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# Alkaloidal Constituents of *Leucojum asetivum* L. (Amaryllidaceae)

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Two novel alkaloids, leucotamine (**1**) and *O*-methylleucotamine (**2**), with a 3*R*-hydroxybutyryl group, and another new alkaloid, 3-*O*-acetylungiminorine (**3**), were isolated from leaves of *Leucojum asetivum* (Amaryllidaceae) together with five known alkaloids. *O*-Methylleucotamine (**2**) and 3-*O*-acetylungiminorine (**3**), as well as four known bases, were also isolated from bulbs of this plant. The stereochemistries of the new compounds **1**, **2**, and **3** were established on the basis of chemical and spectral data.

**Keywords**——*Leucojum asetivum*; Amaryllidaceae; leucotamine; *O*-methylleucotamine; 3-*O*-acetylungiminorine; galanthamine; ungiminorine; pretazettine; demethylhomolycorine; lycorine

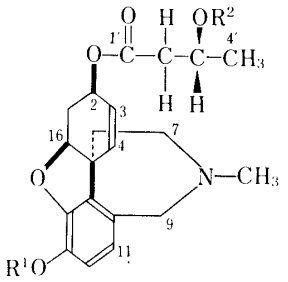
Several Amaryllidaceae alkaloids, galanthamine, pretazettine, lycorine and ungerine, have been isolated from *Leucojum asetivum* L.[1-3] Further, we have recently isolated from an ethanol extract of the leaves of *L. asetivum* L. two novel alkaloids, leucotamine (**1**) and *O*-methylleucotamine (**2**), which have a 3*R*-hydroxybutyryl group.[4] This is of interest from the biogenetic point of view.[5,6] Further examination of the ethanol extract led to the isolation of a new alkaloid, 3-*O*-acetylungiminorine (**3**), together with five known alkaloids, galanthamine (**4**),[7] ungiminorine (**5**),[8-10] pretazettine (**6**),[5] demethylhomolycorine (**7**),[11] and lycorine (**8**).[7] From the bulbs of this plant, compounds **2** and **3** were isolated along with four known bases, **4**, **5**, **6**, and **8**. This paper presents details of the isolation and structural elucidation of leucotamine (**1**), *O*-methylleucotamine (**2**), and 3-*O*-acetylungiminorine (**3**).

Compounds **1** ($C_{20}H_{25}NO_5$) and **2** ($C_{21}H_{27}NO_5$), obtained as needles (mp 168—171 °C) and an oil, respectively, were both optically active. In the $Fe^{3+}$ test, the former gave a positive reaction (blue-violet), but the latter gave a negative reaction. The proton nuclear magnetic resonance ($^1$H-NMR) spectra of compounds **1** and **2** both showed the presence of an *N*-methyl group, two olefinic protons, and two vicinal aromatic protons (see Table I). The ultraviolet (UV) spectra of these compounds were similar to that of **4**. These findings suggested that these compounds have a galanthamine-type skeleton. The $^1$H-NMR spectra of compounds **1** and **2** were very similar (Table I), except for the signal of *O*-methyl protons, and furthermore both spectra showed close similarities to that of **4**, except for the signals around $\delta$ 1.1, 2.4, and 4.1—4.2. These signals were assigned as follows: monitoring of the higher lines ($\delta$ 1.14 and 1.12) of the doublet ($H_3$-4′) in the spectra of **1** and **2**, respectively, gave internuclear double resonance (INDOR) signals at about $\delta$ 4.08 and 4.20, respectively, ascribable to H-3′; monitoring of the lowest lines ($\delta$ 4.14 and 4.27) of H-3′ in **1** and **2** gave INDOR peaks at $\delta$ 1.18 and 1.16 ($H_3$-4′), and $\delta$ 2.48 and 2.44 ($H_2$-2′), respectively. These data indicated that **1** and **2** have the same partial formula $-COCH_2CH(OH)CH_3$. On the basis of

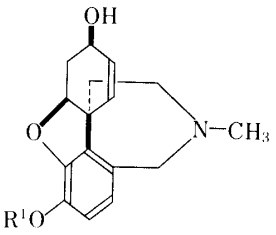
TABLE I. $^1$H-NMR Spectral Data for **1** and **2**, and Related Compounds ($\delta$, $CDCl_3$)

| H | 1 | 2 | 4 | 9 |
|---|---|---|---|---|
| 1a | 2.06 m | 2.02 m | *a)* | *a)* |
| 1b | 2.66 d | 2.71 d | 2.68 d | *a)* |
| 2 | 5.42 t-like | 5.42 t-like | 4.12 m | 4.10 m |
| 3 | 5.91 dd | 5.86 dd | 6.02 s | 6.03 s |
| 4 | 6.30 d | 6.31 d | 6.20 s | 6.03 s |
| 6a | 1.59 d | 1.55 d | 1.58 d | *a)* |
| 6b | 2.07 m | 2.14 m | 2.16 m | *a)* |
| 7a | 3.07 m | 3.02 m | *a)* | *a)* |
| 7b | 3.32 m | 3.27 m | *a)* | *a)* |
| 9a | 3.66 d | 3.64 d | 3.64 d | 3.66 d |
| 9b | 4.09 d | 4.11 d | 4.06 d | 4.05 d |
| 11 | 6.46 d | 6.54 d | 6.62 s | 6.55 s |
| 12 | 6.71 d | 6.66 d | 6.62 s | 6.55 s |
| 16 | 4.59 br s | 4.56 m | 4.59 m | 4.55 m |
| 2′ | 2.48 d | 2.44 d | — | — |
| 3′ | 4.08 m | 4.20 m | — | — |
| 4′ | 1.18 d | 1.16 d | — | — |
| $NCH_3$ | 2.40 s | 2.38 s | 2.40 s | 2.40 s |
| $OCH_3$ | — | 3.83 s | 3.81 s | — |

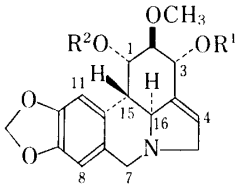
*a)* Obscured signal. $J$ (Hz) values: 1a,1b = 16; 2,3 = 6; 3,4 = 10; 11,12 = 8. For compound **1**: 6a,6b = 13; 9a,9b = 14; 2′,3′ = 7; 3′,4′ = 7. For compound **2**: 6a,6b = 13; 9a,9b = 15; 2′,3′ = 6; 3′,4′ = 6. For compound **4**: 6a,6b = 14; 9a,9b = 14. For compound **9**: 9a,9b = 14.



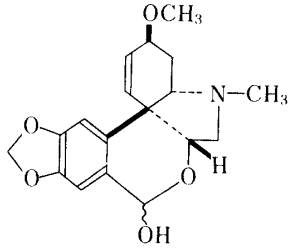
**1** : $R^1 = R^2 = H$
**2** : $R^1 = CH_3$, $R^2 = H$
**10**(**12b**) : $R^1 = CH_3$, $R^2 = Ac$



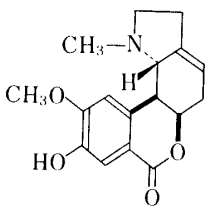
**4** : $R^1 = CH_3$
**9** : $R^1 = H$



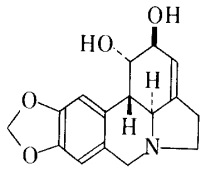
**3** : $R^1 = Ac$, $R^2 = H$
**5** : $R^1 = R^2 = H$
**13** : $R^1 = R^2 = Ac$



**6**



**7**

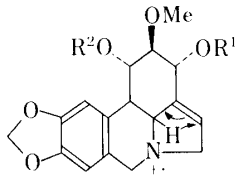


**8**

Chart 1

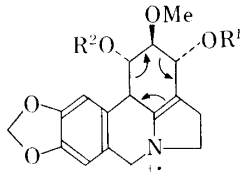
these findings, structural correlations between compounds **1** and **2**, and between compounds **2** and **4** were established as follows. Methylation of **1** with diazomethane in ether gave *O*-methylated **2**, along with **4**. The former product was found to be identical with **2** by direct

comparison. The hydrolysis of **2** with sodium hydroxide–ethanol gave **4**. From these findings, compounds **1** and **2** were established as esters of 3-hydroxybutyric acid with sanguinine (**9**)[7] and galanthamine (**4**), respectively. The acid moieties in **1** and **2** were assigned to be bonded to the C-2 hydroxyl group in **9** and **4** on the basis of the deshielding of the signals of H-2 (see Table I) in **1** and **2**, compared wtih those in **9** and **4**, respectively. This assignment and the stereochemistry of the 3-hydroxybutyryl moieties in **1** and **2** were confirmed by partial synthesis of *O*-methylleucotamine acetate (**10**) from **4**. Acetylation of **2** with acetyl chloride in the presence of boron trifluoride etherate gave the acetate (**10**) as an oil: ($CDCl_3$) $\delta$ 1.261 (3H, d, $J$=6.4 Hz, $H_3$-4′) and 1.942 (3H, s, 3′-$OCOCH_3$). On the other hand, according to Paquette and Freeman,[12] commercially available (±)-3-hydroxybutyric acid was acetylated and partially resolved with quinine to give optically impure (*S*)-(+)- and (*R*)-(−)-3-acetoxybutyric acids ($[\alpha]_D$ +3.4° and −4.0° (EtOH), respectively), which were treated with



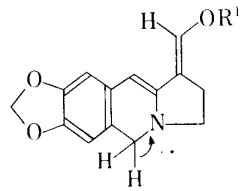
**3**: $R^1$=Ac, $R^2$=H
*m/z* 359 (97.0)
$C_{19}H_{21}NO_6$
Calcd: 359.1367
Found: 359.1320

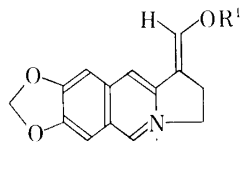
**5**: $R^1$=$R^2$=H
*m/z* 317 (79.9)
$C_{17}H_{19}NO_5$
Calcd: 317.1262
Found: 317.1245



**13**: $R^1$=$R^2$=Ac
*m/z* 401 (94.4)
$C_{21}H_{23}NO_7$
Calcd: 401.1473
Found: 401.1456

(a)





(b)
$R^1$=Ac (from **3**)
*m/z* 285 (100)
$C_{16}H_{15}NO_4$
Calcd: 285.1000
Found: 285.0985
$R^1$=H (from **5**)
*m/z* 243 (28.4)
$C_{14}H_{13}NO_3$
Calcd: 243.0894
Found: 243.0873
$R^1$=Ac (from **13**)
*m/z* 285 (100)
$C_{16}H_{15}NO_4$
Calcd: 285.1001
Found: 285.0980

(c)
$R^1$=Ac (from **3**)
*m/z* 284 (41.6)
$C_{16}H_{14}NO_4$
Calcd: 284.0923
Found: 284.0969
$R^1$=H (from **5**)
*m/z* 242 (80.8)
$C_{14}H_{12}NO_3$
Calcd: 242.0815
Found: 242.0809
$R^1$=Ac (from **13**)
*m/z* 284 (89.5)
$C_{16}H_{14}NO_4$
Calcd: 284.0924
Found: 284.0980

Chart 2

oxalyl chloride in benzene to give the corresponding acid chlorides (**11a** and **11b**, respectively). Esterification of **4** with the chlorides, **11a** and **11b**, in the presence of boron trifluoride etherate afforded optically impure products ($[\alpha]_D$ $-68.2°$ and $-64.6°$ (EtOH), respectively). The former product ($[\alpha]_D$ $-68.2°$) consisted of 3′*S*- and 3′*R*-*O*-methylleucotamine acetates (**12a** and **12b**, respectively) [8 : 2], and the latter ($[\alpha]_D$ $-64.6°$) of **12a** and **12b** [4 : 6], as judged from the relative intensities of *C*-methyl and acetyl proton signals in the $^1$H-NMR spectra: $H_3$-4′ of **12a** at $\delta$ 1.277 (3H,d, $J$=6.1 Hz) and of **12b** at $\delta$ 1.259 (3H, d, $J$=6.4 Hz) and 3′-$OCOCH_3$ of **12a** at $\delta$ 1.971 (3H, s) and of **12b** at $\delta$ 1.941 (3H, s). Comparison of these signals of the acetate (**10**) with those of **12a** and **12b** showed that the stereostructure of **10** was the same as that of **12b**. Therefore, the structures of *O*-methylleucotamine and leucotamine were established as **2** and **1**, respectively. These are the first reported galanthamine-type alkaloids having a 3*R*-hydroxylbutyryl group, which is of interest from the biogenetic point of view.[5,6] Galanthamine (**4**) seems to be an artifact formed from **2** judging from the fact that compound **2** was easily hydrolyzed to a mixture of **2** and **4** on thin layer chromatography (TLC) (see Experimental).

Compound **3**, $C_{19}H_{21}NO_6$, obtained as prisms, mp 157—160 °C, was optically active. Its infrared (IR) spectrum (KBr) showed absorptions due to a hydroxyl group at 3450 $cm^{-1}$, a carbonyl group at 1740 $cm^{-1}$, and a methylenedioxy group at 940 $cm^{-1}$. The $^1$H-NMR spectrum showed the presence of an olefinic proton, a *para*-oriented aromatic proton, a methylenedioxy group, an acetyl group, and an aliphatic *o*-methyl group, but no *N*-methyl group (see Experimental). These findings suggested that **3** has a lycorine-type skeleton. This suggestion was confirmed by the characteristics of its mass fragmentation pattern (see Chart 2): the formation of fragments (b) and (c) is considered to result from hydrogen transfer, the retro-Diels–Alder process, and loss of hydrogen. This fragmentation was supported by the mass spectra (MS) of ungiminorine (**5**), its diacetate (**13**) (see Chart 2), and narcissidine (*m/z* 333 ($M^+$)→259→258),[13] and by the similarity of these spectra to those of lycorine-type alkaloids.[13,14] The $^1$H-NMR spectrum showed close similarities to that of **5**, except for the signals due to the acetyl group. From these findings, compound **3** was concluded to be acetylungiminorine, in which the acetyl group is located at C-3, on the basis of the following spectral results: (i) the signal ($\delta$ 5.89) of H-3 in compound **3** was 1.24 ppm downfield from that ($\delta$ 4.65) of **5**. (ii) The MS of compound **3** showed the presence of fragments (b) (*m/z* 285) and (c) (*m/z* 284) (see Chart 2). Conclusive evidence for the stereochemistry of **3** was obtained by comparison of its acetate with ungiminorine diacetate (**13**):[8] acetylation of **3** and **5** with acetic anhydride and pyridine gave the same diacetate (**13**) of **5**. Thus, compound **3** was established as 3-*O*-acetylungiminorine (**3**).

## Experimental

All melting points are given as uncorrected values. The spectrophotometers used were a Hitachi EPI-G2 for IR spectra, a JEOL JMS-D 300 for MS, a Shimadzu UV-200 for UV spectra, a Yanagimoto OR-50 for optical rotation, and a JEOL JNM-PS-100 or a Hitachi R-22 for $^1$H-NMR spectra, with tetramethylsilane (TMS) as an internal standard. Silica gels 60 ($GF_{254}$ and $PF_{254}$, Merck) were used for TLC and prep. TLC, respectively. The following solvent systems were used: 1) $CHCl_3$–MeOH (10 : 1), 2) $CHCl_2$–$Et_2NH$ (10 : 1), 3) $CH_2Cl_2$–MeOH (10 : 1), 4) MeOH–acetone (3 : 2), 5) $CHCl_3$–MeOH–$Et_2NH$ (92 : 3 : 5), 6) benzene–MeOH (1 : 2). UV light, $I_2$ vapor, $FeCl_3$ and Dragendorff reagents were used for location of compounds.

**Isolation of Alkaloids**——Following the method of Wildman and Bailey,[7] fresh leaves (12.7 kg) of *L. asetivum* L., collected in Tokushima Prefecture, were extracted three times with EtOH (15 l). The ethanolic extract was evaporated to about 5 l *in vacuo*, acidified (pH 4) with tartaric acid, and washed with ether until the ether layer was colorless, to remove neutral and acidic materials. The aqueous acidic solution was made basic (pH 8) with conc. $NH_4OH$ and extracted with $CHCl_3$. The extract was evaporated down *in vacuo* to give crude alkaloids (6.5 g), which were separated into $CHCl_3$-insoluble (1.3 g) and $CHCl_3$-soluble (4.7 g) materials by mixing with $CHCl_3$ (80 mg). The $CHCl_3$-insoluble material (237 mg) was recrystallized from EtOH to give lycorine (**8**, 117 mg, mp 251—

254 °C), which was identical with authentic **8**[7] by direct comparison. The $CHCl_3$-soluble materials (4.7 g) were subjected to prep. TLC (solvent 1) to give three fractions: I, *Rf* 0—0.05 (37 mg); II, *Rf* 0.26—0.41 (510 mg); and III, *Rf* 0.42—0.79 (2.954 g). Fraction I was further subjected to prep. TLC (solvent 5) to give amorphous pretazettine (**6**, 26 mg). On prep. TLC (solvent 4), fraction II gave crude leucotamine (**1**, 43 mg) (*Rf* 0.32—0.44) and ungiminorine (**5**, 216 mg (*Rf* 0.44—0.61). Fraction III was further subjected to prep. TLC (solvent 2) to give two fractions: III-A, *Rf* 0.16—0.27 (60 mg) and III-B, *Rf* 0.52—0.76 (1.9 g). Fraction III-A was purified by prep.TLC (solvent 6) to give crude demethylhomolycorine (**7**, 27 mg). On prep. TLC (solvent 3), fraction III-B gave two fractions: III-B-1 (*Rf* 0.39—0.62; 1.2 g) and III-B-2 (*Rf* 0.62—0.71; 53 mg). Further prep. TLC (solvent 2) of III-B-1 gave *O*-methylleucotamine (**2**, 816 mg) (*Rf* 0.19—0.36) and galanthamine (**4**, 224 mg) (*Rf* 0.40—0.50). The TLC treatment of **2** was repeated to give **2**, along with a small amount of **4**. 3-*O*-Acetylungiminorine (**3**, 12 mg) was obtained by purification of fraction III-B-2 by prep. TLC (solvent 6).

Similar extraction and treatment of fresh bulbs (4.7 kg) of this plant gave crude lycorine (**8**, 1.49 g), pretazettine (**6**, 42 mg), crude ungiminorine (**5**, 409 mg), galanthamine (**4**, 266 mg), *O*-methylleucotamine (**2**, 63 mg), and 3-*O*-acetylungiminorine (**3**, 80 mg).

**Pretazettine (6)**[7]——This amorphous base was crystallized as colorless prisms of its hydrochloride [mp 226—228 °C (from EtOH). *Anal.* Calcd for $C_{18}H_{22}ClNO_5$: C, 58.77; H, 6.03; N, 3.81. Found: C, 58.50; H, 5.98; N, 3.68] and as yellow prisms of its picrate [mp 207—209 °C (from acetone). *Anal.* Calcd for $C_{24}H_{24}N_4O_{12}$: C, 51.43; H, 4.23; N, 10.00. Found: C, 51.59; H, 4.33; N, 9.77]. These derivatives were identical with authentic pretazettine hydrochloride and picrate,[7] respectively, by direct comparison.

**Leucotamine (1)**——Crude **1** was recrystallized from benzene as colorless needles (28 mg), mp 168—171 °C. $[\alpha]_D^{20}$ −52.6° (*c* = 0.74, $CHCl_3$). For $^1$H-NMR ($CDCl_3$) spectrum, see Table I. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 1730. *Anal.* Calcd for $C_{20}H_{25}NO_5$: C, 66.83; H, 7.01; N, 3.90. Found: C, 66.65; H, 7.03; N, 3.75.

**Methylation of Compound 1**——Compound **1** (6 mg) in MeOH (1 ml) was methylated with excess $CH_2N_2$ to give a mixture, which was subjected to prep. TLC on $Al_2O_3$ ($PF_{254}$) with ethyl acetate–benzene (1 : 1) to give an *O*-methylated product and **4**. The former product (High MS *m/z*: Calcd for $C_{21}H_{27}NO_5$: 373.1889. Found: 373.1879) was identical with *O*-methylleucotamine (**2**) (see below) based on a comparison of the TLC behavior, and optical rotatory dispersion (ORD) and IR spectral data.

***O*-Methylleucotamine (2)**——Oil, $[\alpha]_D^{24}$ −36.0° (*c* = 0.75, $CHCl_3$), −49.3° (*c* = 0.75, EtOH). IR $\nu_{max}^{film}$ $cm^{-1}$: 3400, 1720. For $^1$H-NMR spectrum, see Table I. High MS *m/z*: Calcd for $C_{21}H_{27}NO_5$: 373.1888. Found: 373.1874. *O*-Methylleucotamine methiodide, prepared from **2** and methyl iodide, was crystallized from acetone as yellow needles, mp 199—200 °C. *Anal.* Calcd for $C_{22}H_{30}INO_5 \cdot H_2O$: C, 49.54; H, 6.05; N, 2.63. Found: C, 49.52; H, 5.95; N, 2.72.

**Hydrolysis of 2**——Refluxing of **2** (52 mg) with 10% NaOH (2 ml)–EtOH (2 ml) for 0.5 h gave **4** [26 mg, mp 125—127 °C, $[\alpha]_D^{23}$ −112.1° (*c* = 0.68, EtOH)], which was identical with authentic **4**[7] (TLC behavior, IR spectral comparison and mixed mp determination).

**Acetylation of 2**——Treatment of **2** (18 mg) in tetrahydrofuran (3 ml) with acetyl chloride (0.5 ml) and boron trifluoride etherate (0.1 ml) at room temp. for 4 h gave an acetate (**10**) as an oil, $[\alpha]_D^{24}$ −65.7° (*c* = 0.87, $CHCl_3$) and $[\alpha]_D^{23}$ −33.9° (*c* = 0.57, EtOH). IR $\nu_{max}^{film}$ $cm^{-1}$: 1740, 1620. $^1$H-NMR ($CDCl_3$) $\delta$: 1.261 (3H, d, *J* = 6.4 Hz, $H_3$-4′), 1.942 (3H, s, $COCH_3$), 2.41 (3H, s, $NCH_3$), 2.55 (2H, m, H-2′), 2.71 (1H, m, H-1), 3.26 (2H, m, H-7), 3.70 and 4.16 (each 1H, d, *J* = 15 Hz, $H_2$-9), 3.80 (3H, s, $OCH_3$), 4.51 (1H, m, H-16), 5.20 (1H, m, H-3′), 5.33 (1H, m, H-2), 5.89 (1H, dd, *J* = 10, 4 Hz, H-3), 6.28 (1H, d, *J* = 10 Hz, H-4), 6.59 (1H, d, *J* = 8 Hz, H-11), 6.66 (1H, d, *J* = 8 Hz, H-12). High MS *m/z*: Calcd for $C_{23}H_{29}NO_6$: 415.1995. Found: 415.2028.

**Partial Syntheses of 12a and 12b from 2**——According to Paquette and Freeman,[12] commercially available (±)-3-hydroxybutyric acid (1.6 g) was acetylated with acetic anhydride (11 ml) and pyridine (3 ml) to give (±)-3-acetoxybutyric acid (1.5 g), which, in acetone (20 ml), was resolved with quinine (2.7 g) to give (*S*)-(+)- and (*R*)-(−)-3-acetoxybutyric acids [170 mg; $[\alpha]_D^{23}$ +3.4° (*c* = 2.3, EtOH)] and [150 mg; $[\alpha]_D^{21}$ −4.0° (*c* = 10.2, EtOH)], respectively. Treatment of the former acid (65 mg) in benzene (0.5 ml) with oxalyl chloride (0.5 ml) at room temp. for 2.5 h followed by esterification with **4** (21 mg) in ether (1 ml) and boron trifluoride etherate (0.1 ml) at room temp. for 4 h gave an acetate as an oil (11 mg), which consisted of **12a** and **12b** (8 : 2), $[\alpha]_D^{22}$ −68.2° (*c* = 0.73, EtOH). IR $\nu_{max}^{film}$ $cm^{-1}$: 1735, 1620. $^1$H-NMR ($CDCl_3$) $\delta$: 1.277 and 1.259 (total 3H, each d, *J* = 6.1 and 6.4 Hz, respectively, $H_3$-4′), 1.971 and 1.941 (total 3H, each s, $OCOCH_3$), 2.37 (3H, s, $NCH_3$), 3.65 and 4.10 (each 1H, d, *J* = 15 Hz, $H_2$-9), 3.83 (3H, s, $OCH_3$), 4.54 (1H, m, *J* = 6 Hz, H-16), 5.20 (1H, m, H-3′), 5.35 (1H, m, *J* = 10 Hz, H-2), 5.87 (1H, dd, *J* = 10, 4.5 Hz, H-3), 6.30 (1H, d, 10 Hz, H-4), 6.57 (1H, d, *J* = 8 Hz, H-11), 6.65 (1H, d, *J* = 8 Hz, H-12). Its methiodide, mp 212—214 °C, was crystallized from EtOH. *Anal.* Calcd for $C_{24}H_{32}INO_6 \cdot H_2O$: C, 50.09; H, 5.96; N, 2.43. Found: C, 50.26; H, 5.95; N, 2.20. Similar treatment of (*R*)-(−)-3-acetoxybutyric acid (70 mg) with oxalyl chloride (0.5 ml), and then with **4** (20 mg) gave an oil (13 mg), which consisted of **12b** and **12a** (6 : 4), $[\alpha]_D^{23}$ −64.6° (*c* = 0.87, EtOH). IR $\nu_{max}^{film}$ $cm^{-1}$: 1735, 1620. $^1$H-NMR ($CDCl_3$) $\delta$: 1.259 and 1.277 (total 3H, each d, *J* = 6.4 and 6.1, respectively, $H_3$-4′), 1.941 and 1.971 (total 3H, each s, $OCOCH_3$), 2.38 (3H, s, $NCH_3$), 2.54 (2H, d, *J* = 6 Hz, H-2′), 3.66 and 4.11 (each 1H, d, *J* = 15 Hz, $H_2$-9), 3.83 (3H, s, $OCH_3$), 4.56 (1H, m, H-16) 5.20 (1H, m, H-3′), 5.32 (1H, m, *J* = 10 Hz, H-2), 5.89 (1H, dd, *J* = 10, 5 Hz, H-3), 6.29 (1H, d, *J* = 10 Hz, H-4), 6.57 (1H, d, *J* = 8 Hz, H-11), 6.64 (1H, d, *J* = 10 Hz, H-12).

**Ungiminorine (5)**[8,9]——Colorless prisms, mp 208—211 °C (from acetone), $[\alpha]_D^{24}$ −49.0° (*c* = 0.67, EtOH) and

$-31.6°$ ($c=0.73$, $CHCl_3$). IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3430, 940. $^1$H-NMR ($CDCl_3$) $\delta$: 2.67 (1H, dd, $J=11$, 2 Hz, H-15), 3.43 (3H, s, $OCH_3$), 3.50 and 4.01 (each 1H, d, $J=13$ Hz, $H_2$-7), 4.65 (2H, m, H-1 and H-3), 5.56 (1H, br s, H-4), 5.88 (2H, s, $OCH_2O$), 6.63 (1H, s, H-8), 6.86 (1H, s, H-11); (pyridine-$d_5$) $\delta$ 3.13 (1H, dd, $J=11$, 2 Hz, H-15), 3.40 (3H, s, $OCH_3$), 3.63 and 4.11 (each 1H, d, $J=14$ Hz, $H_2$-7), 4.53 (1H, m, H-16), 4.64 (2H, m, H-1 and H-3), 5.74 (1H, dd, $J=3$, 2 Hz, H-4), 5.86 and 5.91 (each 1H, d, $J=2$ Hz, $OCH_2O$), 6.79 (1H, s, H-8), 7.28 (1H, s, H-11). High MS *m/z*: Calcd for $C_{17}H_{19}NO_5$: 317.1263. Found: 317.1272. *Anal.* Calcd for $C_{17}H_{19}NO_5$: C, 64.34; H, 6.04; N, 4.36. Found: C, 64.14; H, 5.96; N, 4.36. Its picrate, mp 170—172 °C (from MeOH). *Anal.* Calcd for $C_{23}H_{22}N_4O_{12}$: C, 50.55; H, 4.06; N, 10.26. Found: C, 50.60; H, 3.96; N, 10.05.

**3-*O*-Acetylungiminorine (3)**——Colorless prisms, mp 157—160 °C (from benzene). $[\alpha]_D^{24}$ $-257.1°$ ($c=0.70$, $CHCl_3$). IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3450, 1740, 940. $^1$H-NMR ($CDCl_3$) $\delta$: 1.99 (3H, s, $COCH_3$), 2.77 (1H, m, $J=11$ Hz, H-15), 3.47 (3H, s, $OCH_3$), 3.62 and 4.04 (each 1H, d, $J=13$ Hz, $H_2$-7), 4.62 (1H, br s, H-1), 5.71 (1H, br s, H-4), 5.89 (3H, br s, H-3 and $OCH_2O$), 6.68 (1H, s, H-8), 6.90 (1H, s, H-11). High MS *m/z*: Calcd for $C_{19}H_{21}NO_6$: 359.1367. Found: 359.1320. *Anal.* Calcd for $C_{19}H_{21}NO_6$: C, 63.50; H, 5.89; N, 3.90. Found: C, 63.60; H, 5.90; N, 3.82.

**Diacetylungiminorine (13)**[8]——(i) From **3**: Refluxing of **3** (50 mg) with acetic anhydride (0.8 ml) and pyridine (0.5 ml) for 1 h gave **13** (31 mg) as colorless needles, mp 172—174 °C (from ether). $[\alpha]_D^{24}$ $-126.8°$ ($c=0.47$, $CHCl_3$). IR $\nu_{max}^{KBr}$ $cm^{-1}$: 1740, 1730, 940. $^1$H-NMR ($CDCl_3$) $\delta$: 1.98 and 2.01 (each 3H, s, $2\times COCH_3$), 2.95 (1H, m, $J=14$ Hz, H-15), 3.51 (3H, s, $OCH_3$), 3.65 and 4.08 (each 1H, d, $J=13$ Hz, H-7), 5.60 (1H, br s, H-4), 5.63 (1H, m, H-1), 5.91 (3H, br s, H-3 and $OCH_2O$), 6.51 (1H, s, H-8), 6.68 (1H, s, H-11). High MS *m/z*: Calcd for $C_{21}H_{23}NO_7$: 401.1473. Found: 401.1456.

(ii) From **5**: Similar treatment of **5** (10 mg) with acetic anhydride (0.1 ml), and pyridine (0.2 ml) gave an acetate (mp 164—167 °C), which was found to be identical with the acetate (**13**) prepared by method (i) on the basis of IR and TLC comparisons and mixed mp determination.

**Galanthamine (4)**[7]——Colorless cubes, mp 125—126 °C (from acetone), $[\alpha]_D^{24}$ $-114.4°$ ($c=0.67$, EtOH). For $^1$H-NMR, see Table I. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3350, 1620. This base was shown to be identical with authentic **4** (TLC behavior, mixed mp, and IR and $^1$H-NMR spectral data).

**Demethylhomolycorine (7)**[11]——Colorless cubes, mp 211—212 °C (from ethyl acetate), $[\alpha]_D^{24}$ $+89.6°$ ($c=0.41$, $CHCl_3$). IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3400, 1720. $^1$H-NMR ($CDCl_3$) $\delta$: 2.04 (3H, s, $NCH_3$), 2.80 (1H, br s, H-11b), 3.90 (3H, s, $OCH_3$), 4.80 (1H, br s, H-5a), 5.54 (1H, br s, H-4), 7.09 (1H, s, H-11), 7.60 (1H, s, H-8). *Anal.* Calcd for $C_{17}H_{19}NO_4$: C, 67.76; H, 6.36; N, 4.65. Found: C, 67.80; H, 6.40; N, 4.71. This base was identical with authentic demethylhomolycorine (**7**) on the basis of TLC behavior, mixed mp, and IR and $^1$H-NMR spectral comparisons.

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