Stereoselective Synthesis of α-Bulnesene

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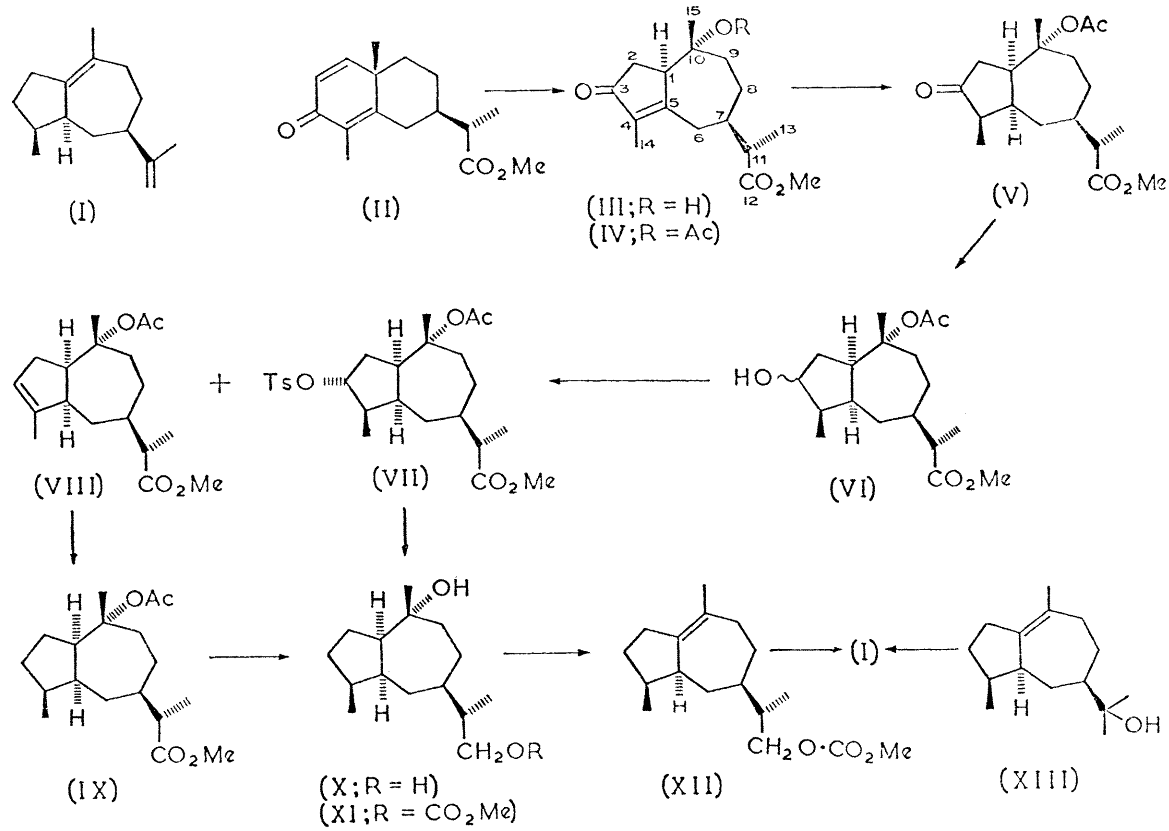
Summary The described stereoselective synthesis of the sesquiterpene α-bulnesene fully corroborates the structure and stereochemistry assigned to this compound and indicates a general approach to the synthesis of guaiane-type sesquiterpenes.

ALTHOUGH the number of known naturally occurring guaiane-type sesquiterpenes has increased rapidly over the past few years,[1] relatively few reports[2] have been concerned with the total synthesis of these compounds. Structurally, one of the simplest members of the guaiane class of sesquiterpenes is α-bulnesene (formerly called δ-guaiene), a $C_{15}H_{24}$ hydrocarbon which has been isolated from a number of different essential oils[1c] and which has been shown[3] to possess the structure and stereochemistry depicted in (I). We report here the stereoselective total synthesis of α-bulnesene(I).

The keto-ester (II),[4] of known absolute stereochemistry, gave, upon irradiation[5] in 45% aqueous acetic acid,† a 79% yield of the substituted hydroazulene (III) [b.p. 175°/0·2 mm.; $[\alpha]_D^{25}$ + 88·5° (*c* 0·1 in methanol). Acetylation (hot acetic anhydride, sodium acetate) of (III), followed by hydrogenation (ethanol, Pd–C) of the resulting acetate (IV), afforded in 63% overall yield the keto-diester (V), an oil. The o.r.d. curve of compound (V) showed a strong negative Cotton effect (*a* = − 232), an



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† A Hanovia 450W high-pressure mercury lamp and a Pyrex filter were employed.

observation which completely corroborated the stereochemical assignment.[6]

Reduction of the ketone (V) with sodium borohydride in methanol gave a mixture of epimeric alcohols (VI) [b.p. 130—140° (bath temperature)/0·2 mm.] which, upon treatment with toluene-*p*-sulphonyl chloride in dry pyridine gave the tosylate (VII) [20% yield] and the olefin (VIII) {55% yield; $[\alpha]_D^{23} + 74{\cdot}5°$ (c 0·4 in methanol)}. Although hydrogenation of olefin (VIII) over Adams catalyst gave a mixture of epimers, hydrogenation of (VIII) in benzene in the presence of the homogeneous catalyst tris(triphenylphosphine)chlororhodium[7] was completely stereoselective and afforded, in 85% yield, the diester (IX) [b.p. 130° (bath temperature)/0·2 mm.]. Lithium aluminium hydride reduction of (IX) gave a quantitative yield of the crystalline diol (X) {m.p. 100—102°; $[\alpha]_D^{22} - 32{\cdot}5$ (c 0·6 in methanol)}. The diol (X) could also be obtained in fair yield by lithium aluminium hydride reduction of the diester tosylate (VII).

Treatment of the diol (X) with methyl chloroformate in dry pyridine, followed by dehydration (thionyl chloride in pyridine) of the resulting monocarbonate (XI) afforded, in good yield, the olefin (XII).‡ Pyrolysis of the latter at 400° gave a mixture of olefins, the major component of which exhibited a g.l.c. retention time identical with that of α-bulnesene. Isolation of this component by preparative g.l.c. gave pure α-bulnesene (I) which exhibited spectra (i.r., n.m.r.) and g.l.c. retention times identical with those of authentic α-bulnesene, obtained by dehydration (thionyl chloride, pyridine) of authentic bulnesol (XIII). It should be noted that synthetic and authentic α-bulnesene also gave identical negative plain o.r.d. curves, thereby establishing the absolute configuration of the latter compound.

All compounds described showed spectral properties in accordance with the structures assigned.

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‡ This compound was contaminated with small amounts of two double-bond isomers.

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