Total Synthesis of Isoishwarane: Structures of the Sesquiterpenoids Ishwarane and Ishwarone

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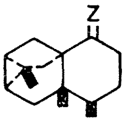
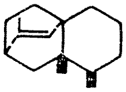
Summary A total synthesis of isoishwarane has been achieved, thus providing corroboration for the structures assigned to ishwarane and ishwarone.

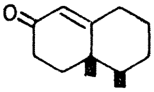
THE sesquiterpenoids ishwarane and ishwarone were very recently assigned the novel and biogenetically significant structures (I)[1,2] and (II),[3] respectively, and their structural relationship was revealed by conversion of ishwarone into ishwarane. During structural studies on ishwarone, it was converted into isoishwarane, to which structure (III) was assigned.[1] We have achieved a total synthesis of (III) and found it to be identical with isoishwarane, thus corroborating the structural assignments[1-3] to ishwarane and ishwarone.



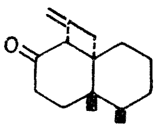
(I) Z = H_2
(II) Z = O



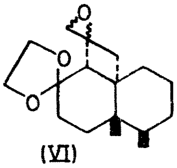
(III)



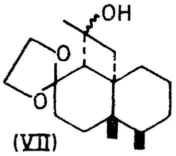
(IV)



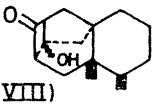
(V)



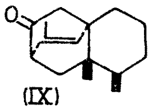
(VI)



(VII)



(VIII)



(IX)

Annelation of 2,3-dimethylcyclohexanone with methyl vinyl ketone and dehydration of the resulting keto-alcohol (m.p. 135°) gave the octalone (IV).[4] Photo-addition of allene to (IV)[5,6] afforded 75% of (V) as an oil, i.r. (film) 1695, 1660, and 880 cm^{-1}; n.m.r. ($CDCl_3$) δ 4·96 (m, 2H). The structure (V) assigned to the photo-adduct is based on the stereospecificity of the photo-addition.[5,6] Acetalization of (V) followed by epoxidation gave (VI) as a mixture of epimers, one of which was isolated (40%), m.p. 64—65°; the i.r. and n.m.r. spectra showed the absence of a keto-group and an olefinic bond. Reduction of (VI) (m.p. 64—65°) with $LiAlH_4$ gave the alcohol (VII) (83%), m.p. 115°; i.r. (Nujol) 3500 cm^{-1}; n.m.r. ($CDCl_3$) δ 1·28 (s, 3H). Treatment of (VII) with aqueous hydrochloric acid in tetrahydrofuran resulted in deacetalization and conversion into a crystalline mixture of epimers (VIII) (97%), one epimer of which was isolated, m.p. 139·5°, i.r. (Nujol) 3300 and 1700 cm^{-1}. The rearrangement of (VII) to (VIII), for which there is ample precedent,[6] was expected. Dehydration of (VIII), either as the pure epimer (m.p. 139·5°) or as a mixture of epimers, gave (IX), i.r. (film) 1725 and 1650 (weak) cm^{-1}; n.m.r. ($CDCl_3$) δ 1·81 (d, 3H), 2·80 (m, 1H), 5·88 (m, 1H). Finally, Wolff–Kishner reduction of (IX) afforded racemic isoishwarane (III) which was identical (i.r. and n.m.r. spectra) with an authentic sample derived from natural sources.

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[2] T. R. Govindichari, K. Nagarajan, and P. C. Parthasarathy, *Chem. Comm.*, 1969, 823.

[3] T. R. Govindichari, P. A. Mohamed, and P. C. Parthasarathy, *Tetrahedron*, 1970, **26**, 615.

[4] *Cf.* E. Piers, R. W. Britton, and W. De Waal, *Canad. J. Chem.*, 1969, **47**, 4307.

[5] K. Wiesner, L. Poon, I. Jirkovsky, and M. Fishman, *Canad. J. Chem.*, 1969, **47**, 433 and references cited.

[6] R. W. Guthrie, Z. Valenta, and K. Wiesner, *Tetrahedron Letters*, 1966, 4645.