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THE DEGRADATION OF RESIN ACIDS TO SYNTHETICALLY USEFUL INTERMEDIATES

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As part of a project aimed at elucidating the biogenesis of diterpene resin acids, the development of suitable procedures for degradation of these acids was necessary. The conjugated diene system present in both neoabietic (Ia) and levopimaric acid (IIa) suggested itself as the most obvious chromophore to concentrate upon. The quest for a simple method of effecting a one-step cleavage of both the double bonds of neoabietic and levopimaric acids to obtain IIIa and IVa in high yields prompted us to conduct a systematic study of the oxidative degradation of resin acids.

The smooth conversion[1] of the enone ester (V) to the keto-acid ester (IIIa) by sodium metaperiodate-potassium permanganate, suggested a study of the Lemieux oxidation[2] of methyl neoabietate (Ib) and methyl levopimarate (IIb). Treatment of Ib with the Lemieux reagent in aqueous dioxan for 48 hours at room temperature afforded the keto-acid ester (IIIa) in yields of about 50%. Under the same conditions, methyl levopimarate (IIb) afforded the keto-acid ester (IVa) and the dihydroxy-oxide (VI) in varying yields. The difficulty of securing reproducible yields in the oxidation of IIb prompted us to reinvestigate the ozonolysis[3,5] of compounds I and II. This paper reports a simple, oxidation procedure for converting Ib to IIIb and IIb to IVb, in good yield, thus providing a convenient source of promising intermediates for the synthesis of many interesting diterpenes.[6]

Exhaustive ozonolysis of Ib in ethyl acetate at -70°, followed by work-up according to the procedure of Bailey[7], afforded an oil which was immediately subjected to Jones[8] oxidation. The product gave an acid fraction in consistent yields of 60-65%. Methylation of this acid fraction with diazomethane and column chromatography over silica gel afforded the pure keto-diester (IIIb) in 55% yield as a pale yellow oil, $C_{18}H_{28}O_5$, νmax 1730 and 1710 cm.$^{-1}$; n.m.r. ($CDCl_3$) τ 6.3 and 6.33 (two carbomethoxyls), 7.5-7.8 [C(7)-methylene], 8.86 [C(4)-CH_3], and 9.2 [C(10)-CH_3].

Partial ozonolysis of Ib, which has been reported[5] to give V in yields varying from 37-58%, afforded a viscous yellow oil, which was separated by chromatography over silica gel to give the enone ester (V) in about 40% yield. The later chloroform eluates afforded a solid (10%), which crystallized as needles from ether-hexane, m.p. 174-176°, $[\alpha]_D$ + 11.5° ($CHCl_3$), $C_{18}H_{28}O_5$[9], νmax 3525, 3470, 3405, 1740 and 1728 cm.$^{-1}$, indicating the presence of hydroxyl, carbonyl and ester functions; n.m.r. ($CDCl_3$): τ 8.94 and 8.76 (two C-methyls), 6.22 (carbomethoxyl) and 6.15 (a proton on a carbon bearing a hydroxyl group). The major peak (83%) in the mass spectrum at m/e 323 (M-1) could be ascribed to the stable oxonium ion (VII), which probably arises by α-fission[10] at C-13. The spectral data coupled with the fact that acetylation of this product afforded only a mono-acetate, m.p. 256-259°, $C_{20}H_{30}O_6$, can be satisfactorily explained by structure VIIIa for this compound. This structure may arise by epoxidation of the double bond of I, cleavage of the isopropylidene moiety and subsequent opening of the epoxide. Such an epoxidation and subsequent opening of the epoxide has ample precedence.[11]

Exhaustive ozonolysis of methyl levopimarate (IIb) has been reported[6] to afford the keto-acid ester (IVa) in yields varying from 20-45%. However, when ozonolysis was conducted in ethyl acetate at -70° and the product oxidized with Jones reagent,[8] the acid fraction was obtained in consistent yields of 60-70%. The acid fraction crystallized to afford the pure keto-acid ester (IVa), m.p. 173-175°, but it was much more convenient to purify this product as the keto-diester (IVb), which was obtained in 57% yield as a pale yellow oil, $C_{17}H_{26}O_5$, ν max 1738 and 1710 cm.$^{-1}$, n.m.r. ($CDCl_3$), τ 6.29 and 6.32 (two carbomethoxyls), 7.5-7.9 [C(7)-methylene], 8.78 [C(4)-CH_3] and 9.24 [C(10)-CH_3].

Thus the present experimental modifications provide convenient methods for preparing the important intermediates (III) and (IV) in good yields. It is worth noting that when the Jones oxidation step is omitted, the yields of III and IV are considerably lower.

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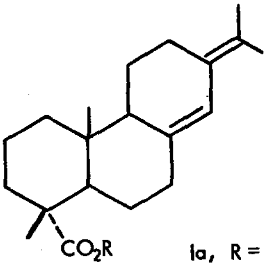
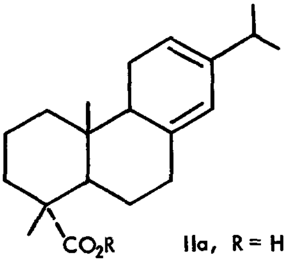


Ia, R = H

Ib, R = CH$_3$



IIa, R = H

IIb, R = CH$_3$

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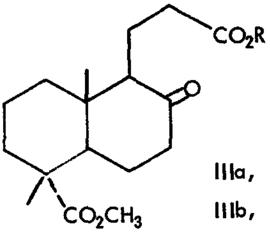
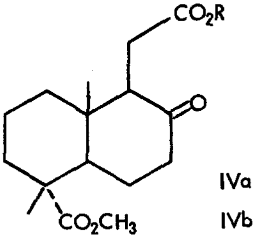


IIIa, R = H

IIIb, R = CH$_3$



IVa, R = H

IVb, R = CH$_3$

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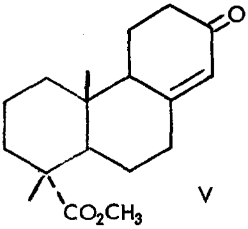
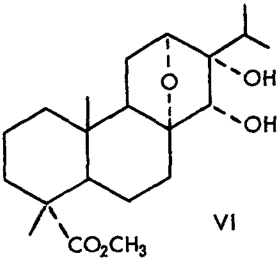
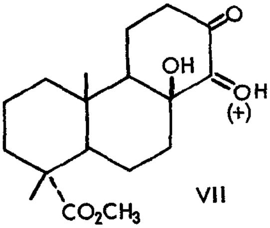


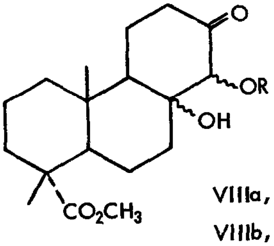
V



VI



VII



VIIIa, R = H

VIIIb, R = COCH$_3$