Phytochemistry, Vol. 29, No. 11, pp. 3547–3552, 1990
Printed in Great Britain.

0031-9422/90 $3.00+0.00

ALKALOIDS FROM THE LEAVES OF *ALSTONIA SCHOLARIS* IN TAIWAN, THAILAND, INDONESIA AND THE PHILIPPINES*

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(*Received* 6 *March* 1990)

Key Word Index—*Alstonia scholaris*; Apocynaceae; leaves; indole alkaloid; 19-epischolaricine; N^a-methylburnamine; N^b-methylscholaricine; vallesamine N^b-oxide.

Abstract—From the leaves of *Alstonia scholaris*, collected in Taiwan, Thailand, Indonesia and Philippines, several new alkaloids, 19-epischolaricine, N^b-methylscholaricine, N^a-methylburnamine and vallesamine N^b-oxide were isolated and their structures determined by spectral and chemical methods. The leaves of plants from Taiwan and Thailand showed similar alkaloid patterns, with picrinine, nareline and alschomine as the major alkaloids. The leaves of plants from Indonesia and Philippines showed different patterns from those of plants from Taiwan or Thailand, and contained mainly angustilobine B group. Picraline and its homologues were obtained from the leaves of Indonesian plants.

INTRODUCTION

Alstonia scholaris R. Br. is a tall tree grown in southeast Asia and south Asia. The barks have been used widely for the remedy of malaria and diarrhoea. In the preceding paper of this series, we described new alkaloids, alschomine and isoalschomine [1], along with known alkaloids, picrinine [2], picralinal [3] and nareline [4], from the leaves cultivated in Taiwan. We also described new alkaloids lagunamine (19-hydroxytubotaiwine), angustilobine B acid and losbanine (6,7-*seco*-6-norangustilobine B) [5], together with known alkaloids, tubotaiwine [6] and 6,7-secoangustilobine B [7] from the leaves of The Philippines plants. Due to the remarkable difference of the alkaloidal patterns between the leaves from Taiwan and The Philippines, a further investigation was attempted on the leaves collected in southeast Asian countries: Taiwan, Thailand, Indonesia and The Philippines. This paper deals with the structure determinations of new alkaloids, including 19-epischolaricine (**1**), N^b-methylscholaricine (**3**), N^a-methylburnamine (**4**), vallesamine N^b-oxide (**6**) and 6,7-*seco*-19,20-epoxyangustilobine B (**8**), and discussion on the alkaloidal pattern in each sample.

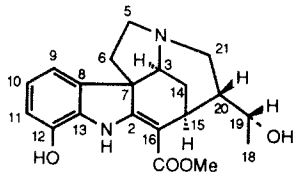
RESULTS

Alkaloids isolated from the leaves are listed in Table 1. Known alkaloids were identified based on the ^{1}H NMR and ^{13}C NMR spectra including ^{1}H–^{1}H and ^{13}C–^{1}H COSY, 2D-NOESY and differential NOE measurements, and EI and FAB mass spectrometry.

19-Epischolaricine (**1**) was isolated from the polar fraction of the leaves collected in Taiwan. A molecular formula, $C_{20}H_{24}N_2O_4$, calculated from an $[M+1]^+$ peak at m/z 357.182 was the same as that of scholaricine (**2**) [8], which was isolated from the leaves of plants from Thailand and Indonesia. In the ^{1}H NMR spectrum of **1**, the signals due to three phenyl protons located on the vicinal carbons, one carbomethoxyl and one secondary methyl groups were observed as in **2**, and the coupling constants of all the signals were in good agreement with those of compound **2**. The sequence from H-3 to H-21 through H-14, H-15 and H-20, was established based on the ^{1}H–^{1}H COSY spectrum. The linkage of two methylene groups (δ2.96, 3.23 and 2.02, 2.42) was assignable to H-5a,b and H-6a,b located between N^b and C-7. Because alkaloids **1** and **2** afforded the same CD spectra as those of akuammicine [9] and alstogustine [10], the configurations at C-15 in **1** and **2** were assigned to be *S*.

In the differential NOE experiment of 1-acetate (**1a**) prepared by usual acetylation, a NOE was observed between H-3 and H-9, suggesting the phenolic hydroxyl group in compound **1** to be located at C-12 (Fig 1). Based on the NOE between axial protons of H-14 and H-21, the piperidine ring of **1** appeared to retain a boat conformation as observed in the structure of alstogustine [10]. As H-20 was observed as a multiplet at δ2.10 in the spectrum of **1a**, orientation of H-20 was assigned to be β (axial). H-14, H-15, H-20 and H-21 showed the same coupling patterns in the spectra of compounds **1** and **2**, suggesting the same configurations at C-20 in the two alkaloids. Due to the evidence described above, compounds **1** and **2** were considered to be the stereoisomers at C-19, although their R_f values on TLC showed a large difference with each other.

*Part 3 in the series '*Alstonia*'. For Part 2, see ref. [5].
†Author to whom correspondence should be addressed.



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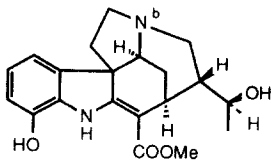
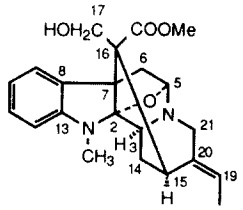


2
3 N^b-CH_3



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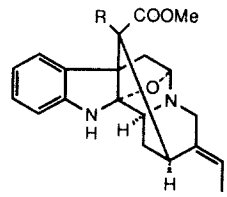
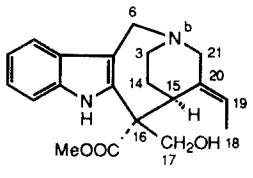
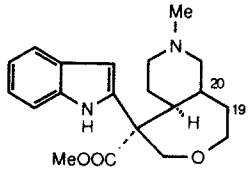


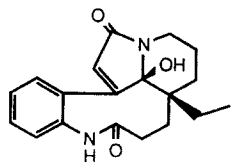
5 R=CH_2OCOCH_3
9 R=H



6 N^b-oxide
7



8 19,20-α-epoxy
10 Δ^{19}



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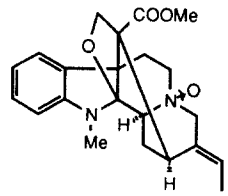


12

Table 1. Yields (mg kg^{-1}) of the alkaloids from the air-dried leaves of *A. scholaris* collected in Taiwan, Thailand, Indonesia and The Philippines

	Taiwan	Thailand	Indonesia	Philippines
Tubotaiwine		7		21
Tubotaiwine N^b-oxide				15
Lagunamine				40
19-Epischolaricine (**1**)	10			
Scholaricine (2)		33	21	
N^b-Methylscholaricine (**3**)			6	
Picrinine (**9**)	535	25		
Picrarinal	(+)			
Alschomine	15	15		
Isoalschomine	8	10		
Nareline	20	20		
φ-Akuammigine			10	
φ-Akuammigine N^b-oxide (**12**)			24	
Akuammidine			21	
N^a-Methylburnamine (**4**)			5	
Picraline (**5**)			7	
Angustilobine B acid				43
6,7-*seco*-Angustilobine B (**10**)	5		25	60
Losbanine				14
Vallesamine N^b-oxide (**6**)			23	
Vallesamine (**7**)	(+)	6	33	
6,7-*seco*-19,20-Epoxy angustilobine B (**8**)			14	
Leuconolam (**11**)			22	

In order to confirm the structures, alkaloids **1** and **2** were subjected to Swern oxidation [11], and **1** and **2** afforded the identical carbonyl compounds. The configurations at C-19 were assigned as 19*R* in **1** and 19*S* in **2** by comparison of the ^{13}C NMR signals with those of alstogustine (19*R*) and 19-epialstogustine (19*S*) [10].

Alkaloid **3** was isolated from the leaves collected in Indonesia along with 11 alkaloids, including **4**, picraline (**5**) [12], **6**, vallesamine (**7**) [13], 6,7-*seco*-19,20-epoxyangustilobine B (**8**) [7] and other known alkaloids. The molecular formula of **3** was suggested to be $C_{21}H_{27}N_2O_4$ based on an $[M+1]^+$ peak at *m/z* 372.207. Three phenolic protons due to an indole moiety and a 3H doublet signal ($J=6$ Hz) assignable to the 18-Me group were observed and the coupling patterns of the signals were the same as those of **2**, except for one 3H singlet signal at

Table 2. ^{1}H Chemical shifts of the compounds **1**, **1a**, **2–6** and **8** [δ(ppm) in $CDCl_3$ unless otherwise mentioned (400 MHz, TMS as int. standard)]

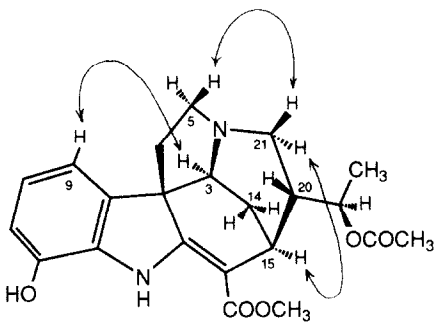
H	1*	1a	2*	3†	4	5	6	8
3	4.15 *br s*	4.08 *br s*	3.96 *br s*	4.50 *br s*	3.76 *br s*	3.60 *br s*	3.40–3.54	1.95 *td* (12, 3) 2.84 *bd* (12)
5	2.96 *m* 3.23 *m*	2.99 *m* 3.25 *m*	2.94 *m* 3.08 *m*	3.71 *dd* (12, 8) 3.80 *m*	4.71 *d* (2)	4.74 *d* (2)		
6	2.02 *m* 2.42 *m*	2.04 *m* 2.30 *m*	1.87 *m* 2.73 *m*	2.08–2.22 3.01 *m*	2.35 *dd* (14, 2) 3.31 *d* (14)	2.44 *dd* (14, 2) 3.21 *d* (14)	4.87 *d* (16) 5.27 *d*)16)	2.27 *s*
7								6.19 *s*
9	6.92 *d* (8)	6.79 *d* (8)	6.92 *d* (8)	7.00 *d* (7)	7.30 *d* (8)	7.41 *d* (7)	7.55 *d* (7)	7.52 *d* (8)
10	6.96 *t* (8)	6.76 *t* (8)	7.00 *t* (8)	6.86 *t* (7)	6.82 *t* (8)	6.81 *t* (7)	7.04 *t* (7)	7.17 *t* (8)
11	7.07 *d* (8)	6.69 *d* (8)	7.08 *d* (8)	6.67 *d* (7)	7.18 *t* (8)	7.03 *t* (7)	7.16 *t* (7)	7.08 *t* (8)
12					6.67 *d* (8)	6.71 *d* (7)	7.25 *d* (7)	7.33 *d* (8)
14	2.47 *br d* (13) 1.19 *dt* (13, 3)	2.21 *br d* (13) 1.21 *dt* (13, 3)	2.01 *br d* (13) 1.34 *dt* (13, 3)	1.59 *br d* (15) 2.34 *dt* (15, 1)	1.97 *m*	1.99 *m*	2.16 *m* 2.34 *m*	1.17 *m* 1.60 *m*
15	3.52 *br s*	3.10 *br s*	3.54 *br s*	3.55 *br s*	3.47 *br s*	3.30 *br s*	3.67 *dd* (12, 3)	3.17 *br d* (13)
17					3.46 *d* (12) 3.67 *d* (12)	3.89 *d* (12) 4.53 *d* (12)	3.87 *d* (10) 4.28 *d* (10)	3.73 *d* (12) 4.76 *dd* (12, 1)
18	1.42 *d* (6)	1.29 *d* (6)	1.24 *d* (6)	1.20 *d* (6)	1.57 *dd* (7, 2)	1.59 *dd* (7, 2)	1.69 *d* (6)	3.95 *d* (14) 4.37 *dd* (14, 3)
19	3.97 *m*	4.90 *m*	3.43 *m*	3.47 *m*	5.35 *qd* (7, 2)	5.39 *q* (7)	5.51 *q* (6)	2.95 *d* (3)
20	2.02 *m*	2.10 *m*	1.87 *m*	2.08–2.22				
21	3.36 *dd* (14, 11) 2.72 *dd* (14, 6)	3.03 *dd* (14, 11) 2.67 *dd* (14, 7)	1.98 *dd* (13, 11) 3.01 *dd* (13, 6)	3.24 *t* (14) 3.38 *dd* (14, 5)	3.12 *br d* (18) 3.82 *dt* (18, 2)	3.11 *br d* (18) 3.79 *dd* (18, 2)	3.84 *d* (15) 4.56 *d* (15)	2.32 *dd* (10, 1) 2.58 *br d* (10)
CO_2Me	3.64 *s*	3.78 *s*	3.66 *s*	3.88 *s*	3.75 *s*	3.68 *s*	3.71 *s*	3.78 *s*
others	9.27 s (NH)	2.08 *s* (OAc)	8.58 *s* (NH)	3.46 *s* (N^+Me)	2.94 *s* (NMe)	1.52 *s* (OAc)	10.93 *s* (NH)	8.36 *s*

*Dissolved in pyridine-d_5.
†Dissolved in methanol-d_4.

Table 3. ^{13}C Chemical shifts of compounds **1–7** and **8** [δ(ppm) in $CDCl_3$ unless otherwise mentioned (100 MHz, TMS as int. standard)]

C	1*†	2*†	3‡	4	5	6*	7	8*
2	168.5[a]	172.7	170.0	109.2	106.9	134.5[a]	134.6[a]	134.1[a]
3	60.2	61.5	73.3	49.4	51.6	64.6	47.3	56.3
5	54.4	54.4	65.5	86.8	87.1			
6	46.6	44.1	41.4	44.8	44.4	69.5	50.5	45.6
7	59.5	58.5	57.6	52.4	52.9	104.0	104.4	100.6
8	138.2	138.1	135.9	132.9[a]	133.7[a]	127.9[b]	127.9	127.8
9	112.3	111.4	113.2	115.8	127.9[b]	117.6	118.1	120.4
10	122.3	122.7	124.9	120.6[b]	120.9[c]	119.8	119.2	120.1
11	115.8	115.6	118.4	128.5	127.6[b]	122.6	122.4	122.4
12	143.1	143.1	144.1	109.2	111.1	111.1	110.7	111.0
13	132.9	132.7	133.1	151.4	148.3	135.0[a]	135.2[a]	135.8[a]
14	28.2	31.6	29.1	21.6	22.0	24.0	23.4	26.7
15	27.9	29.6	29.6	33.2	35.6	33.5	35.9	46.1
16	104.5	97.9	100.2	57.7	56.2	59.0	58.5	53.2
17				64.4	67.1	69.6	70.2	70.4
18	21.3	20.6	20.9	13.1	13.1	14.2	14.0	67.1
19	69.2	68.5	69.0	120.0[b]	120.7[c]	128.5	123.0	62.9
20	44.9	46.8	43.6	137.8[a]	137.4[a]	127.6[b]	133.0[a]	74.3
21	49.2	48.5	59.0	46.6	46.6	72.0	53.4	66.1
CO_2Me	168.0[a]	169.3	169.7	174.5	172.2	173.5	174.8	173.0
	50.7	51.3	53.3	51.6	51.3	52.8	52.8	53.0
NMe			50.1	29.7				
Ac					169.8			
					20.0			

*Signal assignments were based on ^{13}C–^{1}H COSY spectra and in case of **2** also on long range ^{13}C–^{1}H COSY spectrum.
†Dissolved in pyridine-d_5.
‡Disolved in methanol-d_4.
[a–c]Interchangeable within the same column.



1a

Fig. 1.

δ3.46. In the ^{13}C NMR spectrum, one quartet carbon signal was observed at δ50.1, and the C-3, C-5 and C-21 signals were shifted downfield in comparison with those of compound **2**, suggesting the presence of N^b-Me group. The ^{13}C NMR signals due to the non-aromatic portion showed a similarity to those of 19-epialstogustine (19*S*) than alstogustine (19*R*) [10]. Alkaloid **3** was thus determined to be N^b-methylscholaricine.

The EI mass spectrum of **4** afforded a $[M]^+$ peak at *m/z* 382.189, suggesting the molecular formula to be $C_{22}H_{26}N_2O_4$. While coupling constants in the ^{1}H NMR spectrum showed the same pattern as those of compound **5**, no acetyl group was present and the signals of H-17 were shifted upfield in comparison with those of compound **5**. Instead, a 3H singlet signal was observed at δ2.94 and a cross peak was observed between the methyl protons/H-12, together with those between H-18/H-15 and H-19/H-21a, in the 2D-NOESY spectrum. The methyl group therefore seemed to be linked at the nitrogen in the indole moiety. The ^{13}C NMR signals due to the non-aromatic portion and N^a-methyl group were in good agreement with those of 10,11-dimethoxy-1-methyldeacetylpicraline [14], and the structure of **4** was elucidated as N^a-methylburnamine.

The FAB mass spectrum of **6** afforded a $[M+1]^+$ peak at *m/z* 357.181, suggesting the molecular formula to be $C_{20}H_{24}N_2O_4$. ^{1}H–^{1}H COSY and 2D-NOESY spectra disclosed the presence of three isolated methylene groups and an ethylidene side chain with the *E*-configuration, and a structure such as **7** [14] or angustilobine B [7] (alstonamine [15]) was suggested. Based on the downfield shifts of C-3, C-6, C-21 and H-3, H-6 and H-21 in comparison with the corresponding resonances of **7**, as well as a molecular formula, compound **6** was considered to be the N^b-oxide of **7**. When compound **7** was treated with *m*-chloroperbenzoic acid, the product showed the same R_f value on TLC and the ^{1}H and ^{13}C NMR signals were in good agreement with those of **6**. The structure of **6** was thus determined to be vallesamine N^b-oxide.

The structure of **8**, isolated from *Alstonia angustiloba*, was proposed previously by Zeches *et al.* [7]. In this

study, the ^{13}C NMR and ^{13}C–^{1}H COSY measurements were carried out and the epoxide ring was established to retain the α-orientation (19*R*,20*S*) based on cross peaks in the 2D-NOESY spectrum (H-15/H-21α, H-19/H-21β).

DISCUSSION

The leaves from Taiwan showed principally the same alkaloids as those from Thailand, containing picrinine (**9**), nareline and alschomine as major alkaloids (Table 1). As compound **9** is known as one of the main alkaloids in the leaves from India and Thailand [2], these two samples seem to belong to the Continental type, although compound **1** was obtained from the leaves from Taiwan instead of **2** from the leaves of Thai and Indonesian plants.

As described in the preceding paper [5], the leaves from The Philippines contain 6,7-secoangustilobine B (**10**), its 6-*nor*-homologue (losbanine), tubotaiwine and its homologues. Although compound **10** was obtained from the Indonesian plant as well as from the Philippines plant, the former sample also afforded compounds **5**, **8** and leuconolam (**11**) [16] showing the characteristic pattern of *A. scholaris* from Indonesia. Alkaloids **5**, **11** and φ-akuammigine N^b-oxide (**12**) were already known from the other species but this is the first report from *A. scholaris*.

EXPERIMENTAL

General. Mps: uncorr. NMR: 400 and 100 MHz, TMS as int. standard. The following solvent systems were used, S1: $CHCl_3$–MeOH–H_2O (bottom phase), S2: S1 + HOAc or CF_3CO_2H (5%), S3: EtOAc–MeOH–H_2O, S4: $CHCl_3$–MeOH–Me_2CO–NH_4OH (80:10:5:1).

Plant material. The leaves of *Alstonia scholaris* were collected in the following countries. Taiwan: Tainan, R.O.C., February 1989 (deposited in the Herbarium of Fukuoka Univ.); Thailand: the Phucae Botanical Garden, Saraburi, January 1989 (deposited in the Forest Herbarium of Royal Forest Department, Bangkok, voucher number: BKF No. 92987); Indonesia: Medicinal Plant Garden of P.T.Eisai-Indonesia, Gekbrong, Cianjur, April 1989. The Philippines: the campus of University of The Philippines at Los Banos, May 1987 (deposited in the Herbarium of UPLB, voucher number: 16 UPLB-0015).

Extraction and isolation of alkaloids. The powdered air-dried leaves from Taiwan (3.1 kg) were percolated with MeOH. The MeOH soln (40 l) was concd to 1.5 l *in vacuo* and diluted with 1.5 l 20% HOAc. The ppt. was filtered off, the filtrate was made alkaline with NH_4OH and the mixt. was partitioned with $CHCl_3$ (extract, 51 g). The H_2O layer was concd *in vacuo* to remove MeOH, and then partitioned with BuOH (extract, 48 g). The H_2O layer, after partition with BuOH, was passed through a polystyrene column (Mitsubishi Chem. Ind., MCI-gel CHP-20P), and the column eluted with a mixture of H_2O and MeOH with increasing MeOH concentration. The eluate with 50% MeOH was chromatographed on a silica gel column with S1 (7:3:1) to afford compound **1** (30 mg).

The $CHCl_3$ extract (26 g) was chromatographed on a silica gel column with S1 (7:1:1–7:2:2) and S3 (16:2:1) to afford alschomine (23 mg), isoalschomine (12 mg), nareline (31 mg), **9** (830 mg) and **10** (8 mg) [1].

The powdered air-dried leaves collected in Thailand (1.2 kg) were worked-up by the same procedure as above and the following alkaloids were obtained from the $CHCl_3$ extract; tubotaiwine, alschomine, isoalschomine, nareline, **2** and **7** (mp 174–180°, $[\alpha]_D^{24}$ +144.5° (MeOH; *c* 1.20), EIMS *m/z* 340.179 (Calcd for $C_{20}H_{24}N_2O_3$ 340.179)).

From the leaves collected in Indonesia, the following alkaloids were isolated; akuammidine (mp 240–249°, $[\alpha]_D^{11}$ +3.2° (MeOH; *c* 0.5), FABMS *m/z* 353.186 (Calcd for $C_{21}H_{24}N_2O_3$ + H 353.186)), φ-akuammigine [$[\alpha]_D^{28}$ −19.1° (MeOH, *c* 1.34), EIMS *m/z* 366 ($C_{22}H_{26}N_2O_3$)], **2**–**4**, **5** ($[\alpha]_D^{27}$ −109.1° (MeOH); *c* 1.64), EIMS *m/z* 410 ($C_{23}H_{26}N_2O_5$)), **6**–**8**, **10** ($[\alpha]_D^{23}$ +214.4° (MeOH; *c* 0.90), negative FABMS *m/z* 339 $[M-H]^-$), **11** [mp 261–266°, $[\alpha]_D^{25}$ −581.1° (MeOH; *c* 0.55), EIMS *m/z*: 326.164 (Calcd. for $C_{19}H_{22}N_2O_3$ 326.163)] and **12** ($[\alpha]_D^{25}$ −4.1° (MeOH; *c* 1.1), EIMS *m/z* 382.190 (Calcd for $C_{22}H_{26}N_2O_4$ 382.189)).

The alkaloids from the leaves of plants from The Philippines are described in the preceding paper [5].

19-*Epischolaricine* (**1**). Prisms from MeOH, mp 210–230°, $[\alpha]_D^{28}$ −322.4° (MeOH; *c* 0.17), FABMS *m/z* 357.182 ($C_{20}H_{24}N_2O_4$ + H requires 357.181), CD λ_{peak}^{MeOH} nm(Δε): 209 (+43.5), 253 (+1.5), 275 (+5.2), 291 (0), 328 (−23.2). R_f 0.40 (**2**; 0.70, S2). Upon usual acetylation with pyridine and Ac_2O at room temp, **1a** was obtained as a solid, EIMS *m/z* 398 ($C_{22}H_{26}N_2O_5$), 339, 325, 283, 242.

Scholaricine (**2**). Mp 175–185°, $[\alpha]_D^{28}$ −311.3° (MeOH; *c* 0.75), FABMS *m/z* 357.181 (Calcd for $C_{20}H_{24}N_2O_4$ + H 357.181), CD λ_{peak}^{MeOH} nm(Δε): 209 (+71.2), 253 (+1.2), 275 (+7.2), 290 (0), 328 (−27.5). Long-range ^{13}C–^{1}H COSY cross peaks: H-3/C-2,8,15, H-9/C-11,13, H-10/C-8,12, H-11/C-9, H-15/C-2,3,16, CO_2Me, NH/C-7,8,13, CO_2Me/CO_2Me.

Oxidation of compounds **1** *and* **2**. Alkaloids **1** (1 mg) and **2** (25 mg) were subjected to the reaction in principally the same procedure as described for the oxidation of 19-hydroxydihydrogelsevirine [11] with $(COCl)_2$, DMSO, CH_2Cl_2 and triethylamine to give a 19-keto-derivative as a solid from **2**, $[\alpha]_D^{25}$ −283.3° ($CHCl_3$; *c* 0.28), FABMS *m/z* 355.165 ($C_{20}H_{22}N_2O_4$ + H requires 355.166), ^1H NMR ($CDCl_3$): δ 1.49, 2.15 (*dt*, *J* = 13, 1 Hz, H-14), 1.89 (*dd*, *J* = 12, 6 Hz, H-6a), 2.30 (*s*, H-18), 2.15 (*t*, *J* = 13 Hz, H-21a), 2.80–3.20 (*m*, H-5, 6b, 20, 21b), 3.49 (*br s*, H-15), 3.68 (*s*, $-CO_2Me$), 3.92 (*br s*, H-3), 6.66, 6.75 (*br d*, *J* = 7 Hz, H-9, 11), 6.80 (*t*, *J* = 7 Hz, H-10), 8.91 (*s*, NH). The oxidation product from **1** was identified as the 19-keto-derivative of **2** on TLC (S2 and S3).

N^b-*Methylscholaricine* (**3**). A solid, $[\alpha]_D^{26}$ −232.7° (MeOH; *c* 0.85), FABMS *m/z* 372.207 ($C_{21}H_{27}N_2O_4$ + H requires 372.205).

N^a-*Methylburnamine* (**4**). A solid, $[\alpha]_D^{28}$ −116.4° (MeOH; *c* 1.25), EIMS *m/z* 382.189 ($C_{22}H_{26}N_2O_4$ requires 382.189).

Vallesamine N^b-*oxide* (**6**). A solid, $[\alpha]_D^{23}$ +76.1° (MeOH; *c* 1.14), FABMS *m/z* 357.181 ($C_{20}H_{24}N_2O_4$ + H requires 357.181). Alkaloid **7** (20 mg) was dissolved in CH_2Cl_2 (2 ml) and treated with *m*-chloroperbenzoic acid (15 mg) for 30 min at room temp. After addition of 5% NH_4OH (3 ml), the reaction mixt. was extracted with CH_2Cl_2 and purified by silica gel CC with S1 (7:2:1). The product was identified as **6** by means of TLC, ^1H and ^{13}C NMR.

6,7-seco-19,20-α-*Epoxyangustilobine B* (**8**). A solid, $[\alpha]_D^{29}$ +73.6° (MeOH; *c* 1.25), EIMS *m/z* 356.176 (Calcd for $C_{20}H_{24}N_2O_4$ 356.174). 2D-NOESY cross peaks: H-7/H-9, 17a, NH/H-12,15, H-15/H-3α,21α, H-19/H-21β.

Acknowledgements—We thank P. T. Eisai (Indonesia) and Mr. Thawatchai Wongprasert (Phucae Botanical Garden, Saraburi) for supplying the leaves of *Alstonia scholaris*. Our thanks are also due to Misses Y. Iwase, J. Honda and Mr H. Hanazono for NMR and MS measurements. This work was supported in part by a grant from the Central Research Institute of Fukuoka University.

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