S U M M A R Y

The work embodied in the present thesis has been divided into three parts:

A. The first part (Part I) consists of the autoxidation studies on β-amyrone and investigations on the stereochemistry of 2-acetoxy-3-keto-β-amyrin and 3-acetoxy-2-keto-β-amyrin.

B. The second part (Part II) describes the synthesis of isomeric 2,3-diols of isohopane (moretane) (Section B) and isomeric 2, 3-diols of methyl olean-12-en-28-oate. (Section C)

C. The last part (Part III) deals with allylic oxidation and bromination studies with NBS on taraxeryl acetate.

A. Part I:

Chapter II deals with the studies on the stereochemistry of the 2-acetoxy group in 2-acetoxy-3keto-β-amyrin D and 3-acetoxy group in 3-acetoxy-2-keto-β-amyrin G from NMR spectra, O.R.D. spectra and chemical evidences.

β-amyrone A on autoxidation gave the diosphenol B which on acetylation followed by hydrogenation gave 2-acetoxy-β-amyrone D, m.p. 158-60°. NMR spectrum of the compound indicated that it may equally explain both for the 2α-equatorial acetoxy group with the chair conformation of ring A and 2β-acetoxy group with the boat conformation of ring A. The ORD spectra of α-acetoxy ketones have been studied recently by Bull and Enslin and also

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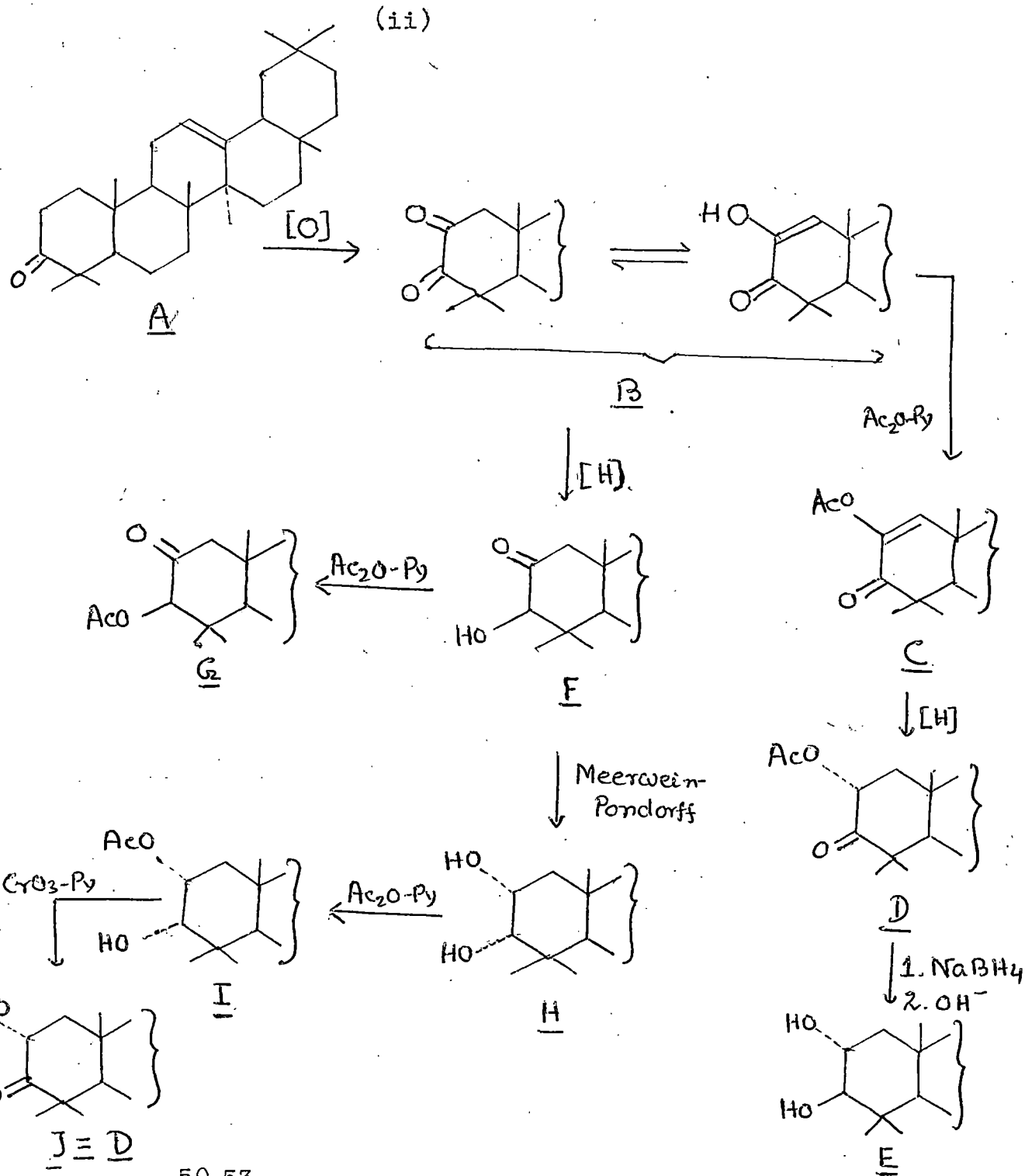


by Klyne et al[50,53]. From their studies it appears that in many cases (though not in all) the effect of an acetoxy to the carbonyl chromophore is anti-octant. The ORD studies revealed that in β-amyrone

(parent ketone) A, the conformation of ring A is a flattened chair (to relieve the diaxial interaction between the 10β-methyl and 4-β methyl groups) and this leads to a positive Cotton effect (Fig. 17). The same conformation is possible for the 2α-acetoxy derivative D but as a consequence of the flattening of ring A, the 2α(equatorial) acetoxy group does not lie in the nodal plane of the carbonyl group but protrudes into the back upper right octant. An alkyl group in that situation would make a negative contribution to the Cotton effect but the acetoxy group shows an '<u>anti-octant</u>' effect and makes a positive contribution. Therefore, as the ORD studies indicate (Fig. 18), if the compound D has the 2α-acetoxy configuration, we would expect it to have a more positive Cotton effect, than the parent ketone. The alternative 2β-acetoxy configuration with the boat conformation of ring A would lead to a small negative Cotton effect. In the ORD curve of the compound D the amplitude is greater than the amplitude in the corresponding parent ketone A. Thus NMR and ORD spectral evidences lead us to conclude that the 2-acetoxy group in D has the α-equatorial configuration with ring A in the chair conformation.

In order to afford further chemical evidences we have prepared Δ^{12}-oleanene-2α, 3β-diol, E m.p. 202-4°, $(\alpha)_D$ 60° from D by $NaBH_4$ reduction followed by hydrolysis. The latter has been found to be identical with an authentic sample of the 2α, 3β-diol[65], indicating α-equatorial orientation of the 2-acetoxy

group in the original compound D .

Further we have also prepared 2α, 3α-diol H m.p. 278-80°, $(\alpha)_D$ 71.28° from 2-keto β-amyrin F. The α, α-configuration is based on NMR spectral data. The monoacetate I, obtained by partial acetylation of H, on CrO_3-pyridine oxidation gave a crystalline solid J, m.p. 158-60°, $(\alpha)_D$ 108.5°, identical with 2α-acetoxy-β-amyrone D obtained by hydrogenation of the diosphenol acetate C. This experiment provided a further support for the assignment of 2α-acetoxy equatorial configuration to the 2-acetoxy group in D.

ORD measurement of 2-keto-3-acetoxy β-amyrone G was also carried out. The compound G with chair conformation of ring A and a 3β-equatorial acetoxy group would be expected to exhibit a positive Cotton effect. This is in accordance with the ORD experimental results. Thus the assignment of stereochemistry as shown in G is consistent with the ORD and NMR measurements.

Above work was presented in the Convention of Chemists held in Madras, India 1970.

B. Part II:

Chapter II describes the synthesis of all the isomeric 2,3-diols of isohopane (moretane) (Section B) and three out of the four possible isomeric 2,3-diols of methyl olean-12-en-28-oate (Section C).

Section B:

Isohopanone (moretanone) on autoxidation gave the diosphenol, m.p. 190-92°, $(\alpha)_D$ 40°. Acetylation of the diosphenol followed by hydrogenation gave the corresponding 2α-acetoxy isohopanone, m.p. 179-81°, $(\alpha)_D$ 86.31°, γ_{max} 276 mμ (ε, 82). Sodium borohydride reduction of the latter at pH 8 gave the 2α-acetoxy-3β-hydroxy isohopane, m.p. 199-200°. The latter on acetylation gave the 2α, 3β-diacetate, m.p. 228-30° $(\alpha)_D$ 50.60°, which on hydrolysis furnished 2α, 3β-dihydroxy isohopane, m.p. 240-2°, $(\alpha)_D$ 82.86°.

Meerwein-Pondorff reduction of 2-keto moretanol, m.p. 181-3°, $(\alpha)_D$ 29.41° (obtained by 1,4 addition of hydrogen during palladium-charcoal hydrogenation of the above diosphenol) furnished a mixture of diols consisting of 5% of the 2α, 3β diol described above and 92% of a diol, m.p. 250-51°, $(\alpha)_D$ 9.37°. The new diol has been assigned 2α, 3α-configuration from its NMR spectrum. It was also found to be identical with an authentic sample of 2α, 3α-diol prepared by osmylation of Δ^2-moretane. The product in the osmylation reaction also gave 2β, 3β-diol as a minor product (8%).

Sodium borohydride reduction of the diosphenol gave 2β, 3β-diol, m.p. 262-4°, $(\alpha)_D$ 23.68°, which on acetylation afforded the 2β, 3β-diacetate, m.p. 214-5°, $(\alpha)_D$ 31.25°.

Performic acid oxidation of Δ^2-moretane by the method reported in literature[1,2,3] afforded the 2β, 3α-diol, m.p. 221-4°, $(\alpha)_D$ 21.18°, acetate m.p. 145-7°.

The structures of the diols were established on the basis of NMR spectra. Acetonide derivatives of two out of the four isomeric diols have been prepared. All the diols described above are new and have not hitherto been reported in the literature.

Section C:

Methyl oleanonate on autoxidation furnished the diosphenol (2,3-dioxo-olean-12-en-28-oate), m.p. 130-35°, $(\alpha)_D$ 104.4°. Hydrogenation of the latter gave methyl-3β-hydroxy-2-keto-olean-12-en-28-oate, m.p. 129-31°, $(\alpha)_D$ 109.09° which on Meerwein-Pondorff reduction gave the methyl 2α, 3α-dihydroxy olean-12-en-28-oate, m.p. 286-7°, $(\alpha)_D$ 71.11°, identical with an authentic sample (supplied by Dr. H.T.Cheung). The diacetate, m.p. 226-8°, $(\alpha)_D$ 95.20° and the acetonide derivative, m.p. 235-9° have also been prepared.

The diosphenol on sodium borohydride reduction gave methyl 2β, 3β-dihydroxy-olean-12-en-28-oate, m.p. 269-72°, $(\alpha)_D$ 88.88°, which on acetylation furnished the diacetate m.p. 220-22°, $(\alpha)_D$ 86.20°. It afforded an acetonide derivative sintering at 75-80°.

Methyl-3-keto-2α-acetoxy olean-12-en-28-oate (obtained by 1,2-addition of hydrogen during palladium-charcoal hydrogenation of diosphenol acetate) on $NaBH_4$ reduction at pH 8 furnished methyl 2α-acetoxy-3β-hydroxy-olean-12-en-28-oate m.p. 199-204°, $(\alpha)_D$ 28.9°. The latter on hydrolysis afforded the 2α, 3β-diol (methyl crategolate) m.p. 220-22°, $(\alpha)_D$ 36°, identical with an authentic sample of methyl crategolate provided by Prof. P.Sengupta.

All the assignments are based on spectral evidences (IR, NMR, UV).

The above work described in Part II was presented in the Convention of Chemists held in Bombay, India.(1971.)

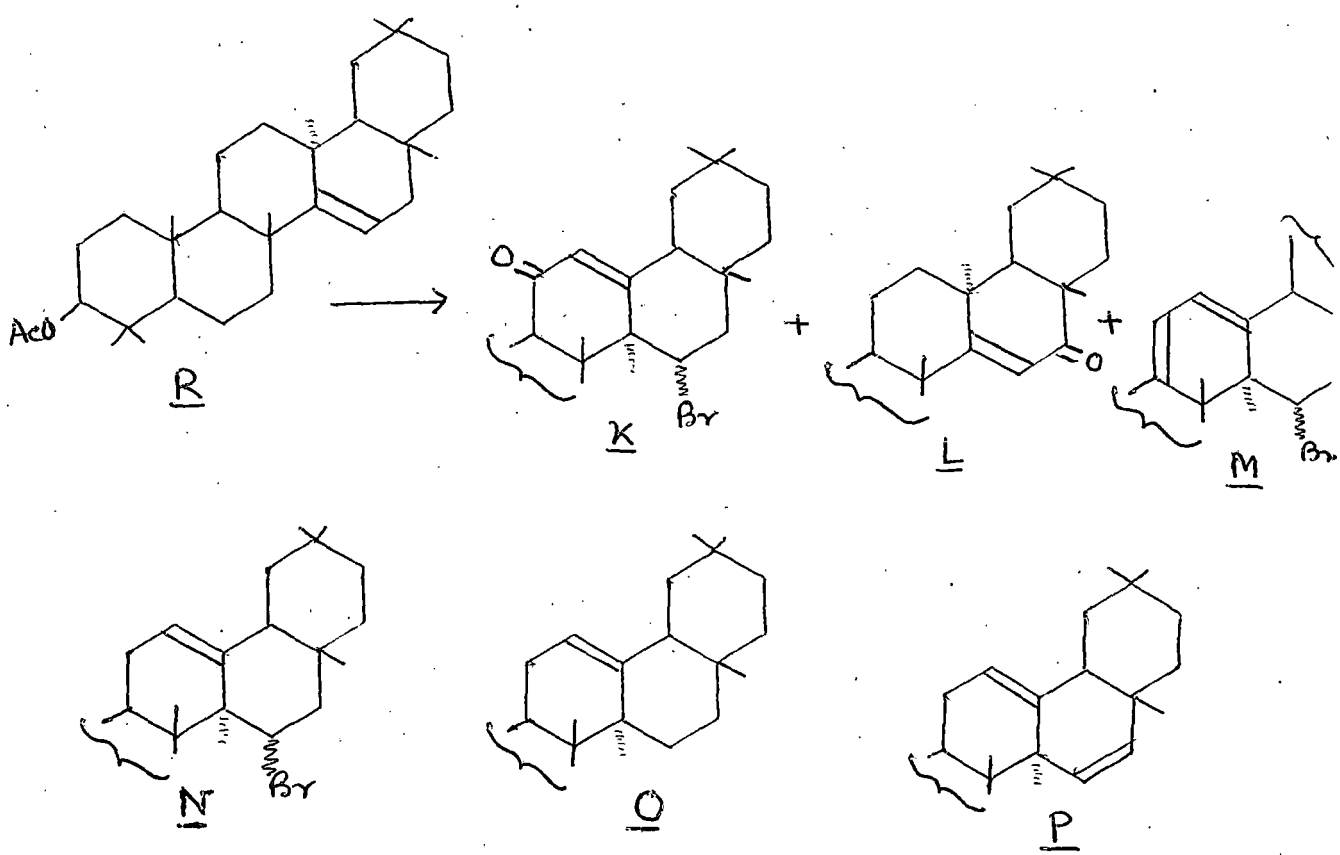
C. Part III

Finucane and Thomson (Chem.Comm. 20, 1220, 1969; J.Chem.Soc. 1856, 1972) recently described a method for allylic oxidation of taraxeryl acetate, β-amyrin acetate etc. using NBS-$CaCO_3$ in aq. dioxan in presence of visilbe light and claimed the isolation of the corresponding $\alpha\beta$-unsaturated ketones in high yield. With a view to preparing 16-OH β-amyrin derivatives oxidation of taraxeryl acetate by their method was taken up. The results were widely different from those recorded by Finucane and Thomson. The reaction product yielded three products after chromatography and crystallisation.

The first compound K, m.p. 238-40°, $C_{32}H_{49}O_3Br$, $(\alpha)_D$ 88.07°,

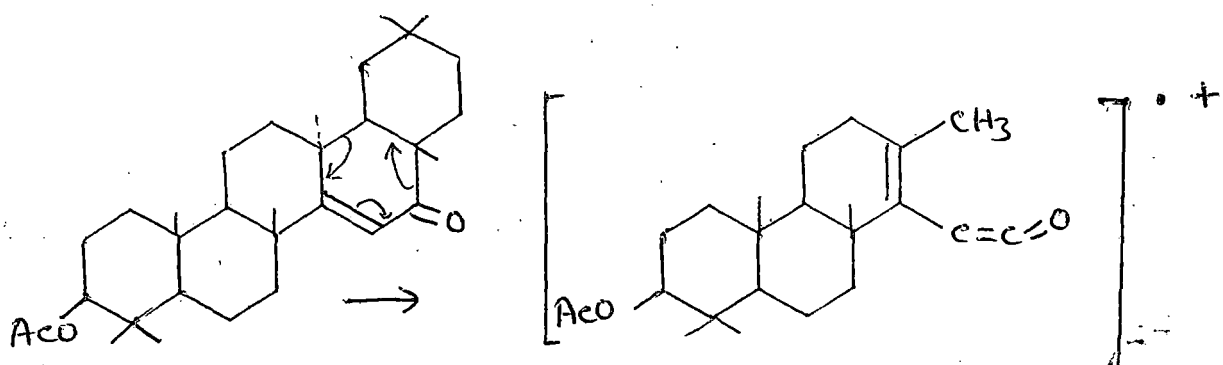
λ_{max} 249.5 mμ (ε, 11,000) was found to be identical with 15-bromo-β-amyrenonyl acetate, established by UV, IR, NMR and its partial synthesis from taraxeryl acetate R. Taraxeryl acetate R on treatment with NBS-DMSO in chloroform gave 15-bromo-β-amyrin acetate N, m.p. 180-2°, $(\alpha)_D$ 47.37°. The latter on treatment with Zn-HOAc gave β-amyrin acetate O indicating that it was a β-amyrin derivative. IR, UV, NMR and mass fragmentation established its structure as depicted in N. Oxidation of 15-bromo-β-amyrin acetate N with CrO_3-HOAc gave 15-bromo-β-amyrenonyl acetate identical with K (m.m.p. and I.R. comparison).

Solvolysis of 15-bromo-β-amyrin acetate N with K-acetate in HOAc gave olean-12, 15-dien-3β-yl-acetate P, m.p. 199-200°. The latter was also obtained when N was treated with dimethyl aniline (IR and m.m.p.).



Probable mechanisms for the formation of 15-bromo-β-amyrenonyl acetate K and 15-bromo-β-amyrin acetate N, have been discussed.

The second compound L, $C_{32}H_{50}O_3$, m.p. 280-82°, $(\alpha)_D$ -38.71°, UV λ_{max} 245 mμ (ε, 10,500) was assigned as 16-oxo taraxeryl acetate from its UV, IR, NMR and mass spectral studies. It showed a mass peak at M^+ 482. Moreover, an abundant base peak at 358 was observed. The appearance of this peak may be explained by assuming that it arises from a 16-oxo taraxeryl acetate by the following genesis S. Our compound was widely different from the sample of 16-oxo taraxeryl acetate, m.p. 251-52°d procured from Dr. Thomson. Their sample was found to give positive bromine test. All physical and chemical evidences prove that our compound m.p. 280-82° is the correct 16-oxo taraxeryl acetate. Attempts to reduce 16-oxo



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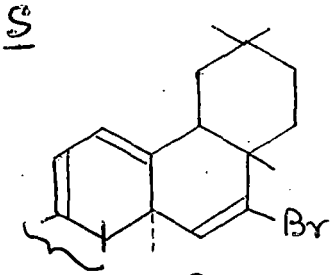
$C_{23}H_{34}O_3$, m/e, 358



Q

taraxeryl acetate to give 16-OH taraxeryl acetate proved futile.

The third compound, M, $C_{32}H_{49}O_2Br$, m.p. 176-8°, $(\alpha)_D$ 249.12°, λ_{max} 276 mμ (ε, 6000) has been assigned as 15-bromo-9(11), 12-olean-diene, on the basis of UV, NMR and mass spectral studies. A probable mechanism for formation of M has also been suggested.

With the expectation of obtaining a 16-bromo taraxeryl acetate we extended our studies on allylic bromination of taraxeryl acetate using NBS in dry CCl_4 in presence of light and benzoyl peroxide as the initiator. The results obtained during these studies were interesting and is summarized below.

When taraxeryl acetate R was refluxed with 2 mole equivalents of NBS in dry CCl_4 using visible light, furnished 16-bromo-olean-9(11), 12,15-trien-3β-yl-acetate Q, $C_{32}H_{47}O_2Br$, m.p. 240°, $(\alpha)_D$ 267.53°, λ_{max} 279 mμ (ε, 6000). The bromine atom in ring D was resistant to reactions (1) Zn-HOAc (2) H_2/Pd-C (3) H_2-PtO_2 (4) Li_2CO_3-LiBr (5) anhydrous KOAc-HOAc (6) $C_6H_5N(CH_3)_2$, indicating that it contained a vinyl bromine atom as shown in structure Q. The mechanism for its formation has also been discussed.

However, with 1 mole equivalent of NBS the product was a bromine free compound, m.p. 199-200°, olean-12,15-dien 3β-yl acetate P, identical with product obtained by solvolysis of 15ξ-

bromo β-amyrin acetate (m.m.p. and IR comparison). The mechanism for the formation of P has been discussed.

This work was presented in the Convention of Chemists, held in Calcutta in 1973.

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