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Synthetic Studies on Lignans and Related Compounds. IV.[1] Synthesis of Taiwanin C and E, and Justicidin D (Neojusticin A), E, and F (Taiwanin E Methyl Ether)[2]

Zen-ichi Horii, Motohide Tsujiuchi, Ken-ichi Kanai, and Takefumi Momose

Faculty of Pharmaceutical Sciences, Osaka University[3]

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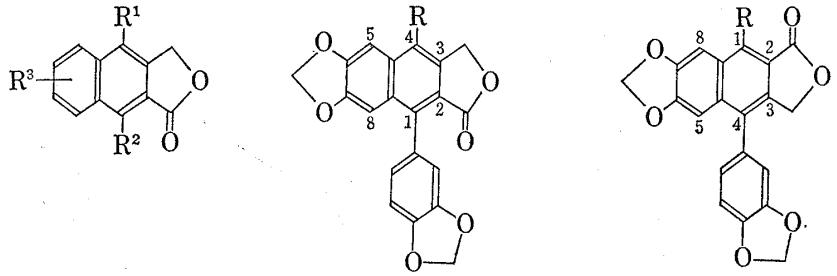
The structure of taiwanin E was re-examined with an empirical proton magnetic resonance (^{1}H-NMR) rule for the lactone methylene in aromatized naphthalide lignans, and concluded to be **5** instead of **4** on the basis of their unambiguous synthesis. Related lignans: taiwanin C (**3**), justicidin D (neojusticin A) (**6**), E (**7**), and F (taiwanin E methyl ether) (**8**) were also synthesized. The ^{1}H-NMR rule was found to be the case also with the lignans synthesized.

Keywords——naphthalide lignan; ^{1}H-NMR rule; synthesis; taiwanin C; taiwanin E; justicidin D; neojusticin A; justicidin E; justicidin F; taiwanin E methyl ether

Upon proton magnetic resonance (^{1}H-NMR) spectral examinations on natural and synthetic naphthalide lignans, we have found that the lactone methylene proton signals of 4-aryl-2,3-naphthalides (**1**), under a shielding effect of the pendant aromatic ring, appear in the region of δ 5.08—5.23 while those of 1-aryl-2,3-naphthalides (**2**) in the δ 5.32—5.52 region.[2]



1: R^1=Ar; R^2=H, OH, OMe
2: R^1=H, OH, OMe; R^2=Ar
3: R=H
5: R=OH
8: R=OMe
4: R=OH
6: R=OMe
7: R=H

Chart 1

Taiwanin C and E isolated from *Taiwania cryptomerioides* Hayata have been assigned by Lin and his co-workers[4] to **3** (type **2**) and **4** (type **1**), respectively, on the basis of the spectral evidences. A revision of the structure of taiwanin E to type **2** (**5**) has been proposed on the basis of ^{1}H-NMR evidences described above[2]: taiwanin E shows the lactone methylene proton signal at δ 5.34.

1) Part III: Z. Horii, K. Ohkawa, S.-W. Kim, and T. Momose, *Chem. Pharm. Bull.* (Tokyo), **19**, 535 (1971).
2) Presented in part as a communication: Z. Horii, M. Tsujiuchi, and T. Momose, *Tetrahedron Lett.*, **1969**, 1079.
3) Location: *133-1, Yamada-kami, Suita, Osaka, 565, Japan.*
4) Y.-T. Lin, T.-B. Lo, K.-T. Wang, and B. Weinstein, *Tetrahedron Lett.*, **1967**, 849.

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We now report the synthesis of compounds **4** and **5** which was carried out for chemical corroboration of the revised structure of taiwanin E. We also report the synthesis of related lignans: justicidin D[5a] (neojusticin A[5b]) (**6**), E (**7**),[6] and F[7] (taiwanin E methyl ether[5b]) (**8**) isolated from *Justicia procumbens* Linn., and taiwanin C (**3**).

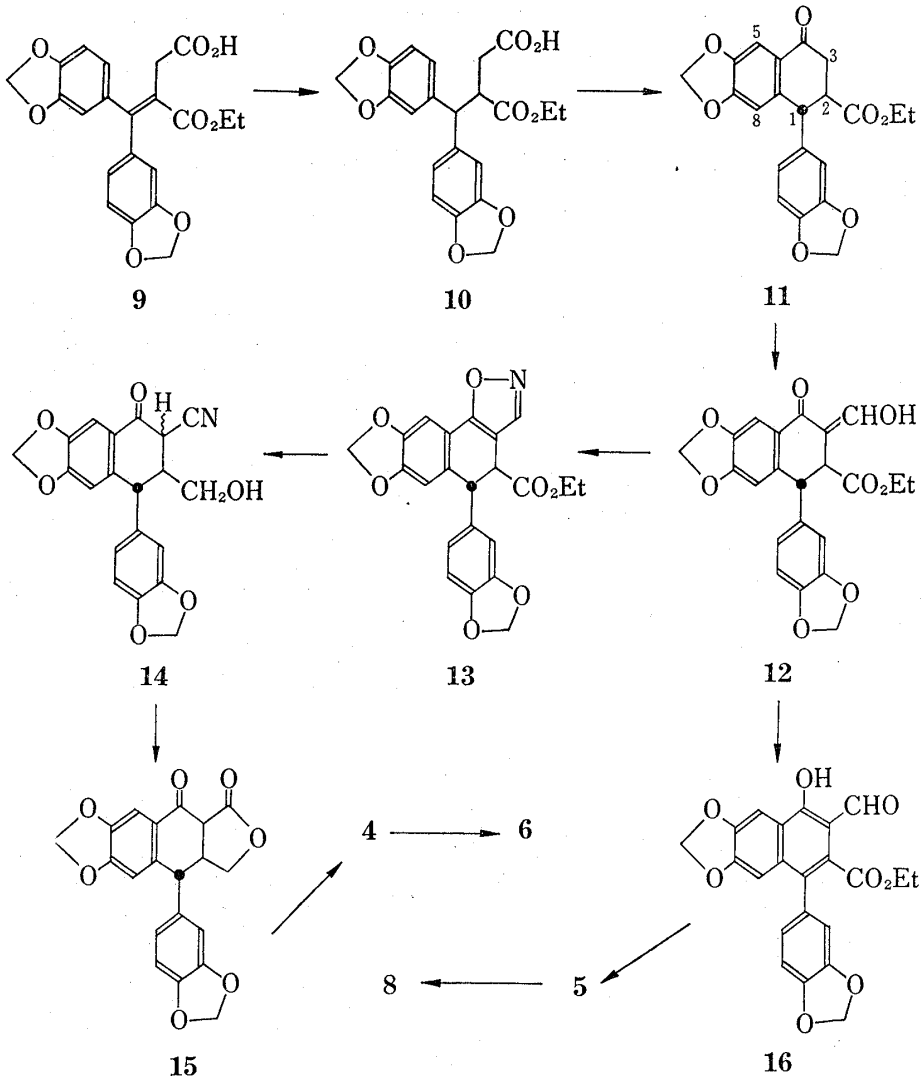

Chart 2

Synthesis of 4 and Justicidin D (Neojusticin A) (6)

The Stobbe condensation of 3,4:3′,4′-bismethylenedioxybenzophenone[8] with diethyl succinate gave a half ester (**9**), which was reduced to a saturated half ester (**10**) with sodium amalgam in a bicarbonate buffer solution. On heating with acetyl chloride, the half ester (**10**) cyclized to a tetralone (**11**), whose structure was evident from the presence of two singlet signals due to a shielded aromatic proton (C_8-H) at δ 6.40 and a deshielded one (C_5-H) at 7.51 in the ^{1}H-NMR spectrum. The stereochemistry of **11** was proved to be a *trans* form by NMR spectral analysis. The ^{1}H-NMR spectrum showed the C_1-H signal at δ 4.48 as a doublet

5) *a*) K. Ohta and K. Munakata, *Tetrahedron Lett.*, **1970**, 923; *b*) M. Okigawa, T. Maeda, and N. Kawano, *Tetrahedron*, **26**, 4301 (1970).
6) K. Wada and K. Munakata, *Tetrahedron Lett.*, **1970**, 2017.
7) K. Ohta and K. Munakata, Abstracts of Papers, 8th Shokubutsu-kagaku Symposium, Tokyo, Jan. 1972, p. 1.
8) T. Garofano, *Ann. Chim.*, **47**, 260 (1957).

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having $J_{1,2}$=6.5 Hz. It is well known that the coupling constants between C_1-H and C_2-H in analogous tetralones are *ca.* 4.5 and 6.5 Hz in *cis* and *trans* configurations, respectively.[9] Condensation of **11** with ethyl formate gave a hydroxymethylene tetralone (**12**), which was converted into an isoxazole (**13**) on treatment with hydroxylamine hydrochloride. A lithium aluminum hydride reduction of **13** at −60° and subsequent ring cleavage of the resulting isoxazole alcohol with sodium ethoxide afforded a keto nitrile (**14**), which was converted into a γ-lactone (**15**) with alcoholic hydrogen chloride. Dehydrogenation of **15** with selenium dioxide gave **4**, mp 250—255°, ν_{max} (KBr) 3401 (OH), 1724 (C=O) cm^{-1}, δ ($(CD_3)_2SO$) 5.18 ($-CH_2OCO-$). The melting point and infrared (IR) spectrum of **4** are quite different from those of authentic taiwanin E which was prepared from taiwanin A[10] according to the method reported.[4]

The lactone (**4**) was methylated with methyl iodide to give a methyl ether (**6**), in 84% yield, which was found to be identical with natural justicidin D on IR and ^{1}H-NMR spectral comparison, and with natural neojusticin A on mixture melting point and IR and ^{1}H-NMR spectral comparison.

Synthesis of Taiwanin E (5) and Justicidin F (Taiwanin E Methyl Ether) (8)

Treatment of **12** with bromine and subsequent dehydrobromination of the resulting bromide with β-picoline afforded a naphthol (**16**) in 35% yield from **12**. Sodium borohydride reduction of **16** followed by purification *via* its acetate gave **5**, mp 302—305° ν_{max} (KBr) 3413, 3407 (OH), 1749 (C=O) cm^{-1}, in 82% yield from **16**. The synthetic sample (**5**) was found to be identical with authentic taiwanin E on mixture melting point and IR spectral comparison.

Taiwanin E (**5**) was methylated with methyl iodide to give a methyl ether (**8**), in 61% yield, which was found to be identical with natural justicidin F on IR and ^{1}H-NMR spectral comparison.

Synthesis of Taiwanin C (3) and Justicidin E (7)

Holmes and Stevenson[11] have reported the synthesis of **3** and **7** *via* a partial oxidation of the lithium aluminum hydride reduction product from 6,7-methylenedioxy-1-(3,4-methylenedioxyphenyl)naphthalene-2,3-dicarboxylic acid anhydride (**17**). Our synthesis is rather simple. Reduction[12] of **17**[13] with sodium borohydride in isopropanol-DMF gave a mixture of **3** (12% yield) and **7** (55% yield). The synthetic sample (**3**) was identical, on IR and ^{1}H-NMR spectral comparison, with authentic taiwanin C which was prepared from taiwanin A accord-

Table I. Chemical Shifts (δ Values) for the Lactone Methylene Protons in Synthetic Lignans

Compound	Solvent	Lactone methylene proton	
		Type 1	Type 2
3	$CDCl_3$		5.33
4	$(CD_3)_2SO$	5.18	
5	$(CD_3)_2SO$		5.35
6	$CDCl_3$	5.09	
7	$(CD_3)_2SO$	5.28	
	$CDCl_3$	5.17	
8	$CDCl_3$		5.46

9) Z. Horii, K. Ohkawa, S.-W. Kim, and T. Momose, *Chem. Pharm. Bull.* (Tokyo), **16**, 2404 (1968).
10) G.A. Swoboda, K.-T. Wang, and B. Weinstein, *J. Chem. Soc.* (*C*), **1967**, 161.
11) T.L. Holmes and R. Stevenson, *J. Org. Chem.*, **36**, 3450 (1971).
12) The procedure is based on the method of Vaughan, *et al.* [W.R. Vaughan, C.T. Goetschel, M.H. Goodrow, and C.L. Warren, *J. Am. Chem. Soc.*, **85**, 2282 (1963)].
13) D. Brown and R. Stevenson, *J. Org. Chem.*, **30**, 1759 (1965); T.L. Holmes and R. Stevenson, *J. Chem. Soc.* (*C*), **1971**, 2091.

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ing to the method reported.[4] Another synthetic sample (**7**) was identical with natural justicidin E on IR and ^{1}H-NMR spectral comparison.

As shown in Table I, an empirical ^{1}H-NMR rule[2] for the lactone methylene in aromatized naphthalide lignans was found to be still the case with the synthetic compounds (**3**, **4**, **5**, **6**, **7**, and **8**).

Experimental

All melting points are uncorrected. ^{1}H-NMR spectra were obtained with a Hitachi Perkin-Elmer R-20A (60 MHz) spectrometer with tetramethylsilane as an internal standard, IR spectra with a Hitachi EPI-G3 spectrophotometer, UV spectra with a Shimadzu MPS-50L spectrophotometer, and Mass Spectrum (MS) with a Hitachi RMU-6E spectrometer. All organic extracts were dried over Na_2SO_4 before evaporation. Column chromatography was effected using Mallinckrodt silicic acid.

3-Ethoxycarbonyl-4,4-di(3,4-methylenedioxyphenyl)-3-butenoic Acid (9)——Metallic K (17.2 g) was dissolved in dry *t*-butanol (400 ml), and to this was added 3,4: 3′,4′-bismethylenedioxybenzophenone[8] (108 g) and diethyl succinate (105 g) at room temperature. The mixture was heated under reflux for 45 min in a stream of dry N_2, and then cooled to room temperature. The separated yellow solid was collected, washed with acetone, and dissolved in ice-water. The solution was acidified with 10% HCl, and the separated oil was taken again in satd. $NaHCO_3$. The alkaline solution was washed with ether, and acidified with conc. HCl, and the separated oil was extracted with AcOEt. The extract was washed with H_2O and evaporated to give a brown solid (74 g), which was recrystallized from isopropyl ether to give **9** (65.4 g, 41%) as colorless crystals, mp 138.5—139.5°. IR ν_{max}^{KBr} cm^{-1}: 1692 (C=O). *Anal.* Calcd. for $C_{21}H_{18}O_8$: C, 63.31; H, 4.55. Found: C, 63.27; H, 4.49. 3,4: 3′,4′-Bismethylenedioxybenzophenone (25.4 g) was recovered.

3-Ethoxycarbonyl-4,4-di(3,4-methylenedioxyphenyl)butyric Acid (10)——To a stirred solution of **9** (60 g) in satd. $NaHCO_3$ (1400 ml) was added 5% Na–Hg (780 g) over 6.5 hr in a stream of CO_2, and the mixture was further stirred for 2 hr. After removal of Hg, the aqueous layer was acidified with conc. HCl, and the separated oil was extracted with AcOEt. The extract was washed with H_2O and evaporated to give **10** (55.7 g, 93%) as colorless rhombs (from EtOH), mp 136—137°. IR ν_{max}^{KBr} cm^{-1}: 1718, 1701 (C=O). *Anal.* Calcd. for $C_{21}H_{20}O_8$: C, 62.99; H, 5.04. Found: C, 63.36; H, 5.00.

Ethyl *trans*-6,7-Methylenedioxy-1-(3,4-methylenedioxyphenyl)-4-oxo-1,2,3,4-tetrahydro-2-naphthoate (11)——A mixture of **10** (50 g) and AcCl (144 g) was refluxed for 2 hr. After removal of AcCl, satd. $NaHCO_3$ was added to the residue, and the separated oil was extracted with benzene. The extract was washed with H_2O and evaporated to give **11** (28.3 g, 59%) as colorless prisms (from EtOH), mp 122—124°. IR ν_{max}^{KBr} cm^{-1}: 1721, 1671 (C=O), 1612 (arom.). ^{1}H-NMR ($CDCl_3$) δ: 1.08 (3H, t, J=7.2 Hz, $-CO_2CH_2C\underline{H}_3$), 2.83 (2H, d, J=6.5 Hz, C_3–H), 3.28 (1H, m, C_2–H), 4.04 (2H, q, J=7.2 Hz, $-CO_2C\underline{H}_2CH_3$), 4.48 (1H, d, J=6.5 Hz, C_1–H), 5.92 (2H, s, $-OCH_2O-$), 5.97 (2H, s, $-OCH_2O-$), 6.40 (1H, s, C_8–H), 6.50—6.83 (3H, m, Ar-H), 7.51 (1H, s, C_5–H). *Anal.* Calcd. for $C_{21}H_{18}O_7$: C, 65.96; H, 4.75. Found: C, 66.45; H, 4.61.

Ethyl *trans*-3-Hydroxymethylene-6,7-methylenedioxy-1-(3,4-methylenedioxyphenyl)-4-oxo-1,2,3,4-tetrahydro-2-naphthoate (12)——Dry EtOH (2.8 g) was added to a stirred suspension of NaH (52.9% in oil, 6.8 g) in dry benzene (100 ml) in a stream of dry N_2, and the suspension was further stirred for 3.5 hr. To this was added ethyl formate (22.2 g) over 8 min and subsequently a solution of **11** (11.5 g) in dry benzene (100 ml) over 45 min at room temperature. The mixture was further stirred for 1 hr and allowed to stand overnight. The mixture was poured into ice water, and the aqueous layer was separated. The organic layer was extracted with 1% NaOH. The combined alkaline layers were washed with benzene and acidified with 1% H_2SO_4. The separated pale yellow solid was collected, washed with satd. $NaHCO_3$, then with H_2O, and dried to give **12** (7.0 g, 57%) as pale yellow rhombs (from benzene–isopropyl ether), mp 149—151°. IR ν_{max}^{KBr} cm^{-1}: 1726, 1635 (C=O), 1612 (arom.). *Anal. Calcd.* for $C_{22}H_{18}O_8$: C, 64.39; H, 4.42. Found: C, 64.77; H, 4.34.

***trans*-3-Ethoxycarbonyl-6,7-methylenedioxy-4-(3,4-methylenedioxyphenyl)-3,4-dihydronaphth[2,1-*d*]isoxazole (13)**——A solution of **12** (3 g) and $NH_2OH\cdot HCl$ (1.52 g) in AcOH (35 ml) was refluxed for 30 min and then poured into ice water (150 ml). The separated oil was extracted with AcOEt. The extract was washed with satd. $NaHCO_3$, then with H_2O, and evaporated to give a brown solid (3 g), which was chromatographed on silica gel in $CHCl_3$ to give **13** (2.0 g, 67%) as colorless crystals (from isopropanol), mp 181—182°. IR ν_{max}^{KBr} cm^{-1}: 1747 (C=O), 1645 (C=N), 1610, 1604 (arom.). *Anal.* Calcd. for $C_{22}H_{17}NO_7$: C, 64.86; H, 4.21; N, 3.44. Found: C, 64.57; H, 4.07; N, 3.38.

***trans*$_{3,4}$-2-Cyano-3-hydroxymethyl-6,7-methylenedioxy-4-(3,4-methylenedioxyphenyl)-3,4-dihydro-1(2*H*)-naphthalenone (14)**——A solution of **13** (1.8 g) in dry tetrahydrofuran (40 ml) was added to a stirred suspension of $LiAlH_4$ (2.5 g) in dry ether (90 ml) at −60° over 1.5 hr, and the suspension was further stirred for 4 hr. After addition of AcOEt (20 ml) and subsequently of 10% HCl (60 ml), the organic layer was separated, and the aqueous layer was extracted with AcOEt. The combined extracts were washed with H_2O and evaporated to give a brown solid (1.5 g). This product was used immediately for the next reaction because its purification was unsuccessful. A solution of the reduction product (1.5 g) in dry EtOH (55 ml) was added to an ice-cooled

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solution of NaOEt [from metallic Na (0.6 g)] in dry EtOH (25 ml) with stirring over 30 min. After being stirred at room temperature for 2 hr, the mixture was poured into ice water (500 ml). The alkaline solution was washed with AcOEt, and the organic layer was extracted with 5% KOH. The combined alkaline layer was acidified with dil. HCl, and the separated oil was extracted with AcOEt. The extract was washed with H_2O and evaporated to give a solid (0.60 g), which was chromatographed on silica gel in $CHCl_3$ to give **14** (0.49 g, 30% from **13**) as colorless crystals (from $CHCl_3$), mp 208—210°. IR ν_{max}^{KBr} cm^{-1}: 3540 (OH), 2245 (C≡N), 1682 (C=O), 1614 (arom.). *Anal.* Calcd. for $C_{20}H_{15}NO_6$: C, 65.75; H, 4.14; N, 3.83. Found: C, 65.81; H, 4.07; N, 3.78.

***trans*$_{3,4}$-3-Hydroxymethyl-6,7-methylenedioxy-4-(3,4-methylenedioxyphenyl)-1-oxo-1,2,3,4-tetrahydro-2-naphthoic Acid γ-Lactone (15)**——An ice-cooled solution of **14** (486 mg) in dry EtOH (40 ml) was saturated with dry HCl. After being allowed to stand overnight at room temperature, the solution was poured into satd. NaCl (200 ml), and the separated oil was extracted with AcOEt. The extract was washed with satd. $NaHCO_3$ and then satd. NaCl and evaporated to give a brown solid (468 mg), which was chromatographed on silica gel in $CHCl_3$ to give **15** (142 mg, 30%) as pale yellow crystals (from AcOEt), mp 187.0—188.5°. IR ν_{max}^{KBr} cm^{-1}: 1785, 1667 (C=O), 1612 (arom.). *Anal.* Calcd. for $C_{20}H_{14}O_7$: C, 65.57; H, 3.85. Found: C, 65.35; H, 3.84.

1-Hydroxy-3-hydroxymethyl-6,7-methylenedioxy-4-(3,4-methylenedioxyphenyl)-2-naphthoic Acid γ-Lactone (4)——A mixture of **15** (130 mg), SeO_2 (63.5 mg), and dry AcOH (10 ml) was refluxed for 2 hr and poured into H_2O (70 ml), and the separated oil was extracted with AcOEt. The extract was washed with satd. $NaHCO_3$ and then satd. NaCl, and evaporated to give **4** (56 mg, 44%) as colorless micro prisms (from tetrahydrofuran), mp 250—255°. IR ν_{max}^{KBr} cm^{-1}: 3401 (OH), 1724 (C=O), 1621 (arom.). ^{1}H-NMR ($(CD_3)_2$SO) δ: 5.18 (2H, s, $-CH_2OCO-$), 6.11 (2H, s, $-OCH_2O-$), 6.16 (2H, s, $-OCH_2O-$), 6.75—7.15 (4H, m, Ar–H), 7.65 (1H, s, C_8–H). MS *m/e*: 364 (M^+). UV λ_{max}^{MeOH} nm (ε): 230 sh. (19000), 237 (19100), 264 sh. (28200), 269 (28700), 287 (16600), 309—314 plateau (8400), 358 (3700). *Anal.* Calcd. for $C_{20}H_{12}O_7$: C, 65.94; H, 3.32. Found: C, 65.78; H, 3.21. Compound **4** was not identical with authentic taiwanin E on IR spectral comparison.

3-Hydroxymethyl-1-methoxy-6,7-methylenedioxy-4-(3,4-methylenedioxyphenyl)-2-naphthoic Acid γ-Lactone (6)——A suspension consisting of **4** (24 mg), MeI (5 g), K_2CO_3 (5 g), and acetone (15 ml) was refluxed for 10 hr. The suspension was filtered while hot, and the filtrate was evaporated. The residual solid was taken again in warm $CHCl_3$ and filtered, and the filtrate was evaporated to give **6** (21 mg, 84%) as colorless micro needles (from $CHCl_3$–MeOH), mp 272—274°. IR ν_{max}^{KBr} cm^{-1}: 1763 (C=O), 1603 (arom.). ^{1}H-NMR ($CDCl_3$) δ: 4.32 (3H, s, OMe), 5.09 (2H, s, $-CH_2OCO-$), 6.07 (4H, s, $-OCH_2O-$), 6.65—7.01 (4H, m, Ar–H), 7.69 (1H, s, C_8–H). MS *m/e*: 378 (M^+). UV λ_{max}^{MeOH} nm (ε): 262 (47600), 298—303 plateau (12400), 316 (13300), 348—357 plateau (4500). *Anal.* Calcd. for $C_{21}H_{14}O_7$: C, 66.67; H, 3.73. Found: C, 66.33; H, 3.54. Compound **6** was found to be identical with natural justicidin D on IR and ^{1}H-NMR spectral comparison, and natural neojusticin A on mixture melting point and IR and ^{1}H-NMR spectral comparison.

Ethyl 3-Formyl-4-hydroxy-6,7-methylenedioxy-1-(3,4-methylenedioxyphenyl)-2-naphthoate (16)——A solution of Br_2 (350 mg) in $CHCl_3$ (20 ml) was added to an ice-cooled solution of **12** (863 mg) in $CHCl_3$ (20 ml) with stirring over 100 min. After being diluted with $CHCl_3$ (20 ml), the solution was washed with aq. $NaHCO_3$–$Na_2S_2O_3$ solution and then H_2O and evaporated to give a brown oil (763 mg). This product was used immediately for the next reaction. A solution of the bromide (763 mg) in β-picoline (4 ml) was heated at 100° for 2 hr. The mixture was poured into ice-conc. HCl, and the separated oil was extracted with $CHCl_3$. The extract was washed with satd. $NaHCO_3$ and then H_2O and evaporated to give a brown solid (628 mg), which was chromatographed on silica gel in $CHCl_3$ to give **16** (300 mg, 35% from **12**) as yellow needles (from EtOH), mp 185—187°. IR ν_{max}^{KBr} cm^{-1}: 3380 (OH), 1701, 1628 (C=O), 1608 (arom.). *Anal.* Calcd. for $C_{22}H_{16}O_8$: C, 64.70; H, 3.95. Found: C, 64.89; H, 3.93.

4-Hydroxy-3-hydroxymethyl-6,7-methylenedioxy-1-(3,4-methylenedioxyphenyl)-2-naphthoic Acid γ-Lactone (5)——To an ice-cooled solution of **16** (105 mg) in MeOH (10 ml) and tetrahydrofuran (1 ml) was added $NaBH_4$ (200 mg) portionwise with stirring, and the solution was further stirred for 3 hr followed by stirring at room temperature for 2 hr. The solution was poured into satd. $NaHCO_3$ (70 ml), and the mixture was extracted with AcOEt. The aqueous layer was acidified with conc. HCl and extracted with AcOEt. The combined extracts were washed with H_2O and evaporated to give a brown solid (104 mg). The crude product was acetylated because a further purification was unsuccessful. A solution of the reduction product (114 mg) in β-picoline (3.8 ml) and Ac_2O (1.9 ml) was heated at 100° for 1 hr. The solution was poured into ice water (60 ml), and the separated oil was extracted with $CHCl_3$. The extract was washed with H_2O and evaporated to give a brown oil (250 mg), which was chromatographed on silica gel in $CHCl_3$ to give the acetate of **5** (107 mg) as pale brown crystals (from EtOH), mp 131—133°. IR ν_{max}^{Nujol} cm^{-1}: 1763 (C=O), 1619 (arom.). ^{1}H-NMR ($CDCl_3$) δ: 2.49 (3H, s, Ac), 5.22 (2H, s, $-CH_2OCO-$), 6.03 (2H, s, $-OCH_2O-$), 6.06 (2H, s, $-OCH_2O-$), 6.69—7.02 (3H, m, Ar–H), 7.10 (1H, s, C_5–H), 7.20 (1H, s, C_8–H). A solution of the acetate (107 mg) in AcOH (8 ml), acetone (8 ml), and conc. HCl (6 ml) was heated at 60° for 1 hr, and then cooled in an ice-bath. The separated solid was collected, washed with AcOH and subsequently with H_2O, and dried to give **5** (78 mg, 82% from **16**) as pale yellow micro needles (from AcOH), mp 302—305°. IR ν_{max}^{KBr} cm^{-1}: 3413, 3407 (OH), 1749 (C=O), 1621 (arom.). ^{1}H-NMR ($(CD_3)_2$SO) δ: 5.35 (2H, s, $-CH_2OCO-$), 6.10 (2H, s, $-OCH_2O-$),

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6.16 (2H, s, $-OCH_2O-$), 6.75—7.08 (4H, m, Ar–H), 7.62 (1H, s, C_8–H). MS *m/e*: 364 (M^+). UV λ_{max}^{MeOH} nm (ε): 230 (31900), 263 sh. (42100), 269 (42300), 290 sh. (12800), 308—313 plateau (10900), 322 (11000), 357 (5500). *Anal.* Calcd. for $C_{20}H_{12}O_7$: C, 65.94; H, 3.32. Found: C, 65.59; H, 3.12. Compound **5** was identical with authentic taiwanin E, prepared[4] by photoreaction of taiwanin A, on mixture melting point and IR spectral comparison.

3-Hydroxymethyl-4-methoxy-6,7-methylenedioxy-1-(3,4-methylenedioxyphenyl)-2-naphthoic Acid γ-Lactone (8)——A suspension consisting of **5** (43 mg), MeI (5 g), K_2CO_3 (5 g), and acetone (15 ml) was refluxed for 10 hr and worked up in a similar manner to that for **6** to give **8** (27 mg, 61%) as colorless crystals (from $CHCl_3$–MeOH), mp 240—243°. IR ν_{max}^{KBr} cm^{-1}: 1770 (C=O), 1626, 1610 (arom.). ^{1}H-NMR ($CDCl_3$) δ: 4.09 (3H, s, OMe), 5.46 (2H, s, $-CH_2OCO-$), 6.06 (4H, s, $-OCH_2O-$), 6.62—7.04 (4H, m, Ar–H), 7.54 (1H, s, C_8–H). MS *m/e*: 378 (M^+). UV λ_{max}^{MeOH} nm (ε): 232 (27200), 262 (44800), 291—294 plateau (11500), 311 (11600), 352 (5100). *Anal.* Calcd. for $C_{21}H_{14}O_7$: C, 66.67; H, 3.73. Found: C, 66.40; H, 3.55. Compound **8** was found to be identical with natural justicidin F and taiwanin E methyl ether on IR and ^{1}H-NMR spectral comparison.

3-Hydroxymethyl-6,7-methylenedioxy-1-(3,4-methylenedioxyphenyl)-2-naphthoic Acid γ-Lactone (3) and 3-Hydroxymethyl-6,7-methylenedioxy-4-(3,4-methylenedioxyphenyl)-2-naphthoic Acid γ-Lactone (7)——A solution of 6,7-methylenedioxy-1-(3,4-methylenedioxyphenyl)naphthalene-2,3-dicarboxylic acid anhydride (**17**)[13] (200 mg) in DMF (5 ml) was added to an ice-cooled suspension of $NaBH_4$ (28 mg) in isopropanol (16 ml) with stirring for 20 min, and the mixture was further stirred at room temperature for 28 hr. After dilution of the mixture with H_2O (100 ml), the separated colorless solid (39 mg) was collected by filtration. The filtrate was acidified with conc. HCl, and the resulting colorless solid was separated into a $CHCl_3$-soluble solid (82 mg) and a $CHCl_3$-insoluble solid (63 mg). The neutral solid (39 mg) and the $CHCl_3$-soluble solid (82 mg) were found to be a mixture of lactones and chromatographed on silica gel in $CHCl_3$ to give **3** (4 mg, 2%) and **7** (89 mg, 46%). A mixture of the $CHCl_3$-insoluble solid (hydroxy acid) (63 mg), *p*-toluenesulfonic acid (50 mg), and EtOH (10 ml) was refluxed for 30 min, and then cooled to room temperature. The separated solid was collected, and recrystallized from AcOH to give **3** (20 mg, 10%). Concentration of the mother liquor gave **7** (18 mg, 9%).

Compound **3**: colorless crystals (from AcOEt), mp 260—266°. IR ν_{max}^{KBr} cm^{-1}: 1768, 1740 sh. (C=O), 1614 (arom.). ^{1}H-NMR ($CDCl_3$) δ: 5.33 (2H, s, $-CH_2OCO-$), 6.04 (4H, s, $-OCH_2O-$), 6.71 —7.17 (5H, m, Ar–H), 7.67 (1H, s, C_4–H). MS *m/e*: 348 (M^+). UV λ_{max}^{MeOH} nm (ε): 217 (18700), 233 (18600), 251 sh. (39000), 257 (42300), 294 (9000), 305 (8700), 350 (4300). *Anal.* Calcd. for $C_{20}H_{12}O_6$: C, 68.96; H, 3.47. Found: C, 69.25; H, 3.95.

Compound **7**: colorless micro needles (from AcOEt), mp 274—276°. IR ν_{max}^{KBr} cm^{-1}: 1762 (C=O), 1627 (arom.). ^{1}H-NMR ($(CD_3)_2SO$) δ: 5.28 (2H, s, $-CH_2OCO-$), 6.11 (2H, s, $-OCH_2O-$), 6.17 (2H, s, $-OCH_2O-$), 6.89—7.15 (4H, m, Ar–H), 7.61 (1H, s, C_8–H), 8.34 (1H, s, C_1–H). MS *m/e*: 348 (M^+). UV $\lambda_{max}^{CHCl_3}$ nm (ε): 252 (46300), 258 (49200), 297—302 plateau (12900), 315 (14400), 348 (5600). *Anal.* Calcd. for $C_{20}H_{12}O_6$: C, 68.96; H, 3.47. Found: C, 68.82; H, 3.44. Compound **3** was identical with authentic taiwanin C on IR and ^{1}H-NMR spectral comparison. Compound **7** was identical with natural justicidin E on IR and ^{1}H-NMR spectral comparison.

Taiwanin C (3) and Taiwanin E (5)——Taiwanin A[10] (40 mg) was dissolved in acetone (10 ml) in a quartz tube, and the tube was allowed to stand in sun light for 5 hr. The solution was evaporated to give a brown paste (40 mg), which was chromatographed on silica gel in $CHCl_3$ to give **3** (8 mg, 20%) as colorless crystals (from AcOEt), mp 260—266° (lit.,[4] 276°), and **5** (2 mg, 5%) as pale yellow micro needles (from AcOH), mp 302—305° (lit.,[4] 263—267°). Both compounds were identical with synthetic compounds (**3** and **5**), respectively, prepared alternatively as described above.

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