

FUNCTIONALIZATION OF THE C-8 METHYL GROUP IN THE ROSANE SKELETON.
POTENTIAL INTERMEDIATES FOR THE SYNTHESSES OF ROSANE TYPE DITERPENOIDS

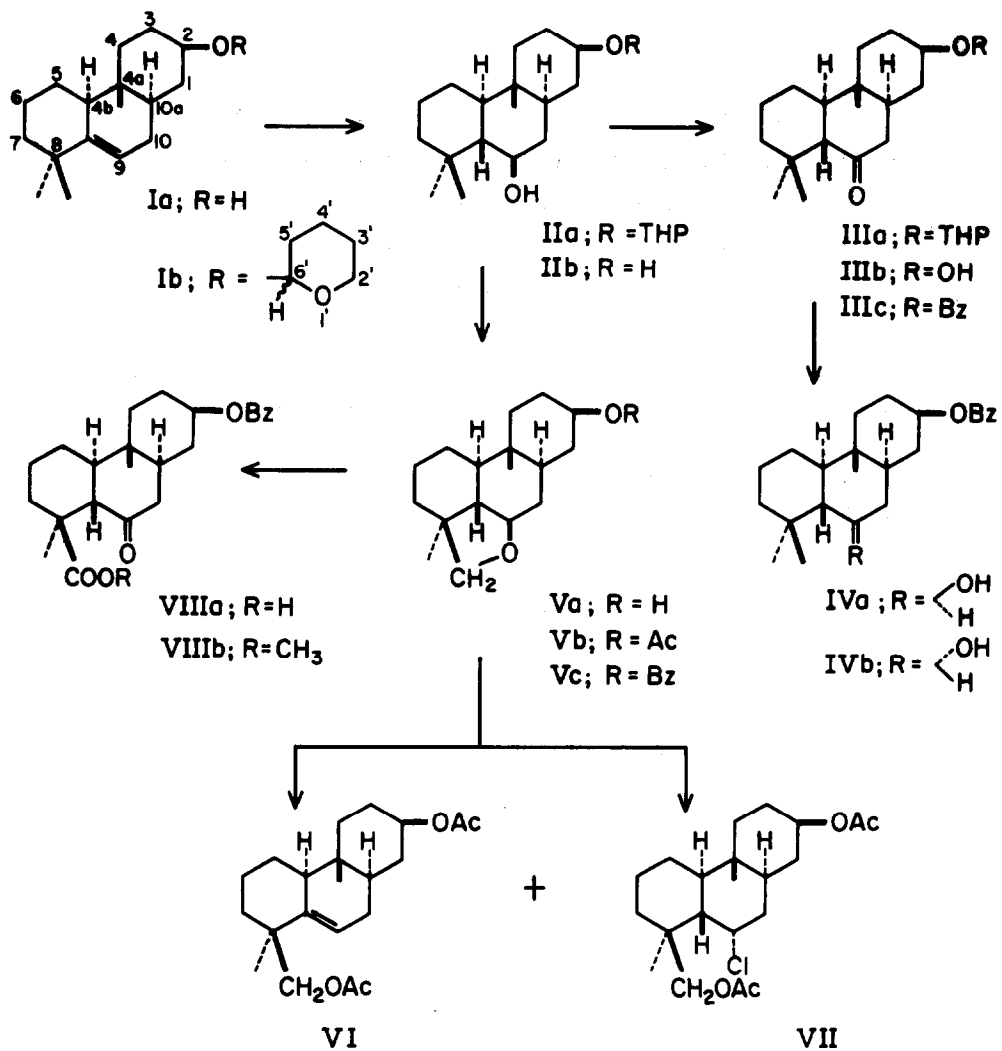
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Functionalization of the C-8 methyl residue in podocarpic acid type compounds has been extensively investigated (1). However, the similar modification of the C-8 methyl groups in the rosane skeleton (2) has not yet been reported (3). We now report an investigation in this area which leads to the synthesis of promising intermediates VI and VIIIa to natural diterpenoids possessing a rosane skeleton, such as erythroxydiol X (2).

2 β -Hydroxy-4 $\alpha\beta$,8,8-trimethyl-1,2,3,4,4a,4ba,5,6,7,8,10,10 $\alpha\alpha$ -dodecahydrophenanthrene (Ia) (4) was prepared according to the method of Ireland and Mander (5). On treatment with dihydropyran in the presence of p-toluenesulfonic acid it yielded a noncrystalline hydroxy ether Ib. Hydroboration of Ib via the standard sequence (6) led to the 9 β -hydroxy ether IIa, m.p. 119-121 $^{\circ}$ (from hexane), δ 1.00 (3H), 1.06 (3H), and 1.15 (3H) (s, quaternary CH₃), 3.21-4.20 (3H) (m, H at C-2' and C-9), 4.76 (1H, m, H at C-6'), and no vinyl proton. Acid hydrolysis of IIa afforded the diol IIb, m.p. 206-208 $^{\circ}$ (from ether). The assignment of the β -configuration to the C-9 hydroxy group was based on the following evidence. Inspection of a molecular model of the olefin Ib shows that the α -side of the molecule is encumbered by the axial 8 α -methyl group. Its β -face is partially shielded by the axial 4 $\alpha\beta$ -methyl group, which, however, is in a 1,4-relationship with the C-9 position. Thus the approach to the β -side of the 8 α ,9-double bond should be more favored to produce the desired 9 β -alcohol. Oxidation of the hydroxy ether IIa with Sarett reagent (7) afforded the ketone IIIa (8), m.p. 149-150 $^{\circ}$ (from ether-hexane), ν_{\max} (cm $^{-1}$) 1700 (C=O), which was hydrolyzed with acid to the hydroxy ketone IIIb, m.p. 120-122 $^{\circ}$ (from ether-hexane). Sodium borohydride reduction of the benzoate IIIc, m.p. 162-164 $^{\circ}$



(from ether-hexane), yielded two alcohols, IVa, m.p. 143-145° (from ether-hexane), ν_{\max} (cm^{-1}) 3555 (OH), and 1694 and 1275 (benzoate), and IVb, m.p. 147-149° (from ether-hexane), ν_{\max} (cm^{-1}) 3500 (OH), 1694 and 1285 (benzoate). In the NMR spectrum of the C-9 β (equatorial) alcohol IVa, the proton at C-9 occurred at δ 3.58 as a broad multiplet (half-width, ca. 25 cps), characteristic of the axial proton, whereas in that of the C-9 α (axial) alcohol IVb, the corresponding proton exhibited a multiplet (half-width, ca. 6 cps) at δ 4.30, which indicated the equatorial nature of this proton (9). Alkaline hydrolysis of the alcohol IVa yielded IIb.

Oxidation of the hydroxy ether IIa with lead tetraacetate in cyclohexane containing iodine and acid hydrolysis of the product furnished the cyclic hydroxy ether Va, m.p. 137-139° (from ether-hexane); acetate Vb, m.p. 110-112° (from ether-hexane), δ 0.86 (3H) and 1.00 (3H) (s, quaternary CH_3), 2.06 (3H, s, OAc), 3.50 (1H, m, H at C-9), 3.66 (2H, AB q, $J = 8$ cps), and 4.80 (1H, broad m, H at C-2). On treatment with pyridine hydrochloride in acetic anhydride the acetoxy ether Vb yielded the expected olefin VI, ν_{\max}^{film} (cm^{-1}) 1735 and 1245 (acetate), δ 5.55 (1H, m, H at C-9), and a chlorine-containing compound VII, δ 2.05 (3H) and 2.08 (3H) (s, OAc), 3.53 (2H, AB q, $J = 11$ cps, $-\text{CH}_2\text{OAc}$), and 4.41-5.16 (2H, m, $-\text{CHCl}$ and $-\text{CHOAc}$). Refluxing of VII with 5% methanolic potassium carbonate gave back the cyclic hydroxy ether Va. Similar oxidation of IIa with lead tetraacetate in benzene in the absence of iodine and acid hydrolysis of the product also yielded Va. Oxidation of the benzoyloxy ether Vc, m.p. 179-181° (from ether), with chromium trioxide in acetic acid furnished the keto acid VIIIa, m.p. 280-282° (from chloroform-hexane), m/e 398 (M^+), ν_{\max} (cm^{-1}) 1701 (unresolved benzoate and acid C=O) and 1270 (benzoate -O-C). Methylation of VIIIa with diazomethane gave the methyl ester VIIIb, m.p. 184-185° (from ether), ν_{\max} (cm^{-1}) 1720 (C=O), 1710 (ester C=O), and 1700 (benzoate C=O) and 1270 (benzoate -O-C), m/e 412 (M^+), δ 1.03 (3H) and 1.16 (3H) (s, quaternary CH_3), 3.63 (3H, s, $-\text{COOCH}_3$), 4.90 (1H, broad m, H at C-2), and 7.20-8.20 (5H, m, benzenoid H).

All crystalline compounds reported here gave satisfactory elemental analyses. NMR spectra were obtained for solutions in deuteriochloroform with a Varian A-60 spectrometer using TMS as an internal standard. The form of signals is expressed as s = singlet, d = doublet, q = quartet, and m = multiplet. Mass spectra were recorded on a Hitachi Perkin-Elmer RMU-6E at 70 eV using a direct inlet system. Unless otherwise specified, IR spectra were taken on a Perkin-Elmer 337 spectrometer for KBr discs.

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