Dry Ozonation of 3β, 28-Diacetoxylypane. A Comment on the Structure of a Pentacyclic Triterpenoid Lactone from *Dillenia indica* (Linn.)

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Recently dry ozonation — *i.e.* the ozonation of a substrate adsorbed on a carrier (e.g. silica gel) without solvent — has been found to be a valuable tool for functionalisation at an unactivated carbon. This oxygenation is often remarkably regioselective and stereospecific with retention of configuration. Usually oxidation at a tertiary carbon to give an alcohol is preferred but attack at secondary carbons may also occur.

Triterpenes are an interesting group for testing this functionalisation method due to their rigid stereostructure, to the environmental diversity of carbon centres, and to the opportunity of selective functionalisation within the fully saturated carbon skeleton — a tedious task by other means. In this field the dry ozonation of a friedelane hydrocarbon was very recently reported to yield compounds resulting from oxidation at secondary carbons. A higher selectivity is shown by substrates containing polar groups, which regulate the orientation of the molecule on the adsorbent and thus direct the spatial attack of ozone.

We now report that the dry ozonation of 3β,28-diacetoxylypane (1) on silica gel yields only one product (conversion ca. 10 %). Its IR spectrum showed the presence of a hydroxyl group and the $^1$H NMR spectrum revealed its tertiary nature. The protons at C-28 appeared at exceptionally low field in the $^1$H NMR spectrum indicating that the new hydroxyl is located in the neighbourhood of C-28.

The suitable tertiary positions on the $\beta$-face are at C-13 and C-19. The physical constants of the ozonation product are in rather good agreement with the known 19β-hydroxy compound 2 and differs clearly from those reported for the 13β-hydroxy compound 3. There was, however, some doubt about the correctness of the reported structure of 3 and therefore we have prepared both of these hydroxy diacetates 2 and 3 for identification. The 19β-hydroxy compound 2 is available from betulin (4) and the 13β-hydroxy compound 3 was prepared from the known ether 5 via NaIO$_4$ – RuO$_4$ oxidation to the lactone 6, LiAlH$_4$ reduction and racetylation to the hydroxy diacetate 3. The hydroxy diacetate from the dry ozonation of 3β,28-diacetoxylypane (1) was found to be identical (m.p., mixed m.p., $\lambda$$_D$, TLC, IR, $^1$H NMR, $m/e$) with the 19β-hydroxy derivative 2.


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The lactone 6 is reported to occur in Nature. The physical constants of our synthetic lactone 6 differ significantly, however, from those reported for the natural compound. The same applies to the hydroxy diacetate prepared from the natural lactone and 3 prepared from the synthetic lactone 6. Therefore at least the stereostructure of the natural compound appears to be at fault. The direct comparison of the acetates of the natural and synthetic lactone showed very similar TLC behaviour (a minor difference in colour after an H₂SO₄ spray was observed). The mass spectra showed significant differences but the overall similarity indicates that these two compounds are closely related possibly stereoisomers. Olefin 7 is reported as a major fraction in BF₃-induced dehydration of the hydroxy diacetate derived from the natural lactone. We have prepared the isomeric olefin 8 via a non-dehydrative route, and the physical constants for 7 and 8 are notably different. Thus the (19αH) configuration 9 is excluded for the natural lactone, although, less emphasis should probably be given to the dehydration result, as isomerisation reactions may intervene under the BF₃ conditions. If the 28→13 lupanolide structure is indeed correct for the natural lactone, the above arguments imply that this lactone has the highly crowded (18βH), (19βH) structure 10. An alternative possibility for the natural lactone is the 27→18 oxide structure 11.

Experimental. For general information see Ref. 6. The ¹H-NMR spectra were recorded in CDCl₃ solution and the IR spectra using KBr pellets.

Dry ozonisation of 3β,28-diacetoxylupane (1). 3β,28-Diacetoxylupane (1) (0.5 g) was dissolved in CH₂Cl₂ and silica gel (50 g) was added. The solvent was removed in vacuo and the silica saturated with ozone at −80 °C and then allowed to reach room temperature during 4 h. Extraction and chromatography on silica plates (CHCl₃ eluent) gave starting material and 3β,28-diacetoxy-19β-hydroxylupane (2) (0.05 g), m.p. (EtOH) 245 °C, [α]D +18° (c 0.9) (Ref. 2, m.p. 272–273 °C, [α]D +19°) ν 3520, 1735, 1715; δ 4.5 (1 H, m, 3 H), 4.4 (2 H, br. s, 28-CH₂); M⁺: 544.

The γ-lactone of 3β-acetoxy-13β-hydroxylupane-28-oic acid (6). 3β-Acetoxy-13β,28-epoxy-lupane 5 (5) (0.2 g) in CCl₄ (25 ml) and NaIO₄ (0.5 g) in H₂O (25 ml) and a catalytic amount of RuO₂ were shaken vigorously overnight. Work-up and crystallisation from EtOH gave the γ-lactone of 3β-acetoxy-13β-hydroxylupane-28-oic acid (6) (0.13 g) m.p. 240 °C, [α]D +1.2° (c 0.84); ν 1755, 1720; δ 4.5 (1 H, m), 2.05 (3 H, s); M⁺: 498.

3β,28-Diacetoxy-13β-hydroxylupane (3). Lactone 6 (0.1 g) was reduced with LiAlH₄ in boiling Et₂O, worked up and reacetylated by refluxing 10 min in Ac₂O (3 ml). 3β,28-Diacetoxy-13β-hydroxylupane (3) (0.05 g) crystallised on cooling m.p. 230 °C, [α]D −5° (c 0.5); ν 3520, 1730, 1725; δ 4.5 (1 H, m), 3.95 and 4.7 (1 H, d, J = 12 Hz), 2.05 (6 H, s); M⁺: absent, M⁺: −60 484.

3β,28-Diacetoxy-(18αH)-lup-13(18)-ene (8). 3β,28-Diacetoxy-lup-12,18-diene 6 (0.2 g) was hydrogenated over PdO (0.1 g) as reported previously for the corresponding lupane derivative. Work-up and crystallisation from EtOH gave 3β,28-diacetoxy-(19αH)-lup-13(18)-ene (8) (0.16 g) m.p. 166 °C, [α]D −43° (c 1.0); ν 1730, 1240; δ 4.5 (1 H, m), 3.95 (2 H, br. s), 2.8–2.1 (3 H, m) 2.05 (6 H, s); M⁺: 526.

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