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# ALKALOIDS OF *GALANTHUS ELWESII*

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**Key Word Index**—*Galanthus elwesii*; Amaryllidaceae: leucotamine; *O*-methyl-leucotamine; 9-*O*-demethylhomolycorine; 5-methoxy-9-*O*-demethylhomolycorine; 16-hydroxygalwesine; 16-hydroxy-9-*O*-demethylgalwesine; galwesine; 9-*O*-demethylgalwesine; galasine.

**Abstract**—Six new lycorenine-type alkaloids, ( + )-5-methoxy-9-*O*-demethylhomolycorine, ( + )-galwesine, ( + )-9-*O*-demethylgalwesine, ( + )-16-hydroxygalwesine, ( + )-16-hydroxy-9-*O*-demethylgalwesine and galasine, were isolated from whole plants of *Galanthus elwesii*. Additionally, 12 known alkaloids, ( − )-galanthamine, ( − )-sanguinine, ( − )-leucotamine, ( − )-*O*-methylleucotamine, ( ± )-narwedine, ( − )-*N*-demethylgalanthamine, ( + )-11-hydroxyvittatine, ( + )-9-*O*-demethylhomolycorine, ( − )-lycorine, ( − )-galanthine, hordenine, and (*E*)-*N*-feruloyltyramine were also obtained. Of these alkaloids, only galanthamine and lycorine have been isolated previously from *G. elwesii*. Identification and structural elucidation were achieved using spectrometric techniques.

## INTRODUCTION

In previous phytochemical investigations of *Galanthus elwesii*, the following alkaloids were isolated: galanthamine (**1**) [1–3], lycorine [4, 5], elwesine, flexine [2], haemanthamine [1] and tazettine [1, 2]. They all belong to the Amaryllidaceae alkaloids, which have been shown to possess interesting pharmacological activities [6]. In this paper, we wish to report the isolation and characterization of the alkaloidal constituents of whole plants of *G. elwesii*.

## RESULTS AND DISCUSSION

Whole plants of *G. elwesii* afforded 12 known and six novel alkaloids. Ten of the known alkaloids belong to the Amaryllidaceae alkaloids and the remaining two are hordenine [7] and (*E*)-*N*-feruloyltyramine [8, 9], which are very common bases found in many other plant families.

Six known galanthamine-type alkaloids: ( − )-galanthamine (**1**), ( − )-sanguinine (**2**), ( − )-*N*-demethylgalanthamine (**3**), ( − )-leucotamine (**4**), ( − )-*O*-methylleucotamine (**5**) and ( ± )-narwedine (**6**), have been isolated and identified by spectroscopic techniques. In the case of **4** [10, 11], identification was confirmed by X-ray diffraction analysis of a single crystal and by hydrolysis to sanguinine (**2**) [12–14]. Spectroscopic data for **4** are consistent with the structure and Fig. 1 shows its ORTEP [15] drawing. The absolute configuration of **4** has been assigned relative to the known configuration at C-3, C-4a, and C-12a (C3, C5, and C12a in Fig. 1) of **2** and is thus *R* at C-3′ (C18 in Fig. 1). The molecule is involved in one intermolecular and one intramolecular hydrogen bond. The intermolecular hydrogen bond links the molecules into infinite one-dimensional chains running parallel to the *a*-axis.

Only one crinine-type alkaloid was isolated, namely ( + )-11-hydroxyvittatine (**7**). Additionally, two lycorine-type alkaloids, ( − )-lycorine and ( − )-galanthine, were isolated and identified. Except for galanthamine [1–3] and lycorine [4, 5], none of these known alkaloids, have been described previously from *G. elwesii*. Furthermore, of the seven lycorenine-type alkaloids which have been isolated and characterized, six are novel compounds.

Compound **8** was isolated from five different subfractions and identified, on the basis of information deduced from thorough-spectral analyses, as the known alkaloid, ( + )-9-*O*-demethylhomolycorine [11, 16–27]. The CD, UV, $^1$H, $^{13}$C NMR and mass spectra were all superimposable with each other. However, their melting points and, to some extent, their optical rotations were different as noticed also by other authors (Table 1). In order to clarify the situation, the structures of recrystallized **8b, 8c, 8d** and **8e** were determined by single crystal X-ray analyses (Fig. 2). The crystal structures of **8d** and **8e** were identical. The configurations of all three molecules appear to be identical, except for the configuration at the N-atom, which is inverted in **8c**; the lone pair and the methyl group have changed places. The crystal lattice of

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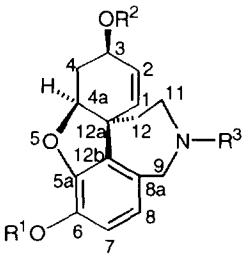
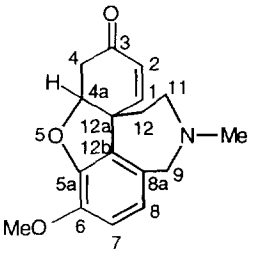
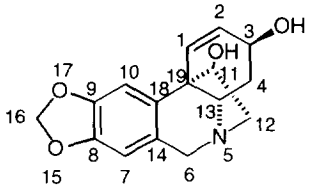


| | $R^1$ | $R^2$ | $R^3$ |
|---|---|---|---|
| **1** | Me | H | Me |
| **2** | H | H | Me |
| **3** | Me | H | H |
| **4** | H | $COCH_2CHOHMe$ | Me |
| **5** | Me | $COCH_2CHOHMe$ | Me |



**6**



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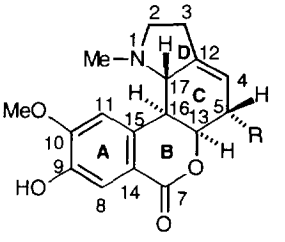
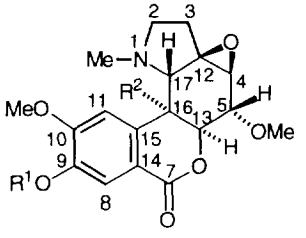
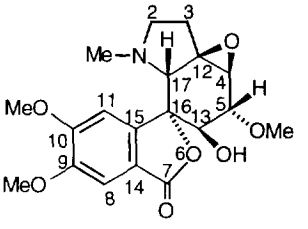


| | R |
|---|---|
| **8** | H |
| **9** | OMe |



| | $R^1$ | $R^2$ |
|---|---|---|
| **10** | Me | OH |
| **11** | H | OH |
| **12** | Me | H |
| **13** | H | H |



**14**

§ The numbering refers to that of *Chemical Abstracts*

**8b** contains two molecules of water and one molecule of **8** in the asymmetric unit (Fig. 3), while that of **8c** contains no solvent. The crystal lattice of **8d** contains two molecules of **8** plus one disordered EtOAc molecule in the asymmetric unit (Fig. 4). Apparently the geometry of the molecule in **8b** and **8d** is such that it cannot pack efficiently in a crystal lattice without leaving significant 'holes' between the molecules. The 'holes' are readily filled with suitable small molecules from the solvent used for recrystallization. On the other hand, compound **8c** seems to have the geometry which can pack without 'holes' and does not need solvent in the crystal lattice. The variations in melting points of the five fractions would therefore be due to the presence of different solvent molecules in the crystals, as well as the different conformers. The differences in optical rotation are well explained by dependency of the true concentration of the sample and the assumed formulae weight.

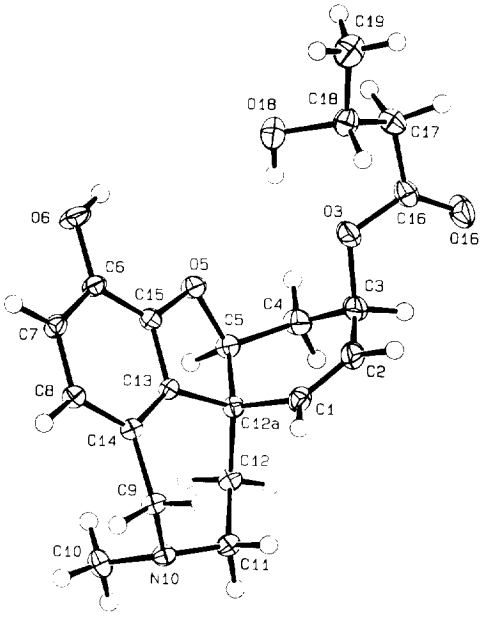



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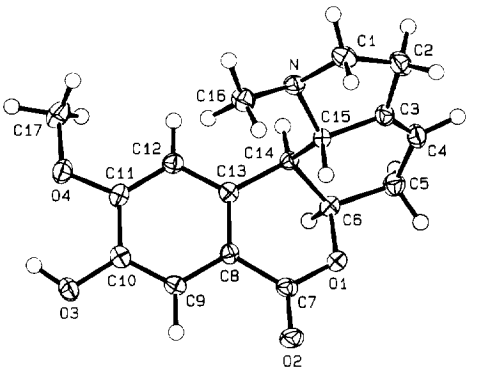
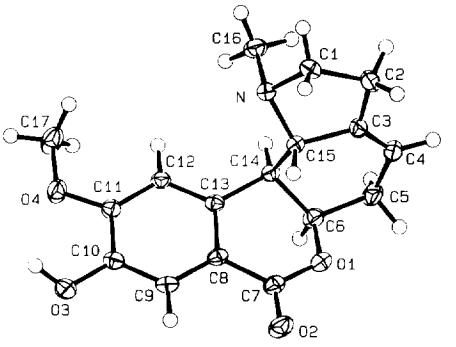
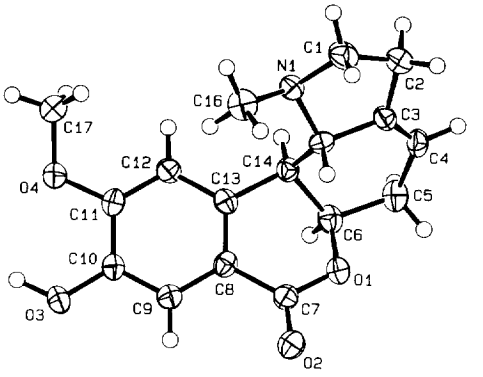
Fig. 1. ORTEP drawing [15] of leucotamine (**4**) (arbitrary numbering of atoms).




**8b**




**8c**



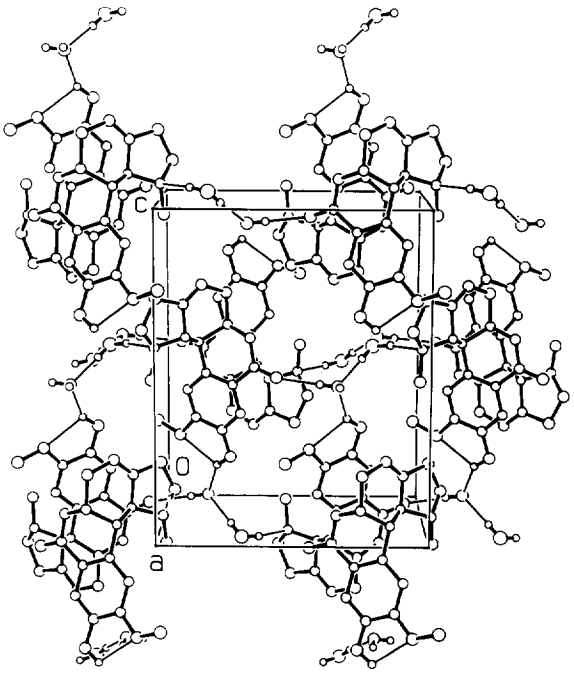

**8d**

Fig. 2. ORTEP drawings [15] of **8b**, **8c** and **8d** (arbitrary numbering of atoms).

The water molecules in **8b** lie in one-dimensional channels within the crystal lattice, which run parallel to the *a*-axis, and combine with molecules of **8** in a complex three-dimensional hydrogen bonding network (Fig. 3). The base **8c** is involved in one weak intramolecular and one stronger intermolecular hydrogen bond, both involving the hydrogen atom of the hydroxyl group, which therefore forms bifurcated hydrogen bonds. The intramolecular hydrogen bond forms a five-membered ring between the methoxyl and hydroxyl groups. The intermolecular interaction links the hydroxyl group with the nitrogen atom of an adjacent molecule, thereby forming infinite one-dimensional chains running parallel to the *c*-axis. The molecules of **8d** have the same pattern of inter- and intramolecular hydrogen bonds that were found in **8c**. The intermolecular interactions link the molecules into infinite, one-dimensional, zig-zag chains running parallel to the *b*-axis (Fig. 4).

Table 1. Physical data of compounds **8a**–**8e** [28, 29]

| Compound | Recrystallization solvent | Mp° | $[\alpha]_D^{22}$ (MeOH; *c*) |
|---|---|---|---|
| **8a** | MeOH | 118–119 | + 99.0° (0.22) |
| **8b** | EtOAc (twins) | 214–216 | + 101.8° (0.33) |
| **8**.2 $H_2O$ (see Figs 2 & 3) | MeOH–$CHCl_3$ | 207–210 | |
| **8c** (see Fig. 2) | EtOAc | 183–185 | + 115.6° (0.85) |
| **8d** | MeOH | 181–184 | + 125.0° (1.18) |
| **8** · 1/2 EtOAc (see Figs 2 & 4) | EtOAc | 217–219 | + 99.4° (0.50) |
| **8e** | EtOAc | 211–213 | |




**8b**

Fig. 3. Crystal packing of **8b** viewed down the a-axis.

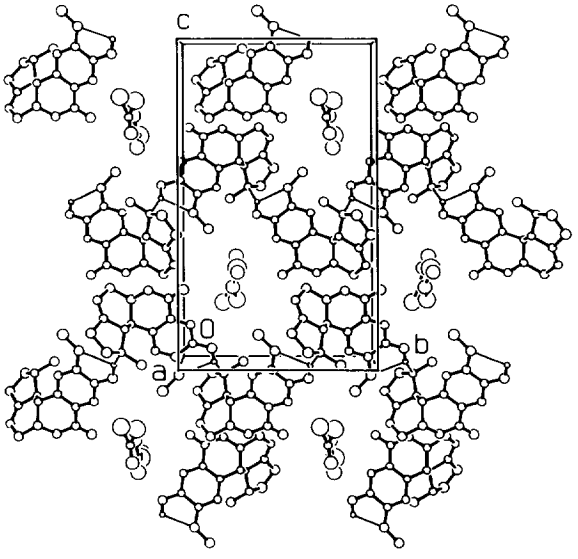



Fig. 4. Crystal packing of **8d** viewed down the a-axis.

The UV spectrum of compound **9** resembles that of **8a–8e** and shows a bathochromic shift in the presence of NaOH. This is typical of non-phenolic lycorenine-type alkaloids having two chromophores, namely a benzene ring with susbstituents and a ketone group conjugated with the benzene ring. In the IR spectrum, the presence of a carbonyl group, demonstrated by an intense absorption at 1718 $cm^{-1}$ is further verified by the signal in the $^{13}C$ NMR spectrum at $\delta$164.9, indicating the presence of a lactone moiety. In the EI mass spectrum of **9**, the base peak is observed at *m/z* 139, along with an intense fragment ion at *m/z* 124, whereas the expected $[M]^+$ at *m/z* 331 is not observed. The fragmentation pattern is in accordance with the retro-*Diels-Alder* reaction of the C ring, which has also been observed for other alkaloids of the homolycorine subgroup having a hydroxyl substituent at C-5 [30, 31]. This $^1H$ NMR spectrum of **9** also shows close similarities to that of **8a–8e** with the exception of a signal at $\delta$3.45, which accounts for an aliphatic methoxyl group. The other difference of these spectra is the presence of an one-proton singlet at $\delta$3.93 (**9**) instead of a two-proton multiplet at $\delta$2.59 for H-5 (**8a–8e**). This singlet is assignable to a methine proton in the $\alpha$-position to the new oxygen atom in **9**. The $^{13}C$ NMR spectrum of **9**, which again bears close similarities with those of **8a–8e**, differs only in having a signal due to a methoxyl group and a $\sim$ 46 ppm downfield shift for the C-5 resonance, which also indicates that the aliphatic methoxyl group is located on C-5. In addition, the positions of the aliphatic methoxyl group on C-5, as well as the position of the aromatic methoxyl group at C-10 were efficiently established through NOE experiments. The stereochemistry of **9** is established by using the information derived from chemical shifts, coupling constants, peak profiles of H-4, H-5, H-13, H-16 and H-17, and by comparison with analogous signals of the congener alkaloids, hippeastrine [20], 5-hydroxyhomolycorine [21] and compound **10**. Alkaloid **9**, identified as 9-hydroxy-5,10-dimethoxy-1-methyllycorenan-7-one, was named (+)-5-methoxy-9-*O*-demethylhomolycorine.

Compound **10** exhibits a UV spectrum which is typical of nonphenolic lycorenine-type alkaloids having a $\delta$-lactone moiety. The presence of a lactone moiety is further verified by a 'quaternary' signal in the $^{13}C$ NMR spectrum at $\delta$163.4 and an intense IR absorption at 1720 $cm^{-1}$. Furthermore, its mass spectrum exhibits a fragment ion at *m/z* 112 as the base peak and a relatively small $[M]^+$ at *m/z* 377, which is more intense than those of **8** and **9**. The fragmentation seems to proceed predominantly by ring C cleavage. Remarkable is the low abundance (< 2%) of the signal for the aromatic lactone moiety at *m/z* 206. On the contrary, the nitrogen-containing fragments at *m/z* 155, 140, and 112 are most abundant.

Conventional $^{13}C$ NMR and DEPT spectra of **10** account for 19 carbon atoms, of which seven are quaternary, six are methine, two are methylene and four are methyl carbons. The chemical shifts of the protonated carbons were assigned with the help of $^{13}C$, $^1H$ COSY [32, 33] experiments. The $^1H$ NMR spectrum displays two singlets at $\delta$7.48 and 7.13 characteristic of the *para*-oriented aromatic protons 8 and 11, respectively, where the relevant chemical shifts are assigned by consideration of the deshielding effect of the *peri*-carbonyl group on H-8. Four singlets of three protons each at $\delta$3.99, 3.93, 3.58 and 2.01 are assigned to two aromatic, one aliphatic methoxyl and an N-methyl group, respectively. These were also verified by the corresponding signals in the

$^{13}$C NMR spectrum at $\delta$59.1, 56.3, 56.3, and 44.0. A singlet at $\delta$4.58 is due to the methine proton on C-13 and shows a NOE with the aliphatic methoxyl group, as well as with the broad singlet at $\delta$3.90. Further NOE experiments verify that both the methoxyl group and the methine proton are located on C-5. On the basis of NOE and decoupling experiments, two signals at $\delta$3.18 (*t*) and 2.64 (*m*) are assigned to the $\alpha$- and $\beta$-protons on C-2, the $\alpha$-proton being more deshielded due to its *cis*-relationship with the nitrogen lone pair. The NOE and decoupling experiments also furnished evidence for the assignment of $\delta$2.32 (*m*) and 1.88 (*dd*) signals to the $\alpha$- and $\beta$-protons on C-3. The presence of these two methylene carbons was also verified by signals at $\delta$56.0 and 30.4 in the $^{13}$C NMR spectrum. Irradiation of the singlet at $\delta$2.69 brings about an enhancement only of the N-Me, indicating that this proton is located on C-17. The broad singlet at $\delta$3.41 is attributable to the methine proton H-4.

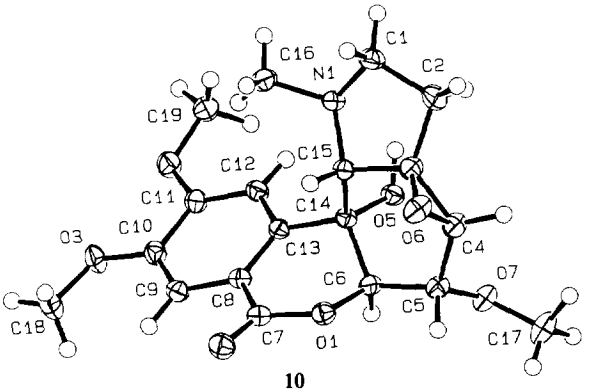
The information provided by the above mentioned spectral data points to the fact that compound **10** is a homolycorine derivative having a methoxy substituent at C-5 and other substituents at C-16, C-12 and C-4, at least one of which is a hydroxyl group, the presence of which is verified by an intense absorption at 3395 cm$^{-1}$ in the IR spectrum. This hydroxyl group is positioned on C-16, since H-17 has no vicinal coupling. Since the mass spectrum furnishes a $[M]^+$ at *m/z* 377, a molecular formula of $C_{19}H_{23}NO_7$ can be suggested. Of the seven oxygens, two belong to the lactone moiety, while four are accounted for by methoxyl and hydroxyl groups. The remaining seventh oxygen must be shared by C-4 and C-12, thus strongly supporting the presence of an epoxy moiety between these two carbon atoms. In agreement with this suggestion is the intense absorption at 1285 cm$^{-1}$ in the IR spectrum, which is attributable to the stretching vibration of an epoxy ring. Furthermore, the optical rotation of compound **10** is very small, $[\alpha]_D^{21} = +1.8°$ ($c$ = 0.224, MeOH) when compared with other lycorenine-type alkaloids. The CD spectrum of **10** has similarities with that of (+)-9-*O*-demethylhomolycorine, indicating that these two compounds have the same configuration in their benzopyrano[3,4-g]indole skeleton and possess a *cis*-B:C ring-junction.

To establish the proposed structure of this novel base with greater certainty, X-ray diffraction analysis was carried out. The X-ray results confirm the structure deduced from the spectral data. The molecular structure of **10** is illustrated in Fig. 5. An attempt to determine the absolute configuration was inconclusive. The molecule is involved in one intermolecular hydrogen bond, which is formed between the hydrogen atom of the hydroxyl group and the epoxide oxygen atom of an adjacent molecule. The hydrogen bonds link the molecules into infinite one-dimensional chains, which run parallel to the *a*-axis. Compound **10** is thus identified as 4,12-epoxy-16-hydroxy-5,9,10-trimethoxy-1-methyllycorenan-7-one and is named 16-hydroxygalwesine.

Compound **11** gives similar spectra to those of 16-hydroxygalwesine (**10**). However, a major difference in the $^1$H NMR spectrum is the lack of one of the signals due to an aromatic methoxyl group, the signal for which is also absent in the $^{13}$C NMR spectrum. Furthermore, the UV spectrum of **11** shows a bathochromic shift in the presence of NaOH, which points to the presence of a phenolic group. NOE experiments proved that an aromatic methoxyl group is positioned at C-10, thus defining the position of the phenolic hydroxyl group as being on C-9. Some other features of the $^1$H NMR spectrum of **11**, which differ from those of compound **10**, are the resonances of $H_\alpha$-2, $H_\beta$-2, and $H_\alpha$-3 ($\delta$3.18, 2.63, and 2.33), which appear as unresolved signals, while the aromatic proton signal at $\delta$7.13 is observed as a broad singlet. However, upon addition of $D_2O$ to the $CDCl_3$ solution of **11**, better resolution is obtained for the signals of $H_\alpha$-2, $H_\beta$-2, and $H_\alpha$-3, while the $\delta$7.13 signal becomes a sharp singlet. It is therefore assumed that compound **11** has a different conformation from compound **10**, as reflected in the original $^1$H NMR data. However, in solution, compound **11** undergoes a conformational change upon deuteration to adopt the conformation of **10**. Thus, the structure of **11** is very similar to that of **10**, being the 9-*O*-demethyl analogue of the latter. Compound **11** is 4,12-epoxy-9,16-dihydroxy-5,10-dimethoxy-1-methyllycorenan-7-one and is named (+)-16-hydroxy-9-*O*-demethylgalwesine.

Compound **12** was obtained in the form of a yellow amorphous powder. It exhibits UV, CD, and mass spectra which are similar to those of **10** and **11**. In addition to conventional 1-D $^1$H and $^{13}$C NMR including DEPT spectra, the 2-D NMR techniques $^1$H, $^1$H COSY [34], ROESY [35], TOCSY [36, 37], $^{13}$C, $^1$H COSY and $^{13}$C, $^1$H long-range COSY [38] were utilized for the assignment of the chemical shifts of the hydrogens and carbons. Once again, a striking similarity between compound **12** and **10** was observable in their $^1$H and $^{13}$C NMR spectra.

The main difference between the $^1$H NMR spectra of **12** and **10** is the appearance of a $\delta$2.81 signal in the former, which is assigned to a methine located on C-16, whereas a hydroxyl group is located in **10**. The signal ($\delta$2.81) interacts with H-17 and H-13, with coupling con-




**10**

Fig. 5. ORTEP drawing [15] of 16-hydroxygalwesine (**10**) (arbitrary numbering of atoms).

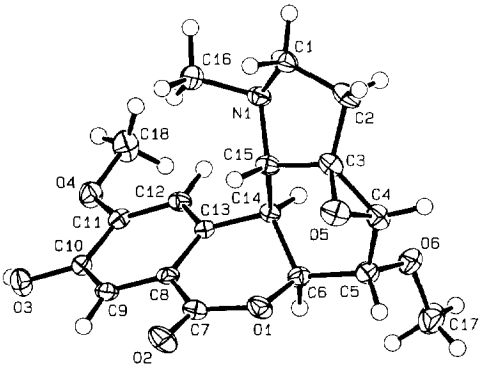
stants of 10.5 Hz and 2.4 Hz, respectively, indicating that H-16 and H-17 are *trans* to each other, while H-16 and H-13 are in a *cis*-relation. H-13 and H-17, which are singlets in the $^1$H NMR spectrum of **10**, appear as a doublet ($J$ 10.5 Hz) and a broad singlet, respectively, in the spectrum of **12**, lending support to the proposed structural difference between the two compounds. Additionally, the chemical shift of H-17 in the spectrum of **12** displays a small shift ($\sim$0.30 ppm) to a higher field as compared to the corresponding signal in **10**.

In the $^{13}$C NMR spectrum of **12**, which closely resembles that of **10**, the resonance of C-16 is observed at $\delta$40.1, while the corresponding signal for **10** is found at $\delta$66.0, the downfield nature of the latter resulting from the hydroxyl group located on C-16. As expected, the $[M]^+$ in the mass spectrum of **12** is found at $m/z$ 361, which is 16 mu less than that for **10**, further verifying that the only structural difference between **12** and **10** is that the former is unsubstituted at C-16, whereas the latter has a hydroxyl substituent at this position. The information gathered from these findings indicates that **12** possesses a homolycorine skeleton without a hydroxyl group on C-16, and that rings B and C have a *cis*-fusion. Thus, **12** is identified as galwesine (4,12-epoxy-5,9,10-trimethoxy-1-methyllycorenan-7-one).

The spectral data of compound **13** closely resemble those of **12**. The major difference is the presence of one less signal due to an aromatic methoxyl group, which is also the case in its $^{13}$C NMR spectrum. The methoxyl substituent of the aromatic ring was established by NOE experiments as being located on C-10. The decoupling experiments indicate that **13**, like other alkaloids of the homolycorine series, has a *cis*-B:C ring-fusion. The structure of compound **13** was deduced from spectral data to be (+)-9-*O*-demethylgalwesine (4,12-epoxy-9-hydroxy-5,10-dimethoxy-1-methyllycorenan-7-one) and was also confirmed by X-ray diffraction analysis. The molecular structure of **13** is presented in Fig. 6. The absolute configuration of the molecule has not been determined directly. The enantiomer used in the refinement is based on the known configuration at C-13, C-16 and C-17 (C6, C14, and C15 in Fig. 6). The enantiomerically pure crystals contain a small amount of water in the lattice. The water molecules sit on a two-fold axis, but only occupy *ca* 16% of these sites, thus giving a ratio of water molecules to **13** of *ca* 13:1. The molecules are interconnected by a single intermolecular hydrogen bond between the hydroxy H-atom and the N-atom of an adjacent molecule. This interaction links the molecules into infinite one-dimensional chains which lie in the $xy$-plane. There is also close contact between the oxygen atom of the hydroxyl and the oxygen atom of water, which is probably a hydrogen bonding interaction with the hydroxyl group acting as the acceptor.

Compound **14** exhibited a mass spectrum, which was strikingly similar to that of 16-hydroxygalwesine (**10**), having the fragment ion $m/z$ 112 as base peak. However, the melting point and other spectral data are different from those of **10**, suggesting that it cannot be 16-hydroxygalwesine but that it does possess the same gross structure. Furthermore, the quaternary signal at $\delta$169.7 in $^{13}$C NMR spectrum and the IR absorption at 1755 cm$^{-1}$ indicate the presence of a lactone moiety, which is typical of lycorenine-type alkaloids. However, the frequency of the carbonyl absorption in the IR spectrum is reminiscent of a five-membered ring lactone rather than a six-membered one. Further structural details are furnished by conventional 600 MHz $^1$H NMR spectra of **14**, while the chemical shifts of protons were assigned with the help of $^1$H, $^1$H COSY experiments. Remarkably, there are no relevant signals due to an olefinic moiety or to H-13 of the homolycorine skeleton. Two singlets at $\delta$7.29 and 7.16 are characteristic of *para*-oriented aromatic protons. A prominent feature of the spectrum is the presence of three three-proton signals at $\delta$3.97, 3.93, and 3.49 due to two aromatic and one aliphatic methoxyl groups. The N–Me resonance of **14** ($\delta$1.66) is shifted $\sim$0.4 ppm upfield as compared to that of the other lycorenine-type alkaloids. The protons at C-2 and C-3 have almost the same chemical shifts as those of other alkaloids of the lycorenine series. Two one-proton singlets at $\delta$3.80 and 3.55 are attributable to the methine protons, H-5 and H-4. The one-proton singlet at $\delta$3.04 is assigned to the isolated H-17, which is shifted downfield when compared with other lycorenine-type alkaloids. The doublet at $\delta$3.74 couples with the doublet at $\delta$2.27. However, upon the addition of $D_2O$ to the $CDCl_3$ solution of **14**, the doublet at $\delta$3.74 collapses to a singlet while the doublet at $\delta$2.27 disappears. Therefore, the latter is assigned to a hydroxyl group at C-13, the presence of which is also verified by the IR absorptions at 3520 and 3290 cm$^{-1}$. The doublet at $\delta$3.74 is assigned to the methine proton located on the same carbon atom.

The $^{13}$C NMR spectrum of **14** exhibits signals due to 19 carbon atoms, the multiplicities of which were determined by DEPT experiments. Like the $^1$H NMR spectrum of **14**, the $^{13}$C NMR spectrum has no signal due to an olefinic moiety. Four of the quaternary signals belong to the aromatic ring ($\delta$154.4, 150.9, 144.9, and 118.5). Of the two quaternary signals in the aliphatic region, the one




**13**

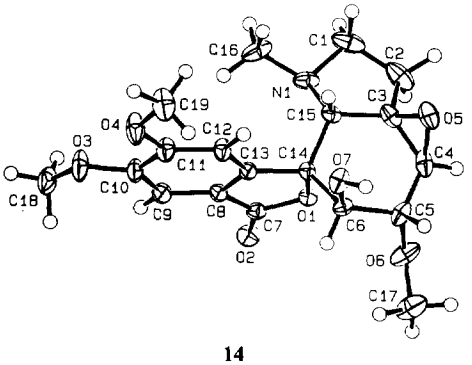
Fig. 6. ORTEP drawing [15] of 9-*O*-demethylgalwesine (**13**) (arbitrary numbering of atoms).

at $\delta$68.2 is assigned to C-12. The other quaternary signal at $\delta$83.0, therefore, belongs to the C-16, since H-17 is isolated. The protonated carbons were assigned with the aid of $^{13}C$, $^{1}H$ COSY. Thus, C-2 and C-3 resonate at $\delta$55.3 and 29.8, respectively. The signals at $\delta$106.0 and 105.5 are due to protonated aromatic carbons, C-8 and C-11. The resonances of the oxygenated methine carbons 5 and 4 are observed at $\delta$78.2 and 58.6. The signal at $\delta$66.7 is due to C-17. Other signals at $\delta$58.6, 56.5, and 56.3 verify the presence of one aliphatic and two aromatic methoxyl groups. The N–Me resonates at $\delta$43.6. Finally, the signal at $\delta$73.3 is assigned to C-13, to which a hydroxyl group is attached. The magnitude of this chemical shift clearly shows that C-13 cannot be fused to the lactone moiety. Thus, compound **14** seems to be the first alkaloid in the lycorenine series possessing a spirocyclic framework and an epoxy moiety between C-4 and C-12. It is named galasine (spiro[3a,4]epoxy-6-hydroxy-5-methoxy-1-methyl-1-azabicyclo[3.4.0]nonan[7,7′]-4,5-dimethoxy-benzo[4,5-*c*]-2-oxofurane). Its optical rotation could not be measured due to the paucity of the compound.

To establish the proposed structure of alkaloid **14** with certainity, X-ray diffraction analysis was carried out. The X-ray results confirm the structure deduced from the spectral data. The molecular structure of **14** is presented in Fig. 7. The absolute configuration of the molecule could not be determined by X-ray analysis. The enantiomer used in the refinement was based on an assumption of the configuration at C-17 (C15 in Fig. 7), which for other lycorenine alkaloids has been found to be always *R*. However, because there was not enough material available, it could not be proven that **14** is converted to **11** in acidic solution. The molecules are linked into infinite one-dimensional chains by intermolecular hydrogen bonds between the hydroxyl group and the N-atom of a neighbouring molecule. These chains run parallel to the *z*-axis.

## EXPERIMENTAL

*General.* Mp.: uncorr. $^{1}H$ NMR: 300 MHz in $CDCl_3$ if not otherwise mentioned. $^{13}C$ NMR: 50 MHz in $CDCl_3$ if not otherwise mentioned. EIMS: direct inlet system, 70 eV. CIMS: in $NH_3$. CC: silica gel 60, 70–230 mesh (Merck). TLC: silica gel 60 precoated plates $F_{254}$ (Merck), detection by UV light or Dragendorff's reagent.




**14**

Fig. 7. ORTEP drawing [15] of galasine (**14**) (arbitrary numbering of atoms).

*Plant material. Galanthus elwesii* Hooker fil. was collected in Karaburun, in the province of Izmir, Turkey, in March 1990 and identified by M.A.Ö. A voucher sample, No. 1094, is deposited in the Herbarium of the Pharmacognosy Department, Faculty of Pharmacy, Ege University, Izmir, Turkey.

*Extraction and isolation.* Dried powdered aerial and underground parts (bulbs) (3.7 kg) were extracted with EtOH at room temp. to furnish crude extracts. These were shaken with 5% aq. HCl soln and filtered. The filtrate was basified with $NH_4OH$ and extracted with $CHCl_3$ to yield the crude alkaloidal mixt. (16.12 g). Preliminary fractionation was achieved by CC using $CHCl_3$ gradually enriched with MeOH (500 ml frs). Further spn of *frs 22–23* (160 mg; eluted with 1% MeOH in $CHCl_3$) by prep. TLC (benzene–$CHCl_3$–$Me_2CO$; 4:4:2 + $NH_3$ vapour) followed by a second prep. TLC (benzene–$CHCl_3$–MeOH; 7:2:1 + $NH_3$ vapour) afforded 39.66 mg **10**. *Frs 28–29* (625 mg, eluted with 2% MeOH in $CHCl_3$) by prep. TLC (benzene–$CHCl_3$–MeOH; 7:2:1 + $NH_3$ vapour) afforded 89.53 mg **12**. *Fr 33–39* (344.6 mg; eluted with 5% MeOH in $CHCl_3$) by prep. TLC (benzene–$CHCl_3$–MeOH; 7:2:1 + $NH_3$ vapour) afforded 4.89 mg **14**. *Frs 40–41* (62.97 mg; eluted with 5% MeOH in $CHCl_3$) by prep. TLC (benzene–$CHCl_3$–$Me_2CO$–MeOH; 5:5:6:4) followed by a second prep. TLC (benzene–$CHCl_3$–$Me_2CO$–MeOH; 6:2:1:1 + $NH_3$ vapour) afforded 21.53 mg **11**. *Frs 42–44* (1.355 g; eluted with 5% MeOH in $CHCl_3$) were first subjected to CC ($CHCl_3$–EtOAc–MeOH; 1:7:2). Further purification by prep. TLC and recrystallization afforded 13.25 mg galanthine, 14.37 mg **13**, 11.0 mg **9**, 268.15 mg **1**, 20.0 mg **6** and 21.0 mg **8a**. *Frs 45–49* (3.5 g; eluted with 7.5% MeOH in $CHCl_3$) were subjected to recrystallization and afforded 71.38 mg **8b** and 281.0 mg **8c**. The residue from recrystallization (1.5 g) was fractionated by CC (benzene–$CHCl_3$–EtOH; 12:5:3) and further purified by prep. TLC (benzene–$CHCl_3$–MeOH; 7:2:1 + $NH_3$ vapour) to furnish 109.5 mg **8d**, 46.54 mg **1**, 53.16 mg **5** and 51.0 mg (*E*)-*N*-feruloyltyramine. *Frs 50–57* (1.95 g; eluted with 7.5% MeOH in $CHCl_3$) was fractionated by CC (benzene–$CHCl_3$–MeOH; 5:3:2) and further purified by recrystallization to furnish 148.4 mg lycorine and 173.89 mg **4**. Further purification by prep. TLC (benzene–$CHCl_3$–$Me_2CO$–$Et_2NH$; 9:9:5:2) and recrystallization yielded 18.0 mg **3** and 154.7 mg **8e**. *Frs 72–75* (166 mg; eluted with 7.5% MeOH in $CHCl_3$) were subjected to prep. TLC (benzene–$CHCl_3$–MeOH; 11:6:3 + $NH_3$ vapour) and recrystallized to yield 32.36 mg **2**. *Frs 76–80* (189 mg; eluted with 7.5% MeOH in $CHCl_3$) were subjected to prep. TLC (benzene–$CHCl_3$–MeOH; 11:6:3 + $NH_3$ vapour) and recrystallized to yield 10.13 mg **2**. *Frs 81–85* (675 mg; eluted with 10% MeOH in $CHCl_3$) were subjected to prep. TLC (hexane–$CHCl_3$–$Me_2CO$–MeOH–EtOAc; 9:1:2:2:6 + $NH_3$ vapour) and recrystallized to yield 66.08 mg hordenine. Finally, prep. TLC

(benzene–$CHCl_3$–$Me_2CO$–MeOH–$Et_2NH$; 12:4:1:1:2) of *frs 86–95* (513 mg; eluted with 10% MeOH in $CHCl_3$) yielded 49.0 mg hordenine and 20.0 mg **7**.

( − )-*Leucotamine* (**4**). Main *frs 50–57* gave a total of 173.89 mg of crude alkaloid **4**. Colourless prisms, mp 185–186° (EtOAc), [10, 11]: 168–171°. $[\alpha]_D^{21} = -77.1°$ (MeOH; *c* 0.24,), [10, 11]: $[\alpha]_D = -52.6°$ ($CHCl_3$; *c* 0.74). CD (MeOH: $c\,2.23 \times 10^{-5}$): $\Delta\varepsilon_{215.0} - 49.19$, $\Delta\varepsilon_{259.2}$ 0, $\Delta\varepsilon_{289.6} + 2.69$. $^{13}$C NMR: $\delta$170.2 (*s*, C-1′), 145.0 (*s*, C-6), 140.5 (*s*, C-5a), 131.8 (*d*, C-2), 131.4 (*s*, C-12b), 128.2 (*s*, C-8a), 122.0 (1*d*, C-1), 121.7 (1*d*, C-8), 116.7 (*d*, C-7), 85.8 (*d*, C-4a), 64.0 and 63.6 (2*d*, C-3, C-3′), 60.3, (*t*, C-9), 53.5 (*t*, C-11), 48.2 (*s*, C-12a), 43.8 (*t*, C-2′), 41.7 (*q*, NMe), 33.6 (*t*, C-12), 27.5 (*t*, C-4), 21.9 (*q*, C-4′). EMS *m/z* (rel. int.): 359 (24, $[M]^+$), 256 (51), 255 (68), 254 (28), 212 (13), 97 (11), 96 (100), 91 (12). CIMS *m/z*: 361 (10), 360 (100, $[M + 1]^+$), 256 (13). (Found: C, 66.84; H, 6.92; N, 3.96. Calcd. for $C_{20}H_{25}NO_5$: C, 66.84; H, 7.01; N, 3.90%). UV, IR, and $^1$H NMR spectra identical to those reported previously [10, 11].

*Hydrolysis of* **4**. A soln of 20 mg (0.056 mmol) of **4** in 5% NaOH-EtOH was refluxed for 1 hr. The solvent was evapd, the residue distributed between $CH_2Cl_2$ and $H_2O$, the organic phases dried and evapd. The crude product was chromatographed by prep. TLC MeOH–$Me_2CO$; (3:1) to give 8.9 mg (0.033 mmol, 59%) of ( − )-sanguinine (**2**), which was identical with an authentic sample with respect to its chemical and physical behaviour, including chiroptical properties.

( − )-O-*Methylleucotamine* (**5**). Main *frs 45–49* gave 53.16 mg of crude alkaloid **5**. Light yellow solid, mp 107–113°, [10, 11]: oil. $[\alpha]_D^{22} = -63.4°$ (MeOH; *c* 0.49), [11]: −49.3° (MeOH; *c* 0.75). [10]: −36° ($CHCl_3$; *c* 0.75). CD (MeOH; $c\,1.76 \times 10^{-5}$): $\Delta\varepsilon_{213.4} - 51.23$, $\Delta\varepsilon_{239.6}$ 0, $\Delta\varepsilon_{241.2} + 0.80$, $\Delta\varepsilon_{246.1}$ 0, $\Delta\varepsilon_{248.6} - 0.64$, $\Delta\varepsilon_{260.0}$ 0, $\Delta\varepsilon_{288.0} + 3.15$, $\Delta\varepsilon_{302.4}$ 0. $^{13}$C NMR: $\delta$171.7 (*s*, C-1′), 146.3 (*s*, C-6), 144.0 (*s*, C-5a), 131.7 (*s*, C-12b), 130.9 (*d*, C-2), 128.5 (*s*, C-8a), 122.4 and 121.4 (2*d*, C-1, C-8), 111.3 (*d*, C-7), 86.1 (*d*, C-4a), 63.8 and 63.2 (2*d*, C-3, C-3′), 60.1 (*t*, C-9), 55.7 (*q*, OMe), 53.5 (*t*, C-11), 47.8 (*s*, C-12a), 43.8 (*t*, C-2′), 41.5 (*q*, NMe), 33.9 (*t*, C-12), 27.4 (*t*, C-4), 22.6 (*q*, C-4′). EIMS *m/z* (rel. int.): 374 (11), 373 (29, $[M]^+$), 372 (22), 271 (16), 270 (100). CIMS *m/z*: 374 $[M + 1]^+$. UV, IR and $^1$H NMR in accordance with those reported previously [10, 11].

( + )-9-O-*Demethylhomolycorine* (**8a–8e**). Subfrs M-17, M-1-D, M-1-E, M-1-F and M-43 of the consecutive main *frs 42–44*, *45–49* and *50–57* gave a total of 637.58 mg of crude alkaloid **8**. CD: (MeOH; $c\,2.39 \times 10^{-5}$): $\Delta\varepsilon_{203.6} + 32.01$, $\Delta\varepsilon_{222.4}$ 0, $\Delta\varepsilon_{232.2} - 12.45$, $\Delta\varepsilon_{242.6}$ 0, $\Delta\varepsilon_{251.4} + 4.32$, $\Delta\varepsilon_{259.4}$ 0, $\Delta\varepsilon_{271.6} - 6.38$. (**8b**: found: C, 61.39; H 6.64; N, 3.71; $C_{17}H_{19}NO_4 \cdot 2H_2O$ requires: C, 60.52; H, 6.87; N, 4.15%. **8c**: found C, 67.47, H, 6.29; N, 4.87; calc. for $C_{17}H_{19}NO_4$: C, 67.76; H, 6.35; N, 4.65%.) other spectral data agree with published values [21, 26].

( + )-5-*Methoxy*-9-O-*demethylhomolycorine* (**9**). From main *frs 42–44*, 11.0 mg of crude alkaloid **9** was isolated. Colourless prisms, mp 232–236° (MeOH–$CHCl_3$). $[\alpha]_D^{21} = +75.2°$ (MeOH; *c* 0.067). CD (MeOH; $c\,2.63 \times 10^{-5}$): $\Delta\varepsilon_{203.4} + 29.10$, $\Delta\varepsilon_{219.6}$ 0, $\Delta\varepsilon_{231.6} - 12.30$, $\Delta\varepsilon_{242.8}$ 0, $\Delta\varepsilon_{250.2} + 3.08$, $\Delta\varepsilon_{259.0}$ 0, $\Delta\varepsilon_{271.0} - 5.61$, $\Delta\varepsilon_{290.0} - 0.50$, $\Delta\varepsilon_{339.0}$ 0. UV $\lambda_{max}^{MeOH}$ nm (log $\varepsilon$): 200 (4.45), 227 (4.51), 265 (4.01), 305 (3.80); $\lambda_{min}^{MeOH}$ 215 (4.35), 247 (3.80), 285 (3.58); $\lambda_{max}^{MeOH+NaOH}$ 245, 275, 340. IR $\nu_{max}^{CHCl_3}$ cm$^{-1}$: 3440, 1718 (br.), 1618, 1505, 1455, 1302, 1282, 1078. $^1$H NMR (400 MHz): $\delta$7.61 (1H, *s*, H-8), 7.02 (1H, *s*, H-11), 5.67 (1H, br *s*, H-4), 4.68 (1H, br *s*, H-13), 3.97 (3H, *s*, OMe), 3.93 (1H, br *s*, H-5), 3.45 (3H, *s*, aliph. OMe), 3.19 (1H, *m*, H-2), 2.77 (1H, *d*, *J* = 7.8 Hz, H-16), 2.70 (1H, *d*, *J* = 9.9 Hz, H-17), 2.55 (2H, *m*, H-3), 2.28 (1H, *dd*, *J* = 18.6, 9.5 Hz, H-2), 2.01 (3H, *s*, NMe). $^{13}$C NMR: $\delta$164.9 (*s*, C-7), 151.1 (*s*, C-10), 145.9 and 145.4 (2*s*, C-9, C-12), 135.8 (*s*, C-15), 117.5 (*s*, C-14), 116.8 and 116.0 (2*d*, C-4, C-8), 110.6 (*d*, C-11), 79.5 (*d*, C-13), 76.7 (*d*, C-5), 66.7 (*d*, C-17), 57.7 (*q*, OMe), 56.1 (*d*, C-2), 56.4 (*q*, OMe), 43.7 (*q*, NMe), 40.6 (*d*, C-16), 28.0 (*t*, C-3). EIMS *m/z* (rel. int.): 331 (1 < , $[M]^+$), 140 (11), 139 (100), 124 (65). CIMS *m/z*: 332 $[M + 1]^+$.

( + )-16-*Hydroxygalwesine* (**10**). Main *frs 22–23* gave 39.66 mg of crude alkaloid **10**. Colourless prisms, mp 154–156° (EtOAc). $[\alpha]_D^{21} = +1.8°$ (MeOH; *c* 0.224). CD (MeOH; $c\,2.06 \times 10^{-5}$): $\Delta\varepsilon_{213.2} + 18.98$, $\Delta\varepsilon_{224.6}$ 0, $\Delta\varepsilon_{232.6} - 10.89$, $\Delta\varepsilon_{242.4}$ 0, $\Delta\varepsilon_{249.4} + 4.71$, $\Delta\varepsilon_{259.8}$ 0, $\Delta\varepsilon_{272.4} - 6.85$, $\Delta\varepsilon_{289.1} - 1.50$, $\Delta\varepsilon_{303.2} - 2.89$, $\Delta\varepsilon_{327.0}$ 0. UV $\lambda_{max}^{MeOH}$ nm (log $\varepsilon$): 202 (4.36), 226 (4.46), 269 (3.99), 303 (3.76); $\lambda_{min}^{MeOH}$ 214 (4.29), 245 (3.63), 287 (3.56). IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3395, 3080, 1720, 1605, 1510, 1460, 1285, 1090, 1035, 938, 878. $^1$H NMR: $\delta$7.48 (1H, *s*, H-8), 7.13 (1H, *s*, H-11), 4.58 (1H, *s*, H-13), 3.99 (3H, *s*, arom. OMe), 3.93 (3H, *s*, arom. OMe), 3.90 (1H, *s*, H-5), 3.58 (3H, *s*, aliph. OMe), 3.41 (1H, *s*, H-4), 3.18 (1H, *t*, *J* = 8.5 Hz, $H_\alpha$-2), 2.69 (1H, *s*, H-17), 2.64 (1H, *m*, $H_\beta$-2), 2.32 (1H, *m*, H-3), 2.01 (3H, *s*, NMe), 1.88 (1H, *dd*, *J* = 14.4, 6.2 Hz, H-3). $^{13}$C NMR*: $\delta$163.4 (*s*, C-7), 153.6 (*s*, C-10), 149.0 (*s*, C-9), 140.4 (*s*, C-15), 114.9 (*s*, C-14), 111.7 (*d*, C-8), 107.0 (*d*, C-11), 79.7 (*d*, C-13), 76.3 (*d*, C-5), 70.0 (*d*, C-17), 67.9 and 66.0 (2*s*, C-12, C-16), 59.1 (*q*, aliph. OMe), 56.3, 56.3, and 56.1 (2*q*, 2 OMe + 1*d*, C-4), 56.0 (*t*, C-2), 44.0 (*q*, NMe), 30.4 (*t*, C-3). EIMS *m/z* (rel. int.): 377 (19, $[M]^+$), 155 (20), 152 (12), 140 (39), 112 (100), 111 (17), 98 (15). CIMS *m/z*: 378 $[M + 1]^+$.

( + )-16-*Hydroxy*-9-O-*demethylgalwesine* (**11**). Main *frs 40–41* gave 21.53 mg of crude alkaloid **11**. Colourless amorphous powder, mp 107–110°. $[\alpha]_D^{21} = +5.2°$ (MeOH; *c* 0.155), $[\alpha]_D^{21} = +23.0°$ ($CHCl_3$; *c* 0.478). CD (MeOH; $c\,2.57 \times 10^{-5}$): $\Delta\varepsilon_{211.2} + 14.49$, $\Delta\varepsilon_{224.4}$ 0, $\Delta\varepsilon_{232.0} - 7.53$, $\Delta\varepsilon_{241.8}$ 0, $\Delta\varepsilon_{249.2} + 2.12$, $\Delta\varepsilon_{257.0}$ 0, $\Delta\varepsilon_{272.0} - 5.62$, $\Delta\varepsilon_{288.2} - 1.24$, $\Delta\varepsilon_{308.4} - 2.20$, $\Delta\varepsilon_{338.0}$ 0. UV $\lambda_{max}^{MeOH}$ nm (log $\varepsilon$): 200 (4.27), 226 (4.31), 266 (3.81), 305 (3.60); $\lambda_{min}^{MeOH}$ 214 (4.17), 245 (3.57), 286 (3.39); $\lambda_{max}^{MeOH+NaOH}$ 243, 276, 341. IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3430 (br.), 1710, 1610, 1510, 1450, 1295, 1210, 1115, 1090. $^1$H NMR ($CDCl_3 + D_2O$): $\delta$7.54 (1H, *s*, H-8), 7.13 (1H, *s*, H-11), 4.56 (1H, *s*, H-13), 4.00 (3H, *s*, arom. OMe), 3.90 (1H, *s*, H-5), 3.57 (3H, *s*, aliph. OMe), 3.41 (1H, *s*, H-4), 3.18 (1H, *t*, *J* = 8.6 Hz, $H_\alpha$-2), 2.69 (1H, *s*, H-17), 2.63 (1H, *m*, $H_\beta$-2), 2.33 (1H, *m*, $H_\alpha$-3), 2.01 (3H, *s*, NMe), 1.88 (1H, *ddd*, *J* = 14.2, 6.5,

* Assignment made by DEPT and $^{13}$C, $^1$H COSY.

1.1 Hz, $H_\beta$-3). $^{13}C$ NMR: $\delta$163.2 (*s*, C-7), 151.3 (*s*, C-10), 145.9 (*s*, C-9), 139.6 (*s*, C-15), 115.9 (*d*, C-14), 115.8 (*s*, C-8), 106.7 (*d*, C-11), 79.7 (*d*, C-13), 76.3 (*d*, C-5), 70.0 (*d*, C-17), 68.1 and 66.1 (2*s*, C-12, C-16), 59.2 (*q*, aliph. OMe), 56.4 and 56.4 (*q*, OMe, *d*, C-4), 56.1 (*t*, C-2), 44.1 (*q*, NMe), 30.4 (*t*, C-3). EIMS *m/z* (rel. int.): 363 (3, $[M]^+$), 323 (28), 322 (16), 155 (9), 149 (15), 148 (88), 140 (19), 112 (100), 111 (10), 98 (10).

( + )-*Galwesine* (**12**). From main *frs 28–29* 89.53 mg of crude alkaloid **12** was isolated as a yellow amorphous powder. $[\alpha]_D^{21}$ = + 13.4° (MeOH; *c* 0.299). CD (MeOH; *c* $2.18 \times 10^{-5}$): $\Delta\varepsilon_{206.6}$ + 16.39, $\Delta\varepsilon_{222.7}$ 0, $\Delta\varepsilon_{232.0}$ − 8.2, $\Delta\varepsilon_{242.4}$ 0, $\Delta\varepsilon_{248.2}$ + 2.80, $\Delta\varepsilon_{256.5}$ 0, $\Delta\varepsilon_{271.8}$ − 6.99, $\Delta\varepsilon_{289.1}$ − 2.25, $\Delta\varepsilon_{301.8}$ − 3.43, $\Delta\varepsilon_{330.9}$ 0. UV $\lambda_{max}^{MeOH}$ nm (log ε): 225 (4.34), 267 (3.85), 303 (3.64); $\lambda_{min}^{MeOH}$ 215 (4.24), 245 (3.55), 2.85 (3.51). IR $\nu_{max}^{KBr}$ $cm^{-1}$: 1720, 1605, 1510, 1465, 1455, 1360, 1295, 1082. $^1H$ NMR† 600 MHz, $CD_3OD$): $\delta$7.47 (1H, *s*, H-8), 7.14 (1H, *s*, H-11), 4.62 (1H, *br s*, H-13), 3.93 and 3.86 (6H, 2*s*, 2 arom. MeO), 3.84 (1H, *d*, *J* = 0.9 Hz, H-5), 3.53 (3H, *s*, aliph. OMe), 3.39 (1H, *s*, H-4), 3.14 (1H, *t*, *J* = 8.5 Hz, $H_\alpha$-2), 2.81 (1H, *dd*, *J* = 10.5, 2.4 Hz, H-16), 2.52 (1H, *m*, $H_\beta$-2), 2.38 (1H, *d*, *J* = 10.5 Hz, H-17), 2.35 (1H, *m*, $H_\alpha$-3), 2.03 (3H, *s*, NMe), 1.81 (1H, *ddd*, *J* = 14.1, 6.2, 0.9 Hz, $H_\beta$-3). $^{13}C$ NMR‡ (600 MHz, $CD_3OD$): $\delta$166.4 (*s*, C-7), 155.2 (*s*, C-10), 150.7 (*s*, C-9), 138.4 (*s*, C-15), 117.9 (*s*, C-14), 113.3 (*d*, C-8), 112.4 (*d*, C-11), 80.2 (*d*, C-13), 76.6 (*d*, C-5), 68.9 (*d*, C-17), 67.9 (*s*, C-12), 59.2 (*q*, aliph. OMe), 57.6 (*d*, C-4), 57.0 (*t*, C-2), 56.9 (*q*, arom. MeO–C-10), 56.6 (*q*, arom. MeO–C-9), 44.4 (*s*, NMe), 40.1 (*d*, C-16), 30.7 (*t*, C-3). EIMS *m/z* (rel. int.): 361 (32, $[M]^+$), 155 (100), 140 (20). CIMS *m/z*: 362 $[M + 1]^+$. (Found: C, 63.42; H, 6.62; N, 4.01. $C_{19}H_{23}NO_6$ requires: C, 63.15; H, 6.41; N, 3.88%).

( + )-9-O-*Demethylgalwesine* (**13**). Main *frs 42–44* gave 14.37 mg of crude alkaloid **13**. Colourless prisms, mp 241–242°. $[\alpha]_D^{21}$ = + 25.7° (MeOH; *c* 0.140). CD (MeOH; *c* $2.40 \times 10^{-5}$): $\Delta\varepsilon_{207.6}$ + 23.46, $\Delta\varepsilon_{223.8}$ 0, $\Delta\varepsilon_{232.6}$ − 9.55, $\Delta\varepsilon_{242.6}$ 0, $\Delta\varepsilon_{249.8}$ + 2.58, $\Delta\varepsilon_{256.0}$ 0, $\Delta\varepsilon_{271.6}$ − 8.14, $\Delta\varepsilon_{286.8}$ − 1.76, $\Delta\varepsilon_{309.2}$ − 3.01, $\Delta\varepsilon_{330.9}$ 0. UV $\lambda_{max}^{MeOH}$ nm (log ε): 227 (4.42), 265 (3.92), 306 (3.72); $\lambda_{min}^{MeOH}$ 215 (4.28), 245 (3.67), 285 (3.46); $\lambda_{max}^{MeOH+NaOH}$ 245, 275, 340. IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 3540, 1720, 1615, 1595, 1500, 1450, 1295, 1278, 1150, 1105, 1075. $^1H$ NMR (600 MHz): $\delta$7.60 (1H, *s*, H-8), 6.96 (1H, *s*, H-11), 4.52 (1H, br *s*, H-13), 3.98 (3H, *s*, arom. OMe), 3.88 (1H, *s*, H-5), 3.53 (3H, *s*, aliph. OMe), 3.33 (1H, *s*, H-4), 3.10 (1H, *t*, *J* = 8.4 Hz, $H_\alpha$-2), 2.74 (1H, *dd*, *J* = 10.2, 2.4 Hz, H-16), 2.51 (1H, *m*, $H_\beta$-2), 2.45 (1H, *d*, *J* = 10.2 Hz, H-17), 2.35 (1H, *d*, $H_\alpha$-3), 2.03 (3H, *s*, NMe), 1.83 (1H, *dd*, *J* = 14.0, 6.3, 0.9 Hz, $H_\beta$-3). $^{13}C$ NMR ($CDCl_3$ + pyridine-$d_5$): $\delta$164.1 (*s*, C-7), 152.3 (*s*, C-10), 147.1 (*s*, C-9), 134.8 (*s*, C-15), 116.9 (*s*, C-14), 116.4 (*d*, C-8), 110.5 (*d*, C-11), 78.7 (*d*, C-13), 75.5 (*d*, C-5), 66.9 (*s*, C-12), 66.7 (*d*, C-17), 58.5 (*q*, aliph. OMe), 56.0 (*d*, C-4), 55.9 (*q*, arom. OMe), 55.8 (*t*, C-2), 43.8 (*q*, NMe), 39.9 (*d*, C-16), 29.6 (*t*, C-3). EIMS *m/z* (rel. int.): 347 (3, $[M]^+$), 164 (14), 155 (63), 140 (100), 112 (31), 99 (19), 98 (36), 96 (18), 94 (18). CIMS *m/z*: 365 $[M + 1 + NH_3]^+$, 348 $[M + 1]^+$.

*Galasine* (**14**). Main *frs 33–39* gave 4.89 mg of crude alkaloid **14**. Colourless prisms, mp 284.9–286.3° (MeOH). CD (MeOH; *c* $3.02 \times 10^{-5}$): $\Delta\varepsilon_{201.4}$ + 5.82, $\Delta\varepsilon_{206.0}$ 0, $\Delta\varepsilon_{214.6}$ − 6.23, $\Delta\varepsilon_{225.8}$ − 8.77, $\Delta\varepsilon_{251.8}$ − 1.69, $\Delta\varepsilon_{265.0}$ − 2.52, $\Delta\varepsilon_{308.8}$ 0. UV $\lambda_{max}^{MeOH}$ nm (log ε): 222 (4.55), 255 (4.02), 293 (3.84), 300 (sh); $\lambda_{min}^{MeOH}$: 237 (3.78), 274 (3.60). IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 3520, 3290, 1755, 1605, 1495, 1465, 1350, 1335, 1300, 1145, 1095, 1065, 1010. $^1H$ NMR§ (600 MHz): $\delta$7.29 (1H, *s*, H-8), 7.16 (1H, *s*, H-11), 3.97 and 3.93 (6H, 2*s*, 2 arom. OMe), 3.80 (1H, *s*, H-5), 3.74 (1H, *d*, *J* = 9.0 Hz, + $D_2O$ *s*, H-13), 3.55 (1H, *s*, H-4), 3.49 (1H, *2*, aliph. OMe), 3.07 (1H, *dt*, *J* = 8.4, 1.6 Hz, $H_\alpha$-2), 3.04 (1H, *s*, H-17), 2.50 (1H, *m*, $H_\beta$-2), 2.37 (1H, *m*, $H_\alpha$-3), 2.27 (1H, *d*, *J* = 9.0 Hz, disappeared when $D_2O$ added, OH), 1.84 (1H, *ddd*, *J* = 13.9, 6.7, 1.8 Hz, $H_\beta$-3), 1.66 (3H, *s*, NMe). $^{13}C$ NMR¶: 169.7 (*s*, C-7), 154.4 (*s*, C-10), 150.9 (*s*, C-9), 144.9 (*s*, C-15), 118.5 (*s*, C-14), 106.0 (*d*, C-8), 105.5 (*d*, C-11), 83.0 (*s*, C-16), 78.2 (*d*, C-5), 73.3 (*d*, C-13), 68.2 (*s*, C-12), 66.7 (*d*, C-17), 58.6 (*d*, C-4), 58.6 (*q*, aliph. OMe), 56.5 and 56.3 (2*q*, 2 arom. OMe), 55.3 (*t*, C-2), 43.6 (*q*, NMe), 29.8 (*t*, C-3). EIMS *m/z* (rel. int.): 377 (4, $[M]^+$), 155 (17), 140 (41), 138 (10), 137 (16), 112 (100), 111 (17), 99 (11), 98 (31), 96 (12). CIMS *m/z*: 378 $[M + 1]^+$.

*X-ray crystal structure analyses.* All measurements were made at − 100(1)° on a *Rigaku AFC5R* diffractometer using graphite-monochromated Mo$K_\alpha$ radiation ($\lambda$ = 0.71069 Å) and a 12 kW rotating anode generator. The $\omega/2\theta$ scan mode was employed for data collection ($\omega$ scans for **13**). The intensities of three standard reflections were measured after every 150 reflections and remained stable, except for those of **13**, which decreased by *ca* 7% during the course of the data collection. A linear correction factor was applied to the intensities of **13** to account for this. The intensities were corrected for Lorentz and polarization effects. Empirical absorption corrections [39] were applied in all cases, except for **8c**. Data collection and refinement parameters are given in Tables 2 and 3. Structures were solved by direct methods using SHELXS86 [40], which revealed the positions of all non-hydrogen atoms. All of the H-atoms were located in a difference electron density map. Anisotropic refinement of the non-H-atoms and isotropic refinement of the H-atoms were carried out on *F* using a full-matrix least-squares procedure [41], which minimized the function $\Sigma w(|F_o| - |F_c|)^2$, where $w = [\sigma^2(F_o) + (0.005F_o)^2]^{-1}$. The final difference electron density maps contained no unusual features. Each of the compounds crystallizes in a chiral space group. For each analysis, the enantiomer chosen for the refinement was based on the known configuration at certain atoms (see Results and Discussion). It was not possible to determine the absolute configuration of any of the compounds by crystallographic means. Neutral atom scattering factors for non-H-atoms were

†Assignment made by $^1H$, $^1H$ COSY, ROESY and TOCSY.

‡Assignment made by DEPT, $^{13}C$, $^1H$ COSY, and $^{13}C$, $^1H$ long range COSY.

§Assignment made by $^1H$, $^1H$ COSY.

¶Assignment made by DEPT and $^{13}C$, $^1H$ COSY.

Table 2. Crystallographic data of compounds **4**, **8b**, **8c**, and **8d**

| | **4** | **8b** | **8c** | **8d** |
|---|---|---|---|---|
| Recrystallized from | EtOAc | MeOH–$CHCl_3$ | EtOAc | EtOAc |
| Empirical formula | $C_{20}H_{25}NO_5$ | $C_{17}H_{19}NO_4 \cdot 2H_2O$ | $C_{17}H_{19}NO_4$ | $C_{17}H_{19}NO_4 \cdot 1{,}2EtOAc$ |
| $M_r$ (g mol$^{-1}$) | 359.42 | 337.37 | 301.34 | 345.39 |
| Crystal colour, habit | colourless, prism | colourless, prism | colourless, prism | colourless, prism |
| Crystal system | monoclinic | orthorhombic | orthorhombic | monoclinic |
| Space group | $P2_1$ (#14) | $P2_12_12_1$ (#19) | $P2_12_12_1$ (#19) | $P2_1$ (#4) |
| Crystal dimensions [mm] | 0.32 × 0.32 × 0.40 | 0.23 × 0.35 × 0.36 | 0.30 × 0.30 × 0.45 | 0.18 × 0.20 × 0.38 |
| Lattice parameters a [Å] | 8.4905 (6)* | 9.320 (2)† | 10.094 (2)‡ | 7.288 (5)$ |
| b [Å] | 5.928 (1) | 11.999 (2) | 14.654 (1) | 12.161 (3) |
| c [Å] | 17.974 (1) | 14.865 (2) | 9.6724 (9) | 20.210 (3) |
| $\beta$ [°] | 97.929 (5) | | — | 92.21 (3) |
| V [Å$^3$] | 896.0 (2) | 1662.2 (5) | 1430.8 (3) | 1790 (1) |
| Z | 2 | 4 | 4 | 4 |
| $D_{calc}$ [g cm$^{-3}$] | 1.332 | 1.348 | 1.399 | 1.282 |
| $\mu$ (Mo$K_\alpha$) [cm$^{-1}$] | 0.890 | 0.955 | 0.932 | 0.866 |
| Absorption corrections min, max | 0.835, 1.162 | 0.897, 1.044 | —, — | 0.814, 1.088 |
| $2\theta$ (max) [°] | 60 | 60 | 60 | 60 |
| Total reflections measured | 3030 | 3188 | 2820 | 5837 |
| Symmetry independent reflections | 2858 | 3081 | 2711 | 5444 |
| Reflections observed [$I > 3\sigma(I)$] | 2663 | 2142 | 2397 | 3290 |
| Variables | 334 | 309 | 275 | 486 |
| R, $R_w$ | 0.0287, 0.0295 | 0.0363, 0.0285 | 0.0352, 0.0340 | 0.0499, 0.0436 |
| Goodness of fit $s$ | 2.072 | 1.320 | 1.951 | 2.053 |
| Final $\Delta_{max}/\sigma$ | 0.0005 | 0.0006 | 0.0001 | 0.001 |
| $\Delta\rho$ (max; min) [eÅ$^{-3}$] | 0.22, −0.14 | 0.24, −0.19 | 0.27, −0.23 | 0.52, −0.30 |

*Cell dimension obtained from 22 carefully centered reflections with $43° < 2\theta < 49°$.
†Cell dimension obtained from 21 carefully centered reflections with $30° < 2\theta < 38°$.
‡Cell dimension obtained from 25 carefully centered reflections with $34° < 2\theta < 44°$.
$Cell dimension obtained from 23 carefully centered reflections with $30° < 2\theta < 40°$.

Table 3. Crystallographic data of compounds **10**, **13**, and **14**

| | **10** | **13** | **14** |
|---|---|---|---|
| Recrystallized from | EtOAc | MeOH | MeOH |
| Empirical formula | $C_{19}H_{23}NO_7$ | $C_{18}H_{21}NO_6 \cdot 0.078H_2O$ | $C_{19}H_{23}NO_7$ |
| $M_r$ (g mol$^{-1}$) | 377.39 | 348.81 | 377.39 |
| Crystal colour, habit | colourless, prism | colourless, prism | colourless, prism |
| Crystal system | orthorhombic | tetragonal | orthorhombic |
| Space group | $P2_12_12_1$ (#19) | $P4_32_12$ (#96) | $P2_12_12_1$ (#19) |
| Crystal dimensions [mm] | 0.20 × 0.32 × 0.50 | 0.15 × 0.20 × 0.33 | 0.25 × 0.26 × 0.46 |
| Lattice parameters a [Å] | 11.011 (2)* | 9.190 (3)† | 1.248 (3)‡ |
| b [Å] | 15.760 (3) | 9.190 (3) | 21.456 (4) |
| c [Å] | 10.240 (2) | 38.779 (7) | 6.434 (1) |
| V [Å$^3$] | 1777.0 (5) | 3275 (2) | 1828.7 (6) |
| Z | 4 | 8 | 4 |
| $D_{calc}$ [g cm$^{-3}$] | 1.411 | 1.414 | 1.372 |
| $\mu$ ($MoK_\alpha$) [cm$^{-1}$] | 1.010 | 0.998 | 0.980 |
| Absorption corrections min, max | 0.919, 1.063 | 0.869, 1.069 | 0.814, 1.110 |
| $2\theta$ (max) [°] | 60 | 55 | 60 |
| Total reflections measured | 5323 | 2995 | 3684 |
| Symmetry independent reflections | 2927 | 2704 | 3547 |
| Reflections observed | 2518 [$I > 3\sigma(I)$] | 1950 [$I > 2\sigma(I)$] | 2888 [$I > 3\sigma(I)$] |
| Variables | 337 | 316 | 336 |
| R, $R_w$ | 0.0282, 0.0274 | 0.0386, 0.0312 | 0.0338, 0.0315 |
| Goodness of fit s | 1.755 | 1.238 | 1.557 |
| Secondary extinction coefficient | $6.31 \times 10^{-9}$ | $7.1 \times 10^{-8}$ | — |
| Final $\Delta_{max}/\sigma$ | 0.0005 | 0.0006 | 0.0005 |
| $\Delta\rho$ (max; min) [eÅ$^{-3}$] | 0.21, −0.13 | 0.20, −0.20 | 0.22, −0.17 |

*Cell dimension obtained from 22 carefully centered reflections with $36° < 2\theta < 40°$.
†Cell dimension obtained from 22 carefully centered reflections with $26° < 2\theta < 36°$.
‡Cell dimension obtained from 22 carefully centered reflections with $35° < 2\theta < 40°$.

taken from ref. [42], scattering factors for H-atoms from ref. [43]. The anomalous dispersion effects were included in $F_{calc}$ [44]; values for $\Delta f'$ and $\Delta f''$ were those of ref. [45]. All calculations were performed using the TEXSAN crystallographic software package [46]. Crystallographic data for all structures has been deposited at the Cambridge Crystallographic Data Centre, U.K. Any deviations from the above refinement procedure in individual cases are detailed below.

The asymmetric unit of **8b** contains two $H_2O$ molecules plus one molecule of **8**. The asymmetric unit of **8d** contains one disordered molecule of EtOAc plus two molecules of **8**. The atoms of the disordered EtOAc molecule were refined only isotropically and H-atoms were not included on this fragment. All other H-atoms, except those of the hydroxyl groups (fixed in the positions indicated by a difference electron density map), were fixed in geometrically calculated positions with a C-H distance of 0.95 Å. Individual isotropic temperature factors were refined for all of the defined H-atoms of **8d**. The neutral atom scattering factors for non-H-atoms of **8d** were taken from ref. [47], values for $Df'$ and $Df''$ were those of ref. [48]. Friedel pair measurements were carried out for **10**, but an attempt to determine the absolute configuration was inconclusive. For **13**, a difference electron density map revealed a significant peak of electron density located on a 2-fold axis. This peak was assigned to the oxygen atom of a $H_2O$ molecule, but it was clear that the site was only partially occupied. Initially, the site occupation factor for this atom was refined and yielded a value of 0.078. For final refinement cycles, the site occupation factor was fixed at this value. The hydrogen atoms of the $H_2O$ molecule could not be located and were omitted from the model. In **14**, two reflections were omitted from the final refinement because of suspected extinction.

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