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THE HOMOLYTIC FRAGMENTATION OF 1-HYDROPEROXY-EUDESMANOLIDES

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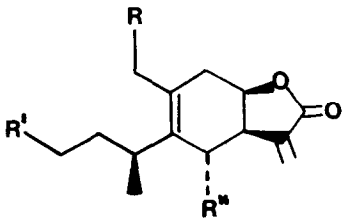
ABSTRACT: The 1-hydroperoxy-eudesmanolides 6 and 7 were prepared,then converted to 1,10-sec-eudesmanolides by homolytic fragmentation.

The 1,10-sec-eudesmanolides are a group of sesquiterpenes,three of which are known, namely,eriolanin 1,eriolangin 2[1]and ivangulin 3[2].These have all synthetized by Grieco et al[3].

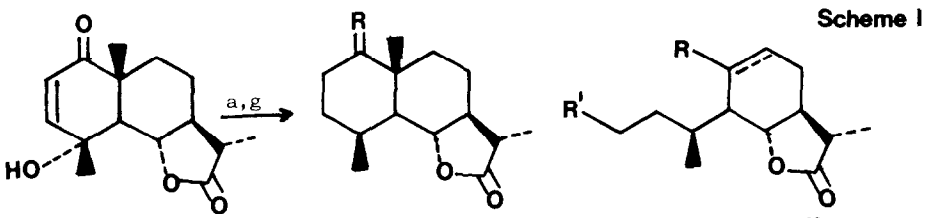


1 R=-OH;R'=-CH_2OH;R"=-OMac
2 R=-OH;R'=-CH_2OH;R"=-OTig
3 R=-H ;R'=-COOMe;R"=-H

Herz has suggested[4] that the biogenesis of the 1,10-sec-eudesmanolides takes place via a 1-hydroperoxy-eudesmanolide fragmentation.

To check out this theory,we prepared the 1-hydroperoxy-eudesmanolides 6 and 7,using vulgarin 4 as starting material[5].Treatment of 4 with Zn-HOAc,followed by reduction, hydrogenation and oxidation yielded 5 (48%)[6].The method described by Cagliotti et al[7] was then applied to 5 which was treated with tosylhidrazine,diborane and sodium peroxide-hydrogen peroxide to give the epimers 6 and 7 (8:10;46%),which then with Ph_3P gave the alcohols 8 and 9 (Scheme I).

Scheme I



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5 R=O
6 R=β-OOH;α-H
7 R=α-OOH;β-H
8 R=β-OH ;α-H
9 R=α-OH ;β-H

10 R=α-Me;R'=-CHO
11 R=α-Me;R'=-COOMe
12 R=-Me ;R'=-CHO ;$\Delta^{9,10}$

a)Zn-HOAc(Δ,1hr.);b)$NaBH_4$;c)H_2-C/Pd;d)Jones;e)NH_2-NHTs;f)B_2H_6-THF;g)H_2O_2-Na_2O_2

When 7 was treated with Ac_2O-py,or $HClO_4$-HOAc,ketone 5 was obtained in 87% and 62% yields respectively,evidently formed by a hydroperoxide transposition,with a hydride migration instead of the desired $\sigma^{1,10}$migration[8].Its epimer 6 yielded identical results, with no fragmentation products discernible in either,thus apparently contradicting Herz' hypothesis.

However,when 6 or 7 was subjected to the action of $FeSO_4$-$Cu(OAc)_2$[9] ,aldehyde 10 was obtained in 59% yield and could be converted to ester 11 by oxidation and diazomethane

esterification (Scheme I).

It seems likely that the reaction may take place trough a alcoxy radical which undergoes β-fragmentation to generate aldehyde 10.Further support for this possibility is provided by the fact that the alcohol 8 when treated with LTA-I_2[10] or iodosobenzene diacetate-I_2[11] gives yields of 72% and 56% respectively of the unsaturated aldehyde 12.[12]

Enzymatic (or perhaps pseudoenzymatic) transformations of hydroperoxides to aldehydes in various plants[13] have been observed any may be the route accounting for the formation of 1,10-sec-eudesmanes.In particular,the enzymatic conversion[14] of linoleic acid 13-hydroperoxide,to generate hexanal and 12-oxo-cis-9-dodecenoic acid,may be considered as formally equivalent to a hydroperoxide transposition with preferred migration for a vinyl radical rather than the hydrogen.

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6.-This route to the preparation of 5 was chosen as the direct hydrogenation of deoxy-vulgarin gives a mixture of epimers at C_4 while the hydrogenation of the corresponding alcohol is stereoselective.
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12.-All spectra (200 Mhz ^{1}H-NMR,IR and high resolution MS)are in agreement with the structures assigned.6:^{1}H-NMR($CDCl_3$)δ:8.02(bs,1H,HOO-,removed by D_2O exchange),3.98 (dd,1H,J=9.9;9.9Hz,H-6),3.67(m,1H,H-1),1.20(d,3H,J=6.8Hz,C_{11}-Me),0.99(d,3H,J=7.5Hz, C_4-Me),0.99(s,3H,C_{10}-Me).IR($CHCl_3$)$\nu_{max.}$ cm^{-1} :3520,1760.MS:m/z 235.1654(M^+-OOH, $C_{15}H_{23}O_2$).7:^{1}H-NMR($CDCl_3$)δ:7.79(bs,1H,HOO-,removed by D_2O exchange),3.90(dd,1H, J=9.9;9.8Hz,H-6),3.68(bs,1H,H-1),1.17(d,3H,J=6.7Hz,C_{11}-Me),1.07(s,3H,C_{10}-Me),1.00 (d,3H,J=6.7Hz,C_4-Me).IR($CHCl_3$)$\nu_{max.}$ cm^{-1} :3520,1760.MS:m/z 235.1579(M^+-OOH,$C_{15}H_{23}O_2$). 11:^{1}H-NMR($CDCl_3$)δ:3.68(dd,1H,J=9.9;10Hz,H-6),3.65(s,3H,-OMe),1.19(d,3H,J=6.9Hz, C_{11}-Me),1.05(d,3H,J=7Hz,C_4-Me),0.98(d,3H,J=6.4Hz,C_{10}-Me).IR($CHCl_3$)$\nu_{max.}$ cm^{-1} :1760, 1725.MS:m/z 251.1628(M^+-OMe,$C_{15}H_{23}O_3$).The stereochemistry of the C_{10}-Me was assigned as α- in the basis of the NOE absence between H-6 and C_{10}-Me.12:^{1}H-NMR($CDCl_3$)δ:9.78 (s,1H,-CHO),5.55(bs,1H,H-9),3.96(dd,1H,J=10;10Hz,H-6),1.69(bs,3H,C_{10}-Me),1.22(d,3H, J=7Hz,C_{11}-Me),1.11(d,3H,J=7Hz,C_4-Me).IR($CHCl_3$)$\nu_{max.}$ cm^{-1} :1760,1716.MS:m/z 250.1550 (M^+,$C_{15}H_{22}O_3$).No exo isomer was detected.
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