Phytochemistry, Vol. 20, No. 7, pp. 1725–1730, 1981.
Printed in Great Britain.

0031-9422/81/071725-06 $02.00/0

(−)-EPILAMPROLOBINE AND ITS *N*-OXIDE, LUPIN ALKALOIDS FROM *SOPHORA TOMENTOSA**

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(*Revised received* 7 *November* 1980)

Key Word Index—*Sophora tomentosa*; Leguminosae; alkaloid; lupin alkaloid; (−)-epilamprolobine; (+)-epilamprolobine *N*-oxide; 5-(3′-methoxycarbonylbutyroyl)aminomethyl-*trans*-quinolizidine *N*-oxide; (+)-lamprolobine; (+)-epilamprolobine; absolute configuration.

Abstract—From the fresh leaves of *Sophora tomentosa*, three new lupin alkaloids, (−)-epilamprolobine, (+)-epilamprolobine *N*-oxide and 5-(3′-methoxycarbonylbutyroyl)aminomethyl-*trans*-quinolizidine *N*-oxide, have further been isolated along with (+)-matrine, (+)-matrine *N*-oxide, (+)-sophocarpine *N*-oxide, (−)-anagyrine, (−)-baptifoline, (−)-cytisine, (−)-*N*-methylcytisine, (−)-*N*-formylcytisine, (−)-*N*-acetylcytisine and (±)-ammodendrine. The absolute configurations of (+)-epilamprolobine *N*-oxide (1*R*:5*R*:6*S*) and (−)-epilamprolobine (5*R*:6*S*) have also been established by spectroscopic data and by comparison with synthetic (+)-epilamprolobine (5*S*:6*R*) derived from (−)-lupinine (5*R*:6*R*). (−)-Epilamprolobine is a diastereomer of (+)-lamprolobine (5*R*:6*R*) in *Lamprolobium fruticosum* and 5-(3′-methoxycarbonylbutyroyl)aminomethyl-*trans*-quinolizidine *N*-oxide is presumed to be an artefact. A biosynthetic pathway for the formation of (−)-epilamprolobine is also proposed.

INTRODUCTION

As part of our studies on lupin alkaloids of leguminous plants growing in Japan [1–10], we have previously reported the presence of (+)-matrine (**12**), (+)-matrine *N*-oxide (**8**), (−)-anagyrine (**10**), (−)-baptifoline (**11**), (−)-cytisine (**13**), (−)-*N*-methylcytisine (**14**) and (−)-*N*-acetylcytisine (**16**) in the dried epigeal parts of *Sophora tomentosa* [1]. Further examination of the basic constituents in the fresh leaves, stems and immature seeds of the same plant has resulted in the isolation of (+)-sophocarpine *N*-oxide, (−)-*N*-formylcytisine (**15**), (±)-ammodendrine and three new lupin alkaloids besides the above seven lupin alkaloids. This paper describes the structure elucidation of the new lupin alkaloids (+)-epilamprolobine *N*-oxide (**1**), (−)-epilamprolobine (**2**) and 5-(3′-methoxycarbonylbutyroyl)aminomethyl-*trans*-quinolizidine *N*-oxide (**3**) and the distribution of the alkaloids in this plant. A possible biosynthetic pathway leading to **1**, **2** and (+)-lamprolobine (**5**) is also proposed from the stereochemical standpoint among the closely related lupin alkaloids.

RESULTS AND DISCUSSION

From the *n*-hexane-insoluble fraction of the total crude alkaloid, obtained from the 75% MeOH extract of the freshly harvested leaves, stems and immature seeds of *S. tomentosa*, two new lupin alkaloids, (+)-epilamprolobine *N*-oxide (**1**) and 5-(3′-methoxycarbonylbutyroyl)aminomethyl-*trans*-quinolizidine *N*-oxide (**3**), were isolated along with (−)-cytisine (**13**), (−)-*N*-methylcytisine (**14**), (−)-*N*-formylcytisine (**15**), (+)-matrine *N*-oxide (**8**), (−)-baptifoline (**11**), (+)-sophocarpine *N*-oxide and other minor alkaloids. From the *n*-hexane-soluble fraction, another new lupin alkaloid, (−)-epilamprolobine (**2**), was isolated together mainly with (+)-matrine (**12**) and (−)-anagyrine (**10**). Distribution of these lupin alkaloids and ammodendrine in the various fresh parts of this plant is listed in Table 1.

The first new alkaloid, (+)-epilamprolobine *N*-oxide (**1**), was a colourless, amorphous solid, $C_{15}H_{24}N_2O_3$ (M^+, *m/z* 280.179, calc. 280.179), $[\alpha]_D^{20}$ +14.9° (EtOH). Its IR spectrum revealed the presence of an imide group at 1715 (weak) and 1660 cm^{-1} (strong). The mass spectrum (70 eV) of **1** showed the parent peak at *m/z* 280 (28%) and the fragment ions at *m/z* 264 (28) and 263 (100) corresponding to $M^+ - O$ and $M^+ - OH$, respectively, characteristic of aliphatic amine *N*-oxides [5, 8, 11]. **1** was quantitatively reduced by H_2SO_3 or by 10% Pd–C/H_2 (MeOH) to a deoxygenated product which was shown to be identical with those of the second alkaloid, (−)-epilamprolobine (**2**), in all measurable respects.

The second new alkaloid, (−)-epilamprolobine (**2**), was isolated as colourless needles from *n*-hexane–benzene, having mp 101.5°, $[\alpha]_{365}^{20}$ −13.8° (EtOH) and a molecular formula of $C_{15}H_{24}N_2O_2$ (M^+, *m/z* 264.182 (35%), calc. 264.183). The IR spectrum of **2** showed the presence of a *trans*-quinolizidine conformation (2800, 2760 and 2670 cm^{-1}) and of an imide group at 1715 (weak) and 1660 (strong) cm^{-1}. The mass spectrum (70 eV) of **2** exhibited fragment ions at *m/z* 152 (48%), 138 (100), 110 (49), 97 (57) and 83 (57) which were similar to those of the

* This work was presented at the 99th Annual Meeting of the Pharmaceutical Society of Japan, August 1979 (Meeting Abstract p. 197).

Table 1. Distribution of lupin alkaloids and (±)-ammodendrine in the various fresh parts of *Sophora tomentosa**

Alkaloids	Leaves	Stems	Immature seeds	Immature pods
Total alkaloids	0.15	0.22	0.64	0.37 %/fr.wt
(+)-Matrine (**12**)	17.3	3.1	10.4	5.8
(+)-Matrine *N*-oxide (**8**)	28.0	10.6	34.9	38.9
(+)-Sophocarpine *N*-oxide	2.1	3.2	tr	0.5
(−)-Anagyrine (**10**)	tr	tr	tr	tr
(−)-Baptifoline (**11**)	0.4	5.7	0.1	0.4
(−)-Cytisine (**13**)	20.6	40.4	13.7	30.8
(−)-*N*-Methylcytisine (**14**)	7.7	5.5	1.5	2.4
(−)-*N*-Formylcytisine (**15**)	0.1	0.3	1.0	0.5
(−)-*N*-Acetylcytisine (**16**)	tr	tr	tr	0.1
(±)-Ammodendrine	tr	tr	tr	tr
(−)-Epilamprolobine (**2**)	1.0	tr	7.0	tr
(+)-Epilamprolobine *N*-oxide (**1**)	10.2	2.9	15.2	13.5
5-(3′-Methoxycarbonylbutyroyl)amino-methyl-*trans*-quinolizidine *N*-oxide (**3**)	tr	tr	tr	tr

* Alkaloid contents were quantitatively estimated by liquid chromatography (HPLC) as described in the Experimental and are shown in %/total alkaloids. *S. tomentosa* was collected in December at the Ishigaki Island, Ryukyu, Japan.

tr = trace.

spectra of (−)-lupinine (**4**) and (+)-epilupinine (**6**) [2–4,6,7,12], suggesting the presence of a lupinane moiety in the molecule. In the ^{13}C NMR spectrum of **2**, the nine signals attributable to the quinolizidine moiety resonated within 1.7 ppm of the corresponding signals for (−)-lupinine (**4**) [13], except for one due to C-4 which was considered to be affected by a bulky substituent at C-11. The other signals, shown in Table 2, at δ 172.6 (*s*), 33.1 (*t*) and 17.3 (*t*) corresponding to two carbonyl, two methylene and one methylene carbons, respectively, suggested the presence of a symmetric glutarimide moiety in the molecule of **2**. From the above results, **2** was presumed to be 5-glutarimidomethylquinolizidine having the same relative configuration as (−)-lupinine (**4**).

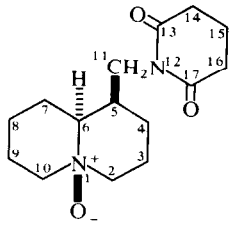
2 was isolated for the first time as a natural product but its racemate has already been synthesized by Yamada *et al.* [14] and named (±)-epilamprolobine. **2** was completely identical with synthetic (±)-epilamprolobine in all measurable respects (TLC, HPLC, MS and ^1H NMR). Therefore, the second and first alkaloids were determined to be (−)-epilamprolobine (**2**) and its *N*-oxide (**1**), respectively. **2** is one diastereomer of (+)-lamprolobine (**5**) which has been found by Hart *et al.* [15] in the leaves of *Lamprolobium fruticosum* of the same family.

The presence of a *trans*-quinolizidine moiety in **2** is apparent from the IR spectrum and the signals due to the two amino-methylene carbons at the C-2 and C-10 positions having the same chemical shifts in the ^{13}C NMR spectrum (Table 2) [8, 16]. The close similarity of the ^1H NMR spectrum of (−)-epilamprolobine (**2**) to that of its *N*-oxide (**1**) also indicates that **1** possesses the same stereochemistry as **2**. Thus, the ^1H NMR spectrum of **2** showed the signals at δ 3.77 (1 H, *dd*, J = 13 and 3 Hz, H_b) and 4.28 (1 H, *dd*, J = 13 and 10.5 Hz, H_a) due to the C-11 methylene protons. Both chemical shifts and coupling characteristics of the methylene protons indicate that the conformation of **2** can be shown as **2a**, in which one (H_a) of the methylene protons is *trans* to 5-H and close to the N-1 lone pair. The ^1H NMR spectrum of **1** showed similar signals due to the C-11 methylene protons at δ 3.83 (1 H, *m* (apparent *br d*), J = 13 Hz, H_b) and 4.92 (1 H, *dd*, J = 13 and 11 Hz, H_a), although they were shifted downfield by the effect of the N^+-O^- bond [5]. These ^1H NMR data also suggest that **1** has the same stereochemistry as **2**, and hence the ring-junction of the quinolizidine moiety is *trans*. This assumption was proved by fact that the ^{13}C

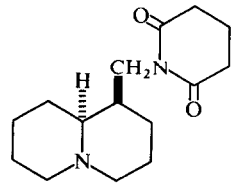
Table 2. ^{13}C NMR spectra of (+)-epilamprolobine *N*-oxide (**1**), (−)-epilamprolobine (**2**) and (−)-lupinine (**4**) in $CDCl_3$*

Carbon No.	1	2	4
2	69.5 (*t*)	57.2 (*t*)	57.2 (*t*)
3	16.6 (*t*)	21.2 (*t*)	22.6 (*t*)
4	25.7 (*t*)	26.7 (*t*)	30.5 (*t*)
5	37.0 (*d*)	37.1 (*d*)	38.8 (*d*)
6	72.6 (*d*)	65.2 (*d*)	65.0 (*d*)
7	24.7 (*t*)	29.6 (*t*)	29.6 (*t*)
8	23.7 (*t*)	25.1 (*t*)	24.8 (*t*)
9	20.6 (*t*)	25.6 (*t*)	25.6 (*t*)
10	69.5 (*t*)	57.6 (*t*)	57.2 (*t*)
11	38.4 (*t*)	37.8 (*t*)	64.7 (*t*)
13	172.7 (*s*)	172.6 (*s*)	
14	33.0 (*t*)	33.1 (*t*)	
15	17.3 (*t*)	17.3 (*t*)	
16	33.0 (*t*)	33.1 (*t*)	
17	172.7 (*s*)	172.6 (*s*)	

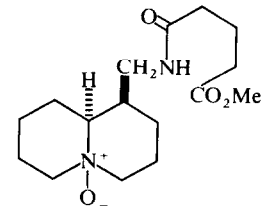
* δ values in ppm from TMS as internal standard.



1



2
(5*R*:6*S*)



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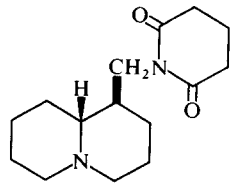

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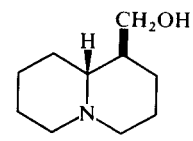
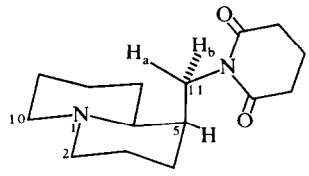
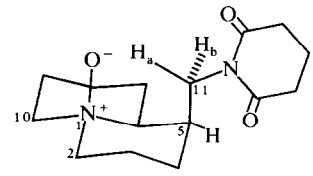
(5*R*:6*R*)



6
(5*S*:6*R*)



2a



1a

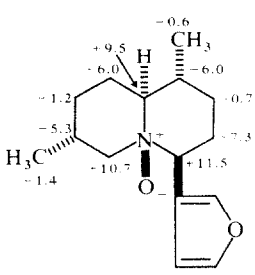
NMR spectrum of **1** exhibited the signal at δ 69.5 assigned to the two magnetically equivalent amino-methylene carbons which were equally deshielded by the positive nitrogen of the *N*-oxide group, compared with that of **2**. The substituent effect of the *N*-oxide bond in the spectrum of **1** agreed with those in (+)-7-epinupharidine (**7**) [17] and (+)-matrine *N*-oxide (**8**) (I. Murakoshi *et al.*, unpublished observation) bearing a *trans*-quinolizidine moiety (Fig. 1).

The absolute configuration of (−)-epilamprolobine (**2**) was shown to be 5*R*:6*S* from the fact that the optical rotation of **2**, $[\alpha]_{365}^{20}$ −13.8° (EtOH), showed an opposite value to that of a synthetic (+)-epilamprolobine (**9**), $[\alpha]_{365}^{20}$ +16.8° (EtOH), derived from (−)-lupinine (**4**, 5*R*:6*R*) [18] as shown in Scheme 1, which was unknown so far in nature.

The third new alkaloid (**3**) has an empirical formula of $C_{16}H_{28}N_2O_4$ (M^+, *m/z* 312.205, calc. 312.205). Its mass spectrum showed the parent peak at *m/z* 312 (4%) and fragment ions at *m/z* 296 (21), 295 (15) and 294 (15) corresponding to $M^+ - O$, $M^+ - H_2O$, respectively, which were characteristic of aliphatic amine *N*-oxides [5, 8, 11]. The ^1H NMR spectrum of **3** exhibited a sharp three-proton singlet at δ 3.65 and a broad one-proton signal at 10.90 assigned to a methoxycarbonyl group and an amide-NH, respectively. From these results, it can be assumed that the third alkaloid is 5-(3′-methoxycarbonyl-butyroyl)aminomethyl-*trans*-quinolizidine *N*-oxide (**3**). **3** is considered to be an artefact produced from **1** during the extraction and purification procedures of the alkaloids, as **3** was easily formed by allowing **1** to stand in MeOH at room temperature.

The absolute configurations of (−)-epilamprolobine (**2**) and its *N*-oxide (**1**) at the C-5 position are the same as those at the C-7 and C-9 positions of the (+)-sparteine-type alkaloids (**17**, **18**) [19] and the (−)-anagyrine-type alkaloids (**10**, **11**) [19], but that of the (+)-matrine-type alkaloids (**8**, **12**) [20], coexisting in the same plant at the C-5 position corresponding structurally to the C-5 position of **2** and **1**, is the opposite. Furthermore, **2** is the enantiomer of (+)-epilamprolobine (**9**) that is chemically derived from (−)-lupinine (**4**) and that has not been found so far in nature. **2** is also the diastereomer of (+)-lamprolobine (**5**) corresponding stereochemically to (+)-epilupinine (**6**).

Judging from the above stereochemical point of view among the lupin alkaloids coexisting in the same plant and from the chemotaxonomic stand-point for the lupin alkaloids in leguminous plants, (−)-epilamprolobine (**2**) and its *N*-oxide (**1**) appear to be either one product arising



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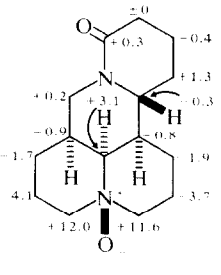

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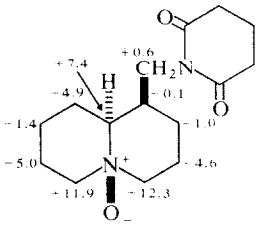


1

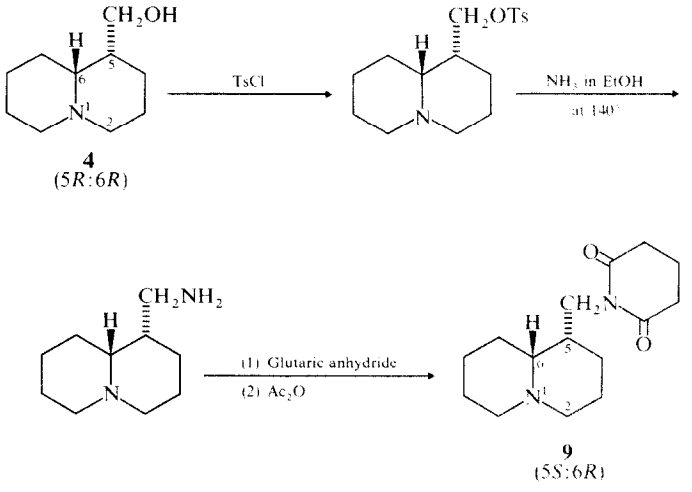
Fig. 1. Substituent effects of *N*-oxide bond on ^{13}C NMR shifts of (+)-7-epinupharidine (**7**), (+)-matrine *N*-oxide (**8**) and (+)-epilamprolobine *N*-oxide (**1**).

from a hypothetical intermediate, 'active lupinine' [21], for the biosynthesis of lupin alkaloids or an oxidative metabolite derived from a C_6–C_7 or C_9–C_{11} bond cleavage of the (+)-sparteine-type alkaloids (**17**, **18**) rather than the (−)-anagyrine-type alkaloids (**10**, **11**) as shown in Scheme 2. (+)-Lamprolobine (**5**) is also assumed to be either one product produced from the 'active lupinine' of (+)-epilupinine-type alkaloids or an oxidative metabolite of the (−)-β-isosparteine-type alkaloids (**19**).

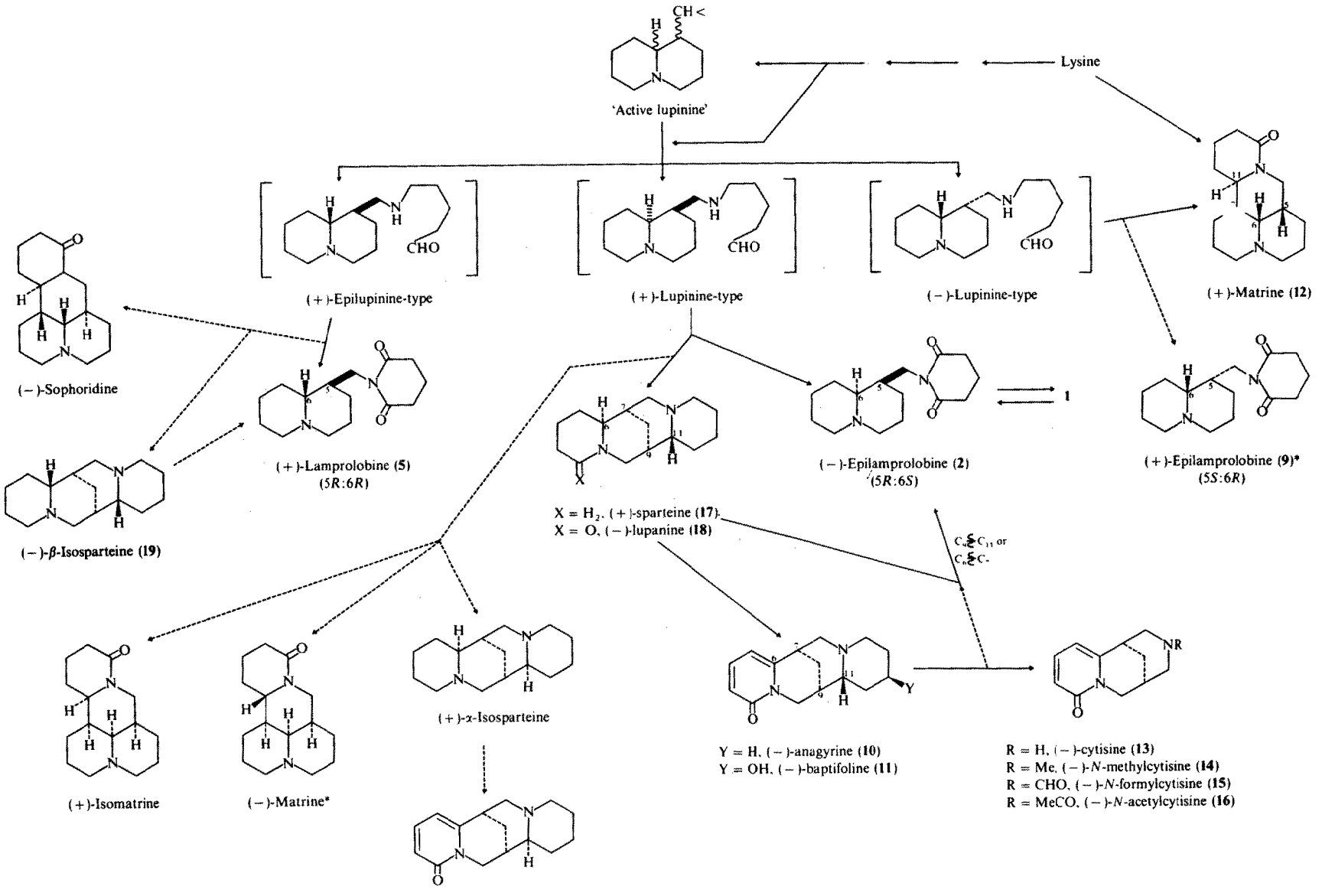
EXPERIMENTAL

Mps are uncorr. The high and low resolution MS were measured at 70 eV. The ^1H NMR (100 MHz) and ^{13}C NMR (25 MHz) were recorded using TMS as an int. standard. TLC was carried out in the following solvent systems: 1, CH_2Cl_2–MeOH–28% NH_4OH (90:9:1) for Si gel; 2, C_6H_6–Me_2CO–MeOH (34:3:3) for Al_2O_3. The R_f values for **1** obtained in these solvents were 0.20 and 0.16, respectively, whilst **2** gave the following values, 0.65 and 0.64, respectively. Under the same conditions, **3** moved at R_fs of 0.16 and 0.11, respectively. Analytical HPLC was performed with solvents 3 [15% MeOH · Et_2O–2.5% NH_4OH (50:1)] and 4 [25% MeOH · Et_2O–H_2O–25% NH_4OH (100:4:3)], using a LiChrosorb SI 100 (Merck, 10 μm, 0.3 × 50 cm) column employing a monitoring flow system (220 and 310 nm) coupled to a recorder at a flow rate of 1 ml/min. The R_t (min) values for **1** and **3** obtained by solvent 4 were 12.5 and 13.5, respectively, whilst **2** moved at R_t of 9.8 in solvent 3. Prep. HPLC was performed on LiChrosorb SI 100 (10 μm, 0.5 × 50 cm or 1 × 50 cm) column using solvents 3 and 4 under the same conditions.

Isolation of (+)-epilamprolobine N-oxide (**1**), *(−)-epilamprolobine* (**2**) *and 5-(3′-methoxycarbonylbutyroyl)aminomethyl-*trans*-quinolizidine N-oxide* (**3**). *Sophora tomentosa* was collected in December, at Ishigaki-island, Ryukyu, Japan. (1) Isolation of (+)-epilamprolobine *N*-oxide (**1**) and the Me ester (**3**) from the fresh leaves. The alkaloid fraction (3.06 g), obtained from the 75% EtOH-extracts of the freshly harvested leaves (2 kg), was extracted with *n*-hexane. The *n*-hexane-insoluble fraction (2.2 g) was chromatographed on a Si gel column (Merck, type 60, 160 g, 2.5 × 63 cm), developing with Et_2O–MeOH–H_2O 28% NH_4OH (50:50:4:3) and 20 ml fractions were collected. After fractions containing **1** and **3** (Nos. 52–67) were pooled, the **1**- and **3**-rich fraction was further applied to a prep. HPLC using solvent 4. **1** and **3** were purified successively by this procedure. **1** (120 mg) was obtained as a colourless, amorphous solid, $[\alpha]_D^{20}$ +14.9° (*c* = 0.77, EtOH). MS *m/z* (rel. int.): 280.179 (M^+, calc. for $C_{15}H_{24}N_2O_3$ 280.179, 28), 264 [M − O]$^+$ (28), 263 [M − OH]$^+$ (100), 168 (25), 154 (73), 150 (50), 138 (38), 136 (40), 110 (20), 100 (20), 98 (32), 83 (24). IR(KBr) cm^{-1}: 1715 (weak), 1660 (strong) (imide C=O). ^1H NMR ($CDCl_3$): δ 2.65 (4 H, *t*, *J* = 6.5 Hz, 14- and 16-H_2), 3.83 (1 H, *m* (apparent *br d*), *J* = 13 Hz, 11-H_b), 4.92 (1 H, *dd*, *J* = 13 and 11 Hz, 11-H_a). ^{13}C NMR ($CDCl_3$): δ 69.5 (*t*, 2-C), 16.6 (*t*, 3-



Scheme 1. Synthetic route of (+)-epilamprolobine (**9**).



Scheme 2. Possible biogenetic relationships between the lupin alkaloids in *Sophora tomentosa* and the other species (*unknown in nature).

C), 25.7 (*t*, 4-C), 37.0 (*d*, 5-C), 72.6 (*d*, 6-C), 24.7 (*t*, 7-C), 23.7 (*t*, 8-C), 20.6 (*t*, 9-C), 69.5 (*t*, 10-C), 38.4 (*t*, 11-C), 172.7 (*s*, 13- and 17-C), 33.0 (*t*, 14- and 16-C), 17.3 (*t*, 15-C). **3** (3 mg) was also obtained as a colourless, amorphous solid. MS *m/z* (rel. int.): 312.205 (M^+, calc. for $C_{16}H_{28}N_2O_4$ 312.205, 4), 296 $[M-O]^+$ (21), 295 $[M-OH]^+$ (15), 294 $[M-H_2O]^+$ (15), 265 (13), 152 (31), 151 (31), 150 (33), 138 (100), 111 (28), 110 (32), 97 (26), 83 (37). ^{1}H NMR ($CDCl_3$): δ 3.65 (3 H, *s*, COOMe), 10.90 (1 H, *br s*, NH).

(2) Isolation of (−)-epilamprolobine (**2**) from immature seeds. The *n*-hexane-soluble fraction (70 mg) of the total crude alkaloid (0.23 g), obtained from the 75% EtOH extracts of the immature seeds (36 g), was subjected to prep. HPLC using solvent 3, as described for **1** and **3**. **2** was obtained as a crystalline solid (13 mg) after elution of (−)-anagyrine. **2**, colourless needles (from *n*-hexane), mp 101.5°, $[\alpha]_D^{20}$ −13.8° (*c* = 0.34, EtOH). MS *m/z* (rel. int.): 264.182 (M^+, calc. for $C_{15}H_{24}N_2O_2$ 264.183, 35), 263 (19), 222 (17), 152 (48), 138 (100), 110 (49), 97 (57), 83 (57). IR (KBr) cm^{-1}: 2800, 2760, 2670 (*trans*-quinolizidine band), 1715 (weak), 1660 (strong) (imide C=O). ^{1}H NMR ($CDCl_3$): δ 2.64 (4 H, *t*, *J* = 6.5 Hz, 14- and 16-H_2), 3.77 (1 H, *dd*, *J* = 13 and 3 Hz, 11-H_b), 4.28 (1 H, *dd*, *J* = 13 and 10.5 Hz, 11-H_a). ^{13}C NMR ($CDCl_3$): δ 57.2 (*t*, 2-C), 21.2 (*t*, 3-C), 26.7 (*t*, 4-C), 37.1 (*d*, 5-C), 65.2 (*d*, 6-C), 29.6 (*t*, 7-C), 25.1 (*t*, 8-C), 25.6 (*t*, 9-C), 57.6 (*t*, 10-C), 37.8 (*t*, 11-C), 172.6 (*s*, 13- and 17-C), 33.1 (*t*, 14- and 16-C), 17.3 (*t*, 15-C).

The alkaloid contents in the various parts of *S. tomentosa* are shown in Table 1.

Reduction of (+)-*epilamprolobine* N-*oxide* (**1**) *into* **2**. (1) A soln of **1** (10 mg) in MeOH was hydrogenated over 10% Pd–C at atm. pres. at room temp. and then the catalyst was filtered off. After the filtrate was concd to dryness, the residue was crystallized from *n*-hexane to give colourless needles (8 mg), mp 101.5°, which was identical to (−)-epilamprolobine (**2**) (IR, MS, co-TLC and co-HPLC).

(2) An aq. soln of **1** (1 mg) was satd with SO_2 under cooling. The reaction mixture was made alkaline with K_2CO_3 under ice-cooling and extracted ×3 with CH_2Cl_2. The organic layer was dried (K_2CO_3) and evapd to dryness *in vacuo*. The residue was purified by HPLC using solvent 3. The product was identical with (−)-epilamprolobine (**2**) (co-TLC, co-HPLC and MS).

Methanolysis of (+)-*epilamprolobine* N-*oxide* (**1**) *into* **3**. **1** (1 mg) was dissolved in MeOH (0.3 ml) and then allowed to stand for a day at room temp. Analysis of the reaction mixture by HPLC with solvent 4 showed the presence of two compounds in the ratio of *ca* 5:1, which were found to be **1** and **3**, respectively, in all measurable respects (MS, TLC and HPLC).

Synthesis of (+)-*epilamprolobine* (**9**) *from* (−)-*lupinine* (**4**). (1) Tosylation of (−)-lupinine. Following the procedure of ref. [22], (−)-lupinine (1 g, 5.9 mmol) and tosyl chloride (0.56 g, 3 mmol) were dissolved in dry Me_2CO (20 ml) and the mixture was stirred for 15 hr at room temp. After the crystalline ppt. (447 mg) of lupinine–HCl was filtered off, Me_2CO was removed *in vacuo* to yield crude lupinine tosylate as a pale yellow oil, which was used for the following step without further purification.

(2) Ammonolysis of lupinine tosylate. 1-Aminomethylquinolizidine was prepared from lupinine tosylate according to a modification of the procedure of ref. [19]. The tosylate (200 mg) in NH_3 satd EtOH was heated in a sealed tube at 130–135° for 15 hr. The reaction mixture was evapd to dryness *in vacuo* to give 1-aminomethylquinolizidine (104 mg) as a pale yellow oil.

(3) Preparation of (+)-epilamprolobine (**9**). Following the procedure of ref. [14], to a soln of 1-aminomethylquinolizidine (104 mg) in dry Et_2O (5 ml), a soln of glutaric anhydride (55 mg) in dry Et_2O (5 ml) was added. The reaction mixture was stirred for 30 min at room temp. After the Et_2O was removed *in vacuo*, the residue was dissolved in 3 ml Ac_2O and was heated on a steam bath for 30 min. The reaction mixture was poured into ice–H_2O, made alkaline with K_2CO_3 and extracted with CH_2Cl_2. The extracts were dried and evapd *in vacuo*. The residue was chromatographed on Al_2O_3 using C_6H_6 to give a crystalline solid (**9**) (62 mg), mp 101.5° (from *n*-hexane), $[\alpha]_{365}^{20}$ +16.8° (*c* = 0.50, EtOH). The synthetic product (**9**) was identical with the naturally occurring (−)-epilamprolobine (**2**) by TLC, HPLC, MS and ^{1}H NMR spectra, except for the optical rotation.

Acknowledgements—We are very grateful to Emeritus Prof. M. Matsui and Prof. K. Mori, Department of Agricultural Chemistry, University of Tokyo, for kindly providing a sample of authentic (±)-epilamprolobine.

REFERENCES

1. Ohmiya, S., Otomasu, H., Murakoshi, I. and Haginiwa, J. (1974) *Phytochemistry* **13**, 1016.
2. Murakoshi, I., Sugimoto, K., Haginiwa, J., Ohmiya, S. and Otomasu, H. (1975) *Phytochemistry* **14**, 2714.
3. Murakoshi, I., Kakegawa, F., Toriizuka, K., Haginiwa, J., Ohmiya, S. and Otomasu, H. (1977) *Phytochemistry* **16**, 2046.
4. Murakoshi, I., Toriizuka, K., Haginiwa, J., Ohmiya, S. and Otomasu, H. (1978) *Phytochemistry* **17**, 1817.
5. Ohmiya, S., Otomasu, H., Haginiwa, J. and Murakoshi, I. (1978) *Phytochemistry* **17**, 2021.
6. Murakoshi, I., Toriizuka, K., Haginiwa, J., Ohmiya, S. and Otomasu, H. (1979) *Chem. Pharm. Bull.* **27**, 144.
7. Murakoshi, I., Toriizuka, K., Haginiwa, J., Ohmiya, S. and Otomasu, H. (1979) *Phytochemistry* **18**, 699.
8. Ohmiya, S., Otomasu, H., Haginiwa, J. and Murakoshi, I. (1980) *Chem. Pharm. Bull.* **28**, 546.
9. Bordner, J., Ohmiya, S., Otomasu, H., Haginiwa, J. and Murakoshi, I. (1980) *Chem. Pharm. Bull.* **28**, 1965.
10. Murakoshi, I., Kidoguchi, E., Haginiwa, J., Ohmiya, S., Higashiyama, K. and Otomasu, H. (1981) *Phytochemistry* **20**, 1407.
11. Bild, N. and Hesse, M. (1967) *Helv. Chim. Acta* **50**, 1885.
12. Neuner-Jehle, N., Nesvadba, H. and Spiteller, G. (1964) *Monatsh. Chem.* **95**, 687.
13. Bohlmann, F. and Zeisberg, R. (1975) *Chem. Ber.* **108**, 1043.
14. Yamada, Y., Hatano, K. and Matsui, M. (1970) *Agric. Biol. Chem.* **34**, 1536.
15. Hart, N. K., Johns, S. R. and Lamberton, J. A. (1968) *Aust. J. Chem.* **21**, 1619.
16. Tourwe, D. and van Binst, G. (1978) *Heterocycles* **9**, 507.
17. Lalonde, R. T., Donvido, T. N. and Tsai, A. I-M. (1975) *Can. J. Chem.* **53**, 1714.
18. Okuda, S., Kataoka, H. and Tsuda, K. (1965) *Chem. Pharm. Bull.* **13**, 487.
19. Okuda, S., Kataoka, H. and Tsuda, K. (1965) *Chem. Pharm. Bull.* **13**, 491.
20. Okuda, S., Yoshimoto, M., Tsuda, K. and Utsugi, N. (1966) *Chem. Pharm. Bull.* **14**, 314.
21. Nowacki, E. and Waller, G. R. (1975) *Phytochemistry* **14**, 165.
22. Edwards, O. E., Fordor, G. and Marion, L. (1966) *Can. J. Chem.* **44**, 13.