Revised Structure and Absolute Configuration of the Sesquiterpene (+)-Bazzanene

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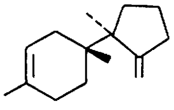
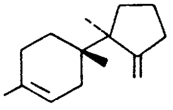
Summary A previous assignment of the structure of (+)-bazzanene is revised based on chemical correlation with (+)-trichodiene (II); the absolute configuration has been determined to be as shown in structure (I), a diastereoisomer of (+)-trichodiene.

In a previous investigation on terpenoids of the liverworts (*Hepaticae*), we isolated a novel bicyclic sesquiterpene hydrocarbon, bazzanene, $C_{15}H_{24}$; $[\alpha]_D$ +48·0°, from the leafy liverwort, *Bazzania pompeana*, and presented a gross structure for it based on chemical and spectral evidence.[1] Since the proposed structure was inconsistent in some respects with a recent examination of the off-resonance ^{13}C n.m.r. spectrum, the structure of the hydrocarbon was reinvestigated in detail, resulting in a revision to structure (I) corresponding to a diastereoisomer of (+)-trichodiene (II), $C_{15}H_{24}$; $[\alpha]_D$ +21°, which has been isolated recently from the fungus *Trichosecium roseum* by Nozoe *et al.*[2] We report evidence for the revised structure and absolute configuration.

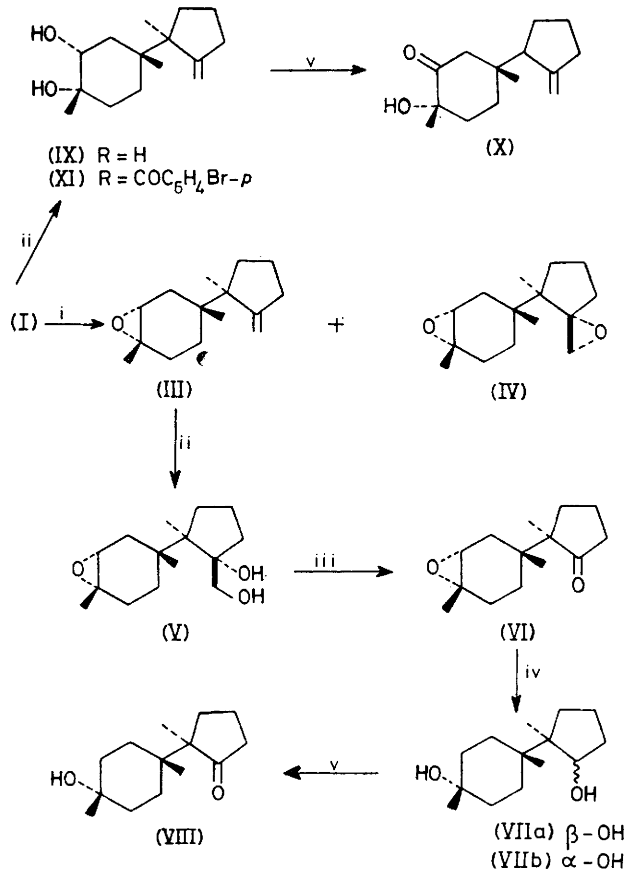


(I)



(II)

Although the off-resonance ^{13}C n.m.r. spectrum[†] of bazzanene [4 s (δ 153·4 and 132·4: olefinic; δ 50·2 and 36·7: aliphatic), 1 d (δ 120·4 olefinic), 7 t (δ 106·2: 1 olefinic; δ 38·9, 37·0, 32·3, 28·0, 27·8, and 23·4: 6 CH_2), and 3 Me q (δ 23·6, 23·4, and 17·6)] was consistent with the structure of trichodiene, the ^1H n.m.r. spectra of the two hydrocarbons were slightly different. Accordingly, (+)-bazzanene was oxidized with *m*-chloroperbenzoic acid in CH_2Cl_2 to give as the major product the monoepoxide (III), $C_{15}H_{24}O$ (M^+ 220); $[\alpha]_D$ +36·6°,[‡] containing an intact *exo* double bond and as a minor product the diepoxide (IV), $C_{15}H_{24}O_2$ (M^+ 236). The ^1H n.m.r. spectrum of the diepoxide (IV) was rather different from that of the diepoxide derived from trichodiene, but the spectra of the monoepoxide (III) resembled the spectra of trichodiene monoepoxide; its ^{13}C n.m.r. spectrum[†] [4 s (δ 159·1, 56·9, 49·8, and 36·0), 1 d (δ 58·9), 7 t (δ 106·8, 38·9, 37·0, 31·8, 26·6, 24·5, and 23·4), and 3 q (δ 23·7, 23·1, and 19·7)] was also reasonably explained by structure (III). As it was thought from the above results that (+)-bazzanene was a diastereoisomer of (+)-trichodiene, a chemical correlation was carried out as follows. Oxidation of the monoepoxide (III) with OsO_4 in pyridine for 30 h[3] gave the epoxy-glycol (V), $C_{15}H_{26}O_3$ (M^+ 254); $[\alpha]_D$ −22·0°, glycol fission of which with $NaIO_4$ afforded the nor-epoxy-ketone (VI), $C_{14}H_{22}O_2$ (M^+ 222); $[\alpha]_D$ +88·2°, containing a cyclopentanone unit. Reduction of (VI) with $LiAlH_4$ in ether afforded two epimeric diols, (VIIa), $C_{14}H_{26}O_2$ (M^+ 226); m.p. 95·5—96 °C; $[\alpha]_D$ −28·8°, and (VIIb), $C_{14}H_{26}O_2$ (M^+ 226); m.p. 98—99 °C; $[\alpha]_D$ +5·1°, in a 2:1 ratio. The major diol (VIIa) was oxidized with CrO_3 in pyridine into the hydroxy-ketone (VIII), $C_{14}H_{24}O_2$ (M^+ 224); $[\alpha]_D$ +95·7°. The i.r., ^1H n.m.r., and mass spectra of (VIII) thus obtained coincided in all respects with those of the hydroxy-ketone prepared from (+)-trichodiene *via* the corresponding nor-epoxy-ketone.[2]



Reagents: i, *m*-$ClC_6H_4CO_3H$ in CH_2Cl_2; ii, OsO_4 in pyridine; iii, $NaIO_4$; iv, $LiAlH_4$ in Et_2O; v, CrO_3 in pyridine.

Further, the o.r.d. and c.d. spectra of the epoxy-ketone (VI) {$[\phi]_{330}$ +5230 (max), $[\phi]_{312}$ 0, $[\phi]_{288}$ −4610 (min); $[\theta]_{312}$ +1380 (max) (in dioxan)} and the hydroxy-ketone (VIII) {$[\phi]_{330}$ +6190 (max), $[\phi]_{311}$ 0, $[\phi]_{288}$ −4620 (min); $[\theta]_{313}$ + 1310 (max) (in dioxan)} showed a positive Cotton effect.[4] These facts indicated that (+)-bazzanene and (+)-trichodiene had the same absolute configuration of the methyl-cyclopentane unit. Thus, the structure of (+)-bazzanene is the same as that of (+)-trichodiene except for the relative position of the *endo* double bond, *i.e.* the configuration of the tertiary methyl group in the cyclohexane ring.

Treatment of (I) with OsO_4 in pyridine for 1·5 h[3] caused attack of the reagent from the less hindered site against the axial tertiary methyl group to the glycol (IX), $C_{15}H_{26}O_2$ (M^+ 238); m.p. 87·5—88 °C; $[\alpha]_D$ +73·0°, which had an equatorial secondary OH group and an axial tertiary OH group as well as an unchanged *exo* methylene group; the glycol (IX) gave the hydroxy-cyclohexanone (X), $C_{15}H_{24}O_2$ (M^+ 236); $[\alpha]_D$ +119°, upon Sarett oxidation. In order to determine the absolute configuration of the cyclohexane unit the glycol (IX) was converted into the *p*-bromobenzoate (XI), $C_{22}H_{29}BrO_3$ (M^+ 420 and 422); $[\alpha]_D$ +27·7°, the molecular rotation of which ($[M]_D$ +113°) showed a decrease compared with that ($[M]_D$ +174°) of the original glycol. In the glycol, accordingly, the carbon atom bearing the secondary equatorial OH group had the (*R*) configuration, as shown in structure (IX), according to the benzoate rule.[5] In addition, the α-hydroxy-ketone (X) showed a positive Cotton effect in the o.r.d. and c.d. spectra {$[\phi]_{326}$ +5180 (max), $[\phi]_{303}$ 0, $[\phi]_{287}$ −1280 (min); $[\theta]_{308}$ +835 (max) (in dioxan)} owing to the contribution of the axial methyl group on the β-carbon of the carbonyl group.[6]

On the basis of the above evidence, the structure and absolute configuration of (+)-bazzanene was shown to be as in the stereostructure (I) which corresponds to a diastereoisomer of (+)-trichodiene (II). It is thought that (+)-bazzanene is an important precursor in the biogenesis of (+)-α-pompene (= isogymnomitrene) and (−)-β-pompene[7] (= gymnomitrene)[8] which has been isolated from the same liverwort.

[†] The ^{13}C n.m.r. spectra were determined in $CDCl_3$ solutions; values of δ are given in p.p.m.

[‡] All new compounds (III)—(VII) and (IX)—(XI) gave spectral data in good accord with the assigned structures. Optical rotations were measured in $CHCl_3$ solutions and i.r. and ^1H n.m.r. spectra in CCl_4 solutions.

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