Phytochemistry, Vol. 28, No. 9, pp. 2447–2450, 1989.
Printed in Great Britain.

0031-9422/89 $3.00+0.00

A TETRAMERIC DERIVATIVE OF CAFFEIC ACID FROM *RABDOSIA JAPONICA**

ISAO AGATA, TSUTOMU HATANO,† SANSEI NISHIBE and TAKUO OKUDA†‡

Faculty of Pharmaceutical Sciences, Higashi Nippon Gakuen University, Ishikari-Tobetsu, Hokkaido 061-02, Japan; †Faculty of Pharmaceutical Sciences, Okayama University, Tsushima, Okayama 700, Japan

(*Received* 28 *November* 1988)

Key Word Index—*Rabdosia japonica*; Labiatae; structure determination; tannin; lignan; rabdosiin; rosmarinic acid; caffeic acid.

Abstract—A component which showed tanning activities, was isolated from *Rabdosia japonica*, and was named rabdosiin. It was shown to be a tetramer of caffeic acid with a lignan skeleton.

INTRODUCTION

Phenolic compounds in nature often condense to form oligomeric products, e.g. lignans, condensed tannins and oligomeric hydrolysable tannins. Oligomers of caffeic acid are also known. Thus rosmarinic acid, widely distributed in plants of the family Labiatae [1], can be regarded as a dimer of caffeic acid, and lithospermic acid (trimer) [2] and lithospermic acid B [3] {or salvianolic acid B[4]} (tetramer) are oligomers of caffeic acid having a benzofuran moiety. In the course of a study of the components responsible for the tanning activities in Labiatae plants [1], we have isolated a new caffeic acid tetramer with a lignan skeleton. This compound, which we have named rabdosiin, was obtained from *Rabdosia japonica* Hara (=*Plectranthus japonicus* Koidz.), the aboveground part of which is used as a common household medicine ('en-mei-so') for gastrointestinal disorders in Japan [5]. The present paper deals with the isolation and the structure determination of rabdosiin including the synthesis of its lignan skeleton.

RESULTS AND DISCUSSION

Rabdosiin was isolated from the powdered stem of *R. japonica* and showed the following tanning activities: RAG (relative astringency based on geraniin) [6–8], 0.20; RMBG (relative affinity to methylene blue based on geraniin) [7, 9], 0.24.

Rabdosiin (**1**), $[\alpha]_D^{25}-78°$ (MeOH), gave $[M+H]^+$ and $[M-H]^-$ ions at *m/z* 719 and 717, corresponding to the molecular formula $C_{36}H_{30}O_{16}$, in its positive ion and negative ion FAB mass spectra. Its UV spectrum (MeOH) showed peaks at 254, 284, 318 (sh) and 346 nm (log ε: 4.20, 4.00, 3.9 and 4.02), the last two of which suggested the presence of a caffeic acid moiety in the molecule. The ^{1}H NMR spectrum (in Me_2CO-d_6) showed three singlets [δ6.56, 6.92 and 7.62 (1H each)], two aliphatic methine protons which couple with each other [δ3.93 (1H, *d*, *J* = 1.5 Hz) and 4.56 (1H, *br s*)], three protons [δ6.38 (1H, *d*, *J* = 2 Hz), 6.41 (1H, *dd*, *J* = 2, 8.5 Hz) and 6.66 (1H, *d*, *J* = 8.5 Hz)] of a 3,4-dihydroxyphenyl group, and the protons of two 3-(3,4-dihydroxyphenyl) lactic acid moieties (Table 1). The protons at δ6.56 and 6.92 can be attributed to a 2,3,5,6-tetrasubstituted benzene moiety, and that at δ7.62 to the β-proton of the caffeoyl group. These data and the ^{13}C NMR spectrum of **1** (Table 2) indicate that rabdosiin consists of a 1,2-dihydro-6,7-dihydroxy-1-(3,4-dihydroxyphenyl) naphthalene-2,3-dicarboxylic acid skeleton and two molecules of 3-(3,4-dihydroxyphenyl) lactic acid.

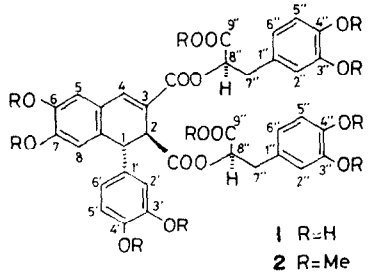
Methylation of **1** with dimethyl sulphate and potassium carbonate afforded the decamethyl derivative **2**, $[\alpha]_D^{25}-88°$ ($CHCl_3$). Treatment of **2** with 1 M sodium hydroxide gave (*R*)-3-(3,4-dimethoxyphenyl) lactic acid (**3**) [2], and compound **4**, $[\alpha]_D^{25}-202°$ ($CHCl_3$).

The ^{1}H NMR spectrum (Me_2CO-d_6) of **4** shows the presence of a 1,2-dihydronaphthalene moiety [δ4.68 (1H, *br s*, H-1), 3.98 (1H, *d*, *J* = 1.5 Hz, H-2), 7.70 (1H, *s*, H-4), 7.10 (1H, *s*, H-5), 6.88 (1H, *s*, H-8)], a 3,4-disubstituted phenyl group [δ6.79 (1H, *d*, *J* = 2 Hz, H-2'), 6.74 (1H, *d*, *J* = 8.5 Hz, H-5'), 6.46 (1H, *dd*, *J* = 2, 8.5 Hz, H-6')], and four methoxyl groups [δ3.71, 3.72, 3.79 and 3.85 (3H each, *s*)].

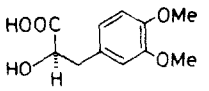
The orientation of the bond C-2–H-2 in **4** is assigned to be *quasi*-equatorial on the basis of the singlet of H-4, as this signal would be a doublet induced by the allyl coupling with H-2 if the orientation of the bond C-2–H-2 is *quasi*-axial. The coupling constant between H-1 and H-2 (1.5 Hz) indicates that the dihedral angle of the bond C-1–H-1 and the bond C-2–H-2 is *ca* 80°. This is attributable to the *quasi*-equatorial orientation of the bond C-1–H-1 (**8**). The conformation of **4** shown in **8** has been confirmed by ROESY measurements. The ROESY spectrum of **4** showed that a NOE is present between H-2 and H-2', and between H-8 and H-1. It is absent between H-8 and H-6', and between H-8 and H-2', while a Dreiding model shows that a NOE should be present for these two sets of protons if the orientation of the bond C-1–H-1 is *quasi*-axial. These findings indicate the *trans*-orienta-

*Part 2 in the series 'Tannins in Labiatae Plants'. For Part 1, see ref. [1]. For a preliminary report, see, Agata, I., Hatano, T., Nishibe, S. and Okuda, T. (1988) *Chem. Pharm. Bull.* **36**, 3223.

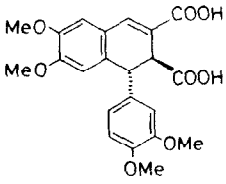
‡Author to whom correspondence should be addressed.



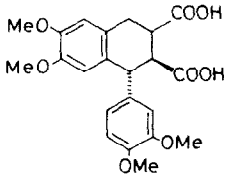
1 R=H
2 R=Me



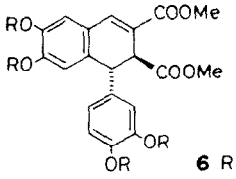
3



4



5



(racemic)

6 R=H
7 R=Me

tion of the phenyl group at C-1 and the carboxyl group at C-2 in **4**.

Hydrogenation of **4** over 5% Pd-C afforded a dihydro derivative (**5**). The CD spectrum of **5** (in MeOH) shows the first positive couplet, $[\theta]_{289}+13\,600$ and $[\theta]_{273}-7200$, and the second positive couplet, $[\theta]_{207}+45\,900$ and $[\theta]_{200}-29\,700$ (lowest wavelength measured), which are analogous to the reported data of the 1-aryltetralin lignans having 1α-substituents [10]. Therefore, the absolute configurations at C-1 and C-2 in **1** should be *R* and *S*, respectively.

The lignan skeleton of **1** was synthesized as follows. The ferric chloride-catalysed condensation of methyl caffeate, which was carried out in a way analogous to that used for the condensation of methyl ferulate [11], gave the dimeric compound **6**. Treatment of **6** with dimethyl sulphate and potassium carbonate yielded the hexamethyl derivative **7**. Hydrolysis of **7** in 1 M sodium hydroxide gave a product identical with **4** although the product was racemic. Thus, the structure of rabdosiin was established to be **1**.

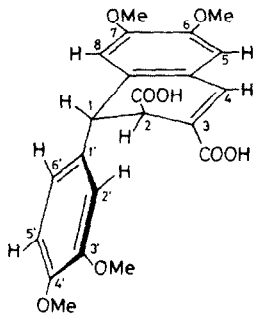
Biogenetically, rabdosiin is regarded as a product of the oxidative coupling between two molecules of rosmarinic acid, occurring in a way analogous to the chemical synthesis of the lignan skeleton from methyl caffeate carried out in the present investigation.

EXPERIMENTAL

^{1}H and ^{13}C NMR: 90 or 500 MHz for ^{1}H and 125 MHz for ^{13}C NMR; chemical shifts are given in δ values (ppm) from TMS.

Isolation of rabdosiin. Powdered stems of *Rabdosia japonica* (1.9 kg) were homogenized in a mixture of Me_2CO and H_2O (7:3; 19 l × 3), and filtered. After concn, the resulting aq. soln (300 ml) was acidified to pH 3 with 10% H_3PO_4, and extracted with EtOAc. The organic layer was evapd, and the EtOAc extract (114 g) thus obtained was chromatographed over Kieselgel 60 silanisiert (Merck) using EtOH–H_2O (7:3) as an eluant. Further chromatography on Sephadex LH-20, and then on Toyopearl HW-40 (fine grade; TOSOH, Japan) afforded rabdosiin (2.3 g).

Rabdosiin (**1**). A light brown amorphous powder, $[\alpha]_D^{25}-78°$ (MeOH; *c* 3.5). (Found: C, 56.5; H, 4.6. $C_{36}H_{30}O_{16}\cdot 3H_2O$ requires: C, 56.0; H, 4.7%). Positive ion FAB-MS: *m/z* 719 $[M+H]^+$. Negative ion FAB-MS: *m/z* 717 $[M-H]^-$. UV λ_{max}^{MeOH} nm (log ε): 254 (4.20), 284 (4.00), 318 sh, 346 (4.02). IR ν_{max}^{KBr} cm^{-1}: 1760–1680 (C=O), 1650–1580 (aromatic). ^{1}H NMR: see Table 1. ^{13}C NMR: see Table 2.



8

Methylation of rabdosiin. A mixture of rabdosiin (179 mg) in Me_2CO (5 ml) and K_2CO_3 (1.2 g) was stirred for 30 min at room temp, and then 0.5 ml of Me_2SO_4 was added to the mixture. The mixture was stirred for 2 hr, and refluxed for 2.5 hr. After centrifugation, the supernatant was evapd and the resulting syrup was chromatographed over silicic acid (Mallinckrodt) with C_6H_6–Me_2CO (9:1), to afford decamethylrabdosiin (**2**) (121 mg) as a colourless amorphous powder, $[\alpha]_D^{25}-88°$ ($CHCl_3$; *c* 8.9). (Found: C, 63.6; H, 5.7. $C_{46}H_{50}O_{16}\cdot 1/2H_2O$ requires: C, 63.7; H, 5.9%). UV λ_{max}^{MeOH} nm (log ε): 232 (4.50), 250 sh, 281 (4.03), 318 sh, 341 (4.10). IR ν_{max}^{KBr} cm^{-1}: 1744, 1710 (C=O), 1632, 1606, 1592, 1568 (aromatic). ^{1}H NMR: Table 1. ^{13}C NMR: Table 2.

Hydrolysis of decamethylrabdosiin. To a soln of decamethylrabdosiin (**2**) (100 mg) in EtOH (7.6 ml), 1 M aq. NaOH (7.6 ml) was added, the mixture refluxed for 5 hr and then concd to half vol. After addition of H_2O (5 ml), the aq. soln was acidified to pH 6 with 1 M H_2SO_4 and then extracted with EtOAc. The EtOAc extract was subjected to CC over silicic acid with $CHCl_3$–EtOH (99:1) as developer, to give (1*R*, 2*S*)-6,7-dimethoxy-1-(3,4-dimethoxyphenyl)-1,2-dihydronaphthalene-2,3-dicarboxylic acid (**4**) (41 mg) as a colourless crystalline powder, mp 125–130°, $[\alpha]_D^{25}-202°$. EIMS *m/z*: 414 $[M]^+$, 396 $[M-18]^+$. UV λ_{max}^{MeOH} nm (log ε): 235 (4.23), 286 (3.81), 310 (3.88), 326 (3.92). IR ν_{max}^{KBr} cm^{-1}: 1694 (C=O), 1632, 1606, 1568, 1514 (aromatic). ^{1}H NMR: Table 1. ^{13}C NMR: Table 2. The aq. mother liquor was treated with 0.5 M H_2SO_4 to pH 1, and extracted with EtOAc. The extract

Table 1. ^{1}H NMR spectral data for compounds **1**, **2** and **4** (Me_2CO-d_6)

H	1	2	4
1	4.56 (*br s*)	4.56 (*br s*)	4.68 (*br s*)
2	3.93 (*d*, J = 1.5 Hz)	3.97 (*d*, J = 1.5 Hz)	3.98 (*d*, J = 1.5 Hz)
4	7.62 (*s*)	7.71 (*s*)	7.70 (*s*)
5	6.92 (*s*)	7.01 (*s*)	7.10 (*s*)
8	6.56 (*s*)	6.79 (*s*)	6.88 (*s*)
2′	6.38 (*d*, J = 2 Hz)	6.66 (*d*, J = 2 Hz)	6.79 (*d*, J = 2 Hz)
5′	6.66 (*d*, J = 8.5 Hz)	6.73 (*d*, J = 8.5 Hz)	6.74 (*d*, J = 8.5 Hz)
6′	6.41 (*dd*, J = 2, 8.5 Hz)	6.42 (*dd*, J = 2, 8.5 Hz)	6.46 (*dd*, J = 2, 8.5 Hz)
2″	6.80 (*d*, J = 2 Hz)	6.84 (*d*, J = 2 Hz)	
	6.85 (*d*, J = 2 Hz)	6.96 (*d*, J = 2 Hz)	
5″	6.73 (*d*, J = 8 Hz)	6.78 (*d*, J = 8 Hz)	
	6.74 (*d*, J = 8 Hz)	6.79 (*d*, J = 8.5 Hz)	
6″	6.61 (*dd*, J = 2, 8 Hz)	6.68 (*dd*, J = 2, 8 Hz)	
	6.64 (*dd*, J = 2, 8 Hz)	6.75 (*dd*, J = 2, 8.5 Hz)	
7″	3.01–3.05 (4H, *m*)	3.00–3.11 (4H, *m*)	
8″	5.03 (*dd*, J = 5.5, 6 Hz)	5.07 (*dd*, J = 4.5, 9 Hz)	
	5.07 (*dd*, J = 5.5, 7 Hz)	5.13 (*dd*, J = 4.5, 9 Hz)	
COOMe		3.61, 3.65, 3.67 (3H each, *s*)	
OMe		3.72, 3.74, 3.75 3.76, 3.77, 3.79 3.86 (3H each, *s*)	3.71, 3.72, 3.79 3.85 (3H each, *s*)

was chromatographed over silicic acid using $CHCl_3$ as eluant to afford (*R*)-3-(3,4-dimethoxyphenyl) lactic acid (**3**) (13 mg) [2] as a white crystalline powder, mp 99–100°, $[\alpha]_D^{25}$ + 31° ($CHCl_3$; *c* 1). EIMS *m/z*: 226 $[M]^+$, 209 $[M-OH]^+$, 181 $[M-COOH]^+$. UV λ_{max}^{MeOH} nm (log ε): 230 (3.87), 279 (3.43), 285 sh. IR ν_{max}^{KBr} cm^{-1}: 1742 (C=O), 1608, 1518 (aromatic). ^{1}H NMR (Me_2CO-d_6): δ2.70–3.17 (2H, *m*), 3.76, 3.78 (3H each, *s*, OMe), 4.29–4.43 (1H, *m*), 6.82–6.90 (3H, *m*, aromatic). ^{13}C NMR ($CDCl_3$): δ40.0 (C-3), 56.3 (2 × OMe), 71.3 (C-2), 112.5 (C-5′), 113.8 (C-2′), 121.9 (C-6′), 128.8 (C-1′), 148.9 (C-4′), 149.7 (C-3′), 176.3 (COOH).

Hydrogenation of **4**. To a soln of **4** (20 mg) in EtOH, 10 mg of charcoal containing Pd (5%) was added and the mixture stirred for 6 hr under H_2 at room temp. After filtration, the filtrate was evapd to give (1*R*,2*S*,3*RS*)-6,7-dimethoxy-1-(3,4-dimethoxyphenyl)tetralin-2,3-dicarboxylic acid (**5**) (10 mg) as white amorphous powder. EIMS *m/z*: 416 $[M]^+$, 398 $[M-H_2O]^+$. UV λ_{max}^{MeOH} nm (log ε): 281 (3.76), 285 sh. IR ν_{max}^{KBr} cm^{-1}: 1728, 1716 (C=O), 1644, 1612, 1518. ^{1}H NMR (CD_3OD): δ2.9–3.2 (4H, *m*, H-2, 3, 4), 3.51, 3.75, 3.80, 3.80 (3H each, *s*, 4 × OMe), 4.13 (1H, *d*, J = 10.5 Hz, H-1), 6.24 (1H, *s*, H-8), 6.70–6.74 (3H, *m*, H-4, 2′, 6′), 6.88 (1H, *d*, J = 8 Hz, H-5′). CD (MeOH) $[\theta]_{289}$ + 13 600, $[\theta]_{273}$ − 7200, $[\theta]_{238}$ − 15 300, $[\theta]_{207}$ + 45 900, $[\theta]_{200}$ − 29 700 (lowest wavelength measured).

Dimerization of methyl caffeate. To a soln of methyl caffeate (2 g) in Me_2CO (75 ml), an aq. soln (3.2 ml) of $FeCl_3 \cdot 6H_2O$ (3.2 g) was added at 5° over 1.5 hr, and the mixture was further stirred for 4.5 hr at 5°. After being kept at 0° for 18 hr, the mixture was concd to 75 ml, and extracted with hexane–EtOAc (1:1) (500 ml). The extract was chromatographed over silicic acid with $CHCl_3$ as eluant, to afford the dimethyl ester of *trans*-6,7-dihydroxy-1-(3,4-dimethoxyphenyl)-1,2-dihydronaphthalene-2,3-dicarboxylic acid (**6**) (1.1 g), as a white crystalline powder, mp 239–242°. (Found: C, 60.8; H, 4.6. $C_{20}H_{18}O_8 \cdot 1/2H_2O$ requires: C, 60.8; H, 4.8%). EIMS *m/z*: 386 $[M]^+$, 327 $[M-COOMe]^+$, 268 $[M-2 \times COOMe]^+$. UV λ_{max}^{MeOH} nm (log ε): 253 (4.28), 292 sh, 313 (3.99), 340 (4.09). IR ν_{max}^{KBr} cm^{-1}: 1714, 1690 (C=O), 1614, 1590 (aromatic). ^{1}H NMR (Me_2CO-d_6): δ3.56, 3.67 (3H each, *s*, 2 × OMe), 3.87 (1H, *d*, J = 3 Hz, H-2), 4.43 (1H, *d*, J = 3 Hz, H-1), 6.41 (1H, *dd*, J = 2.5, 8.5 Hz, H-6′), 6.62 (1H, *s*, H-8), 6.64 (1H, *d*, J = 2.5 Hz, H-2′), 6.66 (1H, *d*, J = 8.5 Hz, H-5′), 6.95 (1H, *s*, H-5), 7.55 (1H, *s*, H-4). ^{13}C NMR (Me_2CO-d_6): δ46.1 (C-1), 48.3 (C-2), 51.8, 52.3 (2 × OMe), 115.4 (C-2′), 116.0 (C-5′), 116.8 (C-5), 117.0 (C-8), 119.7 (C-6′), 122.9 (C-3), 124.7 (C-4a), 130.8 (C-8a), 136.0 (C-1′), 138.4 (C-4), 144.6, 145.1, 145.6, 148.3 (C-6, C-7, C-3′, C-4′), 167.5 (ester carbonyl at C-3), 173.2 (ester carbonyl at C-2).

Methylation of **6**. To a soln of **6** (0.6 g) in Me_2CO (15 ml), Me_2SO_4 (0.9 g) and K_2CO_3 (2 g) were added, and the mixture was refluxed for 3 hr. After cooling, the solvent was evapd, and the residue passed through a column of silicic acid (40 g) with C_6H_6–Me_2CO (19:1) as eluant, to give the dimethyl ester of *trans*-6,7-dimethoxy-1-(3,4-dimethoxyphenyl)-1,2-dihydronaphthalene-2,3-dicarboxylic acid (**7**) (524 mg), as colourless prisms, mp 150–152°. (Found: C, 64.4; H, 6.4. $C_{24}H_{26}O_8$ requires: C, 65.1; H, 5.9%). EIMS *m/z*: 442 $[M]^+$. UV λ_{max}^{MeOH} nm (log ε): 246 (4.36), 290 sh, 312 sh, 3.66 (4.10). IR ν_{max}^{KBr} cm^{-1}: 1734, 1708 (C=O), 1632, 1606 (aromatic). ^{1}H NMR (Me_2CO-d_6): δ3.57, 3.69, 3.70, 3.71, 3.77, 3.85 (3H each, *s*, 6 × OMe), 3.96 (1H, *d*, J = 2.5 Hz, H-2), 4.63 (1H, *d*, J = 2.5 Hz, H-1), 6.42 (1H, *dd*, J = 2.5, 8.5 Hz, H-6′), 6.74 (1H, *d*, J = 8.5 Hz, H-5′), 6.76 (*d*, J = 2.5 Hz, H-2′), 6.84 (1H, *s*, H-8), 7.11 (1H, *s*, H-5), 7.67 (1H, *s*, H-4). ^{13}C NMR (Me_2CO-d_6): δ46.2 (C-1), 47.9 (C-2), 51.9, 52.4 (2 × OMe), 56.0, 56.1, 56.2, 56.2 (4 × OMe), 112.6 (C-2′), 112.7 (C-5′), 113.3 (C-5), 113.4 (C-8), 120.3 (C-6′), 123.4 (C-3), 125.2 (C-4a), 131.3 (C-8a), 136.5 (C-1′), 138.2 (C-4), 149.3, 149.6, 150.2, 152.2 (C-6, C-7, C-3′, C-4′), 167.4 (ester carbonyl at C-3), 172.9 (ester carbonyl at C-2).

Hydrolysis of **7**. To a soln for **7** (227 mg) in EtOH (8 ml), 1 M NaOH (8 ml) was added, and the mixture was refluxed for 5 hr. After cooling, the mixture was concd to half vol. The aq. soln was acidified with 0.5 M H_2SO_4 to pH 1, and then extracted with EtOAc. The extract was purified by CC over silicic acid with

Table 2. ^{13}C NMR chemical shifts for compounds **1**, **2** and **4**

C	**1** (Me_2CO-d_6)	**2** (Me_2CO-d_6)	**4** ($CDCl_3$)
1	45.4	45.7	45.1
2	47.8	47.3	46.7
3	121.1	121.9	120.9
4	140.0	139.4	140.0
4a	124.3	124.5	123.8
5	119.4	119.9	112.0
6	148.3	152.1	148.9
7	148.3	152.1	151.4
8	121.7	122.1	112.2
8a	130.7	131.3	130.5
COO at C-2	171.9	171.5	177.8
COO at C-3	166.6	166.1	172.1
1′	136.5	136.4	130.5
2′	115.2	112.0	110.7
3′	145.4	149.9	147.9
4′	145.6	150.0	148.3
5′	116.8	113.1	111.1
6′	117.3	122.3	119.3
1″	128.8, 128.9	129.4, 129.5	
2″	115.8, 115.9	112.4, 112.5	
3″	144.4, 144.7	149.1, 149.3	
4″	144.6, 144.9	149.1, 150.0	
5″	117.1, 117.1	113.2, 113.2	
6″	117.3, 117.3	114.1, 114.1	
7″	37.1, 37.4	37.2, 37.6	
8″	74.2, 74.3	74.2, 74.3	
9″	170.9, 171.2	170.0, 170.4	
COOMe		52.3, 52.4	
OMe		55.9, 55.9, 55.9 55.9, 56.0, 56.1 56.1	55.8, 55.8 55.9, 56.0

$CHCl_3$–EtOH (99:1), to give *trans*-6,7-dimethoxy-1-(3,4-dimethoxyphenyl)-1,2-dihydronaphthalene-2,3-dicarboxylic acid (141 mg), as a white crystalline powder, mp 125–130°. (Found: C, 61.7; H, 5.6. $C_{22}H_{22}O_8 \cdot H_2O$ requires: C, 61.1; H, 5.6%). The UV, IR, ^{1}H and ^{13}C NMR spectra of this compound were identical with those of **4**.

REFERENCES

1. Okuda, T., Hatano, T., Agata, I. and Nishibe, S. (1986) *Yakugaku Zasshi* **106**, 1108.
2. Kelly, C. J., Mahajan, J. R., Brooks, L. C., Neubert, L. A., Breneman, W. R., Carmack, M. (1975) *J. Org. Chem.* **40**, 1804.
3. Wagner, H. (1977) in *Biochemistry of Plant Phenolics* (Swain, T., Harborne, J. B. and Van Sumere, C. F., eds), p. 598. Plenum Press, New York.
4. Ai, C.-B. and Li, L.-N. (1988) *J. Nat. Prod.* **51**, 145.
5. Fujita, E. and Node, M. (1984) *Fortschr. Chem. Org. Naturst.* **46**, 77.
6. Okuda, T., Mori, K. and Aoi, K. (1977) *Yakugaku Zasshi* **97**, 1267.
7. Okuda, T., Mori, K. and Hatano, T. (1985) *Chem. Pharm. Bull.* **33**, 1424.
8. Hatano, T., Kagawa, H., Yasuhara, T. and Okuda, T. (1988) *Chem. Pharm. Bull.* **36**, 2090.
9. Okuda, T., Mori, K. and Murakami, R. (1977) *Yakugaku Zasshi* **97**, 1273.
10. Hulbert, P. B., Klyne, W. and Scopes, P. M. (1981) *J. Chem. Res. (S)* 27.
11. Kuo, Y.-H., Kuo, P.-C. and Lin, S.-T. (1983) *Proc. Natl Sci. Counc. Repub. China, Part B* **7**, 28; *Chem. Abstr.* (1983) **99**, 53253k.