

BACCATIN, A NOVEL NOR-TRITERPENE PEROXIDE ISOLATED FROM SAPIUM BACCATUM ROXB.

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We already reported the isolation of taraxerone, taraxerol¹ and 3-acetoxy aleuritic acid² from the benzene extract of the bark of S.baccatum Roxb. From the more polar fractions of the neutral portion of the same extract we have been able to isolate a new nor-triterpene peroxide, baccatin 2 ($R_1 = H$), $C_{29}H_{46}O_4$ (M^+ 458), m.p. 228-9° (d), $(\alpha)_D^{20} -9.09^\circ$, ν_{max}^{KBr} 3360(OH), 1389, 1369 (gem-dimethyl), 890, 875 cm^{-1} (-CH = CH-), having no UV absorption in the region 220-300 nm. It readily formed a diacetate, $C_{33}H_{50}O_6$ (M^+ 542), $(\alpha)_D^{20} 47.5^\circ$, $\nu_{max}^{CHCl_3}$ 1737(-O.CO.CH₃), 1389, 1368 (gem-dimethyl), 1245, 892, 875 (-CH = CH-). The NMR (100 MHz) spectrum of the alcohol showed signals at δ 0.88-1.18 (7-tert. CH₃ grs), 2.16 & 2.20 (d), 2.28 & 2.32(d) (two OH groups), 3.25 (unsym. d H-C₃-OH), 3.9 (q of d, H-C₂-OH, J = 10 Hz, 10.4 Hz) and a AB quartet at δ_A 6.69 & δ_B 6.43 ($J_{AB} \sim 9$ Hz, -C₁-CH = CH-C₁-) and NMR of the diacetate showed peaks at δ 0.88-1.025 (7-tert. CH₃ grs), 1.99 and 2.05 (6H, two O.CO.CH₃ grs) and peaks centred at 4.6 (unsym. d H-C₃-O.CO.CH₃, J = 10 Hz) and 5.08 (q of d H-C₂-O.CO.CH₃, J = 10 Hz, 10.5 Hz) and a AB quartet at δ_A 6.68 and δ_B 6.42 ($J_{AB} \sim 9$ Hz). The 10 Hz coupling between the C₂ and C₃ protons implied the presence of trans 2 α , 3 β -diol system^{3(a),(b)} in ring A of the nor-triterpene.

KI-acetic acid titration on the diacetate 2 ($R_1 = Ac$) indicated the presence of two active oxygen atoms, either as a peroxide or two epoxide groupings. However, as the compound was found to be very sensitive to alkali the presence of epoxide may be excluded. Thus when 2 ($R_1 = H$ or Ac) was treated with 10% MeOH-KOH it afforded a new product m.p. 237-40°, $C_{29}H_{46}O_2$ (M^+ 426), ν_{max}^{nujol} 3280 (OH), 840 cm^{-1} , λ_{max}^{MeOH} 282 nm (ϵ , 8300), indicating a homoannular diene structure as in 3 ($R = H$).

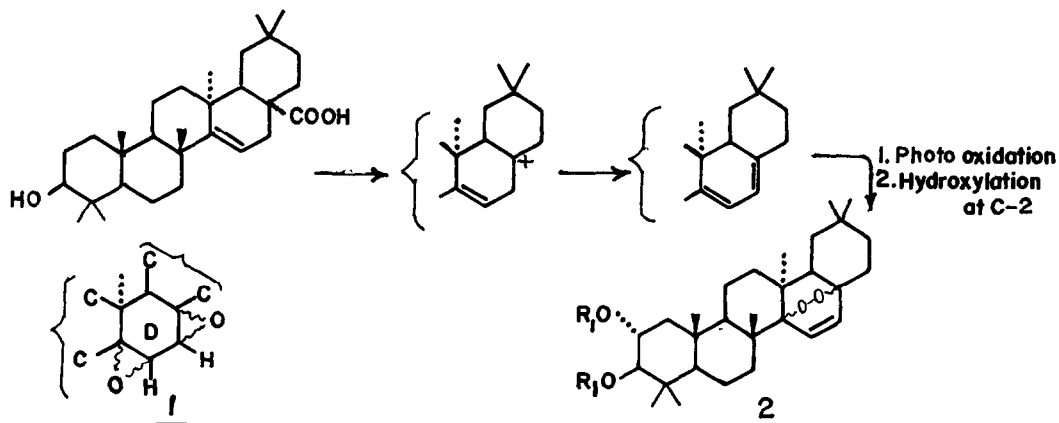
The diene on acetylation gave a diacetate, m.p. 226-7°, $C_{33}H_{50}O_4$ (M^+ 510), λ_{max}^{MeOH} 282 nm (ϵ , 8032), NMR(100 MHz) spectrum showed resonances at δ 0.9-1.15

(7-tert. CH₃ grs), 2.0 & 2.03 (6H, two -O.CO.CH₃ grs), 4.7, 4.8(d, H-C₃-O.CO.CH₃) peaks centred at 5.1 (q of d, H-C₂-O.CO.CH₃) and at 5.58 (m, two vinyl protons). These observations led us to believe that two of the oxygen atoms in baccatin might be present as a peroxy linkage. This was unequivocally demonstrated by conversion of the diene-diol 3(R = H) to a peroxide identical with the original diol-peroxide 2(R₁ = H) (Photooxidation-O₂-eosin). Furthermore, the presence of the more abundant peaks at M⁺-32^{4,5} in the mass spectra of baccatin (2, R₁ = H) and its diacetate (2, R₁ = Ac) gave added support to the presence of a peroxide bridge (-O-O-) in these compounds. Thus 2 (R₁ = H) gave peaks at m/e 426 (M⁺-32, 95%), 458 (M⁺, 8%) and the diacetate 2(R₁ = Ac) showed peaks at m/e 510 (M⁺-32, 96%) and 542 (M⁺, 10%).

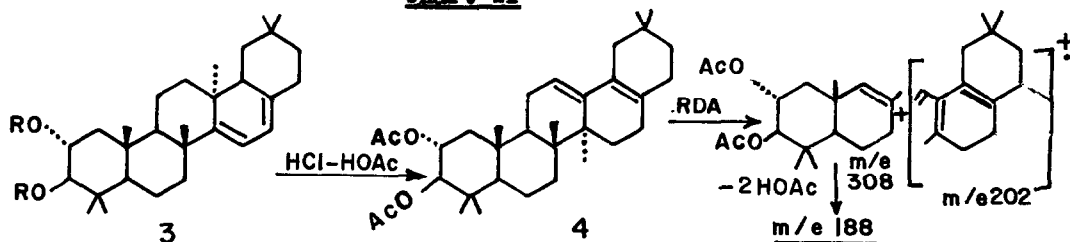
Having thus been sure of the presence of a peroxide linkage we can infer that the four line signal in the NMR spectra of both the diol and the diacetate (δ_A 6.69 and δ_B 6.43) arise from a disubstituted double bond (- $\overset{\text{O}}{\underset{|}{\text{C}}}$ - CH = CH - $\overset{\text{O}}{\underset{|}{\text{C}}}$ -) present in the same ring as the peroxide as shown in 2.

When a benzene solution of the diacetate 2(R₁ = Ac) was adsorbed in a column of basic alumina (48 hrs) it rearranged to a new product, C₃₃H₅₀O₆ (M⁺ 542), m.p. 263-4°, $\nu_{\text{max}}^{\text{nujol}}$ 1720, 1250 (-O.CO.CH₃), 1040 cm⁻¹, NMR (100 MHz) spectrum showed signals at δ 0.9-1.18 (7-tert.CH₃ grs), 2.0, 2.06 (2-O.CO.CH₃) 3.0 (J = 2Hz, sym. d), 3.5 (J = 2Hz, sym. d), 4.7, 4.8 (C₃-proton, unsym. d), and a peak centred at 5.05 (C₂-H, q of d). The diepoxy structure ⁶1 is consistent with the NMR signals at δ 3.0 and 3.5 (Chart I).

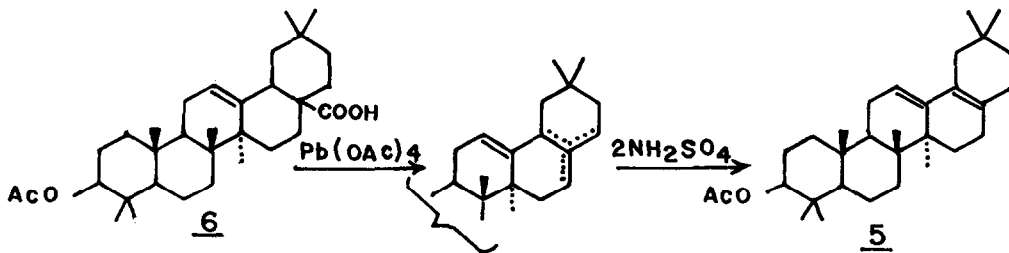
Computation of m.f. of the diol and the diene indicated that the nor-triterpene peroxide is pentacyclic. The absence of lupane, hopane or friedlane type of skeleton was deduced from the NMR and mass spectra of baccatin. As the nor-triterpene peroxide was found to occur with triterpenes having Δ^{14} -taraxerene system^{1,2}, it appeared to us from biogenetic considerations that the same Δ^{14} -taraxerene type of nucleus might be involved in the formation of triterpene peroxide in the plant (Chart I). We therefore propose structure 2(R₁ = H) from biogenetic point of view as well as from the fact that it could explain all the chemical and physical evidence in a satisfactory manner.

Chart I (Probable biogenesis)

- Further confirmation of the proposed structure 2 has been obtained by the following experiment. The diene-diacetate, which may now be depicted as 3 (R = Ac) on treatment with HCl-HOAc gave a compound, $C_{33}H_{50}O_4$, m.p. $189-90^\circ$, λ_{max}^{MeOH} 237, 244 (ϵ , 22,000), 252 nm, NMR (100 MHz) δ 5.2 (m, 1 vinyl proton), mass: m/e 510 (M^+), 495 (M^+-15), 450 (M^+-60), 435 ($M^+-60-15$), 390 (M^+-120), 375 ($M^+-120-15$), 308, 202 and 188. We assign structure 4 to this product. The fragments m/e 308, 202 and 188 are diagnostic of the system (Chart II).

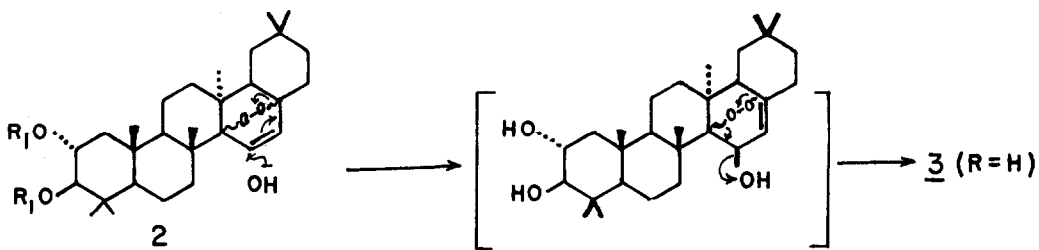
Chart II

To correlate the above observation we prepared 5, m.p. $185-6^\circ$, from 3-acetoxy

Chart III

oleanolic acid 6 as shown in Chart III. 5 showed similar mass fragmentation pattern as 4.

Chart IV



A probable mechanism for the transformation of 2 ($R_1 = Ac$) to 3 ($R = H$) is shown in Chart IV. The Dreiding model of 3 with β -peroxide linkage showed that both rings C and D assume rigid boat conformation with considerable interaction between the hydrogen atoms at C-12 and C-19. In the diene the C-ring takes up half-chair conformation and D-ring becomes almost flat with complete disappearance of above interactions. Most probably this relief of strain facilitates the transformation of the peroxide to the diene.

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