In Vitro Conversion of Labdadienols into Pimara- and Rosa-dienes

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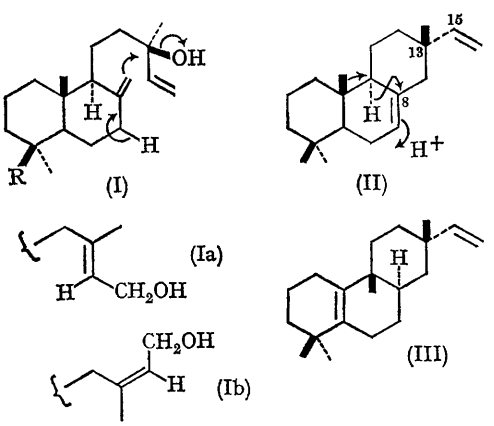
RUZICKA first suggested[1] that tricyclic diterpenoids of the pimarane group (II) are formed *in vivo* from bicyclic labdane-type (I) precursors. Further rearrangement can lead[2] (with or without the intervention of dienic intermediates) to the rosane group (III) which counts rosenonolactone[3] and rimuene[4] among its members.

In vitro demonstrations of the first suggestion are on record. The acid-catalysed cyclisation of manool (I; R = Me) to a tricyclic hydrocarbon was observed by Bory and Asselineau.[5] Edwards and Rosich have more recently established[6,7] that



agathadiol (Ia; R = CH_2OH) and manool are converted by formic acid into (*ca.* 1 : 1) mixtures of the corresponding C-13-epimeric pimara-8,15-dienes (*cf.* ref. **2**). While *in vivo* incorporation of alcohol (Ia; R = Me) into rosenonolactone has been reported,[8] the *in vitro* formation of the rosane skeleton from bicyclic (or tricyclic) precursors has not been previously realised.

In search of a biogenetically-patterned synthetic route to rosane derivatives, we have subjected manool,† 13-epimanool,[9]† and the allylic primary alcohols (Ia; R = Me)[10]†‡ [τ **9·33, 9·21, 9·15,** 3H singlets; 8·34, 3H, s; 5·88, 2H, d; 4·62, 1H, t] and (1b; R = Me)†‡ [τ **9·33,** 9·21, **9·15,** 3H singlets; 8·28, 3H, s; **5·96,** 2H, d; 4·59, 1H, t], all potential progenitors of the same mesomeric cation, to acid-promoted dehydration [AcOH–H_2O–H_2SO_4 (83 : 10 : 7)[5] at 50°]. We find that the four labdadienols give product mixtures of essentially similar composition (g.l.c.) which varies with time. Cyclisation cannot therefore be concerted with formation of the cationic centre at C-13.

After 3 hr. the hydrocarbon fraction (60%) consisted predominantly (> 95%) of pimara-8,15-diene (II; Δ^8, 13α-Me) and its C-13 epimer (1 : 1·3), both isolated by preparative t.l.c. ($AgNO_3$–SiO_2) and indistinguishable [g.l.c.; g.c.–m.s. (LKB 9000) and n.m.r.] from the authentic dienes prepared[11] from pimaric and isopimaric acids respectively.

† G.l.c.-homogeneous on (a) 10% poly(ethylene glycol adipate); (b) 1% silicone elastomer 30; (c) 5% Apiezon L The same columns were used for g.l.c. comparisons throughout.

‡ (Ia) and (Ib) were obtained *via* oxidative rearrangement of sclareol (S. Bory and E. Lederer, *Croat. Chem. Acta*, 1957, **29**, 163).

The mixture of bicyclic trienes consisting of *cis*- and *trans*-biformene and sclarene (obtained[12] by $POCl_3$–pyridine on manool) accounted for less than 5% (g.l.c.) of the hydrocarbon fraction.

After 150 hr. under the same acidic conditions the two pimaradienes had been further transformed into a more complex mixture of isomeric hydrocarbons (g.c.–m.s.) (at least 8 major peaks on g.l.c.). Its analysis was simplified by separating the two C-13-epimeric series by subjecting isopimara-8,15-diene (II; Δ^8-isomer) (A), and its C-13 epimer (B) (obtained from the 3 hr. experiment) individually to the same acid conditions as before. Combination of the resultant g.l.c. traces essentially reconstituted the trace of the hydrocarbon mixture obtained from manool after 150 hr.

The hydrocarbon fraction from diene (A) furnished three major products of *M* 272: (i) the rosadiene (III)† (50%). Separated by preparative t.l.c., this showed in its n.m.r. spectrum only 3 vinyl protons (τ 3·9– 5·3; 3H, multiplets characteristic of the C-13 vinyl group) and four tertiary methyls [singlets at τ 9·16 (3H) and 9·07 (9H)]. It was indistinguishable by g.l.c. and g.c.–m.s. from the component of shorter retention time obtained[4a] when rimuene is epxosed to moist chloroform–hydrogen chloride. (ii) a diene (10%) identical (g.l.c.; g.c.–m.s.) with the component of longer retention time obtained from rimuene. Although its retention times† equal those of rimuene, the m.s. indicates at least one other isomer in admixture.

Diene (B) afforded the rosadiene (III; 13α-Me) (30% of hydrocarbon fraction) as one of four major peaks. It was identified by comparison with the antipode (obtained[13] from erythroxydiol Y) from which it was indistinguishable by g.l.c. and g.c.–m.s. The mass spectrum showed only minor intensity differences from that of its C-13 epimer (III). Isolation by preparative t.l.c. has been foiled by the presence of other major products of similar mobility. The hitherto unidentified major products are receiving attention.

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