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The Constituents of *Kadsura japonica* Dunal. I. The Structures of Three New Lignans, Acetyl-, Angeloyl- and Caproyl-binankadsurin A

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Three new dibenzocyclooctadiene lignans, named acetyl (**1**)-, angeloyl (**2**)- and caproyl-binankadsurin A (**3**), were isolated from the fruits of *Kadsura japonica* Dunal (Schizandraceae). Their absolute structures were elucidated by chemical and spectral studies.

Keywords——*Kadsura japonica* Dunal; Schizandraceae; dibenzocyclooctadiene; lignan; acetyl-binankadsurin A; angeloyl-binankadsurin A; caproylbinankadsurin A; ^{13}C-NMR; CD spectrum

Kadsura japonica Dunal (Schizandraceae) (Japanese plant name: "Binan-kadsura" or "Sane-kadsura") is a climber growing in the southern part of Japan. In ancient times, the dry fruits of this plant were used as an antitussive and a tonic under the name of "Nan-gomishi" as a substitute for the fruits of *Schizandra chinensis* Baill. (Schizandraceae, "Hoku-(or "Kita-) gomishi"),[1] and the mucilage from the stems was used to dress the hair and to make paper.

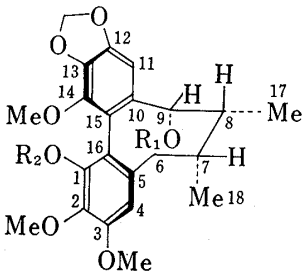
Sesquiterpenoids[germacrenes C(from fruits) and D(from stems and leaves)],[2] anthocyanin[cyanidin-3-O-β-(2G-xylorutinoside)][3] and fatty acids[4] have been isolated from the fruits of the plant. Recently, two dibenzocyclooctadiene lignans (kadsurin and kadsurarin)[5] and a triterpenoid (kadsuric acid)[6] have been isolated from the stems.

This paper describes the structure elucidation of three new dibenzocyclooctadiene lignans, acetyl (**1**)-, angeloyl (**2**)- and caproyl-binankadsurin A (**3**), isolated from the fruits of this plant.

Acetyl-binankadsurin A (**1**), $C_{24}H_{28}O_8$, mp 188—192°, $[\alpha]_D^{24} \simeq 0°$ (in $CHCl_3$) was isolated as colorless needles (from acetone–EtOH) in a yield of 0.19%. The ultraviolet (UV) spectrum, with absorption maxima at 218 (log ε: 4.59), 254 (sh. 3.98) and 288 nm (3.46), and the infrared (IR) spectrum, with bands at 3325 (OH), 1740 (ester), 1605 and 1580 (aromatic), suggest that **1** is a dibenzocyclooctadiene lignan[7] possessing a hydroxy group and an ester linkage. The proton nuclear magnetic resonance (^{1}H-NMR) and carbon (^{13}C)-NMR spectra of **1** reveal that **1** possesses three methoxy groups, a methylenedioxy moiety and a hydroxy group ($FeCl_3$ in EtOH, green; Gibbs test, blue) on the aromatic rings, and two secondary methyls, a benzylic methylene, a benzylic methine and an acetyl group on the cyclooctadiene ring (see Table I for ^{13}C-NMR and "Experimental" for ^{1}H-NMR). The chemical shift of the acetyl group in the ^{1}H-NMR spectrum (δ 1.55 in $CDCl_3$) indicates that it is shielded by the aromatic ring. The mass spectrum (MS), with peaks at m/z: 444 (M^+) and 384 ($M^+ - 60$), also supports the presence of the acetyl group in **1**.

Hydrolysis of **1** with 3% KOH in a mixture of EtOH and $CHCl_3$ afforded compound **4**, named binankadsurin A, as colorless prisms (from ether–hexane), $C_{22}H_{26}O_7$, mp 153—155°, $[\alpha]_D^{26}$ −20.7° (in $CHCl_3$). Methylation of **1** with ethereal diazomethane afforded a monomethyl ether (**5**), $C_{25}H_{30}O_8$, mp 157—158°, $[\alpha]_D^{24}$ −19.7° (in $CHCl_3$), which was identified as kadsurin by direct comparison of ^{1}H-NMR and IR spectra, and $[\alpha]_D$ value. These results indicate that **1** corresponds to norkadsurin.

The position of the phenolic hydroxy group in **1** was confirmed as mentioned below. First, the ^{13}C-NMR spectrum (in $CDCl_3$) of **1** was compared with that of **5**, the carbon shifts of which were assigned by comparison with the data for lignans (gomisins) isolated from *Schizandra chinensis*.[8] The signals of C-11 and C-4 in **5** appear at δ 102.4 and δ 110.5, re-



1: R_1=-OCCH$_3$, R_2=H

2: R_1= -OC(H$_3$C)C=C(H)CH$_3$, R_2=H

3: R_1=-OC(CH$_2$)$_4$CH$_3$, R_2=H

4: R_1=R_2=H

5: R_1=-OCCH$_3$, R_2=CH$_3$

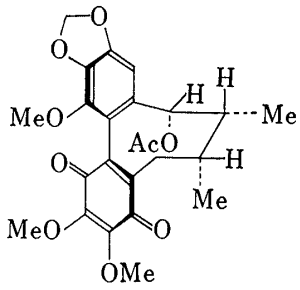


Chart 1. (Me=CH$_3$, Ac=CH$_3$CO) **6**

TABLE I. ^{13}C-NMR Spectral Data for **1**, **2**, **3**, **4** and **5** [δ in CDCl$_3$, ^{13}C: 20 MHz, at 25°]

Carbon (multiplicity)	Compound 1	2	3	4	5
1(s)	146.7	147.1	146.6	147.4	151.0[a]
2(s)	133.4	133.8	133.5	133.9	139.7
3(s)	150.4	150.6	150.4	151.3	151.6[a]
4(d)	107.3	107.2	107.2	107.5	110.5
5(s)	133.7	133.4	133.6	133.9	133.3
6(t)	38.6	38.6	38.7	38.8	38.8
7(d)	35.0	34.8	35.0	34.9	34.9
8(d)	41.6	41.8	41.6	43.1	42.0
9(d)	82.6	82.7	82.5	83.7	82.3
10(s)	135.7	136.0	135.9	138.9	134.9
11(d)	102.7	102.9	102.8	102.8	102.4
12(s)	148.9	149.0	148.9	148.9	148.7
13(s)	136.1	136.1	136.1	135.7	136.0
14(s)	141.3	141.3	141.3	141.3	141.4
15(s)	119.1	119.4	119.2	118.3	120.7
16(s)	117.1	117.2	117.1	115.3	123.3
17(q)	19.7	19.8	19.7	19.7	19.5
18(q)	14.8	14.9	14.9	15.4	14.7
OCH$_3$ ($C_{(14)}$)	59.7	59.6	59.8	59.8	60.2, 59.7[b]
OCH$_3$ ($C_{(2)}$)	60.8	60.3	60.8	61.1	60.7
OCH$_3$ ($C_{(3)}$) (q)	55.8	55.9	55.8	55.8	56.0
OCH$_2$O (t)	101.3	101.3	101.2	101.2	101.2
Acid moiety	167.0 (s, CO)	166.7 (s,C-1′)	172.9 (s, C-1′)		170.0 (s, CO)
	20.3 (q, CH$_3$)	127.2 (s,C-2′)	33.7 (t, C-2′)		20.7 (q, CH$_3$)
		139.3 (d, C-3′)	24.1 (t,C-3′)		
		15.6 (q,C-4′)	31.2 (t,C-4′)		
		20.5 (q,C-2′-CH$_3$)	22.3 (t,C-5′)		
			13.8 (q,C-6′)		

a) Signals may be reversed.
b) $C_{(1)}$ and $C_{(14)}$-OCH$_3$
c) d=doublet; q=quartet; s=singlet; t=triplet.

spectively. In the spectrum of **1**, the C-11 signal (δ 102.7) appears at the same region as that of **5**, but the C-4 signal (δ 107.3) shows an upfield shift of 3.2 ppm, compared with that of 5. Furthermore, C-1, -2 and -16 in **1** show upfield shifts of 4.3 (or 4.9), 6.3 and 6.2 ppm, respectively, compared with those of 5. These findings indicate that the hydroxy group in **1** is linked to C-1 as mentioned in our previous paper.[8] Next, oxidation of **1** with Fremy's salts[7b] [(SO$_3$K)$_2$NO] gave compound **6**, $C_{24}H_{26}O_9$, mp 147—149°, which shows absorption bands at 1660 and 1642 cm^{-1} due to *p*-quinone in the IR spectrum and only one aromatic proton signal in the ^{1}H-NMR spectrum (δ 6.44). The chemical shift of C-11 (δ 102.9) in the ^{13}C-NMR spectrum of **6** is almost the same as the C-11 shift of **1**. All of the above observations indicate that the hydroxy group in **1** is linked to C-1.

On the other hand, the CD spectra of **1** and **4** show that these compounds possess S-biphenyl configuration.[7a] The absolute structure of acetyl-binankadsurin A was thus elucidated as **1**, and therefore the biphenyl configuration of kadsurin was also confirmed to be S.

Angeloyl-binankadsurin A (**2**, yield 0.19%) was obtained as colorless prisms (from ether–hexane), $C_{27}H_{32}O_8$, mp 121—122°, $[\alpha]_D^{25}$ +61.5° (in $CHCl_3$) and caproyl-binankadsurin A (**3**, yield 0.02%) was obtained as colorless prisms (from ether–hexane), $C_{28}H_{36}O_8$, mp 83—87°, $[\alpha]_D^{25}$ +14.7° (in $CHCl_3$). The spectral (UV, IR, MS, ^{1}H- and ^{13}C-NMRs) data for **2** and **3** show that they possess the same skeleton as **1**, that **2** possesses an angeloyl group[^{13}C-NMR(δ in $CDCl_3$): 15.6 (q), 20.5 (q), 127.2 (s), 139.3 (d) and 166.7 (s); MS, *m/z* (%): 484 (M^+, 10), 384 (100), 100 (27), 83 (16), 55 (26)] and that **3** possesses a caproyl group[^{13}C-NMR(δ in $CDCl_3$): 13.8 (q), 22.3 (t), 24.1 (t), 31.2 (t), 33.7 (t), 172.9 (s); MS, *m/z* (%): 500 (M^+, 11), 384 (100), 73 (13), 60 (23)] (see "Experimental").

Hydrolysis of **2** and **3** in 3% ethanolic KOH afforded **4** and the corresponding acids.[9] The absolute structures of angeloyl- and caproyl-binankadsurin A were thus elucidated as **2** and **3**, respectively. The pharmacological activities of these compounds are under investigation in our laboratory.

Experimental

All melting points were determined on a Yanagimoto micromelting point apparatus (hot stage type) and are uncorrected. The UV spectra were recorded with a Hitachi 624 digital spectrophotometer and the IR spectra with a Hitachi EPI-G2 unit. The ^{1}H-NMR and ^{13}C-NMR spectra were recorded with Varian T-60 and Varian FT 80A spectrometers, respectively, with tetramethylsilane as an internal standard. Mass spectra were measured with a Hitachi RMU-7L double focusing mass spectrometer. The specific rotations were measured with a JASCO DIP-SL spectrometer and the CD spectra with a JASCO J-20 spectrometer. Gas liquid chromatography (GLC) was carried out on a Hitachi 073 gas chromatograph with FID. For silica gel column chromatography, Kieselgel 60 (Merck) was used. Thin layer chromatography (TLC) was carried out on Merck plates precoated with Kieselgel $60F_{254}$. Preparative layer chromatography (PLC) was carried out on plates (20×20 cm, 0.75 mm thick) coated with Kieselgel PF_{254} (Merck).

Extraction——The dried fruits (250 g) of *Kadsura japonica* collected in October, 1978, were pulverized and extracted with pet.ether (bp 37—39°, 1.2 l×3, 7 hr each) under reflux and then with hot MeOH (1.2 l ×3, 7 hr each). The pet.ether extracts were concentrated to give a brown mass (31.62 g). The MeOH extracts were also concentrated to give a brown mass (73.09 g), which was dissolved in H_2O (200 ml). This solution was extracted with AcOEt (200 ml×3). The AcOEt extract (12.59 g), after concentration, was dissolved in MeOH and mixed with Celite (No. 535, Wako Pure Chemical Industries Ltd., 70 g). The mixture was dried at room temperature and chromatographed. Elution was carried out with pet.ether (2.5 l), CH_2Cl_2 (1.5 l) and then MeOH (1 l). The pet.ether eluate was concentrated to give a residue (7.01 g), which was combined with the pet. ether extract. The combined extract (total 38.63 g) was chromatographed on silica gel (SiO_2, 600 g, 7×30 cm) with hexane–benzene, benzene, and benzene–acetone solvent systems. The fractions eluted with benzene–acetone (94: 6) were concentrated to give a residue (1.54 g), which was purified by PLC [hexane–acetone (3: 2)] to give **2** (*Rf* 0.51, yield 468.5 mg, 0.19%) and **3** (*Rf* 0.54, 54.6 mg, yield 0.02%). The fractions eluted with benzene–acetone (9: 1) were purified by PLC [i) benzene–ether (1: 1), *Rf* 0.46; ii) hexane–acetone (3: 2), *Rf* 0.42] to give **1** (463 mg, yield 0.19%).

Acetyl-binankadsurin A (1)——Colorless needles (from acetone–EtOH), mp 188—192°, $[\alpha]_D^{24} \simeq 0°$ (c=1.16, $CHCl_3$). $FeCl_3$ in EtOH: green. Gibbs test: blue. UV λ_{max}^{EtOH} nm (log ε): 218 (4.59), 254 (sh, 3.98), 288 (3.46). IR ν_{max}^{KBr} cm^{-1}: 3325 (OH), 1740 (C=O), 1605, 1580 (aromatic). CD (c=0.0212, MeOH), $[\theta]^{23}$ (nm): −64000 (253), −8400 (232), −9300 (230), 0 (223), +61000 (202). ^{1}H-NMR (δ in $CDCl_3$): 0.91 (3H, d, J= 7 Hz, H–$\overset{|}{C}_{(7)}$–CH_3), 1.05 (3H, d, J=7 Hz, H–$\overset{|}{C}_{(8)}$–CH_3), 1.9—2.12 (2H, m, 2×–$\overset{|}{C}$H), 2.64 (2H, d, J=4 Hz, $C_{(6)}$–H), 3.84 (3H, s), 3.92 (6H, s) (3×OCH_3), 5.55 (1H, s, $C_{(9\beta)}$–H), 5.58 (1H, s, $C_{(1)}$–OH, D_2O-exchangeable), 5.91 (2H, s, OCH_2O), 6.41, 6.48 (each 1H, s, 2×arom.–H), 1.55 (3H, s, CH_3CO). MS, *m/z* (%): 444 (M^+, 16), 384 (M^+-CH_3COOH, 100). *Anal.* Calcd for $C_{24}H_{28}O_8$: C, 64.85; H, 6.35. Found: C, 65.10; H, 6.48.

Hydrolysis of 1——A solution of **1** (26 mg) in a mixture of EtOH (2 ml) and $CHCl_3$ (1 ml) containing 3% KOH was kept at 75—80° for 8.5 hr. The reaction mixture was neutralized with 1 N HCl, diluted with H_2O (10 ml) and extracted with ether. The ethereal extract was washed with 5% $NaHCO_3$, then H_2O, dried over Na_2SO_4 and concentrated. The residue was purified by PLC[$CHCl_3$–EtOH (19: 1)] to give **4** as colorless prisms (from ether–hexane), $[\alpha]_D^{26}$ −20.7° (c=1.35, $CHCl_3$), mp 153—155°, 11.3 mg. $FeCl_3$ in EtOH: brown. UV λ_{max}^{EtOH} nm (log ε): 22 (4.59), 254 (sh. 3.90), 282 (3.14). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3505, 3490 (OH), 1610, 1575 (aromatic). CD (c=0.0223, MeOH), $[\theta]^{23}$ (nm): −84000 (254), −5400 (232), −9900 (227), 0 (223), +66000 (207).

^{1}H-NMR (δ in $CDCl_3$): 0.93 (3H, d, J=7 Hz, H-C$_{(7)}$-C$\underline{H}_3$), 1.15 (3H, d, J=7 Hz, H-C$_{(8)}$-C$\underline{H}_3$), 1.78—2.08 (2H, m, 2×-C$\underline{H}$), 2.62 (2H, d, J=4 Hz, C$_{(6)}$-H), 3.83, 3.87, 3.88 (each 3H, s, 3×OCH_3), 4.60 (1H, s, C$_{(9\beta)}$-H), 5.85 (1H, s, C$_{(1)}$-OH, D_2O-exchangeable), 5.93 (2H, s, OCH_2O), 6.33, 6.40 (each 1H, 2×arom.-H), 1.38 (1H, br s, C$_{(9)}$-OH, D_2O-exchangeable). *Anal.* Calcd for $C_{22}H_{26}O_7$: C, 65.66; H, 6.51. Found: C, 65.51; H, 6.52.

Oxidation of 1 with Fremy's Salts——A solution of **1** (29.7 mg) and Fremy's salts (potassium nitrosobisulfite, 105 mg) in a mixture of H_2O (1 ml) and acetone (2 ml) was kept at 55—60° for 6 hr, then the reaction mixture was diluted with H_2O and extracted with ether. The ethereal extract was washed with H_2O, dried over Na_2SO_4 and concentrated to give a residue, purification of which by PLC [benzene–ether (1: 1), *Rf* 0.62] gave **6** as orange prisms (from ether–hexane), mp 147—149°, $[\alpha]_D^{26}$ −85.1° (c=1.14, $CHCl_3$), 22.8 mg (74.5%). UV λ_{max}^{EtOH} nm (log ε): 220 (4.57), 246 (sh, 3.94), 278 (4.11), 355 (3.34). IR ν_{max}^{KBr} cm^{-1}: 1738 (ester), 1660, 1642 (p-quinone), 1625, 1608 (aromatic). ^{1}H-NMR (δ in $CDCl_3$): 0.85 (3H, d, J=7 Hz, H-C$_{(7)}$-C$\underline{H}_3$), 1.05 (3H, d, J=7 Hz, H-C$_{(8)}$-C$\underline{H}_3$), 1.97 (2H, m, 2×-C$\underline{H}$), 2.01 (1H, dd, J=14/2 Hz, C$_{(6\beta)}$-H), 3.17 (1H, dd, J=14/8 Hz, C$_{(6\alpha)}$-H), 3.82, 3.98, 4.05 (each 3H, s, 3×OCH_3), 5.73 (1H, d, J=2 Hz, C$_{(9\beta)}$-H), 5.94 (2H, s, OCH_2O), 6.44 (1H, s, arom.-H), 1.78 (3H, s, CH_3CO). ^{13}C-NMR (δ in $CDCl_3$): 184.1 (s, C=O), 183.3 (s, C=O), 169.4 (s, $CH_3\underline{C}O$), 150.2 (s), 144.8 (s), 144.2 (s), 141.3 (s), 140.7 (s, ×2), 135.7 (s), 135.5 (s), 116.8 (s), 102. 9 (d, C-11), 101.6 (t, OCH_2O), 81.2 (d, C-9), 61.2, 61.1, 59.5 (each q, 3×OCH_3), 40.6 (d, C-8), 34.1 (d, (C-7), 30.0 (t, C-6), 20.7 (q, $\underline{C}H_3CO$), 18.1 (q, C-17), 15.5 (q, C-18). High resolution MS, Calcd for $C_{24}H_{26}O_9$ (M^+): 458.1576. Found: 458.1565.

Methylation of 1——A solution of **1** (20.4 mg) in ethereal diazomethane (2 ml) was kept at 0—5° for 7 days, and then concentrated. The residue was purified by PLC [benzene–ether (1: 1), *Rf* 0.72] to give **5** (7.8 mg, 37.1%) as colorless needles (from EtOH), $[\alpha]_D^{21}$ −19.7° (c=1.52, $CHCl_3$), mp 157—158°, UV λ_{max}^{EtOH} nm (log ε): 221 (4.63), 244 (sh. 4.05), 280 (sh. 3.50). IR ν_{max}^{KBr} cm^{-1}: 1735 (C=O), 1617, 1595, 1580 (aromatic). ^{1}H-NMR (δ in $CDCl_3$): 0.93 (3H, d, J=7 Hz, H-C$_{(7)}$-C$\underline{H}_3$), 1.07 (3H, d, J=7 Hz, H-C$_{(8)}$-C$\underline{H}_3$), 1.88—2.13 (2H, m, 2×-CH), 2.65 (2H, d, J=4 Hz, C$_{(6)}$-H), 3.63, 3.80, 3.87, 3.90 (each 3H, s, 4×OCH_3), 5.65 (1H, s, C$_{(9\beta)}$-H), 5.97 (2H, s, OCH_2O), 6.45, 6.57 (each 1H, s, 2×arom.-H), 1.55 (3H, s, CH_3CO). *Anal.* Calcd for $C_{25}H_{30}O_8$: C, 65.49; H, 6.60. Found: C, 65.57; H, 6.67. This compound was identified as kadsurin by direct comparison (IR, ^{1}H-NMR and $[\alpha]_D$).

Angeloyl-binankadsurin A (**2**)——Colorless prisms (from ether–hexane), mp 121—122°, $[\alpha]_D^{25}$ +61.5° (c=2.26, $CHCl_3$). $FeCl_3$ in EtOH: green. UV λ_{max}^{EtOH} nm (log ε): 218 (4.65), 254 (sh. 3.95), 276—282 (sh. 3.38). IR ν_{max}^{KBr} cm^{-1}: 3360 (OH), 1720 (C=O), 1645 (C=C), 1608, 1585 (aromatic). ^{1}H-NMR (δ in $CDCl_3$): 0.93 (3H, d, J=7 Hz, H-C$_{(7)}$-C$\underline{H}_3$), 1.08 (3H, d, J=7 Hz, H-C$_{(8)}$-C$\underline{H}_3$), 2.08 (center, 2H, m, 2×-C$\underline{H}$), 2.60 (2H, d, J=4 Hz, C$_{(6)}$-H), 3.77, 3.80, 3.83 (each 3H, s, 3×OCH_3), 5.55 (1H, s, C$_{(9\beta)}$-H), 5.37 (1H, s, C$_{(1)}$-OH, D_2O-exchangeable), 5.90 (2H, s, OCH_2O), 6.33, 6.50 (each 1H, s, 2×arom.-H), 1.30 (3H, m), 1.87 (3H, dq, J= 7/1.5 Hz), 5.72 (1H, m) (angeloyl group). MS, m/z (%): 484 (M^+, 10), 384 [M^+-CH_3CH=C(CH_3)COOH, 100], 100 [CH_3CH=C(CH_3)COOH, 27], 83 [CH_3CH=C(CH_3)CO, 16], 55 [CH_3CH=C(CH_3), 26]. *Anal.* Calcd for $C_{27}H_{32}O_8$: C, 66.92; H, 6.66. Found: C, 67.06; H, 6.71.

Hydrolysis of 2——A solution of **2** (98.1 mg) in 3% KOH in EtOH (2 ml) was kept at 65—70° for 7 hr, neutralized with 1 N HCl, diluted with H_2O (10 ml) and extracted with ether. The ethereal extract was washed with 5% $NaHCO_3$, then with H_2O, dried over Na_2SO_4 and concentrated. The residue was purified by PLC [benzene–ether (1: 1)] to give **4** as colorless prisms, mp 153—155°, $[\alpha]_D^{25}$ −17.0° (c=2.00, $CHCl_3$), 39.2 mg. *Anal.* Calcd for $C_{22}H_{26}O_7$: C, 65.66; H, 6.51. Found: C, 65.58; H, 6.51. This compound was identical with **4** prepared from **1** on direct comparison (IR, mixed mp, ^{1}H-NMR and $[\alpha]_D$). The 5% $NaHCO_3$ solution was acidified with 1 N HCl and extracted with ether. The ethereal extract was washed with H_2O, dried over Na_2SO_4 and concentrated. Sublimation (70°, 15 mmHg) of the residue gave colorless needles. The presence of angelic acid and tiglic acid in this sublimate in a ratio of 1: 10 was demonstrated by GLC.[10] GLC conditions: column, SP-1200 (10%)+H_3PO_4 (1%) on Chromosorb WAW (80—100 mesh), 3 mm×2 m; column temperature, 130°; injection temperature, 150°; carrier gas, N_2, 29.4 ml/min; t_R(min): angelic acid, 6.4; tiglic acid, 8.3.

Caproyl-binankadsurin A (**3**)——Colorless prisms (from ether–hexane), mp 83—87°, $[\alpha]_D^{25}$ +14.7° (c=2.73, $CHCl_3$). $FeCl_3$ in EtOH: green. UV λ_{max}^{EtOH} nm (log ε): 218 (4.54), 255 (sh. 3.92), 275—282 (sh. 3.40). IR ν_{max}^{KBr} cm^{-1}: 3330 (OH), 1735, 1725 (C=O), 1615, 1600, 1580 (aromatic). ^{1}H-NMR (δ in $CDCl_3$): 2.63 (2H, d, J=4 Hz, C$_{(6)}$-H), 3.82 (3H, s), 3.88 (6H, s) (3×OCH_3), 5.55 (1H, s, C$_{(9\beta)}$-H), 5.57 (1H, s, C$_{(1)}$-OH, D_2O-exchangeable), 5.95 (2H, s, OCH_2O), 6.37, 6.47 (each 1H, s, 2×arom.-H). The signals of the C$_{(7)}$- and C$_{(8)}$-methyl groups and the caproyl group were not clear due to overlapping (δ 0.80—2.30). MS, m/z (%): 500 (M^+, 11), 384 [$M^+-CH_3(CH_2)_4COOH$, 100], 73 [$(CH_2)_2COOH$, 13], 60 [CH_2=C$(OH)_2$, 23]. *Anal.* Calcd for $C_{28}H_{36}O_8$: C, 67.18; H, 7.25. Found: C, 66.97; H, 7.27.

Hydrolysis of 3——A solution of **3** (17.3 mg) in 3% KOH in EtOH (2 ml) was kept at 65~70° for 2.5 hr. The reaction mixture was neutralized with 1 N HCl, diluted with H_2O (10 ml) and extracted with ether. The ethereal extract was washed with 5% $NaHCO_3$, then H_2O, dried over Na_2SO_4 and concentrated. The residue was purified by TLC [benzene–ether (1: 1)] to give **4** as colorless prisms (from ether–hexane), mp 153—155°, $[\alpha]_D^{25}$ −18.3° (c=0.60, $CHCl_3$), 10.4 mg. *Anal.* Calcd for $C_{22}H_{26}O_7$: C, 65.66; H, 6.51. Found: C, 65.77; H, 6.54. This compound was identical with **4** prepared from **1** on direct comparison (IR, mixed

mp, ^{1}H-NMR and $[\alpha]_D$). The 5% $NaHCO_3$ solution was acidified with 1 N HCl and extracted with ether. The ethereal extract was washed with H_2O, dried over Na_2SO_4 and concentrated to give an oil, which was identified as caproic acid by GLC. GLC conditions were the same as those used for the identification of angelic acid in the case of hydrolysis of **2**. Caproic acid: t_R(min), 10.5.

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