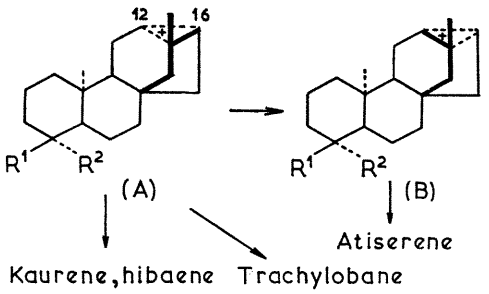
# Biogenetic-like Rearrangements of Isosteviol Derivatives: π-Route to the Atiserene System

By ROBERT M. COATES* and EDWARD F. BERTRAM

(*Department of Chemistry and Chemical Engineering, University of Illinois, Urbana, Illinois* 61801)

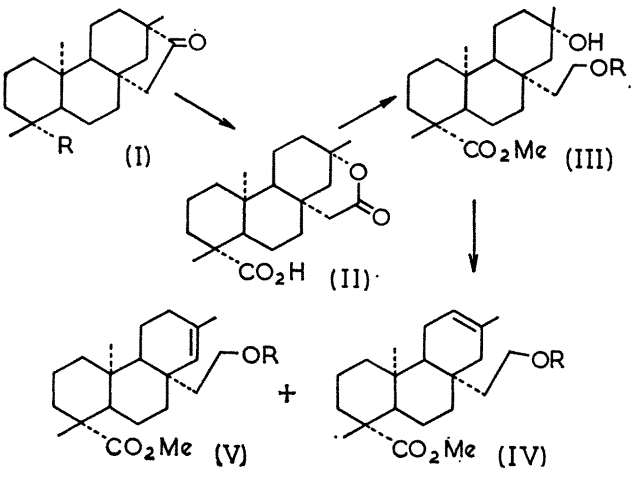
*Summary* Solvolytic cyclization of the unsaturated tricyclic toluene-*p*-sulphonate (IV) affords the atiseran-13-ol derivative (VI), which at higher temperature undergoes Wagner–Meerwein rearrangement to the hibaan-12-ol isomer (IX).

THE two bridged ions (A) and (B)† provide a biogenetic rationalization for a number of known tetracyclic diterpene skeletons.[1] We[2a] and others[2b,3] have been interested in examining the carbonium ion rearrangements represented by these processes *in vitro*. Most of the previous studies[2,3] have dealt with rearrangements originating from an ion of type (A). We have now used the π-route[4] in order to gain direct entry to the hydrogen-shift isomer, ion (B), presumably the immediate biogenetic precursor of atiserene and atisine.




† Wenkert's original biogenetic scheme[1a] employs a face-protonated, trachylobane-type intermediate. Since the evidence now seems to weigh against face-protonated nortricyclene intermediates in norbornyl rearrangements (*cf.* C. J. Collins and M. H. Lietzke, *J. Amer. Chem. Soc.*, 1967, **89**, 6565), we prefer the bridged-ion representation shown.

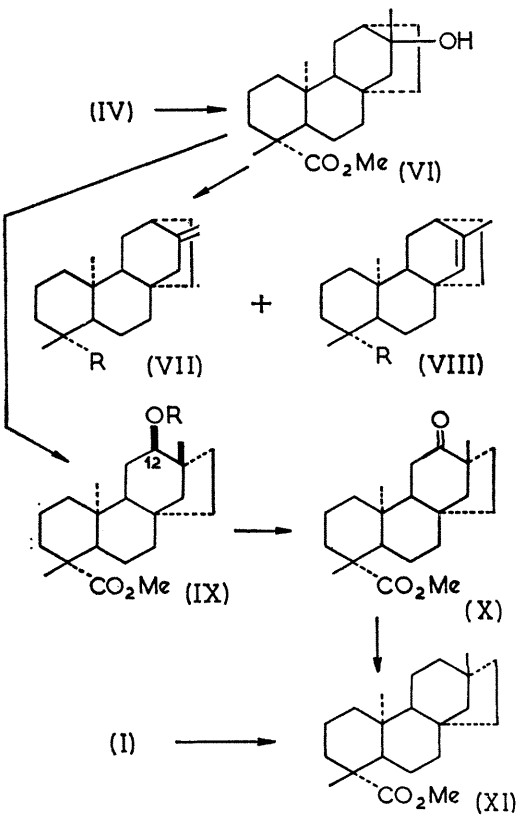
The toluene-*p*-sulphonate (IV; R = Ts) was prepared from isosteviol (I; R = $CO_2H$) as outlined in the Scheme. Baeyer–Villiger oxidation of (I) with buffered peroxyacetic acid produces the lactone acid (II), [m.p. 264—265°, $\tau$ 6·89 and 7·99 (AB doublet, $J$ 19 Hz.)] in 89% yield. Partial reduction with $LiAlH_4$ in tetrahydrofuran, followed by esterification, furnished the diol ester (III; R = H) (86%, m.p. 220—221°). The monoacetate (III; R = Ac), (m.p. 145—145·5°), was dehydrated with thionyl chloride and collidine in methylene chloride to a 2 : 1 mixture of the endocyclic double-bond isomers (IV; R = Ac) ($\tau$ 4·67, $w_{\frac{1}{2}}$ 9 Hz.) and (V; R = Ac), ($\tau$ 4·90, $w_{\frac{1}{2}}$ 4 Hz).




SCHEME

Buffered formolysis of the toluene-*p*-sulphonate mixture (IV and V; R = Ts) left the $\Delta^{13}$-isomer unaffected while the $\Delta^{12}$-component was completely consumed. Alkaline hydrolysis of the product followed by column chromatography enabled a clean separation of unreacted (V; R = Ts) from the tertiary alcohol (VI), m.p. 148—148·5°. Dehydration of (VI) produced a mixture of the two olefin esters (VII; R = $CO_2Me$) [36%, m.p. 126—127°, $\tau$ 5·28 and 5·42 (qt., 1 H, $J$ 2 Hz.)] and (VIII; R = $CO_2Me$) [51%, m.p. 90—91°, $\tau$ 4·42 (br., 1H), 8·28 (d, 3H, $J$ 1·7 Hz.)], which were separately transformed into atiserene (VII; R = Me) [m.p. 81·5—82·5°, $[\alpha]_D^{23}$ −75° (lit.[5] m.p. 84—85°, $[\alpha]_D$ −74°)] and isoatiserene (VIII; R = Me), m.p. 58—58·5°, $[\alpha]_D^{23}$ −41° (lit.[5] m.p. 57—58°, $[\alpha]_D$ −40·5°). The i.r. and n.m.r. spectra of natural atiserene compare well with the spectra of (VII; R = Me) and the literature spectral data[5] for isoatiserene agree with those of (VIII; R = Me).

If (VI) is subjected to more vigorous formolysis, the secondary isomer (IX) is obtained, and isolated as its acetate (IX; R = Ac) [74%, m.p. 137—139°, $\tau$ 5·30 (m, 1H)]. The structure of (IX) follows from its conversion into the saturated ester (XI) *via* keto-ester (X) [m.p. 205—206°, $\nu_{max}$ (KBr) 1695 and 1720 cm.$^{-1}$].




Presumably bridged ion (B) is an intermediate (or transition state) in the (IV) → (VI) → (IX) solvolytic reactions. The tertiary isomer is the result of kinetic control under mild conditions, while the thermodynamically more stable secondary product (IX) is formed at higher temperature.[6] There seems[2] to be a reluctance to undergo the crossover rearrangement (12 ⇌ 16 hydride shift) between (A) and (B). However, in the absence of the C-13 methyl group[3] and in the related bicyclo-octane derivatives[7] such hydride rearrangements occur in solvolysis reactions.

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[1] (a) E. Wenkert, *Chem. and Ind.*, 1955, 282; (b) W. B. Whalley, *Tetrahedron*, 1962, **18**, 43; (c) R. McCrindle and K. H. Overton, *Adv. Org. Chem.*, 1965, **5**, 47.
[2] (a) R. M. Coates and E. F. Bertram, *Tetrahedron Letters*, 1968; 5145; (b) Pertinent references cited therein.
[3] R. A. Appleton, P. A. Gunn, and R. McCrindle, *Chem. Comm.*, 1968, 1131.
[4] *cf.* H. L. Goering and G. N. Fickes, *J. Amer. Chem. Soc.*, 1968, **90**, 2856.
[5] A. H. Kapadi, R. R. Sobti, and S. Dev, *Tetrahedron Letters*, 1965, 2729.
[6] See J. A. Berson in "Molecular Rearrangements" vol. I, ed. P. de Mayo, Wiley, New York, 1963, pp. 133—138.
[7] R. A. Appleton, J. C. Fairlie, R. McCrindle, and W. Parker, *J. Chem. Soc.* (*C*), 1968, 1716.