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# SESQUITERPENE GLYCOSIDES AND SESQUILIGNAN GLYCOSIDES FROM STEMS OF *ALANGIUM PREMNIFOLIUM*

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**Key Word Index**—*Alangium premnifolium*; Alangiaceae; sesquiterpene glycosides; cadinane glycosides; calamenene glycoside; alangicadinosides F–I; sesquilignan glucoside; alangisesquins A–D.

**Abstract**—From the stems of *Alangium premnifolium*, collected on Okinawa island, four sesquiterpene (calamenene) glycosides, named alangicadinosides F–I, and four sesquilignan glucosides, named alangisesquins A–D, were isolated. The structures of the glycosides were determined on the basis of spectroscopic evidence.


## INTRODUCTION

On chemical investigation of the constituents in the leaves of *Alangium premnifolium* Ohwi, collected on Okinawa island, several ionol glycosides were isolated [1]. The *n*-BuOH-soluble fraction of a MeOH extract of stems of the title plant has yielded sesquiterpene and sesquilignan glycosides. This paper deals with their structural elucidation.

## RESULTS AND DISCUSSION

A total of 11 compounds was isolated from the *n*-BuOH-soluble fraction by means of a combination of various kinds of chromatography.

Three known compounds isolated were identified as salicin (**1**), henryoside (**2**) [2] and loganic acid (**3**) [3] by comparison of their physical data with those of authentic samples or reported values.

Compound **4**, $[\alpha]_D$ −33.6°, was obtained as a pale yellow amorphous powder, whose elemental composition was determined to be $C_{26}H_{40}O_{12}$ by analysis of the quasi molecular ion peak on HR-FAB mass spectrometry. The IR (1610 and 1490 $cm^{-1}$) and UV (280 nm) absorption maxima indicated the presence of an aromatic ring system. The $^{13}C$ NMR spectrum showed 11 signals assignable to a terminal β-xylopyranose moiety and a 6-glycosylated β-glucopyranose moiety [4] (Table 1). Six of the remaining 15 signals were attributed to pentasubstituted aromatic ring carbons, two of which must carry hydroxyl functions ($\delta_C$ 143.4 and 147.8), and eight to aliphatic carbons, whose protons appeared close and finely coupled each other. The remaining signal with three protons, which resonated at $\delta_H$ 2.29 as a singlet, had to be a methyl group on the aromatic ring. The H—H and C—H COSY spectra revealed the connectivities of the eight aliphatic carbon atoms, namely $C(15)H_3$-C(10)H-C(9)$H_2$-C(8)$H_2$-C(7)H-C(11)H $<^{C(12)H_2O-}_{C(13)H_3}$.

Since significant enhancement of the anomeric proton signal ($\delta_H$ 4.45) was observed on irradiation of the aromatic methyl protons and vice versa in the difference NOE experiments, the sugar moiety was linked through the hydroxyl group adjacent to the aromatic methyl position. Whereas, on irradiation of the aromatic proton ($\delta_H$ 6.47), the increase in the signal intensity of the proton at C-11 ($\delta_H$ 1.93) and the aromatic methyl suggested the partial structure (a) shown in Fig. 1. Finally, the results of the C—H long-range COSY ($J$ = 7 Hz) experiment revealed that C-1 and C-10 must be connected to make up a sesquiterpene skeleton of a cadinane, or more strictly, a calamenene type [see (b) in Fig. 1] [5]. Therefore, the disposition of all substituents on the aromatic ring was clarified and the structure of compound **4** was concluded to be 2,3,12-trihydroxycalamenene-3-*O*-β-

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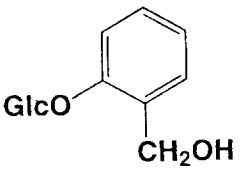


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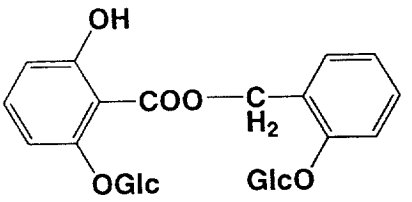


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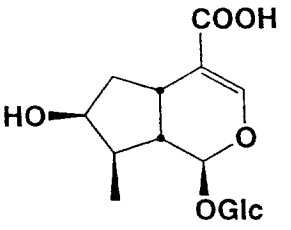


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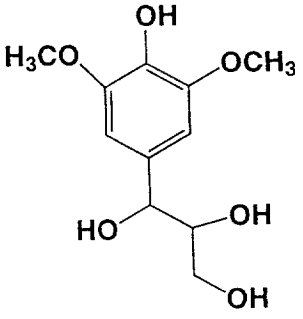


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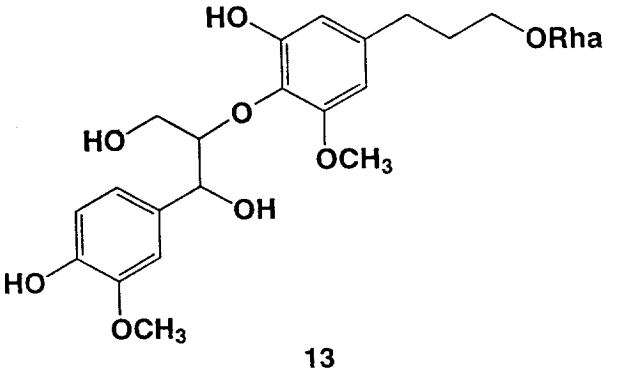


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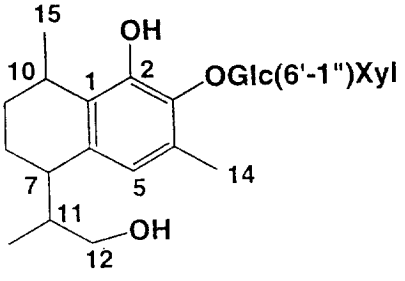


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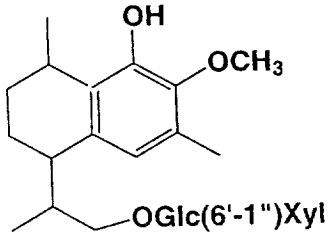


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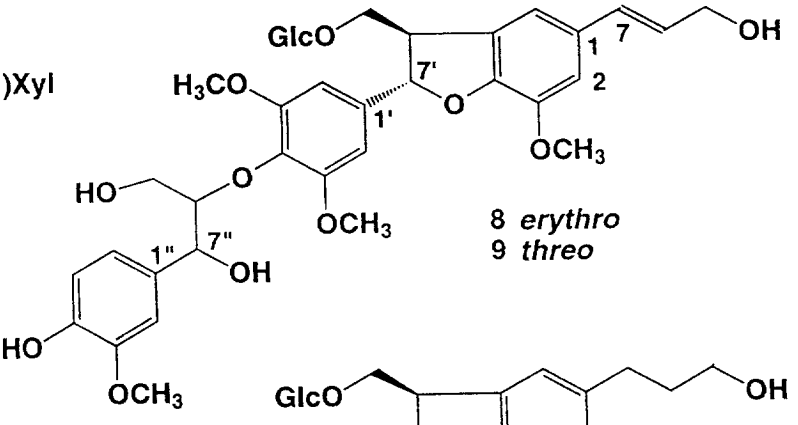
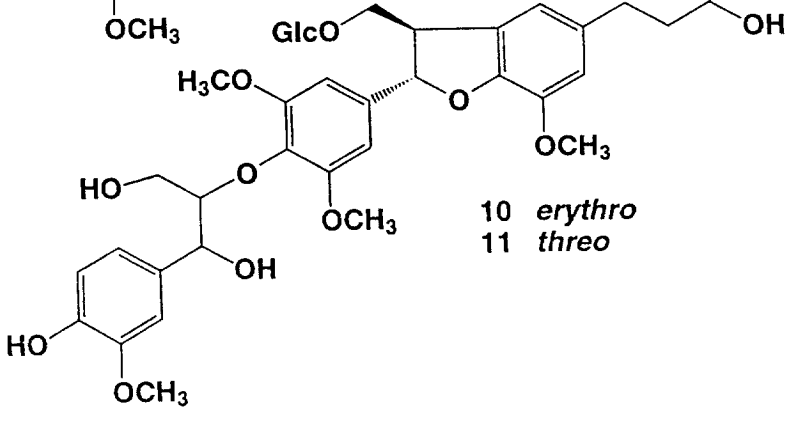



8 *erythro*
9 *threo*




10 *erythro*
11 *threo*

Table 1. $^{13}C$ NMR data for alangicadinosides F–I (**4**–**7**) ($CD_3OD$, 100 MHz)

| C | 4 | 5 | 6 | 7 |
|---|---|---|---|---|
| 1 | 129.5 | 129.6 | 129.4 | 129.6 |
| 2 | 147.8 | 147.6 | 145.1 | 144.9 |
| 3 | 143.4 | 143.2 | 148.0 | 148.0 |
| 4 | 129.5 | 129.8 | 128.1 | 128.2 |
| 5 | 123.3 | 122.7 | 123.3 | 122.8 |
| 6 | 136.8 | 137.4 | 135.6 | 136.2 |
| 7 | 40.8 | 38.2 | 40.9 | 38.1 |
| 8 | 21.3 | 19.9 | 21.2 | 20.1 |
| 9 | 28.0 | 28.3 | 28.2 | 28.5 |
| 10 | 28.2 | 28.3 | 28.2 | 28.3 |
| 11 | 43.2 | 42.5 | 40.6 | 40.2 |
| 12 | 66.4 | 66.9 | 74.2 | 74.6 |
| 13 | 17.1 | 14.3 | 17.6 | 14.6 |
| 14 | 17.1 | 17.1 | 16.0 | 15.9 |
| 15 | 21.6 | 21.6 | 21.5 | 21.6 |
| –OMe | | | 60.7 | 60.7 |
| 1′ | 107.8 | 107.8 | 104.2 | 104.7 |
| 2′ | 75.4 | 75.4 | 75.1 | 75.2 |
| 3′ | 77.9 | 77.9 | 78.1 | 78.1 |
| 4′ | 71.2 | 71.2 | 71.5 | 71.5 |
| 5′ | 77.2 | 77.1 | 77.0 | 77.0 |
| 6′ | 70.1 | 70.1 | 69.7 | 69.8 |
| 1″ | 105.5 | 105.5 | 105.5 | 105.6 |
| 2″ | 75.0 | 75.0 | 74.9 | 74.9 |
| 3″ | 77.6 | 77.6 | 77.7 | 77.7 |
| 4″ | 71.2 | 71.2 | 71.2 | 71.2 |
| 5″ | 66.9 | 66.9 | 66.9 | 66.9 |

D-xyloglucosyl(1 → 6)-β-D-glucopyranoside. As alangicadinosides A–E with a cadinane skeleton have been isolated from the leaves of this plant [6], compound **4** was named alangicadinoside F.

Alangicadinoside G (**5**), $[\alpha]_D$ −64.7°, was obtained as an amorphous powder and its elemental composition analyzed by HR-FAB-MS was the same as that of alangicadinoside F (**4**). Other spectroscopic data were essentially similar to those for **4**. Thus, **5** had the same planar structure as **4**, but some of the absolute configurations at the three chiral centres were different. Since the Cotton effects observed in the CD spectra of **4** and **5** were similar in the longer wave range [243 (−3.81 and −3.21, respectively), 248 (0, both) and 278 (−2.62 and −2.07, respectively) nm ($\Delta\varepsilon$)], they must be diastereomers formed on oxidation of one of the two prochiral methyl groups at the C-11 position of a common precursor.

Alangicadinoside H (**6**), $[\alpha]_D$ −33.6°, was obtained as a pale yellow amorphous powder. Its elemental composition was determined to be $C_{27}H_{42}O_{12}$, which was 14 amu greater compared to langicadinosides G (**4**) and H (**5**). The $^{13}C$ and $^1H$ NMR spectra indicated that **6** was an analogous compound to **4** and **5**, and a methoxyl signal ($\delta_C$ 60.7 and $\delta_H$ 3.70, respectively) was observed as a new functional group. While the same sugar moiety as that found in **4** and **5** was present in the molecule, the position was expected to be on the alcoholic hydroxyl group at the 13-position, since the C-13 carbon signal appeared at a lower field ($\delta_C$ 74.6) than those of **4** ($\delta_C$ 66.4) and **5** ($\delta_C$ 66.9) due to a glycosylation-induced downfield shift. The position of the methoxyl group was determined in the difference NOE experiments. On irradiation of the aromatic methyl protons ($\delta_H$ 2.21), significant NOEs were detected for both the methoxy methyl protons and the aromatic proton ($\delta_H$ 6.58), and vice versa. NOE correlations between the aromatic proton and the aromatic methyl, and the C-7 and C-11 protons confirmed that **6** had a cadinane backbone. Therefore, the structure of alangicadinoside H is that presented as **6** by formula.

Alangicadinoside I (**7**), $[\alpha]_D$ −66.8°, was also obtained as a pale yellow powder. Its molecular formula was the same as that of **6**, and its NMR spectroscopic properties were similar to those of **6** cf. **4** and **5**. As **7** had essentially the same CD spectrum as that of **6** this led to the conclusion that **7** is a diastereomer of **6**, probably at the C-11 position.

Alangisesquin A (**8**), $[\alpha]_D$ −29.0°, was obtained as a pale yellow amorphous powder, whose elemental composition was determined to be $C_{37}H_{46}O_{16}$ by HR-FAB mass spectrometry. The IR (1590 and 1490 $cm^{-1}$) and UV (224 and 276 nm) spectra indicated the presence of aromatic rings. The $^{13}C$ and $^1H$ NMR spectra showed the presence of one aromatic ring with three protons coupled in an ABX system, and two aromatic rings with two protons each which were located at *meta* sites relative to each other. The presence of a β-glucopyranose moiety was confirmed by the $^{13}C$ NMR spectrum, a *trans* double bond by the $^1H$ NMR spectrum [$\delta_H$ 6.53 (*d*, $J$ = 16 Hz) and 6.22 (*dd*, $J$ = 6, 16 Hz)], and four methoxyl groups by $\delta_C$ 56.4, 56.8 × 2 and 56.9. The $^{13}C$ NMR signals at $\delta_C$ 61.7 (*t*) [$\delta_H$ 3.75 (*dd*, $J$ = 3, 12 Hz)], 87.4 (*d*) [$\delta_H$ 4.24 (*dd*, $J$ = 3, 5 Hz)] and 74.1 (*d*) [$\delta_H$ 4.90 (*d*, $J$ = 5 Hz)], and 61.7 (*t*) [$\delta$ 3.57 (*dd*, $J$ = 3, 12 Hz)] were indicative of a glycerol moiety like C-7″–C-9″, and $\delta_C$ 89.1 (*d*) [$\delta_H$ 5.69 (*d*, $J$ = 6 Hz)] and 53.3 (*d*) [$\delta_H$ 3.66 (*m*)] indicated a part of a neolignan with a benzofuran ring. The above evidence and the fact that the number of $^{13}C$ NMR signals was 27 implied that **8** was a β-glucopyranoside of a sesquilignan, such as buddlenol B, which was previously isolated from *Buddleja davidii* [7]. The H—H and C—H COSY spectra enabled us to correlate the protons on the carbons of three $C_3$ units, and the secondary alcohol, whose carbon signal appeared at the lowest field ($\delta_C$ 72.5), was expected to carry the glucose residue. This was confirmed by the observation of a cross peak between the aromatic proton and the 9′-position in the C—H long-range COSY ($J$ = 7 Hz) spectrum (Fig. 2). The long-range correlation also indicated that aromatic ring B has two methoxyl groups, which is the same as in the case of buddlenol B.

The ether linkage between the C-4′-position and the

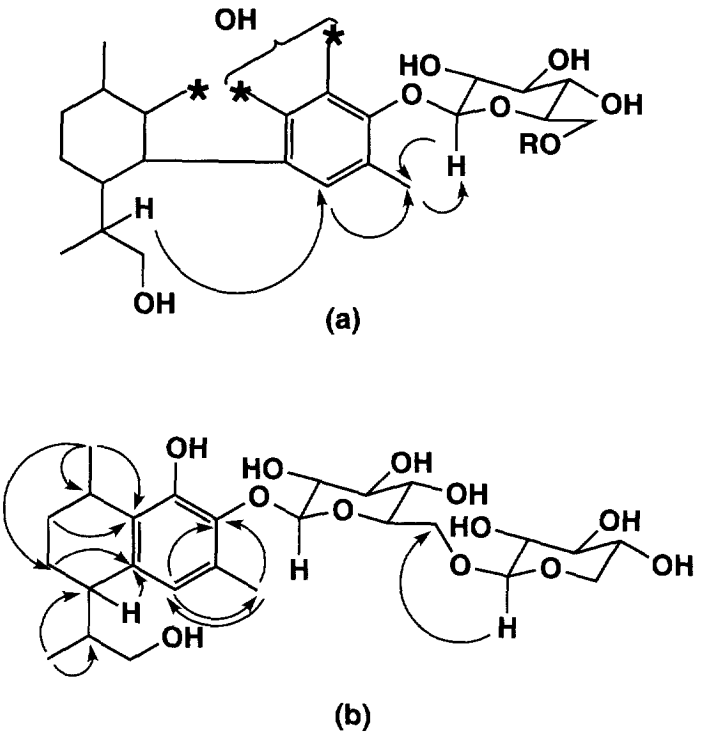



Fig. 1. NOE and C—H long-range correlations for alangicadinoside F (**4**). (a) NOE correlations were acquired by the difference NOE experiments. (b) Selected C—H long-range correlations ($J$ = 7 Hz). Arrowheads denote carbons and arrow tails denote protons.

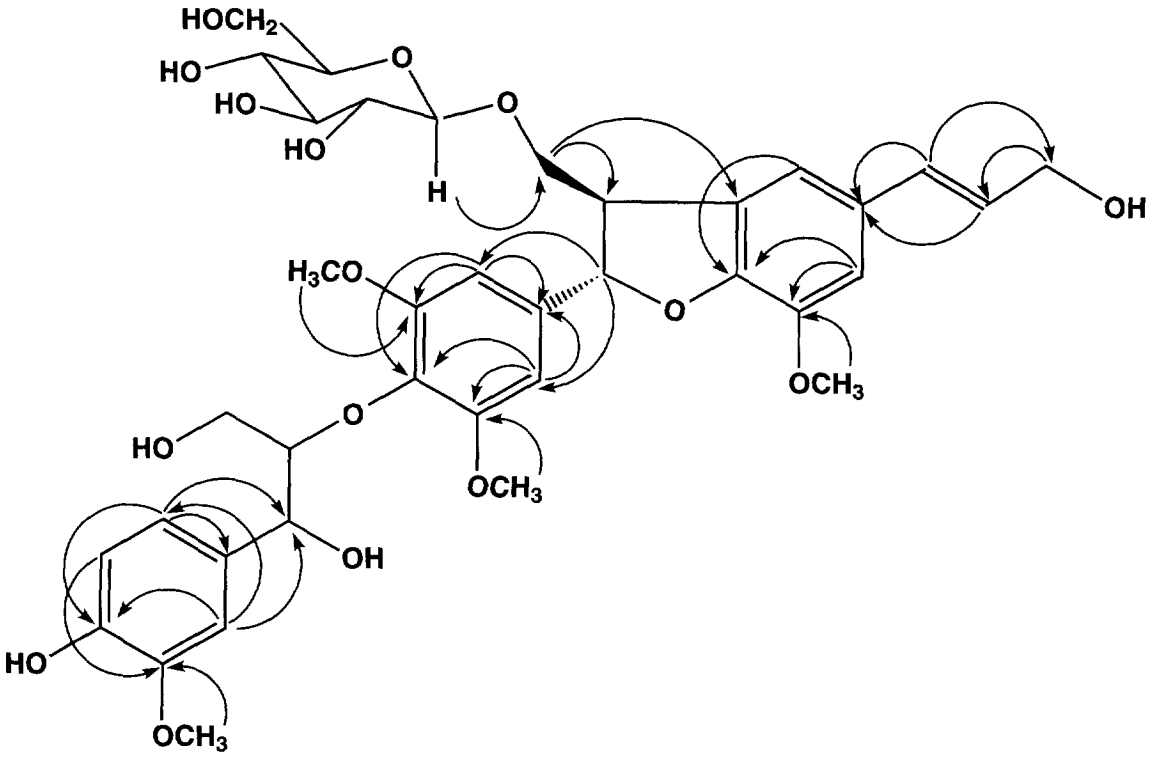



Fig. 2. Diagnostic C—H long-range correlations of alangisesquin A (**8**) ($J$ = 7 Hz).

glycerol moiety was expected to be at the C-8-position from its chemical shift ($\delta_C$ 87.4), and this was confirmed by acetylation of **8**, which induced low field shifts of the protons at C-7 ($\delta_H$ 4.24 → 6.06) and C-9 ($\delta_H$ 3.57 → 4.46), while the C-8 proton remained almost unchanged [$\delta_H$ 4.42 ($CD_3OD$) → 4.58 ($CDCl_3$)] in the $^1H$ NMR spectrum. The $^1H$ NMR spectrum of the octaacetate (**8a**) showed that the rotation of the C-8—O—C-4′ axis was restricted, showing that some proton signals around these positions appeared with satellite signals. The absolute configurations at the C-7′ and C-8′ position, were considered to be *S* and *R*, respectively, as the CD spectrum showed a negative Cotton effect at 273 nm [8]. Therefore, the structure of alangisesquin A was determined to be as shown in formula **8**.

Alangisesquin B (**9**), $[\alpha]_D$ −14.5°, was obtained as a pale yellow amorphous powder. The spectroscopic properties indicated the same planar structure for **9** as that of **8**. However, the $R_f$s of **8** and **9** were obviously different on HPLC (41 and 55 min, respectively), and the proton coupling constant between H-7 and H-8 was 5 Hz in **8**, but 7 Hz in **9**. These findings and the similarity of the CD spectrum to that of **8** suggested that **8** and **9** were isomers at the C-7 and C-8 positions. It has been reported that in the cases of syringoylglycerols (**12**) and guaiacylglycerol derivatives like **13** the erythro isomer is eluted faster than the threo isomer on reversed-phase HPLC [9], and that the coupling constant between H-7 and 8 of **13** was about 5 Hz for the erythro isomer and 7 Hz for the threo isomer [10]. Thus, alangisesquin A is considered to be the erythro isomer and alangisesquin B the threo isomer with respect to the glycerol moiety.

Alangisesquins C (**10**), $[\alpha]_D$ −8.7°, and D (**11**), $[\alpha]_D$ −3.2°, were expected to be similar compounds to **8** and **9** from their spectroscopic data. In the $^{13}C$ NMR spectra of **10** and **11**, *trans* double bonds, which were seen for **8** and **9**, were reduced to single bonds [e.g. $\delta_C$ 127.9 (*d*) and 131.9 (*d*) in **8** to 32.9 (*t*) and 35.8 (*t*) in **10**]. Therefore, alangisesquins C (**10**) and D (**11**) were the 7″,8″-dihydroalangisesquins A and B. On catalytic hydrogenation, alangisesquin A (**8**) gave a reduced compound, which was identical with alangisesquin C (**10**) in all spectroscopic properties.

Table 2. $^{13}C$ NMR data for alangisesquins A–D (**8**–**11**) ($CD_3OD$, 100 MHz)

| C | **8** | **9** | **10** | **11** |
|---|---|---|---|---|
| 1 | 133.8 | 133.5 | 133.8 | 133.5 |
| 2 | 111.5 | 111.7 | 111.5 | 111.7 |
| 3 | 148.7 | 148.8 | 148.7 | 148.8 |
| 4 | 146.9 | 147.2 | 146.9 | 147.2 |
| 5 | 115.7 | 115.9 | 115.7 | 115.9 |
| 6 | 120.7 | 120.9 | 120.7 | 120.9 |
| 7 | 74.1 | 74.5 | 74.1 | 74.5 |
| 8 | 87.4 | 88.9 | 87.4 | 89.0 |
| 9 | 61.7 | 61.9 | 61.7 | 61.7 |
| 1′ | 136.4 | 136.9 | 136.3 | 136.8 |
| 2′ | 104.1 | 104.0 | 104.2 | 104.1 |
| 3′ | 154.6 | 154.4 | 154.6 | 154.3 |
| 4′ | 139.5 | 139.7 | 139.7 | 139.9 |
| 5′ | 154.6 | 154.4 | 154.6 | 154.3 |
| 6′ | 104.1 | 104.0 | 104.2 | 104.1 |
| 7′ | 89.1 | 89.1 | 88.8 | 88.8 |
| 8′ | 53.3 | 53.4 | 53.6 | 53.7 |
| 9′ | 72.5 | 72.5 | 72.7 | 72.6 |
| 1″ | 132.9 | 132.9 | 137.2 | 137.3 |
| 2″ | 112.4 | 112.4 | 114.4 | 114.4 |
| 3″ | 145.6 | 145.6 | 145.3 | 145.3 |
| 4″ | 149.2 | 149.2 | 147.5 | 147.5 |
| 5″ | 129.7 | 129.6 | 129.2 | 129.2 |
| 6″ | 116.8 | 116.8 | 118.2 | 118.2 |
| 7″ | 131.9 | 131.9 | 32.9 | 32.9 |
| 8″ | 127.9 | 127.9 | 35.8 | 35.8 |
| 9″ | 63.9 | 63.9 | 62.8 | 62.3 |
| Glucose | | | | |
| 1 | 104.6 | 104.6 | 104.6 | 104.6 |
| 2 | 75.3 | 75.3 | 75.3 | 75.3 |
| 3 | 78.4 | 78.4 | 78.4 | 78.4 |
| 4 | 71.7 | 71.7 | 71.7 | 71.7 |
| 5 | 78.1 | 78.1 | 78.1 | 78.2 |
| 6 | 62.9 | 62.9 | 62.9 | 62.9 |
| 3-O$\underline{C}H_3$ | 56.4 | 56.4 | 56.4 | 56.4 |
| 3′-O$\underline{C}H_3$ | 56.8 | 56.8 | 56.8 | 56.8 |
| 5′-O$\underline{C}H_3$ | 56.8 | 56.8 | 56.8 | 56.8 |
| 3″-O$\underline{C}H_3$ | 56.9 | 56.9 | 56.9 | 56.9 |

## EXPERIMENTAL

### *General*

$^1H$ NMR and $^{13}C$ NMR: 400 MHz and 100 MHz, respectively; EI-MS: 70 eV; Highly porous synthetic resin: Diaion HP-20 CC ($\phi$ = 60 mm, $L$ = 60 cm, fractions of 1 l being collected). The DCCC was equipped with 500 columns ($\phi$ = 2 mm, $L$ = 40 cm). The ascending method was used with $CHCl_3$–MeOH–$H_2O$–*n*-PrOH (9:12:8:2), and 5 g fractions were collected and numbered according to the elution of the mobile phase. Reversed-phase gravity CC (RPCC) was performed with Cosmosil 75$C_{18}$-OPN ($\phi$ = 40 mm, $L$ = 25 cm, fractions of 10 g being collected). Prep. HPLC was performed with Inertsil ($\phi$ = 20 mm, $L$ = 200 mm), the flow rate and detection wavelength being 6 ml $min^{-1}$ and 254 nm, respectively at 25°.

### *Plant material*

Stems of *A. premnifolium* were collected in Okinawa island in 1990. The plant was identified by one (A.T.) of the authors and a voucher specimen was deposited in the Herbarium of the Institute of Pharmaceutical Sciences, Hiroshima University School of Medicine.

*Extraction and isolation*

Powdered stems of *A. premnifolium* (12.8 kg) were extracted with MeOH (45 l) three times at about 20°. The MeOH extract was concentrated to 1.5 l and, after the addition of 75 ml of $H_2O$, extracted with 1.5 l of *n*-hexane (44.7 g). The methanolic layer was evaporated to leave a black mass, which was suspended in 1.5 l of $H_2O$ and extracted with 1.5 l of EtOAc (49.6 g) and then with *n*-BuOH (1.5 l × 2) (106 g).

The residue (105 g) of the *n*-BuOH layer was subjected to Diaion HP-20 CC with 20% (8 l), 40% (12 l), 60% (12 l), and 80% (14 l) MeOH in $H_2O$. The residue of the 20% MeOH eluate (14.7 g, frs 5–10) was subjected to silica gel CC ($CHCl_3$–$CHCl_3$–MeOH), and the residue of the 10% MeOH eluate on silica gel CC (1.32 g) was purified by RPCC [MeOH–$H_2O$ (1:9, 1 l)–(1:1, 1 l)]. The residue of frs 60–65 (188 mg) was further purified by DCCC to give 41 mg of **1** in frs 31–37 as crystals. Compound **3** (473 mg) was obtained in a similar manner to **1** from the residue of the 20% MeOH eluate on silica gel CC (2.23 g).

The residue of the 40% MeOH eluate on Diaion HP-20 CC (8.46 g, frs 13–15) was separated by silica gel CC (1.04 g in the residue of the 12% MeOH in $CHCl_3$ eluate), followed by RPCC (390 mg in frs 150–156). Purification by DCCC (314 mg in frs 29–39), prep. HPLC [30 mg, 41.8 min with MeOH–$H_2O$ (3:7)] and prep. TLC [silica gel, Merck, 0.5 mm thickness, 20 cm × 20 cm, developed with $CHCl_3$–MeOH–$H_2O$ (15:6:1), eluted with $CHCl_3$–MeOH (4:1)] gave 10 mg of **2**.

The residue of the 60% MeOH eluate on Diaion HP-20 CC (30.8 g in frs 16–22) was subjected to silica gel CC with $CHCl_3$–MeOH with increasing MeOH contents. The residue of the 8% MeOH eluate (3.64 g) was separated by RPCC [MeOH–$H_2O$ (1:9, 1 l)–(7:3, 1 l)]. Fractions 131–133 (240 mg) were purified by DCCC to concentrate compounds **8** and **10** in frs 123–151 (106 mg), and compounds **9** and **11** in frs 152–182 (55 mg). These fractions were finally purified by prep. HPLC [MeOH–$H_2O$ (2:3) to give 39 mg of **8** (*R*t 41 min), 32 mg of **10** (*R*t 45 min), 3.2 mg of **9** (*R*t 55 min), and 6.2 mg of **11** (*R*t 60 min). RPCC frs 156–161 (31 mg) and 169–171 (21 mg) were purified by Sephadex LH-20 CC ($\phi$ = 20 mm, $L$ = 130 cm, MeOH, frs of 7 g being collected) to give 13 mg of **7** in frs 40–42 and 10 mg of **6** in frs 68–71, respectively. A portion (2.11 g) of the residue of the 10–12% MeOH elute on silica gel CC (2.695 g) was separated by RPCC [MeOH–$H_2O$ (1:9, 1 l)–(7:3, 1 l)] to give compound **5** (82 mg in frs 167–171) and **4** (51 mg in frs 174–179) enriched fractions, and then pure **5** (51 mg) and **4** (31 mg) were obtained by DCCC in frs 39–44 and 43–46, respectively.

*Known compounds isolated*

Salicin (**1**), colourless needles, mp 198–201° (MeOH), $[\alpha]_D^{22}$ −46.8° (MeOH, *c* 1.09), was identified by comparison with a commercially available authentic sample. Henryoside (**2**), colourless needles, mp 142° (MeOH), $[\alpha]_D^{22}$ −22.6° (MeOH, *c* 0.44) [3]. Loganic acid (**3**), an amorphous powder, $[\alpha]_D^{22}$ −74.2° (MeOH, *c* 0.89) [3].

*Alangicadinoside F* (**4**). Pale yellow powder, $[\alpha]_D^{25}$ −67.0° (MeOH, *c* 0.93). IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3300, 2900, 1610, 1490, 1460, 1425, 1365, 1320, 1220, 1165, 1035; UV $\lambda_{max}^{MeOH}$ nm (log ε): 223 (4.11), 280 (3.43); $^1H$ NMR ($CD_3OD$): δ 0.96 (3H, *d*, *J* = 7 Hz, $H_3$-13), 1.15 (3H, *d*, *J* = 7 Hz, $H_3$-15), 1.48 (H, *m*, H-9a), 1.71 (H, *m*, H-8a), 1.79 (H, *m*, H-9b), 1.87 (H, *m*, H-8b), 1.93 (H, *m*, H-11), 2.29 (3H, *s*, $H_3$-14), 2.62 (H, *dt*, *J* = 3, 6 Hz, H-7), 3.09 (H, *m*, H-10), 3.19 (H, *dd*, *J* = 10, 11 Hz, H-5″a), 3.24 (H, *dd*, *J* = 7, 9 Hz, H-2″), 3.32 and 3.43 (2H, overlapped by the sugar ring protons, $H_2$-12), 3.50 (H, *dd*, *J* = 8, 9 Hz, H-8, 9 Hz, H-2′), 3.78 (H, *dd*, *J* = 5, 11 Hz, H-6′a), 3.86 (H, *dd*, *J* = 5, 11 Hz, H-5″b), 4.08 (H, *dd*, *J* = 2, 11 Hz, H-6′b), 4.27 (H, *d*, *J* = 7 Hz, H-1″), 4.45 (H, *d*, *J* = 8 Hz, H-1′), 6.47 (H, *s*, H-5); $^{13}C$ NMR ($CD_3OD$): see Table 1; CD (MeOH, *c* 0.00463) Δε (λ nm): +0.24 (214), −3.81 (234), 0 (248); HR-FAB-MS (negative centroid) *m/z*: 543.2416 $[M-H]^-$ ($C_{26}H_{39}O_{12}$ requires 543.2441).

*Alangicadinoside G* (**5**). Pale yellow powder, $[\alpha]_D^{26}$ −64.7° (MeOH, *c* 0.91). UV $\lambda_{max}^{MeOH}$ nm (log ε): 223 (4.18), 279 (3.58); $^1H$ NMR ($CD_3OD$): δ 0.79 (3H, *d*, *J* = 7 Hz, $H_3$-13), 1.16 (3H, *d*, *J* = 7 Hz, $H_3$-15), 1.48 (H, *m*, H-9a), 1.69 (H, *m*, H-8a), 1.82 (H, *m*, H-9b), 1.90 (H, *m*, H-8b), 1.99 (H, *m*, H-11), 2.29 (3H, *s*, $H_3$-14), 2.76 (H, *dt*, *J* = 2, 5 Hz, H-7), 3.13 (H, *m*, H-10), 3.20 (H, *dd*, *J* = 10, 11 Hz, H-5″a), 3.25 (H, *dd*, *J* = 7, 9 Hz, H-2″), 3.78 (H, *dd*, *J* = 5, 11 Hz, H-6′a), 3.87 (H, *dd*, *J* = 5, 11 Hz, H-5″b), 4.09 (H, *dd*, *J* = 2, 11 Hz, H-6′b), 4.28 (H, *d*, *J* = 7 Hz, H-1″), 4.46 (H, *d*, *J* = 8 Hz, H-1′), 6.50 (H, *s*, H-5); $^{13}C$ NMR ($CD_3OD$): see Table 1; CD (MeOH, *c* 0.00456) Δε (λ nm): −2.44 (210), −0.99 (219), −3.21 (234), 0 (248), −2.07 (278); HR-FAB-MS (negative centroid) *m/z*: 543.2426 $[M-H]^-$ ($C_{26}H_{39}O_{12}$ requires 543.2441).

*Alangicadinoside H* (**6**). Pale yellow powder, $[\alpha]_D^{26}$ −66.8° (MeOH, *c* 0.60). UV $\lambda_{max}^{MeOH}$ nm (log ε): 224 *sh* (4.06), 279 (3.35); $^1H$ NMR ($CD_3OD$): δ 0.99 (3H, *d*, *J* = 7 Hz, $H_3$-13), 1.15 (3H, *d*, *J* = 7 Hz, $H_3$-15), 1.49 (H, *m*, H-9a), 1.74–1.90 (3H, *m*, H-8a, 8b and 9b), 2.13 (H, *m*, H-11), 2.20 (3H, *s*, $H_3$-14), 2.64 (H, *m*, H-7), 3.15 (H, *m*, H-10), 3.15 (H, *dd*, *J* = 9, 12 Hz, H-5″a), 3.69 (3H, *s*, $C\underline{H}_3$-), 3.69 (H, overlapped by the methoxyl signal, H-12b), 3.73 (H, *dd*, *J* = 5, 11 Hz, H-6′a), 3.85 (H, *dd*, *J* = 5, 12 Hz, H-5″b), 4.03 (H, *br d*, *J* = 12 Hz, H-6′b), 4.13 (H, *d*, *J* = 8 Hz, H-1′), 4.32 (H, *d*, *J* = 8 Hz, H-1″), 6.48 (H, *s*, H-5); $^{13}C$ NMR ($CD_3OD$): see Table 1; CD (MeOH, *c* 0.00299) Δε (λ nm): −3.39 (235), −0.15 (251), −2.06 (279); HR-FAB-MS (negative centroid) *m/z*: 557.2596 $[M-H]^-$ ($C_{27}H_{41}O_{12}$ requires 557.2598).

*Alangicadinoside I* (**7**). Pale yellow powder, $[\alpha]_D^{26}$ −33.6° (MeOH, *c* 0.92). UV $\lambda_{max}^{MeOH}$ nm (log ε): 224 *sh* (4.11), 279 (3.72); $^1H$ NMR ($CD_3OD$): δ 0.82 (3H, *d*, *J* = 7 Hz, $H_3$-13), 1.16 (3H, *d*, *J* = 7 Hz, $H_3$-15), 1.48

(H, *m*, H-9a), 1.70 (H, *m*, H-8a), 1.82 (H, *m*, H-8b), 1.90 (H, *m*, H-9b), 2.17 (H, *dd* $J = 6$, 13 Hz, H-11), 2.21 (3H, *s*, $H_3$-14), 2.86 (H, *m*, H-7), 3.13 (H, *m*, H-10), 3.19 (H, *dd*, $J = 10$, 12 Hz, H-5″a), 3.45 (H, overlapped by the sugar ring protons, H-12a), 3.70 (3H, *s*, $C\underline{H}_3O$-), 3.75 (H, *dd*, $J = 5$, 12 Hz, H-6′a), 3.86 (H, *dd*, $J = 5$″b), 3.90 (H, *dd*, $J = 7$, 10 Hz, H-12b), 4.08 (H, *dd*, $J = 2$, 12 Hz, H-6′b), 4.27 (H, *d*, $J = 8$ Hz, H-1′), 4.34 (H, *d*, $J = 7$ Hz, H-1″), 6.57 (H, *s*, H-5); $^{13}$C NMR ($CD_3OD$): see Table 1; CD (MeOH, *c* 0.00451) $\Delta\varepsilon$ ($\lambda$ nm): −2.96 (235), −0.15 (250), −1.73 (279); HR-FAB-MS (negative centroid) *m/z*: 557.2601 $[M-H]^-$ ($C_{27}H_{41}O_{12}$ requires 557.2598).

*Alangisesquin A* (**8**). White powder, $[\alpha]_D^{24}$ −29.0° (MeOH, *c* 0.90). IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3300, 2850, 1590, 1490, 1450, 1410, 1320, 1221, 1121; UV $\lambda_{max}^{MeOH}$ nm (log $\varepsilon$): 224 *sh* (4.60), 276 (4.26), 284 *sh* (4.16); $^1$H NMR ($CD_3OD$): $\delta$ 3.24 (H, *dd*, $J = 8$, 9 Hz, H-G-2), 3.57 (H, *dd*, $J = 3$, 12 Hz, H-9a), 3.66 (2H, *m*, H-8′ and G-6a), 3.78 (6H, *s*, $C\underline{H}_3O$- on C-3′ and 5′), 3.79 (H, overlapped by the methoxyl signals, H-9′a), 3.81 (6H, *s*, $C\underline{H}_3O$- on C-3 and 3″), 3.88 (2H, *m*, H-9b and G-6b), 4.19 (2H, *dd*, $J = 1$, 6 Hz, $H_2$-9″), 4.24 (H, *dt*, $J = 3$, 5 Hz, H-8), 4.26 (H, *dd*, $J = 5$, 9 Hz, H-9′b), 4.39 (H, *d*, $J = 8$ Hz, H-G-1), 4.90 (H, *d*, $J = 5$ Hz, H-7), 5.69 (H, *d*, $J = 6$ Hz, H-7′), 6.22 (H, *td*, $J = 6$, 16 Hz, H-8″), 6.53 (H, *br d*, $J = 16$ Hz, H-7″), 6.72 (H, *d*, $J = 8$ Hz, H-5), 6.75 (2H, *s*, H-2′ and 6′), 6.78 (H, *dd*, $J = 2$, 8 Hz, H-6), 6.94 (H, *br s*, H-2″), 6.95 (H, *d*, $J = 2$ Hz, H-2), 7.00 (H, *br s*, H-6″); $^{13}$C NMR ($CD_3OD$): see Table 2; CD (MeOH, *c* 0.00123) $\Delta\varepsilon$ ($\lambda$ nm): +0.16 (215), −3.53 (219), 0 (225) +7.42 (238), 0 (252), −5.48 (273); HR-FAB-MS (negative centroid) *m/z*: 745.2748 $[M-H]^-$ ($C_{37}H_{45}O_{16}$ requires 745.2708).

*Alangisesquin B* (**9**). White powder, $[\alpha]_D^{24}$ −14.3° (MeOH, *c* 0.21). UV $\lambda_{max}^{MeOH}$ nm (log $\varepsilon$): 225 *sh* (4.45), 275 (4.09), 284 *sh* (4.02); $^1$H NMR ($CD_3OD$): $\delta$ 3.24 (H, *dd*, $J = 8$, 9 Hz, H-G-2), 3.35 (H, in the solvent signals, H-9a), 3.66 (2H, *m*, H-8′ and G-6a), 3.75 (overlapped by the methoxyl signals, H-9b), 3.81 (3H, *s*, $C\underline{H}_3O$- on C-3), 3.84 (6H, *s*, $C\underline{H}_3O$- on C-3′ and 5′), 3.87 (2H, overlapped by the methoxyl signals, H-9′a and G-6b), 3.90 (3H, *s*, $C\underline{H}_3O$- on C-3″), 4.08 (H, *dt*, $J = 3$, 6 Hz, H-8), 4.20 (2H, *dd*, $J = 1$, 6 Hz, $H_2$-9″), 4.27 (H, *dd*, $J = 5$, 10 Hz, H-9′b), 4.39 (H, *d*, $J = 8$ Hz, H-G-1), 4.97 (H, *d*, $J = 7$ Hz, H-7), 5.71 (H, *d*, $J = 6$ Hz, H-7′), 6.23 (H, *td*, $J = 6$, 16 Hz, H-8″), 6.54 (H, *br d*, $J = 16$ Hz, H-7″), 6.73 (H, *d*, $J = 8$ Hz, H-5), 6.77 (2H, *s*, H-2′ and 6′), 6.85 (H, *dd*, $J = 2$, 8 Hz, H-6), 6.96 (H, *br s*, H-2″), 6.99 (H, *br s*, H-6″), 7.00 (H, *br s*, H-2); $^{13}$C NMR ($CD_3OD$): see Table 2; CD (MeOH, *c* 0.00105) $\Delta\varepsilon$ ($\lambda$ nm): −0.06 (214), −2.59 (218), 0 (224), +4.90 (237), 0 (251), −3.23 (273); HR-FAB-MS (negative centroid) *m/z*: 745.2723 $[M-H]^-$ ($C_{37}H_{45}O_{16}$ requires 745.2708).

*Alangisesquin C* (**10**). White powder, $[\alpha]_D^{24}$ −8.7° (MeOH, *c* 0.63). IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3300, 2850, 1590, 1490, 1455, 1420, 1325, 1270, 1215, 1121, 1020; UV $\lambda_{max}^{MeOH}$ nm (log $\varepsilon$): 228 (4.34), 281 (3.77); $^1$H NMR ($CD_3OD$): $\delta$ 1.80 (2H, *m*, $H_2$-8″), 2.61 (2H, *dd*, $J = 7$, 8 Hz, $H_2$-7″), 3.24 (H, *dd*, $J = 8$, 9 Hz, H-G-2), 3.55 (2H, *br t*, $J = 6$ Hz, $H_2$-9″), 3.58 (H, overlapped by the sugar ring signals, H-9a), 3.65 (2H, *m*, H-8′ and G-6a), 3.75 (H, overlapped by the methoxyl signals, H-9′a), 3.78 (6H, *s*, $C\underline{H}_3O$- on C-3′ and 5′), 3.81 (6H, *s*, $C\underline{H}_3O$- on C-3 and 3″), 3.86 (H, overlapped by the methoxyl signals, H-G-6b), 3.89 (H, in the envelopes of the methoxyl signals, H-9b), 4.23 (H, *dt*, $J = 3$, 5 Hz, H-8), 4.25 (H, *dd*, $J = 5$, 8 Hz, H-9′b), 4.38 (H, *d*, $J = 8$ Hz, H-G-1), 4.90 (H, *d*, $J = 5$ Hz, H-7), 5.66 (H, *d*, $J = 6$ Hz, H-7′), 6.73 (H, *br s*, H-2″), 6.73 (H, *d*, $J = 8$ Hz, H-5), 6.76 (3H, *s*, H-2′, 6′ and 6″), 6.78 (H, *dd*, $J = 2$, 8 Hz, H-6), 6.96 (H, *br s*, H-2); $^{13}$C NMR ($CD_3OD$): see Table 2; CD (MeOH, *c* 0.00126) $\Delta\varepsilon$ ($\lambda$ nm): +8.7 (207), −4.29 (216), +0.17 (225), −0.16 (232), +1.58 (244), −0.69 (292); HR-FAB-MS (negative centroid) *m/z*: 747.2873 $[M-H]^-$ ($C_{37}H_{47}O_{16}$ requires 747.2864).

*Alangisesquin D* (**11**). White powder, $[\alpha]_D^{24}$ −3.2° (MeOH, *c* 0.41). UV $\lambda_{max}^{MeOH}$ nm (log $\varepsilon$): 229 (4.33), 280 (3.75); $^1$H NMR ($CD_3OD$): $\delta$ 1.80 (2H, *m*, $H_2$-8″), 2.62 (2H, *t*, $J = 8$ Hz, $H_2$-9″), 3.24 (H, *dd*, $J = 8$, 9 Hz, H-G-2), 3.34 (H, overlapped by the solvent signal, H-9a), 3.56 (2H, *t*, $J = 6$ Hz, $H_2$-9″), 3.65 (2H, *m*, H-8′ and G-6a), 3.75 (H, in the envelopes of the methoxyl signals, H-9b), 3.81 (3H, *s*, $C\underline{H}_3O$- on C-3), 3.83 (6H, *s*, $C\underline{H}_3O$- on C-3′ and 5′), 3.86 (H, overlapped by the methoxyl signals, H-G-6b), 3.87 (3H, *s*, $C\underline{H}_3O$- on C-3″), 3.87 (H, overlapped by the methoxyl signals, H-9′a), 4.06 (H, *dt*, $J = 3$, 7 Hz, H-8), 4.26 (H, *dd*, $J = 5$, 10 Hz, H-9′b), 4.38 (H, *d*, $J = 8$ Hz, H-G-1), 4.97 (H, *d*, $J = 7$ Hz, H-7), 5.68 (H, *d*, $J = 6$ Hz, H-7′), 6.73 (H, *br s*, H-2″), 6.73 (H, *d*, $J = 8$ Hz, H-5), 6.75 (H, *br s*, H-6″), 6.77 (2H, *s*, H-2′ and 6′), 6.85 (H, *dd*, $J = 2$, 8 Hz, H-6), 6.99 (H, *br s*, H-2); $^{13}$C NMR ($CD_3OD$): see Table 2; CD (MeOH, *c* 0.00816) $\Delta\varepsilon$ ($\lambda$ nm): −3.57 (215), 0 (220), +1.56 (227), +0.90 (239), +0.94 (243), +0.81 (250), +1.06 (262), −0.19 (290); HR-FAB-MS (negative centroid) *m/z*: 747.2836 $[M-H]^-$ ($C_{37}H_{47}H_{16}$ requires 747.2864).

*Alangisesquin A octaacetate* (**8a**). Alangisesquin A (**8**) (about 3 mg) was acetylated with a mixture of $Ac_2O$ (50 $\mu$) and pyridine (50 $\mu$) for 18 h at 20°. The reaction mixture was evaporated under a stream of $N_2$ and then purified by prep. TLC [Merck precoated silica gel $F_{254}$, 0.25 mm thickness, 4 cm × 9 cm, developed with $C_6H_6$–$Me_2CO$ (4:1), eluted with $CHCl_3$–MeOH (9:1)]. Amorphous powder, $^1$H NMR ($CDCl_3$): $\delta$ 1.903 and 1.908 (major) (3H, both *s*), 1.956 and 1.962 (major) (3H, both *s*) ($C\underline{H}_3CO$- on C-7-O and 9-O), 2.00, 2.03, 2.089, 2.093, 2.13 (each 3H, each *s*, $C\underline{H}_3CO$- ×5 on alcoholic hydroxyl groups), 2.29 (3H, *s*, on a phenolic hydroxyl group), ~3.62 (2H, *m*, H-8′ and 9a), ~3.66 (H, *m*, H-G-5), 3.79 and 3.80 (major) (3H, both *s*, $C\underline{H}_3O$- on C-3), 3.72 (6H, *s*, $C\underline{H}_3CO$- ×2 on C-3′ and 5′), 3.92 (3H, *s*, $C\underline{H}_3O$- on C-3″), 4.14 (H, *dd*, $J = 2$, 12 Hz, H-G-6a), 4.18–4.25 (2H, *m*, H-9b and 9′b), 4.30 (H, *dd*, $J = 4$, 12 Hz, H-G-6b), 4.46 (major) and 4.50 (H, both *dd*, $J = 6$, 12

Hz, H-9b), 4.53 (H, *d*, $J = 8$ Hz, H-G-1), 4.58 (H, *dt*, $J = 4$, 5 Hz, H-8), 4.70 (2H, *dd*, $J = 1$, 6 Hz, H-9″), 5.07 (H, *dd*, $J = 8$, 10 Hz, H-G-2), 5.11 (H, *t*, $J = 10$ Hz, H-G-4), 5.21 (H, *t*, $J = 10$ Hz, H-3), 5.53 (H, *br d*, $J = 4$ Hz, H-7′), 6.067 (major) and 6.073 (H, both *d*, $J = 5$ Hz, H-7), 6.15 (H, *td*, $J = 6$, 16 Hz, H-8″), 6.56 (2H, *s*, H-2′ and 6′), 6.58 (H, *d*, $J = 16$ Hz, H-7″), 6.84 and 6.87 (each H, both *br s*, H-2″ and 6″), 6.90 (major) and 6.91 (H, both *dd*, H-2, 8 Hz, H-6), 6.97 (H, *d*, $J = 8$ Hz, H-5), 6.99 (major) and 7.00 (H, both *d*, $J = 2$ Hz, H-2); FAB-MS (*m*-nitrobenzyl alcohol) *m/z*: 1083 $[M+H]^+$, 1105 $[M+Na]^+$ (+NaI), 1121 $[M+K]^+$ (+KI); EI-MS *m/z*: (rel. int.): 1082 $[M]^+$ (1.8), 802 (38), 412 (17), 331 $[Glu(OAc)_4$ oxonium ion$]^+$ (9), 222 (61), 179 (38), 169 (26), 131 (70), 60 (100).

*Catalytic reduction of* **8** *to alangisesquin C* (**10**). An ethanolic soln (10 ml) of **8** (7.0 mg) was reduced with 2 mg of $PtO_2$ and $H_2$ for 3 h. The catalyst was filtered off and then the filtrate was concentrated to give the reduced compound (5.0 mg). Amorphous powder, UV $\lambda_{max}^{MeOH}$ nm (log $\varepsilon$): 228 *sh* (4.21), 280 (3.58); $^1$H NMR ($CD_3OD$): essentially the same as those of alangisesquin C (**10**); CD (MeOH, *c* 0.00167) $\Delta\varepsilon$ ($\lambda$ nm): +4.29 (206), 0 (211), −3.99 (216), −0.41 (287); HR-FAB-MS (negative centroid) *m/z*: 747.2879 $[M-H]^-$ ($C_{37}H_{47}O_{16}$ requires 747.2864).

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