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THREE ISOCOUMARINS FROM *CORIANDRUM SATIVUM*

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Key Word Index—*Coriandrum sativum*; Umbelliferae; isocoumarins; coriandrones C–E.

Abstract—Three new isocoumarins, coriandrones C–E, were isolated from whole plants of *Coriandrum sativum* and their structures established from spectral and chemical evidence.

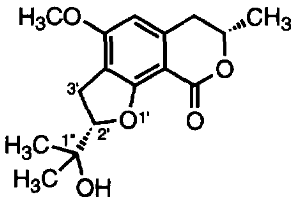
INTRODUCTION

In a previous paper [1], we reported the isolation of two new isocoumarins, coriandrones A (**4**) and B, together with two known isocoumarins, coriandrin (**5**) and dihydrocoriandrin (**6**) [2] from the aerial parts of *Coriandrum sativum*. In the present work, we have isolated three more new isocoumarins, coriandrones C–E (**1**–**3**).

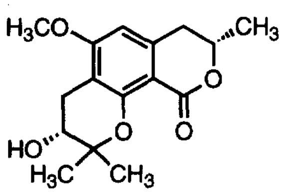
RESULTS AND DISCUSSION

A methanolic extract of the whole plant yielded the three new compounds (**1**–**3**) after chromatographic purification, together with 20 other compounds, viz. coriandrones A (**4**) and B, coriandrin (**5**), dihydrocoriandrin (**6**), *p*-hydroxyphenethyl ferulate, (*R*)-(−)-4, *β*-dihydroxyphenethyl ferulate, umbelliferone, isoscopoletin, escletin dimethyl ether, daphnetin-8-*O*-glucoside, syringaldehyde, ferulic acid, veratric acid, *p*-hydroxycinnamic acid, *p*-hydroxybenzoic acid, 2-(4-hydroxyphenyl)-ethanol, 2-(4-hydroxyphenyl)-2-methoxyethanol, 1-(4-hydroxyphenyl)-1,2-ethanediol, kaempferol 3-*O*-*α*-L-[2,3-di-(*E*)-*p*-coumaroylrhamnopyranoside] and kaempferol 3-*O*-*α*-L-[3-(*E*)-*p*-coumaroylrhamnopyranoside].

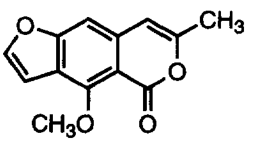
Compound **1** was isolated as needles and assigned the molecular formula $C_{13}H_{10}O_5$ by HR mass spectrometry (*m/z* 246.0530 $[M]^+$). The UV spectrum showed absorption maxima at 249.2, 277.0, 286.0, 297.7 and 334.4 nm, and the IR spectrum showed absorption bands at 3527, 3414, 3269, 1709, 1672, 1609 and 1568 cm^{-1}, suggesting the presence of a hydroxyl group, an aromatic ring and an unsaturated lactone. The ^{1}H NMR spectrum (Table 1) showed the presence of a 4,5,6-trisubstituted benzofuran ring [δ



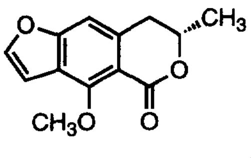
Coriandrone A (4)



Coriandrone B



Coriandrin (5)



Dihydrocoriandrin (6)

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Table 1. NMR spectral data for compounds **1** and **5** (values in parentheses are coupling constants in Hz; δ in $CDCl_3$, TMS)

	H		C	
	1	**5**	**1**	**5**
1			160.0	160.7
3			154.9	153.9
4	6.51 *s*	6.23 *q* (1.0)	103.9	104.2
4a			136.4	137.3
5	7.18 *d* (0.9)	7.10 *d* (1.0)	103.1	102.0
6			160.5	160.4
7			119.9	119.4
8			158.3	158.1
8a			107.6	107.2
2′	7.64 *d* (2.4)	7.61 *d* (2.4)	145.9	145.6
3′	7.09 *dd* (2.4, 0.9)	7.06 *dd* (2.4, 1.0)	106.4	106.2
OMe-8	4.25 *s*	4.23 *s*	61.8	61.8
CH_3-3		2.25 *d* (1.0)		19.6
CH_2-3	4.48 *s*		61.7	
OH	2.00 *br s*			

Assignments confirmed by ^1H–^1H COSY, ^1H–^{13}C COSY and NOE experiments.

7.64 (1H, *d*, $J = 2.4$ Hz), 7.18 (1H, *d*, $J = 0.9$ Hz) and 7.09 (1H, *dd*, $J = 2.4$ and 0.9 Hz)], an olefinic proton [δ 6.51 (1H, *s*)] and a methoxyl group [δ 4.25 (3H, *s*)]. These functional groups were also identified by ^{13}C NMR (Table 1). These spectral data were closely related to those of **5**, except for the presence of the signals assignable to a hydroxymethyl group [^1H: δ 4.48 (2H, *s*), 2.00 (1*H*, *br s*), ^{13}C: δ 61.7] instead of signals due to a methyl group [^1H: δ 2.25 (3H, *d*, $J = 1.0$ Hz), ^{13}C: δ 19.6]. In the NOE difference spectrum of **1**, on irradiation of the hydroxylmethyl group at δ 4.48, a NOE was observed at the olefinic proton at δ 6.51. When the olefinic proton at δ 6.51 was irradiated, NOEs were observed at the aromatic proton at δ 7.18 and the hydroxylmethyl group at δ 4.48. On irradiation of the methoxyl proton at δ 4.25, NOE was only observed at the β-proton of the furan ring at δ 7.09. In the coupled ^{13}C NMR spectrum of **1**, the carbonyl carbon signal at δ 160.0 was exhibited as a singlet signal. Thus, the structure of **1** was decided.

Compound **2** was isolated as prisms and assigned the molecular formula $C_{18}H_{24}O_7$ by HR mass spectrometry (*m*/*z* 352.1523 $[M]^+$). The UV spectrum showed absorption maxima at 223.1, 272.8 and 300.0sh nm, and the IR spectrum showed absorption bands at 3460, 1728, 1667, 1628, 1580 and 1520 cm^{-1}, indicating the presence of a hydroxyl group, an aromatic ring and a lactone. The ^1H NMR spectrum (Table 2) exhibited signals assignable to a methoxyl group [δ 3.88 (3H, *s*)], a 2-acetoxy-3-hydroxy-3-methylbutyl group [δ 5.07 (1H, *dd*, $J = 9.7$ and 3.0 Hz), 3.06 (1H, *dd*, $J = 14.2$ and 9.7 Hz), 2.88 (1H, *dd*, $J = 14.2$ and 3.0 Hz), 1.90 (3H, *s*), 1.31 and 1.27 (each 3H, *s*)] and a hydroxyl

Table 2. NMR spectral data for compounds **2** and **4** (values in parentheses are coupling constants in Hz; δ in $CDCl_3$, TMS)

	H		C	
	2	**4**	**2**	**4**
1			170.7	164.2
3	4.67 *dqd* (10.3, 6.4, 4.5)	4.55 *dqd* (10.6, 6.3, 4.8)	75.9	74.8
4	2.93 *dd* (16.0, 10.3)	2.89 *dd* (16.1, 10.6)	35.3	36.2
	2.84 *dd* (16.0, 4.5)	2.77 *dd* (16.1, 4.8)		
4a			140.0	142.3
5	6.23 *s*	6.23 *s*	101.5	102.6
6			164.1	160.5
7			112.9	115.2
8			162.0	163.6
8a			102.3	102.5
CH_3-3	1.50 *d* (6.4)	1.48 *d* (6.3)	20.9	21.0
OMe-6	3.88 *s*	3.87 *s*	56.2	55.9
OH-8	11.41 *s*			
1′	3.06 *dd* (14.2, 9.7)		23.3	
	2.88 *dd* (14.2, 3.0)			
2′	5.07 *dd* (9.7, 3.0)	4.80 *t* (9.2)	79.4	92.7
3′		3.04 *d* (9.2)	72.8	27.2
$\underline{CH_3}CO$	1.90 *s*		21.1	
$CH_3\underline{CO}$			171.3	
CH_3-3′	1.31 *s*		26.7	
	1.27 *s*		25.4	
1″				71.8
CH_3-1″		1.39 *s*		26.2
		1.21 *s*		23.6
OH-2″		2.75 *br s*		

Assignments confirmed by ^1H–^1H COSY, ^1H–^{13}C COSY and NOE experiments.

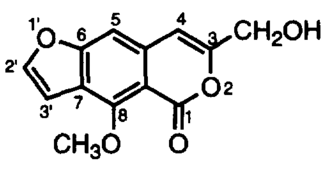
Table 3. NMR spectral data for compounds **3** and **6** (values in parentheses are coupling constants in Hz; δ in $CDCl_3$, TMS)

	H		C	
	3	**6**	**3**	**6**
1			162.3	163.7
3	4.40 *dq* (8.2, 6.4)	4.58 *dqd* (9.2, 6.4, 5.0)	79.1	74.7
4	4.67 *ddd* (8.2, 7.3, <0.1)	3.05 *dd* (16.1, 9.2) 2.94 *dd* (16.1, 5.0)	70.8	37.0
4a			140.9	138.2
5	7.44 *dd* (1.0, <0.1)	7.05 *d* (1.0)	103.5	105.2
6			159.8	159.3
7			120.1	119.4
8			157.8	157.8
8a			109.4	111.1
2′	7.63 *d* (2.3)	7.58 *d* (2.3)	145.7	145.1
3′	7.04 *dd* (2.3, 1.0)	7.00 *dd* (2.3, 1.0)	106.4	106.1
OMe-8	4.21 *s*	4.19 *s*	61.7	61.6
CH_3-3	1.53 *d* (6.4)	1.51 *d* (6.4)	17.9	20.8
OH-4	2.36 *d* (7.3)			

Assignments confirmed by ^1H–^1H COSY, ^1H–^{13}C COSY and NOE experiments.

group chelated with a carbonyl group [δ 11.41 (1H, *s*)], in addition to signals due to a 3-methyl-6,7,8-trisubstituted 3,4-dihydro-isocoumarin [δ 6.23 (1H, *s*), 4.67 (1H, *dqd*, $J = 10.3$, 6.4 and 4.5 Hz), 2.93 (1H, *dd*, $J = 16.0$ and 10.3 Hz), 2.84 (1H, *dd*, $J = 16.0$ and 4.5 Hz) and 1.50 (3H, *d*, $J = 6.4$ Hz)] as shown in that of **4**. From the above spectral data, the structure of **2** was established. This structure was confirmed by a NOE experiment (data not shown). The absolute configuration at C-3 was concluded to be *S* from the fact that the circular dichroic spectrum of **2** showed a positive Cotton effect ascribed to the *K*-absorption band at 273 nm [1, 3–6].

Compound **3** was isolated as colourless needles and assigned the molecular formula $C_{13}H_{12}O_5$ by HR mass spectrometry (*m/z* 248.0676 $[M]^+$). The UV spectrum showed absorption maxima at 232.0, 259.0sh and 306.2 nm, and the IR spectrum showed absorption bonds at 3332, 1702, 1693, 1613, 1592, 1542 and 1477 cm^{-1}, suggesting the presence of a hydroxyl group, an aromatic ring and a lactone. The ^1H NMR spectrum (Table 3) exhibited signals due to a 4,5,6-trisubstituted benzofuran ring [δ 7.63 (1H, *d*, $J = 2.3$ Hz), 7.44 (1H, *dd*, $J = 1.0$ and <0.1 Hz), and 7.04 (1H, *dd*, $J = 2.3$ and 1.0 Hz)], a methine proton linked to an oxygen atom [δ 4.40 (1H, *dq*, $J = 8.2$ and 6.4 Hz)], a methyl group [δ 1.53 (3H, *d*, $J = 6.4$ Hz)] and a methoxyl group [δ 4.21 (3H, *s*)]. These signals were closely related to those of **6**, except for the presence of signals assignable to a benzylmethine proton [δ 4.67 (1H, *ddd*, $J = 8.2$, 7.3 and <0.1 Hz)] coupled with a hydroxyl group [δ 2.36 (1H, *d*, $J = 7.3$ Hz)], instead of the signal due to a benzylmethylene proton [δ 3.05 (1H, *dd*, $J = 16.1$ and 9.2 Hz), 2.94 (1H, *dd*, $J = 16.1$ and 5.0 Hz)]. In the NOE difference spectrum of **3**, on irradiation of the methyl group at δ 1.53, a NOE was observed at a benzylmethine proton at δ 4.67. When the benzylmethine proton at δ 4.67 was irradiated, NOEs were observed at the aromatic proton at δ 7.44 and the methyl proton at δ 1.53. On irradiation of the methoxyl proton at δ 4.21, NOE was observed only at the β-proton of the furan ring at δ 7.04. Thus, the structure of **3** was decided as shown in the formula. The absolute configurations of C-3 and C-4 were concluded to be *S* and *R*, respectively, from the coupling constant between C-3 and C-4 protons ($J = 8.2$ Hz) in the ^1H NMR spectrum of **3**, and from analysis of the circular dichroic spectrum of **3** [7, 8].



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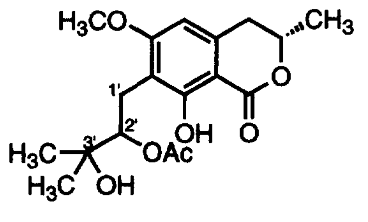

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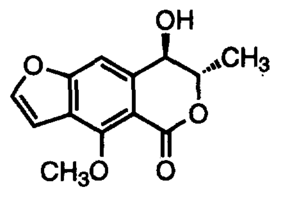

3

EXPERIMENTAL

General. Mps: uncorr. EIMS: 70 eV. ^{1}H and ^{13}C NMR: 300 and 75.4 MHz with TMS as int. standard. CC: Merck silica gel 60 (70–230 mesh) and Sephadex LH-20. TLC: Merck silica gel 60 F_{254} (0.25 mm) and Whatman silica gel 150A PLK5F (1 mm). Spots and bands were detected by UV irradiation (254 and 365 nm).

Plant material. Plants of *C. sativum* L. were cultivated and collected in the botanical garden of the Osaka University of Pharmaceutical Sciences in June 1993. A voucher specimen is deposited at this university.

Extraction and isolation. Air-dried whole plants (26 kg) were chopped into small pieces and extracted with MeOH (600 l × 2) under reflux. The combined MeOH extracts were concd to dryness *in vacuo*. The residue obtained (3 kg) was subjected to CC on silica gel, eluting successively with *n*-hexane–EtOAc and $CHCl_3$–MeOH mixts of increasing polarity. The 15% EtOAc eluates were rechromatographed on silica gel with *n*-hexane–EtOAc (6:1), and Sephadex LH-20 with MeOH, to give **5** (11.9 mg) and **6** (9.4 mg). The 25% EtOAc eluates were rechromatographed on silica gel with *n*-hexane–EtOAc (4:1) followed by Sephadex LH-20 with MeOH to give **2** (2.3 mg), **3** (16.0 mg), 2-(4-hydroxyphenyl)-2-methoxyethanol (324.3 mg), *p*-hydroxyphenethyl ferulate (31.1 mg), umbelliferone (2.1 mg), isoscopoletin (2.5 mg) and 2-(4-hydroxyphenyl)-ethanol (6.4 mg). The 50% EtOAc eluates were rechromatographed on silica gel with *n*-hexane–EtOAc (1:1) and Sephadex LH-20 with MeOH to give **1** (3.2 mg), (*R*)-(−)-4,*β*-hydroxyphenethyl ferulate (73.0 mg), escletin dimethyl ether (4.7 mg) and syringaldehyde (1.9 mg). The 5% MeOH eluates were rechromatographed on silica gel with $CHCl_3$–MeOH (20:1), after Sephadex LH-20 with MeOH, to give **4** (334.1 mg), coriandrone B (35.2 mg), kaempferol 3-*O*-*α*-L-[2,3-di-(*E*)-*p*-coumaroylrhamnopyranoside] (220.0 mg), kaempferol 3-*O*-*α*-L-[3-(*E*)-*p*-coumaroylrhamnopyranoside] (49.1 mg), 1-(4-hydroxyphenyl)-1,2-ethandiol (98.3 mg), ferulic acid (275.6 mg), veratric acid (7.0 mg), *p*-hydroxycinnamic acid (30.5 mg) and *p*-hydroxybenzoic acid (23.7 mg). The 10% MeOH eluates were rechromatographed on silica gel with $CHCl_3$–MeOH (10:1), followed by Sephadex LH-20 with MeOH, to give daphnetin-8-*O*-glucoside (3.3 mg).

Coriandrone C (**1**). Needles, mp 142–143°. UV λ_{max}^{MeOH} nm (log ε): 334.4 (3.57), 297.7 (4.11), 286.0 (4.02), 277.0 (3.86), 249.2 (4.44). IR ν_{max}^{KBr} cm^{-1}: 3527, 3414, 3269, 1709, 1672, 1609, 1568. HR-MS *m/z*: 246.0530 $[M]^+$ (calc. for $C_{13}H_{10}O_5$ 246.0528). ^{1}H and ^{13}C NMR in Table 1.

Coriandrone D (**2**). Prisms, mp 172–173°. UV λ_{max}^{MeOH} nm (log ε): 300.0sh (3.57), 272.8 (4.06), 223.1 (4.34). IR ν_{max}^{KBr} cm^{-1}: 3460, 1728, 1667, 1628, 1580, 1520. CD (MeOH, *c* 2.84×10^{-5}) $\Delta\varepsilon^{23}$ (nm): 0 (295), +1.81 (273), 0 (253), −0.43 (246), 0 (240). HR-MS *m/z*: 352.1523 $[M]^+$ (calc. for $C_{18}H_{24}O_7$ 352.1522). ^{1}H and ^{13}C NMR in Table 2.

Coriandrone E (**3**). Needles, mp 148–150°. UV λ_{max}^{MeOH} nm (log ε): 306.2 (3.33), 259.0sh (3.84), 232.0 (4.59). IR ν_{max}^{KBr} cm^{-1}: 3332, 1702, 1693, 1613, 1592, 1542, 1477. HR-MS *m/z*: 248.0676 $[M]^+$ (calc. for $C_{13}H_{12}O_5$ 248.0685). CD (MeOH, *c* 1.79×10^{-4}) $\Delta\varepsilon^{23}$ (nm): 0 (346), +0.220 (310), +0.102 (284), +0.135 (276), +0.119 (271), +0.440 (260), +0.846 (245), +0.694 (240). ^{1}H and ^{13}C NMR in Table 3.

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