

A New Example under Novel Conditions of Backbone Rearrangement of Steroids; Conversion of Methyl Lithocholates into Δ -Homoandrostane Derivatives

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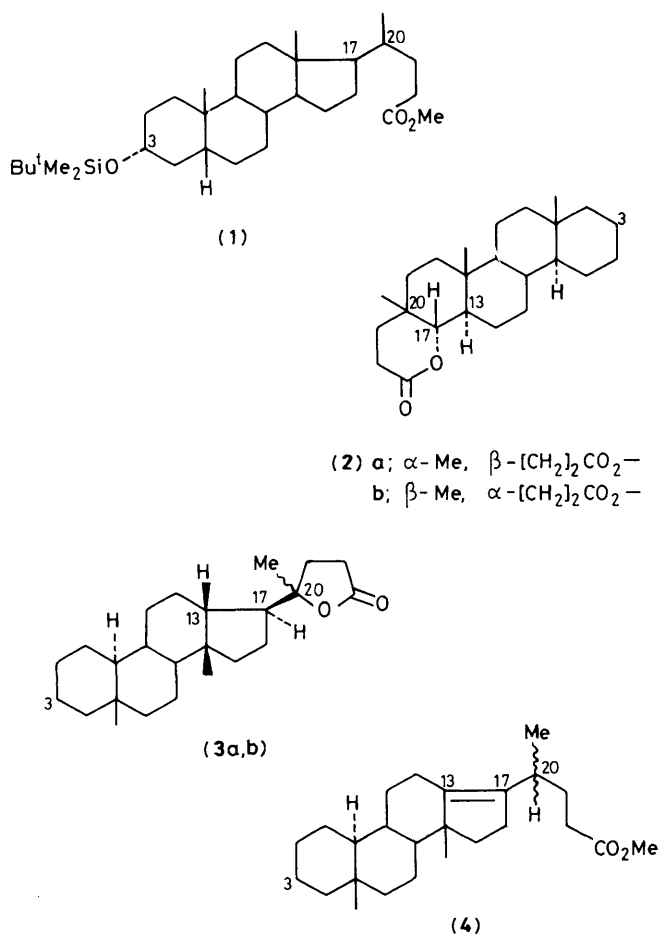
The backbone rearrangement of the silyl ether of methyl lithocholate (**1**) leads to Δ -homoandrostane epimeric lactones (**2**) in 40% yield.

This note reports the first backbone rearrangement observed in the lithocholic acid series,¹ under unusually mild conditions and ending in a novel manner, whereby the silyl ether of methyl lithocholate (**1**) can be transformed into Δ -homoandrostane derivatives.

Treatment of a solution of (**1**) in hexafluoropropan-2-ol-

methylene dichloride (1 : 1), with trifluoroacetic anhydride (3 equiv.) at 0 °C over 18 h, gave the Δ -homoandrostane lactones (**2a**) and (**2b**) (45 : 55) in 46% yield[†] (isolated: 39%), and the lactones (**3a**) and (**3b**) (55 : 45) in 11% yield[†] (isolated: 9%).

[†] Determined by capillary g.l.c.



(2a): m.p. 231–234 °C (EtOH), $[\alpha]_{546}^{22} -48.7^\circ$; (2b): m.p. 185–191 °C, $[\alpha]_{546}^{22} +9.7^\circ$. The structures (of the D-homo

ring and the δ -lactones) and the configuration assignments of (2a) and (2b) were determined by n.m.r. spectroscopy (¹H and ¹³C).[‡] The structures of the lactones (3a) and (3b) were also determined by spectroscopic means (¹H and ¹³C n.m.r., i.r.), but their relative configurations were not determined. (3a) or (3b): m.p. 187.5–190 °C, $[\alpha]_{546}^{27} +29.6^\circ$.

It is noteworthy that if the reaction is performed in methylene dichloride alone, the main product is a mixture of the methyl 20(*R*) and 20(*S*) diacholenates (4) in 41% yield[†] (isolated 30%),^{2,3} which were transformed into lactones (2) and (3) by protonation (HF, SbF₅) in CH₂Cl₂. This result shows that these lactones are formed from interactions between the carboxylate group and the positive centres at the C(20) or C(17) positions, arising from different rearrangements.[‡]

Furthermore, when the reaction is performed in CH₂Cl₂, work-up after 5 min shows that the first fast step in the reaction pathway is the formation of methyl Δ^2 - and Δ^3 -cholenate. Evidently in this reaction medium, the transformation of methyl Δ^2 - and Δ^3 -cholenate into (4) is a slow process.

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References

- 1 The only other example of a backbone rearrangement in the Δ^2/Δ^3 series was reported in D. M. Tal, E. Keinan, and Y. Mazur, *Tetrahedron*, 1981, **37**, 4327, but no yields were given.
- 2 By analogy with 'diacholestene' according to the nomenclature proposed for backbone rearranged chol-13(17)-enes in A. Ensminger, G. Joly, and P. Albrecht, *Tetrahedron Lett.*, 1978, 1575.
- 3 D. M. Tal, H. E. Gottlieb, C. Ben-Ari, and Y. Mazur, *Tetrahedron*, 1981, **37**, 4331.

[‡] Details of structure determination and mechanistic aspects will be published elsewhere in a full paper.