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Short Note

1,1,4,7-Tetramethyldecahydro-1*H*-cyclopropa[*e*]azulen-7-ol from the Stembark *Chisocheton pentandrus*

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Abstract: A new aromadendrane-type sesquiterpenoid, namely dehydrosphatulenol (**1**), has been isolated from the stembark of *Chisocheton pentandrus*. The chemical structure of **1** was characterized on the basis of spectroscopic evidences including mainly one dimension and two dimension Nuclear Magnetic Resonance, and Mass Spectroscopy as well as through a comparison with those related compounds previously reported.

Keywords: aromadendrane *Chisocheton pentandrus;* Meliaceae; sesquiterpenoid

1. Introduction

Chisocheton plants have been known to be a rich source of secondary metabolites including various sterols, limonoids, terpenoids, and alkaloids with biologically properties such as antifungal, antibacterial, antiviral, anti-inflammatory, cytotoxic, and antiplasmodial agents [1–4]. In our previous research for novel cytotoxic constituents from Indonesia *Chisocheton*, we isolated and described limonoids, dysobinol from the seed *C. macrophyllus* [5], pentandricine from stem bark *C. pentandrus* [6], four new apo-euphane-type triterpenoid from the bark of *C. patens* [1] and a triterpenoid from *C. cumingianus* and *C. celebicus* [7,8]. In the further search for anticancer candidate compounds from *C. pentandrus,* we found a new aromadendrane-type sesquiterpenoid, namely dehydrospatulenol **(1)** from the stembark of *C. pentandrus*. In this communication, the isolation and structural determination of the new aromadendrane-type sesquiterpenoid are described.

2. Results

Extraction and Isolation

The dried stem bark of *C. pentandrus* (3.8 kg) was extracted with MeOH at room temperature to give a crude MeOH extract (560 g) after solvent was removed. The crude MeOH extract (560 g) was partitioned between *n*-hexane and water to give the *n*-hexane fraction (96.6 g) after evaporation of the solvent. The *n*-hexane soluble fraction was separated by column chromatography (CC) using gradient *n*-hexane/EtOAc to give eight fractions (A–H). Fraction A (3.3 g) was separated by medium

pressure liquid chromatography (MPLC) on silica using isocratic of MeOH:H_2O (8:2) to give 12 subfractions (A1–12). Subfraction A9 (1.5 g) was subjected to column chromatography (CC) using CH_2Cl_2 to give three subfractions (A9.1–9.3). Compound **1** (335 mg) (Figure 1) was obtained by further purification of subfraction A9.3 (0.6 g) on silica gel eluted with *n*-hexane as a mobile phase.

Dehydrosphatulenol (**1**), colorless oil, $[\alpha]^{D}_{23^o}$ +7.2 (*c*, 0.17, CH_3OH), ^{1}H NMR ($CDCl_3$, 500 MHz), see Table 1. ^{13}C NMR ($CDCl_3$, 125 MHz), δ_C (ppm), see Table 1. HR-TOFMS *m*/*z* 223.2064 $[M + H]^+$ (calcd. for $C_{15}H_{26}O$, *m*/*z* 222.2084).

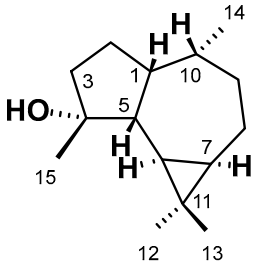

Figure 1. Chemical structure of compound **1**.

Table 1. Nuclear Magnetic Resonance data for compound **1** (500 MHz for ^{1}H and 125 MHz for ^{13}C in $CDCl_3$).

C	δ_C	δ_H (ΣH., mult., *J* = Hz)
1	39.7	1.72 (1H, m)
2	29.1	1.15 (1H, m) 1.68 (1H, m)
3	37.8	1.45 (1H, m) 1.59 (1H, m)
4	76.6	-
5	58.2	1.69 (1H, m)
6	22.3	0.10 (1H, t, 9.3)
7	28.6	0.51 (1H, ddd, 6.0, 9.6)
8	18.8	1.29 (1H, m) 1.52 (1H, m)
9	25.8	1.49 (1H, m) 1.54 (1H, m)
10	38.5	1.85 (1H, m)
11	18.4	-
12	16.3	0.88 (3H, s)
13	28.7	0.92 (3H, s)
14	16.1	0.84 (3H, d, 6.8)
15	32.1	1.04 (3H, s)

3. Discussion

Compound **1** was obtained as a colorless oil with $[\alpha]^{D}_{23^o}$ +7.2 (*c*, 0.17, CH_3OH) and the High Resolution Time of Flight-Mass Spectroscopy (HRTOF-MS) spectra showed a pseudomolecular ion peak at 223.2064 $[M + H]^+$, corresponding to the molecular formula $C_{15}H_{26}O$ (calculated *m*/*z* 222.2084). The ^{1}H NMR spectrum of **1** showed four methyls at δ_H 0.82 (3H, *d*, *J* = 6.82 Hz, Me-14), 0.88 (3H, *s*, Me-12), 0.92 (3H, *s*, Me-13), and 1.04 (3H, *s*, Me-15), each 3H, four methylene proton at δ_H 1.15 and 1.68 (2H, *m*, H-2), 1.29 and 1.52 (2H, *m*, H-8), 1.49 and 1.54 (2H, *m*, H-9), 1.45 and 1.59 (2H, *m*, H-3), five methine protons at δ_H 0.01 (1H, *t*, *J* = 9.3 Hz, H-6), 0.51 (1H, *ddd*, *J* = 6.05 and 9.6 Hz, H-7), 1.69 (1H, *m*, H-5), 1.72 (1H, *m*, H-1), and 1.85 (1H, *m*, *overlap*, H-10). The ^{13}C NMR (Table 1) and Distortionless Enhancement by Polarization Transfer (DEPT) spectra revealed 15 carbon resonances due to two sp^3 quaternary carbons at δ_C 18.4 (C-11) and 76.6 (C-4) and five sp^3 methines at δ_C 22.3 (C-6), 28.6 (C-7),

38.5 (C-10), 39.7 (C-1), and 58.2 (C-5). In addition, there were four sp^3 methylene at δ_C 18.8 (C-8), 25.8 (C-9), 29.1 (C-2), and 37.8 (C-3) and four methyls at δ_C 16.1 (C-14), 16.3 (C-12), 28.7 (C-13), and 32.1 (C-15). Among them, one sp^3 quaternary carbon (δ_C 74.60) was ascribed bearing an oxygen atom.

A comparison of the NMR data of **1** with a ledol isolated from *Renealmia chrysotrycha* [9] revealed that the structures of the compound are closely related. The main difference was the position of an oxygenated sp^3 quaternary carbon. In order to clarify the position of the hydroxyl group, Heteronuclear Multiple Bond Correlation (HMBC) and ^1H-^1H Corelated Spectroscopy (COSY) experiments were conducted and the results are shown in Figure 2 and supplementary materials. The HMBC spectrum of **1** showed correlation from the proton signal of Me-15 (δ_H 1.04) and methylene proton at δ_C 1.45 to oxygenated sp^3 quaternary carbon C-14 (δ_C 74.60), indicating that a tertiary alcohol was located at C-4. The HMBC spectrum also showed correlations of proton methine H-6 (δ_H 0.10), proton methine H-7 (δ_H 0.51), Me-12 (δ_H 0.88), and Me-13 (δ_H 0.92) to sp^3 quaternary carbon C-11 (δ_C 18.4), suggesting that a cyclopropane ring is located at C-6, C-7, and C-11, respectively. Furthermore, in the HMBC spectrum, a proton methyl with doublet multiplicity signal at δ_H 0.82 (H-14) was correlated with methine carbon C-10, indicating a secondary methyl located at C-10. The ^1H-^1H COSY spectrum of the isolated compound showed correlation in H1–H2, H1–H10, H5–H6, H6–H7, H7–H8, H8–H9, and H14–H10, supporting the presence of an aromadendrane structure in **1**.

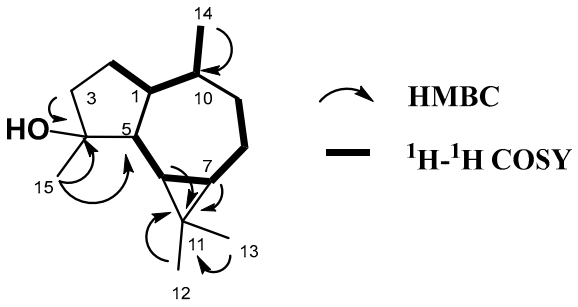

Figure 2. Selected ^1H-^1H Corelated Spectroscopy (COSY) and Heteronuclear Multiple Bond Correlation (HMBC) correlations for **1**.

The ring-junction between cycloheptane and cyclopropane is *cis*. This was confirmed by the ~9 Hz vicinal coupling constant ($^3J_{HH}$) of H-6 and H-7 from the experimental data and literature [9]. In the Nuclear Overhauser Effect-one dimension (NOE-1D) spectrum, there was correlation between H-6 with H-7. In addition, there are also correlation between H-6 with CH_3-14 and CH_3-13 when the signal H-6 was irradiated. As there was no correlation signal in the NOE-1D spectrum between CH_3-14 with H-1 and H-5 with H-5, this indicates that the configuration of methine H-1 and H-5 is *cis* to each other. The proton CH_3-15 showed no NOE interaction with H-5, this indicates the stereochemistry of CH_3-15 at the β-side of the molecule. Based on the literature, another aromadendrane-type sesquiterpenoid was isolated from *Chisocheton penduliflorus* [10], compound **1** was determined as a new aromadendrane-type sesquiterpenoid, 1,1,4,7-tetramethyldecahydro-1*H*-cyclopropa[*e*]azulen-7-ol, namely dehydrospathulenol (**1**).

4. Materials and Methods

4.1. General Experimental Procedures

The optical rotation was measured with an Autopol IV automatic polarimeter. The mass spectra was measured with a Water Xevo QTOFMS (Waters, Milford, MA, USA). NMR data were recorded on a Bruker Topspin spectrometer at 600 MHz for ^1H and 150 MHz for ^{13}C using Tetramethylsilane (TMS) as an internal standard (Bruker, Billerica, MA, USA). Medium performance liquid chromatography was undertaken using a Buchi Pump Controller C-610, Buchi Pump Modules C-605 with FLH-R10030B SiliCycle column-ISO04 (Siliasep™, Buchi, Swizerland). Silica gel 60 was used for

column chromatography (Merck, Darmstadt, Germany). Thin layer chromatography plates were precoated with silica gel GF_{254} (Merck, Darmstadt, Germany, 0.25 mm) and detection was achieved by spraying with 10% H_2SO_4 in EtOH, followed by heating and irradiation under UV–Vis light at wavelengths of 254 and 364 nm.

4.2. Plant Material

The stem bark of *C. pentandrus* was collected in Halimun Salak Mountain National Park, Sukabumi, West Java Province, Indonesia. The plant was identified by the staff of the Bogoriense Herbarium, Bogor, Indonesia. A voucher specimen (MSF-G01) was deposited at the herbarium.

5. Conclusions

A new aromadendrane-type sesquiterpenoid, namely, dehydrospathulenol (**1**), was isolated from the stembark of *Chisocheton pentandrus*. This examination confirms that *Chisocheton pentandrus* is capable of producing sesquiterpenoid-type compounds.

Supplementary Materials: The following are available online, Figure S1: ^{1}H-NMR Spectrum of **1** (500 MHz in $CDCl_3$), Figure S2: ^{13}C-NMR Spectrum of **1** (125 MHz in $CDCl_3$), Figure S3: DEPT-135° Spectrum of **1** (in $CDCl_3$), Figure S4: HSQC Spectrum of **1**, Figure S5: HMBC Spectrum of **1**, Figure S6: ^{1}H-^{1}H-COSY Spectrum of **1**, Figure S7: NOE-1D Spectrum of **1** (500 MHz in $CDCl_3$), Figure S8: HRESI-TOF-MS Spectrum of **1**, Figure S9: TLC profile of **1**.

Author Contributions: Conceptualization, Khalijah Awang; Data curation, Dewa Katja; Formal analysis, Muhamad Husna; Investigation, Muhamad Fareza; Methodology, Nurlelasari Nurlelasari; Supervision, Unang Supratman.

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Conflicts of Interest: The authors declare no conflicts of interest.

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