral analysis, while lupan 3β-ol, **21** on similar treatment afforded lupan 3-one,**22** and 3,4 seco lupan 4→3 olide **23**.

17, R = -OH
21, R = -H





18, R = -OH
22, R = -H



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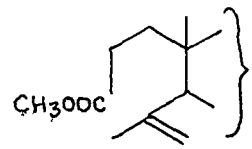

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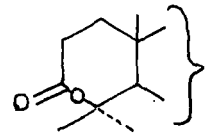


23 (4.3%)

Lupan 3β,28 diyl diacetate **24** subjected to same reaction[24] gave only one product,19β-hydroxy lupane 3β,28 diyl diacetate **25**.

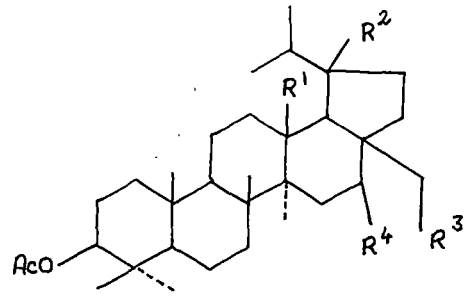
24, R_1 = R_2 = R_4 = H, R_3 = OAc

25, R_1 = R_4 = H, R_2 = OH, R_3 = OAc

26 R_1 = R_2 = R_3 = R_4 = H

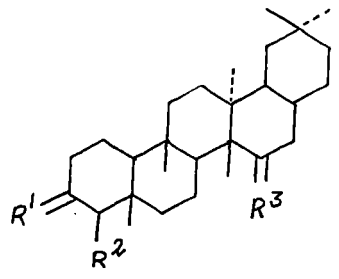
27, R_1 = OH, R_2 = R_3 = R_4 = H

28, R_1 = R_2 = R_3 = H, R_4 = OH



Lupan 3β-yl acetate, **26** on treatment[24] *with* mCPBA gave two compounds, 13β hydroxy 3β-yl acetate,**27** and 16β hydroxy 3β-yl acetate **28**.

Friedelan 3β-ol 29 on same reaction with mCPBA yielded friedelin 30, 4-epi friedelin 31 and 3,4 seco friedelin 3→4 olide 32. while-friedelin 3β-yl acetate 33 furnished only one product as 15-oxo friedelan 3β-yl acetate 34.



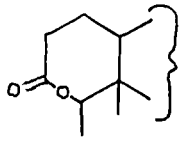
29, R_1= ; R_2= β-Me ; R_3= H_2

30, R_1= O ; R_2= β-Me ; R_3= H_2

31, R_1= O ; R_2= α-Me ; R_3= H_2

33, R_1= ; R_2= β-Me ; R_3= H_2

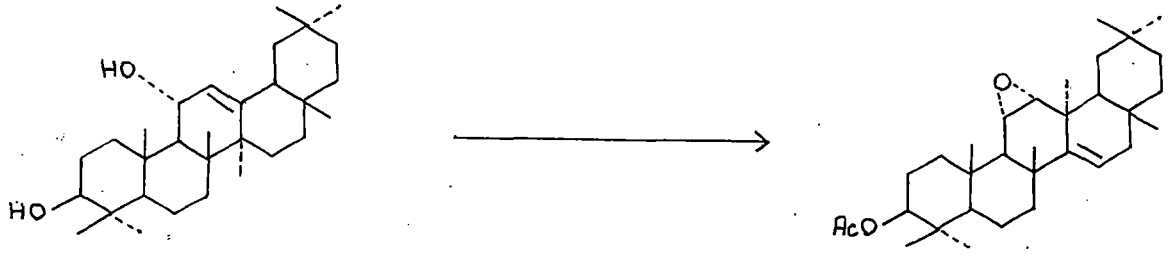
34, R_1= ; R_2= β-Me ; R_3= O



32, R_1= O ; R_2= β-Me ; R_3= H

OXIDATIVE REARRANGEMENTS

Corey et al[29] reported that 3β,11α-dihydroxy Δ^{12}-pentacyclic triterpenoid 35 on treatment in methylene chloride with a solution of H_2O_2 (30%) – p-toluenesulphonic acid in tertiary butanol, after acetylation, gave 11α,12α epoxide, 36 with a rearranged skeletal system (C_{14} C_{13} methyl migration and shift of the double bond). The free epoxy alcohol is similar to the product obtained from photoxidation of β-amyrin.

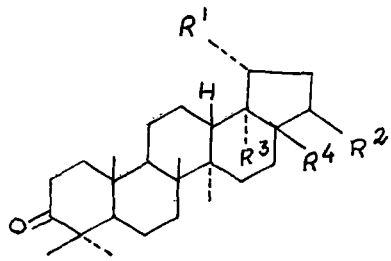


35 36

Pradhan et al[30] studied the action of mCPBA in presence of p-toluene-sulphonic acid on friedelin 30 as a member of 4-mono methyl 3-keto

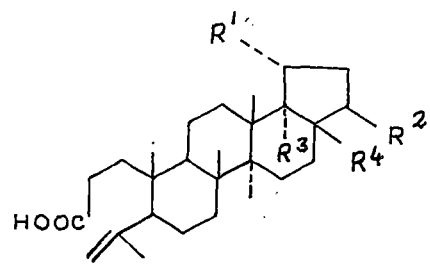
triterpenoids and lupanone 22 and moretanone 37 for 4,4 dimethyl 3-keto triterpenoids. They observed that 30 gave only a ε-lactone, 32 while 22 and 37 first furnished the corresponding ε-lactones,which being unstable due to the sterical strain from C-4 axial methyl group resulted the corresponding 3,4 seco acids 38 and 39 by opening of the ring system in situ under the influence of p-toluenesulphonic acid.

30



22, R_1= ⟨ ; R_2= H
R_3 = H ; R_4 = CH_3

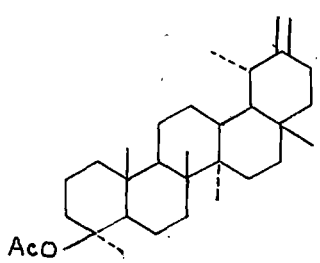
37, R_1= H ; R_2= ⟨
R_3 = CH_3 ; R_4 = H



38, R_1= ⟨ ; R_2= H
R_3 = H ; R_4 = CH_3

39, R_1= H ; R_2= ⟨
R_3 = CH_3 ; R_4 = H

Dutta et al[25] studied the action of mCPBA on taraxasteryl acetate 41 and reported three compounds formed as taraxa-20α,30α oxido-3β-yl acetate 42 and E-ring enlarged products 43 and 44.



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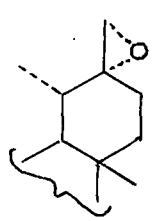

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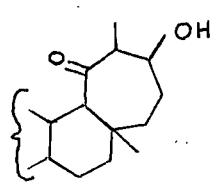

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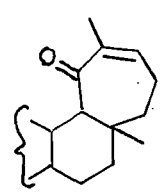
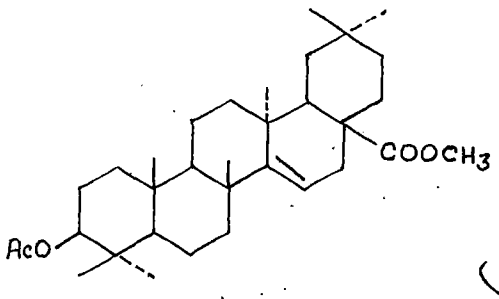


44,

They[26] extended the reaction on olean-14-en-28-carbomethoxy 3β-yl acetate 45 and reported the isolation of olean 14α,15α oxido 28 carbomethoxy 3β-yl acetate 46 along with two rearranged products as olean 12-en-28-carbomethoxy 15α-hydroxy 3β-yl acetate 47 and olean 12--en-28-carbomethoxy 15-oxo-3β-yl acetate 48.



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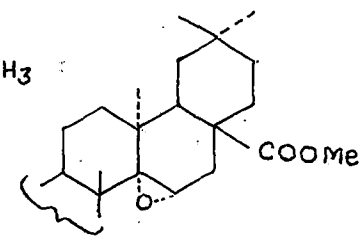

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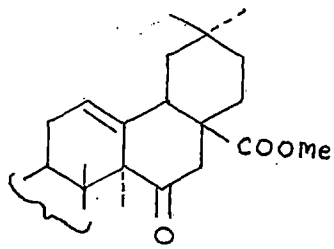

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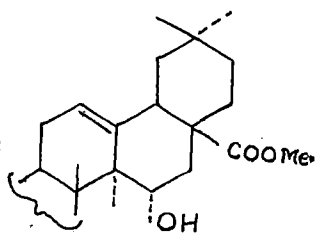
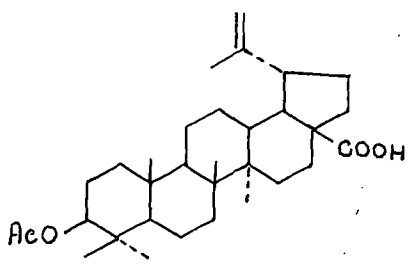


47,

Patra et al[27] studied the action of mCPBA on 3-acetylbetulinic acid 49 in dichloro methane and reported the isolation of three products as 3β-acetoxy lupan 28,29 di-oic acid 50, 3β-acetoxy 30-hydroxy lup-20 (29)-en 28-oic acid 51 and 3β-acetoxy 20-hydroxy lupan-29-al-28-oic acid 52.



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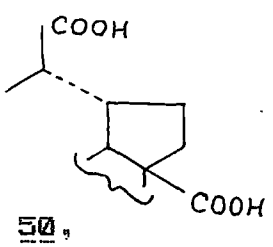

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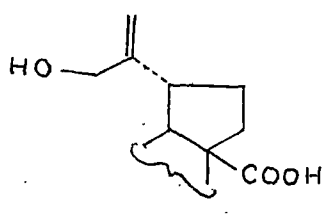

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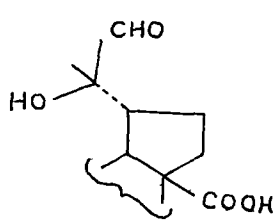

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They proposed the mechanism as shown below :-