(−)-Herbertene, an Aromatic Sesquiterpene with a Novel Carbon Skeleton from the Liverwort *Herberta adunca*

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Summary  The structure of (-)-herbertene, an aromatic sesquiterpene hydrocarbon isolated from the liverwort Herberta adunca, has been determined as (1S)-1,2,2-trimethyl-m-tolylcyclopentane (3) on the basis of chemical and spectral evidence.

(+)-Cuparene (1), one of the few sesquiterpenes containing a benzene nucleus, was first isolated from some species of the Cupressaceae, and it is widely distributed in the higher plants. From the liverwort Bazzania pompeana we have isolated the (-)-enantiomer (2). Indeed, in general, a significant biochemical characteristic of the liverworts (Hepaticae) is that they produce sesquiterpenoid metabolites which are enantiomers of those compounds produced by higher plants. In our continuing studies of the constituents of liverworts, we have isolated a sesquiterpene which we have called hydrocarbon (-)-herbertene, (3), with a novel 1,3-disubstituted benzene carbon skeleton, from a methanolic extract of the leafy liverwort Herberta adunca Dicks belonging to the family Herbertaceae of the order Jungermanniales. The structure and absolute configuration of (3) was shown to be (1S)-1,2,2-trimethyl-m-tolylcyclopentane from the following chemical and spectroscopic evidence.

(-)-Herbertene (3), C_{19}H_{22}, [\alpha]D_{D} -48.3° (c 1.31, CHCl₃), was isolated as an oil from the methanolic extract by a combination of column chromatography and thin layer chromatography. Both the i.r., ¹H n.m.r., and ¹³C n.m.r. spectra and the degree of unsaturation revealed that the compound was a bicyclic sesquiterpene hydrocarbon containing a benzene ring [v_{max} 1610, 1500, and 720 cm⁻¹].

† I.r. spectra were measured in CHCl₃ solution, and n.m.r. spectra in CDCl₃ solution. All new compounds (3)—(5) gave spectral data in good agreement with the assigned structures.
Δοδο 1H 6.70–7.15 (4 H, complex); δH 124.2 (d), 126.2 (d), 127.9 (d), 136.8 (s), and 147.6 (s) p.p.m. substituted with a methyl group [δH 2.34 (3 H, s); δH 21.8 (q) p.p.m.] as well as a cyclopentane ring [δH 19.8 (t), 30.9 (t), 39.9 (t), 44.2 (s), and 50.5 (s) p.p.m.] with three tertiary methyl groups [δH 0.58, 1.10, and 1.27 (each 3 H, s); δH 24.4 (q x 2) and 26.5 (q) p.p.m.]. These spectral properties resemble those of cuparene (1) which differs from (3) in a para-substitution pattern and shows different signals in the aromatic region [δH 6.96 and 7.12 (each 2 H, d, J 8.5 Hz); δH 127.0 (d x 2), 128.3 (d x 2), 134.7 (s), and 144.6 (s) p.p.m.].

Compound (3) when treated with bromine, gave the benzyl bromide (4), [δH 4.43 (2 H, s)] (Scheme). However, bromination of (3) using iron and iodine as catalyst produced the aryl bromide (5) showing 1H n.m.r. data consistent with a 1,2,4-trisubstituted benzene nucleus [δH 6.94 (1 H, dd, J 8.5 and 2.0 Hz), 7.11 (1 H, d, J 2.0 Hz), and 7.32 (1 H, d, J 8.5 Hz)]. For confirmation of the meta-substitution pattern of the aromatic ring in herbertene, (3) was oxidized with dilute nitric acid in a sealed tube followed by methylation (CH₂N₂) to afford the dimethyl ester (6) which was identified as dimethyl benzene-1,3-dicarboxylate by its m.p. and spectral data, identical with those of an authentic specimen. By prolonged ozonolysis and subsequent oxidation of the ozonide formed (3) was converted into the acid (7) which was then methylated (CH₂N₂) to give the ester (8). The spectra and optical rotation values of these compounds coincided with those of (-)-camphonanic acid and (-)-methyl camphonanate, respectively, prepared from (-)-ent-cupaxene (2).

Accordingly, the structure and absolute configuration of (3) is represented by (1S)-1,2,2-trimethyl-2-tolylcyclopentane. The biosynthetic route to this novel carbon skeleton, enantiomeric to the configurations of higher-plant sesquiterpenes, apparently does not follow the isoprene rule; it may be formed by 1,2-methyl migration of the ent-cuparene skeleton produced from farnesyl pyrophosphate through a stereospecific cyclization.

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References: