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

Muhamad Salman Fareza 1, Nurlelasari 2, Unang Supratman 2,*, Dewa Gede Katja 4, Muhamad Hafiz Husna 5 and Khalijah Awang 5

1 Department of Pharmacy, Faculty of Public Health Sciences, Universitas Jenderal Soedirman, Purwokerto 53123, Central Java, Indonesia; muhamad.fareza@unsoed.ac.id
2 Department of Chemistry, Faculty of Mathematics and Natural Sciences, Universitas Padjadjaran, Jatinangor 45363, West Java, Indonesia; nurlelasari@unpad.ac.id
3 Central Laboratory, Universitas Padjadjaran, Jatinangor 45363, West Java, Indonesia
4 Department of Chemistry, Faculty of Mathematics and Natural Sciences, Universitas Sam Ratulangi, Kampus Bahu, Manado 95115, North Sulawesi, Indonesia; dewakatja20@gmail.com
5 Department of Chemistry, Faculty of Science, University of Malaya, Kuala Lumpur 59100, Malaysia; hafiz_husna@um.edu.my (M.H.H.); khalijah@um.edu.my (K.A.)

* Correspondence: unang.supratman@unpad.ac.id; Tel.: +62-022-779-4391

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Abstract: A new aromadendrane-type sesquiterpenoid, namely dehydrospatulenol (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. putens [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:H2O (8:2) to give 12 subfractions (A1–12). Subfraction A9 (1.5 g) was subjected to column chromatography (CC) using CH2Cl2 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, [α]D23o +7.2 (c, 0.17, CH3OH). 1H NMR (CDCl3, 500 MHz), see Table 1. 13C NMR (CDCl3, 125 MHz), δC (ppm), see Table 1. HR-TOFMS m/z 223.2064 [M + H]+ (calcd. for C15H26O, m/z 222.2084).

Figure 1. Chemical structure of compound 1.

Table 1. Nuclear Magnetic Resonance data for compound 1 (500 MHz for 1H and 125 MHz for 13C in CDCl3).

| C   | δc  | δH (ΣH., mult., J = Hz) |
|-----|-----|-------------------------|
| 1   | 39.7| 1.72 (1H, m)             |
| 1   | 39.7| 1.15 (1H, m)             |
| 2   | 29.1| 1.68 (1H, m)             |
| 3   | 37.8| 1.45 (1H, m)             |
| 3   | 37.8| 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)             |
| 8   | 18.8| 1.52 (1H, m)             |
| 9   | 25.8| 1.49 (1H, m)             |
| 9   | 25.8| 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 [α]D23o +7.2 (c, 0.17, CH3OH) 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 C15H26O (calculated m/z 222.2084). The 1H NMR spectrum of 1 showed four methyls at δH 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 δH 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 δH 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 13C NMR (Table 1) and Distortionless Enhancement by Polarization Transfer (DEPT) spectra revealed 15 carbon resonances due to two sp3 quaternary carbons at δc 18.4 (C-11) and 76.6 (C-4) and five sp3 methines at δc 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 sp² methylene at δ 18.8 (C-8), 25.8 (C-9), 29.1 (C-2), and 37.8 (C-3) and four methylys at δ 16.1 (C-14), 16.3 (C-12), 28.7 (C-13), and 32.1 (C-15). Among them, one sp³ quaternary carbon (δ 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 sp³ 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 (δH 1.04) and methylene proton at δ 1.45 to oxygenated sp³ quaternary carbon C-14 (δC 74.60), indicating that a tertiary alcohol was located at C-4. The HMBC spectrum also showed correlations of proton methine H-6 (δH 0.10), proton methine H-7 (δH 0.51), Me-12 (δH 0.88), and Me-13 (δH 0.92) to sp³ quaternary carbon C-11 (δC 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 δH 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.](image)

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 CH₃-14 and CH₃-13 when the signal H-6 was irradiated. As there was no correlation signal in the NOE-1D spectrum between CH₃-14 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 CH₃-15 showed no NOE interaction with H-5, this indicates the stereochemistry of CH₃-15 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-1H-cycloprop[a]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 ¹³C 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, Switzerland). 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% H2SO4 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 stem bark 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: 1H-NMR Spectrum of 1 (500 MHz in CDCl3), Figure S2: 13C-NMR Spectrum of 1 (125 MHz in CDCl3), Figure S3: DEPT-135° Spectrum of 1 (in CDCl3), Figure S4: HSQC Spectrum of 1, Figure S5: HMBC Spectrum of 1, Figure S6: 1H-1H-COSY Spectrum of 1, Figure S7: NOE-1D Spectrum of 1 (500 MHz in CDCl3), Figure S8: HRES-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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