Total Synthesis of the Sesquiterpenoid Ishwarane: Structure of Ishwarone

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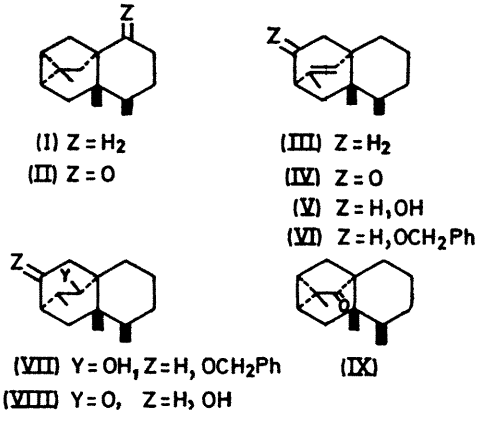
Summary A total synthesis of ishwarane has been completed, thus providing proof of the correctness of the structure assigned to ishwarane and corroboration of the structure assigned to ishwarone.

THE novel, biogenetically significant structures (I)[1] and (II)[2–4] were recently suggested for the sesquiterpenoids ishwarane and ishwarone, respectively, and their structural relationship was demonstrated by reduction of ishwarone to ishwarane.[1] More recently[5] we provided corroboration for these suggestions[1–4] by a total synthesis of isoishwarane (III),[2,4] a conversion product of ishwarone. We have now completed a total synthesis of ishwarane (I), thus providing proof of the correctness of structure (I) for ishwarane and further corroboration of structure (II) for ishwarone.

We have previously reported[5] the total synthesis of (IV) and we now describe its conversion into ishwarane (I). The enone (IV), on reduction with $LiAlH_4$, gave two epimeric alcohols (V) (m.p. 116° and 110°, 40% of each). One epimer (V) [m.p. 116°; i.r. (Nujol) 3300 cm^{-1}; n.m.r. ($CDCl_3$) δ 3·87 (br m, 1H), 5·63 (m, 1H)] was converted into the benzyl ether (VI) and then, by hydroboration in 82% yield, into a single alcohol (VII), m.p. 104°; i.r. (Nujol) 3465 cm^{-1}; n.m.r. ($CDCl_3$) δ 3·60 (br m, 1H), 3·88 (d, 1H), 4·46 (s, 2H), 7·27 (m, 5H). Oxidation of (VII) with Jones' reagent followed by hydrogenolysis of the benzyl ether afforded 75% of the keto-alcohol (VIII), m.p. 91°; i.r. (Nujol) 3410 and 1705 cm^{-1}; n.m.r. ($CDCl_3$) δ 4·05 (m, 1H). Treatment of the tosylate of (VIII) with methylsulphinyl carbanion[6] in Me_2SO at 60° for 2 h resulted in cyclization, in 71% yield, to the cyclopropyl ketone (IX) as an oil, λ_{max} (EtOH) 208 nm (ϵ 4000); i.r. (film) 1715 cm^{-1}; n.m.r. ($CDCl_3$) δ *ca.* 0·5 (m, 2H). Finally, Wolff-Kishner reduction of (IX) afforded racemic ishwarane (I)



(60%) which was identical (i.r. and n.m.r. spectra and behaviour on t.l.c. chromatograms) with an authentic sample of ishwarane obtained from natural sources.

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