

Paxillarines A and B, New Steroidal Alkaloids from *Pachysandra axillaris*, and Conformation of Their Ring A Moieties

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Two new steroidal alkaloids, paxillarines A (1) and B (2), were isolated from *Pachysandra axillaris*. Their structures were determined by means of spectrometric methods as 3 α -*N*-methylbenzoylamino-4 β -acetoxy-16 β -hydroxy-20 α -dimethylamino-5 α -pregnane and 3 α -*N*-methylbenzoylamino-4 β -acetoxy-12 β -hydroxy-20 α -dimethylamino-5 α -pregnane, respectively. Some of the expected characteristic ¹H-NMR signals were not observed due to hindered rotation when the spectra were measured on a 400 MHz spectrometer, although all of the signals appeared clearly on a 90 MHz machine. The conformation of the ring A moiety of these alkaloids is discussed.

Key words NMR; paxillarine A; paxillarine B; *Pachysandra axillaris*; rotational isomerism; steroidal alkaloid

Pachysandra axillaris FRANCH (Buxaceae) is distributed in the southern part of China and is used as a folk medicine for pain.¹⁾ A lot of interest has been shown in *P. axillaris* because of the abundance of its alkaloidal constituents.²⁾ More than 20 kinds of pregnane-type alkaloids have already been isolated³⁾ from a related plant, *P. terminalis* SIEB *et* ZUCC. In this paper, we describe the isolation and structure elucidation of two new alkaloids, paxillarines A (1) and B (2).

Dried whole plants (45 kg) of *P. axillaris* were extracted with 95% ethanol. The extract was then treated with aqueous acetic acid to give a crude alkaloid fraction. This fraction was separated into strongly basic and weakly basic alkaloid fractions. The weakly basic alkaloid fraction was further purified by column chromatography on alumina to afford alkaloids 1 (7.2 g) and 2 (50 mg).

Paxillarine A (1), mp 263–265 °C, has the molecular formula C₃₃H₅₀N₂O₄. In this compound, isolated from the weakly basic fraction, one of the two nitrogens may be an amide nitrogen. The IR spectrum indicated a hydroxy group, an ester and an amide group at 3400, 1720, and 1620 cm⁻¹, respectively, and the MS showed the molecular ion peak at *m/z* 538 and characteristic fragment peaks at *m/z* 174 [CH₂=CH-CH=N⁺(CH₃)–

COC₆H₅] and 72 [base peak, CH₃-CH=N⁺(CH₃)₂] which were suggestive of a pregnane-type alkaloid possessing a dimethylamino group at C-20 and an *N*-

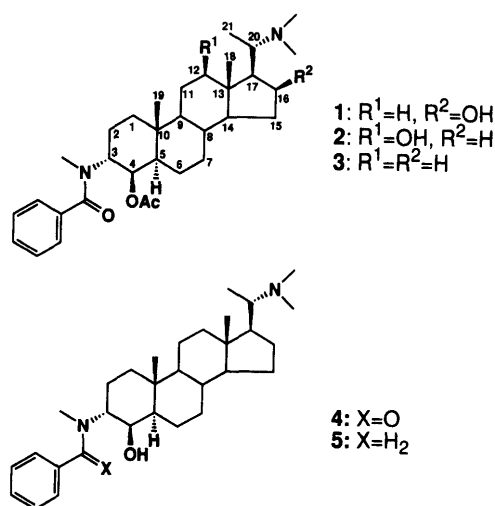


Chart 1

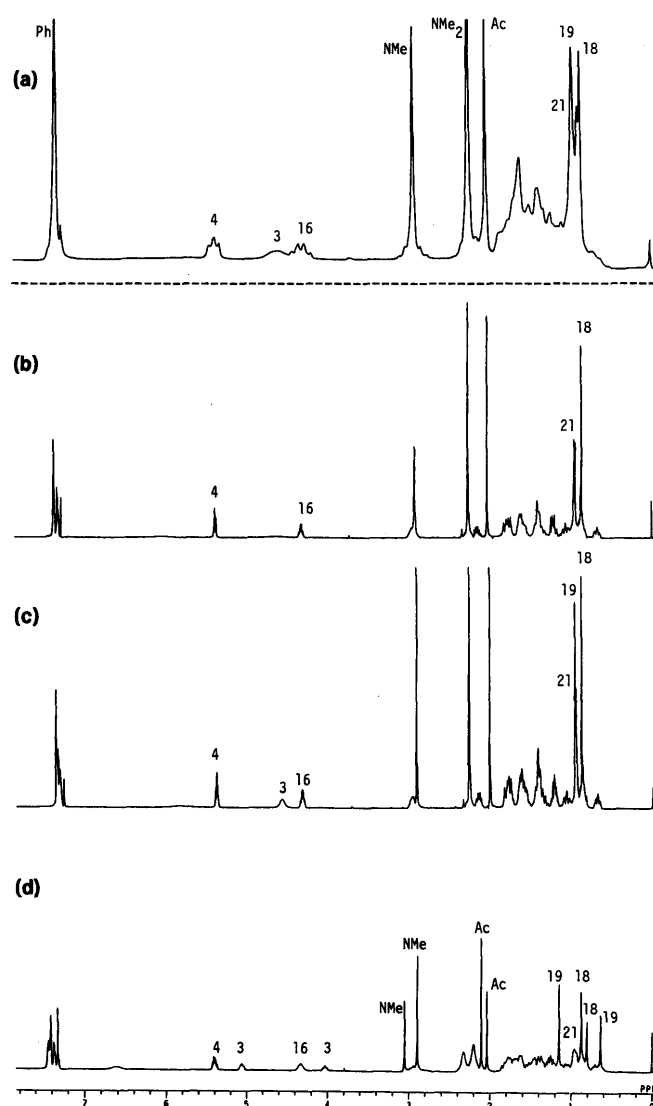


Fig. 1. ¹H-NMR Spectra of Paxillarine A (1)

(a) 90 MHz at 27 °C; (b) 400 MHz at 27 °C; (c) 400 MHz at 60 °C; (d) 400 MHz at -50 °C.

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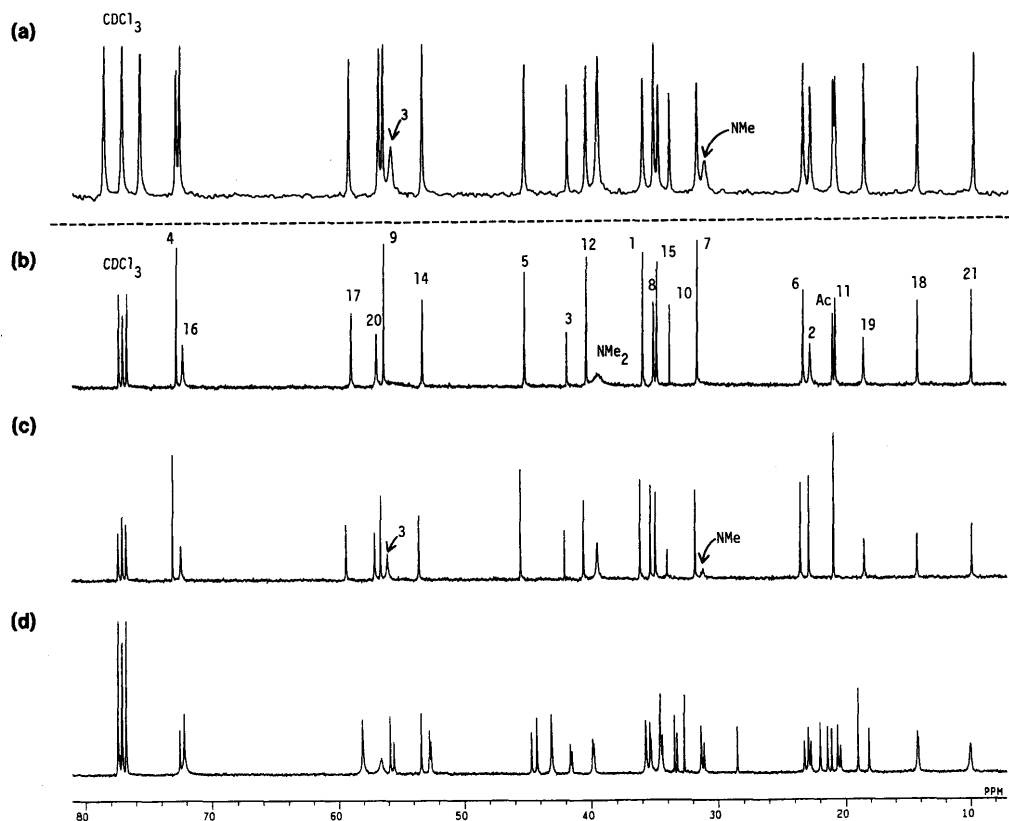


Fig. 2. ^{13}C -NMR Spectra of Paxillarine A (**1**)

(a) 22.5 MHz at 27 °C; (b) 100 MHz at 27 °C; (c) 100 MHz at 60 °C; (d) 100 MHz at -50 °C.

methylbenzoylamino group at C-3.³⁾ In addition, the ^1H -NMR spectrum showed the presence of an acetoxy group. From these observations, this compound was considered to be a pregnane alkaloid closely related to pachysandrine A (**3**)⁴⁾ (previously isolated from *P. terminalis*), but bearing an additional hydroxy group.

However, the proton and carbon signals of the 19-methyl, the 3-methine, and the *N*-methyl groups of **1** were not clearly observed in the 400 MHz ^1H - and 100 MHz ^{13}C -NMR spectra taken at 27 °C. In addition, the ^1H - ^{13}C COSY spectrum also showed no correlation peaks for the proton and carbon signals within each of the three groups. Thus we repeated the ^1H -NMR determination of **1** on a 90 MHz NMR spectrometer. All the hitherto missing signals of **1** were now clearly observed. It was thought that the signals had disappeared owing to the occurrence of conformational isomerism in the ring A moiety for some reason. We therefore examined the NMR spectrum at various temperatures. As expected, when we repeated the ^1H -NMR measurement at 60 °C on a 400 MHz spectrometer, both the 19-methyl and 3-methine signals were clearly observed, and at -50 °C, these signals appeared as two sets each. Using a 22.5 MHz apparatus at 27 °C, both the *N*-methyl and 3-methine carbon signals clearly appeared in the ^{13}C -NMR spectrum. Even on the 100 MHz apparatus at 60 °C, both the *N*-methyl and 3-methine carbon signals clearly appeared in the ^{13}C -NMR spectrum, and at -50 °C, these signals appeared in duplicate. It should be noted that pachysandrine A (**3**) showed quite similar NMR phenomena.

The position of the additional hydroxy group in **1** was

determined to be C-16 by analysis of the ^1H - ^1H correlation spectroscopy (COSY) measured at 60 °C, in which the signal at δ 4.31 (q, $J=7.0$ Hz) due to the methine proton geminal to the hydroxyl group showed a correlation with H-17 at δ 1.22 (dd, $J=11.0, 7.0$ Hz) and the latter with H-20 at δ 2.96 (dq, $J=11.0, 6.4$ Hz). The configuration of the hydroxy group was determined to be β because of the great downward shift of the 18-methyl signal in the ^1H -NMR spectrum as compared to that of **3**. Since the ^1H - and ^{13}C -NMR data of **1** agreed quite well with those of **3** (Table 1), the configurations at the C-3 and C-4 position should be the same for both compounds. Thus paxillarine A was concluded to be 3 α -*N*-methylbenzoylamino-4 β -acetoxy-16 β -hydroxy-20 α -dimethylamino-5 α -pregnane (**1**).

Paxillarine B (**2**), mp 234–237 °C, has the same molecular formula as paxillarine A (**1**), $\text{C}_{33}\text{H}_{50}\text{N}_2\text{O}_4$, as determined by HR-MS. It showed hydroxyl, ester and amide carbonyl absorptions (3400, 1725, and 1620 cm^{-1} , respectively) in the IR spectrum, and diagnostic fragment peaks at m/z 174 [$\text{CH}_2=\text{CH}-\text{CH}=\text{N}^+(\text{CH}_3)-\text{COC}_6\text{H}_5$] and 72 [base peak, $\text{CH}_3-\text{CH}=\text{N}^+(\text{CH}_3)_2$] in the MS. The ^1H -NMR spectra measured at 27 °C and 60 °C on a 400 MHz spectrometer were closely similar to those of **1** measured under similar conditions. However, the position of the hydroxy group in **2** differed from that of **1**. From the analyses of the ^1H - ^1H COSY and ^1H - ^{13}C COSY and comparison of the ^1H - and ^{13}C -NMR spectra with those of **1**, we concluded that the hydroxy group in **2** was at the C-12 position. The attached methine proton at the C-12 position was shown to be axial by the J values (11.0,

Table 1. ^1H - (400 MHz) and ^{13}C - (100 MHz) NMR Data for Paxillarine A, Paxillarine B, and Pachysandrine A in CDCl_3 at 60°C

	Paxillarine A		Paxillarine B		Pachysandrine A	
	δ_{H} (J in Hz)	δ_{C}	δ_{H} (J in Hz)	δ_{C}	δ_{H} (J in Hz)	δ_{C}
1	1.56 m 1.62*	36.1 t	1.57* (2H)	36.0 t	1.56* (2H)	36.1 t
2	1.62* 1.78*	22.8 t	1.66* 1.79*	22.9 t	1.65* 1.76*	22.9 t
3	4.56 br s	56.1 d	4.52 br s	56.2 d	4.56 br s	56.1 d
4	5.37 t (6.3)	73.1 d	5.37 t (6.3)	73.2 d	5.36 t (6.3)	73.1 d
5	1.62*	45.5 d	1.61*	45.7 d	1.65*	45.6 d
6	1.40* (2H)	23.5 t	1.38—1.43 (2H)	23.7 ^{b)} t	1.38* (2H)	23.6 t
7	0.87* 1.76*	31.8 t	0.85 td (12.0, 6.0) 1.73*	31.3 t	0.87* 1.71*	31.7 t
8	1.40*	35.3 d	1.27*	34.3 d	1.26*	35.8 d
9	0.67 td (10.5, 4.5)	56.6 d	0.76 td (11.0, 3.5)	55.2 d	0.67 td (11.0, 4.0)	56.6 ^{c)} d
10	—	34.0 s	—	34.1 s	—	34.0 s
11	1.32 td (13.5, 3.5) 1.42*	20.9 ^{d)} t	1.31* 1.64*	28.4 t	1.31* 1.42*	21.1 ^{d)} t
12	1.06 td (11.5, 4.5) 1.81 dt (11.5, 3.0)	40.5 t	3.22 dd (11.0, 4.3)	77.9 d	1.11 td (11.0, 4.0) 1.89 dt (11.0, 3.5)	40.0 ^{e)} t
13	—	42.0 s	—	49.3 s	—	42.1 s
14	0.85*	53.5 d	0.94*	54.6 d	1.01*	56.6 ^{c)} d
15	1.19 m 2.14 ddd (12.5, 7.0, 6.0)	34.8 t	1.22* 1.69*	23.6 ^{b)} t	1.04* 1.60*	24.1 t
16	4.31 q (7.0)	72.5 d	1.61* (2H)	25.7 t	1.48* 1.81*	27.7 t
17	1.22 dd (11.0, 7.0)	59.5 d	2.03 m	51.5 d	1.34*	55.1 d
18	0.87 s	14.3 q	0.72 s	9.6 q	0.65 s	12.4 q
19	0.96 s	18.5 q	0.94 s	18.3 q	0.94 s	18.4 q
20	2.96 dq (11.0, 6.4)	56.9 d	2.21 qd (7.0, 4.0)	62.8 d	2.42 dq (10.5, 6.4)	61.5 d
21	0.95 d (6.4)	9.8 q	1.13 d (7.0)	15.0 q	0.87 d (6.4)	10.4 q
NMe ₂	2.26 s	39.5 q	2.33 s	43.9 q	2.17 s	39.9 ^{e)} q
N-Me	2.91 s	31.1 q	2.92 s	31.3 q	2.91 s	31.2 q
CO-Ph 3', 5'	—	126.7 d	—	126.7 d	—	126.7 d
2', 6'	7.30—7.36 (5H)	128.3 d	7.30—7.36 (5H)	128.4 d	7.30—7.36 (5H)	128.3 d
4'	—	129.2 d	—	129.2 d	—	129.2 d
1'	—	137.4 s	—	137.4 s	—	137.4 s
C=O	—	170.6 s	—	170.6 s	—	170.6 s
Ac CH ₃	2.01 s	20.9 ^{d)} q	2.03 s	20.9 q	2.00 s	20.9 ^{d)} q
C=O	—	171.9 s	—	172.0 s	—	171.9 s

Multiplicities of ^1H - and ^{13}C -signals are indicated as s (singlet), d (doublet), t (triplet), and q (quartet). Those of ^{13}C -signals were determined by the DEPT method. Chemical shifts with asterisks are approximate values; exact values were not obtained because of signal overlappings. a) At 23°C , $\text{C}_{(11)}$ and $\text{C}(\text{COCH}_3)$ in paxillarine A appeared separately at δ 20.8 and 21.0, respectively. b) At 23°C , $\text{C}_{(6)}$ and $\text{C}_{(15)}$ in paxillarine B appeared at δ 23.4 and 23.5, respectively. c) At 23°C , $\text{C}_{(9)}$ and $\text{C}_{(14)}$ in pachysandrine A appeared separately at δ 56.3 and 56.4, respectively. d) At 23°C , $\text{C}_{(11)}$ and $\text{C}(\text{COCH}_3)$ in pachysandrine A were overlapped and appeared at δ 21.0. e) At 23°C , $\text{C}_{(12)}$ and $\text{C}(\text{NMe}_2)$ in pachysandrine A appeared at δ 39.8 and 39.9, respectively.

4.3 Hz), and the hydroxyl group was thus determined to have β -configuration. Since the ^1H -NMR data of the ring A moiety of **2** agreed with those of **1**, the configuration at the C-3 and C-4 positions must be the same for both compounds. Consequently paxillarine B was determined to be 3α -*N*-methylbenzoylamino-4 β -acetoxy-12 β -hydroxy-20 α -dimethylamino-5 α -pregnane (**2**).

Next, we further investigated the conformational isomerism of these compounds (**1**, **2**, and **3**). ^1H -NMR spectral analyses of the ring A moieties of the three compounds obtained at -50°C on a 400 MHz spectrometer showed similar values for the chemical shifts and coupling constants for all three compounds, suggesting that all three compounds exhibited the same conformational isomerism.

In this type of conformational isomerism, the interconversion rate between conformers is too fast for a low magnetic field NMR apparatus such as a 90 MHz spectrometer to be able to distinguish the conformers. In this case, the spectrum obtained shows only one signal

Table 2. Coupling Constants (Hz) between Protons at the 2-, 3-, 4-, and 5-Positions (400 MHz)

Compounds	Temp. ($^\circ\text{C}$)	Conformation	$J_{3-2\alpha}$	$J_{3-2\beta}$	J_{3-4}	J_{4-5}
1—3	−50	A (Boat)	11.0	3.5	6.5	6.5
		B (Boat)	11.5	4.0	6.5	6.5
4	−50	Boat	10.5	3.5	5.0	5.0
5	27	Chair	3.0	3.0	3.0	3.0

which is an average of the chemical shifts of the conformers. On the other hand, on a high magnetic field apparatus such as a 400 MHz spectrometer, the difference between the chemical shifts of conformers is similar to the rate of interconversion of the conformers and thus the corresponding signals are broadened and become unobservable.⁵⁾

Initially, we thought that this phenomenon was due to the boat–chair interconversion of the ring A moiety. However, the J values between 2-H₂, 3-H, 4-H, and

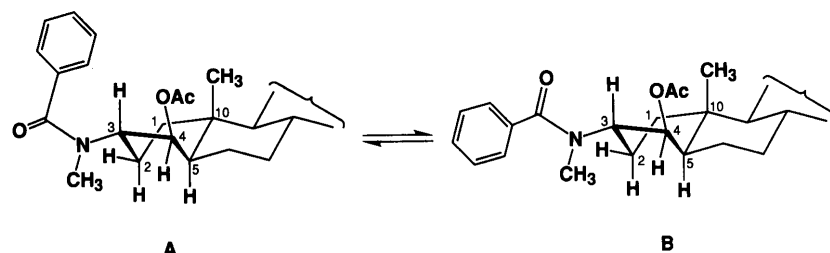


Chart 2

5-H obtained from the ^1H -NMR spectra determined at -50°C on a 400 MHz spectrometer were identical with each other in both conformers as shown in Table 2 and also they were practically identical with those of the deacyl compound (4). In view of the large $J_{3-2\alpha}$ value (11.0–11.5 Hz), it was clear that ring A was not in a chair form, but rather in a twist-boat form. We therefore concluded that the conformational isomerism exhibited by these compounds could be due to rotational isomerism of the amide bond⁵⁾ as shown in Chart 2. The chemical shifts of the 19-methyl, 3-methine, and 3-*N*-methyl groups of the conformers A and B are very different and clearly explain the above phenomena observed in the 90 and 400 MHz NMR spectrometer. The free energy of activation for the interconversion between the conformers can be deduced using Eyring's Eq. 1 and 2 as modified by Shanan-Atidi and Bar-Eli.⁶⁾

$$\Delta G_A^\ddagger = 4.57T_c\{10.62 + \log\{X/2\pi(1 - \Delta P)\} + \log(T_c/\Delta\nu)\} \quad (1)$$

$$\Delta G_B^\ddagger = 4.57T_c\{10.62 + \log\{X/2\pi(1 + \Delta P)\} + \log(T_c/\Delta\nu)\} \quad (2)$$

where $X = 2\pi\tau\Delta\nu$ and $\Delta P = P_A - P_B$, P_A and P_B representing the population of the species A and B ($P_A + P_B = 1$), respectively, and τ is the mean lifetime. T_c and $\Delta\nu$ are the coalescence temperature and the chemical shift difference between A and B, respectively. X is obtained by the use of Eq. 3. The calculated values of the activation energy ($\Delta G_A^\ddagger$, $\Delta G_B^\ddagger$) for 1, 2, and 3 were all about 13 kcal/mol.

$$P_A - P_B = (X^2 - 2/3)^{3/2}/X \quad (3)$$

It is of interest to note that the ring A of the reduced amine compound (5) exists in the chair form (see Table 2). Thus, the twist-boat form of ring A in 1–3 was due mainly to the 3 α -amide group.

Experimental

Melting points were taken on a Yanagimoto micro melting point apparatus, and are uncorrected. Optical rotations were measured in CHCl_3 at 25°C . IR spectra were taken in CHCl_3 solution and are given in cm^{-1} . ^1H - and ^{13}C -NMR spectra were measured on JEOL JNM-GX400 and JEOL JNM-FX90Q spectrometers in CDCl_3 with tetramethylsilane as an internal standard, and chemical shifts are given in δ values. MS and HR-MS were measured with a JEOL D-300 at an ionization voltage of 70 eV.

Free energies of activation were obtained by substituting coalescence temperatures (T_c), chemical shifts differences at -50°C (223 K) ($\Delta\nu$), and their intensities (populations) (P_A , P_B) into the modified Eyring equation.⁶⁾

Isolation of Paxillarines A and B Dried whole plants (45 kg) of *Pachysandra axillaris*, collected in Yunnan Province, China, in October 1985, were cut into small pieces and extracted three times with boiling 95% ethanol. After concentration of the combined extracts, the residue was dissolved in 5% aqueous AcOH and the insoluble material was removed by filtration. The acidic solution was basified with 28% NH_4OH

and extracted thoroughly with CHCl_3 . The CHCl_3 solution was washed with H_2O , dried, and concentrated *in vacuo* to give a crude alkaloid mixture (928 g). This was dissolved in CHCl_3 (3 l) and shaken well with an equal volume of 3% HCl. The CHCl_3 layer was separated, and it was washed with water, dried, and concentrated *in vacuo* to give a weakly basic alkaloid fraction (560 g). This substance was extracted with acetone and the insoluble material was separated by filtration. Then, the acetone solution was concentrated *in vacuo* and the residue was repeatedly chromatographed over alumina with ether–benzene (1:9, 2:8, and 3:7) and MeOH– CHCl_3 (1:9) to give paxillarines A (1) (7.2 g) and B (2) (50 mg), together with 13 other compounds.²⁾

Paxillarine A (1) Colorless prisms (acetone), mp $263\text{--}265^\circ\text{C}$. IR: 3400 (OH), 1720 (ester), 1620 (amide). 400 MHz ^1H -NMR at 60°C : see Table 1. 400 MHz ^1H -NMR at -50°C , conformer A: 1.15 (s, 19- CH_3), 2.10 (s, COCH_3), 2.89 (s, NCH_3), 5.05 (ddd, $J = 11.0, 6.5, 3.5$ Hz, 3-CH), 5.40 (t, $J = 6.5$ Hz, 4-CH); conformer B: 0.64 (s, 19- CH_3), 2.03 (s, COCH_3), 3.05 (s, NCH_3), 4.02 (ddd, $J = 11.5, 6.5, 4.0$ Hz, 3-CH), 5.38 (t, $J = 6.5$ Hz, 4-CH). 100 MHz ^{13}C -NMR at 60°C : see Table 1. MS m/z (%): 538 (M^+ , 14), 523 (11), 521 (5), 494 (16), 434 (13), 255 (1), 174 (6, $\text{CH}_2=\text{CH}-\text{CH}=\text{N}^+(\text{CH}_3)-\text{COC}_6\text{H}_5$), 136 (12), 105 (26), 72 (100, $\text{CH}_3-\text{CH}=\text{N}^+(\text{CH}_3)_2$). HR-MS: Found 538.3805. Calcd for $\text{C}_{33}\text{H}_{50}\text{N}_2\text{O}_4$ (M^+): 538.3771. Anal. Found: C, 73.60; H, 9.37; N, 5.06. Calcd for $\text{C}_{33}\text{H}_{50}\text{N}_2\text{O}_4$: C, 73.61; H, 9.29; N, 5.20. $[\alpha]_D^{25} + 77.7^\circ$ ($c = 0.515$, CHCl_3).

Paxillarine B (2) Colorless prisms (acetone– CH_2Cl_2), mp $234\text{--}237^\circ\text{C}$. IR: 3410 (OH), 1725 (ester), 1620 (amide). 400 MHz ^1H -NMR at 60°C : see Table 1. 400 MHz ^1H -NMR at -50°C , conformer A: 1.15 (s, 19- CH_3), 2.10 (s, COCH_3), 2.90 (s, NCH_3), 5.02 (ddd, $J = 11.0, 6.5, 3.5$ Hz, 3-CH), 5.39 (t, $J = 6.5$ Hz, 4-CH); conformer B: 0.64 (s, 19- CH_3), 2.03 (s, COCH_3), 3.04 (s, NCH_3), 4.05 (ddd, $J = 11.5, 6.5, 4.0$ Hz, 3-CH), 5.38 (t, $J = 6.5$ Hz, 4-CH). 100 MHz ^{13}C -NMR at 60°C : see Table 1. MS m/z (%): 538 (M^+ , 3), 174 (7, $\text{CH}_2=\text{CH}-\text{CH}=\text{N}^+(\text{CH}_3)-\text{COC}_6\text{H}_5$), 136 (10), 105 (42), 72 (100, $\text{CH}_3-\text{CH}=\text{N}^+(\text{CH}_3)_2$). HR-MS: Found 538.3775. Calcd for $\text{C}_{33}\text{H}_{50}\text{N}_2\text{O}_4$ (M^+): 538.3771. $[\alpha]_D^{25} + 65.2^\circ$ ($c = 0.537$, CHCl_3).

Pachysandrine A (3) This compound was isolated from *P. terminalis*.⁴⁾ 400 MHz ^1H -NMR at 60°C : see Table 1. 400 MHz ^1H -NMR at -50°C , conformer A: 1.13 (s, 19- CH_3), 2.10 (s, COCH_3), 2.89 (s, NCH_3), 5.05 (ddd, $J = 11.0, 6.5, 3.5$ Hz, 3-CH), 5.40 (t, $J = 6.5$ Hz, 4-CH); conformer B: 0.63 (s, 19- CH_3), 2.03 (s, COCH_3), 3.05 (s, NCH_3), 4.03 (ddd, $J = 11.5, 6.5, 4.0$ Hz, 3-CH), 5.37 (t, $J = 6.5$ Hz, 4-CH). 100 MHz ^{13}C -NMR at 60°C : see Table 1.

O-Deacylpachysandrine A (3 α -*N*-Methylbenzoylamino-4 β -hydroxy-20 α -dimethylamino-5 α -pregnane) (4) 3 was hydrolyzed with 5% NaOH–MeOH to give 4, colorless needles (acetone), mp $194\text{--}195^\circ\text{C}$.⁴⁾ 400 MHz ^1H -NMR at -50°C : 0.67 (3H, s, 18- CH_3), 0.87 (3H, d, $J = 6.5$ Hz, 21- CH_3), 1.15 (3H, s, 19- CH_3), 2.18 (6H, s, $\text{N}(\text{CH}_3)_2$), 2.42 (1H, dq, $J = 10.0, 6.5$ Hz, 20-CH), 2.95 (3H, s, NCH_3), 3.94 (1H, t, $J = 5.0$ Hz, 4-CH), 4.60 (1H, ddd, $J = 10.5, 5.0, 3.5$ Hz, 3-CH), 7.43–7.49 (5H, Ph).

3 α -*N*-Methylbenzoylamino-4 β -hydroxy-20 α -dimethylamino-5 α -pregnane (5) 3 was reduced with LiAlH_4 in THF to give 5, colorless needles (acetone), mp $123\text{--}125^\circ\text{C}$.³⁾ 400 MHz ^1H -NMR at 27°C : 0.66 (3H, s, 18- CH_3), 0.93 (3H, d, $J = 6.0$ Hz, 21- CH_3), 1.06 (3H, s, 19- CH_3), 2.14 (3H, s, NCH_3), 2.16 (6H, s, $\text{N}(\text{CH}_3)_2$), 2.37 (1H, q, $J = 3.0$ Hz, 3-CH), 2.43 (1H, dq, $J = 11.0, 6.0$ Hz, 20-CH), 3.57 (2H, s, Ph-CH_2), 3.88 (1H, brs, 4-CH), 7.21–7.33 (5H, Ph).

Coalescence Temperatures of 1, 2, and 3 Paxillarine A (1): 3-CH: $P_A = 0.61$, $P_B = 0.39$, $T_c = 16^\circ\text{C}$; 4-OCOCH₃: $P_A = 0.62$, $P_B = 0.38$, $T_c = -11^\circ\text{C}$; 3-*N*-CH₃: $P_A = 0.62$, $P_B = 0.38$, $T_c = -6^\circ\text{C}$.

Paxillarine B (2): 3-CH: $P_A = 0.49$, $P_B = 0.51$, $T_c = 17^\circ\text{C}$; 4-OCOCH₃: $P_A = 0.50$, $P_B = 0.50$, $T_c = -8^\circ\text{C}$; 3-*N*-CH₃: $P_A = 0.50$, $P_B = 0.50$, $T_c = -5^\circ\text{C}$.

Pachysandrine A (3): 3-CH: $P_A=0.61$, $P_B=0.39$, $T_C=19^\circ\text{C}$; 4-OCOCH₃: $P_A=0.61$, $P_B=0.39$, $T_C=-11^\circ\text{C}$; 3-N-CH₃: $P_A=0.59$, $P_B=0.41$, $T_C=-2^\circ\text{C}$.

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