

# Quinolizidines. XV. A Racemic Synthesis of 10-Demethyltubulosine, an Alkaloid from *Alangium lamarckii*

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confirmed the correctness of the above indication. A brief account of the results described here has been published in a preliminary form.<sup>9)</sup>

The synthesis of the target molecule ( $\pm$ )-**2** proceeded from the *trans*-lactam ester ( $\pm$ )-**5** through a "lactim ether route,"<sup>10)</sup> which paralleled that employed for our recent synthesis<sup>1,7)</sup> of the 9-demethyl isomer ( $\pm$ )-**1**. The key intermediate was the tricyclic amino acid ( $\pm$ )-**7**, and it was obtained from ( $\pm$ )-**5** in eight steps *via* the lactim ether ( $\pm$ )-**6** according to the previously reported procedure.<sup>11)</sup> Application of the diethyl phosphorocyanidate method<sup>12)</sup> to the condensation of ( $\pm$ )-**7** with 5-benzyloxytryptamine in *N,N*-dimethylformamide (DMF)

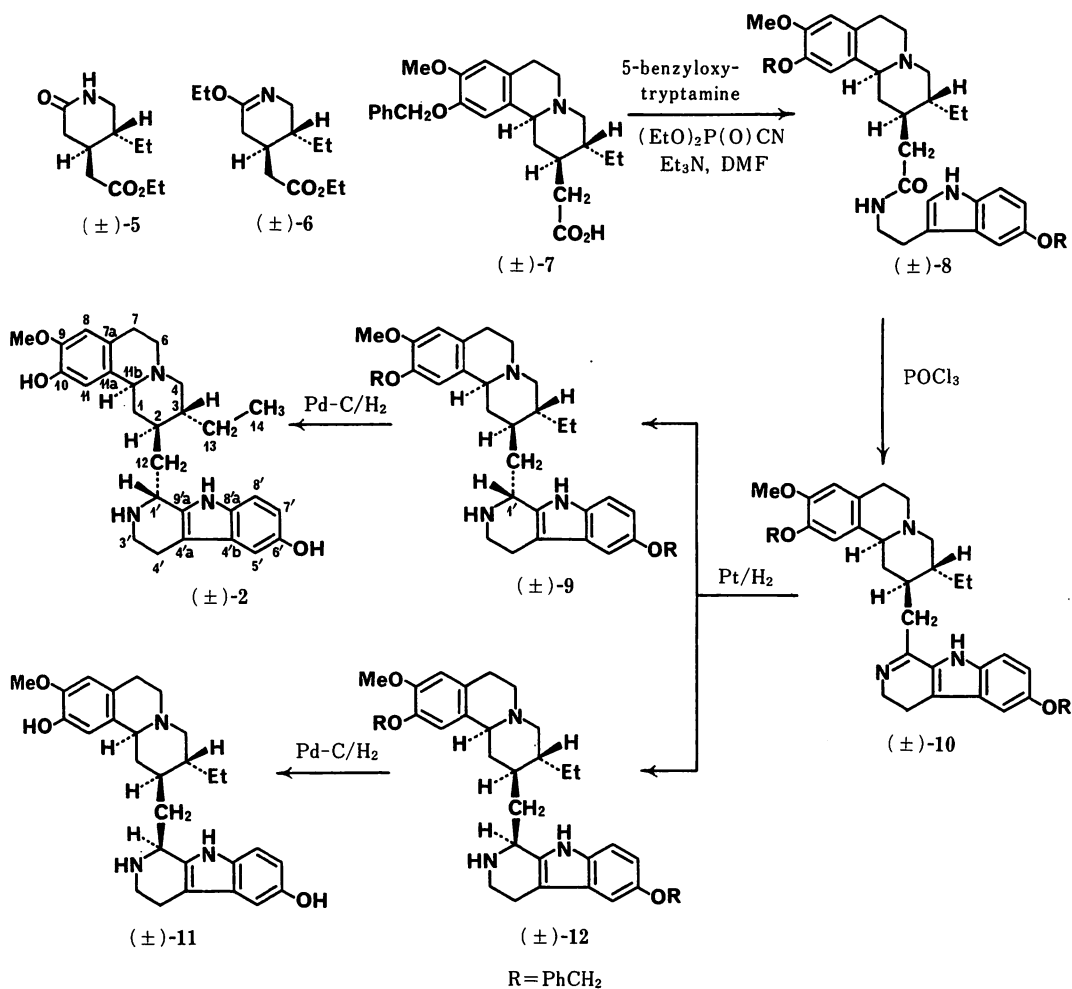


Chart 1

produced the amide ( $\pm$ )-**8** (96% yield), which was then cyclized with POCl<sub>3</sub> in boiling toluene to afford the dihydro- $\beta$ -carboline ( $\pm$ )-**10** in 59% yield. Catalytic hydrogenation of ( $\pm$ )-**10** in dioxane over Adams catalyst and subsequent chromatographic separation of the products gave ( $\pm$ )-*O,O*-dibenzyl-10-demethyltubulosine [( $\pm$ )-**9**] and its 1'-epimer [( $\pm$ )-**12**] in 25% and 54% yields, respectively.

The assignments of the relative configuration at C-1' of ( $\pm$ )-**9** and ( $\pm$ )-**12** were based on the following evidence. In the catalytic reduction of ( $\pm$ )-**10**, the formation of ( $\pm$ )-**12** predominated over that of ( $\pm$ )-**9** in a 2.2:1 molar ratio. On thin-layer chromatography

TABLE I.  $^{13}\text{C}$ -NMR Data for  $(\pm)$ -10-Demethyltubulosine (**2**),  $(\pm)$ -*O*, *O*-Dibenzyl-10-demethyltubulosine (**9**), and the  $1'\alpha$ -H Isomer  $(\pm)$ -**12**

Carbon <sup>b)</sup>	Chemical shift <sup>a)</sup>			Carbon <sup>b)</sup>	Chemical shift <sup>a)</sup>		
	$(\pm)$ - <b>2</b> <sup>c)</sup>	$(\pm)$ - <b>9</b> <sup>d)</sup>	$(\pm)$ - <b>12</b> <sup>d)</sup>		$(\pm)$ - <b>2</b> <sup>c)</sup>	$(\pm)$ - <b>9</b> <sup>d)</sup>	$(\pm)$ - <b>12</b> <sup>d)</sup>
C(1)	36.3	36.8	38.9 <sup>k)</sup>	C(4')	22.4	23.0	22.9
C(2)	35.8	36.3	38.4	C(4'a)	106.1	108.7	108.6
C(3)	— <sup>e)</sup>	41.8	42.7	C(4'b)	127.8	128.0	127.9
C(4)	61.1	61.3	61.4	C(5')	101.7	102.2	102.1
C(6)	52.1	52.5	52.5	C(6')	150.0	153.2	153.2
C(7)	28.8	29.2	29.1	C(7')	110.0	112.1 <sup>h)</sup>	111.9 <sup>l)</sup>
C(7a)	124.7	127.5	127.5	C(8')	110.9	111.3	111.4
C(8)	111.9 <sup>f)</sup>	111.9 <sup>h)</sup>	111.9 <sup>l)</sup>	C(8'a)	130.0	131.0	130.9
C(9)	144.2 <sup>g)</sup>	148.2 <sup>i)</sup>	148.2 <sup>m)</sup>	C(9'a)	138.3	137.5 <sup>j)</sup>	137.3 <sup>n)</sup>
C(10)	145.7 <sup>g)</sup>	146.1 <sup>i)</sup>	146.2 <sup>m)</sup>	9-OMe	55.5	56.0	55.9
C(11)	112.1 <sup>f)</sup>	112.3 <sup>h)</sup>	111.7 <sup>l)</sup>	10-OCH <sub>2</sub> Ph	—	71.7	71.5
C(11a)	130.5	130.2	129.8	6'-OCH <sub>2</sub> Ph	—	71.0	70.9
C(11b)	62.0	62.2	62.5	OCH <sub>2</sub> Ph	—	137.8 <sup>j)</sup>	137.7 <sup>m)</sup>
C(12)	— <sup>e)</sup>	38.7	39.2 <sup>k)</sup>		—	—	137.6 <sup>n)</sup>
C(13)	22.9	23.5	23.9		—	128.4	128.3
C(14)	11.0	11.1	11.3		—	127.6	127.6
C(1')	48.7	49.3	52.3		—	127.2	127.5
C(3')	41.6	42.2	42.6				

a) In ppm downfield from internal Me<sub>4</sub>Si. b) See formula  $(\pm)$ -**2** 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<sub>2</sub>SO-*d*<sub>6</sub>. d) Measured in CDCl<sub>3</sub>. e) Overlapped with the signals of the solvent, Me<sub>2</sub>SO-*d*<sub>6</sub>. f-n) Assignments indicated by a given superscript may be interchanged.

TABLE II.  $^1\text{H}$ -NMR Data for  $(\pm)$ -*O*, *O*-Dibenzyl-10-demethyltubulosine (**9**) and Its  $1'\alpha$ -H Isomer  $(\pm)$ -**12** in CDCl<sub>3</sub>

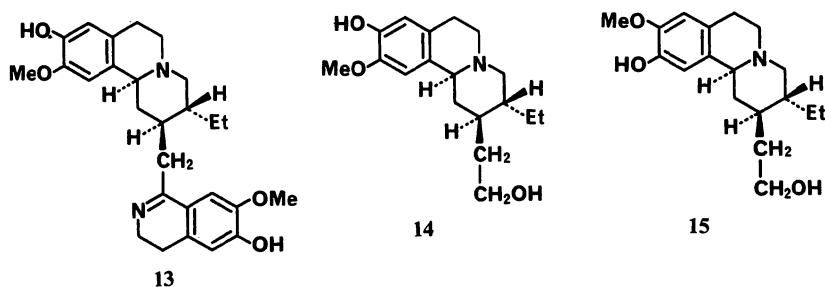
Proton <sup>a)</sup>	Chemical shift ( $\delta$ )		Proton <sup>a)</sup>	Chemical shift ( $\delta$ )	
	$(\pm)$ - <b>9</b>	$(\pm)$ - <b>12</b>		$(\pm)$ - <b>9</b>	$(\pm)$ - <b>12</b>
CH <sub>2</sub> Me	0.86 (t) <sup>b)</sup>	0.91 (t) <sup>e)</sup>	C(11)H	6.72 (s)	6.58 (s) <sup>f)</sup>
C(9)OMe	3.83 (s)	3.80 (s)	C(5')H	7.04 (d) <sup>g)</sup>	7.01 (d) <sup>h)</sup>
C(1')H	4.08 (d) <sup>d)</sup>	4.08 (t) <sup>e)</sup>	C(7')H	6.85 (dd) <sup>i)</sup>	6.82 (dd) <sup>j)</sup>
C(10)OCH <sub>2</sub> Ph	5.08 (s)	4.92 (s)	C(8')H	7.16 (d) <sup>k)</sup>	7.17 (d) <sup>l)</sup>
C(6')OCH <sub>2</sub> Ph	5.08 (s)	5.01 (s)	OCH <sub>2</sub> Ph	7.1—7.5 (m)	7.15—7.5 (m) <sup>l)</sup>
C(8)H	6.59 (s)	6.56 (s) <sup>f)</sup>	N(9')H	7.80 (s)	7.97 (s)

a) See formula  $(\pm)$ -**2** 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  $J=6.8$  Hz. c) With  $J=6.4$  Hz. d) With  $J=10.5$  Hz. e) Dull triplet with  $J=5.0$  Hz. f) Assignments indicated by this superscript may be reversed. g) With  $J=2.4$  Hz. h) With  $J=2.2$  Hz. i) With  $J=8.6$  and  $2.4$  Hz. j) With  $J=8.8$  and  $2.2$  Hz. k) With  $J=8.6$  Hz. l) With  $J=8.8$  Hz.

(TLC),  $(\pm)$ -**9** moved faster than  $(\pm)$ -**12**. In the  $^{13}\text{C}$  nuclear magnetic resonance ( $^{13}\text{C}$ -NMR) spectra in CDCl<sub>3</sub> (see Table I), the C(1), C(2), and C(1') carbon signals of  $(\pm)$ -**9** resonated at higher field than the corresponding carbon signals of  $(\pm)$ -**12** by 2.1—3.0 ppm. In the  $^1\text{H}$ -NMR spectra in CDCl<sub>3</sub> (see Table II), the methylene protons of the C(10)-benzyloxy group in  $(\pm)$ -**12** were more shielded than those in  $(\pm)$ -**9** by 0.16 ppm. A similar upfield shift of the C(11)H proton signal of  $(\pm)$ -**12**, relative to that of  $(\pm)$ -**9**, was also observed. Furthermore, the C(1')H proton signal of  $(\pm)$ -**9** appeared as a doublet with  $J=10.5$  Hz, whereas that of  $(\pm)$ -**12** appeared as a dull triplet with  $J=5.0$  Hz. These chemical, TLC, and  $^{13}\text{C}$ -NMR and

$^1\text{H-NMR}$  spectral features of ( $\pm$ )-**9** and ( $\pm$ )-**12** fulfilled all the recently reported<sup>1,13)</sup> criteria for the  $1'\beta\text{-H}$  and  $1'\alpha\text{-H}$  isomers, which had been shown to function satisfactorily in analogous ring systems.

On hydrogenolysis using hydrogen and Pd-C catalyst, ( $\pm$ )-**9** furnished the target molecule ( $\pm$ )-**2** (79% yield), which was characterized as a dihydrate, mp 199—201 °C (dec.). A similar debenzoylation of the epimeric base ( $\pm$ )-**12** afforded the corresponding phenolic base ( $\pm$ )-**11** in 88% yield. The ultraviolet (UV) (MeOH, 0.1 N aqueous NaOH, or 0.1 N aqueous HCl), infrared (IR) (Nujol),  $^1\text{H-NMR}$  (Me<sub>2</sub>SO-*d*<sub>6</sub>), and mass spectra and TLC mobility of the synthetic ( $\pm$ )-**2**·2H<sub>2</sub>O were found to be identical with those of natural (–)-demethyltubulosine dihydrate [mp 198—200 °C (dec.)].



Thus, the above results, together with the previous chemical correlation,<sup>5)</sup> establish the structure of the *Alangium lamarckii* alkaloid demethyltubulosine as 10-demethyltubulosine [**2** (absolute configuration shown)]. Interestingly, the positions of the methoxy and the hydroxy groups in ring A of this base are just the reverse of those of desmethylpsychotrine (**13**),<sup>6,11,14)</sup> a co-occurring alkaloid.<sup>6)</sup> However, this turned out to be not uncommon when Pakrashi and co-workers<sup>15)</sup> quite recently isolated from the seeds of *A. lamarckii* two new alkaloids inferred to be 9-demethylprotoemetinol (**14**) and 10-demethylprotoemetinol (**15**), the structure and stereochemistry of the latter having been confirmed by us *via* synthesis.<sup>16)</sup>

### Experimental

**General Notes**—All melting points were determined with a Yamato MP-1 capillary melting point apparatus and are corrected. See ref. 11*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.

( $\pm$ )-**10**-Benzyloxy-*N*-[2-(5-benzyloxy-1*H*-indol-3-yl)ethyl]-3 $\alpha$ -ethyl-1,3,4,6,7,11*b* $\alpha$ -hexahydro-9-methoxy-2*H*-benzo[*a*]quinolizine-2 $\beta$ -acetamide [( $\pm$ )-**8**]—Diethyl phosphorocyanidate<sup>17)</sup> (1.31 g, 8.03 mmol) and Et<sub>3</sub>N (810 mg, 8.00 mmol) were successively added to an ice-cooled, stirred solution of ( $\pm$ )-**7**·H<sub>2</sub>O<sup>11)</sup> (1.71 g, 4.00 mmol) and 5-benzyloxytryptamine<sup>18)</sup> (1.60 g, 6.01 mmol) in HCONMe<sub>2</sub> (20 ml). The mixture was stirred at room temperature for 6 h and extracted with CHCl<sub>3</sub> after addition of H<sub>2</sub>O (30 ml). The CHCl<sub>3</sub> extracts were combined, washed with H<sub>2</sub>O, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated *in vacuo* to leave an orange glass, which crystallized from AcOEt to afford ( $\pm$ )-**8** (2.53 g, 96%) as almost colorless, minute prisms, mp 148.5—150 °C. Recrystallization from AcOEt gave an analytical sample as colorless prisms, mp 150.5—152 °C; IR  $\nu_{\text{max}}^{\text{CHCl}_3}$  cm<sup>-1</sup>: 3490 and 3460 (NH's), 2820 and 2760 (*trans*-quinolizidine ring),<sup>19)</sup> 1658 (amide CO);  $^1\text{H-NMR}$  (CDCl<sub>3</sub>)  $\delta$ : 0.88 (3H, t, *J* = 6.6 Hz, CCH<sub>2</sub>Me), 3.84 (3H, s, OMe), 4.97 and 5.04 (2H, AB type d's, *J* = 11.6 Hz, OCH<sub>2</sub>Ph), 5.06 (2H, s, OCH<sub>2</sub>Ph), 5.53 (1H, t, *J* = 5.5 Hz, CONH), 6.60 (1H, s, H<sub>(8)</sub> or H<sub>(11)</sub>), 6.74 (1H, s, H<sub>(11)</sub> or H<sub>(8)</sub>), 6.88 (1H, dd, *J* = 8.6 and 2.2 Hz, H<sub>(6)</sub>), 6.90 (1H, d, *J* = 2.0 Hz, H<sub>(2)</sub>), 7.09 (1H, d, *J* = 2.2 Hz, H<sub>(4')</sub>), 7.11 (1H, d, *J* = 8.6 Hz, H<sub>(7')</sub>), 7.15—7.5 (10H, m, two OCH<sub>2</sub>Ph's), 8.18 (1H, br, indole NH).<sup>20)</sup> *Anal.* Calcd for C<sub>42</sub>H<sub>47</sub>N<sub>3</sub>O<sub>4</sub>: C, 76.68; H, 7.20; N, 6.39. Found: C, 76.54; H, 7.21; N, 6.41.

( $\pm$ )-**10**-Benzyloxy-2 $\beta$ -[(6-benzyloxy-4,9-dihydro-3*H*-pyrido[3,4-*b*]indol-1-yl)methyl]-3 $\alpha$ -ethyl-1,3,4,6,7,11*b* $\alpha$ -hexahydro-9-methoxy-2*H*-benzo[*a*]quinolizine [( $\pm$ )-**10**]—A solution of ( $\pm$ )-**8** (2.17 g, 3.3 mmol) and POCl<sub>3</sub> (5.06 g, 33 mmol) in dry toluene (100 ml) was heated under reflux in an atmosphere of nitrogen for 2.5 h. The reaction mixture was evaporated *in vacuo* to leave an orange gum, which was treated with a mixture of CH<sub>2</sub>Cl<sub>2</sub> (80 ml) and 5%

aqueous KOH (80 ml) under ice-cooling and stirring for 10 min. The  $\text{CH}_2\text{Cl}_2$  layer was separated from the aqueous layer, which was further extracted with  $\text{CH}_2\text{Cl}_2$ . The combined  $\text{CH}_2\text{Cl}_2$  extracts were washed with saturated aqueous NaCl, dried over anhydrous  $\text{Na}_2\text{SO}_4$ , and concentrated *in vacuo* to leave a dark orange glass. The glass was purified by means of column chromatography [silica gel (40 g), benzene-EtOH (10:1, v/v)] to furnish ( $\pm$ )-**10** (1.24 g, 59%) as a yellow glass, MS *m/e*: 639 ( $\text{M}^+$ ); IR  $\nu_{\text{max}}^{\text{CHCl}_3}$   $\text{cm}^{-1}$ : 3490 (NH), 2760 (*trans*-quinolizidine ring);  $^{19}\text{F}$ -NMR ( $\text{CDCl}_3$ )  $\delta$ : 0.92 (3H, t,  $J=6.6$  Hz,  $\text{CCH}_2\text{Me}$ ), 3.80 (3H, s, OMe), 4.82 and 5.03 (2H each, s, two  $\text{OCH}_2\text{Ph}$ 's), 6.48 (1H, s,  $\text{H}_{(8)}$  or  $\text{H}_{(11)}$ ), 6.54 (1H, s,  $\text{H}_{(11)}$  or  $\text{H}_{(8)}$ ), 6.9–7.5 (13H, m,  $\text{H}_{(5)}$ ,  $\text{H}_{(7)}$ ,  $\text{H}_{(8)}$ ), and two  $\text{OCH}_2\text{Ph}$ 's), 8.25 (1H, br, NH).

**[2R\*-[2 $\alpha$ (S\*),3 $\beta$ ,11b $\beta$ ]]- and [2R\*-[2 $\alpha$ (R\*),3 $\beta$ ,11b $\beta$ ]]-10-Benzoyloxy-2-[(6-benzoyloxy-2,3,4,9-tetrahydro-1H-pyrido[3,4-*b*]indol-1-yl)methyl]-3-ethyl-1,3,4,6,7,11b-hexahydro-9-methoxy-2H-benzo[*a*]quinolizines [( $\pm$ )-**9** and ( $\pm$ )-**12**]**—A solution of ( $\pm$ )-**10** (1.00 g, 1.56 mmol) in dioxane (25 ml) was hydrogenated over Adams catalyst (120 mg) at atmospheric pressure and 19°C for 1.5 h. Removal of the catalyst by filtration with the aid of EtOAc (30 ml) and concentration of the filtrate under reduced pressure left an orange oil, which was dissolved in  $\text{CHCl}_3$  (80 ml). The  $\text{CHCl}_3$  solution was washed successively with 5% aqueous NaOH and saturated aqueous NaCl, dried over anhydrous  $\text{Na}_2\text{SO}_4$ , and evaporated *in vacuo*, leaving a dark orange glass (995 mg). The glass was then chromatographed on a Merck Lobar column (LiChroprep Si 60) using  $\text{CHCl}_3$ -EtOH (10:1, v/v) as eluent. Earlier fractions yielded ( $\pm$ )-*O*,*O*-dibenzyl-10-demethyltubulosine [( $\pm$ )-**9**] (254 mg, 25%) as a pale yellow glass, TLC *Rf* 0.5 [silica gel,  $\text{CHCl}_3$ -EtOH (10:1, v/v)]; MS *m/e*: 641 ( $\text{M}^+$ ); IR  $\nu_{\text{max}}^{\text{CHCl}_3}$   $\text{cm}^{-1}$ : 3490 (indole NH), 3390 [ $\text{N}(2')\text{H}$ ], 2820 and 2760 (*trans*-quinolizidine ring);  $^{19}\text{F}$ -NMR (Table II);  $^{13}\text{C}$ -NMR (Table I). This sample crystallized from EtOH, and further recrystallizations from EtOH and drying over  $\text{P}_2\text{O}_5$  at 2 mmHg and 40°C for 18 h produced an analytical sample of ( $\pm$ )-**9** · 1/2EtOH as colorless needles, mp 89–91°C; IR  $\nu_{\text{max}}^{\text{Nujol}}$   $\text{cm}^{-1}$ : 2760 (*trans*-quinolizidine ring);  $^{19}\text{F}$ -NMR ( $\text{CDCl}_3$ )  $\delta$ : 0.88 (3H, t,  $J=6.8$  Hz,  $\text{CCH}_2\text{Me}$ ), 1.23 (1.5H, t,  $J=7.1$  Hz,  $\text{MeCH}_2\text{OH}$ ), 3.71 (1H, q,  $J=7.1$  Hz,  $\text{MeCH}_2\text{OH}$ ), 3.86 (3H, s, OMe), 4.11 (1H, d,  $J=10.5$  Hz,  $\text{H}_{(1)}$ ), 5.11 (4H, s, two  $\text{OCH}_2\text{Ph}$ 's), 6.60 (1H, s,  $\text{H}_{(8)}$ ), 6.71 (1H, s,  $\text{H}_{(11)}$ ), 6.88 (1H, dd,  $J=8.8$  and 2.4 Hz,  $\text{H}_{(7)}$ ), 7.05 (1H, d,  $J=2.4$  Hz,  $\text{H}_{(5)}$ ), 7.22 (1H, d,  $J=8.8$  Hz,  $\text{H}_{(8)}$ ), 7.1–7.5 (10H, m, two  $\text{OCH}_2\text{Ph}$ 's), 7.57 (1H, br, NH). *Anal.* Calcd for  $\text{C}_{42}\text{H}_{47}\text{N}_3\text{O}_3 \cdot 1/2\text{C}_2\text{H}_5\text{OH}$ : C, 77.68; H, 7.58; N, 6.32. Found: C, 77.53; H, 7.42; N, 6.53.

Later fractions obtained from the above chromatography gave the 1' $\alpha$ -H isomer ( $\pm$ )-**12** (541 mg, 54%) as a yellow glass, TLC *Rf* 0.48 [silica gel,  $\text{CHCl}_3$ -EtOH (10:1, v/v)]; MS *m/e*: 641 ( $\text{M}^+$ ); IR  $\nu_{\text{max}}^{\text{CHCl}_3}$   $\text{cm}^{-1}$ : 3490 (indole NH), 3390 [ $\text{N}(2')\text{H}$ ], 2820 and 2760 (*trans*-quinolizidine ring);  $^{19}\text{F}$ -NMR (Table II);  $^{13}\text{C}$ -NMR (Table I).

**[2R\*-[2 $\alpha$ (S\*),3 $\beta$ ,11b $\beta$ ]]-3-Ethyl-1,3,4,6,7,11b-hexahydro-10-hydroxy-2-[(6-hydroxy-2,3,4,9-tetrahydro-1H-pyrido[3,4-*b*]indol-1-yl)methyl]-9-methoxy-2H-benzo[*a*]quinolizines [( $\pm$ )-**10**-Demethyltubulosine] [( $\pm$ )-**2**]**—A solution of ( $\pm$ )-**9** · 1/2EtOH (166 mg, 0.25 mmol) in MeOH-AcOH (1:1, v/v) (12 ml) was hydrogenated over 10% Pd-C (160 mg) at atmospheric pressure and 18°C for 3 h. The catalyst was removed by filtration and washed with MeOH (15 ml). The filtrate and washings were combined and concentrated *in vacuo*, and  $\text{H}_2\text{O}$  (3 ml) was added to the oily residue. The aqueous mixture was filtered and the filtrate was made alkaline with 10% aqueous  $\text{Na}_2\text{CO}_3$ . The crystals that resulted were filtered off, washed with  $\text{H}_2\text{O}$ , and dried to yield ( $\pm$ )-**2** · 2H $_2\text{O}$  (98 mg, 79%). Recrystallization from MeOH- $\text{CH}_2\text{Cl}_2$  (1:1, v/v) and drying over  $\text{P}_2\text{O}_5$  at 2 mmHg and room temperature for 18 h gave an analytical sample as colorless minute needles, mp 199–201°C (dec.); TLC *Rf* 0.46 [silica gel,  $\text{CHCl}_3$ -MeOH (2:1, v/v)]; MS *m/e* (relative intensity): 461 ( $\text{M}^+$ ) (65), 261 (27), 260 (39), 259 (30), 258 (78), 256 (38), 232 (63), 230 (41), 201 (93), 200 (57), 199 (59), 198 (27), 191 (36), 187 (100), 185 (27), 178 (41), 177 (33), 176 (42); UV  $\lambda_{\text{max}}$  (MeOH): 281 nm ( $\epsilon$  12500);  $\lambda_{\text{max}}$  (0.1 N aqueous NaOH): 283 (10500), 304 (sh) (8920), 327 (sh) (3740);  $\lambda_{\text{max}}$  (0.1 N aqueous HCl): 277.5 (11800);  $^1\text{H}$ -NMR ( $\text{Me}_2\text{SO}-d_6$ )  $\delta$ : 3.72 (3H, s, OMe), 4.10 (1H, d,  $J=9.8$  Hz,  $\text{H}_{(1)}$ ), 6.50 (1H, dd,  $J=8.5$  and 2.2 Hz,  $\text{H}_{(7)}$ ), 6.59 (1H, s,  $\text{H}_{(8)}$ ), 6.66 (1H, d,  $J=2.2$  Hz,  $\text{H}_{(5)}$ ), 6.72 (1H, s,  $\text{H}_{(11)}$ ), 7.03 (1H, d,  $J=8.5$  Hz,  $\text{H}_{(8)}$ ), 8.47 (1H, br, indole NH), 10.28 [1H, s,  $\text{N}(2')\text{H}$ ];  $^{13}\text{C}$ -NMR (Table I). *Anal.* Calcd for  $\text{C}_{28}\text{H}_{35}\text{N}_3\text{O}_3 \cdot 2\text{H}_2\text{O}$ : C, 67.58; H, 7.90; N, 8.44. Found: C, 67.42; H, 7.67; N, 8.36. The TLC mobility and mass, UV, IR (Nujol), and  $^1\text{H}$ -NMR spectra of this sample were identical with those of the *Alangium lamarckii* alkaloid (–)-demethyltubulosine dihydrate<sup>5</sup> [mp 198–200°C (dec.);  $[\alpha]_{\text{D}}^{23}$  –51.9° ( $c=1$ , pyridine)].

**[2R\*-[2 $\alpha$ (R\*),3 $\beta$ ,11b $\beta$ ]]-3-Ethyl-1,3,4,6,7,11b-hexahydro-10-hydroxy-2-[(6-hydroxy-2,3,4,9-tetrahydro-1H-pyrido[3,4-*b*]indol-1-yl)methyl]-9-methoxy-2H-benzo[*a*]quinolizines [( $\pm$ )-**11**]**—Debenzylation of ( $\pm$ )-**12** and work-up of the reaction mixture were effected in a manner similar to that described above for ( $\pm$ )-**2**, giving ( $\pm$ )-**11** (88% yield) as a pale brown solid. Recrystallization of the solid from EtOH and drying over  $\text{P}_2\text{O}_5$  at 2 mmHg and 50°C for 15 h produced an analytical sample as colorless minute prisms, mp 215–217°C (dec.); TLC *Rf* 0.31 [silica gel,  $\text{CHCl}_3$ -MeOH (2:1, v/v)]; MS *m/e*: 461 ( $\text{M}^+$ ); UV  $\lambda_{\text{max}}$  (MeOH): 278 nm ( $\epsilon$  11900);  $\lambda_{\text{max}}$  (0.1 N aqueous NaOH): 284 (10200), 304 (sh) (8520), 327 (sh) (3530);  $\lambda_{\text{max}}$  (0.1 N aqueous HCl): 277.5 (10800);  $^1\text{H}$ -NMR ( $\text{Me}_2\text{SO}-d_6$ )  $\delta$ : 3.71 (3H, s, OMe), 3.94 (1H, dull t,  $J=5$  Hz,  $\text{H}_{(1)}$ ), 6.51 (1H, dd,  $J=8.5$  and 2.4 Hz,  $\text{H}_{(7)}$ ), 6.56 (1H, s,  $\text{H}_{(8)}$  or  $\text{H}_{(11)}$ ), 6.64 (1H, s,  $\text{H}_{(11)}$  or  $\text{H}_{(8)}$ ), 6.66 (1H, d,  $J=2.4$  Hz,  $\text{H}_{(5)}$ ), 7.07 (1H, d,  $J=8.5$  Hz,  $\text{H}_{(8)}$ ), 8.46 (1H, br, indole NH), 10.31 [1H, s,  $\text{N}(2')\text{H}$ ]. *Anal.* Calcd for  $\text{C}_{28}\text{H}_{35}\text{N}_3\text{O}_3 \cdot 2/3\text{H}_2\text{O}$ : C, 71.01; H, 7.73; N, 8.87. Found: C, 70.84; H, 7.48; N, 8.60.

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