Total Synthesis of Sesquicarene

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Summary Sesquicarene (Ia) has been synthesized from farresol by two separate routes, both involving intramolecular carbenoid addition as the key step.

SESQUICARENE (Ia), an isoprenylogue of the well known monoterpene Δ^2 -carene, represents a new structural type among sesquiterpenes.^{1a} The important plant sex hormone serenin has recently shown to be a dihydroxylated version (Ib) of sesquicarene.^{1b} We now report two separate syntheses of sesquicarene originating from farnesol.[†]

Geranylacetone (III) was obtained by retro-aldolization² of farmesal and reduced to the carbinol (IVa). The corresponding toluene-*p*-sulphonate (IVb) affords a mixture of the nitrile (IVc) 46%, ν_{max} 2210 cm.⁻¹ and the isonitrile (IVd) 11%, ν_{max} 2110 cm.⁻¹ upon reaction with an excess of sodium cyanide in dimethyl sulphoxide at 59°. Alkaline hydrolysis of (IVc) produced the liquid carboxylic acid (IVe) 93%, amide m.p. 76·5–77·5° from which the diazo-ketone (IVf) ν_{max} 2080 cm.⁻¹ was obtained by

successive treatment with oxalyl chloride and diazomethane. Copper powder in tetrahydrofuran effected cyclization of (IVf) to a 1:1 mixture of the two sesquicarone isomers, (\pm) -(II) 54%, ν_{max} 1670 cm.⁻¹, δ C-7 Me, *cis* 1.09, *trans* 1.20.³ Equilibration, as expected,⁴ enriched the proportion of the *trans*-epimer to *ca.* 80%.

Pyrolysis of synthetic sesquicarone toluene-p-sulphonyl hydrazone (V) m.p. 99—100° as its sodium salt in diglyme⁵ at 140° furnished a mixture of two hydrocarbons (71%). The major product (VI) 53%, ν_{max} 3300, 2100 cm.⁻¹, δ 1·17 (d, 3H, J 7 Hz), 1·87 (d, 1H, J 2·2 Hz.) is the result of



† An independent synthesis of sesquicarene has recently been reported: E. J. Corey and K. Achiwa, Tetrahedron Letters, 1969, 1837.

fragmentation⁶ while the minor isomer is sesquicarene (Ia) (15%). The i.r., n.m.r., and mass spectral data of synthetic (\pm) -(Ia) are in good agreement with the literature values for the natural product.¹

A direct, though inefficient, synthesis of sesquicarene can be accomplished by copper-catalysed cyclization of farnesal toluene-p-sulphonylhydrazone (VII, cis,trans + trans,trans) in the presence of sodium hydride. After chromatography on silver nitrate-silica gel, (Ia) was obtained in 5.3% yield. The intramolecular addition appears to be at least partially specific since the yield diminished to 1.5%when the trans, trans-(VII) was used.

As well as confirming the gross structure of sesquicarene, these syntheses also establish unequivocally the stereochemistry of the natural product at position 7 since farnesol



from commercial sources is known to have a trans-configuration about the central 6,7-double bond.8



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