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Sesquiterpenoids from the Rhizome of *Curcuma zedoaria*

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In the course of searching for biologically active sesquiterpenoids from *Curcuma* genus, two sesquiterpenoids were isolated from the rhizome of *Curcuma zedoaria* (Zingiberaceae). Their structures were identified as ar-turmerone (**1**) and β-turmerone (**2**). The structure elucidation of compounds **1** and **2** was carried out by comparison of their physical and spectral data with previously reported values.

Key words: *Curcuma zedoaria*, Zingiberaceae, sesquiterpenoids, ar-turmerone, β-turmerone

INTRODUCTION

Curcuma zedoaria Roscoe (Zingiberaceae) is a perennial plant originated from Himalya, India and mainly distributed in Asian country including China, Vietnam, India, and Japan. The rhizome, Zeodaria Rhizoma, has been used for a stomachic, treatment of blood stagnation, hepatoprotection, and promoting menstruation as an oriental medicine (Han, 1998; Matsuda *et al.*, 1998; Yoshioka *et al.*, 1998).

Previous phytochemical studies on this plant led to the isolation of various curcuminoids and sesquiterpenoids such as zedoarol, germacrone, curdione, β-elemene, and curzeone (Yoshinori *et al.*, 1985; Yoshinori *et al.*, 1986). Several sesquiterpenes isolated from *C. zedoaria* have been reported to exhibit hepatoprotective activity against D-galactosamine/LPS induced toxicity, and some of them, germacrone and curdione, used to treat hepatitis (Hisashi *et al.*, 1998). β-elemene showed antithrombotic and inhibitory effect on 6-keto-prostagladin F_1 α and thromboxane B_2 production (Xie *et al*, 1998) and dehydrocurdione did anti-inflammatory activity (Yoshioka *et al.*, 1998).

In the course of searching for biologically active sesquiterpenoids from *Curcuma* genus, Zedoaria rhizome was investigated. The chromatographic separation of the methylene chloride extract of this plant led to the isolation of two sesquiterpenoids, ar-turmerone (**1**) and β-turmerone (**2**). We report herein the isolation and structural characterization of these compounds.

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MATERIALS AND METHODS

General experimental procedure

IR spectra were recorded on a FTS 135 spectrometer (Bio-RAD, Cambridge, MA). The NMR spectra were recorded on a Varian UNITY INOVA 400 (9.4T) spectrometer (^{1}H, 400 MHz; ^{13}C, 100 MHz), using $CDCl_3$ and chemical shifts were reported in ppm downfield from TMS as an internal standard. MS were obtained on a JMS AX505 WA (EI+) spectrometer. UV data were recorded on a Hitachi U-3000 spectrophotometer. Column chromatography was performed over silica gel 60 (230-400 mesh, Merck) and preparative TLC (1.5 mm, Merck).

Plant materials

The rhizome of *C. zedoaria* was purchased from herbal market (Hanyang Yutong Co.) in Seoul, Korea. A voucher specimen (No. EWHA 068) was deposited in the herbarium of College of Pharmacy, Ewha Womans University.

Extraction and isolation

The air-dried powered rhizomes (600 g) were extracted three times with methanol (3 × 1000 ml). The methanol extract (28.5 g) was then suspended in distilled water and partitioned with methylene chloride. The methylene chloride fraction (18.5 g) was loaded on a silica gel (360 g) column and eluted with a gradient of methylene chloride-methanol (20:1 to 1:1) to afford eight fractions (Z1-Z8). The fraction Z2 (3 g) was further separated using a silica gel (80 g) column chromatography with elution of gradient

of methylene chloride-methanol (100:1 to 1:1), and five fractions were obtained (Z2-1-Z2-5). The fraction Z2-1 (250 mg) was further fractionated with preparative TLC (1.5 mm thickness, hexane-ethyl acetate=97:3), and gave compounds **1** (15 mg) and **2** (13 mg).

Compound **1** (ar-turmerone): light yellowish oil; $[\alpha]_D^{25}$ +54.0 (*c* 1.0, $CHCl_3$); UV ($CHCl_3$) λ_{max} 244 nm; IR (KBr) ν_{max} 1685 (C=O), 1620, 1515 (aromatic C=C), 819 cm^{-1}; EIMS (70 eV, *m/z*): 216 $[M]^+$, 201 $[M\text{-}CH_3]^+$, 119, 83, 55; ^{1}H-NMR (400 MHz, $CDCl_3$, δ) and ^{13}C-NMR (100 MHz, $CDCl_3$, δ): see the Table I.

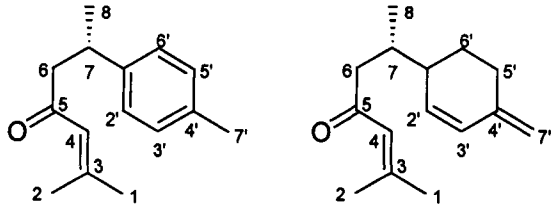
Compound **2** (β-turmerone): light yellowish oil; $[\alpha]_D^{25}$ -0.03 (*c* 2.2, $CHCl_3$); UV ($CHCl_3$) λ_{max} 241 nm; IR (KBr) ν_{max} 1680 (C=O), 1615 (aromatic C=C), 870 cm^{-1} ; EIMS (*m/z*): 218 $[M]^+$, 120, 83, 55; ^{1}H-NMR (400 MHz, $CDCl_3$, δ) and ^{13}C-NMR (100 MHz, $CDCl_3$, δ): see the Table I.

RESULTS AND DISCUSSION

The methanolic extracts of the rhizoma of *C. zedoaria* were evaporated *in vacuo,* suspended in H_2O and partitioned with CH_2Cl_2. The CH_2Cl_2 fraction was subjected to column chromatography over silica gel eluting with gradient solvent system (CH_2Cl_2: MeOH=20:1→1:1). Two sesquiterpenoids (compounds **1** and **2**) were isolated by repetitive chromatography on silica gel column and preparative TLC.

Compound **1** was obtained as a light yellowish oil with $[\alpha]_D^{25}$ +54.0 (*c* 1.0, $CHCl_3$). The molecular formula of **1** was established as $C_{15}H_{20}O$ observation of molecular ion peak at *m/z* 216 $[M]^+$ in the EI mass spectrum. The IR spectrum exhibited absorption typical of conjugated carbonyl (1685 cm^{-1}) and aromatic (1620 and 1515 cm^{-1}) functionalities. The ^{13}C NMR spectrum revealing 15 signals suggested that **1** has a sesquiterpene skeletone (Table I). The ^{1}H- and ^{13}C-NMR spectra showed a ketone (δ_C: 200.1), 4 methyls (δ_H: 1.17, 1.78, 2.0, 2.24), an α,β-unsaturated olefine (δ_C: 124.3, 155.3), a pair of geminal coupled protons (δ_H: 2.54, 2.65), and a symmetrically substituted aromatic ring (δ_H: 7.3, 4H, s; δ_C: 126.9 × 2, 129.3 × 2, 135.8, 143.9). HMBC correlations suggested that compound **1** is a bisabolane type, and spectral as well as other physical data were well accordance with the literature (Itokawa *et al.*, 1985). Therefore, the structure of compound **1** was identified as ar-turmerone.

Compound **2** was obtained as a light yellowish oil with $[\alpha]_D^{25}$ -0.03 (*c* 2.2, $CHCl_3$). The IR, ^{1}H- and ^{13}C- NMR spectra were very similar to **1**, and the EI MS of compound **2** gave the molecular peak at *m/z* 218, implying



Compound 1 ar-Turmerone **Compound 2** β-Turmerone

Fig. 1. Chemical structures of ar-turmerone and β-turmerone.

Table I. ^{1}H- and ^{13}C-NMR spectral data of compounds **1** and **2** in $CDCl_3$

Position	1		2	
	δ ^{13}C	δ ^{1}H (multiplicity., *J* Hz)	δ ^{13}C	δ ^{1}H (multiplicity., *J* Hz)
1	20.9	2.24 (3H, s)	20.9	2.05 (3H, s)
2	27.9	1.78 (3H, d, *J*=1.6 Hz)	27.8	1.80 (3H, s)
3	155.3		155.7	
4	124.3	5.96 (1H, m)	124.7	6.00 (1H, m)
5	200.1		201.7	
6	52.9	2.54 (1H, m)	48.8	2.60 (2H, m)
		2.65 (1H, m)		
7	35.5	3.2 (1H, m)	33.7	2.13 (1H, m)
8	22.2	1.17 (3H, d, *J*=6.9 Hz)	16.6	0.8 (3H, m)
1′	143.9		40.7	2.21 (1H, m)
2′	126.9	7.3 (1H, s)	133.9	5.53 (1H, m)
3′	129.3	7.3 (1H, s)	130.3	6.08 (1H, *d*, *J*=10.2 Hz)
4′	135.8		143.6	
5′	129.3	7.3 (1H, s)	30.3	2.37 (2H, m)
6′	126.9	7.3 (1H, s)	25.1	1.64 (2H, m)
7′	21.2	2.0 (3H, d, *J*=1.2 Hz)	110.5	4.68 (2H, s)

the presence of two additional protons compared with **1**. The ^{1}H and ^{13}C NMR spectra suggested that **2** has two pairs of double bonds and a pair of methylene group instead of aromatic ring. On the basis of the ^{1}H- and ^{13}C-NMR spectra and other physical data compared with the data reported in the literature (Kiso *et al.*, 1983), the structure of compound **2** was characterized as β-turmerone.

In summary, ar-tumerone has been reported to exhibit various biological activities including mosquitocidal (Roth *et al.*, 1998) and antimicrobial activities against Gram-positive and Gram-negative bacteria (Martins *et al.*, 2001). To the best of our knowledge, the isolation of ar- and β-turmerone has not been reported previously from *C. zedoaria*. Thus, the phytochemical investigation of *C. zedoaria* in this study will be a informative in terms of constituents of biologically active components.

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