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Acid-catalyzed Reactions of 3β -Acetoxy- 9α -hydroxy-11-keto- 5α -lanostane: $19(10 \rightarrow 9\beta)abeo$ -lanostenes¹

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OLIVER E. EDWARDS and ZDSISLAW PARYZEK. Can. J. Chem. 53, 3498 (1975). Acid-catalyzed dehydration of 3 β -acetoxy-9-hydroxy-11-keto-5 α -lanostane gave under varying conditions 3 β -acetoxy-11-keto-14(13 \rightarrow 12)*abeo*-lanost-12-ene, or the two cucurbitanes 3 β acetoxy-11-keto-19(10 \rightarrow 9 β)*abeo*-lanost-1(10)-ene and the corresponding 5(10)-ene.

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La déshydratation, en milieu acide, de l'acétoxy-3 β hydroxy-9 oxo-11 5 α -lanostane conduit, suivant les conditions, à l'acétoxy-3 β oxo-11 14(13 \rightarrow 12) *abéo*-lanostène-12 ou aux deux cucurbitanes acétoxy-3 β oxo-11 19(10 \rightarrow 9 β) *abéo*-lanostène-1(10) et l'alcène correspondant avec une double liaison en 5.10.

[Traduit par le journal]

Attempts have been made without success in several laboratories to convert lanostane derivatives, by processes involving cationic carbon, into cucurbitanes (1-3).³ We now report the first such transformation.

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The ketol 1, m.p. 183 °C, $[\alpha]_D$ 63° (c, 1.3 in chloroform), v_{max} (CHCl₃) 1712, and 1691 cm⁻¹, was prepared from 3β-acetoxylanost-9(11)-ene(4) via the 9 α ,11 α -diol, m.p. 164 °C. Its structure was confirmed by thionyl chloride – pyridine de-hydration to 3β-acetoxy-11-keto-5 α -lanost-8-ene. Under Westphalen dehydration conditions (sulfuric acid in acetic acid – acetic anhydride mixture at room temperature), 1 gave two olefinic products A and B in 19 and 15% yields respectively.



¹Issued as NRCC No. 14960.

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³The multifunctional cucurbitacins are derivatives of $19(10 \rightarrow 9\beta)abeo$ -lanostane. We suggest that this skeleton be named cucurbitane.



Compound A was a trisubstituted olefin, m.p. 84 °C, with v_{max} (CHCl₃) 1725, and 1685 cm⁻¹. The following evidence established its structure as **2** (R = Ac). It gave ¹H n.m.r. signals at δ 5.14 (br s, 1H), 4.84 (dd, 1H), a pair of doublets (2H, $\Delta\delta$ 23 Hz, J = 15 Hz) centered at δ 2.59, and a 3H singlet at δ 2.06. It could be hydrolyzed to an alcohol (**2**, R = H) with c.d._{max} 300 nm, $\Delta\epsilon$ 4.65 which gave ¹³C n.m.r. signals at 214, 139, and 119.6 p.p.m. The action of pyridine on the tosylate of this alcohol produced a homo-annular diene **3**, m.p. 115 °C, v_{max} (CHCl₃) 1695 cm⁻¹, M⁺ 424, λ_{max} 270 nm, ϵ 6450. Its ¹H n.m.r. spectrum had a complex group of signals (3H) between δ 5.2 and 5.8.

Oxidation of 2 (R = H) with Jones' reagent gave an amorphous diketone with v_{max} (CHCl₃) 1710 and 1690 cm⁻¹. This gave ¹H n.m.r. signals at δ 5.26 (m, 1H), 2.82 (m, 2H), and 2.62 (pair of doublets, 2H, $\Delta\delta$ 27 Hz, J = 14 Hz). Double irradiation showed that the olefinic proton was coupled with the methylene resonating at δ 2.82. The action of selenium dioxide in hot

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wet dioxane on the diketone produced pale yellow needles of a compound with possible structure **4**, m.p. 205 °C, λ_{max} 370 nm, ε 2340, ν_{max} 1690, 1646, and 1623 cm⁻¹, ¹H n.m.r. signals at δ 7.18 (1H) and 2.6 (2H).

Compound B was a tetrasubstituted olefin, m.p. 149 °C whose structure proved to be **5**. It had v_{max} 1725 and 1690 cm⁻¹, ¹H n.m.r. signals at δ 4.65 (1H), 2.55 (2H), and 2.05 (3H), ¹³C n.m.r. signals at 216, 180, 134, and 128 p.p.m. and c.d._{max} 300 nm, $\Delta\epsilon$ 7.5. On hydrolysis this gave an amorphous keto alcohol ($\Delta\epsilon$ 8.0 at 300 nm) which could be oxidized to an amorphous diketone with v_{max} 1712 and 1693 cm⁻¹. This diketone was oxidized by selenium dioxide in hot wet dioxane to a mixture of a homoannular dienone **6** (36%) (λ_{max} 325 nm, ϵ 4750, v_{max} 1690, 1660, and 1625 cm⁻¹) and a 16% yield of **4** thus relating it to A.



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The action of anhydrous *p*-toluenesulfonic acid in hot benzene on B gave among other products a 20% yield of an amorphous aromatic compound with v_{max} (CHCl₃), 1690 cm⁻¹; λ_{max} 271 nm (ɛ 178), 263 nm (ɛ 220) with intense end absorption. It had ¹H n.m.r. signals at δ 7.08 (s, 3H), 2.7 (t, 2H), 2.53 (s, 2H), 2.30 (s, 3H), and 2.23 (s, 3H). Its mass spectrum had M⁺ 424 and intense peaks at m/e 317, 304, and 291 corresponding to loss of the aromatic ring and one or two extra carbons respectively. The use of Eu(dpm)₃ shift reagent caused rapid movement of both the signal from a methylene group which was originally at $\delta 2.5$ (finally transforming it into a pair of doublets with $\Delta\delta$ 42 Hz and J =16 Hz (-CH₂CO-)) and a broad signal for a third hydrogen (CHCO). A 3H doublet (CH₃-

CHCO) moved with moderate speed as the shift reagent concentration increased. This evidence is consistent with structure 7, formed in a mechanistically plausible way from a protonated species such as 8.



24-Deoxybryogenin acetate 9 was prepared from bryogenin. It had m.p. 140 °C, c.d._{max} 298 nm, $\Delta\epsilon$ 6.6. When treated with *p*-toluenesulfonic acid in benzene as for B it gave a 60% yield of 7 thus interrelating A and B with an authentic cucurbitacin.

As far as we are aware, A and B are the first $19(10 \rightarrow 9\beta)abeo$ -lanostane derivatives to be obtained by partial or total synthesis.

The action of *p*-toluenesulfonic acid hydrate in hot benzene on **1**, followed by alkaline hydrolysis, gave among other products the *C*nor-*D*-homo derivative **10** (3β-hydroxy-11-keto-14(13 \rightarrow 12)*abeo*-lanost-12-ene). It had m.p. 159 °C, v_{max} (CH₂Cl₂) 1620 and 1695 cm⁻¹, and λ_{max} 255 nm (ε 15 000) and 356 nm (ε 100). Its ¹H n.m.r. spectrum contained a 3H singlet at δ 2.1. This appears to be the first report of a *C*-nor-*D*homo lanostane derivative.

We thank Mr. R. Kolt for valuable technical assistance, Dr. R. E. Williams for the circular dichroism measurements, and Dr. I. C. P. Smith and co-workers for the ¹³C n.m.r. spectra.

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