

ISOLATION OF TWO UNUSUAL TETRAHYDROISOQUINOLINE-MONOTERPENE GLUCOSIDES FROM *ALANGIUM LAMARCKII* AS POSSIBLE INTERMEDIATES IN THE NON-ENZYMATIC FORMATION OF ALANGIMARINE FROM ALANGISIDE

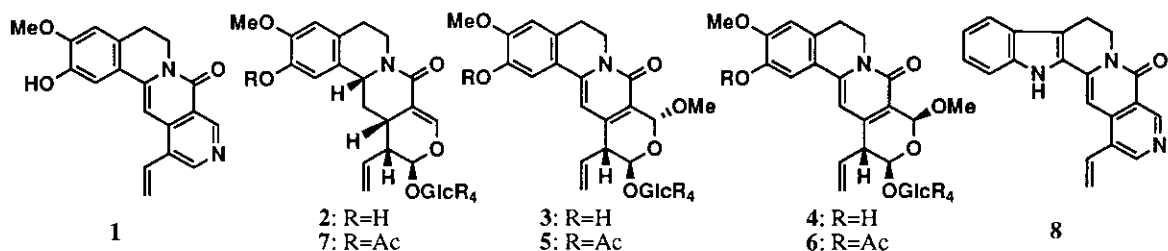
Atsuko Itoh\*, Takao Tanahashi, and Naotaka Nagakura

Kobe Pharmaceutical University, 4-19-1 Motoyamakita-machi, Higashinada-ku, Kobe 658-8558, Japan

**Abstract-** From the fruits of *Alangium lamarckii*, two new glucosides (3) and (4), which possessed unusual structures different from any known tetrahydroisoquinoline-monoterpene glucosides, have been isolated. Their structures were determined on the basis of spectroscopic and chemical methods. These same glucosides were also obtained by storage of alangiside (2) in MeOH for a prolonged period and glucoside (4) was further converted to alangimarine (1), a benzopyridoquinolizine alkaloid from this plant, by the usual treatment for isolation of alkaloids, suggesting the possibility of non-enzymatic formation of alangimarine (1) from alangiside (2) via the isolated glucosides (3) and (4).

*Alangium lamarckii* Thwaites (Alangiaceae) is a traditional medicinal plant in India. The decoction from the root barks has been used as anthelmintic, purgative, emetic and febrifuge and for the treatment of leprosy and other skin diseases.<sup>1</sup> From this plant the isolation of such alkaloids including ipecac alkaloids, e.g. emetine and cephaeline, and benzo[a]pyrido[3,4-g]quinolizine alkaloids such as alangimarine (1) has been reported.<sup>1-3</sup> This plant is also known to be a rich source of alangiside (2), a tetrahydroisoquinoline-monoterpene glucoside, the structure of which is closely related to these alkaloids.<sup>4</sup> From our interests in the biosynthesis of the *Alangium* alkaloids, we have investigated the constituents of the fruits of *A. lamarckii*, isolated a variety of nitrogenous glucosides and characterized eighteen of them.<sup>5-9</sup> In continuation of this study, we report here the structure elucidation of two more unusual tetrahydroisoquinoline-monoterpene glucosides (3) and (4), and the possibility of artificial formation of alangimarine (1) from alangiside (2) via these isolated glucosides.

Compound (3), a pale yellow powder,  $[\alpha]_D +8.5^\circ$ , and compound (4), pale yellow needles, mp 219-220°,  $[\alpha]_D -105^\circ$ , have the same molecular formula,  $C_{26}H_{31}NO_{11}$ , from their HR-SIMS. Their IR spectra showed adsorption bands due to the hydroxyl and lactam carbonyl groups. Conventional acetylation of 3 and 4 gave pentaacetates (5) and (6), respectively. Their <sup>1</sup>H NMR spectra showed a signal for a phenolic acetyl group (5:  $\delta$  2.35; 6:  $\delta$  2.34), indicating the presence of one phenolic hydroxyl group in each glucoside.



The  $^1\text{H}$  NMR spectrum of **3** showed a singlet for an aromatic methoxyl group at  $\delta$  3.92, signals for a terminal vinyl group at  $\delta$  5.20 (br d,  $J=10.5$  Hz), 5.24 (dt,  $J=17.0, 1.0$  Hz), 5.83 (ddd,  $J=17.0, 10.5, 8.0$  Hz), a doublet for an acetal proton at  $\delta$  5.53 ( $J=1.0$  Hz), and signals for a glucosyl moiety at  $\delta$  3.17-4.78, implying its structural similarity to alangiside (**2**). However, the  $^1\text{H}$  NMR of **3** lacked an olefinic proton signal for H-9 and a methin proton signal for H-13a, but alternatively exhibited three singlets in the aromatic region ( $\delta$  6.61, 6.89 and 7.23), a signal for a methoxyl group ( $\delta$  3.66) and a singlet for an acetal proton ( $\delta$  5.46). This acetal proton signal was correlated with the methoxyl singlet ( $\delta$  3.66) in the ROESY spectrum, and showed a long-range correlation with C-11 ( $\delta$  96.9) in the HMBC spectrum. From these results, the signal at  $\delta$  5.46 was assigned to H-9 and the methoxyl was located at C-9. On the other hand, the singlet at  $\delta$  6.61 was assigned to H-13 by ROESY correlation with H-12 [ $\delta$  3.49 (br d,  $J=8.0$  Hz)]. Further correlations in ROESY and HMBC spectra (Figure 1) revealed the planar structure of **3**.

The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectral features of **4** (Table 1) were closely related to those of **3**. Moreover, its HMBC and ROESY spectra suggested that **4** possessed the same structure as **3** except for the configuration of C-9.

These proposed structures were confirmed by preparation of **3** and **4** from alangiside pentaacetate (**7**).<sup>4</sup> Oxidation of **7** with DDQ<sup>10</sup> followed by Zemplen deacetylation afforded two isomeric products which were identified with **3** and **4**.

The stereochemistry at C-9 of **3** and **4** was determined by a detailed comparison of NMR data for **3** and **4** which showed a remarkable difference in the coupling constant between H-11 and H-12. The coupling constant ( $J_{11,12}=1.0$  Hz) of **3** required that both H-11 and H-12 adopted quasi-equatorial positions similar to those of **2**,<sup>5</sup> while the coupling constant ( $J_{11,12}=7.5$  Hz) of **4** suggested that both H-11 and H-12 adopted

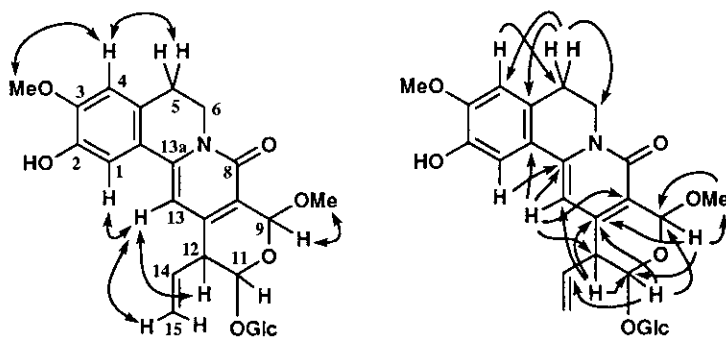


Figure 1. Correlations of ROESY ( $\longleftrightarrow$ ) and HMBC ( $\longrightarrow$ ) of **3**

quasi-axial positions (Figure 2). This conformation was also supported by the ROESY correlation between H-9 and H-11 in both **4** and **6**. Accordingly, the absolute structures of compounds (**3**) and (**4**) were deduced as shown.

The occurrence of the unusual glucosides (**3**) and (**4**) gave an important clue to the genesis of the benzo[*a*]pyrido[3,4-*g*]quinolizine alkaloids of the plant. Although Pakrashi *et al.* have claimed that these alkaloids were natural products biosynthesized from alangiside (**2**),<sup>3</sup> we could assume that alangimarine (**1**) would be an artifact, as in the same case as for angustine (**8**), a related pyridino-indolo-quinolizidinone alkaloid, which was proposed to be formed during extraction procedures by the action of ammonia on the lactam compound.<sup>11</sup> Alangimarine (**1**) might possibly arise by reaction with AcOH and/or HCl and then with ammonia of the isolated glucosides (**3**) and (**4**), both of which were non-enzymatically derived from alangiside (**2**) by oxidation processes followed by addition of methanol during extraction. To prove this assumption, the following reactions were performed. On heating in MeOH for a short period, alangiside (**2**) was converted neither to **3** nor to **4**. On the other hand, when a methanolic solution of alangiside (**2**) was

Table 1. <sup>1</sup>H and <sup>13</sup>C NMR spectral data of compounds **3** and **4** in CD<sub>3</sub>OD (500 and 125 MHz).

C	3		4	
	δ <sub>H</sub>	δ <sub>C</sub>	δ <sub>H</sub>	δ <sub>C</sub>
1	7.23 s	113.1	7.14 s	112.8
2	-	147.2 <sup>a</sup>	-	147.4
3	-	151.8	-	151.8
4	6.89 s	111.7	6.88 s	111.8
4a	-	129.5	-	129.4
5	2.92 t (6.5)	28.1	2.90 t (6.5)	28.1
5	2.92 t (6.5)	-	2.90 t (6.5)	-
6	4.17 dt (13.0, 6.5)	41.0	4.17 dt (13.0, 6.5)	40.9
6	4.24 dt (13.0, 6.5)	-	4.21 dt (13.0, 6.5)	-
8	-	161.6	-	161.7
8a	-	119.2	-	120.5
9	5.46 s	96.3	5.63 s	97.6
11	5.53 d (1.0)	96.9	5.49 d (7.5)	93.9
12	3.49 br d (8.0)	48.1	3.41 br t (8.5)	n.d. <sup>b</sup>
12a	-	147.4 <sup>a</sup>	-	149.0
13	6.61 s	104.5	6.57 s	103.6
13a	-	145.2	-	145.1
13b	-	122.3	-	122.3
14	5.83 ddd (17.0, 10.5, 8.0)	137.0	5.78 dt (17.5, 9.5)	135.6
15	5.20 br d (10.5)	119.0	5.39-5.44 m	121.6
15	5.24 dt (17.0, 1.0)	-	5.39-5.44 m	-
1'	4.78 d (8.0)	99.5	4.80 d (8.0)	99.6
2'	3.17 dd (9.0, 8.0)	75.0	3.23 dd (9.0, 8.0)	74.8
3'	3.42 t (9.0)	78.3	3.41 t (9.0)	78.3
4'	3.26 dd (9.5, 9.0)	71.5	n.d. <sup>b</sup>	71.7
5'	3.37 ddd (9.5, 6.0, 2.0)	78.5	n.d. <sup>b</sup>	78.6
6'	3.67 dd (12.0, 6.0)	62.8	3.68 dd (12.0, 5.5)	62.8
6'	3.91 dd (12.0, 2.0)	-	3.87 dd (12.0, 2.0)	-
OMe	3.66 s	56.6	3.57 s	56.3
OMe	3.92 s	57.9	3.91 s	56.6

<sup>a</sup> Values are interchangeable.

<sup>b</sup> Not determined.

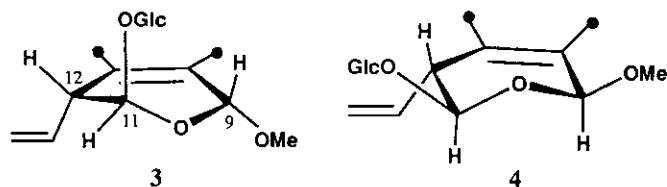


Figure 2. Conformations of dihydropyran ring in **3** and **4** from  $^1\text{H}$  NMR analysis.

kept for a prolonged period, **3** and **4** were formed in a small quantity. Glucosides with the same 2-methoxy dihydropyran ring have already been reported as artifacts of iridoid glucosides and the mechanism of their formation was proposed.<sup>12</sup> Formation of compounds (**3**) and (**4**) should also involve oxidation processes and an addition of MeOH.

Furthermore, glucoside (**4**) was treated with *dil.* HCl and then with 14% ammonia to give alangimarine (**1**) in 19% yield. From these results, we concluded that the isolated glucosides (**3**) and (**4**) could be artifacts derived from alangiside (**2**) through reactions during exposure to air and the separation procedure. We assume that part of alangimarine (**1**) could be non-enzymatically formed, although the possibility of its being a natural alkaloid could not be ruled out.

## EXPERIMENTAL

Melting points were measured on a Büchi melting point apparatus and are reported uncorrected. UV spectra were recorded on a Shimadzu UV-240 spectrophotometer and IR spectra on a Shimadzu FTIR-8200 spectrophotometer. Optical rotations were measured on a Jasco DIP-370 digital polarimeter. MS and HR-MS were obtained with a Hitachi M-4100 mass spectrometer. For SIMS, glycerol was used as the matrix. The NMR experiments were performed with Varian VXR-500 and Varian Gemini-200 spectrometers, with TMS as internal standard. HPLC was performed using a Waters system (600E multisolvent delivery system, 486 tunable absorbance detector). CC was carried out with Silica gel 60 (70-230 mesh, Nacalai Tesque). TLC was performed on precoated Kieselgel 60F<sub>254</sub> plates (Merck).

### Plant material and isolation of glucosides.

The source of plant material and isolation of glucosides were as described in a previous paper.<sup>7</sup> Compound E and H in ref. 7 correspond to **4** and **3**, respectively.

### Compound (**3**)

Pale yellow powder.  $[\alpha]_{\text{D}}^{27} +8.5^\circ$  ( $c=1.0$ , MeOH). UV  $\lambda_{\text{max}}^{\text{MeOH}}$  nm (log  $\epsilon$ ): 221 (4.32), 226 (4.32), 243sh (4.02), 258sh (3.79), 267 (3.84), 351 (4.33), 366sh (4.24). IR  $\nu_{\text{max}}^{\text{KBr}}$   $\text{cm}^{-1}$ : 3385 (OH), 1647 (NCO), 1591 (Ar), 1558 (Ar), 1512 (Ar).  $^1\text{H}$  NMR: Table 1.  $^{13}\text{C}$  NMR: Table 1. SIMS  $m/z$ : 556  $[\text{M}+\text{Na}]^+$ , 502, 340. HR-SIMS  $m/z$ :  $[\text{M}+\text{Na}]^+$  Calcd for  $\text{C}_{26}\text{H}_{31}\text{NO}_{11}\text{Na}$ : 556.1796. Found: 556.1783.

**Compound (4)**

Pale yellow needles. mp 219-220° (MeOH).  $[\alpha]_D^{20}$  -105° ( $c=1.0$ , MeOH). UV  $\lambda_{\max}^{\text{MeOH}}$  nm (log  $\epsilon$ ): 226.5 (4.38), 244sh (4.10), 260sh (3.89), 266.5 (3.91), 334sh (4.21), 351.5 (4.37), 367sh (4.28). IR  $\nu_{\max}^{\text{KBr}}$   $\text{cm}^{-1}$ : 3448 (OH), 1644 (NCO), 1592 (Ar), 1558 (Ar), 1514 (Ar).  $^1\text{H}$  NMR: Table 1.  $^{13}\text{C}$  NMR: Table 1. ROESY: H-1 / H-13; H-4 / OMe ( $\delta$  3.91); H-4 / H<sub>2</sub>-5; H-9 / OMe ( $\delta$  3.57); H-9 / H-11; H-11 / H-14; H-11 / H-1'; H-12 / H-13; H-12 / H<sub>2</sub>-15; H-13 / H<sub>2</sub>-15. HMBC: H-1 to C-13a; H-4 to C-5; H-9 to C-8a; H-9 to C-11; H-9 to C-12a; H-9 to OMe ( $\delta$  56.3); H-11 to C-14; H-11 to C-1'; H-12 to C-11; H-12 to C-12a; H-12 to C-14; H-13 to C-8a; H-13 to C-13a; H-13 to C-13b; H-2' to C-1'; OMe ( $\delta$  3.57) to C-9. SIMS  $m/z$ : 556  $[\text{M}+\text{Na}]^+$ . HR-SIMS  $m/z$ :  $[\text{M}+\text{Na}]^+$  Calcd for  $\text{C}_{26}\text{H}_{31}\text{NO}_{11}\text{Na}$ : 556.1796. Found: 556.1805.

**Acetylation of 3**

Compound (3) (12.2 mg) was acetylated with  $\text{Ac}_2\text{O}$  (0.2 mL) in pyridine (0.2 mL) overnight in a refrigerator and the crude acetate was purified by prep. TLC with  $\text{CHCl}_3$ -MeOH (97:3) to afford pentaacetate (5) (13.9 mg) as an amorphous powder.

$[\alpha]_D^{32}$  -64° ( $c=1.39$ ,  $\text{CHCl}_3$ ). UV  $\lambda_{\max}^{\text{MeOH}}$  nm (log  $\epsilon$ ): 218 (4.43), 242sh (3.79), 259sh (3.90), 266 (3.95), 330sh (4.21), 346 (4.32), 362sh (4.20). IR  $\nu_{\max}^{\text{CHCl}_3}$   $\text{cm}^{-1}$ : 1755 (OAc), 1655 (NCO), 1593 (Ar), 1562 (Ar), 1508 (Ar).  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$ : 1.87, 1.99, 2.03, 2.10, 2.35 (15H, each s, 5xAc), 2.94 (2H, t,  $J=6.5$  Hz, H<sub>2</sub>-5), 3.38 (1H, br d,  $J=8.0$  Hz, H-12), 3.67 (3H, s, OMe), 3.78 (1H, ddd,  $J=10.0, 5.0, 2.5$  Hz, H-5'), 3.89 (3H, s, OMe), 4.16 (1H, dd,  $J=12.5, 2.5$  Hz, H-6'), 4.23 (1H, dt,  $J=13.5, 6.5$  Hz, H-6), 4.29 (1H, dt,  $J=13.5, 6.5$  Hz, H-6), 4.31 (1H, dd,  $J=12.5, 5.0$  Hz, H-6'), 4.98 (2H, m, H-1', H-2'), 5.09 (1H, dd,  $J=10.0, 9.5$  Hz, H-4'), 5.20 (1H, dt,  $J=17.0, 1.0$  Hz, H-15), 5.23 (1H, br d,  $J=10.0$  Hz, H-15), 5.24 (1H, m, H-3'), 5.39 (1H, d,  $J=1.5$  Hz, H-11), 5.52 (1H, s, H-9), 5.75 (1H, ddd,  $J=17.0, 10.0, 8.5$  Hz, H-14), 6.32 (1H, s, H-13), 6.82 (1H, s, H-4), 7.37 (1H, s, H-1). ROESY: H-4 / H<sub>2</sub>-5; H-4 / OMe ( $\delta$  3.89); H-9 / OMe ( $\delta$  3.67); H-11 / H-14; H-11 / H-1'; H-12 / H-13; H-12 / H-15 ( $\delta$  5.20); H-13 / H-15 ( $\delta$  5.23). MS  $m/z$  (rel. int.): 743  $[\text{M}]^+$  (0.01), 713 (0.02), 395 (28), 364 (100), 336 (23), 43 (50). HR-MS  $m/z$ :  $[\text{M}]^+$  Calcd for  $\text{C}_{36}\text{H}_{41}\text{NO}_{16}$ : 743.2427. Found: 743.2430.

**Acetylation of 4**

Conventional acetylation of 4 (15.1 mg) and subsequent purification by prep. TLC with  $\text{CHCl}_3$ -MeOH (97:3) afforded pentaacetate (6) (15.4 mg) as an amorphous powder.

$[\alpha]_D^{27}$  -61° ( $c=0.85$ ,  $\text{CHCl}_3$ ). UV  $\lambda_{\max}^{\text{MeOH}}$  nm (log  $\epsilon$ ): 217 (4.40), 243sh (3.79), 258sh (3.84), 266 (3.91), 334sh (4.24), 348 (4.33), 364sh (4.19). IR  $\nu_{\max}^{\text{CHCl}_3}$   $\text{cm}^{-1}$ : 1757 (OAc), 1651 (NCO), 1591 (Ar), 1558 (Ar), 1508 (Ar).  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$ : 2.01, 2.03, 2.04, 2.08, 2.34 (15H, each s, 5xAc), 2.93 (2H, t,  $J=6.5$  Hz, H<sub>2</sub>-5), 3.29 (1H, br t,  $J=8.0$  Hz, H-12), 3.65 (3H, s, OMe), 3.75 (1H, ddd,  $J=10.0, 5.5, 2.5$  Hz, H-5'), 3.88 (3H, s, OMe), 4.13 (1H, dd,  $J=12.0, 2.5$  Hz, H-6'), 4.14 (1H, dt,  $J=14.0, 6.5$  Hz, H-6), 4.27 (1H, dd,  $J=12.0, 5.5$  Hz, H-6'), 4.37 (1H, dt,  $J=14.0, 6.5$  Hz, H-6), 5.00 (1H, d,  $J=7.5$  Hz, H-1'), 5.04 (1H, br t,  $J=8.5$  Hz, H-2'), 5.10 (1H, t,  $J=9.0$  Hz, H-4'), 5.27 (1H, t,  $J=9.0$  Hz, H-3'), 5.33 (1H, d,  $J=7.0$  Hz, H-11), 5.39 (1H, br d,  $J=17.0$  Hz, H-15), 5.42 (1H, dd,  $J=10.0, 1.5$  Hz, H-15), 5.68 (1H, s, H-9), 5.72 (1H, ddd,  $J=17.0, 10.0, 9.0$  Hz, H-14), 6.38 (1H, s, H-13), 6.81 (1H, s, H-4), 7.34 (1H, s, H-1). ROESY: H-1 / H-13; H-4 / H<sub>2</sub>-5; H-4 / OMe ( $\delta$  3.88); H-9 / OMe ( $\delta$  3.65); H-9 / H-11; H-11 / H-1'; H-11 / H-14; H-12 / H-13; H-12 / H-15

( $\delta$  5.39); H-12 / OMe ( $\delta$  3.65); H-13 / H-14; H-13 / H-15 ( $\delta$  5.39). MS  $m/z$  (rel. int.): 743 [M]<sup>+</sup> (4.8), 713 (4.7), 396 (26), 382 (20), 364 (55), 336 (38), 331 (11), 43 (100). HR-MS  $m/z$ : [M]<sup>+</sup> Calcd for C<sub>36</sub>H<sub>41</sub>NO<sub>16</sub>: 743.2427. Found: 743.2425.

#### Preparation of 3 and 4 from alangiside pentaacetate (7)

Alangiside pentaacetate (7) (200 mg, 0.28 mmol) was treated with DDQ (200 mg, 0.88 mmol) in toluene-MeOH (1:1, 10 mL) at 50° for 1 h. The reaction mixture was diluted with toluene (90 mL), the solution was chromatographed on a silica gel column with toluene-MeOH (19:1) as eluent and the product was further purified by prep. TLC (toluene-MeOH, 3:1) to afford a mixture of 5 and 6 (212.2 mg). To a solution of the mixture in MeOH (10 mL) was added a solution of 0.1 N NaOMe (2.0 mL) and the whole stirred at rt for 4 h. The reaction mixture was neutralized by Amberlite IR-120B (H<sup>+</sup> form) and evaporated *in vacuo*. The resulting residue was subjected to prep. TLC (CHCl<sub>3</sub>-MeOH, 4:1) to afford 3 (22.4 mg, 15% from 7) and 4 (104.2 mg, 70% from 7).

3. [ $\alpha$ ]<sub>D</sub><sup>26</sup> +8.0° ( $c=1.0$ , MeOH). SIMS  $m/z$ : 556 [M+Na]<sup>+</sup>, 534 [M+H]<sup>+</sup>, 502, 340.

UV, IR and <sup>1</sup>H NMR spectra of this compound were identical with those of 3 from natural source.

4. [ $\alpha$ ]<sub>D</sub><sup>27</sup> -110° ( $c=1.0$ , MeOH). SIMS  $m/z$ : 556 [M+Na]<sup>+</sup>, 534 [M+H]<sup>+</sup>, 502, 340.

UV, IR and <sup>1</sup>H NMR spectra of this compound were identical with those of 4 from natural source.

#### Conversion of alangiside (2) into 3 and 4

A solution of alangiside (2) (100 mg) in MeOH (5 mL) was allowed to stand at rt for 9 months. After evaporation of the solvent, the resulting residue was purified by prep. HPLC (MeOH-H<sub>2</sub>O, 1:1) to give 3 (1.8 mg) and 4 (4.9 mg) along with the recovered 2 (75.6 mg).

A MeOH solution (2 mL) of 2 (10.0 mg) was then refluxed for 18 h, but neither 3 nor 4 was detected in the reaction mixture by HPLC analysis.

#### Preparation of alangimarine (1) from 4

To a solution of 4 (60 mg) in THF (3 mL) was added 1N HCl (3.0 mL) and the whole stirred at rt for 1 h. The reaction mixture was basified with 14% NH<sub>4</sub>OH at 0° and stirred at rt for 1 h. The mixture was then extracted with CHCl<sub>3</sub> and the organic layer was washed and dried over MgSO<sub>4</sub> and the solvent removed under reduced pressure. The resulting residue was purified by prep. TLC with CHCl<sub>3</sub>-MeOH (93:7) to afford 1 (7.0 mg, 19%).

UV  $\lambda_{\max}^{\text{MeOH}}$  nm (log  $\epsilon$ ): 220sh (4.40), 247 (4.11), 260 (4.14), 290sh (3.85), 364 (4.41), 377sh (4.37). IR  $\nu_{\max}^{\text{KBr}}$  cm<sup>-1</sup>: 1645 (NCO), 1599 (Ar), 1510 (Ar). <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>)  $\delta$ : 2.95 (2H, t,  $J=6.0$  Hz, H<sub>2</sub>-5), 3.98 (3H, s, OMe), 4.35 (2H, t,  $J=6.0$  Hz, H<sub>2</sub>-6), 5.58 (1H, dd,  $J=11.0, 1.0$  Hz, H-15), 5.84 (1H, dd,  $J=17.5, 1.0$  Hz, H-15), 6.75 (1H, s, H-4), 6.98 (1H, s, H-1), 7.13 (1H, dd,  $J=17.5, 11.0$  Hz, H-14), 7.42 (1H, s, H-13), 8.76 (1H, s, H-11), 9.51 (1H, s, H-9). (200 MHz, C<sub>5</sub>D<sub>5</sub>N)  $\delta$ : 2.82 (2H, t,  $J=6.0$  Hz, H<sub>2</sub>-5), 3.83 (3H, s, OMe), 4.35 (2H, t,  $J=6.0$  Hz, H<sub>2</sub>-6), 5.48 (1H, dd,  $J=11.0, 1.0$  Hz, H-15), 5.86 (1H, dd,  $J=17.5, 1.0$  Hz, H-15), 6.84 (1H, s, H-4), 7.06 (1H, s, H-1), 7.19 (1H, dd,  $J=17.5, 11.0$  Hz, H-14), 7.80 (1H, s, H-13), 8.97 (1H, s, H-11), 9.84 (1H, s, H-9). MS  $m/z$  (rel. int.): 320 [M]<sup>+</sup> (100), 305 (59). HR-MS  $m/z$ : [M]<sup>+</sup> Calcd for C<sub>19</sub>H<sub>16</sub>N<sub>2</sub>O<sub>3</sub>: 320.1162. Found: 320.1169.

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## REFERENCES

1. T. Fujii and M. Ohba, "*The Alkaloids*", ed. by A. Brossi, Academic Press, New York, 1983, Vol. XXII, p. 1.
2. M. Shamma, "*The Isoquinoline Alkaloids*", Academic Press, New York, 1972, p.426.
3. S.C. Pakrashi, R. Mukhopadhyay, R.R. Sinha, P.P.G. Dastidar, B. Achari, and E. Ali, *Indian J. Chem.*, 1985, **24B**, 19.
4. A. Shoeb, K. Raj, R.S. Kapil, and S.P. Popli, *J. Chem. Soc., Perkin Trans. 1*, 1975, 1245.
5. A. Itoh, T. Tanahashi, N. Nagakura, and H. Nayeshiro, *Phytochemistry*, 1994, **36**, 383.
6. A. Itoh, T. Tanahashi, and N. Nagakura, *Chem. Pharm. Bull.*, 1994, **42**, 2208.
7. A. Itoh, T. Tanahashi, and N. Nagakura, *J. Nat. Prod.*, 1995, **58**, 1228.
8. A. Itoh, T. Tanahashi, and N. Nagakura, *Phytochemistry*, 1996, **41**, 651.
9. A. Itoh, T. Tanahashi, and N. Nagakura, *Phytochemistry*, 1997, **46**, 1225.
10. C.R. Hutchinson, M.-T.S. Hsia, A.H. Heckendorf, and G.J. O'loughlin, *J. Org. Chem.*, 1976, **41**, 3493.
11. J.D. Phillipson and S.R. Hemingway, *Phytochemistry*, 1974, **13**, 973.
12. C.A. Boros, F.R. Stermitz, and G.H. Harris, *J. Nat. Prod.*, 1990, **53**, 72.

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