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Structure of Naematolin C and Naematolin G, Novel 4,8,11,11-Tetramethyltricyclo[5.4.0.0^{2,3}]undecane Sesquiterpenoids

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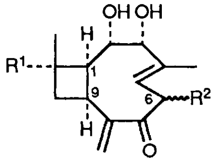
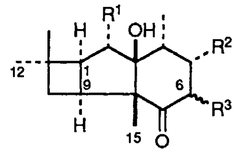
Naematolins C and G, metabolites of *Naematoloma fasciculare*, have the novel (1*S*,2*S*,3*S*,4*R*,5*S*,6*R*,8*R*,9*S*)-6-acetoxy-2,3,5-trihydroxy-4,8,11,11-tetramethyltricyclo[5.4.0.0^{2,3}]undecan-7-one (**4**) structure and its 6-epimer (**7**), respectively, as shown by a crystal structure determination of the chloroacetate (**5**).

We reported previously the structures of naematolin (**1**) and naematolin B (**2**), metabolites from culture filtrates of *Naematoloma fasciculare* (Fr.) Karst. (Nigakuritake in Japanese; basidiomycete).[1] Two additional metabolites, naematolins C[†] and G, were later isolated and their structural elucidation has now been carried out.[‡] Naematolin C (**4**), colourless needles, m.p. 142 °C, $[\alpha]_D^{24}$ −19° (*c* 0.31 in dioxane), has the molecular formula $C_{17}H_{26}O_6$ (high-resolution mass spectrometry). Its IR (KBr), and ^1H (270 MHz) and ^{13}C (67.8 MHz) NMR spectra show the presence of one secondary acetoxy, two secondary hydroxy, one tertiary hydroxy, one keto, one secondary methyl, and three tertiary methyl groups, two of which are *gem*. The absence of alkenic unsaturation shows (**4**) to be tricyclic. The framework and the absolute stereochemistry of (**4**) were determined by crystallographic analysis of its chloroacetate (**5**), colourless prisms, m.p. 140—141 °C, $[\alpha]_D^{19}$ −6.9° (*c* 0.16 in $CHCl_3$) (Figure 1).[§] The CD spectrum of the dibenzoate (**6**), $C_{31}H_{34}O_8$, colourless powder, m.p. 171—172 °C, $[\alpha]_D^{21}$ +11.9° (*c* 0.51 in $CHCl_3$), UV $\lambda_{max.}$ (MeOH) 231 nm (ε 27 500), showed a negative first Cotton effect ($\Delta\varepsilon_{234}$ −3.42) and a positive second Cotton effect ($\Delta\varepsilon_{218}$ +1.47), indicating that the 1,4-bisbenzoyloxy arrangement in (**6**) has negative exciton chirality.[2] This shows that the configurations of 2-OH and 5-OH in (**4**) are both α, and that the absolute stereochemistry of naematolin C is as in structure (**4**), consistent with its NMR data.



(**1**) R^1 = Me, R^2 = β-OAc
(**2**) R^1 = CH_2OH, R^2 = β-OAc
(**3**) R^1 = Me, R^2 = α-OAc



(**4**) R^1 = R^2 = OH, R^3 = β-OAc
(**5**) R^1 = $OCOCH_2Cl$, R^2 = OH, R^3 = β-OAc
(**6**) R^1 = R^2 = OCOPh, R^3 = β-OAc
(**7**) R^1 = R^2 = OH, R^3 = α-OAc

[†] An erroneous structure for naematolin C was proposed by K. Doi, T. Shibata, and O. Kamo, 'Symposium on Chemistry of Terpenes, Essential Oils, and Aromatics,' Hiroshima, 1969, p. 237.

[‡] The numbering system for caryophyllene was applied for convenience; see A. Aebi, D. H. R. Barton, and A. S. Lindsey, *J. Chem. Soc.*, 1953, 3124.

[§] *Crystal data*: $C_{19}H_{27}ClO_7$, M = 402.63, orthorhombic, space group $P2_12_12_1$ (No. 19), a = 17.217(2), b = 24.205(1), c = 14.665(2) Å, U = 6112(1) Å^3, Z = 12, D_c = 1.313 g cm^{-3}, $F(000)$ = 2568, $\mu(Cu\text{-}K_\alpha)$ = 19.89 cm^{-1}, crystal dimensions 0.45 × 0.33 × 0.33 mm. Intensity data were collected at 22 °C with a Rigaku AFC-5 diffractometer using Ni-filtered Cu-K_α radiation; 5030 unique data in the range $3 < 2\theta < 120°$ and 140 Bijvoet pairs with $1 \leqslant h \leqslant 5$, $1 \leqslant k \leqslant 7$, $1 \leqslant |l| \leqslant 4$. 5030 Unique reflections were used in the analysis, 4878 of which had $F > \sigma(F)$. The structure was solved by MULTAN84[3] and refined by full-matrix least-squares technique with anisotropic thermal parameters for non-H atoms, taking into consideration the anomalous-dispersion effect of Cl atoms. All the H atoms were located on a difference electron density map and their parameters were refined isotropically. Final R, R_w, and S values were 0.048, 0.050, 1.34, respectively for 5030 reflections. For seven reflections with $\Delta F_o[= |F_o(+)| - |F_o(-)|] > 9\sigma(F_o)$, the signs of ΔF_o were the same as those of ΔF_c. Least-squares refinements assuming z parameters with inverted signs increased R to 0.052. The absolute configuration suggested by the X-ray analysis was inconsistent with that from CD results. Programs used were from the UNICS-Osaka package. Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

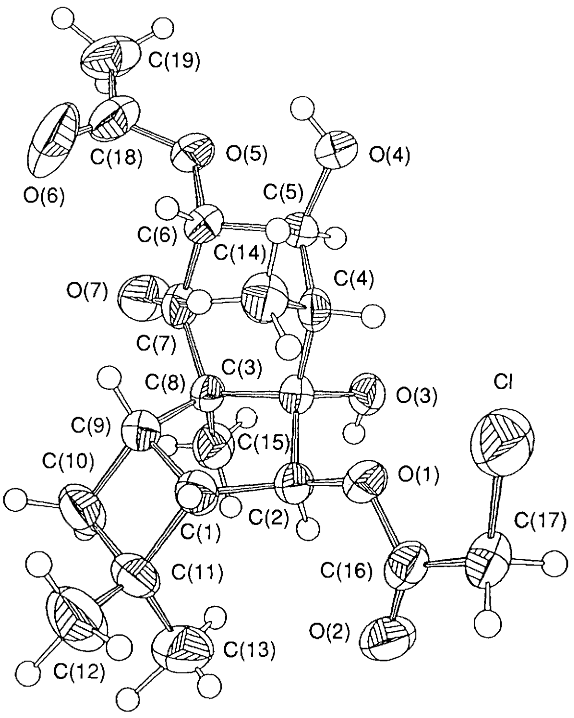


Figure 1. ORTEP drawing of (**5**).

Naematolin G (**7**), $C_{17}H_{26}O_6$, colourless needles, m.p. 176—177 °C, $[\alpha]_D^{22}$ −64.5° (*c* 0.16 in dioxane), was shown unambiguously to be the 6-epimer of (**4**) by nuclear Overhauser enhancement experiments. Since a new metabolite (**3**), the 6-epimer of (**1**), has recently been isolated, we assumed that the tricyclic metabolite is biosynthesised by *in vivo* cyclisation of the bicyclic precursor.

Although a tetramethyltricyclo[5.4.0.0^{2,3}]undecane skeleton had been assigned to a dehydrochlorination product of caryophyllene dihydrochloride,[4] naematolins C and G are the first examples of such a skeleton in naturally occurring sesquiterpenoids.

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