Constituents of Zingiberaceae. I. Diarylheptanoids from the Rhizomes of Ginger (*Zingiber officinale* ROSCOE)

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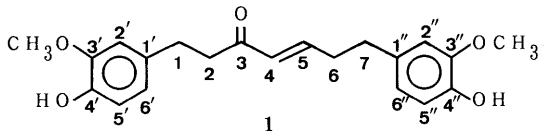
Two new diarylheptanoids, *meso*-3,5-diacetoxy-1,7-bis(4-hydroxy-3-methoxyphenyl)heptane (3a) and 3,5-diacetoxy-1-(4-hydroxy-3,5-dimethoxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)heptane (4a) were isolated from the rhizomes of ginger (*Zingiber officinale* ROSCOE), together with dehydroxytetrahydrocurcumin (gingerenone A, 1) and hexahydrocurcumin (2). Their structures were elucidated on the basis of chemical and spectroscopic evidence.

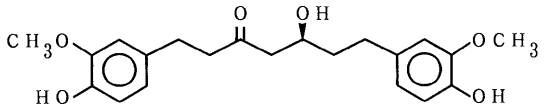
Keywords ginger; *Zingiber officinale*; Zingiberaceae; diarylheptanoid; curcuminoid; spice

Ginger, the rhizome of *Zingiber officinale* ROSCOE, is one of the most popular spices and is also used as an oriental folk medicine. Its chemical constituents reportedly include a large number of terpenoids such as zingiberene and geraniol[1] and pungent components, *e.g.* shogaol and gingerol.[2] Many diarylheptanoids were isolated from the plants belonging to Zingiberaceae,[3] however, only a few were obtained from *Z. officinale* ROSCOE.[4] In this paper, we describe the isolation and structural elucidation of four diarylheptanoids including two new ones from ginger.

Dried rhizomes of ginger were extracted with dichloromethane and the extract was stream-distilled. The non-volatile components were subjected to chromatography on a silica gel column using benzene–acetone as an eluent to afford eleven fractions. The sixth and seventh fractions were successively chromatographed on a Sephadex LH-20 column and a silica gel column to give compound **1**. Compounds **2**, **3a** and **4a** were isolated from the eighth fraction in a similar way.



1



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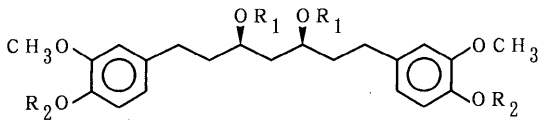
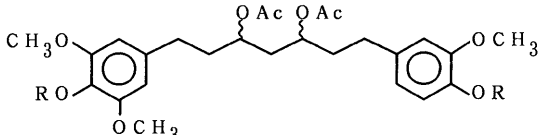
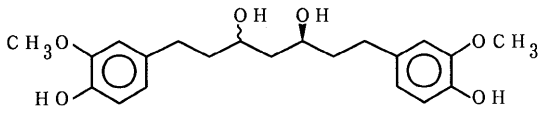


3a : R_1 = Ac, R_2 = H
3b : R_1 = R_2 = Ac



4a : R = H
4b : R = Ac



5a : 3*R*
5b : 3*S*

Chart 1

Compound **1** was obtained as an oil, and gave a molecular ion peak in the high-resolution mass spectrum (HRMS) at *m/z* 356.1578, which indicated the molecular formula of $C_{21}H_{24}O_5$. On the basis of the spectral and physical data, compound **1** was identified as gingerenone A [1,7-bis(4-hydroxy-3-methoxyphenyl)hept-4-en-3-one], which has recently been isolated from the same source.[4b]

Compound **2** was colorless needles, mp 87 °C, and identified as hexahydrocurcumin [5-hydroxy-1,7-bis(4-hydroxy-3-methoxyphenyl)heptan-3-one]. It is known that authentic hexahydrocurcumin has the specific rotation of +9.0° and the stereochemistry at the 5-position is of S configuration.[3b,4a] The specific rotation of this compound was +6.0°, so the configuration at the 5-position of **2** must be *S*.

Compound **3a** was obtained as an oil and gave a molecular ion peak in the HRMS at *m/z* 460.2091, which indicated the molecular formula of $C_{25}H_{32}O_8$. The infrared (IR) spectrum showed the presence of a hydroxyl group at 3420 cm^{-1} and an ester at 1720 cm^{-1}. In the proton nuclear magnetic resonance (^{1}H-NMR) spectrum, the signal at δ 2.01 (6H, s) showed the presence of two acetyl groups. This fact was supported by the mass fragments of *m/z* 400 and 340 in the mass spectrum (MS), the former being yielded by deacetoxylation from the molecular ion of *m/z* 460 and the latter from the ion of *m/z* 400. A set of a two proton double triplet at δ 2.50 (J=7.9, 14.0 Hz) and 2.56 (J=7.9, 14.0 Hz) was attributed to the geminal protons of the benzylic methylene (H-1, 7), which were coupled with two methylene protons at C-2 and 6, observed as an apparent quartet at δ 1.84 (4H, J=7.9 Hz). When the signal at δ 1.84 (H-2, 6) was irradiated, the apparent quintet at δ 4.94 (2H, J=6.1 Hz) assignable to acetoxymethine protons, changed into a double doublet (J=6.1, 7.3 Hz), which coupled with geminal methylene protons at δ 1.75 (1H, dt, J=6.1, 14.0 Hz), and 1.95 (1H, dt, J=7.3, 14.0 Hz). Furthermore, when the signal at δ 4.94 was irradiated, the quartet at δ 1.84 was collapsed into a triplet (J=7.9 Hz), and the double triplets at δ 1.75 and 1.95 into two doublets with a coupling constant of 14.0 Hz each. This fact indicated that both C-3 and 5 are substituted by acetoxyl groups. Six aromatic protons [δ 6.63 (2H, br d, J=7.9 Hz), 6.65 (2H, br s), 6.81 (2H, d, J=7.9 Hz)] accompanied by two arylic methoxyl ones [δ 3.87 (6H, s)] in the ^{1}H-NMR and six

TABLE I. ^{13}C-NMR Spectral Data for Compounds **3a**—**5b**

Carbon No.	3a	3b	4a	4b	5a	5b
1	31.25	31.60	31.79	32.25	31.98	32.40
2	35.99	35.67	36.02[a)]	35.65[c)]	41.13	41.02
3	70.73	70.65	70.63[b)]	70.64	71.66	68.40
4	38.51	38.69	38.59	38.73	44.37	44.88
5	70.73	70.65	70.68[b)]	70.64	71.66	68.40
6	35.99	35.67	35.97[a)]	35.68[c)]	41.13	41.02
7	31.25	31.60	31.25	31.61	31.98	32.40
1′	133.12	140.20	132.99	139.72	134.74	134.86
2′	114.29	112.61	105.04	105.01	112.82	112.86
3′	146.43	150.90	147.00	151.99	148.12	148.12
4′	143.86	137.97	132.27	120.35	145.39	145.39
5′	110.98	122.60	147.00	151.99	115.78	115.58
6′	120.89	120.39	105.04	105.01	121.47	121.50
1″	133.12	140.20	133.11	140.18	134.74	134.86
2″	114.29	112.61	114.29	112.61	112.82	112.86
3″	146.43	150.90	146.45	150.90	148.12	148.12
4″	143.86	137.97	143.86	137.97	145.39	145.39
5″	110.98	122.60	110.98	122.60	115.78	115.58
6″	120.89	120.39	120.87	120.39	121.47	121.50
3′OMe	55.90	55.87	56.29	56.13	56.16	56.19
5′OMe			56.29	56.13		
3″OMe	55.90	55.87	55.90	55.87	56.16	56.19
3,5OAc	170.64	170.69	170.64	170.70		
	21.16	21.15	21.14	21.13		
4′OAc		169.20		168.90		
		20.68		20.47		
4″OAc		169.20		169.20		
		20.68		20.68		

a—*c*) Assignments interchangeable. The measurements were made in $CDCl_3$ (**3a**, **3b**, **4a** and **4b**) and acetone-d_6 (**5a** and **5b**) with TMS as internal standard.

TABLE II. ^{1}H-NMR Spectral Data for Compounds **3a**—**5b**

Proton No.	3a	3b	4a	4b	5a	5b
H-1a	2.50 dt	2.56 dt	2.49 dt	2.50—2.60 m	2.57 dt	2.57 ddd
H-1b	2.56 dt	2.62 dt	2.57 dt	2.61 dt	2.68 dt	2.69 ddd
H-2	1.84 q	1.88 q	1.84 q	1.88 q	1.71 q	1.72 m
H-3	4.94 quint	4.97 quint	4.94 quint	4.97 quint	3.78—3.84 m	3.90 m
H-4a	1.75 dt	1.76 dt	1.75 dt	1.76 dt	1.52 dt	1.58 t
H-4b	1.95 dt	1.97 dt	1.95 dt	1.97 dt	1.65 dt	1.58 t
H-5	4.94 quint	4.97 quint	4.94 quint	4.97 quint	3.78—3.84 m	3.90 m
H-6	1.84 q	1.88 q	1.84 q	1.88 q	1.71 q	1.72 m
H-7a	2.50 dt	2.56 dt	2.50 dt	2.50—2.60 m	2.57 dt	2.57 ddd
H-7b	2.56 dt	2.62 dt	2.57 dt	2.61 dt	2.68 dt	2.70 ddd
H-2′	6.65 br s	6.76 d	6.37 s	6.40 s	6.81 d	6.81 d
H-5′	6.81 d	6.92 d			6.72 d	6.72 d
H-6′	6.63 br d	6.72 dd	6.37 s	6.40 s	6.64 dd	6.64 dd
H-2″	6.65 br s	6.76 d	6.64 br s	6.76 d	6.81 d	6.81 d
H-5″	6.81 d	6.92 d	6.81 d	6.92 d	6.72 d	6.72 d
H-6″	6.63 br d	6.72 dd	6.63 br d	6.72 dd	6.64 dd	6.64 dd
3′OMe	3.87 s	3.82 s	3.87 s	3.80 s	3.81 s	3.82 s
5′OMe			3.87 s	3.80 s		
3″OMe	3.87 s	3.82 s	3.87 s	3.82 s	3.81 s	3.82 s
3OAc	2.01 s	2.01 s	2.02 s[a)]	2.02 s[b)]		
5OAc	2.01 s	2.01 s	2.01 s[a)]	2.01 s[b)]		
4′OAc		2.30 s		2.32 s		
4″OAc		2.30 s		2.30 s		

a, *b*) Assignments interchangeable. The measurements were made in $CDCl_3$ (**3a**, **3b**, **4a** and **4b**) and acetone-d_6 (**5a** and **5b**) with TMS as internal standard. Multiplicities come from observed spectra (400 MHz). *J* (Hz) **3a**, **3b**, **4a**, **4b** and **5a**: 1a, 1b = 7a, 7b = 14.0; 1, 2 = 7, 6 = 7.9; 4a, 4b = 14.0. **5b**: 1a, 1b = 7a, 7b = 14.0; 1a, 2a = 7a, 6a = 6.7; 1a, 2b = 7a, 6b = 9.2; 1b, 2a = 7b, 6a = 6.1; 1b, 2b = 7b, 6b = 9.2. **3a**: 5′, 6′ = 5″, 6″ = 7.9. **3b**, **5a** and **5b**: 2′, 6′ = 2″, 6″ = 1.8; 5′, 6′ = 5″, 6″ = 7.9. **4a**: 5″, 6″ = 7.9. **4b**: 2″, 6″ = 1.8; 5″, 6″ = 7.9.

aromatic carbons (δ 133.12, 114.29, 146.43, 143.86, 110.98, 120.89) in the carbon-13 nuclear magnetic resonance (^{13}C-NMR) suggested the presence of two 4-hydroxy-3-methoxyphenyl groups, which was supported by the stable fragment ion at *m/z* 137 as a base peak in the MS. The ^{13}C-NMR spectrum revealed only thirteen peaks in spite of the molecular formula of $C_{25}H_{32}O_8$. This fact and a specific rotation of 0° suggested that this compound (**3a**) had a symmetrical skeleton and that the structure was 3,5-diacetoxy-1,7-bis(4-hydroxy-3-methoxyphenyl)heptane.

Acetylation of **3a** with acetic anhydride and pyridine introduced two more acetyl groups on the structure of **3a**, exhibiting a molecular ion peak at *m/z* 544. The IR spectrum of this compound (**3b**) showed a new absorption band of acetate at 1755 cm^{-1} with the disappearance of the hydroxyl peak at 3240 cm^{-1} in the spectrum of **3a**. The signal of two phenolic acetates was observed at δ 2.30 in the ^{1}H-NMR.

In order to determine the stereochemistry at C-3 and 5, compound **2** (5*S* configuration) was reduced with $NaBH_4$ to afford **5a** and **5b**, and separated by silica gel column chromatography. Compound **5a** was a colorless oil and showed the molecular ion peak at *m/z* 376 in the MS. The absorption band of a carbonyl group at 1702 cm^{-1} in the IR spectrum of **2** disappeared. The ^{13}C-NMR spectrum revealed a new signal of oxymethine carbon at δ 71.66 instead of that of the carbonyl one at δ 211.35 of **2**. The specific rotation ($[\alpha]_D^{25}$ 0°) together with the results of ^{13}C-NMR data[3c)] indicated that this compound was *meso* type, namely (3*R*,5*S*)-1,7-bis(4-hydroxy-3-methoxyphenyl)-heptan-3,5-diol. Compound **5b** was obtained as colorless needles, mp 136 °C. A comparison of **5b** with **5a** in the ^{13}C-NMR spectrum showed upfield shifts of C-2, 6 (0.1 ppm) and C-3, 5 (3.3 ppm), and downfield shifts of C-1, 7 (0.4 ppm) and C-4 (0.5 ppm).[3c,5)] The specific rotation ($[\alpha]_D^{25}$ −7.4°) confirmed the configuration of **5b** to be (3*S*, 5*S*). Alkaline hydrolysis of compound **3a** gave 3,5-dihydroxyl compound. The behavior of thin layer chromatography (TLC) and spectral data of this compound was identical with those of **5a**. Furthermore, the spectral data of **3b** was identical with those of acetyl derivative of compound **5a**. Thus, the structure of compound **3a** was concluded to be *meso*-3,5-diacetoxy-1,7-bis(4-hydroxy-3-methoxyphenyl)heptane.

Compound **4a** was obtained as an oil and gave a molecular ion peak at *m/z* 490.2202 in the HRMS, corresponding to the molecular formula of $C_{26}H_{34}O_9$. Spectral characteristics of this compound indicated that **4a** had a similar structure to **3a**. In the IR spectrum, absorption bands of a hydroxyl group and an ester were observed at 3480 and 1725 cm^{-1}, respectively. The presence of two acetyl groups was supported by the signals at *m/z* 430 and 370 in the MS, which were produced stepwise by deacetoxylation from the molecular ion (*m/z* 490). In the ^{1}H-NMR, the signal of a nine proton singlet at δ 3.87 showed the presence of three methoxyl groups, which suggested that compound **4a** was a methoxylated derivative of **3a**, considering that the molecular size of **4a** was 30 mass (OCH_2) larger than that of **3a**. Three aromatic protons [δ 6.63 (br d, *J* = 7.9 Hz), 6.64 (br s), 6.81 (d, *J* = 7.9 Hz)] and ^{13}C-NMR data suggested the presence of a 4-hydroxy-3-methoxyphenyl group. Other aromatic protons were observed at δ 6.37 as a two proton singlet. It is deduced from this fact that **4a** had a symmetrical tetrasubstituted benzene ring in place of the 1,3,4-trisubstituted one of **3a**. The typical mass fragment

ion peak at m/z 167 indicated the presence of dimethoxy-monohydroxyphenyl group. The substitution pattern of the aromatic ring was determined to be two methoxyl groups at C-3′ and 5′ and a hydroxyl one at C-4′, by the chemical shifts of ^{13}C-NMR data based on the results of calculations.

Acetylation of **4a** gave compound **4b** as a colorless oil. The IR spectrum showed a new absorption band of acetate at 1760 cm^{-1}, with disappearance of the hydroxyl peak at 3420 cm^{-1} in the spectrum of **4a**. The signals of two phenolic acetates were observed at δ 2.30 and 2.32. Other spectral data (^{1}H-NMR, ^{13}C-NMR) supported the structure of compound **4b**.

On the basis of all the above data, **4a** was concluded to be 3,5-diacetoxy-1-(4-hydroxy-3,5-dimethoxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)heptane. The absolute configuration of the acetoxy groups is now under investigation.

Experimental

Melting points were taken on a Yanagimoto micro melting point apparatus and are uncorrected. Ultraviolet (UV) absorption spectra were determined on a Hitachi 220 spectrophotometer and IR spectra were recorded with a Perkin Elmer 1720X. ^{1}H-NMR (400 MHz) and ^{13}C-NMR (100 MHz) spectra were run on a JEOL GX-400 using tetramethylsilane (TMS) as an internal standard. MS were obtained on a Hitachi M-2000. Optical rotation was measured with a Union PM-101. Column chromatographies were performed using Merck silica gel 60 (70—230 mesh) and Pharmacia Sephadex LH-20, and TLC was done using silica gel GF-254.

Extraction and Isolation Dried ground rhizomes of ginger (955 g) from China were extracted five times with dichloromethane (CH_2Cl_2, 2 l each) at room temperature. The combined CH_2Cl_2 extract was concentrated on a rotary evaporator to yield a brown viscous residue (62.8 g). This extract was steam-distilled to give the non-volatile fraction (29.5 g), which was subjected to chromatography on a silica gel column eluted stepwise with benzene–acetone to give eleven fractions. The sixth and seventh fractions eluted with benzene–acetone (97 : 3) were rechromatographed on a Sephadex LH-20 column using isopropyl alcohol as an eluent to separate six fractions, the fifth of which was purified by column chromatography on silica gel using *n*-hexane–acetone (4 : 1) as an eluent to give compound **1** (130 mg). The eighth fraction eluted with benzene–acetone (97 : 3) was subjected to column chromatography on silica gel eluted with *n*-hexane–acetone (2 : 1) to separate six fractions. The fourth fraction was rechromatographed on a silica gel column with *n*-hexane–acetone (2 : 1) as an eluent to give compound **3a** (39 mg) and **4a** (29 mg). The fifth fraction was purified by column chromatography on silica gel using benzene–methanol (95 : 5) as an eluent to afford compound **2** (24 mg).

Compound **1** (Gingerenone A): MS m/z (%): 356 (M$^+$, 25), 205 (5), 179 (3), 151 (5), 137 (100). HRMS m/z: 356.1578 (M$^+$, Calcd for $C_{21}H_{24}O_5$: 356.1621). UV λ_{max}^{EtOH} nm (log ε): 230.0 (4.27), 281.5 (3.85). IR ν_{max}^{film} cm^{-1}: 3435, 1696, 1615, 1516, 1034, 975. ^{1}H-NMR ($CDCl_3$) δ: 2.49 (2H, q, J=7.3 Hz, H-6), 2.70 (2H, t, J=7.3 Hz, H-7), 2.83 (4H, m, H-1, 2), 3.858 (3H, s, OCH_3), 3.864 (3H, s, OCH_3), 5.50 (1H, s, OH), 5.51 (1H, s, OH), 6.10 (1H, d, J=16.1 Hz, H-4), 6.65 (1H, br s, H-2′ or 2″), 6.69 (1H, br s, H-2′ or 2″), 6.65—6.70 (2H, m, H-6′, 6″), 6.82 (1H, d, J=7.8 Hz, H-5′ or 5″), 6.83 (1H, d, J=8.5 Hz, H-5′ or 5″). ^{13}C-NMR ($CDCl_3$) δ: 29.87, 34.16, 34.44, 42.13, 55.91, 110.95, 111.15, 114.34, 114.38, 120.83, 120.93, 130.74, 132.61, 133.19, 143.95, 144.05, 146.37, 146.43, 146.60, 199.60.

Compound **2** (Hexahydrocurcumin): mp 87 °C (benzene). $[\alpha]_D^{20}$: +6.0° (c=1.68, $CHCl_3$). MS m/z (%): 374 (M$^+$, 3), 356 (5), 194 (27), 180 (21), 151 (10), 137 (100). HRMS m/z: 374.1763 (M$^+$, Calcd for $C_{21}H_{26}O_6$: 374.1728). UV λ_{max}^{EtOH} nm (log ε): 227.0 (4.36), 281.0 (4.05). IR ν_{max}^{film} cm^{-1}: 3435, 1702, 1603, 1516, 1033. ^{1}H-NMR ($CDCl_3$) δ: 1.63 (1H, dddd, J=4.3, 6.7, 10.1, 14.0 Hz, H-6), 1.77 (1H, dddd, J=5.5, 9.2, 9.2, 14.0 Hz, H-6), 2.51 (1H, dd, J=7.9, 17.4 Hz, H-4), 2.57 (1H, dd, J=3.1, 17.4 Hz, H-4), 2.59 (1H, ddd, J=6.7, 9.2, 12.9 Hz, H-7), 2.71 (2H, t, J=7.3 Hz, H-2), 2.72 (1H, ddd, J=5.5, 10.1, 12.9 Hz, H-7), 2.82 (2H, t, J=7.3 Hz, H-1), 3.85 (3H, s, OCH_3), 3.86 (3H, s, OCH_3), 4.03 (1H, dddd, J=3.1, 4.3, 7.9, 9.2 Hz, H-5), 5.53 (1H, s, OH), 5.55 (1H, s, OH), 6.64 (1H, dd, J=1.8, 7.9 Hz, H-6′ or 6″), 6.66 (1H, d, J=1.8 Hz, H-2′ or 2″), 6.67 (1H, dd, J=1.8, 7.9 Hz, H-6′ or 6″), 6.70 (1H, d, J=1.8 Hz, H-2′ or 2″), 6.81 (2H, d, J=7.9 Hz, H-5′, 5″). ^{13}C-NMR ($CDCl_3$) δ: 29.27, 31.40, 38.34, 45.39, 49.35, 55.88, 66.92, 111.01, 111.12, 114.29, 114.44, 120.74, 120.92, 132.55, 133.69, 143.76, 144.02, 146.45, 146.49, 211.35.

Compound **3a**: $[\alpha]_D^{20}$: 0° (c=0.95, $CHCl_3$). MS m/z (%): 460 (M$^+$, 22), 400 (4), 340 (3), 204 (8), 190 (25), 175 (11), 163 (14), 150 (11), 137 (100). HRMS m/z: 460.2091 (M$^+$, Calcd for $C_{25}H_{32}O_8$: 460.2094). UV λ_{max}^{EtOH} nm (log ε): 227.5 (sh, 3.72), 281.0 (3.40). IR ν_{max}^{film} cm^1: 3420, 1720, 1600, 1025.

Acetyl Derivative of **3a**: To a solution of 6 mg of compound **3a** in pyridine (0.5 ml), acetic anhydride (0.5 ml) was added, and the mixture was allowed to stand overnight at room temperature. The reaction mixture was poured into cold 2 N HCl and then extracted with CH_2Cl_2. The organic layer was washed with water, dried over anhydrous $CaCl_2$ and evaporated to dryness. The crude product was purified by column chromatography on silica gel using *n*-hexane–acetone (2 : 1) as an eluent to give a colorless oil (**3b**). MS m/z (%): 544 (M$^+$, 2), 502 (31), 484 (1), 460 (11), 442 (12), 400 (13), 340 (15), 204 (10), 190 (26), 175 (8), 163 (12), 150 (11), 137 (100). IR ν_{max}^{film} cm^{-1}: 1763, 1735, 1605, 1509.

Compound **4a**: $[\alpha]_D^{20}$: −1.4° (c=0.72, $CHCl_3$), MS m/z (%): 490 (M$^+$, 34), 430 (3), 370 (3), 234 (5), 220 (11), 205 (2), 204 (7), 193 (14), 190 (11), 180 (7), 175 (7), 167 (53), 163 (21), 150 (13), 137 (100), HRMS m/z: 490.2202 (M$^+$, Calcd for $C_{26}H_{34}O_9$: 490.2201). UV λ_{max}^{EtOH} nm (log ε): 230.0 (sh, 4.05), 280.0 (3.56). IR ν_{max}^{film} cm^{-1}: 3480, 1725, 1600, 1030.

Acetyl Derivative of **4a**: Acetylation of **4a** (6 mg) was carried out as described above. Compound **4b**: IR ν_{max}^{film} cm^{-1}: 1763, 1734, 1604, 1510.

Hydrogenation of **2**: To a solution of compound **2** (16.8 mg) in EtOH (5 ml), 3.5 mg of $NaBH_4$ was added at room temperature, and the mixture was allowed to stand for 1 h. After removing the solvent *in vacuo*, the reaction mixture was poured into cold 0.2 N HCl, and then extracted with CH_2Cl_2. The organic layer was washed with water, dried over anhydrous $CaCl_2$ and concentrated. The product was chromatographed on a silica gel column with CH_2Cl_2–methanol (97 : 3) as an eluent to give compounds **5a** and **5b**. Compound **5a**: $[\alpha]_D^{25}$: 0° (c=0.68, EtOH). MS m/z (%): 376 (M$^+$, 13), 358 (9), 340 (1), 190 (9), 163 (6), 151 (6), 150 (13), 138 (36), 137 (100). HRMS m/z: 376.1875 (M$^+$, Calcd for $C_{21}H_{28}O_6$: 376.1884). UV λ_{max}^{EtOH} nm (log ε): 227.5 (3.81), 281.0 (3.48). IR ν_{max}^{film} cm^{-1}: 3391, 1603, 1516, 1034. Compound **5b**: mp 136 °C (benzene–chloroform). $[\alpha]_D^{25}$: −7.4° (c=0.27, EtOH). MS m/z (%): 376 (M$^+$, 17), 358 (12), 340 (1), 190 (9), 163 (7), 151 (10), 150 (7), 138 (37), 137 (100). HRMS m/z: 376.1871 (M$^+$, Calcd for $C_{21}H_{28}O_6$: 376.1884). IR ν_{max}^{film} cm^{-1}: 3368, 1602, 1516, 1033.

Acetyl Derivative of Compound **5a**: Spectral data from MS, IR, ^{1}H- and ^{13}C-NMR of this compound were identical in all respects with those of compound **3b**.

Alkaline Hydrolysis of Compound **3a**: Compound **3a** (6.6 mg) was dissolved in 0.5 ml of 2% methanolic KOH, and the mixture was left overnight at room temperature. After removing the solvent *in vacuo*, the reaction mixture was poured into cold 0.1 N HCl, and subsequently extracted with CH_2Cl_2. The organic layer was washed with water, dried over anhydrous $CaCl_2$ and evaporated to dryness (5.3 mg). The residue was chromatographed on a silica gel column with a mixture of CH_2Cl_2–methanol as an eluent to give a colorless oil. Spectral data from MS, IR, ^{1}H- and ^{13}C-NMR of this compound was identical in all respects with those of compound **5a**.

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