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Quinolizidines. XIV.[1] A Racemic Synthesis of 9-Demethyltubulosine, an Alkaloid Isolated from *Alangium vitiense*

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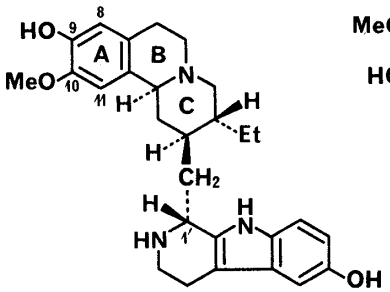
The first total synthesis of the *Alangium vitiense* alkaloid 9-demethyltubulosine (**1**) has been achieved in the form of a racemic modification through a "lactim ether route," which included the intermediates (±)-**7**, (±)-**8**, (±)-**10**, and (±)-**9**. The 1′α-H isomers (±)-**12** and (±)-**11** were also produced through this synthetic route. On the other hand, the nonconformity of synthetic (±)-**1** with another (−)-demethyltubulosine from *A. lamarckii* indicated the alternative 10-demethyl structure (**2**) to be correct for the *A. lamarckii* alkaloid. The assignments of the configuration at C-1′ of (±)-**1**, (±)-**9**, (±)-**11**, and (±)-**12** were based on four criteria, namely, the ratio of products from the catalytic reduction of (±)-**10**, thin-layer chromatographic mobility, and ^{1}H and ^{13}C nuclear magnetic resonance spectral features.

Keywords——*Alangium vitiense* alkaloid 9-demethyltubulosine; diethyl phosphorocyanidate amide formation; Bischler–Napieralski cyclization; carbon–nitrogen double-bond catalytic reduction; benzyl ether catalytic hydrogenolysis; TLC epimer differentiation; NMR epimer differentiation

It is known that twenty-two species of the genus *Alangium* constitute a monogeneric plant family, Alangiaceae.[2] Several of these species have been investigated chemically, and *A. lamarckii*, an Indian medicinal plant, was found to be a particularly rich source of a number of benzoquinolizidine alkaloids.[3] A new phenolic base designated as demethyltubulosine was among them,[4,5] and Popelak *et al.*[4] proposed two possible alternative structures (**1** and **2**) for this alkaloid on the basis of its two-step methylation to *O*-methyltubulosine (**4**) through tubulosine (**3**), as well as mass spectral evidence. Its structure has now been established as 10-



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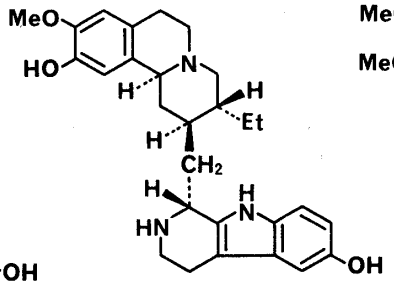

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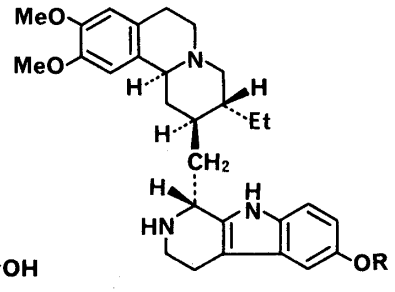

3: R=H
4: R=Me

demethyltubulosine (**2**) as a result of the syntheses of (±)-**1** and (±)-**2** by our group.[6,7] While the synthetic (±)-9-demethyltubulosine [(±)-**1**] did not match the *A. lamarckii* alkaloid, it was quite recently found to correspond to a new alkaloid isolated from another species of the same genus, *A. vitiense*.[8] Interestingly, this *A. vitiense* alkaloid has been reported to increase the survival time of mice infected with leukemia L1210 or P388.[8a] The present paper describes the details of the synthesis of (±)-**1**, which was accomplished through a "lactim ether

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route."[9] A brief account of the results reported here has been published in a preliminary form.[6]

The key intermediate generated in our synthetic plan was the racemic tricyclic amino acid (±)-**7**, which was prepared in eight steps from the *trans*-lactam ester (±)-**5** *via* the lactim ether (±)-**6** according to the previously reported procedure.[10] Condensation of (±)-**7** with 5-benzyloxytryptamine in *N*,*N*-dimethylformamide (DMF) by the diethyl phosphorocyanidate method[11] gave the amide (±)-**8** in 93% yield. The amide (±)-**8** was then cyclized with $POCl_3$ in boiling toluene to furnish the dihydro-β-carboline (±)-**10** in 69% yield. Catalytic

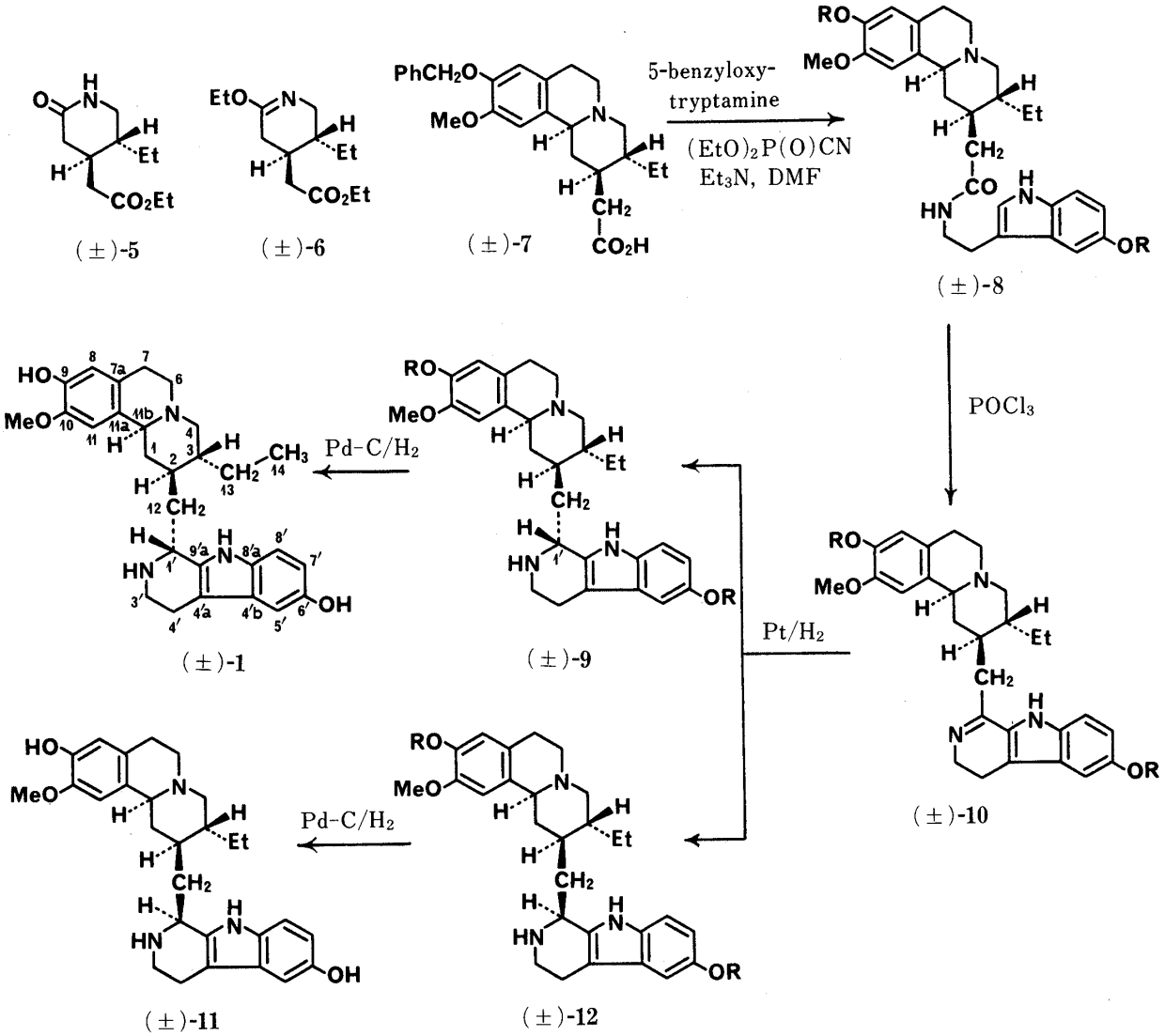

Chart 1

hydrogenation of this base in dioxane over Adams catalyst and chromatographic separation of the products afforded (±)-*O*,*O*-dibenzyl-9-demethyltubulosine [(±)-**9**] and its 1′-epimer [(±)-**12**] in 29% and 54% yields, respectively. On debenzylation using hydrogen and Pd–C catalyst, (±)-**9** produced the target molecule (±)-**1** (81% yield), which was characterized as a crystalline dihydrate. A similar debenzylation of the epimeric base (±)-**12** gave the corresponding phenolic base (±)-**11** in 86% yield.

The assignments of the configuration at C-1′ of (±)-**1**, (±)-**9**, (±)-**11**, and (±)-**12** were based on four criteria, namely, the ratio of the two C-1′ isomers formed, thin-layer

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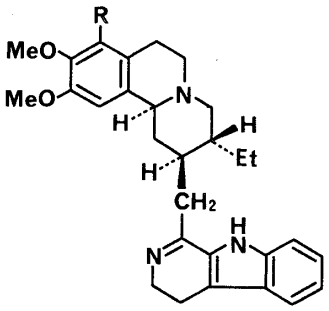
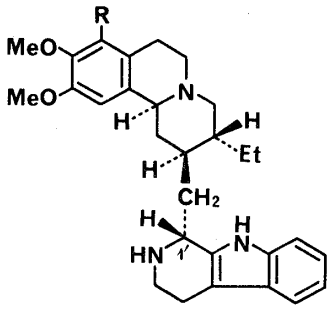
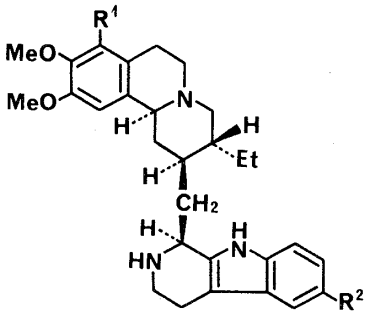
chromatographic (TLC) mobility, and ^{13}C nuclear magnetic resonance (^{13}C-NMR) and ^{1}H-NMR spectral features. As regards the first criterion, the formation of a 1 : 1.9 mixture of (±)-**9** and (±)-**12** in the above catalytic reduction of (±)-**10** is comparable to that[12] of a 1 : 2 mixture of deoxytubulosine (**15**) and isodeoxytubulosine (**18**) or to that[1] of a 1 : 1.9 mixture of *O*-benzylalangimarckine (**16**) and the 1′α-H isomer (±)-**20** in the analogous reduction of the dihydro-β-carboline **13** or **14**. As regards the second criterion, the TLC mobilities of (±)-**1** and (±)-**9** were found to be greater than those of their 1′-epimers (±)-**11** and (±)-**12**, respectively. This chromatographic behavior corresponds to that observed for the analogous 1′-epimeric pairs tubulosine (**3**)–isotubulosine (**19**),[13] emetine (**26**)–isoemetine (**27**),[1] **16**–**20**,[1] and alangimarckine (**17**)–**21**.[1]



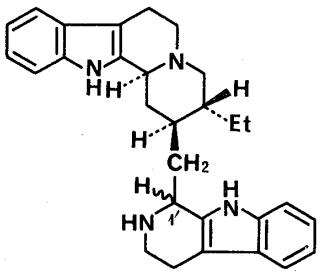
13 : R=H
14 : R=OCH_2Ph



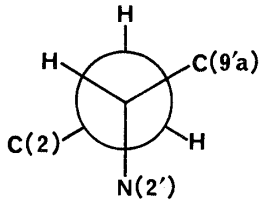
15 : R=H
16 : R=OCH_2Ph
17 : R=OH



18 : R^1=R^2=H
19 : R^1=H; R^2=OH
20 : R^1=OCH_2Ph; R^2=H
21 : R^1=OH; R^2=H



22 : 1′β-H
23 : 1′α-H



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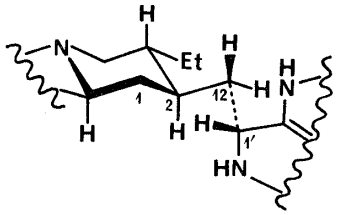

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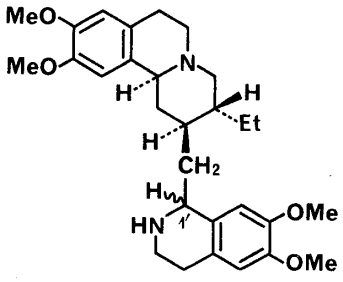
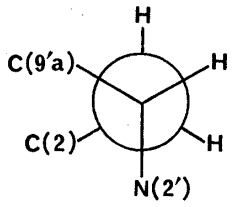


26 : 1′β-H
27 : 1′α-H



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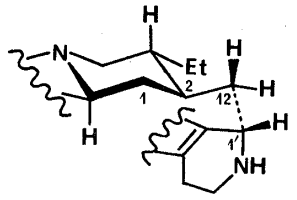

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As regards the third criterion (^{13}C-NMR), it may be seen from Table I that the C(1), C(2), and C(1′) carbon signals of (±)-**9** appeared upfield from the corresponding signals of the 1′-epimer (±)-**12** by 1.4—2.9 ppm, whereas the differences in chemical shift between the other corresponding carbons of the two isomers were insignificant. A similar feature has been found by Koch *et al.*[14] for ochrolifuanine A (**22**) and ochrolifuanine B (**23**), and they

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proposed a preferred conformation, as represented by the partial structure **25**, for the 1′β-H isomer **22**. We have observed the same trends for the isomeric pair emetine (**26**)–isoemetine (**27**) and utilized them successfully for differentiating alangimarckine (**17**) from its 1′-epimer (**21**).[1] The ^{13}C-NMR spectral features of (±)-**1** in Me_2SO-d_6 (Table I) also indicated the 1′β-H configuration to be correct for this phenolic base.

The fourth criterion employed for the stereochemical assignment was the ^{1}H-NMR spectral features, as shown in Table II and in the experimental section. It may be seen that the C(10)-methoxy protons of (±)-**12** and (±)-**11** resonated at higher field than did those of (±)-**9** and (±)-**1** by 0.29 and 0.22 ppm, respectively. Such a relationship has been found by

TABLE I. ^{13}C-NMR Data for (±)-9-Demethyltubulosine (**1**), (±)-*O*,*O*-Dibenzyl-9-demethyltubulosine (**9**), and the 1′α-H Isomer (±)-**12**

Carbon[b]	Chemical shift[a]			Carbon[b]	Chemical shift[a]		
	(±)-**1**[c]	(±)-**9**[d]	(±)-**12**[d]		(±)-**1**[c]	(±)-**9**[d]	(±)-**12**[d]
C(1)	36.5	36.9	38.3[i]	C(4′)	22.4	22.8	22.8
C(2)	35.9	36.5	37.9	C(4′a)	106.1	108.6	108.7
C(3)	—[e]	41.6	42.5	C(4′b)	127.8	127.9	128.0
C(4)	61.1	61.3	61.4	C(5′)	101.6	102.2	102.0
C(6)	52.0	52.4	52.6	C(6′)	150.0	153.2	153.2
C(7)	28.7	28.9	28.9	C(7′)	110.0	111.9	111.8
C(7a)	126.8	126.9	126.3	C(8′)	110.9	111.4	111.4
C(8)	115.2	114.4	114.3	C(8′a)	129.9	130.6	130.3
C(9)	144.7[f]	146.9[g]	146.6[j]	C(9′a)	138.3	137.2[h]	137.2[k]
C(10)	145.7[f]	147.9[g]	147.8[j]	10-OMe	56.1	56.6	56.0
C(11)	109.6	109.7	108.8	9-O$\underline{C}H_2$Ph	—	71.0	71.0
C(11a)	128.9	131.0	130.9	6′-O$\underline{C}H_2$Ph	—	71.0	71.0
C(11b)	62.2	62.5	62.7	O$\underline{C}H_2$Ph	—	137.7[h]	137.7[k]
C(12)	—[e]	38.6	38.6[i]		—	137.5[h]	137.4[k]
C(13)	23.0	23.5	23.9		—	128.4	128.4
C(14)	11.0	11.1	11.3		—	127.6	127.6
C(1′)	48.6	49.4	52.3		—	127.5	127.5
C(3′)	41.5	42.0	42.9		—	127.2	127.2

a) In ppm downfield from internal Me_4Si. *b*) See formula (±)-**1** in Chart 1 for the numbering system. The carbon(s) indicated by underscoring in the partial structures is that to which the signal has been assigned. *c*) Measured in Me_2SO-d_6. *d*) Measured in $CDCl_3$. *e*) Overlapped with the signals of the solvent, Me_2SO-d_6. *f*—*k*) Assignments indicated by a given superscript may be interchanged.

TABLE II. ^{1}H-NMR Data for (±)-*O*,*O*-Dibenzyl-9-demethyltubulosine (**9**) and Its 1′α-H Isomer (±)-**12** in $CDCl_3$

Proton[a]	Chemical shift (δ)		Proton[a]	Chemical shift (δ)	
	(±)-**9**	(±)-**12**		(±)-**9**	(±)-**12**
$CH_2\underline{Me}$	0.88 (t)[b]	0.94 (t)[b]	C(11)H	6.78 (s)	6.43 (s)
C(10)OMe	3.83 (s)	3.54 (s)	C(5′)H	7.03 (d)[f]	7.01 (d)[f]
C(1′)H	4.23 (d)[c]	4.18 (t)[d]	C(7′)H	6.86 (dd)[g]	6.85 (dd)[g]
C(9)OC$\underline{H}_2$Ph	5.10 (s)	5.06 (s)[e]	C(8′)H	7.19 (d)[h]	7.19 (d)[h]
C(6′)OC$\underline{H}_2$Ph	5.10 (s)	5.09 (s)[e]	O$\underline{CH}_2$Ph	7.2—7.5 (m)	7.2—7.5 (m)
C(8)H	6.60 (s)	6.55 (s)	N(9′)H	7.81 (s)	7.86 (s)

a) See formula (±)-**1** in Chart 1 for the numbering system. The protons indicated by underscoring in the partial structures are those to which the signal has been assigned. *b*) With J=6.6 Hz. *c*) With J=10.0 Hz. *d*) Indistinct triplet with J=5.0 Hz. *e*) Assignments indicated by this superscript may be reversed. *f*) With J=2.4 Hz. *g*) With J=8.8 and 2.4 Hz. *h*) With J=8.8 Hz.

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Popelak *et al.*[13] for isotubulosine (**19**) and tubulosine (**3**) and by us[1] for **21** and alangimarckine (**17**). The shielding of the C(10)-methoxy protons in these and the present cases may be explained by assuming a preferred conformation (type **29**) of the 1′α-H isomer in which the C(10)-methoxy group overhangs the indole moiety within the same molecule. This view is supported by the observation of an about 0.35-ppm upfield shift of the C(11)H proton signal of (±)-**12** or (±)-**11**, relative to that of (±)-**9** or (±)-**1**. It is of particular interest that the C(1′)H proton signal of the 1′β-H isomer (±)-**9** or (±)-**1** appeared as a doublet with $J=$ 10 Hz, whereas that of the 1′α-H isomer (±)-**12** or (±)-**11** appeared as a dull triplet with $J=$ 5.0 or 5.5 Hz. We have observed that in $CDCl_3$ the C(1′)H protons of the 1′β-H isomers emetine (**26**) and alangimarckine (**17**) also resonate as a doublet ($J=10.5$ Hz) at δ 4.16 and 4.27, respectively; those of the 1′α-H isomers isoemetine (**27**) and **21** appear as a dull triplet ($J=5.5$ Hz) at δ 4.10 and 4.22, respectively. The doublet pattern observed for the 1′β-H isomers may be explained by assuming a C(1′)–C(12) bond conformation close to that represented by the Newman projection formula **24**, whereas the triplet pattern of the 1′α-H isomers may be a reflection of a **28**-type conformer. Thus, the coupling pattern of the C(1′)H proton served as an additional diagnostic tool for the C(1′) stereochemistry. On the basis of the above discussions on the ^{13}C- and ^1H-NMR spectral data, we propose the preferred conformations **25** for the 1′β-H isomers and **29** for the 1′α-H isomers.

The synthetic sample of (±)-9-demethyltubulosine [(±)-**1**] described above was then compared directly with a natural sample[4] of (−)-demethyltubulosine isolated from *A. lamarckii*. Although the ultraviolet (UV) (in MeOH, 0.1 N aqueous NaOH, and 0.1 N aqueous HCl) and mass spectra of (±)-**1** were virtually identical with those of the natural sample, the ^1H-NMR spectra and TLC behavior of the two samples were not identical. Thus, the above results definitely exclude the structure **1** and indicate the alternative 10-demethyl structure (**2**) to be correct for the *A. lamarckii* alkaloid. This was subsequently confirmed by a racemic synthesis of **2** *via* a similar "lactim ether route";[7] the details will be published elsewhere shortly. On the other hand, it happened quite recently that our (±)-**1** was found to be identical, apart from the chiroptical properties and melting point, with a $C_{28}H_{35}N_3O_3$ alkaloid from *Alangium vitiense*.[8] Interestingly, the above synthesis of (±)-9-demethyltubulosine [(±)-**1**] thus turned out to have completed incidentally the racemic synthesis of the *A. vitiense* alkaloid demethyltubulosine instead of the *A. lamarckii* alkaloid demethyltubulosine, establishing the structure and relative stereochemistry of the former.

Experimental

General Notes——All melting points were determined with a Yamato MP-1 capillary melting point apparatus and are corrected. See ref. 10*b* for details of instrumentation and measurements. Microanalyses were performed by Mr. Y. Itatani and his associates at Kanazawa University. The following abbreviations are used: br=broad, d=doublet, dd=doublet-of-doublets, m=multiplet, q=quartet, s=singlet, sh=shoulder, t=triplet.

(±)-9-Benzyloxy-*N*-[2-(5-benzyloxy-1*H*-indol-3-yl)ethyl]-3α-ethyl-1,3,4,6,7,11bα-hexahydro-10-methoxy-2*H*-benzo[*a*]quinolizine-2β-acetamide [(±)-8]——Diethyl phosphorocyanidate[15] (587 mg, 3.6 mmol) and Et_3N (364 mg, 3.6 mmol) were successively added to a chilled, stirred solution of (±)-**7**·1/3EtOH[10] (765 mg, 1.8 mmol) and 5-benzyloxytryptamine[16] (719 mg, 2.7 mmol) in $HCONMe_2$ (10 ml). The mixture was stirred at room temperature for 6 h and extracted with $CHCl_3$ after addition of H_2O (20 ml). The $CHCl_3$ extracts were washed with H_2O, dried over anhydrous Na_2SO_4, and concentrated *in vacuo* to leave an orange glass. The glass was crystallized from AcOEt to give (±)-**8**·1/2AcOEt (1.18 g, 93%) as colorless fluffy needles. Recrystallization from AcOEt and drying over P_2O_5 at 2 mmHg and room temperature for 20 h yielded an analytical sample, mp 92.5—94 °C; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3490 and 3460 (NH's), 2820 and 2760 (*trans*-quinolizidine ring),[17] 1730 (AcOEt), 1659 (amide CO); ^1H-NMR ($CDCl_3$) δ: 0.88 (3H, t, $J=7$ Hz, $CH_2\underline{Me}$), 1.25 (1.5H, t, $J=7$ Hz, $AcOCH_2\underline{Me}$), 2.04 (1.5H, s, $\underline{Me}CO_2Et$), 3.77 (3H, s, OMe), 4.12 (1H, q, $J=7$ Hz, $AcOC\underline{H}_2Me$), 5.09 (4H, s, two $OC\underline{H}_2Ph$'s), 5.57 (1H, t, $J=5.5$ Hz, CONH), 6.61 (1H, s, $H_{(8)}$ or $H_{(11)}$), 6.70 (1H, s, $H_{(11)}$ or $H_{(8)}$), 6.91 (1H, dd, $J=8.8$ and 2.4 Hz, $H_{(6')}$), 6.94 (1H, d, $J=2.0$ Hz, $H_{(2')}$), 7.11 (1H, d, $J=2.4$ Hz, $H_{(4')}$), 7.20 (1H, d, $J=8.8$ Hz, $H_{(7')}$), 7.2—7.5 (10H, m, two $OCH_2\underline{Ph}$'s), 8.15 (1H, br, indole NH).[18] *Anal.* Calcd for $C_{42}H_{47}N_3O_4\cdot 1/2CH_3CO_2C_2H_5$: C, 75.29; H, 7.32; N, 5.99. Found: C, 75.54; H, 7.27; N, 6.20.

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(±)-9-Benzyloxy-2β-[(6-benzyloxy-4,9-dihydro-3*H*-pyrido[3,4-*b*]indol-1-yl)methyl]-3α-ethyl-1,3,4,6,7,11bα-hexahydro-10-methoxy-2*H*-benzo[*a*]quinolizine [(±)-10]——A solution of (±)-**8**·1/2AcOEt (1.12 g, 1.6 mmol) and $POCl_3$ (2.45 g, 16 mmol) in dry toluene (50 ml) was heated under reflux in an atmosphere of nitrogen for 2.5 h. The reaction mixture was concentrated *in vacuo*, and 5% aqueous KOH (40 ml) and CH_2Cl_2 (50 ml) were added to the oily residue under ice-cooling. The resulting mixture was stirred for 10 min, and the CH_2Cl_2 layer was separated from the aqueous layer, which was further extracted with CH_2Cl_2. The combined CH_2Cl_2 extracts were washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, and evaporated *in vacuo* to leave a brown glass. The glass was chromatographed on a silica gel column [benzene–EtOH (10 : 1, v/v)] to give (±)-**10** (704 mg, 69%) as a yellow glass, which crystallized from EtOH. Recrystallization from EtOH and drying over P_2O_5 at 2 mmHg and room temperature for 20 h furnished an analytical sample of (±)-**10**·$2H_2O$·EtOH as yellow minute needles, mp 105—106 °C; IR ν_{max}^{Nujol} cm^{-1}: 2770 (*trans*-quinolizidine ring);[17] ^{1}H-NMR ($CDCl_3$) δ: 0.93 (3H, t, J=7 Hz, CCH_2Me), 1.23 (3H, t, J=7 Hz, MeCH_2OH), 1.98 (H_2O), 3.51 (3H, s, OMe), 3.70 (2H, q, J=7 Hz, MeCH_2OH), 5.04 and 5.10 (2H each, s, two OCH_2Ph's), 6.40 (1H, s, $H_{(8)}$ or $H_{(11)}$), 6.55 (1H, s, $H_{(11)}$ or $H_{(8)}$), 6.9—7.5 (13H, m, $H_{(5')}$, $H_{(7')}$, $H_{(8')}$, and two OCH_2Ph's), 8.46 (1H, br, NH). *Anal.* Calcd for $C_{42}H_{45}N_3O_3\cdot 2H_2O\cdot C_2H_5OH$: C, 73.20; H, 7.68; N, 5.82. Found: C, 73.19; H, 7.48; N, 5.96.

[2*R-[2α(*S**),3β,11bβ]]- and [2*R**-[2α(*R**),3β,11bβ]]-9-Benzyloxy-2-[(6-benzyloxy-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-1-yl)methyl]-3-ethyl-1,3,4,6,7,11b-hexahydro-10-methoxy-2*H*-benzo[*a*]quinolizines [(±)-9 and (±)-12]**——A solution of (±)-**10**·$2H_2O$·EtOH (541 mg, 0.75 mmol) in dioxane (10 ml) was hydrogenated over Adams catalyst (80 mg) at atmospheric pressure and 29 °C for 40 min. Removal of the catalyst by filtration and evaporation of the filtrate under reduced pressure left a yellowish oil, which was dissolved in $CHCl_3$ (60 ml). The $CHCl_3$ solution was washed successively with 5% aqueous NaOH and saturated aqueous NaCl, dried over anhydrous Na_2SO_4, and concentrated *in vacuo* to leave a brown glass (470 mg). This material was then chromatographed on a silica gel column using $CHCl_3$–EtOH (10 : 1, v/v) as eluent. Earlier fractions afforded (±)-*O*,*O*-dibenzyl-9-demethyltubulosine [(±)-**9**] (140 mg, 29%) as a pale yellowish glass, TLC *Rf* 0.59 or 0.45 [silica gel, $CHCl_3$–EtOH (10 : 1, v/v) or benzene–EtOH (10 : 1, v/v)]; MS *m/e*: 641 (M^+); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3490 (indole NH), 3390 [N(2′)H], 2820 and 2760 (*trans*-quinolizidine ring);[17] ^{1}H-NMR (Table II); ^{13}C-NMR (Table I).

Later fractions in the above chromatography furnished the 1′α-H isomer (±)-**12** (262 mg, 54%) as a pale yellowish glass, TLC *Rf* 0.50 or 0.40 [silica gel, $CHCl_3$–EtOH (10 : 1, v/v) or benzene–EtOH (10 : 1, v/v)]; MS *m/e*: 641 (M^+); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3490 (indole NH), 3390 [N(2′)H], 2820 and 2760 (*trans*-quinolizidine ring);[17] ^{1}H-NMR (Table II); ^{13}C-NMR (Table I).

[2*R-[2α(*S**),3β,11bβ]]-3-Ethyl-1,3,4,6,7,11b-hexahydro-9-hydroxy-2-[(6-hydroxy-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-1-yl)methyl]-10-methoxy-2*H*-benzo[*a*]quinolizine [(±)-9-Demethyltubulosine] [(±)-1]**——A solution of (±)-**9** (120 mg, 0.19 mmol) in MeOH–AcOH (1 : 1, v/v) (10 ml) was hydrogenated over 10% Pd–C (120 mg) at atmospheric pressure and 27 °C for 3 h. The catalyst was removed by filtration and washed with MeOH (20 ml). The filtrate and washings were combined and concentrated *in vacuo*, and H_2O (3 ml) was added to the oily residue. The aqueous mixture was filtered and the filtrate was alkalified with 10% aqueous Na_2CO_3. The precipitate that resulted was filtered off, washed with H_2O, and dried to give (±)-**1**·$2H_2O$ (75 mg, 81%) as a pale yellowish solid, mp 212—214 °C (dec.). Recrystallization from MeOH–CH_2Cl_2 (1 : 3, v/v) and drying over P_2O_5 at 2 mmHg and room temperature for 20 h produced an analytical sample as colorless minute needles, mp 213—214 °C (dec.); TLC *Rf* 0.39 [silica gel, $CHCl_3$–MeOH (2 : 1, v/v)]; MS *m/e* (relative intensity): 462 (M^++1) (21), 461 (M^+) (75), 272 (20), 271 (22), 261 (28), 260 (30), 259 (31), 258 (86), 256 (36), 232 (51), 230 (41), 201 (59), 200 (39), 199 (44), 191 (39), 187 (100), 178 (42), 177 (31); UV λ_{max} (MeOH) 281.5 nm (ε 12800); λ_{max} (0.1 N aqueous NaOH) 282 (10800), 304 (sh) (8020), 326 (sh) (3940); λ_{max} (0.1 N aqueous HCl) 276.5 (11500); ^{1}H-NMR (Me_2SO-d_6) δ: 3.71 (3H, s, OMe), 4.15 (1H, d, J=10 Hz, $H_{(1')}$), 6.47 (1H, s, $H_{(8)}$), 6.49 (1H, dd, J=8.7 and 2.0 Hz, $H_{(7')}$), 6.66 (1H, d, J=2.0 Hz, $H_{(5')}$), 6.78 (1H, s, $H_{(11)}$), 7.03 (1H, d, J=8.7 Hz, $H_{(8')}$), 8.45, 8.68, and 10.25 (br, NH's and OH's); ^{13}C-NMR (Table I). *Anal.* Calcd for $C_{28}H_{35}N_3O_3\cdot 2H_2O$: C, 67.58; H, 7.90; N, 8.44. Found: C, 67.59; H, 7.68; N, 8.44. The spectral data and TLC mobility were identical with those of the $C_{28}H_{35}N_3O_3$ alkaloid [mp 200 °C; $[\alpha]_D^{20}$ −40° (c=1, pyridine)] isolated from *Alangium vitiense*.[8] On the other hand, the ^{1}H-NMR spectrum and TLC behavior of this (±)-**1** were not identical with those of (−)-demethyltubulosine[4] isolated from *A. lamarckii*.

[2*R-[2α(*R**),3β,11bβ]]-3-Ethyl-1,3,4,6,7,11b-hexahydro-9-hydroxy-2-[(6-hydroxy-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-1-yl)methyl]-10-methoxy-2*H*-benzo[*a*]quinolizine [(±)-11]**——Debenzylation of (±)-**12** and work-up of the reaction mixture were carried out as described above for (±)-**1**, producing (±)-**11** (86% yield) as a yellowish solid. Recrystallization of the solid from EtOH provided an analytical sample as colorless prisms, mp 235—236.5 °C (dec.); TLC *Rf* 0.27 [silica gel, $CHCl_3$–MeOH (2 : 1, v/v)]; MS *m/e*: 461 (M^+); UV λ_{max} (MeOH) 281.5 nm (ε 11900); λ_{max} (0.1 N aqueous NaOH) 282 (10300), 304 (sh) (7720), 326 (sh) (4300); λ_{max} (0.1 N aqueous HCl) 276.5 (10700); ^{1}H-NMR (Me_2SO-d_6) δ: 3.49 (3H, s, OMe), 4.18 (1H, dull t, J=5.5 Hz, $H_{(1')}$), 6.41 (1H, s, $H_{(8)}$ or $H_{(11)}$), 6.44 (1H, s, $H_{(11)}$ or $H_{(8)}$), 6.51 (1H, dd, J=8.5 and 2.0 Hz, $H_{(7')}$), 6.67 (1H, d, J=2.0 Hz, $H_{(5')}$), 7.07 (1H, d, J=8.5 Hz, $H_{(8')}$), 8.50, 8.61, and 10.41 (br, NH's and OH's). *Anal.* Calcd for $C_{28}H_{35}N_3O_3$: C, 72.86; H, 7.64; N, 9.10. Found: C, 73.00; H, 7.62; N, 8.93.

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