[Chem. Pharm. Bull. 31(7)2491—2496(1983)]

Synthesis of Diarylheptanoids and Assessment of Their Pungency

HIDEJI ITOKAWA,* RITSUO AIYAMA and AKIRA IKUTA

Tokyo College of Pharmacy, 1432–1 Horinouchi, Hachioji, Tokyo 192–03, Japan

(Received November 22, 1982)

With the aim of correlating pungency with substituent groups on one benzene ring, various analogues of yakuchinones were synthesized by means of the Claisen–Schmidt reaction. Their pungencies were assessed by direct comparison of the threshold concentrations obtained in taste experiments. The presence of a phenolic hydroxyl group was indispensable for high pungency, while that of a 1,2-double bond of the heptanone part tended to decrease the pungency.

Keywords——diarylheptanoid; pungency; yakuchinone-A; yakuchinone-B; zingerone

Since the first isolation of zingerone, a strong pungent principle, in 1917 by Nomura,[1] many pungent principles and related compounds (*e.g.* gingerols,[2] shogaol[3] and paradols[4]) of Zingiberaceous plants have been reported from *Zingiber* and *Amomum* spp. In 1978, Inoue *et al.* isolated a pungent principle having a diarylheptanoid-type structure from *Alpinia officinarum*.[5] Recently we also reported the isolation and structure determination of two pungent principles, yakuchinone-A (Ia) and yakuchinone-B (Ib), which are linear diarylheptanoids, from *Alpinia oxyphylla* MIQUEL together with an evaluation of their pungency.[6] In 1972, from the standpoint of the relationship between pungency and structure Locksley *et al.* prepared eleven paradols, from [0]-paradol (zingerone) to [10]-paradol, with different sizes of alkyl chains. On the basis of taste evaluation experiments on these paradols, they found a close relationship between the pungency and the length of side chain.[7]

As a part of a more general program aimed at correlating pungency with several substituent groups on one benzene ring, we synthesized analogues of yakuchinone-A and -B by using the Claisen–Schmidt reaction and hydrogenation. Yakuchinone-A was previously

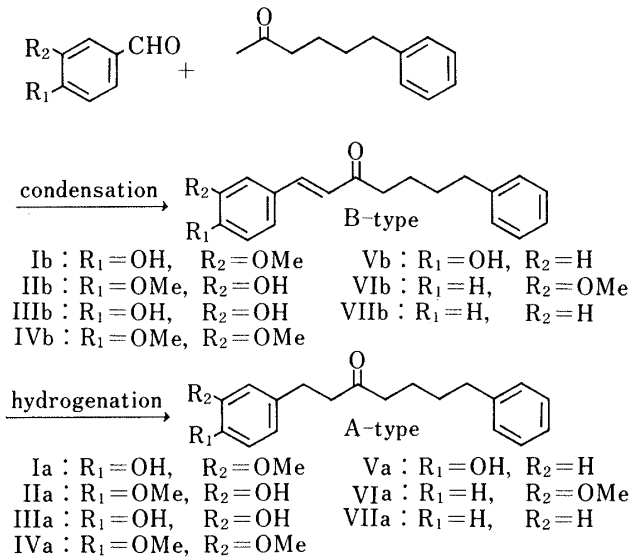


Chart 1

prepared by condensation of benzylvanillin with 6-phenyl-2-hexanone followed by hydrogenation.[6a] For the preparation of yakuchinone-B, which contains a double bond, however, we employed a condensation method using vanillin without blocking of the phenolic hydroxyl group[6b] based on the weak aicd-weak base combination which was previously used by Locksley *et al.* for the synthesis of the paradol series.[7] Thus, the condensation of vanillin with 6-phenyl-2-hexanone by the use of equimolar quantities of acetic acid and pyrrolidine in ether gave yakuchinone-B (80% yield), from which yakuchinone-A was obtained by hydrogenation in the presence of palladium-carbon (5%) in benzene. Therefore, we applied this method (method A) for the analogues of yakuchinones and obtained compounds IIb,

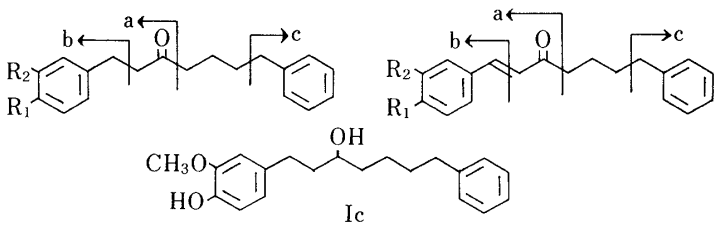
Table I. Reaction Conditions and Yields of Diarylheptanoids

Starting material	Condensation conditions	Condensation product (yield %)		Hydrogenation product (yield %)	
Vanillin	Ac–Py/Et_2O	Ib	(80)[6b]	Ia	(98)[6b]
Isovanillin	Ac–Py/Et_2O	IIb	(65)	IIa	(95)
Protocatechualdehyde	Ac–Py/THF	IIIb	(72)	IIIa	(65)
Veratrum aldehyde	NaOH/EtOH	IVb	(69)	IVa	(90)
p-Hydroxybenzaldehyde	Ac–Py/Et_2O	Vb	(70)	Va	(73)
m-Anisaldehyde	NaOH/EtOH	VIb	(37)	VIa	(85)
Benzaldehyde	NaOH/EtOH	VIIb	(93)	VIIa	(92)

Ac–Py, acetic acid–pyrrolidine.

Table II. Mass Data and Threshold Concentrations for Pungency of Diarylheptanoids

Compound No.	Formula	High resolution MS		Fragment				Threshold $\bar{x}$ (mol/ml)
		Found	Calcd	M^+	a	b	c	
Ia	$C_{20}H_{24}O_3$	312.1705	312.1723	312	179	137	91	7.85×10^{-9}
IIa	$C_{20}H_{24}O_3$	312.1714	312.1723	312	179	137	91	6.34×10^{-8}
IIIa	$C_{19}H_{22}O_3$	298.1557	298.1567	298	165	123	91	2.98×10^{-8}
IVa	$C_{21}H_{26}O_3$	326.1871	326.1880	326	193	151	91	5.12×10^{-7}
Va	$C_{19}H_{22}O_2$	282.1597	282.1618	282	149	107	91	1.18×10^{-7}
VIa	$C_{20}H_{24}O_2$	296.1755	296.1774	296	163	121	91	8.75×10^{-7}
VIIa	$C_{19}H_{22}O$	266.1666	266.1669	266	133	91	91	3.64×10^{-7}
Ib	$C_{20}H_{22}O_3$	310.1548	310.1567	310	177	137	91	1.64×10^{-7}
IIb	$C_{20}H_{22}O_3$	310.1567	310.1567	310	177	137	91	Weak
IIIb	$C_{19}H_{20}O_3$	296.1431	296.1412	296	163	123	91	8.00×10^{-7}
IVb	$C_{21}H_{24}O_3$	324.1725	324.1724	324	191	151	91	1.13×10^{-6}
Vb	$C_{19}H_{20}O_2$	280.1455	280.1461	280	147	107	91	3.04×10^{-7}
VIb	$C_{20}H_{22}O_2$	294.1614	294.1618	294	161	121	91	Weak
VIIb	$C_{19}H_{20}O$	264.1513	264.1513	294	131	91	91	2.53×10^{-7}
Ic	$C_{20}H_{26}O_3$	314.1886	314.1881	314	—	—	—	1.30×10^{-8}
Zingerone								1.25×10^{-6}



Ic

IIIb and Vb.

On the other hand, some analogues having no hydroxyl group, IVb, VIb and VIIb, were obtained by using the usual condensation process in the presence of aqueous sodium hydroxide (method B)

In the mass spectra of the diarylheptanoids (Table II), the pattern of four major fragments (molecular ion, acyl cation and two benzylic fissions) was a common observation.

TABLE III. ^{13}C NMR Chemical Shifts for Diarylheptanoids

Carbon No.	IIa	IIIa	IVa	Va	VIa	VIIa	Ic
1	29.1	29.2	29.5	28.9	29.8	29.8	31.4[a]
2	44.2	44.4	44.5	44.5	44.1	44.2	39.3
3	210.1	212.7	209.9	210.9	209.9	209.7	71.3
4	42.8	43.3	42.8	42.8	42.8	42.8	37.4
5	23.3	23.4	23.4	23.4	23.4	23.4	25.3
6	30.8	30.8	31.0	30.8	30.9	31.0	31.7[a]
7	35.7	35.6	35.7	35.6	35.6	35.7	35.9
1′	134.2	133.4	133.7	132.7	142.5[a]	141.1[a]	134.0
2′	110.7	115.5	111.3[a]	129.3	114.0	128.3	111.0
3′	145.5	143.9	148.8	115.3	159.5	128.3	146.4
4′	144.9	142.2[a]	147.3	153.9	111.3	126.0[b]	143.7
5′	114.4	115.5	111.7[a]	115.3	129.3	128.3	114.3
6′	119.5	120.3	120.0	129.3	120.6	128.3	120.9
1″	142.1	142.1[a]	142.1	142.0	141.8[a]	142.1[a]	142.5
2″ and 6″	128.2	128.3	128.3	128.2	128.2	128.3	128.2[b]
3″ and 5″	128.2	128.3	128.3	128.2	128.2	128.3	128.3[b]
4″	125.6	125.7	125.7	125.6	125.6	125.7[b]	125.7
3′-OMe	—	—	55.8	—	55.1	—	55.9
4′-OMe	55.9	—	55.8	—	—	—	—

Carbon No.	IIb	IIIb	IVb	Vb	VIb	VIIb	P.H
1	142.3	144.1	142.4	144.3	142.4	142.3	—
2	122.1[a]	123.0[a]	122.9[a]	123.0	126.6	126.2	(29.8)
3	200.3	202.3	200.1	202.6	200.1	200.1	208.7
4	40.6	40.5	40.5	40.4	40.8	40.7	43.5
5	24.1	24.4	24.1	24.4	24.1	24.0	23.4
6	31.1	31.1	31.0	31.0	31.1	31.0	30.8
7	35.7	35.9	35.7	35.7	35.9	35.7	35.7
1′	128.2	127.2	128.3	126.2	136.0	134.5	—
2′	110.6	114.5[b]	109.8	130.5	113.2	128.9	—
3′	145.9	144.3[c]	149.2	116.2	160.0	130.3	—
4′	148.7	147.3	151.2	159.4	116.4	128.9	—
5′	113.1	115.6[b]	111.1	116.2	130.0	130.3	—
6′	124.4[a]	123.8[a]	124.4[a]	130.5	121.0	128.9	—
1″	142.1	144.0[c]	142.1	142.1	142.4	142.1	142.0
2″ and 6″	128.2	128.4	128.2[b]	128.2[a]	128.3[a]	128.1	128.2
3″ and 5″	128.2	128.4	128.3[b]	128.3[a]	128.5[a]	128.1	128.2
4″	125.6	125.9	125.6	125.7	125.8	125.7	125.6
3′-OMe	—	—	55.9[c]	—	55.4	—	—
4′-OMe	56.0	—	56.1[c]	—	—	—	—

P.H, 6-phenyl-2-hexanone.

a—c) The assignments may be reversed.

The measurements were made on a JEOL FX-100 spectrometer in $CDCl_3$ with TMS as an internal reference and were expressed in ppm.

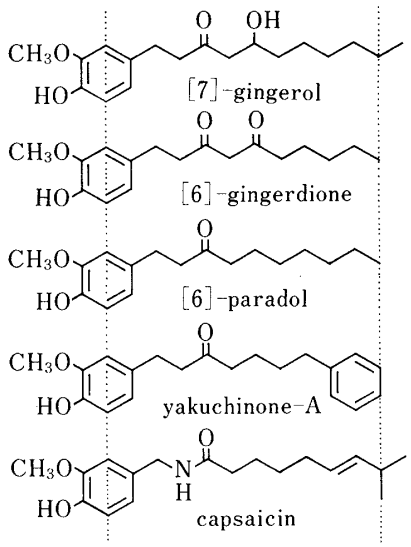


Fig. 1

Another peak due to McLafferty rearrangement was also observed at low intensity. The carbon nuclear magnetic resonance (^{13}C NMR) spectral data for diarylheptanoids are listed in Table III. The signal assignments were made by means of chemical shift rules,[8] off-resonance proton decoupling experiments and comparison with the spectra of Ia and Ib.

The pungency of these diarylheptanoids was assessed by direct comparison of their threshold concentrations, which are listed in Table II. The threshold concentration of Ia was found to be 7.85×10^{-9} mol/ml, and that of zingerone, classified as a strongly pungent compound, was found to be 1.25×10^{-6} mol/ml, *i.e.* the pungency of Ia was more than 100 times stronger than that of zingerone. The data reported for the [*n*]-paradols[7] show that [6]-paradol is the most pungent principle among natural compounds, although the unnatural [5]- and [7]-members have similar thresholds. Among the [*n*]-gingerols, the [7]- and [8]-members are the most pungent,[9] while among [*n*]-gingerdiones and [*n*]-dehydrogingerdiones, the [6]-homologue is the hottest in each case.[9] In our studies, many diarylheptanoids were found to be more pungent than zingerone, possibly because the diarylheptanoids have similar molecular lengths to [6]-paradol, [7]-gingerol and [6]-gingerdione, which are the most pungent compounds in their series (Fig. 1). The presence of a 1,2-double bond appeared to decrease the pungency, whereas the presence of a free phenolic hydroxyl group was indispensable for high pungency; the lack of a hydroxyl group or its replacement by a methoxyl group on the aromatic ring led to a decrease in the pungency compared with the corresponding free phenolic compound. From this point of view, our taste experiments gave results approximately similar to those of the pain-producing experiments with capsaicin congeners by Szolcsányi and Jancsó-Gábor;[10] the relationships between structure and pungency described in this paper are similar to those in the capsaicin series.

Experimental

All mps were determined on a micro-melting point apparatus (Yanagimoto) and are uncorrected ^{13}C NMR spectra were recorded on a JEOL FX-100 spectrometer at 25.2 MHz with tetramethylsilane as an internal standard, and all data are listed in Table III. MS were obtained on a Hitachi M-80 double-focusing mass spectrometer with perfluorokerosene as a standard, and the data are listed in Table II.

6-Phenyl-2-hexanone——6-Phenyl-2-hexanone was prepared *via* 6-phenylhexa-3,5-dien-2-one, which was obtained by the condensation of (*E*)-cinnamaldehyde (25.0 g, 0.19 mol) with acetone (28 ml, 0.38 mol) in the presence of aq. 10% NaOH soln. (about 30 ml) at room temp. for 3 h. This reaction mixture was partitioned between benzene and water in a separatory funnel. The former fraction was washed with water, and chromatographed on silica gel using *n*-hexane–ethyl acetate (9 : 1) to afford a yellow amorphous material, from which 6-phenyl-2-hexanone (22.1 g) was

obtained by hydrogenation in the presence of 5% Pd-C in $CHCl_3$ for 9 h (total yield: 66% from (*E*)-cinnamaldehyde). A colorless oil, IR ν_{max}^{neat} cm^{-1}: 1715 and 1595; ^1H NMR (in $CDCl_3$) δ: 1.64 (4H, m), 2.12 (3H, s), 2.42 (2H, br t), 2.62 (2H, br t), 7.0—7.3 (5H, m); MS *m/z* (rel. int. %): 176 (47), 129 (22), 118 (42), 117 (29), 104 (13), 91 (100).

Method A——6-Phenyl-2-hexanone (2.00 g, 1.12×10^{-2} mol) was added to a stirred mixture of acetic acid (0.7 g) and pyrrolidine (0.8 g) in Et_2O. An aromatic aldehyde (1.12×10^{-2} mol; isovanillin 1.70 g; protocatechualdehyde 1.55 g; *p*-hydroxybenzaldehyde 1.37 g) in Et_2O or tetrahydrofuran (THF) was added slowly at room temp., and the mixture was stirred for 2 d. When thin-layer chromatography (TLC) showed that almost no aldehyde remained, the mixture was poured into dil. HCl, and extracted with Et_2O or EtOAc. The organic phase was washed successively with water, sat. $NaHSO_3$ and water, and concentrated. The product was purified by silica gel chromatography with benzene–EtOAc, and finally by recrystallization (IIb: 2.26 g, 65%. IIIb: 2.39 g, 72%. Vb: 2.20 g, 70%).

Method B——A nonhydroxy aromatic aldehyde (1.12×10^{-2} mol; veratrum aldehyde 1.86 g; *m*-anisaldehyde 1.52 g; benzaldehyde 1.19 g) in EtOH was added slowly to an ethanolic solution of 6-phenyl-2-hexanone (2.00 g, 1.12×10^{-2} mol) containing aq. 10% NaOH (5 ml) at room temp., and the mixture was stirred overnight. The reaction mixture was poured into dil. HCl, and partitioned between large amounts of Et_2O and water. The organic layer was washed successively with water, sat. $NaHSO_3$ and water, and concentrated. The product was purified by silica gel chromatography with *n*-hexane–EtOAc (IVb: 2.51 g, 69%. VIb: 1.23 g, 37%. VIIb: 2.75 g, 93%.).

Hydrogenation of B-type Diarylheptanoids to A-type Diarylheptanoids: A B-type diarylheptanoid (200 mg) in benzene or EtOAc containing 5% Pd-C (about 30 mg) was stirred under an atmosphere of H_2 for 3—8 h. The product was purified by silica gel chromatography with benzene–EtOAc.

(*E*)-1-(3-Hydroxy-4-methoxyphenyl)-7-phenylhept-1-en-3-one (IIb)——Colorless needles, mp 77.5—78.5 °C (MeOH). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550, 2940, 1680, 1650, 1605, 1585, 1510, 1460, 1440, 1030, 975. ^1H NMR ($CDCl_3$) δ: 1.68 (4H, m), 2.62 (4H, m), 3.84 (3H, s), 6.08 (1H, br), 6.57 (1H, d, J=16 Hz), 6.79 (1H, d, J=8 Hz), 7.03 (1H, dd, J=2, 8 Hz), 7.0—7.3 (6H, overlap. m), 7.64 (1H, d, J=16 Hz).

(*E*)-1-(3,4-Dihydroxyphenyl)-7-phenylhept-1-en-3-one (IIIb)——Yellow needles mp 112.0—112.5 °C (benzene), IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3560, 3500, 2940, 1680, 1650, 1595, 1515, 1445, 1280, 1105, 975; ^1H NMR ($CDCl_3$) δ: 1.69 (4H, m), 2.61 (4H, m), 6.56 (1H, d, J=16 Hz), 6.7—7.3 (8H, m), 7.48 (1H, d, J=16 Hz).

(*E*)-1-(3,4-Dimethoxyphenyl)-7-phenylhept-1-en-3-one (IVb)——A yellow oil, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2940, 1680, 1600, 1590, 1515, 1465, 1270, 1140, 1020; ^1H NMR ($CDCl_3$) δ: 1.71 (4H, m), 2.64 (4H, m), 3.90 (6H, s), 6.60 (1H, d, J=16 Hz), 6.8—7.3 (8H, m), 7.48 (1H, d, J=16 Hz).

(*E*)-1-(4-Hydroxyphenyl)-7-phenylhept-1-en-3-one (Vb)——Yellow needles, mp 70—71 °C (benzene–hexane). IR $\nu_{max}^{CHCl_3}$ cm^{-1}; 3600, 3280, 2940, 1675, 1650, 1600, 1585, 1510, 1165, 1100; ^1H NMR ($CDCl_3$) δ: 1.70 (4H, m), 2.67 (4H, m), 6.60 (1H, d, J=16 Hz), 6.87 (2H, d, J=8 Hz), 7.0—7.4 (5H, m), 7.40 (2H, d, J=8 Hz), 7.52 (1H, d, J=16 Hz).

(*E*)-1-(3-Methoxyphenyl)-7-phenylhept-1-en-3-one (VIb)——A yellow oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2940, 1685, 1655, 1610, 1580, 1490, 1465, 1455, 1430, 1275, 1160, 1105, 980; ^1H NMR ($CDCl_3$) δ: 1.71 (4H, m), 2.67 (4H, m), 3.82 (3H, s), 6.67 (1H, d, J=16 Hz), 6.8—7.4 (9H, overlap. m), 7.50 (1H, d, J=16 Hz).

(*E*)-1,7-Diphenylhept-1-en-3-one (VIIb)——A yellow oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2940, 1685, 1655, 1610, 1580, 1500, 1450, 1100, 980; ^1H NMR ($CDCl_3$) δ: 1.70 (4H, m), 2.67 (4H, m), 6.71 (1H, d, J=16 Hz), 7.0—7.4 (10H, m), 7.51 (1H, d, J=16 Hz).

1-(3-Hydroxy-4-methoxyphenyl)-7-phenyl-3-heptanone (IIa)——A colorless oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3560, 2940, 1710, 1595, 1515, 1455, 1445, 1275, 1135, 1030; ^1H NMR ($CDCl_3$) δ: 1.57 (4H, m), 2.38 (2H, br t), 2.58 (2H, br t), 2.6—2.9 (4H, m), 3.82 (3H, s), 5.51 (1H, OH), 6.61 (1H, dd, J=2, 8 Hz), 6.73 (1H, d, J=2 Hz), 6.78 (1H, d, J=8 Hz), 7.0—7.4 (5H, m).

1-(3,4-Dihydroxyphenyl)-7-phenyl-3-heptanone (IIIa)——A slightly red oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3560, 3380, 2940, 1705, 1605, 1520, 1500, 1450, 1405, 1365, 1280, 1110, 950; ^1H NMR ($CDCl_3$) δ: 1.56 (4H, m), 2.38 (2H, br t), 2.60 (2H, br t), 2.70 (4H, m), 5.98 (2H, OH), 6.53 (1H, dd, J=2, 8 Hz), 6.68 (1H, d, J=2 Hz), 6.74 (1H, d, J=8 Hz), 7.0—7.4 (5H, m).

1-(3,4-Methoxyphenyl)-4-phenyl-3-heptanone (IVa)——A colorless oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2940, 1710, 1605, 1595, 1515, 1465, 1455, 1140, 1025. ^1H NMR ($CDCl_3$) δ: 1.57 (4H, m), 2.38 (2H, br t), 2.58 (2H, br t), 2.6—2.9 (4H, m), 3.82 (6H, s), 6.6—6.8 (3H, m), 7.0—7.4 (5H, m).

1-(4-Hydroxyphenyl)-7-phenyl-3-heptanone (Va)——A colorless oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600, 3370, 2940, 1710, 1615, 1600, 1520, 1500, 1455, 1365, 1255, 1170, 1100, 830; ^1H NMR ($CDCl_3$) δ: 1.57 (4H, m), 2.38 (2H, br t), 2.57 (2H, br t), 2.6—2.9 (4H, m), 5.96 (1H, OH), 6.79 (4H, d, J=8 Hz), 7.00 (2H, d, J=8 Hz), 7.0—7.4 (5H, m).

1-(3-Methoxyphenyl)-7-phenyl-3-heptanone (VIa)——A colorless oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2940, 1710, 1600, 1585, 1495, 1465, 1455, 1435, 1365, 1255, 1150, 1040; ^1H NMR ($CDCl_3$) δ: 1.60 (4H, m), 2.38 (2H, br t), 2.69 (2H, br t), 2.7—3.0 (4H, m), 3.77 (3H, s), 6.6—6.8 (4H, m), 7.0—7.4 (5H, m).

1,7-Diphenyl-3-heptanone (VIIa)——A colorless oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2940, 1705, 1605, 1500, 1455, 1405, 1370, 1100, 1080, 1030, 910; ^1H NMR ($CDCl_3$) δ: 1.60 (4H, m), 2.39 (2H, br t), 2.57 (2H, br t), 2.6—2.9 (4H, m), 7.0—7.4 (10H, m).

1-(4-Hydroxy-3-methoxyphenyl)-7-phenyl-3-heptanol (Ic)——Reduction of **Ia** with $NaBH_4$ in MeOH yielded **Ic**

as colorless needles. mp 55—56 °C (benzene–hexane). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550, 2940, 1600, 1515, 1465, 1455, 1265, 1130; ^1H NMR ($CDCl_3$) δ: 1.3—1.8 (8H, m), 2.61 (4H, m), 3.60 (1H, m) 3.84 (3H, s), 5.60 (1H, OH), 6.6—6.8 (2H, overlap. m), 6.83 (1H, d, $J=8$ Hz), 7.0—7.4 (5H, m). MS *m/z* (ref. int. %): 314 (M^+, 35), 137 (100), 91 (90).

Evaluation of Pungency——A panel of ten tasters was used to assess the pungency of diarylheptanoids in ethanol solutions which were diluted to 1 part in 50 (v/v), 1 part in 100 (v/v), *etc.*, with 5% sucrose soln. containing 1% sodium carboxymethyl cellulose. Samples (0.5 ml) of each soln. were placed on the tongue of each taster. After few minutes, each taster was asked to report any pungent effect. The minimal concentration which could be detected by each taster was recorded in each case. The average value for each compound was taken, and regarded as the threshold concentration of the diarylheptanoid.

Acknowledgements The authors gratefully acknowledge the assistance of Mr. Asao Kobayashi, Mr. Tetsuo Takeda and Miss Junko Miyamoto. We also thank Mr. Yasuo Shida, Mrs. Chiseko Sakuma and Miss Yukiko Kaneko, Analytical Center of Tokyo College of Pharmacy, for measurements of mass spectra and ^{13}C NMR spectra.

References

1) H. Nomura, *J. Chem. Soc.*, **1917** 769; H. Nomura, *Sci. Rep. Tohoku Imp. Univ.*, **6** (i), 41 (1917); H. Nomura, *ibid.*, **17** (i), 973 (1928).
2) A. Lapworth, L. K. Pearson and R. A. Royle, *J. Chem. Soc.*, **1917**, 777; D. W. Connell and M. D. Sutherland, *Aust. J. Chem.*, **22**, 1033 (1969).
3) H. Nomura, *Sci. Rep. Tohoku Imp. Univ.*, **7** (i), 67 (1918).
4) D. W. Connell, *Aust. J. Chem.*, **23**, 369 (1970).
5) T. Inoue, T. Shinbori, M. Fujioka, K. Hishimoto and Y. Masada, *Yakugaku Zasshi*, **98**, 1255 (1978).
6) *a*) H. Itokawa, R. Aiyama and A. Ikuta, *Phytochemistry*, **20**, 769 (1981); *b*) H. Itokawa, R. Aiyama and A. Ikuta, *ibid.*, **21**, 241 (1982).
7) H. D. Locksley, D. K. Rainey and T. A. Rohan, *J. Chem. Soc., Perkin Trans. 1*, **1972**, 3001.
8) J. B. Stothers, "Carbon-13 NMR Spectroscopy," Academic Press, New York, 1972.
9) P. Denniff, I. Macleod and D. A. Whiting, *J. Chem. Soc., Perkin Trans. 1*, **1981**, 82.
10) J. Szolčsanyi and A. Jancsó-Gábor, *Arzneim.-Forsch.*, **25**, 1877 (1975).