# The Stereochemistry at C-17 of Baccharis Oxide. The Synthesis of Baccharan-3β-ol and Baccharan-3-one

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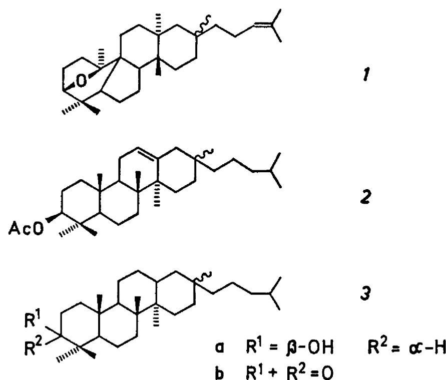
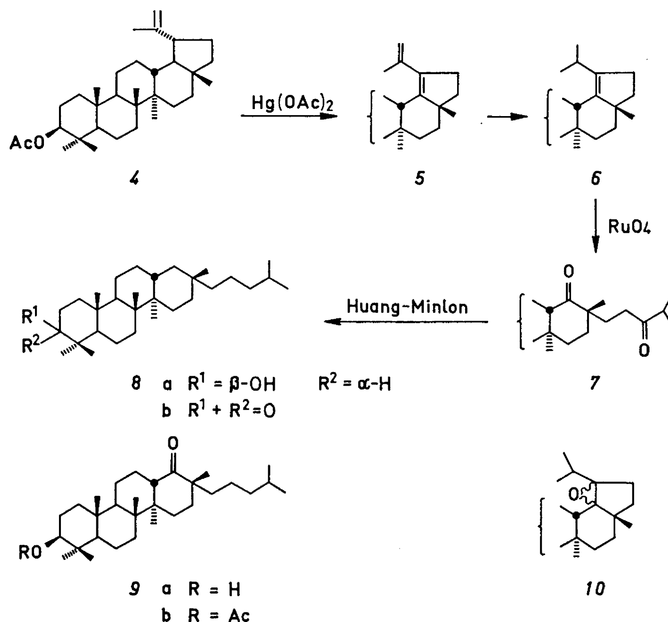



Recently the isolation and structure elucidation of a new triterpenoid, baccharis oxide (*1*), was described.[1] The ether (*1*) was converted by hydrogenation, $BF_3$-catalysed rearrangement and acetylation into (*2*), which furnished the alcohol (*3*a) by epoxidation, rearrangement and Mozingo reduction. The structure of (*1*) was deduced by spectrometry of (*1*), (*2*), (*3*a, b) and other derivatives, but in none of these compounds was the stereochemistry at C-17 established.

We have now synthetised the alcohol (*8*a) and the ketone (*8*b) by the route shown in the chart.

18,19-*Seco*lupan-3-one (*8*b) (from *8*a by Jones oxidation) was found to be identical with baccharan-3-one (*3*b) (mixed m.p., TLC, and mass spectra) when compared with an authentic sample. Synthetic 18,19-*seco*lupan-3β-ol (*8*a) has m.p. 163°C, $[\alpha]_D$ +7.5° (lit.[1] for baccharan-3β-ol (*3*a) m.p. 162–163°C, $[\alpha]_D$ +12°). Direct comparison of the two alcohols (*3*a and *8*a) was not possible, but their mass spectra are virtually identical. Thus the compounds (*8*a, b) establish the stereochemistry at C-17 in baccharis oxide (*1*) itself.

Although all the intermediates involved in the transformation of lupenyl acetate



(*4*) into baccharan-3$\beta$-ol (*8*a) are known compounds, certain aspects of their synthesis deserve mention. The dehydrogenation of (*4*) into (*5*) is usually [2] effected by a large excess of mercuric acetate (12 g per 1 g of lupenyl acetate) in acetic acid (reflux 5 h). We found that a reasonable yield of (*5*) (60 %) can be obtained with a smaller amount of mercuric acetate (4.5 g per 1 g of lupenyl acetate) in propionic acid (reflux 30 min).

The oxidation of the dihydroacetate (*6*) [3] (in mixture with the tetrahydroacetate) in $CCl_4$ with ruthenium dioxide and aqueous sodium metaperiodate leads to the diketone (*7*).[2,4] Ozonisation with aqueous work-up,[5] on the other hand, gives the epoxide (*10*), m.p. 238°C, $[\alpha]_D + 40°$, which is probably the same as that obtained by treatment of (*6*) with perbenzoic acid.[2,4] This is a further example of epoxide formation in the ozonolysis of highly hindered olefins.[6-9]

For the Huang-Minlon reduction of the highly hindered C-18 carbonyl in the diketone (*7*), anhydrous hydrazine and prolonged refluxing time is required. Only 10 % of baccharan-3$\beta$-ol (*8*a) is produced, the main product being the ketone (*9*a),* m.p. 199–200°C, $[\alpha]_D + 31.9°$ ($c = 0.37$), $\nu_{max}$ (KBr pellet) 3450 and 1698 $cm^{-1}$; acetate (*9*b),* m.p. 184°C, $[\alpha]_D + 31°$ ($c = 1.58$), $\nu_{max}$ 1725, 1698 and 1245 $cm^{-1}$.

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* Both new compounds gave acceptable analyses. Melting points are uncorrected.

# Use of Flow Microcalorimetry for the Determination of Cholinesterase Activity and Its Inhibition by Organophosphorus Pesticides

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Recently a general analytical technique was described for the determination of enzyme activities by the use of flow microcalorimetry.[1] The present study is part of a project where the usefulness of this technique in pesticide research and related areas is explored.

The experimental procedure adopted consists simply of pumping an enzyme solution, or suspension, mixed with an excess of a suitable substrate, through the calorimetric cell. In the ideal case the kinetics of the process follows zero order for some time and there will be established a steady state heat effect signal. This is recorded as a voltage-time curve parallel to the instrument baseline. The baseline displacement is directly proportional to the heat effect and will thus provide a measure of the enzymatic activity under the conditions of the experiment.

In the earlier study [1] assay methods were described for several enzymes, including cholinesterase. In the present work the calorimetric technique has been used for a study of the inhibition of cholinesterase by the organophosphorus pesticide Dimefox. From the calorimetric results the inhibition rate constant was calculated.

*Experimental. Apparatus.* The flow microcalorimeter, a prototype to the LKB 10700-1 microcalorimeter, has been described in detail elsewhere.[2] The flow-through cell used for the present experiments was of the same design as those used in the commercial instruments.

Throughout the work the 10 $\mu$V range of a Keithley 150 B Microvolt Ammeter was used. The calorimetric signal was recorded by means of a Servogor RE511 recorder, 100 mV range. A calorimetric baseline shift ($\Delta$) of 1 mm corresponded to 0.05 $\mu$V being equivalent to 0.9 $\mu$W. The reaction mixtures were pumped through the calorimeter at a flow rate of 20 ml/h. All