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Full Papers

Four Dimeric Aporphine-Containing Alkaloids from *Thalictrum fauriei*[1]

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Four dimeric alkaloids (**1**−**4**) containing an aporphine unit and representing unique structural features were obtained from *Thalictrum fauriei* and were characterized by spectral and chemical methods. Fauripavine (**1**), with a munitagine pavine unit, is the first such dimer with an aporphine C-1 diphenyl ether connection; although fauridine (**2**), also the first of its class, has codamine, a benzyl tetrahydroisoquinoline, linked at the same position. Faurithaline (**3**) and its 3-methoxy analogue **4**, both with reticuline, a benzyl tetrahydroisoquinoline as the second unit, are the first dimers with the diphenyl ether linkage at C-8 of an aporphine oxygenated at C-10 and C-11. Oconovine (**8**) was converted to 8-hydroxy-*O*-methyloconovine (**12**) to determine the effect of oxygenation at C-8 on the proton chemical shift of the C-7 hydrogens in a study to support the C-8 ether linkage of alkaloids **3** and **4**. All the alkaloids have the *S*-configuration at their asymmetric centers as established from their CD spectra when compared with those of model compounds.

Recently, we described the isolation and structure elucidation of the dimeric alkaloid faurine and its *O*-methyl derivative from the Taiwanese *Thalictrum fauriei* Hayata (Ranunculaceae). These alkaloids have a diphenyl ether linkage joining a dimethoxybenzyl unit to the unusual and previously unreported 1-position of an aporphine.[1] In this study, evidence is presented for two additional dimers, fauripavine (**1**) and fauridine (**2**), with similar connections to the aporphine unit. The former alkaloid has the pavine munitagine[2] as the second component of the dimer, while the latter has the benzyl tetrahydroisoquinoline codamine.[3] The aporphine unit, in both cases, as in faurine, is corydine, a reported constituent of the plant.[4] The literature records two types of dimeric alkaloids containing a pavine, the earliest being the aporphine−pavine dimers, pennsylpavoline and its *O*-methyl derivative pennsylpavine, from the North American *Thalictrum polyganum* Muhl.[5] In these cases the pavine is likewise munitagine, but the aporphines are isoboldine and *N*-methyllaurotetanine and have ether connections to the 9-position. More recently, three pavine−benzyl tetrahydroisoquinoline dimers, hervelines A, B, and C, from a Madagascan Hernandiaceae, *Hernandia voyronii* Jumelle, were characterized as variously methylated products of a basic unit derived from the pavine norargemonine and *N*-methylcoclaurine and oxygen linked at the 7-position.[6] This position is biogenetically equivalent to the 1-position of aporphines.

The other dimers of this report, faurithaline (**3**) and 3-methoxyfaurithaline (**4**), are ether linked at the aporphine C-8 to reticuline. Several dimers are known with the same connection, but the aporphine precursor is oxygenated at positions 9 and 10, and the benzyl tetrahydroisoquinoline precursor is coclaurine derived, forming the so-called thalifaberine group.[7−9] Faurithaline (**3**) and 3-methoxyfaurithaline (**4**), on the other hand, have the 10- and 11-positions of the aporphine oxygenated with reticuline as the benzyl tetrahydroisoquinoline component and thus represent a new class of aporphine−benzyl isoquinoline dimers.

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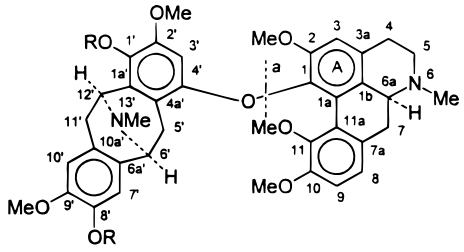
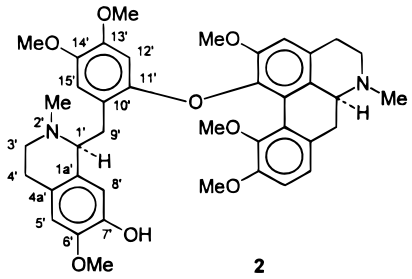


1 R=H
5 R=Ac
6 R=Me



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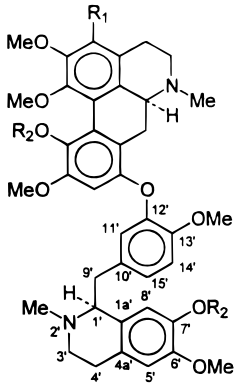


3 $R_1=R_2=H$
4 $R_1=MeO$, $R_2=H$
7 $R_1=H$, $R_2=Ac$
13 $R_1=MeO$, $R_2=Ac$

Results and Discussion

Fauripavine (**1**) was isolated from the Et_2O-soluble phenolic alkaloid fraction[10] of the entire *T. fauriei* plant after solvent partition countercurrent and Si gel chromatographies. The amber amorphous solid was optically active, and in laser-desorption Fourier transform ion cyclotron resonance mass spectrometry (LD-FT-ICRMS) showed a molecular ion peak corresponding to the formula $C_{39}H_{42}N_2O_8$. The relatively weak (6%) molecular ion in EIMS suggested a dimeric alkaloid with one diphenyl ether linkage. The ^{1}H NMR spectrum revealed six aromatic protons, two *N*-methyl and five *O*-methyl groups, and, with the ^{13}C NMR DEPT results, three methines and five methylenes. These aliphatic groups and the UV spectrum pointed to a pavine and an aporphine as the monomeric units.[5] Although the ^{1}H NMR spectrum did not show discrete phenolic hydroxyls, the IR spectrum had a peak at 3550 cm^{-1}, and the bathochromic and hyperchromic changes for the 292-nm absorption in the UV spectrum with strong alkali, as well as the preparation of the diacetate **5** and dimethyl **6** derivatives, required two phenolic groups. Thus, with seven oxygenated substituents, six aromatic protons, and one diphenyl ether oxygen, all of the substitution positions were accounted for.

The ^{1}H NMR spectrum of **1** showed several features observed for faurine:[1] two aromatic doublets (δ 6.83 and 6.71, $J = 8.1$ Hz) as an AB quartet, an aromatic singlet (δ 5.62), and a methoxyl (δ 3.40), both at unusually high field positions. This suggested the dimer contained the same aporphine (corydine) as faurine with the diphenyl ether linkage at C-1. On the pavine side, the ortho position to the diphenyl ether oxygen must have a proton; and the meta position, a methoxyl to get the large upfield shifts for these groups. The EIMS base peak at *m*/*z* 321, formed by cleavage at bond 'a' of **1** and aromatization are also present in the spectra of the diacetate **5** and the dimethyl derivative **6**. This supported the corydine unit and required the phenolic groups to be located on the pavine. The fragment at *m*/*z* 341 from fauripavine, and those at *m*/*z* 427 and 371 from the diacetate **5** and the dimethyl derivative **6**, respectively, confirmed this location as they represent the pavine component and are also derived from bond 'a' cleavage with either loss or gain of a hydrogen. Additional fragmentation to isoquinoline units, for example, to ions *m*/*z* 190 and 204 from the pavine unit, required a phenolic hydroxyl in each ring. Corresponding fragments were observed from the diacetate and the dimethyl derivatives.

The ^{1}H−^{1}H COSY 2D NMR experiment at 500 MHz and homonuclear decoupling identified four spin-coupled units; a four-spin system for the dimethylene group of the aporphine and three ABX systems. The two from the pavine were recognized by the characteristic downfield doublets (δ 4.33 and 4.04) for the methine protons.[11] Arrangement of these units along with the aromatic substituents was possible from NOE studies by difference spectroscopy (NOED) at 270 MHz and are shown in part in Figure 1.[12] Confirmation of the phenolic hydroxyl positions was obtained from the dimethyl derivative **6**, where irradiation of H-7′ (δ 6.59) showed NOE enhancements to H-6′ (δ 4.06, 7%), H-5β′ (δ 2.98, 3%), and MeO-8′ (δ 3.84, 13%), the previous phenolic position, and irradiation at MeO-8′ gave enhancement of H-7′ (14%). The other phenolic position, now MeO-1′ (δ 3.76), when irradiated, caused relaxation to H-12′ (δ 4.26, 7%). Two other enhancements of significance for this derivative were to H-3′ (δ 5.60, 3%) and MeO-2′ (δ 3.37, 1%) when H-7β (δ 2.31) was irradiated. The foregoing evidence established the pavine component as munitagine linked at C-4′ to the aporphine corydine via the C-1 phenolic hydroxyl.

The 2D CH-correlation NMR experiment allowed assignments of the proton-bearing carbons, and the related COLOC experiment for detection of long-range CH-coupling identified the quaternary carbons, except the four (C-1a′, -4a′, -6a′, and -10a′) bearing the aliphatic carbons of the pavine unit. The HMBC experiment at 600 MHz located only C-10a′ by a three-bond correlation from H-7′. The remaining three carbons were assigned by comparison to those of munitagine to which were added the empirical shifts from a phenyloxy substituent placed at C-4′.[13] For this calculation, the complete assignment of the ^{13}C NMR spectrum of munitagine, previously not reported, was made by 2D NMR CH-correlation and COLOC studies after verification of the ^{1}H NMR assignments from NOED experiments. Additional evidence for placing the diphenyl ether linkage at C-1 (δ 141.1) of the corydine unit is the clear doublet ($^3J_{CH} = 8$ Hz) observed for it from coupling to H-3 in the fully ^{1}H-coupled ^{13}C NMR spectrum. Inci-

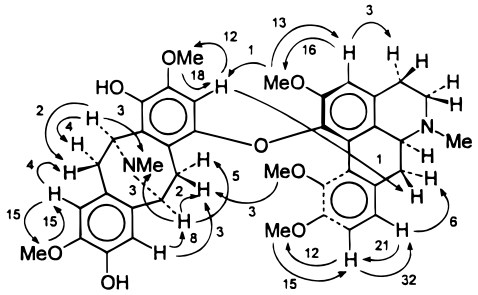


Figure 1. NOED enhancements (in percent) for fauripavine (**1**) at 270 MHz.

dentally, C-1a (δ 127.0) appears as a sharp singlet, thereby revealing no ^{1}H-coupling, although H-6a is three bonds away.

The stereochemistry of **1** was established by comparison of its circular dichroism (CD) spectrum to that of the sum of faurine and munitagine. This is possible because in faurine the diphenyl ether-linked benzyl unit is oriented in the same position as the comparable ring of munitagine, as witnessed by the sizable upfield shifts for H-3′ and MeO-2′ in **1**. Any contribution to the CD spectrum from this orientation would be the same in both compounds. The chirality of the pavine unit would thus be a separate and additive component. The calculated and observed spectra were essentially indistinguishable and thereby required the stereochemistry of **1** to be that of faurine and (−)-munitagine. The chiral centers at C-6a, C-6′, and C-12′ are thus all *S*-configured. Fauripavine (**1**) is the third known pavine−aporphine dimer and the only one with a C-1 connection at the aporphine. A pavine−aporphine dimer designated EP-10 and also isolated from *T. fauriei* is undoubtedly **1** from good agreement with the limited spectral values (UV, MS, and ^{1}H NMR) reported.[4] The proposed structure had the diphenyl ether linkage at C-11 of the aporphine. Spectral and stereochemical assignments were not made, and the ^{13}C NMR values are at considerable variance from those reported here.

Fauridine (**2**), a minor alkaloid, was obtained as an optically active amorphous solid. The HRMS showed a very weak molecular ion at *m*/*z* 682 (0.2%) corresponding to the formula $C_{40}H_{46}N_2O_8$, which was confirmed by the M + K$^+$ ion at *m*/*z* 721 (100%) in the LD-FT-ICRMS analysis. The weak molecular ion and the formula support a dimeric alkaloid with one diphenyl ether group, and the UV spectrum (311 nm) supported an aporphine component. This unit would provide 10 of the 19 double-bond equivalents required by the formula, with the remaining nine from a benzyl tetrahydroisoquinoline as the most probable unit. The IR spectral peak at 3540 cm^{-1} and a bathochromic shift of the UV absorption at 290 nm were consistent with the presence of a phenolic hydroxyl located in the nonaporphine unit. The base peak in the HRMS at *m*/*z* 192 is observed on fragmentation between C-1 and the benzylic carbon of benzyl tetrahydroisoquinolines bearing *N*-methyl, methoxyl, and hydroxyl substituents (vide infra) in the isoquinoline part.[14]

The ^{1}H NMR spectrum of **2** (Table 2) revealed two *N*-methyls, six *O*-methyls, and seven aromatic protons, of which the upfield shifted *O*-methyl at δ 3.41 and the aromatic proton at δ 5.65 are as observed for faurine and **1** and were assigned the substituents residing over the shielding region of the aporphine ring A. Thus **2** belongs to the same C-1-linked class of dimeric alkaloids. Three of the *O*-methyl groups must be located on the aporphine, since the MS contains fragments at *m*/*z* 324 and 321 that were already discussed for faurine and **1**. In addition, the aromatic doublets at δ 6.89 and 6.73 are in agreement with corydine as the aporphine. The NOED experiments (Figure 2) confirmed the nature of the dimer and allowed for the ordering of the substituents on the benzyl tetrahydroisoquinoline−aporphine framework.

The ^{1}H NMR spectrum exhibited a considerable broadening of the protons of the benzyl isoquinoline component such that the methylene patterns, which are in the same region as those of the aporphine, but with the latter clearly delineated, prevented their characterization. The H-1′ methine was observable, however, in an unobstructed region (δ 4.28), but was a broad hump spread over 80 Hz. These featureless patterns undoubtedly result from the greater fluctuation or flexion of the benzyl isoquinoline component as compared to the rigid aporphine. Attempts to sharpen the features by increasing the temperature to 55° in $CDCl_3$ did not significantly alter the spectrum. However, in DMSO-d_6 it was only at 110°−120° that peak sharpening resulted; for example, H-1′ became a triplet with J = 6.2 Hz, but decomposition was occurring. Because of limited material and fear of its loss, NMR data were only collected at room temperature. The 2D CH-correlation NMR experiment allowed assignment of all the ^{1}H-bearing carbons, including the methylenes and methine of the benzyl isoquinoline. The quaternary carbons were assigned by comparison to those of faurine, **1**, and related benzyl tetrahydroisoquinolines, as well as from the patterns in the fully ^{1}H-coupled ^{13}C NMR spectrum. Specifically, the latter involved C-1, C-1a, and C-7′.

The absolute stereochemistry of **2** was established as *S*,*S* by comparison of its CD spectrum with the sum of those for faurine and (+)−(*S*)-reticuline. The latter compound represented the benzyl tetrahydroisoquinoline component of **2** and exhibited three positive Cotton effect peaks at 290, 235, and 210 nm. The sum clearly matched the observed CD spectrum for **2**.

Faurithaline (**3**) with the formula $C_{39}H_{44}N_2O_8$ as supported by HREIMS was isolated from the phenolic Et_2O-soluble alkaloid fraction. The weak molecular ion at *m*/*z* 668 (0.3%) indicated a single diphenyl ether oxygen-linked dimer, and the UV absorption at 220, 273, and 307 nm pointed to a 1,2,10,11-substituted aporphine.[15] The molecular formula required 19 double-bond equivalents, of which the aporphine unit provided 10, leaving the remainder to a benzyl tetrahydroisoquinoline as the most likely choice. The bathochromic shift of the UV spectrum under alkaline conditions and the formation of the diacetate **7** supported two phenolic hydroxyls. This, when taken with the seven aromatic protons and five *O*-methyl peaks found in the ^{1}H NMR spectrum, accounted for all the aromatic substitution positions of the oxygen-linked aporphine−benzyl tetrahydroisoquinoline dimer. The ^{13}C NMR spectrum with 24 aromatic carbons between 152 and 105 ppm were in accord with the proposed dimer.

The ^{1}H NMR spectrum also showed two *N*-methyls but lacked any aromatic proton absorption near 8 ppm, a diagnostic position for the aporphine H-11. That a phenolic δ 8.57 and an *O*-methyl group were present in the tetrahydroisoquinoline part was supported by the base peak at *m*/*z* 192 corresponding to the ion fragment formed on breaking the C-1′ to C-9′ bond. The other phenolic group was assigned to the aporphine component from the *m*/*z* 338 peak, which formed from cleavage on the aporphine side of the diphenyl ether and aromatization of the heteroring.

The ABX pattern typical of a 1,2,4-substituted benzene ring observed in the ^{1}H NMR spectrum agreed with the

Table 1. ^{1}H NMR Data for Compounds **1**, **5**, and **6**, and COLOC Data for **1**[a]

	compound			COLOC[f]
proton	**1**[b]	**5**[c]	**6**[d]	**1**
MeO-2	3.61	3.62	3.64	C-2
H-3	6.67	6.68	6.68	C-1, C-2, C-1b, C-3a
H-4	2.72α br d (16.5)	2.73α br dd (16.2, 2.7)	2.73α dd (16.5, 2.6)	C-3, C-3a
	3.18*β* ddd (16.0, 12.5, 5.7)	3.18*β* ddd (16.6, 11.8, 5.4)	3.17*β* ddd (17.0, 12.3, 6.0)	
H-5	2.55α h m	2.54α h m	2.55α h m	
	3.04*β* h dd (11.0, 6.8)	3.03*β* h m	3.03*β* dd (13.1, 5.6)	C-3a, C-6a
MeN-6	2.54	2.54	2.56[e]	C-6a
H-6a	2.90 br d (13.6)	2.89 h dd (12.6, 3.8)	2.88 br d (11.7)	MeN-6
H-7	3.03α h dd (13.2, 3.2)	3.03α h dd (13.3, 3.5)	3.04α dd (13.3, 3.2)	C-1b, C-7a, C-8, C-11a
	2.33*β* dd (12.9, 12.9)	2.30*β* h dd (12.7, 12.7)	2.31*β* dd (12.9, 12.9)	C-7a, C-8
H-8	6.83 d (8.1)	6.85 d (8.1)	6.84 d (8.0)	C-10, C-11a
H-9	6.71 d (8.1)	6.73 d (8.1)	6.68 d (8.0)	C-7a, C-11
MeO-10	3.63	3.70	3.56	C-10
MeO-11	3.60	3.56	3.52	C-11
MeO-2′	3.40	3.37	3.37	C-2′
H-3′	5.62	5.71	5.60	C-1′, C-2′, C-4′
H-5′	3.33α dd (17.1, 5.7)	3.33α dd (16.8, 6.1)	3.35α h m	
	2.91*β* h d (17.7)	2.84*β* d (17.3)	2.98*β* d (17.0)	C-4′
H-6′	4.04 d (5.2)	4.06 d (5.4)	4.06 d (5.5)	
H-7′	6.60	6.77	6.59	C-8′, C-9′
MeO-9′	3.73	3.66	3.76	C-9′
H-10′	6.37	6.51	6.40	C-8′
H-11′	3.33α dd (17.1, 5.7)	3.32α dd (17.4, 5.9)	3.35α h m	
	2.73*β* h d (16.5)	2.61*β* d (15.7)	2.62*β* d (16.7)	C-10′
H-12′	4.33 d (5.2)	4.06 d (5.4)	4.26 d (5.6)	C-6′
MeN-13	2.54	2.50	2.54[e]	C-6′, C-12′
miscellaneous		2.31 (Ac-1′)	3.76 (MeO-1′)	
		2.28 (Ac-8′)	3.84 (MeO-8′)	

[a] Taken at 300 MHz or stated otherwise with data point resolution of 0.4 Hz and chemical shift (*δ*) in ppm as referenced to TMS with residual solvent peak ($CHCl_3$) taken as internal standard at 7.26 ppm. The spin-coupling constant (*J*) is given in parentheses in Hertz. Some hidden (h) patterns were clarified by homonuclear decoupling and NOE studies and are given in brackets. [b] At 500 MHz. [c] Assigned by comparison to spectrum of **1** except for MeO-1′ and MeO-8′, which were identified from NOED irradiations of the acetate methyls. [d] Assigned from NOED studies. [e] May be interchanged. [f] Performed at 125 MHz with 30, 60, and 90 ms delays set for *J* values of 16.7, 8.3, and 5.6 Hz.

Table 2. ^{1}H NMR Data for Compounds **2**−**4** and **7**[a]

	compound			
proton	**2**[b]	**3**	**4**	**7**
H-3	6.75	6.70		6.69
H-4	2.78α br dd (16.3, 4)	2.67α hm [dd] (16.9, 2.8)	2.77α hm	2.67α hm [dd] (16.4, 3.3)
	3.22*β* ddd (16.2, 11.8, 6.3)	3.21*β* ddd (16.9, 11.2, 5.6)	2.95*β* ddd (16.8, 11.0, 5.5)	3.11*β* ddd (17.2, 11.2, 5.9)
H-5	2.60α ddd (11.8, 11.8, 3.8)	2.48α ddd (11.9, 11.9, 3.5)	2.39α hm	2.46α ddd (11.9, 11.9, 3.9)
	3.10*β* hm	3.01*β* dd (11.5, 5.6)	3.05*β* hm	2.98*β* dd (11.4, 5.5)
H-6a	2.97 dd (12.3, 3.7)	2.82 br d (12.4)	2.77 hm [dd] (13.6, 4.0)	2.78 hm [dd] (12.6, 3.5)
H-7	3.09α dd (13.5, 3.7)	3.31α dd (13.8, 3.4)	3.31α dd (14.0, 3.5)	3.48α dd (14.0, 3.5)
	2.36*β* t (12.5)	1.89*β* t (13.5)	1.88*β* t (13.6)	1.98*β* t (13.3)
H-8	6.89 d (8.1)			
H-9	6.73 d (8.2)	6.63	6.60	6.56
H-1′	4.28 vbr s	3.60 br t (6.5)	3.58 t (5.3)	3.58 t (6.0)
H-3′	h	3.08 hm	3.06 hm	3.05 ddd (12.8, 8.0, 4.8)
		2.67 hm	2.67 hm	2.66 hm
H-4′	h	2.66 hm	2.67 hm	2.75 hm
		2.47 hm	2.47 hm	2.52 ddd (16.2, 5.0, 5.0)
H-5′	6.55	6.39	6.39	6.59
H-8′	6.56 br	6.14	6.13	6.43
H-9′	3.14 dd (14.3, 8.1)	3.07 hm	3.05 hm	2.93 dd (14.2, 6.2)
	h	2.65 hm	2.65 hm [dd] (14.0, 7.7)	2.77 hm [dd] (14.2, 6.2)
H-11′		6.35 br	6.34 d (1.4)	6.71 hm
H-12′	5.65 br			
H-14′		6.87 d (8.3)	6.88 d (8.3)	6.83 d (8.8)
H-15′	6.45 br	6.78 br d (8.2)	6.78 dd (8.3, 1.3)	6.71 hm
MeN-6	2.57	2.37	2.36	2.42
MeN-2′	2.53 br	2.42	2.41	2.35
MeO-1		3.67	3.71	3.44
MeO-2	3.71	3.91	3.97	3.87
MeO-3			3.93	
MeO-10	3.67	3.81	3.81	3.71
MeO-11	3.69			
MeO-6′	3.84	3.71	3.71	3.76
MeO-13′	3.41	3.91	3.91	3.86
MeO-14′	3.64			
miscellaneous		8.57 HO-11		2.23 AcO-11
				2.24 AcO-7′

[a] Taken at 500 MHz in $CDCl_3$ or stated otherwise. See Table 1 footnote for symbols and other information. [b] Taken at 270 MHz.

benzylic component bearing the diphenyl ether and the fifth *O*-methyl. The AMX system in the aliphatic region at *δ* 3.31, 2.82, and 1.89 showed patterns for H-7α, H-6a, and H-7*β*, respectively, that were observed for simple aporphines with unsubstituted C-8 and C-9 positions,[16] except that, for **3**, H-7α was shifted farther downfield and H-7*β* farther upfield. The average chemical difference (7α−7*β*) of 0.6 ppm was increased to 1.4 ppm, suggesting the

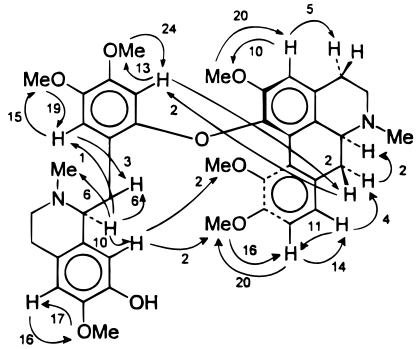


Figure 2. NOED enhancements (in percent) for fauridine (**2**) at 270 MHz.

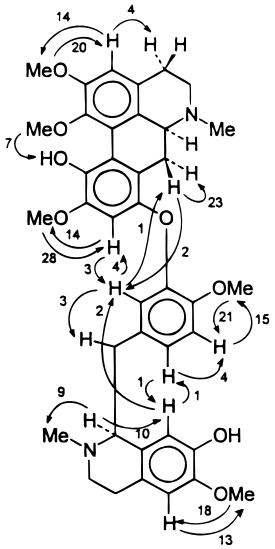
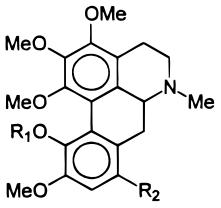


Figure 3. NOED enhancements (in percent) for faurithaline **3** at 270 MHz.

diphenyl ether linkage was located at C-8. To test this possibility oconovine (**8**), a component of *T. fauriei*, was converted to 8-bromooconovine (**9**), methylated to 8-bromo-*O*-methyloconovine (**10**), and oxidized with nitrobenzene via the 8-litho derivative in the Buck-Köbrich reaction, to 8-hydroxy-*O*-methyloconovine (**11**).[17] When compared to *O*-methyloconovine (**12**) with H-7α and H-7β at δ 3.00 and 2.36, respectively, the 8-hydroxy derivative **11** showed these protons at δ 3.40 and 2.04. The farther upfield shift of H-7β to δ 1.89 in **3** must be from the diamagnetic anisotropy of the benzylic ring.



8 R_1=R_2=H
9 R_1=H, R_2=Br
10 R_1=Me, R_2=Br
11 R_1=Me, R_2=OH
12 R_1=Me, R_2=H

Extensive NOED studies at 270 MHz (Figure 3) with **3** and its diacetate **7**, allowed the placement of substituents and supported C-8 and C-12′ as the oxygen-bridge positions for the dimer. Comparison of the highfield (500 MHz) ^{1}H NMR spectral patterns for the aliphatic protons of the aporphine unit to several aporphines allowed their assignment,[16] while those of the tetrahydroisoquinoline were made from the CH-correlation experiment based on the characteristic C-3′ and C-4′ chemical shifts[18] and those of **2**. The COLOC experiment located the quaternary carbons except those at C-1a, C-3a, C-1a′, C-4a′, and C-10′. The very sharp singlet at δ 126.0 in the fully ^{1}H-coupled ^{13}C NMR spectrum was assigned to C-1a, as was observed for faurine, **1**, and **2**, while the remainder were designated by comparison to related compounds. The ^{13}C NMR spectrum is given in Table 3.

The absolute configuration of **3** was established from its CD spectrum by comparison with the sum of the CD spectra of the aporphine (+)-(*S*)-isocorydine and (+)-(*S*)-reticuline, the likely monomeric biogenetic precursors. This is possible because **3**, with one diphenyl ether linkage, would not significantly prevent the two compounds from behaving conformationally as individual monomers. The addition spectrum showed five Cotton effect maxima (3 positive and 2 negative) matching those of **3** in position and relative intensities. Thus, **3** has the *S*,*S*-configuration.

3-Methoxyfaurithaline (**4**), obtained from the phenolic Et_2O-soluble fraction, showed a weak molecular ion by HREIMS at *m*/*z* 698 corresponding to formula $C_{40}H_{46}N_2O_9$ and supportive of a dimeric alkaloid with one diphenyl ether linkage. The ^{1}H NMR spectrum was nearly the same as that of **3** but contained an additional methoxyl and lacked one aromatic singlet. The fragmentation ions at *m*/*z* 506, 386, 370, 328, and 192 (base peak) required the methoxyl to reside in the aporphine unit, with C-3, the biogenetically preferred position. The presence of two phenolic groups was substantiated by the UV spectral evidence and preparation of the diacetate **13**.

Extensive NOED studies and homonuclear decoupling arranged the substituents on the benzyl tetrahydroisoquinoline−aporphine skeleton and allowed the ^{1}H NMR assignments (Table 2) to be made, with location of the methylene protons aided by the 2D NMR CH-correlation study. The COLOC experiment identified 13 of the 18 quaternary carbons, and the remaining five carbons (C-1a, -1b, -3a, -11a, and -10′) were assigned as follows: the fully ^{1}H-coupled ^{13}C NMR spectrum showed a sharp singlet at δ 121.2, which was designated C-1a, in accord with the other compounds in this report. It also gave further support for differentiating C-1 (δ 147.7) from C-12′ (δ 147.5), the latter appearing as a sharp double-doublet (J = 8.0, 4.0 Hz) from two-bond (H-11′) and three-bond (H-14′) couplings. Faurithaline (**3**) was the model compound for designating C-11a (δ 120.9) and C-10′ (δ 133.0), while oconovine (**8**) was the model for C-1b (δ 133.3) and C-3a (δ 124.6) showing, respectively, shifts at δ 133.2 and 124.5.

The absolute stereochemistry for 3-methoxyfaurithaline (**4**) was found to be *S*,*S* from the nearly identical appearance of its CD spectrum with that of the addition spectrum, formed from those of (+)−(*S*)-oconovine (**8**) and (+)−(*S*)-reticuline, putative biosynthetic precursors of **4**.

Experimental Section

General Experimental Procedures. The equipment used is already recorded.[1] The LD-FT-ICRMS was obtained on a Nicolet FTMS-1000 spectrometer, operating at a field strength of 3.019 T, interfaced to a Tachisto 215G pulsed CO_2 laser operating at 10.6 μm.

Plant Material. The plant material, its source, extraction, and initial separation of the crude residue into the various alkaloid-containing fractions is already recorded.[1]

Table 3. ^{13}C NMR Data for Compounds **2**−**4**[a]

	compound					compound			
carbon	**2**[b]	multiplicity	**3**	**4**	carbon	**2**	multiplicity	**3**	**4**
C-1	139.5	s	142.7	147.7	C-5′	110.4	d	110.7	110.8
C-1a	126.9	s	126.0	121.2	C-6′	147.9[c]	s	145.9	145.8
C-1b	129.3	s	129.6	133.3	C-7′	144.2	s	143.5	143.4
C-2	150.3	s	151.5	144.5	C-8′	115.3	d	114.6	114.6
C-3	112.2	d	111.7	150.6 s	C-9′	36.6	t	40.3	40.4
C-3a	129.6	s	130.1	124.6	C-10′	116.5	s	132.9	133.0
C-4	29.2	t	29.3	24.0	C-11′	151.6	s	118.1 d	118.1 d
C-5	53.0	t	52.9	52.7	C-12′	97.6	d	147.7 s	147.5 s
C-6a	63.2	d	62.5	62.7	C-13′	148.1[c]	s	147.9	147.9
C-7	36.1	t	28.1	27.8	C-14′	142.6	s	112.7 d	112.7 d
C-7a	130.5	s	120.9	120.9	C-15′	114.4	d	123.6	123.6
C-8	122.1	d	145.4 s	145.5 s	MeN-6	44.1	q	43.7	43.8
C-9	112.8	d	105.8	105.4	MeN-2′	42.6	q	42.9	43.0
C-10	151.8	s	149.8	149.7	MeO-1		q	62.2	62.8
C-11	146.0	s	141.0	140.4	MeO-2	56.3	q	56.5	61.5
C-11a	125.0	s	121.3	120.9	MeO-3		q		60.6
C-1′	63.0	d	64.8	64.7	MeO-10	56.6	q	56.5	56.5
C-1a′	127.5	s	130.0	130.2	MeO-11	61.0	q		
C-3′	48.8	t	47.7	47.7	MeO-6′	56.0	q	55.9	55.8
C-4′	25.2	t	25.9	26.0	MeO-13′	55.7	q	56.2	56.5
C-4a′	123.4	s	125.7	125.8	MeO-14′	56.3	q		

[a] Taken at 75 MHz on $CDCl_3$ unless stated otherwise with multiplicities determined by SFORD or DEPT and chemical shifts (δ) relative to TMS using the solvent peak (center) as reference at 77.2 ppm. Abbrevations are as follows: s = singlet, d = doublet, t = triplet, and q = quartet. [b] Taken at 67.9 MHz. [c] May be interchanged.

Chromatography of the Et_2O-Soluble Tertiary Phenolic Alkaloid Fraction. A 2.0-g sample of the Et_2O-soluble tertiary phenolic alkaloids from the 1982 plant collection was separated by rotation locular countercurrent chromatography (RLCC), with the aqueous phase of the solvent system $CHCl_3$−MeOH−25mM HOAc (3:5:5) as the mobile phase. Effluent fractions (5.5 mL) were collected at 0.4 mL/min and monitored by TLC on Si gel with $CHCl_3$−MeOH (9:1), developed twice, and visualized by Dragendorff's spray reagent. The alkaloids **1**, **2**, ocobotrine, **3**, 3-demethyloconovine, **4**, and oconovine were isolated, in that order.

The residue (190 mg) from fractions 30−56 was placed on a Si gel (12 g) column and eluted with 2% MeOH in $CHCl_3$ (100 mL), then 10-mL fractions were collected with mixtures from the same solvents, 5% (1−80), 10% (81−120), 15% (121−134), and 25% (135−150). Fractions 11−42 gave 65 mg of **1** and fractions 52−103 yielded 33 mg of **2**.

Fauripavine (1): amorphous off-white solid, $[\alpha]^{26}_D$ +67.8° (*c* 0.9, MeOH); CD (*C* 1.5 × 10^{-5}M, MeOH) (deg) $[\theta]_{315}$ +20 600, $[\theta]_{293}$ −27 300, $[\theta]_{280}$ −25 600 (trough), $[\theta]_{269}$ −37 000, $[\theta]_{253}$ 0, $[\theta]_{235}$ +426 000, $[\theta]_{226}$ 0, and $[\theta]_{210}$ −263 000 (end); UV (MeOH) λ_{max} (log ϵ) 220 (sh, 4.96), 271 (4.44), 292 (sh, 4.29), and 310 (sh, 3.86) nm; (0.05N KOH, MeOH) 220 (end, 5.09), 268 (4.50), and 2.95 (4.39) nm; IR ($CHCl_3$) ν_{max} 3550 (OH), 1650, 1600, 1510, 1490, 1462, 1442, 1330, 1290−1200 (C−O−C), 1140, 1112, 1080, 972, and 870 cm^{-1}; EIMS *m/z* 666 (6, M^+), 635 (4, M-OMe), 341 (30, $C_{19}H_{19}NO_5$), 321 (100, $C_{20}H_{19}NO_3$), 306 (55), 263 (42), 206 (13), 204 (14, $C_{11}H_{10}NO_3$) and 190 (93, $C_{11}H_{12}NO_2$); LD-FT-ICRMS *m/z* 666.3069, $C_{39}H_{42}N_2O_8$ requires 666.2941; ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.1 (C-1), 127.0 (C-1a), 129.2 (C-1b), 151.4 (C-2), 112.3 (C-3), 129.0 (C-3a), 29.1 (C-4), 53.1 (C-5), 63.3 (C-6a), 36.2 (C-7), 130.6 (C-7a), 121.5 (C-8), 113.7 (C-9), 153.0 (C-10), 148.5 (C-11), 125.0 (C-11a), 56.3 (MeO-2), 56.8 (MeO-10), 60.8 (MeO-11), 44.1 (MeN-6), 136.2 (C-1′), 123.5 (C-1a′), 143.8 (C-2′), 96.8 (C-3′), 149.4 (C-4′), 113.9 (C-4a′), 27.6 (C-5′), 55.9 (C-6′), 130.7 (C-6a′), 113.0 (C-7′), 144.1 (C-8′), 145.7 (C-9′), 111.0 (C-10′), 123.7 (C-10a′), 31.8 (C-11′), 52.0 (C-12′), 55.7 (MeO-2′), 55.9 (MeO-9′), and 40.6 ppm (MeN-13′); and ^1H NMR in Table 1.

Fauripavine Diacetate (5). Fauripavine (**1**) (16.8 mg), Ac_2O (0.5 mL), and pyridine (0.5 mL) were reacted overnight at room temperature. The reaction mixture was evaporated to dryness with aid of toluene and the residue purified by preparative TLC on Si gel (0.5 mm) with 5% MeOH in $CHCl_3$. The major band was then passed through a Si gel (3 g) column with 3% MeOH to give 14 mg of the amorphous diacetate **5**: $[\alpha]^{24}_D$ +67.5° (*c* 0.6, MeOH); UV (MeOH) λ_{max} (log ϵ) 305 (sh, 4.11), 273 (4.63), and 218 (sh, 4.93) nm; IR ($CHCl_3$) ν_{max} 1763 (C=O, Ac) and 1190 (C−O−C, Ac) cm^{-1}; EIMS *m/z* 750 (3, M^+), 427 (31) 384 (16), 342 (12), 321 (100), 306 (50), 263 (40), 248 (30), 232 (75), 206 (24), and 190 (60); and ^1H NMR in Table 1.

***O,O*-Dimethylfauripavine (6).** Fauripavine (**1**) (20 mg) in MeOH (2 mL) was treated with excess CH_2N_2 in Et_2O (5 mL) at 4 °C for 3 days. The residue, after evaporation of solvent, was purified as described for acetate **5** to give 9 mg of dimethylfauripavine (**6**): $[\alpha]^{25}_D$ +24.3° (*c* 0.7, MeOH); IR ($CHCl_3$) ν_{max} 1610, 1518, 1490, 1467, 1326, 1280−1200, 1140, 1115, 1050, 988, 855, and 660 cm^{-1}; EIMS *m/z* 694 (3,M^+), 371 (40), 356 (9), 321 (87), 306 (46), 263 (35), 220 (39), 204 (100), 190 (11), and 161 (10); and ^1H NMR in Table 1.

(−)-Munitagine: CD (*C* 6.0 × 10^{-4} M, MeOH) (deg) $[\theta]_{292}$ +1810, $[\theta]_{289}$ 0, $[\theta]_{275}$ −14 100, $[\theta]_{253}$ 0, $[\theta]_{241}$ +13 300, $[\theta]_{234}$ 0, $[\theta]_{226}$ −56 000 (sh), $[\theta]_{207}$ −403 000, $[\theta]_{201}$ 0, $[\theta]_{195}$ +252 000; ^1H NMR (250 MHz, $CDCl_3$) δ 3.78 (MeO-2), 6.63 (d, *J* = 8.3 Hz, H-3), 6.46 (d, *J* = 8.3 Hz, H-4), 3.36 (dd, *J* = 16.4, 5.9 Hz, H-5α), 2.57 (d, *J* = 16.6 Hz, H-5*β*), 3.91 (d, *J* = 5.4 Hz, H-6), 6.56 (H-7), 3.71 (MeO-9), 6.39 (H-10), 3.33 (dd, *J* = 16.4, 5.9, H-11α), 2.73 (d, *J* = 16.5, H-11*β*), 4.39 (d, *J* = 5.5 Hz, H-12), 2.52 (MeN-13); and ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 142.2 (C-1), 144.5 (C-2), 109.6 (C-3), 119.8 (C-4), 125.6 (C-4α), 33.1 (C-5), 56.3 (C-6), 130.4 (C-6α), 113.3 (C-7), 144.3 (C-8), 146.0 (C-9), 111.3 (C-10), 124.2 (C-10α), 31.1 (C-11), 51.9 (C-12), 40.7 (MeN-13), 56.1 (MeO-2), 55.9 (MeO-9) ppm.

Fauridine (2): amorphous solid, $[\alpha]^{24}_D$ +285.6° (*c* 1.04, MeOH); CD (*C* 1.52 × 10^{-5} M, MeOH) (deg) $[\theta]_{330}$ 0; $[\theta]_{316}$ +9180, $[\theta]_{308}$ 0, $[\theta]_{302}$ −4590, $[\theta]_{296}$ 0, $[\theta]_{284}$ +15 700, $[\theta]_{265}$ 0, and $[\theta]_{236}$ +504 000; UV (MeOH) λ_{max} (log ϵ) 222 (sh, 4.90), 272 (4.30), 290 (sh, 4.21) and 311 (sh, 3.83); (0.01 KOH, MeOH) 220 (end, 4.56), 268 (4.31), and 2.94 (4.25) nm; IR ($CHCl_3$) ν_{max} 3540 (OH), 1660, 1510, 1468, 1270, 1250−1200, 1138, 1076, 1028, 998, 820, and 653 cm^{-1}; HRMS *m/z* (int. formula, dev.) 682.3591 (0.2 M^+, $C_{40}H_{46}N_2O_8$, +33.7), 491.2626 (2, $C_{29}H_{33}NO_6$, +31.8), 492.2482 (2, $C_{28}H_{34}NO_6$, +19.3), 324.1637 (1, $C_{20}H_{22}NO_3$, +3.7), 322.1436 (1, $C_{20}H_{20}NO_3$, +0.7), 192.1028 (100%, $C_{11}H_{14}NO_2$, +0.4), 190.0893 (8, $C_{11}H_{12}NO_2$, +2.5), 177.0827 (10, $C_{10}H_{11}NO_2$, +3.7), 177.0804 (8, $C_{10}H_{11}NO_2$, +7.9); LD-FT-ICRMS *m/z* 721 (100, M + K^+) and 705 (13, M + Na^+); ^1H and ^{13}C NMR in Tables 2 and 3.

(+)-(*S*)-Reticuline: isolated from *T. foetidum* L. (unpublished and identified from physical data in the literature[19]): $[\alpha]^{26}_D$ +124° (*c* 0.5, MeOH); CD (*C* 1.52 × 10^{-5} M, MeOH) (deg)

$[\theta]_{302}$ 0°, $[\theta]_{290}$ +15 400, $[\theta]_{253}$ 0, $[\theta]_{235}$ +25 500, $[\theta]_{226}$ +22 500 (trough), $[\theta]_{210}$ +97 500, and $[\theta]_{202}$ 0.

Isolation of Faurithaline (3) and 3-Methoxyfaurithaline (4). Fractions 170−220 (120 mg) from the RLCC separation of the Et_2O-soluble tertiary phenolic alkaloid fraction were chromatographed on Si gel (10 g) taking 8-mL fractions with 2% (1−39) and 5% (40−70) MeOH in $CHCl_3$. Fractions 6−9 yielded 30 mg of crystalline 3-*O*-demethyloconovine, mp 171−173°, and fractions 17−50 afforded 83 mg of **3**.

RLCC fractions 271−320 (112 mg) were chromatographed on basic Al_2O_3 (10 g) collecting 10 mL of effluent with 0.5% (1−40), 1.25% (40−70) MeOH in $CHCl_3$ to give 93 mg of **4** from fractions 9−60.

Faurithaline (3): amorphous solid, $[\alpha]^{25}{}_D$ +83.3° (*c* 0.9, MeOH); CD (*C* 6.59 × 10^{-5} M, MeOH) (deg) $[\theta]_{355}$ 0, $[\theta]_{323}$ +3800, $[\theta]_{303}$ 0, $[\theta]_{299}$ −380, $[\theta]_{297}$ 0, $[\theta]_{293}$ +2360, $[\theta]_{289}$ 0, $[\theta]_{270}$ −31 500, $[\theta]_{248}$ 0, $[\theta]_{232}$ +104 700, and $[\theta]_{215}$ +15 700 (end); UV (MeOH) λ_{max} (log ϵ) 220 (end, 4.82), 268 (sh, 4.27), 273 (4.28), and 307 (3.72) nm; IR ($CHCl_3$) ν_{max} 3550 (OH), 3200 (OH), 3010, 1582, 1513, 1448, 1268−1200, 1140, 1102, 1047, 1030, 990, 857, and 836 cm^{-1}; ^{13}C NMR (75 MHz, $CDCl_3$) COLOC correlations H-3/C-1, C-1b, C-2; H-7α/C-7a, C-8, C-11a; H-7*β*/C-1b, C-8, C-11a; H-9/C-8, C-10, C-11; H-5′/C-6′, C-7′; H-8′/C-6′, C-7′; H-11′/C-13′; H-14′/C-12′; H-15′/C-13′; MeO-1/C-1; MeO-2/C-2; MeO-10/C-10; MeO-6′/C-6′; MeO-13′/C-13′; HREIMS *m/z* 668.3520 (0.3, M^+, $C_{39}H_{44}N_2O_8$ requires 668.3098), 477.2189 (1.4, $C_{28}H_{31}NO_6$, +3.8), 476.2100 (0.9, $C_{23}H_{30}NO_6$, +2.7), 446.2010 (5, $C_{27}H_{28}NO_5$, +4.3), 338.1437 (0.5, $C_{20}H_{20}NO_4$, +4.5), 325.1391 (4, $C_{20}H_{21}O_4$, −4.9), 192.1014 (100, $C_{11}H_{14}NO_2$, −1.0) and 177.0810 (12, $C_{10}H_{11}NO_2$, +2.1); ^1H- and ^{13}C NMR in Tables 2 and 3.

Faurithaline Diacetate (7). Faurithaline (**3**) (16 mg) was reacted overnight at room temperature with Ac_2O (3 mL) and pyridine (1 mL). The residue after evaporation was chromatographed on silica gel (3 g) with 1%, 2%, and 5% MeOH in $CHCl_3$ to give from the last eluant diacetate **7** (16 mg) as an amorphous solid; $[\alpha]^{25}{}_D$ +58.5° (*c* 1.0, MeOH); IR ($CHCl_3$) ν_{max} 3005, 2940, 1765, 1515, 1467, 1375, 1265, 1240−1180, 1140, 1100, and 1012 cm^{-1}; and ^1H NMR in Table 2; NOED showed MeO-1 to AcO-11 (2%) and MeO-2 (1); H-3 to MeO-2 (18) and H-4 (5); MeN-6 to H-5 (14), H-6a (21) and H-7α (13); H-9 to MeO-10 (15) and H-11′ (2); H-1′ to MeN-2′ (5), H-8′ (9), H-9′s (15 each); MeN-2′ to H-3′ (*δ* 2.67, 4), H-3′ (*δ* 3.05, 2), H-1′ (11); H-5′ to H-4′ (2) and MeO-6′ (14); H-8′ to H-11′ and H-15′ (together 2), and H-14′ to H-15′ (7) and MeO-13′(12); FABMS (with m-$NO_2C_6H_4CH_2OH$) *m/z* 753 (100%, MH^+), 711 (27), 234 (95), and 192 (70).

(+)-(***S***)-**Oconovine (8):** isolated from *T. fauriei*,[1] identified from physical data in the literature:[20] $[\alpha]^{25}{}_D$ +120° (*c* 0.31, $CHCl_3$); CD (*C* 1.62 × 10^{-4} M, MeOH) (deg) $[\theta]_{345}$ 0, $[\theta]_{315}$ +1360, $[\theta]_{307}$ 0, $[\theta]_{272}$ −24 700, $[\theta]_{251}$ 0, $[\theta]_{234}$ +265 000, and $[\theta]_{205}$ +11 100 (end).

8-Bromo-*O*-methyloconovine (10). Oconovine[1] (**8**) (67 mg) in 3 mL HOAc was treated dropwise with 29 mg of Br_2 in 0.9 mL of HOAc at ambient temperature. The reaction mixture was mixed with 100 mL each of $CHCl_3$ and H_2O. The $CHCl_3$ layer was extracted twice with 100 mL of 6% aqueous NH_4OH, dried (anhydrous $MgSO_4$), and the residue (80 mg) chromatographed on 3 g of Si gel with 2% Me_2CO in PhH. The brominated product (61 mg) in 3 mL of MeOH was treated with 6 mL of 1.5% CH_2N_2 in Et_2O for 4 days at 4 °C. The reaction residue (59 mg) was separated on 3 g of silica gel with $CHCl_3$ and 0.5% MeOH in $CHCl_3$. The last solvent gave product **10** as a crystalline solid: mp 121−122 °C, $[\alpha]^{25}{}_D$ +191.5° (*c* 0.86, MeOH); CD (*C* 1.2 × 10^{-5} M, MeOH) (deg) $[\theta]_{335}$ 0, $[\theta]_{312}$ +7380, $[\theta]_{302}$ 0, $[\theta]_{278}$ −35 200, $[\theta]_{258}$ 0, and $[\theta]_{239}$ +445 000; UV (MeOH) (log ϵ) λ_{max} 225 (4.81) and 279 (4.41)-nm; IR ($CHCl_3$) ν_{max} 1572, 1456, 1402,1378, 1348, 1108, 1073, 1033, 1013, and 963 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) *δ* 7.03 (1H, s, H-9), 3.93 (3H, s, MeO-11), 3.90 (3H, s, MeO-2), 3.87 (3H, s, MeO-10), 3.69 (3H, s, MeO-1), 3.66 (3H, s, MeO-11), 3.46 (1H, dd, *J* = 14.4, 3.6 Hz, H-7α), 3.06 (1H, ddd, *J* = 11.5, 5.8, 1.2 Hz, H-5*β*), 2.91 (1H, dddd, *J* = 17.0, 12.0, 6.0, 1.6 Hz, H-4*β*), 2.81 (1H, dddd, *J* = 12.7, 3.5, 1.7, 1.7 Hz, H-6a), 2.76 (1H, dddd, *J* = 16.9, 3.9, 1.3, 1.3 Hz, H-4α), 2.55 (3H, s, MeN-6), 2.43 (1H, ddd, *J* = 11.8, 11.8, 3.9 Hz, H-5α), and 2.17 (1H, dd, *J* = 14.3, 12.7 Hz, H-7*β*); ^{13}C NMR ($CDCl_3$, 20 MHz) *δ* 152.4 (s), 151.1 (s), 150.9 (s), 147.3 (s), 144.7 (s), 132.6 (s), 130.0 (s) 127.2 (s), 121.5 (s), 120.0 (s), 116.0 (d, C-9), 115.9 (s), 63.3 (d, C-6a), 61.1 (q, MeO-1), 60.9 (2C, q, MeO-2 and MeO-11), 60.5 (q, MeO-3), 56.7 (q, MeO-10), 53.0 (t, C-5), 44.1 (q, MeN-6), 35.2 (t, C-7), and 24.0 (t, C-4); HREIMS *m/z* (int. formula, dev.) 465.0978 (M^+, 60, $C_{22}H_{26}NO_5{}^{81}Br$, 0.4), 463.0998 ($M^+$, 70, $C_{22}H_{26}NO_5{}^{79}Br$, 0.3), 450.0813 (M-Me, 70, $C_{21}H_{23}NO_5{}^{81}Br$, 7.4), 448.0805 (M-Me, 82, $C_{21}H_{23}NO_5{}^{79}Br$, 4.6), 434.0815 (M-MeO, 99, $C_{21}H_{23}NO_4{}^{81}Br$, 2.5), 432.0814 (M-MeO, 100, $C_{21}H_{23}NO_4{}^{79}Br$, 0.3), and 384.1803 (M-Br, 2, $C_{22}H_{26}NO_5$, −0.7).

8-Hydroxy-*O*-methyloconovine (11). Compound **10** (38 mg) in 1 mL of dry THF was added dropwise to a solution of 2.6M *n*-BuLi in hexane (0.12 mL) in 1.5 mL THF under N_2 cooled by dry ice−Me_2CO. After 55 min, 0.12 mL of $PhNO_2$ was added and stirred for 4 h. At ambient temperature, 20 mL of 10% H_2SO_4 was added and the mixture extracted with Et_2O (3 × 50 mL). The aqueous layer was basified (NH_4OH) and extracted with $CHCl_3$ (3 × 50 mL). The $CHCl_3$ layer after washing (H_2O) and drying ($MgSO_4$) gave a 35-mg residue on evaporation, which was separated by preparative TLC on Si gel (0.75 mm thick) with MeOH−PhH−NH_4OH (6:94:0.5). The R_f 0.50 band (15 mg) was *O*-methyloconovine (**12**), and the R_f 0.30 band (10 mg) was compound **11**: amorphous, $[\alpha]^{25}{}_D$ +32° (*c* 1, MeOH); CD (*C* 2.5 × 10^{-5} M, MeOH) (deg) $[\theta]_{350}$ 0, $[\theta]_{314}$ +15 400, $[\theta]_{297}$ 0, $[\theta]_{274}$ −33 300, $[\theta]_{253}$ 0, $[\theta]_{235}$ +185 000, and $[\theta]_{223}$ 0; UV (MeOH) λ_{max} (log ϵ) 221 (sh, 4.56), 2.73 (4.15), and 320 (sh, 3.64) and (in 0.01N KOH) 221 (end abs 4.60), 2.53 (sh, 4.12), 275 (4.12), and 329 (3.68) nm; IR ($CHCl_3$) ν_{max} 3590 and 3300 (OH), 1592, 1570, 1460, 1410, 1373, 1340, 1230−1190, 1122, 1105, and 1010 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) *δ* 6.43 (1H, s, H-9), 3.92 (3H, s, MeO-3), 3.90 (3H, s, MeO-2), 3.79 (3H, s, MeO-10), 3.71 (3H, s, MeO-1), 3.58 (3H, s, MeO-11), 3.40 (1H, dd, *J* = 13.9, 3.6 Hz, H-7α), 3.14 (1H, dd, *J* = 11.5, 5.7 Hz, H-5*β*), 2.98 (1H, ddd, *J* = 17.5, 12.6, 6.3 Hz, H-4*β*), 2.95 (1H, h br d, *J* = 13 Hz, H-6a), 2.79 (1H, dd, *J* = 16.9, 3.5 Hz, H-4α), 2.58 (3H, s, MeN-6), 2.54 (1H, ddd, *J* = 11.9, 11.9, 3.6 Hz, H-5α), and 2.04 (1H, dd, *J* = 13.2, 13.2 Hz, H-7*β*); ^{13}C NMR ($CDCl_3$, 125 Hz) *δ* 152.1 (s), 151.0 (s), 150.5 (s), 148.3 (s), 145.0 (s), 141.4 (s), 131.1 (s), 125.8 (s), 120.6 (s), 120.4 (s), 114.7 (s), 101.2 (d, C-8), 63.2 (d, C-6a), 61.20 (q, MeO-1), 61.15 (q, MeO-2), 60.9 (q, MeO-11), 60.7 (q, MeO-3), 56.2 (q, MeO-10), 52.8 (t, C-5), 43.4 (q, MeN-6), 27.1 (t, C-7) and 23.1 (t, C-4); HREIMS *m/z* (int. formula, dev.) 401.1780 (M^+, 16, $C_{22}H_{27}NO_6$, −5.8), 399.1677 (M-2H, 15, $C_{22}H_{25}NO_6$, −0.4), 386.1594 (M-Me, 38, $C_{21}H_{24}NO_6$, −0.9), 371.1687 (M-CH_2O, 10, $C_{21}H_{25}NO_5$, −4.6), 370.1676 (M-MeO, 24, $C_{21}H_{24}NO_5$, 22), and 57 (100%).

***O*-Methyloconovine (12).** Prepared from **8** (25 mg) by treatment with excess CH_2N_2 in Et_2O for 12 days; and separated from unreacted starting material by preparative TLC on Si gel with Et_2O−PhH (1:1) and on a 3-g column of Si gel with 0.8% MeOH in $CHCl_3$ to give 15 mg of compound **12**: amorphous, $[\alpha]^{25}{}_D$ +182.5° (*c* 1.31, $CHCl_3$); IR ($CHCl_3$) ν_{max} 1583, 1483, 1460, 1410, 1372, 1342, 1290−1260, 1103, 1075, 1033, and 1016 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) *δ* 6.94 and 6.82 (1H each, d, *J* = 8.0 Hz, H-8 and H-9), 3.93 (3H, s, MeO-3), 3.91 (3H, s, MeO-2), 3.89 (3H, s, MeO-10), 3.72 (3H, s, MeO-1), 3.68 (3H, s, MeO-11), 3.06 (1H, dd, *J* = 11.3, 5.6 Hz, H-5*β*), 3.00 (1H, dd, *J* = 13.6, 3.5 Hz, H-7α), 2.93 (1H, dddd, *J* = 16.9, 12.2, 6.1, 1.5 Hz, H-4*β*), 2.84 (1H, brd, *J* = 12.9 Hz, H-6a), 2.77 (1H, ddd, *J* = 16.9, 3.9 Hz, H-4α), 2.52 (3H, s, MeN-6), 2.43 (1H, ddd, *J* = 11.8, 11.8, 4.1 Hz, H-5α) and 2.36 (1H, dd, *J* = 13.1 Hz, H-7*β*).

3-Methoxyfaurithaline (4): amorphous solid, $[\alpha]^{25}{}_D$ +66.6° (*c* 0.78, MeOH); CD (*C* 1.12 × 10^{-5} M, MeOH) (deg) $[\theta]_{340}$ 0, $[\theta]_{318}$ +5340, $[\theta]_{305}$ 0, $[\theta]_{297}$ −5340, $[\theta]_{295}$ −4900 (min), $[\theta]_{276}$ −40 500, $[\theta]_{251}$ 0, $[\theta]_{234}$ +185 000, and $[\theta]_{222}$ 0; UV (MeOH) λ_{max} (log ϵ) 220 (sh, 4.81), 275 (4.30), and 315 (sh, 3.54) nm; (0.05 N KOH, MeOH) 220 (end, 4.84), 273 (4.26), 282 (sh, 4.22), 304 (sh, 3.90), and 340 (3.83) nm; IR ($CHCl_3$) ν_{max} 3550 (OH), 3220 (OH), 1615−1575, 1515, 1475, 1448, 1418, 1377, 1345, 1300−1200, 1137, 1112, 1098, and 910 cm^{-1}; HREIMS *m/z* 698.3166 (0.4, M^+, $C_{40}H_{46}N_2O_9$ requires 698.3203), 506.2177

(1.5, $C_{29}H_{32}NO_7$, −0.2), 386.1601 (0.7, $C_{21}H_{24}NO_6$, −0.3), 370.1649 (1.5, $C_{21}H_{24}NO_5$, −0.5), 328.1547 (1.3, $C_{19}H_{22}NO_4$, −0.2), 192.1064 (100, $C_{11}H_{14}NO_2$, 3.9), and 190.0912 (8, $C_{11}H_{12}NO_2$, 4.4); ^{1}H and ^{13}C NMR in Tables 2 and 3; NOED (270 MHz) showed HO-11 to MeO-1(8%); MeO-1 to MeO-2 (5); MeO-2 to MeO-1(4), MeO-3(4); MeO-3 to MeO-2(2), H-4α(1); MeN-6 to H-5β (8), H-6a (10), H-7α (6); H-7α to MeN-6 (6), H-6a (11), H-7β (23); H-9 to MeO-10 (14), H-11′ (2); H-11′ to H-9(4), H-9′A (3), H-9′B (1); H-1′ to MeN-2′ (5), H-8′ (10), H-9′A (11), H-9′B (2), H-11′ (4), H-15′ (5); H-15′ to H-8′ (1), H-14′ (10); H-14′ to H-15′ (9), MeO-13′ (9); MeO-13′ to H-14′ (18); H-5′ to H-4′A (3), H-4′B (3); and MeO-6′ to H-5′ (20).

3-Methoxyfaurithaline Diacetate (13). Compound **4** (10 mg) was acetylated as given for diacetate **7** to give 8 mg of diacetate **13**: $[\alpha]^{26}_D$ +40.0° (*c* 0.2, MeOH); UV (MeOH) λ_{max} (log ϵ) 218 (5.00), 275 (4.55), and 306 (sh, 3.85); IR ($CHCl_3$) ν_{max} 1765, 1515, 1413, 1375, 1270, and 1230−1190 cm^{-1}; ^{1}H NMR (90 MHz, $CDCl_3$) δ 6.85 (H-14′, d, 8.8 Hz), 6.71 (H-11′, d, 1.9), 6.69 (H-15′, dd, 8.8, 1.9), 6.59 (H-5′, s), 6.54 (H-9, s), 6.43 (H-8′, s), 3.95 (MeO-2), 3.92 (MeO-3), 3.85 (MeO-13′), 3.76 (MeO-6′), 3.71 (MeO-10), 3.48 (MeO-1), 2.42 (MeN-2′), 2.35 (MeN-6), and 2.24 (2 × Ac); EIMS *m*/*z* 782 (1%, M^+) 740 (1), 549 (3), 369 (4), 353 (13), 324 (11), 310 (19), 234 (100), 192 (30), and 177 (8).

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