(+)-Bicyclohumulenone, a Novel Sesquiterpene Ketone of the Humulane Group from *Plagiochila acanthophylla* subsp. *japonica* (Liverwort): *X*-Ray Crystal and Molecular Structure of the *p*-Bromobenzoate Derivative

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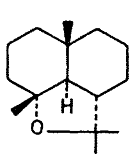
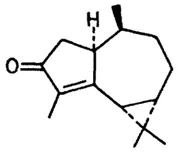
Summary A novel sesquiterpene ketone, (+)-bicyclohumulenone (**3**), has been isolated from *Plagiochila acanthophylla* subsp. *japonica*, and its structure and absolute configuration have been determined by *X*-ray analysis of the triol mono *p*-bromobenzoate (**6**).



(1)



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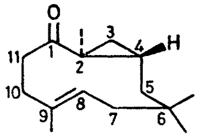
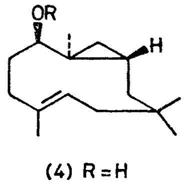
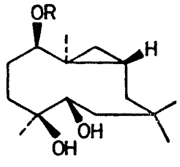


(3)



(4) R = H
(5) R = COC_6H_4Br-*p*



(6) R = COC_6H_4Br-*p*

IN connection with a previous paper on the isolation of two enantiomeric sesquiterpenoids,[1] (−)-maalioxide (**1**) and (+)-cyclocolorenone (**2**), a novel sesquiterpene ketone with a cyclopropane ring, (+)-bicyclohumulenone, was isolated from the leafy liverwort, *Plagiochila acanthophylla* subsp. *japonica*. Its structure and absolute configuration were determined by single-crystal *X*-ray diffraction analysis of the triol mono *p*-bromobenzoate (**6**) to be as shown by formula (**3**).

Repeated silicic acid column chromatography of an ethanol extract of the air-dried plant gave (+)-bicyclohumulenone, $C_{15}H_{24}O$, $[\alpha]_D$ +60·0°, ν_{max} 1684 cm^{-1}, λ_{max} (EtOH) 205 nm (ϵ 10,400), as needles, m.p. 76 °C from ethanol, 2,4-dinitrophenylhydrazone, m.p. 174—176 °C.

The i.r., ^1H n.m.r., and ^{13}C n.m.r. spectra of the ketone† (**3**) revealed that it was a bicyclic sesquiterpene containing a cyclopropane ring conjugated with a carbonyl group,[2] a trisubstituted double bond bearing a methyl group, together with an active methylene adjacent to the carbonyl, and three tertiary methyls. Since this result could not be

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† Optical rotations were measured in $CHCl_3$ solutions and ^1H n.m.r. and i.r. spectra in CCl_4 solutions. ^{13}C n.m.r. spectra were determined in $CDCl_3$ solutions. The compound, as well as saturated alcohol and glycol derivatives gave spectral data in good accord with the assigned structure.

accommodated by any known sesquiterpene skeleton, a single-crystal X-ray diffraction analysis was undertaken.

X-ray analysis of the ketone itself was unsuccessful because of its instability in the X-ray beam. However, the triol mono-*p*-bromobenzoate (**6**), prepared by OsO_4 oxidation of the *p*-bromobenzoate (**5**) of the unsaturated alcohol (**4**) obtained by $LiAlH_4$ reduction of the ketone (**3**), formed suitable monoclinic crystals belonging to the $P2_1$ space group with $a = 22{\cdot}88(2)$, $b = 6{\cdot}32(1)$, $c = 15{\cdot}25(1)$ Å, $\beta = 99{\cdot}0(2)^\circ$: the density [$D_c = 1{\cdot}34$ g cm^{-1}, $D_m = 1{\cdot}36$ (in $ZnCl_2$ solution)] indicated two molecules per asymmetric unit ($Z = 4$). 2559 independent reflections were obtained by visual estimation of equi-inclination Weissenberg photographs (*h0l*–*h5l* and *hk0*) with Cu-K_α radiation ($\lambda = 1{\cdot}5418$ Å), and corrected for Lorentz and polarization effects. The positions of the bromine atoms in the two independent molecules were determined from Patterson synthesis. The subsequent electron density syntheses were finally interpreted to yield the non-hydrogen atom skeleton of both molecules. 34 hydrogen atoms (excluding those of the four methyl groups) were placed at calculated positions. Refinement by block-diagonal least-squares, using anisotropic thermal parameters, converged to a current R-value of 0·119.‡ The absolute configuration was determined by comparing the observed intensities and calculated values of $|\mathrm{F}(hkl)|^2$ and $|F(h\bar{k}l)|^2$ for 30 Friedel pairs using the anomalous dispersion effect of the bromine atoms.[3] The Figure shows a perspective drawing of the resulting X-ray model of the triol mono-*p*-bromobenzoate (**6**).§

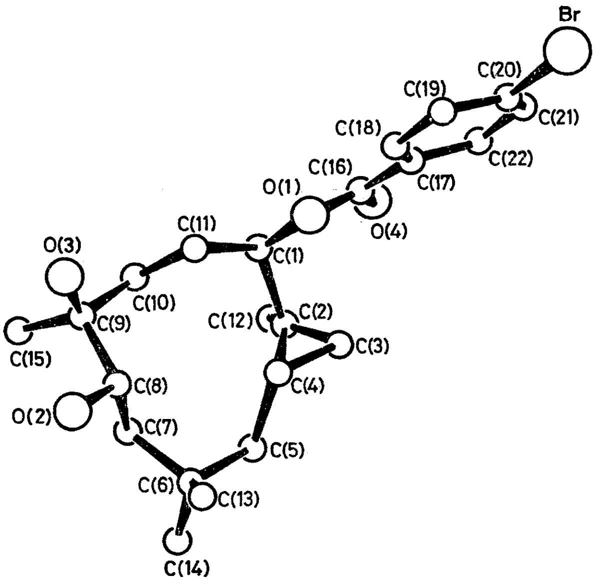

FIGURE. Perspective drawing of an X-ray model of the triol mono-*p*-bromobenzoate (**6**).

Both molecules in an asymmetric unit have the same configuration and similar bond lengths and angles (within experimental error), and most of them agreed well with accepted values.[4] The shortest intermolecular contact is a hydrogen bond between the hydroxy groups of two independent molecules (2·85 Å).

The structure and absolute configuration of (+)-bicyclohumulenone should thus be represented by the stereostructure (**3**) consisting of a novel carbon skeleton. The trisubstituted double bond is between C(8) and C(9) and the cyclopropane ring is between C(2) and C(4), in conjugation with the carbonyl group.

This novel sesquiterpene ketone may be biosynthesized from *trans*-farnesyl pyrophosphate, together with the two constituents (**1**) and (**2**) isolated from this liverwort.

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‡ All computations were carried out a HITAC 8700 computer at Hiroshima University, using the UNICS programs of the Crystallographic Society of Japan (1965) and slightly modified forms.

§ The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

[1] A. Matsuo, M. Nakayama, S. Sato, T. Nakamoto, S. Uto, and S. Hayashi, *Experientia*, 1974, **30**, 321.

[2] J. M. Greenwood, M. D. Solomon, J. K. Sutherland, and A. Torre, *J. Chem. Soc.* (*C*), 1968, 3004; Y. Naya and M. Kotake, *Bull. Chem. Soc. Japan*, 1969, 2405.

[3] J. M. Bijvoet, A. F. Peerdeman, and A. J. van Bommel, *Nature*, 1951, **168**, 271.

[4] O. Kennard and D. G. Watson, 'Molecular Structure and Dimensions,' Crystallographic Data Centre, Cambridge, 1970.