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# Structure and Synthesis of Bicalamenene

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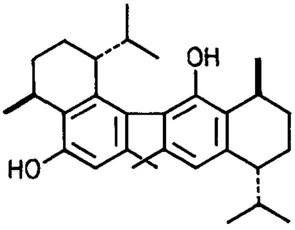
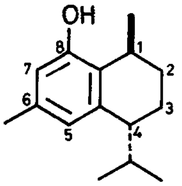
Summary: The structure of an unsymmetrical dimeric sesquiterpene named bicalamenene has been established based on the spectral study and synthesis.

Recently, we have reported the isolation of (+)-8-hydroxycalamenene (2) from a Meliaceous plant Dysoxylum alliaceum as its major poisonous principle.[1] A minor constituent of the same plant has been characterized to be a novel unsymmetrical dimer of 2,[2] and the absolute structure has been established by the synthesis to be formula 1.



**1**

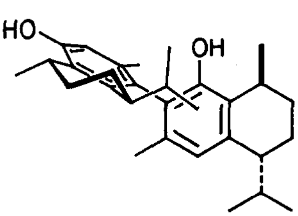


**2**

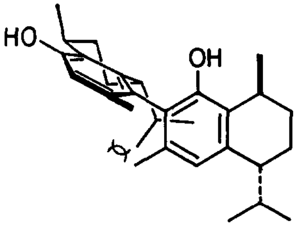
Bicalamenene (1), $[\alpha]_D^{27}$ +32.4° ($c$ 1.55, $CHCl_3$); UV $\lambda_{max}$ 284 nm ($\varepsilon$ 2581, isooctane), was isolated as a pale yellow syrup in ca 0.04% yield by the silica gel column chromatography of the hexane extract of the dried peel of D. alliaceum collected in Bogor, Indonesia. The molecular formula $C_{30}H_{42}O_2$ was estimated by the high resolution mass spectrum. IR spectrum indicated the presence of hydroxyl groups (3600 and 3550 $cm^{-1}$). Six signals due to methyls ($\delta$ 0.60, 0.64, 0.85, 0.99, 1.10, and 1.18) were observed as doublets with $J$ = 7 Hz in $^1H$ NMR. A pair of singlets due to aromatic methyls appeared at $\delta$ 1.76 and 1.84. Aromatic protons appeared as a single broard peak at $\delta$ 6.58.[3] From these spectral evidence, an unsymmetrical dimeric structure of 8-hydroxycalamenene is suggested to this new natural product, which was confirmed by the following synthesis.

When an aqueous suspension of (+)-8-hydroxycalamenene (2), $[\alpha]_D^{15}$ +38.0° ($c$ 1.37, $CHCl_3$), UV $\lambda_{max}$ 282 nm ($\varepsilon$ 1812, isooctane), was heated at reflux with two equiv. of ferric chloride for 21 h, a single unsymmetrical dimer and two kinds of symmetrical dimers were isolated in 14%, 23%, and 10% yields, respectively, along with 18% of the recovered starting material. The unsymmetrical dimer was fully identified with the natural product including optical rotation. Among the two possible conformers of the unsymmetrical dimer on the basis of the rotation around $C_5$-$C_{7'}$ bond, **1a** contains more serious overlapping between the aromatic methyl group of one half of the molecule and the isopropyl group of the other half than that of **1**. Thus, the absolute configuration of the natural product was represented by the formula **1**.

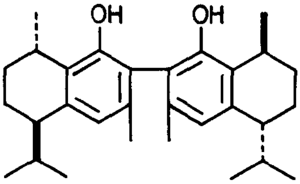
The symmetrical dimers **3a**, 10% yield; $R_f$ 0.35 (5:1 mixture of hexane and dichloromethane); $[\alpha]_D^{21}$ +3.8° ($\underline{c}$ 0.40, $CHCl_3$); UV $\lambda_{max}$ 284 nm ($\varepsilon$ 4476, isooctane), and **3b**, 23% yield; $R_f$ 0.37; $[\alpha]_D^{21}$+52.9° ($\underline{c}$ 0.35, $CHCl_3$); UV $\lambda_{max}$ 284 nm ($\varepsilon$ 4130, isooctane), were separated each other by using HPLC (Develosil 5D-ODS, a 15:1 mixture of acetonitrile and water). Lower polarity of these two compounds compared with **1** ($R_f$ 0.01 in the same solvent system) or **2** ($R_f$ 0.11) suggests the existence of intramolecular hydrogen bond in **3a** and **3b**. IR spectrum determined under high dilution supported this conclusion. Thus, both of the isomers are assigned to be the $C_7$-$C_{7'}$ dimers rather than the more hindered $C_5$-$C_{5'}$ dimeric structures. These two compounds showed quite similar spectral properties ($^1H$ and $^{13}C$ NMR, IR, and UV). Only the chemical shift values due to aromatic methyl protons are distinguishable; **3a** $\delta$ 1.94(6H,s); **3b** $\delta$ 1.89(6H,s).



**1**



**1a**



**3a, 3b**

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## REFERENCES

1. M. Nishizawa, A. Inoue, S. Sastrapradja, and Y. Hayashi, Phytochemistry, 22, 2083 (1983).
2. Symmetrical dimer of cadinane type sesquiterpenoids are well known; See A. Adams, T. A. Geissman, and J. D. Edwards, Chem. Rew., **60**, 555 (1960).
3. $^{13}C$ NMR data of 1 are as follows; ($\delta$, $CDCl_3$) 18.1, 19.6, 19.9, 20.8, 21.7, 22.2, 26.7, 27.0, 27.3, 32.0, 33.2, 39.7, 43.2, 114.7, 123.0, 123.6, 125.9, 126.2, 128.5, 132.0, 136.4, 139.3, 142.5, 150.5, 153.1.

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