

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

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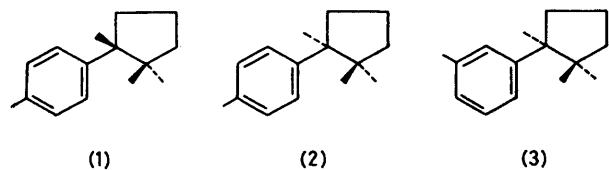
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Summary The structure of (-)-herbertene, an aromatic sesquiterpene hydrocarbon isolated from the liverwort *Herberta adunca*, has been determined as (1*S*)-1,2,2-trimethyl-*m*-tolylcyclopentane (**3**) on the basis of chemical and spectral evidence.

(+)-CUPARENE (**1**), one of the few sesquiterpenes containing a benzene nucleus, was first isolated from some species of the Cupressaceae,¹ and it is widely distributed in the higher plants. From the liverwort *Bazzania pompeana* we have isolated the (-)-enantiomer (**2**).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.³ 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 (1*S*)-1,2,2-trimethyl-*m*-tolylcyclopentane from the following chemical and spectroscopic evidence.

(-)-Herbertene (**3**), C₁₅H₂₂, [α]_D -48.3° (*c* 1.31, CHCl₃), was isolated as an oil from the methanolic extract by a combination of column chromatography and thick 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 [ν_{\max} 1610, 1500, and 720 cm⁻¹;

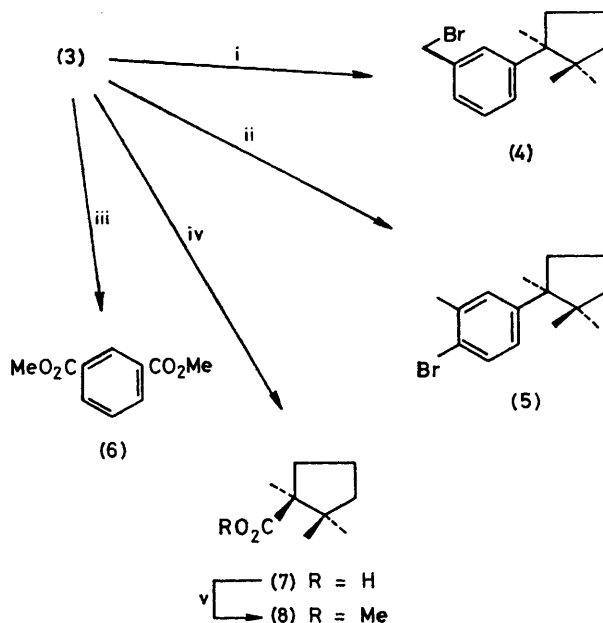


† I.r. spectra were measured in CCl₄ solution, and n.m.r. spectra in CDCl₃ solution. All new compounds (**3**)—(**5**) gave spectral data in good agreement with the assigned structures.

δ_{H} 6.70—7.15 (4 H, complex); δ_{C} 124.2 (d), 126.2 (d), 127.4 (d), 127.9 (d), 136.8 (s), and 147.6 (s) p.p.m.] substituted with a methyl group [δ_{H} 2.34 (3 H, s); δ_{C} 21.8 (q) p.p.m.] as well as a cyclopentane ring [δ_{C} 19.8 (t), 36.9 (t), 39.9 (t), 44.2 (s), and 50.5 (s) p.p.m.] with three tertiary methyl groups [δ_{H} 0.58, 1.10, and 1.27 (each 3 H, s); δ_{C} 24.4 (q \times 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 [δ_{H} 6.95 and 7.12 (each 2 H, d, J 8.5 Hz); δ_{C} 127.0 (d \times 2), 128.3 (d \times 2), 134.7 (s), and 144.6 (s) p.p.m.].

Compound (3) when treated with bromine, gave the benzyl bromide (4), [δ_{H} 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 [δ_{H} 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 (CH_2N_2) 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 (CH_2N_2) to give the ester (8). The spectra and optical rotation values of these compounds coincided with those of (–)-camphonic acid and (–)-methyl camphonate, respectively, prepared from (–)-*ent*-cuparene (2).²

Accordingly, the structure and absolute configuration of (3) is represented by (1*S*)-1,2,2-trimethyl-*m*-tolylcyclopentane. The biosynthetic route to this novel carbon



SCHEME. Reagents: i, Br_2 ; ii, Br_2 with Fe and I_2 ; iii, dil. HNO_3 , then CH_2N_2 ; iv, O_3 - H_2O_2 ; v, CH_2N_2 .

skeleton, enantiomeric to the configurations of higher-plant sesquiterpenes, apparently does not follow the isoprene rule;⁴ it may be formed by 1,2-methyl migration of the *ent*-cuparene skeleton produced from *cis*-farnesyl pyrophosphate through a stereospecific cyclization.

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¹ C. Enzell and H. Erdtman, *Tetrahedron*, 1958, 4, 361.

² A. Matsuo, M. Nakayama, T. Maeda, Y. Noda, and S. Hayashi, *Phytochemistry*, 1975, 14, 1037.

³ S. Hayashi and A. Matsuo, *Chemistry (Kyoto)*, 1976, 31, 518 and references therein; A. Matsuo, S. Sato, M. Nakayama, and S. Hayashi, *J. Chem. Soc., Perkin Trans. 1*, 1979, 2652 and references therein; A. Matsuo, K. Atsumi, M. Nakayama, and S. Hayashi, *ibid.*, in the press and references therein.

⁴ L. Ruzika, *Experientia*, 1953, 9, 357.