Communications to the Editor

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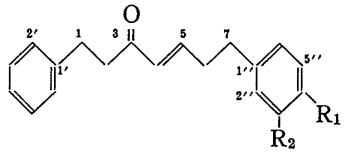
Two New Diarylheptanoids from *Alpinia officinarum* Hance

Two new and two known diarylheptanoids were isolated from the rhizomes of *Alpinia officinarum* Hance (Zingiberaceae). The structure of the new compounds was determined to be 1,7-diphenylhept-4-en-3-one (**1**) and 7-(4″-hydroxy-3″-methoxyphenyl)-1-phenylhept-4-en-3-one (**3**) on the basis of the spectral data and chemical correlation.

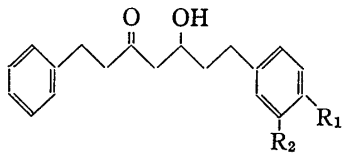
Keywords——Zingiberaceae; *Alpinia officinarum*; diarylheptanoid; 1,7-diphenylhept-4-en-3-one; 7-(4″-hydroxy-3″-methoxyphenyl)-1-phenylhept-4-en-3-one; 1,7-diphenyl-5-hydroxy-3-heptanone; 5-hydroxy-7-(4″-hydroxy-3″-methoxyphenyl)-1-phenyl-3-heptanone; MS; ^{13}C-NMR

The rhizomes of *Alpinia officinarum* (Zingiberaceae)(Ryôkyô in Japanese) have been used as a component of some formulae in Chinese medicine to relieve gastro-intestinal disorders. *n*-Hexane and chloroform soluble fractions of this drug have been shown to have pharmacological activity against the contraction of the ileum of guinea pigs.[1] Here we report the isolation of two new and two known diarylheptanoids from these fractions.

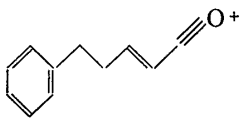
The commercial crude drug was extracted with methanol. The extract was separated into the *n*-hexane and chloroform fractions by the usual procedure. After chromatographic purification, the former fraction yielded compound **1**, and the latter fraction compounds **2**, **3**, and **4** in increasing order of polarity.



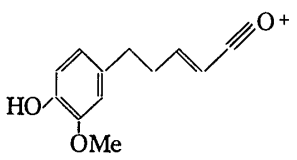
1 : $R_1=R_2=H$
3 : $R_1=OH$, $R_2=OMe$



2 : $R_1=R_2=H$
4 : $R_1=OH$, $R_2=OMe$



5 *m/z* 159



6 *m/z* 205

Chart 1

Compounds **2** and **4** were identified as dihydroyashabushiketol(1,7-diphenyl-5-hydroxy-3-heptanone, **2**)[2] and 5-hydroxy-7-(4″-hydroxy-3″-methoxyphenyl)-1-phenyl-3-heptanone (**4**),[3] respectively, by comparing their spectral data with those of authentic specimens. Compound **4**, a pungent principle,[3] has recently been isolated from the same source.

Compound **1** is a colorless oil, $C_{19}H_{20}O$ (*Anal.* Calcd: C, 86.32; H, 7.63. Found: C, 86.57; H, 7.72), with three isolated chromophores, two nonsubstituted phenyl groups and an α,β-unsaturated ketone grouping in its UV (EtOH, 209 and 221 nm (ε=21000 and 16200)) and IR (liquid film, 1695 cm^{-1}) spectra. In the ^{1}H-NMR spectrum ($CDCl_3$) four methylene proton signals were observed in the range of δ 2.30—3.0 ppm (8Hz, m) in addition to proton signals of the phenyl groups (δ 7.00—7.30 ppm, 10H, m) and of the *trans*-α,β-unsaturated ketone grouping (δ 6.04 ppm, 1H, d, J=16 Hz and δ 6.78, double t, J=16Hz and 6 Hz). A mass

Table I. The ^{13}C-NMR ($CDCl_3$, δ ppm) Spectra of **1**, **2**, **3**, and **4**

No.	1	2	3	4
1	30.0 t	31.7 t	30.0 t	31.4 t
2	41.6 t	44.2 t	41.6 t	44.9 t
3	199.0 s	210.7 s	199.3 s	210.9 s
4	130.5 d	49.2 t	130.5 d	49.2 t
5	146.0 d	66.7 d	146.3 d	66.9 d
6	34.3 t [a]	38.1 t	33.3 t [b]	38.3 t
7	34.0 t [a]	29.4 t	34.1 t [b]	29.5 t
1′	141.1 s	141.7 s	141.1 s	140.6 s
2′	128.2 d	128.1 d	128.2 d	128.2 d
3′	128.3 d	128.2 d	128.2 d	128.4 d
4′	126.0 d	126.0 d	126.0 d	126.1 d
5′	128.3 d	128.2 d	128.2 d	128.4 d
6′	128.2 d	128.1 d	128.2 d	128.2 d
1″	140.5 s	140.5 d	132.4 s	133.6 s
2″	128.2 d	128.2 d	111.0 d	111.1 d
3″	128.3 d	128.1 d	146.3 s	146.4 s
4″	125.9 d	125.7 d	144.0 s	143.7 s
5″	128.3 d	128.1 d	114.4 d	114.3 d
6″	128.2 d	128.2 d	120.8 d	120.8 d
3″-OMe	—	—	55.8 q	55.8 q

a) and *b*) are changeable. s=singlet, d=doublet, t=triplet, q=quartet.

fragment at *m/z* 159 (76%) (**5**) suggests that the whole structure of **1** is 1,7-diphenylhept-4-en-3-one. Acid treatment of compound **2** gave an α,β-unsaturated ketone which was identical with compound **1** and this finally established the structure of **1**.

Compound **3**, a colorless oil, $C_{20}H_{22}O_3$ (M^+: *m/z* 310.1594, Calcd: 310.1568) showed UV absorption maxima (EtOH) at 216 and 281 nm (ε=20100 and 3500), and the bathochromic shift (211, 247 (infl.), and 295 nm) occurred on addition of alkali. The ^{1}H-NMR spectrum ($CDCl_3$) of **3** revealed methylene proton signals at δ 2.12—2.96 ppm (8H, m), a methoxyl signal at δ 3.80 ppm (3H, s), a hydroxyl proton signal at δ 5.64 ppm (1H, s, which disappeared on addition of D_2O), an α-proton signal of an α,β-unsaturated ketone grouping centered at δ 6.06 ppm (1H, d, J=16 Hz), and aromatic proton signals of a phenyl group at δ 7.12—7.30 (5H, m). The β-proton signal of the unsaturated ketone overlapped three proton signals on a disubstituted phenyl group at δ 7.12—7.30 ppm (4H, m). The mass spectrum showed a peak at *m/z* 205 (2%) (**6**), indicating the position of the α,β-unsaturated ketone grouping. The presence of a 4″-hydroxy-3″-methoxyphenyl moiety was assumed by comparison of the ^{13}C-NMR spectrum of compound **3** with those of **4** (Table I) and the analogous compounds.[4] Accordingly, compound **3** is identified as 7-(4″-hydroxy-3″-methoxyphenyl)-1-phenylhept-4-en-3-one. This formulation was also verified by acid conversion of **4** into **3** as in the case of compound **1**.

It is possible that compound **1** and **3** may be formed from compounds **2** and **4**, respectively, during preparation of the crude drug.

References and Notes

1) These fractions have an inhibitory effect on the contraction of the isolated guinea pig ileum induced by histamine (1×10^{-7} g/ml) and barium chloride (2×10^{-4} g/ml) as shown below.

	Histamine	Barium Chloride
n-Hexane fr.	73% (4.2×10^{-5} g/ml)	25% (2.1×10^{-5} g/ml)
Chloroform fr.	95% (1×10^{-4} g/ml)	100% (1×10^{-4} g/ml)

A detailed study will be published elsewhere.

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Tumor Visualization by ^{99m}Tc-Labeled Ethylenediamine-N,N-diacetic Acid[1)]

Tumor tissues were clearly visualized in scintigrams of mice bearing Ehrlich ascites tumor a few hours after the administration of ethylenediamine-N,N-diacetic acid labeled with ^{99m}Tc.

Keywords——radiopharmaceuticals; tumor scintigraphy; ^{99m}Tc; ethylenediamine-N,N-diacetic acid; Ehrlich ascites tumor

Among many radiodiagnostic agents developed for the scintigraphic visualization of tumors, clinically favored are ^{67}Ga, ^{201}Tl, and bleomycin labeled with various radionuclides.[2)] Though they are effective in imaging certain types of tumors, specific scanning agents are not available for a number of other malignant diseases. ^{99m}Tc is an ideal radionuclide for the scintigraphy because of its favorable physical characteristics and is widely used clinically for the scanning of various organs.

We have been working on ^{99m}Tc labeled amino acids to evaluate them as radiopharmaceuticals.[1)] In the course of the study, we found that ^{99m}Tc radioactivity was concentrated in Ehrlich ascites tumors after the administration of ethylenediamine-N,N-diacetic acid (EDDA) labeled with ^{99m}Tc to experimental animals. This communication presents the *in vivo* behavior and the scintigram of ^{99m}Tc EDDA and suggests that it can be a new radiodiagnostic agent for tumor visualization.

EDDA was prepared by the reported method[3)] and labeled with ^{99m}Tc by the $SnCl_2$ method as described previously.[1)] The labeling yield was greater than 99% when estimated by the thin layer chromatography. The ^{99m}Tc EDDA complex thus prepared was stable in neutral saline solution, other radiochromatographic peak being undetectable on standing it for 24 h at room temperature.

A group of mice (male; 30±2 g body weight) were implanted with Ehrlich ascites tumor cells at the right foreleg. The mice were left for 3 weeks for the growth of the tumors. A saline solution of ^{99m}Tc EDDA (0.1 ml, 500 μCi) was injected through the tail vein in the mice showing tumor growth. The animals were sacrificed 5 h after the injection. The organs, blood, some muscle, and the tumor were removed, weighed, and the radioactivity was measured with an autogamma scintillation spectrophotometer (Packard 5360). The percentages of the injected dose per gram of organs and tissues were calculated.

The results were blood, 0.19±0.12; liver, 1.90±0.46; spleen, 1.12±0.21; stomach 0.41±0.22; intestine, 1.25±0.16; kidney, 12.61±2.41; muscle, 0.38±0.11; and tumor, 4.15±1.01. The values are mean ±SD of three animals.

Very high uptake of radioactivity by the tumor and the kidneys is noted. The tumor/blood and tumor/muscle ratios were 4,61 and 10.92, respectively, 5 h after the injection.