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STUDIES ON EPOXIDES IV. REARRANGEMENTS IN TRITERPENOIDS[1]

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Recently we have reported studies on the constituents of two Melia species: M. azedarach L.[2] and M. azadirachta L. (syn. M. indica and Azadirachta indica A. Juss)[3]. In the seed oil of the latter (Nim oil), compounds having carbon skeletons of both the tirucallane and the meliacin[4] types, have been identified. In the meliacins which possess a carbocyclic apoeuphol type skeleton, a β-oriented methyl group is present at C_8, while an α-oriented hydroxyl (acetoxyl) group is at C_7.

In view of the possible role played in nature by epoxides as demonstrated by the enzymatic conversion of squalene-2,3-oxide to lanosterol and cholesterol[5], as well as the conversion of simpler terpenes with terminal epoxides yielding cyclic compounds[6] when reacted with $SnCl_4$, it was assumed that epoxides could also be involved in various secondary elaborations and transformations in the plant. Thus, a rearrangement induced by opening of a 7α,8α-epoxide in a euphane-tirucallane type carbon skeleton may lead to its conversion to an apoeuphol structure as in the meliacin series, whereby a migration of the C_{14}-β methyl group to C_8 would take place with the formation of a C_7 hydroxy-group having the correct α-orientation, and a double bond at Δ^{14}. A recent publication[7] along these lines prompted us to report some of our results.

Upon complete reduction of melianone (I)[2] with lithium aluminium hydride the melianotetrol (IIa)[2] was obtained. Acetylation yielded the triacetate (IIb), which was the model compound chosen for our sequence, m.p. 161-162°, $C_{36}H_{58}O_7$, (M^+ 602); the C_{7-8} double bond is indicated in the n.m.r. by the C_7 vinylic proton signal at δ 5.29 (t). Epoxidation of (IIb) with perbenzoic acid afforded the 7α,8α-epoxide (III), m.p. 70-71°, $C_{36}H_{58}O_8$, (M^+ 618) which showed now a signal at δ 2.89 (t) for the C_7 epoxidic proton.

Treatment of the epoxide in dry benzene solution for 5 min. at room temperature with $SnCl_4$ afforded the 7α-hydroxy-14-ene derivative (IV). This compound can be rationalised by a sequence involving the opening of the epoxide ring followed by migration of the C_{14}

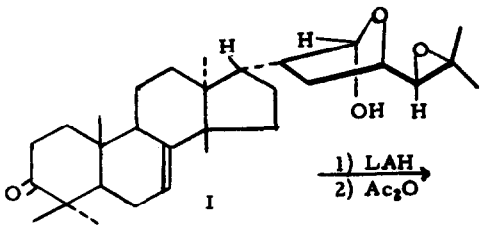
methyl group to C_8 with generation of a double bond at C_{14-15}. The new compound m.p. 118-120°, $C_{36}H_{58}O_8$, (M^+ 618), showed in its n.m.r. spectrum a triplet at δ 5.30 assigned to the C_{15} vinylic proton. In order to support this structure, the 14,15-epoxide (probably β) (V) was prepared with perbenzoic acid, m.p. 110-112°, $C_{36}H_{58}O_9$, (M^+ 634), and in the n.m.r. the C_{15} epoxidic proton appeared as a triplet at δ 3.45.

Compound (IV) has therefore a meliacin carbocyclic skeleton produced from a rearrangement of an euphol type skeleton, thus being a model for a possible biogenetic pathway between these two types of structures occurring in the same species.

The second example selected for the study of the effect of epoxide ring opening with concomitant methyl group migration was epoxyazadiradione (VI)[3] a compound isolated from M. azadirachta. It has previously been reported[8] that when cedrelone acetate was treated with boron trifluoride etherate, migration of a methyl group from C_{13} to C_{14} took place with generation of a C_{13-17} double bond. The treatment of epoxyazadiradione (VI) with $SnCl_4$ for 25 min. gave a product, $C_{28}H_{34}O_6$, m.p. 270-272° dec. $[\alpha]_D$ + 5° ($CHCl_3$), which was identified as having structure (VII) on the following grounds: λ_{max}^{KBr} 225 and 307 mμ (ε 14,300 and 15,550), (KOH) 225 and 343 mμ (ε 14,300 and 11,500); ν_{max}^{KBr} 1764 (cyclopentenone), 1736 (acetate), 1700 (cyclohexenone), 886 (furan) cm^{-1}; n.m.r., singlet at δ 2.57 for the C_{14}-H; the signals of the epoxidic proton (previously observed in epoxyazadiradione[3] at δ 3.33*), and the C_{17}-H are missing in the spectrum of this compound. It is noteworthy that the signals of the furan protons exhibited a paramagnetic shift under the influence of the Δ^{16} and are now at δ 8.05 for the α proton and 6.94 and 7.52 for the α', β' protons respectively, all being multiplets. The signal of the proton of the C_{16} enolic-OH at δ 6.55 disappeared upon addition of D_2O. With ferric chloride the compound gave a positive test.

The formation of (VII) can be explained through a cleavage of the C_{14}-O bond concerted with the migration of a hydride ion from C_{15} to C_{14} producing a diketone which is then enolised to form the keto-enol system. A similar sequence was also observed when 1,2-dihydroepoxyazadiradione (dihydro VI) was treated with the same reagent, compound (VIIIa), $C_{28}H_{36}O_6$, m.p. 241-243°, $[\alpha]_D$ - 3° ($CHCl_3$) was obtained, in which the chromophore of the α,β unsaturated carbonyl group was missing; λ_{max}^{EtOH} 217 (furan) and 307 mμ (ε 22,400), (KOH) 343 mμ (ε 17,400); the 16-enol acetate (VIIIb) showed the expected spectroscopic values[9] for such a system, λ_{max}^{EtOH} 291 (ε 9100), and $\nu_{max}^{CHCl_3}$ 1773 cm^{-1}.

* This signal was erroneously reported as a triplet[3].



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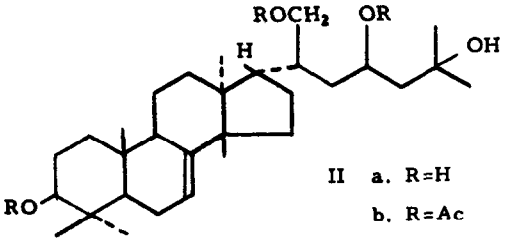
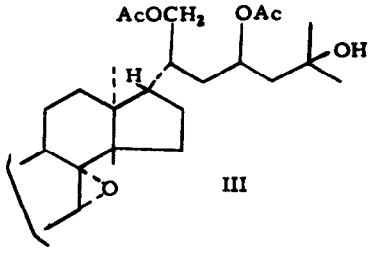
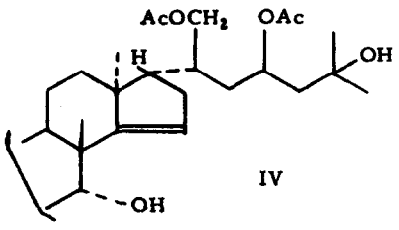


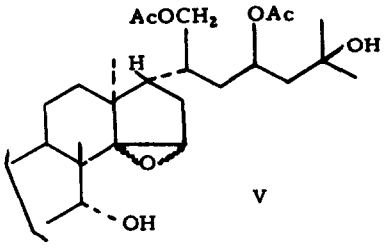
II a. R=H
b. R=Ac



III



IV



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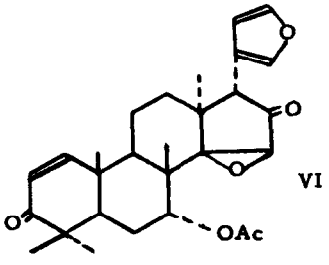

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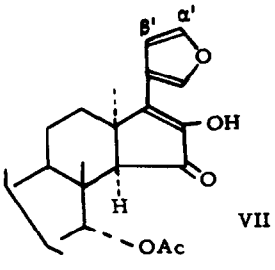
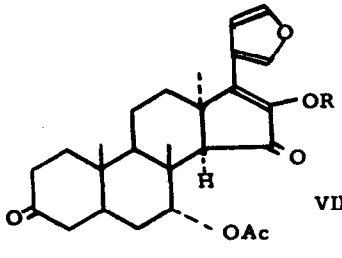


VII



VIII a. R=H
b. R=Ac

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