The Atisane → Aconane Conversion: Stereospecific Skeletal Rearrangements during the Pyrolysis of Epimeric Toluene-*p*-Sulphonates†

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A POSSIBLE biosynthetic relationship between the atisine and aconitine–lycoctonine groups of diterpene alkaloids was suggested independently by Valenta and Wiesner[1] and by Cookson and Trevett in 1956.[2] In essence, both schemes consist of the two steps depicted in (I) → (II): (a) Wagner–Meerwein rearrangement of a C_{19} (loss of C-17 of atisine) intermediate (I) derivable from atisine, leading from a 6–6 to a 7–5 B/C ring system; (b) formation of the C-7 → C-20 bond by Mannich addition. The order of steps (a) and (b) might be reversed. A re-evaluation[3,4] of the mechanism which generates the well-known "pyro" compounds in the aconitine series, suggests a modification of the original Wiesner–Cookson hypothesis. According to this, the intermediate alkene (III) participates in a Prins-type addition

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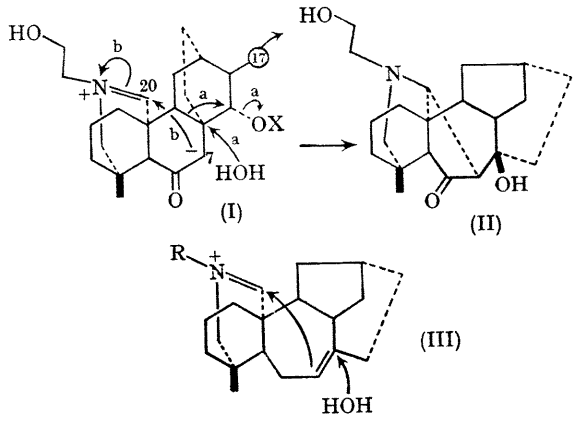
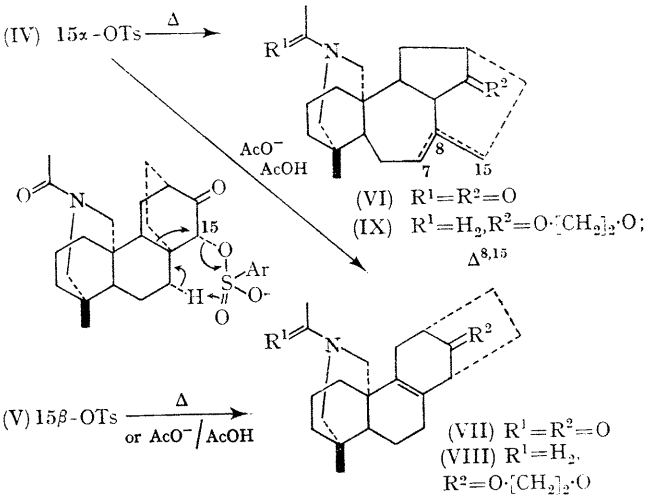
(III; arrows), which generates the C-7–C-20 bond and a C-8 hydroxy-group of the correct configuration. We have for practical reasons chosen this model as the basis of our experiments.



Acetolysis of the α- and β-*p*-tolylsulphonyloxyketones (IV) and (V) (obtainable from atisine in eleven and seven steps, respectively; all intermediates characterised), was expected to lead to the rearranged olefinic ketones (VI) and (VII), respectively, as major products. We expected that the carbonyl group (which replaces C-17 of atisine by an oxygen function invariably found at this position in the aconite alkaloids) adjacent to the departing ester residue would facilitate a concerted and therefore stereospecific rearrangement. On the contrary, the sole observed acetolysis (AcO⁻–AcOH; 150°/48 hr.) product from *both* esters (IV) and (V) was the unsaturated ketone (VII) [ν_{max} (CCl_4) 1760 cm.$^{-1}$; no vinyl H in n.m.r.], characterised as the hydriodide, m.p. 228—232°, and hydrobromide, m.p. 250° (sublimes), of the derived ethylamine acetal (VIII). Analogous observations in experiments directed towards similar objectives, were reported[5] soon after we had made these discoveries.

By contrast, *pyrolysis* (550°; 0·5 mm. N_2) of the toluene-*p*-sulphonates (IV) and (V) led stereospecifically (g.l.c.) to the olefinic ketones (VI)‡ [ν_{max} (CCl_4) 1760 cm.$^{-1}$; τ 4·73, 1H, m], and (VII) in 75—80% yields estimated by g.l.c. The constitution and stereochemistry of (VI)‡ were confirmed by an *X*-ray analysis (see accompanying Communication) of the hydriodide of (IX). The corresponding acetates survived the pyrolytic conditions unchanged.



The stereospecific pyrolytic rearrangements which we have observed can be visualised as proceeding through a seven-membered transition state[6,7] [shown for ease of illustration for the case of (IV; arrows) proceeding to (VI; Δ⁷)]. The available stereochemistry in the two cases studied (C–H and C–O bonds broken in the reaction are 1,3-diaxial and both anti-periplanar to the bond migrating from the intermediate carbon) may be optimal for such pyrolytic rearrangements.

The final step in the construction of the aconane skeleton, C-7 → C-20 bond formation, has already been accomplished in principle[3,4] and is currently receiving our experimental attention, as is the necessary prior isomerisation of the double bond from the 8(15) to the 7(8) position.

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‡ It is not clear at present whether the pyrolysis product contains minor amounts of the Δ⁷-isomer.

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