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STEREOCHEMISTRY OF THE C-19 ISOPROPENYL SUBSTITUENT IN THE MERCURIC ACETATE OXIDATION PRODUCT OF THE TRITERPENES OF LUPANE SERIES

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Allison and coworkers [1,2] carried out mercuric acetate oxidation on lupeol acetate (Ia), betulindiacetate (Ib) and methyl acetyl betulinate (Ic) and assigned structures (IIa), (IIb) and (IIc) to the respective products. They also performed the same oxidation on betulin (IIIa) and acetyl betulinic acid (IIIb) and formulated the products as (IV) and (V) respectively. The stereochemistry of the isopropenyl group at C-19 in the products of oxidation was not established by them. Recently Chopra et al[3] repeated this oxidation on methyl acetyl betulinate and established structure (VI) for the product on the basis of UV absorption NMR spectrum and osmic acid hydroxylation of the tetrasubstituted double bond but did not assign the stereochemistry of the C-19 isopropenyl group.

In the present communication we report the evidences which indicated that the stereochemical assignment of the isopropenyl group should be cis in relation to the β-substituent at C-17. On mechanistic grounds we thought it probable that the dehydrogenation may lead to cis orientation of the isopropenyl group with respect to the C-17 substituent. Most probably the initial product of dehydrogenation is (VII) which then isomerizes to the thermodynamically more stable (VIII), the addition of proton at C-19 taking place from rearside.

To provide reasonable evidences regarding the stereochemical assignment of the isopropenyl group we chose the lactone 3β-acetoxy-lup-20 (30)-en-28,13β-olide (V*), m.p. 300-2°, $[\alpha]_D$ + 56°

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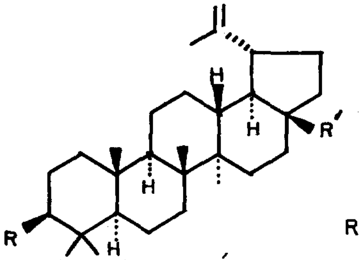
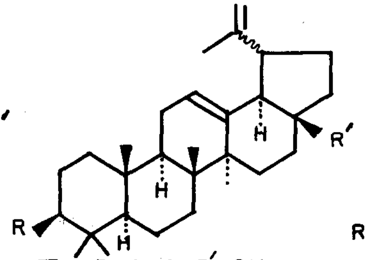
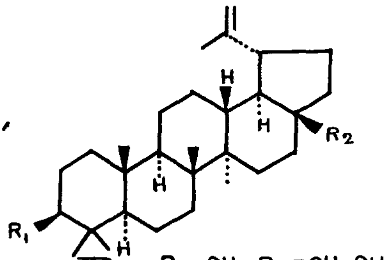
* In the lactone (V) the C-19 H is necessarily α-oriented.



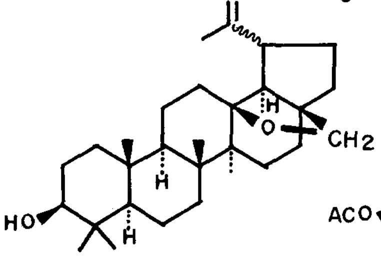
Ia; $R=OAC$, $R'=CH_3$
Ib; $R=OAC$, $R'=CH_2OAC$
Ic; R OAC, $R'=COOCH_3$



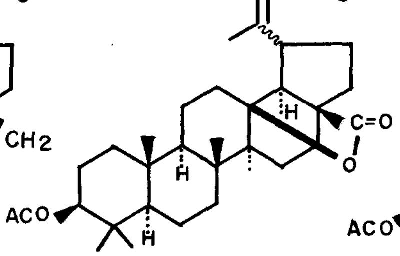
IIa; $R=OAC$, $R'=CH_3$
IIb; $R=OAC$, $R'=CH_2OAC$
IIc; $R=OAC$, $R'=COOCH_3$



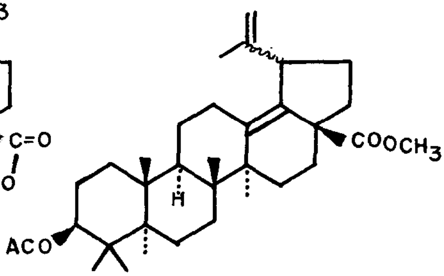
IIIa; $R_1=OH$, $R_2=CH_2OH$
IIIb; $R_1=OAC$, $R_2=COOH$



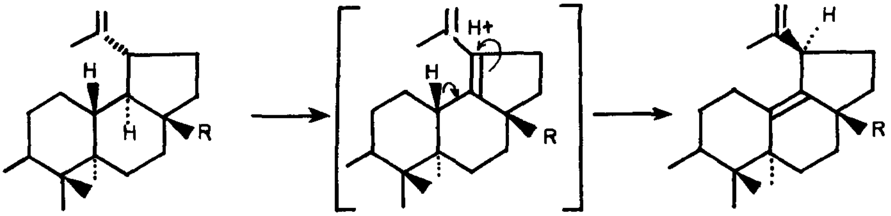
IV



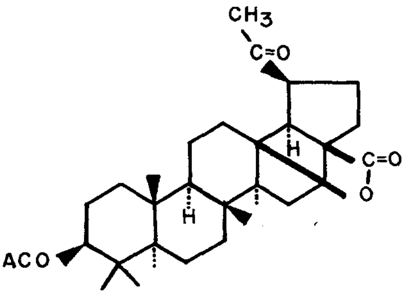
V



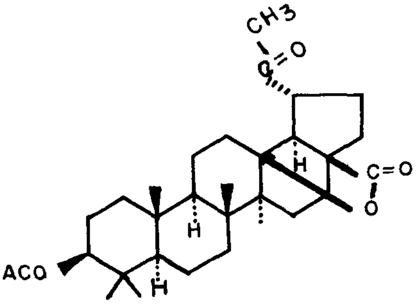
VI



VII VIII



IX



X

$\nu_{max}^{CHCl_3}$ 1730, 1775 cm^{-1} (reported[1] m.p. 315-17°, $[\alpha]_D$ + 60°) as our starting material. The presence of terminal methylene protons was indicated by an nmr signal at 4.9 ppm. Examination of the Dreiding model of this compound clearly indicated that if the C-19 substituent were trans to the C-17 group as in lupeol and betulinic acid then it should be amenable to acid induced isomerization[4a, b] as observed in the lupeol series with expansion to six membered ring E with chair conformation. But if the original orientation were cis no skeletal rearrangement would occur. Accordingly, we exposed the lactone (V) to the action of $HCl-CHCl_3$[5,6], 98% formic acid[7,8] HCl-acetic acid [1,2] and in each case the starting material was recovered in good yield (mixed melting point and comparison of infrared spectra) and no isomerized product could be detected. These experiments suggested that the skeleton of the lactone and the stereochemistry of the substituents in the compounds is preserved unchanged. The lactone was ozonised at 0°C in $CHCl_3$ solution and the ozonide on decomposition under neutral conditions furnished the ketone (IX), melting point 301-3°, $[\alpha]_D$ - 9°, $\nu_{max}^{CHCl_3}$ 1715, 1780 cm^{-1} (reported[1] m.p 317°, $[\alpha]_D$ - 2°). The latter on equilibration with potassium tertiary butoxide in benzene solution, reacetylation and chromatography furnished a new ketone (X), m.p. 300-2°, $[\alpha]_D$ - 24° $\nu_{max}^{CHCl_3}$ 1714, 1780^{cm-1} in 60% yield thus demonstrating that the cis ketone (IX) has isomerized to the more stable trans ketone (X). The mixture melting point of the two ketones showed considerable depression. The epimerization of the ketone (IX) by base is an expected process. Thus the sterochemistry of (IX) requires that $-CO-CH_3$ group at C-19 be cis to the C-17 lactone.

Satisfactory analytical data have been secured for the compounds reported here. Further studies are in progress and more complete details will be reported later.

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Melting points are uncorrected. Optical rotations were determined in chloroform solution unless stated otherwise.