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A 1,7-DIARYLHEPTANOID FROM *ALPINIA CONCHIGERA*

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Key Word Index—*Alpinia conchigera*; Zingiberaceae; rhizomes; 1,7-diarylheptanoids; flavonoids; phenylpropanoids.

Abstract—The rhizomes of *Alpinia conchigera* were found to contain a new 1,7-diarylheptanoid, which was identified as 1,7-diphenyl-3,5-heptanedione, together with four other diarylheptanoids, two flavonoids and four phenylpropanoids.

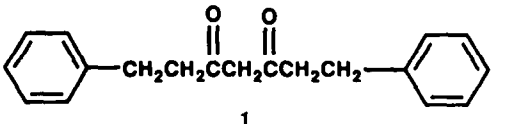
INTRODUCTION

The rhizomes of *Alpinia conchigera* Griff. are used in traditional Thai medicine to relieve gastro-intestinal disorders and in the preparation of Thai food dishes. The aqueous extract of the rhizomes has been shown to prevent the contraction of the bronchial tubes of guinea pig (Sunbhanich, M., unpublished results). Little is known about the chemical constituents of the rhizomes. In the only publication to date [1], it was reported that the phenylpropanoid derivatives, chavicol acetate and eugenol acetate are present in the fruit of *A. conchigera*, and that they show anti-inflammatory activity. In this paper, we have investigated the chemical constituents of both fresh and dried rhizomes of this plant. A new naturally occurring diarylheptanoid together with 10 known compounds were isolated and identified.

RESULTS AND DISCUSSION

Steam distillation of the fresh rhizomes of *A. conchigera* yielded 0.15% of an essential oil. GC-MS of the oil showed the presence of 12 components: chavicol acetate, α-pinene, β-pinene, *p*-cymene, cineol, terpinen-4-ol, α-terpineol, chavicol and four unidentified components. PLC of the oil resulted in the separation of the major component (chavicol acetate [2]) in 45% yield. The purified compound was characterized on the basis of its spectral data. The aqueous layer obtained from the steam distillation was extracted with ethyl acetate. Chromatography of the extract revealed the presence of chavicol acetate, 1-hydroxychavicol acetate [3], 4-acetoxycinnamyl alcohol and 4-acetoxycinnamyl acetate [4].

The dried rhizomes of *A. conchigera* were extracted consecutively with hexane, dichloromethane and methanol. After chromatographic separation, the hexane and dichloromethane fractions gave a new diarylheptanoid (**1**) [shown as the diketo form, but infact largely enolized] and four known diarylheptaniods, 1,7-diphenyl-5-hydroxy-3-heptanone, **2** [5–10], 5-hydroxy-7-(4′-hydroxy-3′-methoxyphenyl)-1-phenyl-3-heptanone, **3** [6, 7, 10, 11], 1,7-diphenylhept-4-en-3-one [6] and 7-(4′-hydroxy-3′-methoxyphenyl)-1-phenylhept-4-en-3-one, **4** [6, 10], while the methanol fraction gave two known flavonoids, 3,5,7-trihydroxyflavone [12] and 3,5,7-trihydroxy-4′-methoxyflavone [12].



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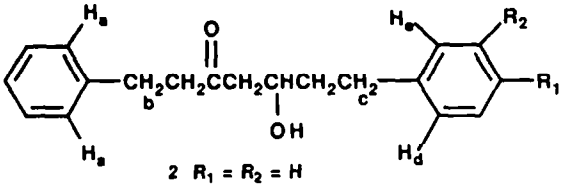
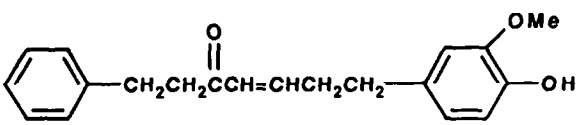


2 $R_1 = R_2 = H$

3 R_1 = OH, R_2 = OMe



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*Author to whom correspondence should be addressed.

The diarylheptanoid (**1**) was obtained as a pale yellow oil. It showed a $[M]^+$ peak at *m/z* 280.1453 in its HRMS spectrum suggesting the formula $C_{19}H_{20}O_2$ (calcd 280.1463). The ^1H NMR spectrum contained the signal of a H-bonded hydroxyl proton [δ15.45 (0.6H, *brs*)], the signals of two unsubstituted phenyl groups [δ7.15–7.23 (6H, *m*) and 7.25–7.33 (4H, *m*)], the signal of an olefinic proton in the enol form [δ5.43 (1.3H, *s*)], the signal of methylene protons in the diketo form [δ3.50 (0.7H, *s*)], α-methylene signals of ketones [δ2.72–2.93 (4H, *m*)], and the signals of benzyl protons [δ2.58 (4H, *t*, $J = 7.8$ Hz)]. These spectral data established that **1** is 1,7-diphenyl-3,5-heptanedione. This structure was supported by the presence of signals of the enol and keto carbonyl carbons at δ193.0 and 202.2 in the ^{13}C NMR spectrum as well as significant MS peaks at *m/z* 175 [($PhCH_2CH_2COCH_2CO$), 133 ($PhCH_2CH_2CO$), 105 ($PhCH_2CH_2$) and 91 ($PhCH_2$). Finally, oxidation of **2** with CrO_3–pyridine reagent gave **1**.

Other compounds were identified by comparison of their spectral data with those reported in the literature. In addition, the location and position of two aromatic substituents (OH and OMe) in the structures of **3** and **4** were confirmed by NOE experiments. When the signal at δ7.15 (H_a) of **3** was irradiated, enhancement of the signal at δ2.89 (H_b) was observed. As two H_c protons appeared separately at δ2.58 and 2.69, irradiation of the H_d and H_e signals at δ6.67 and 6.70 enhanced both signals of H_c as well as the methoxy signal at δ3.85. Enhancement of the signals of H_d and H_e was observed when either the signal of H_c at δ2.58 or that of H_c at δ2.69 was irradiated. These results indicated that the methoxyl and hydroxyl substituents are located at C-3 and C-4 on the right-hand aromatic ring. Similar results obtained with the acetate derivative confirmed the structure of **4**.

Many diarylheptanoids [5–18] have been isolated, but this is the first report of **1** as a natural product. Several groups [19–22] have synthesized **1**.

EXPERIMENTAL

General procedures. Mps: uncorr.; NMR: 400 MHz (^1H) and 100 MHz (^{13}C), $CDCl_3$, TMS as an int. standard; GC-MS (Hewlett Packard 5989 A) HP-1 column.

Plant material. The rhizomes of *A. conchigera* Griff. were collected in Songkla Province in 1990 and identified by Prof. Puangpen Siriruksa. The voucher specimen was deposited in the herbarium of the Department of Biology, Faculty of Science, Prince of Songkla University, Hatyai, Songkla.

Steam distillation. The fr. rhizomes (2.58 kg) were cut into small pieces and steam-distilled, yielding an essential oil (slightly yellow, 3.76 g, 0.15%). The major component was sepd by PLC ($CHCl_3$) to yield chavicol acetate in 45% yield. The aq. phase was filtered and then extracted with EtOAc. Evapn of the EtOAc layer to dryness *in vacuo* gave an orange-red syrup (10.3 g). The crude syrup was purified by quick CC on silica gel using a stepwise gradient system (hexane to MeOH). The resulting eluates were combined on the basis of their TLC patterns to give 5 frs. Fr. 2 (35% CH_2Cl_2–hexane–75% CH_2Cl_2–hexane) was further subjected to chromatographic sepn to yield 1-hydroxychavicol acetate and 4-acetoxycinnamyl acetate. Frs 3 and 4 (20% EtOAc–CH_2Cl_2–55% EtOAc–CH_2Cl_2), upon standing at room temp., gave 4-acetoxycinnamyl alcohol.

Isolation and extraction. Powdered and dried rhizomes (5 kg) were extracted twice with hexane, CH_2Cl_2 and MeOH, respectively. Removal of the solvents *in vacuo* afforded 132 g of hexane extract, 152 g of CH_2Cl_2 extract and 268 g of MeOH extract.

A portion (30 g) of the crude hexane extract was subjected to quick CC on silica gel using a stepwise gradient system (hexane to MeOH) to give 12 frs. Fr. 6 (13% hexane–CH_2Cl_2–30% hexane–CH_2Cl_2), after CC over silica gel (hexane to MeOH) and then PLC (hexane–CH_2Cl_2, 1:1) yielded **1** (40 mg) and 1,7-diphenylhept-4-en-3-one (20 mg). Fr. 8 (CH_2Cl_2–15% EtOAc–CH_2Cl_2), after CC on silica gel (hexane to MeOH), gave **2** (1.25 g) and **4** (450 g). Fr. 9 (20% EtOAc–CH_2Cl_2–EtOAc) was further dissolved in hexane and the soluble hexane fr., upon standing at room temp., afforded **2** (600 mg).

A portion (30 g) of the CH_2Cl_2 extract was subjected to quick CC over silica gel using a stepwise gradient system (hexane to MeOH) to afford 12 frs. Fr. 4 (15% hexane–CH_2Cl_2–CH_2Cl_2) was purified by CC on silica gel (hexane to MeOH) and then PLC (30% Et_2O–hexane), to yield **1** (30 mg) and **2** (85 mg), while fr. 7, upon standing at room temp., afforded **3** (40 mg).

A portion (12.4 g) of the MeOH extract was subjected to CC over silica gel using a stepwise gradient system (hexane to MeOH) to afford 9 frs. Fr. 5 (13% EtOAc–CH_2Cl_2–70% EtOAc–CH_2Cl_2) was recrystallized in EtOAc–CH_2Cl_2 (1:4) to yield 3,5,7-trihydroxyflavone (20 mg), 3,5,7-trihydroxy-4′-methoxyflavone (15 mg), and a mixt. of these flavones. This mixt. was methylated with Me_2SO_4 in the presence of excess K_2CO_3 in refluxing Me_2CO. The resulting products were purified by PLC (hexane–EtOAc, 1:1) to yield 3,5,7-trimethoxyflavone and 3,5,7,4′-tetramethoxyflavone.

1,7-Diphenyl-3,5-heptanedione (**1**). Pale yellow oil. ^1H NMR: δ2.58 (4H, *t*, $J = 7.8$ Hz), 2.72–2.93 (4H, *m*), 3.50 (0.7H, *s*), 5.43 (1.3H, *s*), 7.15–7.25 (6H, *m*), 7.25–7.33 (4H, *m*), 15.45 (0.6H, *brs*); ^{13}C NMR: δ29.3, 31.4, 39.9, 45.0, 57.4, 99.5, 126.1, 128.2, 128.4, 140.4, 140.5, 193.0, 202.2; MS *m/z* (rel. int.): 280 $[M]^+$ (23), 175 (46), 133 (12), 105 (61), 91 (100), 77 (18), 65 (20); HRMS 280.1453 $[M]^+$.

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