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A NEW NORSESQUITERPENOID FROM THE RHIZOMES OF *Curcuma longa*

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*A new norsesquiterpenoid, 4-(1′,5′-dimethyl-3′-oxo-4′-hexenyl)-2-cyclohexen-1-one (**1**), was isolated from the rhizomes of* Curcuma longa *(Zingiberaceae). The structure of the new norsesquiterpenoid was elucidated by chemical and physical evidence.*

Keywords: *Curcuma longa*, Zingiberaceae, rhizome, norsesquiterpenoid.

The traditional system of medicinals consists of a large number of plants with various medicinal and pharmacological importances and hence represents a priceless resource of new bioactive molecules. *Curcuma* (family Zingiberaceae) is a genus containing 70 known species that has been historically used as a spice, food preservative and coloring material. *Curcuma longa* L. is distributed throughout tropical and subtropical regions of the world. It is used in traditional medicine as a household remedy for various diseases. Also, it has been reported that *C. longa* possesses multiple pharmacological activities, including antioxidant, antimicrobial, anti-inflammatory, anticancer, anticoagulant, antidiabetic, and immunological [1, 2]. In continuation of some studies of the chemotaxonomy and biologically active metabolites from *Zingiberaceous* plants [3–20], a methanol extraction of the rhizomes of *C. longa* afforded one new norsesquiterpenoid, 4-(1′,5′-dimethyl-3′-oxo-4′-hexenyl)-2-cyclohexen-1-one (**1**). In this paper, we report the isolation and structural elucidation of this new compound (**1**).

Norsesquiterpenoid (**1**), a yellow oil, was deduced as $C_{14}H_{20}O_2$ by HR-MS-ESI (*m/z* 243.1354 $[M + Na]^+$; calcd 243.1361). IR bands at 1685 (C=O) and 1620 (C=C) cm^{-1} and a signal appearing at δ 199.7 in the ^{13}C NMR spectrum indicate the characteristic of the turmerone homologues [21]. The ^1H NMR spectrum of **1** showed two aromatic protons at δ 6.83 (1H, dt, J = 10.0, 2.0 Hz, H-2) and 6.03 (1H, ddd, J = 10.0, 2.0, 1.2 Hz, H-3), three methylene protons at δ 2.32/2.51 (H-6), 2.31/2.48 (H-2′), and 1.78/1.96 (H-5), three methine protons at δ 6.07 (1H, m, H-4′), 2.50 (1H, m, H-4), and 2.36 (1H, m, H-1′), and three methyl protons at δ 2.15 (3H, s, H-7′), 1.90 (3H, s, H-6′), and 0.92 (3H, d, J = 6.8 Hz, H-8′), indicating that **1** was probably a turmerone. The carbons of **1** were assigned, from ^{13}C NMR and DEPT experiments, to three methyls at δ 16.5 (C-8′), 20.8 (C-7′), and 27.7 (C-6′), three methylenes at δ 24.2 (C-5), 37.4 (C-6), and 48.2 (C-2′), five methines at δ 32.7 (C-1′), 40.6 (C-4), 123.8 (C-4′), 130.0 (C-3), and 154.4 (C-2), and three quaternary carbons at δ 156.2 (C-5′), 199.7 (C-3′, C=O), and 199.9 (C-1, C=O). Complete unambiguous assignments for the ^1H and ^{13}C NMR signals were made by a combination of the COSY, HETCOR, long-range HETCOR, and NOESY spectrum (Table 1). COSY correlations were observed between H-2, H-3, H-4, H-5 and H-6, and between H-1′, H-2′, H-4, and H-8′. The HETCOR experiment showed that the carbon/proton signals at δ 16.5/0.92 for C-8′, 20.8/2.15 for C-7′, 24.2/1.78, 1.96 for C-5, 27.7/1.90 for C-6′, 32.7/2.36 for C-1′, 37.4/2.32, 2.51 for C-6, 40.6/2.50 for C-4, 48.2/2.31, 2.48 for C-2′, 123.8/6.07 for C-4′, 130.0/6.03 for C-3, and 154.4/6.83 for C-2.

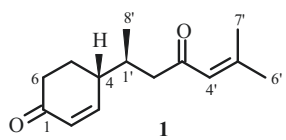

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TABLE 1. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR Data of **1** ($CDCl_3$, δ, ppm, J/Hz)

C atom	δ_H	δ_C	HMBC ($^{1}H \rightarrow ^{13}C$)
1	–	199.9	
2	6.83 (dt, J = 10.0, 2.0)	154.4	C-1, 3, 4, 6
3	6.03 (ddd, J = 10.0, 2.0, 1.2)	130.0	C-1, 2, 4, 5, 1′
4	2.50 (m)	40.6	C-2, 3, 5, 6, 1′
5	1.78 (m)	24.2	C-1, 3, 4, 6, 1′
	1.96 (m)		C-1, 3, 4, 6, 1′
6	2.32 (m)	37.4	C-1, 2, 4, 5
	2.51 (m)		C-1, 2, 4, 5
1′	2.36 (m)	32.7	C-3, 5, 2′, 3′, 8′
2′	2.31 (m)	48.2	C-4, 1′, 3′, 4′, 8′
	2.48 (m)		C-4, 1′, 3′, 4′, 8′
3′	–	199.7	
4′	6.07 (m)	123.8	C-2′, 3′, 6′, 7′
5′	–	156.2	
6′	1.90 (s)	27.7	C-4′, 7′
7′	2.15 (s)	20.8	C-4′, 6′
8′	0.92 (d, J = 6.8)	16.5	C-4, 2′

The observation of the NOESY correlations between H-6′ and H-7′, between H-1′, H-2′, H-8′, H-3, and H-4, between H-2 and H-3, and between H-5 and H-6 established the connective site as shown in structure **1**. Thus, the structure of this compound was determined to be 4-(1′,5′-dimethyl-3′-oxo-4′-hexenyl)-2-cyclohexen-1-one, which was further confirmed by HMBC experiments (Table 1).

The compound was dehydrogenated to give (+)-*ar*-turmerone, which was indicative that the absolute configuration at C-1′ was *S*. In the ^{1}H NMR spectrum, an intramolecular NOESY was observed between the secondary methyl hydrogens at C-8′ and the olefinic hydrogen at C-3, showing that these hydrogens were situated in a spatially close relationship. Provided that the hydrogens at C-4 and C-1′ adopted the thermodynamically most stable *anti*-arrangement, the above observation of the NOESY allowed the absolute configuration at C-4 to be *S*. The combined evidence pointed to the stereostructure **1** for 4*S*-(1′*S*,5′-dimethyl-3′-oxo-4′-hexenyl)-2-cyclohexen-1-one.

EXPERIMENTAL

General. UV spectra were obtained in MeCN, IR spectra were measured on a Hitachi 260-30 spectrophotometer. ^{1}H NMR (400 MHz), ^{13}C NMR (100 MHz), HETCOR, HMBC, COSY, and NOESY spectra were obtained on a Varian (Unity Plus) NMR spectrometer. Low-resolution ESI-MS spectra were obtained on an API 3000 (Applied Biosystems), and high-resolution ESI-MS spectra on a Bruker Daltonics APEX II 30e spectrometer. Silica gel 60 (Merck, 70–230 mesh, 230–400 mesh) was used for column chromatography. Precoated Silica gel plates (Merck, Kieselgel 60 F-254), 0.20 mm and 0.50 mm, were used for analytical TLC and preparative TLC, respectively, visualized with 50% H_2SO_4.

Plant Material. The rhizomes of *Curcuma longa* were collected from Chiayi County, Taiwan, in April 2017. Plant material was identified by Dr. Fu-Yuan Lu (Department of Forestry and Natural Resources, College of Agriculture, National Chiayi University). A voucher specimen was deposited at the Department of Medical Technology, School of Medical and Health Sciences, Fooyin University, Kaohsiung, Taiwan.

Extraction and Isolation. The rhizomes (0.1 kg) of *C. longa* were extracted repeatedly with MeOH (3 L × 2) at room temperature for 24–48 h. The MeOH extract was dried and evaporated to leave a viscous residue (21.2 g). The residue was placed on a silica gel column (4.8 kg, 70–230 mesh) and eluted with CH_2Cl_2 gradually enriched with MeOH to afford five fractions. Part of fraction 2 (2.1 g) was subjected to silica gel chromatography (0.9 kg, 70–230 mesh) by eluting with *n*-hexane–acetone (100:1) and enriched with acetone to furnish five fractions (2-1–2-5). Part of fraction 2-2 (0.4 g) was further purified on a silica gel column using *n*-hexane–acetone mixtures to obtain 4-(1′,5′-dimethyl-3′-oxo-4′-hexenyl)-2-cyclohexen-1-one (12.2 mg).

4*S*-(1′*S*,5′-Dimethyl-3′-oxo-4′-hexenyl)-2-cyclohexen-1-one (1). Yellow oil, $[\alpha]_D^{25}$ –0.21° (*c* 0.51, CH_2Cl_2). UV/Vis (CH_3CN, λ_{max}, nm) (log ε): 233 (4.11), 238 (3.65). IR (neat, ν_{max}, cm^{-1}): 1685 (C=O), 1620 (aromatic C=C), 870. ESI-MS *m/z* 243 $[M + Na]^+$; HR-ESI-MS *m/z* 243.1354 $[M + Na]^+$ (calcd for $C_{14}H_{20}O_2Na$, 243.1361). For ^1H and ^{13}C NMR, see Table 1.

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