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PHENYLBUTENOID MONOMERS FROM THE RHIZOMES OF *ZINGIBER CASSUMUNAR*

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Key Word Index—*Zingiber cassumunar*; Zingiberaceae; phenylbutenoid; rhizome.

Abstract—Four new phenylbutenoid monomers, (*E*)-4-(4-hydroxy-3-methoxyphenyl)but-3-en-1-yl acetate, (*E*)-4-(4-hydroxy-3-methoxyphenyl)but-2-en-1-ol, (*E*)-2-hydroxy-4-(3,4-dimethoxyphenyl)but-3-en-1-ol and (*E*)-2-methoxy-4-(3,4-dimethoxyphenyl)but-3-en-1-ol, have been isolated from fresh rhizomes of *Zingiber cassumunar* along with the three known phenylbutenoid monomers.

INTRODUCTION

Zingiber cassumunar is an important medicinal plant in southeast Asia. The rhizomes are known to have antioxidant [1] and antiinflammatory [2] activities. We have isolated new curcuminoids as both antioxidant and antiinflammatory active substances from the rhizomes [3–5]. Recently, Ozaki *et al.* reported that some phenylbutenoids from *Z. cassumunar* also have antiinflammatory activity [6]. Phenylbutenoids are typical non-polar substances in the rhizomes and various monomeric and dimeric phenylbutenoids are found in the rhizomes [7–10]. We now report on the isolation and structural elucidation of four new monomeric phenylbutenoids from the fresh rhizomes of *Z. cassumunar*.

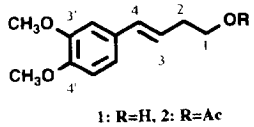
RESULTS AND DISCUSSION

The acetone extract of the fresh rhizomes of *Zingiber cassumunar* was suspended in water and successively extracted with hexane and ethyl acetate. The ethyl acetate fraction was purified by repeated silica gel column chromatography and TLC to give seven phenylbutenoid monomers (**1**–**7**).

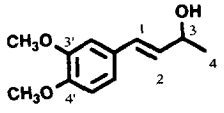
Compounds **1**–**3** were identified as (*E*)-4-(3,4-dimethoxyphenyl)but-3-en-1-ol, (*E*)-4-(3,4-dimethoxyphenyl)but-3-en-1-yl acetate, and (*E*)-3-hydroxy-1-(3,4-dimethoxyphenyl)but-1-ene, respectively, from their NMR and mass spectral data [7, 10].

Compound **4** had the molecular formula $C_{13}H_{16}O_4$ (HR-MS). Although the ^{1}H NMR spectrum of **4** was similar to that of **2**, a hydroxyl signal [δ5.42 (1H, *br s*)] was observed instead of one of the phenolic methoxyl signal in the ^{1}H NMR spectrum of **2**. The position of the hydroxyl group was placed at C-4 of the trisubstituted benzene, because the remaining methoxyl group was at C-3 of the benzene ring as shown by the NOE between H-2′ (δ6.63) and the methoxyl protons (δ3.14). Thus, the structure of **4** was (*E*)-4-(4-hydroxy-3-methoxyphenyl)-but-3-en-1-yl acetate.

Compound **5** had the molecular formula $C_{11}H_{14}O_3$ (HR-MS). The ^{1}H NMR spectrum of **5** in benzene-d_6 indicated that a 1-butenyl-3-methoxy-4-hydroxybenzene moiety was present. A NOE between the two signals at δ6.39 and 3.10 also confirmed the position of methoxyl group at C-3 of the benzene ring. The ^{1}H NMR spectrum also indicated that the butenyl group was a 4-substituted 1-hydroxybut-2-ene. Acetylation of **5** gave a diacetate **8** ($[M]^+$, *m/z* 278), which also supported the structure (*E*)-4-(4-hydroxy-3-methoxyphenyl)but-2-en-1-ol for **5**.



1: R=H, **2**: R=Ac



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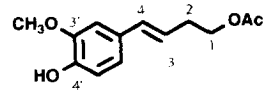

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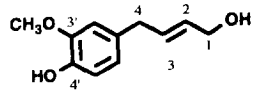

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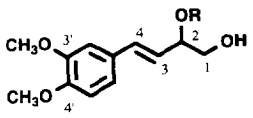

6: R=H, **7**: R=CH_3

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Compound **6** has a molecular formula $C_{12}H_{16}O_4$ (HR-MS). The ^{1}H NMR data for **6** indicated that its butenyl moiety was different from that of **1** and that the structure was a 1,2-dihydroxybut-3-ene, as deduced from coupling constants of each proton in the butenyl group. Acetylation of **6** gave a diacetate **9** [δ2.06 (3H, *s*) and 2.09 (3H, *s*)], which confirmed that both of the 1- and the 2-positions of the butenyl group were hydroxylated. Thus, the structure of **6** is (*E*)-2-hydroxy-4-(3,4-dimethoxyphenyl)but-3-en-1-ol.

Compound **7** had the molecular formula $C_{13}H_{18}O_4$ (HR-MS). Although the ^{1}H NMR data of **7** were similar to those of **6**, an additional methoxyl signal (δ3.37) was observed. Acetylation of **7** gave a monoacetate (**10**) [δ2.08 (3H, *s*)]. In the ^{1}H NMR spectrum of **10**, the signal of H-1 (δ3.63 in **7**) was shifted to δ4.10 and 4.21 while the signal of H-2 (δ3.85 in **7**) was slightly shifted to δ3.98. These results indicated that the methoxyl group was at the 2-position of the butenyl group and the 1-position of the butenyl group was hydroxylated. Thus, the structure of **7** is (*E*)-2-methoxy-4-(3,4-dimethoxyphenyl)but-3-en-1-ol.

EXPERIMENTAL

General. NMR: ^{1}H at 400 MHz, ^{13}C at 100 MHz; MS: EI and HR MS 70 eV.

Plant material. Rhizomes of *Zingiber cassumunar* Roxb. cultivated in Tabanan Village, Bali, Indonesia were collected in January 1991, and identified by Dr I. G. P. Tengah (Udayana University, Indonesia). The rhizomes were continuously cultivated in a research field of the Institute of Tropical Agriculture, University of Ryukyu, Taketomi, Okinawa, Japan.

Extraction and isolation. Fresh rhizomes (2.9 kg) were crushed and soaked in Me_2CO (5 l × 3) at room temp for nine days. After filtration, the extract was concd. The residue (111 g) was suspended in H_2O (2 l), extracted with hexane and EtOAc, successively, and the extracts concd. The EtOAc-soluble fraction (40 g) was sepd into 13 frs by silica gel CC eluted with EtOAc–hexane (1:9) and 15% MeOH in EtOAc. Fr. 10 (3.8 g) was purified by silica gel CC to give **1** (1.1 g). Fr. 7 (370 mg; 6.7 g) was filtered with EtOH–H_2O and the filtrate was purified by silica gel CC (CH_2Cl_2–hexane, 2:1) and silica gel TLC to give **2** (1 mg) and **4** (1 mg). Fr. 9 (33 mg; 1 g) was purified by silica gel CC (Me_2CO–hexane, 1:3) and silica gel TLC ($CHCl_3$ and EtOAc–hexane, 1:2) to give **3** (2 mg). Fr. 11 was filtered with CH_2Cl_2 and the filtrate (329 mg) was purified by silica gel CC (Me_2CO–CH_2Cl_2, 1:40) and silica gel TLC (EtOAc–hexane, 1:2) to give **5** (2 mg) and **7** (2 mg). Fr. 13 (9.8 g) was subjected to Diaion HP-20™ CC eluted with a H_2O–MeOH gradient. The 60–70% MeOH eluate was concd and the residue (0.5 g) purified by silica gel CC (5% MeOH in CH_2Cl_2) and silica gel TLC (Me_2CO–hexane, 1:1) to give **6** (5 mg).

(E)-4-(3,4-*dimethoxyphenyl*)*But*-3-*en*-1-*ol* (**1**). EI-MS, *m/z* (rel. int.): 208 $[M]^+$ (49), 177 (100), 146 (43); ^{1}H NMR ($CDCl_3$): δ2.48 (2H, *q*, *J* = 6.7 Hz, H-2), 3.76 (2H, *t*, *J* = 6.7 Hz, H-1), 3.88 (3H, *s*, OMe), 3.90 (3H, *s*, OMe), 6.08 (1H, *dt*, *J* = 15.9, 6.7 Hz, H-3), 6.44 (1H, *d*, *J* = 15.9 Hz, H-4), 6.81 (1H, *d*, *J* = 8.5 Hz, H-5′), 6.90 (1H, *dd*, *J* = 8.5, 1.8 Hz, H-6′), 6.93 (1H, *d*, *J* = 1.8 Hz, H-2′).

(E)-4-(3,4-*dimethoxyphenyl*)*But*-3-*ene*-1-*yl acetate* (**2**). EI-MS, *m/z* (rel. int.): 250 $[M]^+$ (24), 190 (100), 159 (92); ^{1}H NMR ($CDCl_3$): δ2.06 (3H, *s*, OAc), 2.53 (2H, *q*, *J* = 6.7 Hz, H-2), 3.88 (3H, *s*, OMe), 3.90 (3H, *s*, OMe), 4.17 (2H, *t*, *J* = 6.7 Hz, H-1), 6.03 (1H, *dt*, *J* = 15.9, 6.7 Hz, H-3), 6.41 (1H, *d*, *J* = 15.9 Hz, H-4), 6.81 (1H, *d*, *J* = 8.5 Hz, H-5′), 6.89 (1H, *dd*, *J* = 8.5, 1.8 Hz, H-6′), 6.91 (1H, *d*, *J* = 1.8 Hz, H-2′).

(E)-3-*Hydroxy*-1-(3,4-*dimethoxyphenyl*)*but*-1-*ene* (**3**). EI-MS, *m/z* (rel. int.): 208 $[M]^+$ (65), 190 (14), 165 (27), 151 (100); ^{1}H NMR ($CDCl_3$): δ1.36 (3H, *d*, *J* = 6.1 Hz, H-4), 3.86 (3H, *s*, OMe), 3.88 (3H, *s*, OMe), 4.46 (1H, *quint*, *J* = 6.1 Hz, H-3), 6.11 (1H, *dd*, *J* = 15.9, 6.1 Hz, H-2), 6.49 (1H, *d*, *J* = 15.9 Hz, H-1), 6.79 (1H, *d*, *J* = 8.6 Hz, H-5′), 6.89 (1H, *dd*, *J* = 8.6, 1.8 Hz, H-6′), 6.92 (1H, *d*, *J* = 1.8 Hz, H-2′).

(E)-4-(4-*hydroxy*-3-*methoxyphenyl*)*But*-3-*en*-1-*yl acetate* (**4**). EI-MS, *m/z* (rel. int.): 236 $[M]^+$ (25), 176 (100); HR-MS, *m/z* 236.1057 $[M]^+$ (calcd for $C_{13}H_{16}O_4$: 236.1048); ^{1}H NMR (C_6D_6): δ1.67 (3H, *s*, OAc), 2.30 (2H, *quart*, *J* = 6.7 Hz, H-2), 3.14 (3H, *s*, OMe), 4.06 (2H, *t*, *J* = 6.7 Hz, H-1), 5.42 (1H, *br s*, OH), 5.83 (1H, *dt*, *J* = 15.9, 6.7 Hz, H-3), 6.25 (1H, *d*, *J* = 15.9 Hz, H-4), 6.63 (1H, *d*, *J* = 1.8 Hz, H-2′), 6.76 (1H, *dd*, *J* = 7.9, 1.8 Hz, H-6′), 6.96 (1H, *d*, *J* = 7.9 Hz, H-5′); ^{13}C NMR ($CDCl_3$): δ21.0 (OCOMe), 32.2 (C-2), 55.9 (OMe), 63.8 (C-1), 108.1 (C-2′), 114.4 (C-5′), 119.8 (C-6′), 123.3 (C-3), 130.0 (C-1′), 132.2 (C-4), 145.3 (C-4′), 146.6 (C-3′), 171.1 (OCOMe).

(E)-4-(4-*hydroxy*-3-*methoxyphenyl*)*But*-2-*en*-1-*ol* (**5**). EI-MS, *m/z* 194 $[M]^+$; HR-MS *m/z* 194.0965 $[M]^+$ (calcd for $C_{11}H_{14}O_3$: 194.0942); ^{1}H NMR (C_6D_6): δ3.09 (2H, *d*, *J* = 6.7 Hz, H-1), 3.10 (3H, *s*, OMe), 3.78 (2H, *d*, *J* = 6.1 Hz, H-4), 5.33 (1H, *br s*, OH), 5.43 (1H, *dt*, *J* = 15.3, 6.1 Hz, H-3), 5.61 (1H, *dt*, *J* = 15.3, 6.7 Hz, H-2), 6.39 (1H, *d*, *J* = 1.8 Hz, H-2′), 6.55 (1H, *dd*, *J* = 8.5 and 1.8 Hz, H-6′), 6.82 (1H, *d*, *J* = 8.5 Hz, H-5′).

(E)-2-*Hydroxy*-4-(3,4-*dimethoxyphenyl*)*but*-3-*el*-1-*ol* (**6**). EI-MS, *mz* (rel. int.): 224 $[M]^+$ (76), 206 (85), 193 (100); HR-MS, *m/z* 224.1058 $[M]^+$ (calcd for $C_{12}H_{16}O_4$: 224.1047); ^{1}H NMR ($CDCl_3$): δ3.59 (1H, *dd*, *J* = 11.0, 7.3 Hz, H-1), 3.74 (1H, *dd*, *J* = 11.0, 3.7 Hz, H-1), 3.86 (3H, *s*, OMe), 3.88 (3H, *s*, OMe), 4.40 (1H, *ddd*, *J* = 7.3, 6.7, 3.7 Hz, H-2), 6.05 (1H, *dd*, *J* = 15.9, 6.7 Hz, H-3), 6.60 (1H, *d*, *J* = 15.9 Hz, H-4), 6.80 (1H, *d*, *J* = 8.6 Hz, H-5′), 6.90 (1H, *dd*, *J* = 8.6, 1.8 Hz, H-6′), 6.92 (1H, *d*, *J* = 1.8 Hz, H-2′).

(E)-2-*Methoxy*-4-(3,4-*dimethoxyphenyl*)*but*-3-*en*-1-*ol* (**7**). EI-MS, *m/z* (rel. int.): 238 $[M]^+$ (10), 207 (100); HR-MS *m/z* 238.1234 $[M]^+$ (calcd for $C_{13}H_{18}O_4$: 238.1204); ^{1}H NMR ($CDCl_3$): δ3.37 (3H, *s*, OMe-2), 3.63 (2H, *m*, H-1), 3.85 (1H, H-2), 3.87 (3H, *s*, Ar-OMe), 3.89 (3H, *s*, Ar-OMe), 5.89 (1H, *dd*, *J* = 15.9, 7.9 Hz, H-3), 6.57 (1H, *d*, *J* = 15.9 Hz, H-4), 6.81 (1H, *d*, *J* = 7.9 Hz, H-5′), 6.92

(1H, *dd*, J = 7.9, 1.8 Hz, H-6′), 6.94 (1H, *d*, J = 1.8 Hz, H-2′).

Acetylation of compounds **5–7**. Small amount (0.2–0.4 mg) of **5–7** were acetylated in the usual way (Ac_2O–pyridine at room temp.) to give **8–10**, respectively. Compound **8**: EI-MS, *m/z* (rel. int.): 278 $[M]^+$ (15), 236 (100), 176 (75). Compound **9**: ^{1}H NMR ($CDCl_3$): δ2.06 (3H, *s*, OAc), 2.09 (3H, *s*, OAc), 3.87 (3H, *s*, OMe), 3.88 (3H, *s*, OMe), 4.16 (1H, *dd*, J = 11.6, 7.3 Hz, H-1), 4.31 (1H, *dd*, J = 11.6, 3.7 Hz, H-1), 5.63 (1H, *dt*, J = 7.3, 3.7 Hz, H-2), 5.96 (1H, *dd*, J = 15.9, 7.3 Hz, H-3), 6.63 (1H, *d*, J = 15.9 Hz, H-4), 6.80 (1H, *d*, J = 8.6 Hz, H-5′), 6.91 (2H, *m*, H-2′ and H-6′). Compound **10**: ^{1}H NMR ($CDCl_3$): δ2.08 (3H, *s*, OAc), 3.36 (3H, *s*, OMe), 3.87 (3H, *s*, OMe), 3.89 (3H, *s*, OMe), 3.98 (1H, *dt*, J = 7.3, 3.7 Hz, H-2), 4.10 (1H, *dd*, J = 11.6, 7.3 Hz, H-1), 4.21 (1H, *dd*, J = 11.6, 3.7 Hz, H-1), 5.89 (1H, *dd*, J = 15.9, 7.3 Hz, H-3), 6.57 (1H, *d*, J = 15.9 Hz, H-4), 6.81 (1H, *d*, J = 8.6 Hz, H-5′), 6.29 (2H, *m*, H-2′ and H-6′).

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