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NORPALLIDINE, A NEW MORPHINANDIENONE ALKALOID FROM *FUMARIA VAILLANTII**

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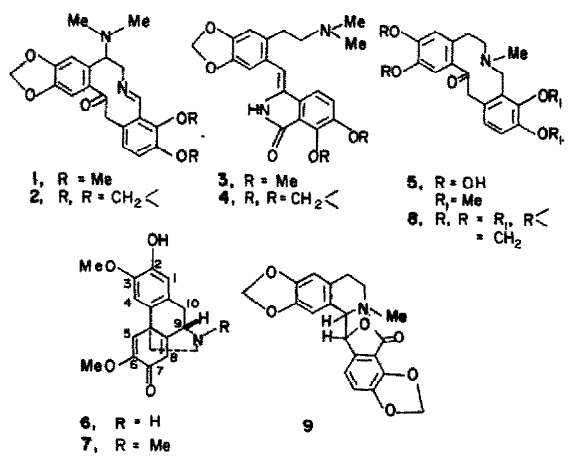
Key Word Index—*Fumaria vaillantii*; Fumariaceae; new morphinandienone alkaloid, norpallidine, pallidine, bicuculline and protopine.

Previously recorded investigations of *Fumaria vaillantii*, var. Schrammii (Fumariaceae) have yielded fumaridine and fumaramine whose original structural assignments **1** and **2**, respectively [1, 2], were later corrected to **3** and **4** [3]. More recently, a new alkaloid was reported, vaillantine, supposedly **5** [4] and this structure is again probably in error since it incorporates a catecholic system which would oxidize readily in air to a quinone.

In our hands, an investigation of *F. vaillantii* collected in northern Pakistan yielded the colorless new base norpallidine (**6**), mp 102° ($CHCl_3$), $[\alpha]_D^{23}$ −11° (MeOH, 0.0019 gm/ml), along with the known protopine (**8**) and (−)-bicuculline (**9**). The NMR spectrum of norpallidine (**6**) in $CDCl_3$ showed two methoxyl singlets at δ3.73 and 3.82, and four downfield singlets at δ6.22, 6.30, 6.62, and 6.73 for H-8, H-1, H-4 and H-5, respectively [5, 6]. The most significant feature of the IR spectrum obtained in $CHCl_3$ was the display of the three bands characteristic of an α-methoxy cross-conjugated cyclohexadienone system at 1668, 1642, and 1625 cm^{-1} [6]. The mass spectrum showed a parent peak at *m/e* 313 for $C_{18}H_{19}O_4N$ which was also the base peak.



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Since (−)-pallidine (**7**) was also found in the same plant, it was immediately suspected that alkaloid **6** corresponded to the so far unknown norpallidine. Indeed, Eschweiler–Clarke *N*-methylation of **6** yielded pallidine, identical in all respects with the known natural product [5].

It is interesting to note that it still remains to be settled whether norpallidine (**6**) is the biogenetic precursor of pallidine (**7**) via methionine *N*-methylation, or whether *N*-demethylation occurs *in vivo* so that **7** is transformed into **6**. This problem bears direct analogy to the aporphine series where the exact biogenetic sequence relating aporphines to noraporphines is still unclear. It is, of course, a distinct possibility that both *N*-methylation and *N*-demethylation occur as *in vivo* processes, and are involved in the biogenesis of these secondary and tertiary bases.

EXPERIMENTAL

General procedure. Mp's are uncorrected. NMR spectra are at 60 MHz. CD curves were obtained using a J-20 Japan Spectroscopic Co. apparatus. TLC was on Merck Si gel plates; the solvent system was MeOH–$CHCl_3$ (1:4).

Extraction and isolation. Dried and ground roots (9 kg) of *F. vaillantii* were extracted with light petroleum for 4 days. Plant material was then extracted with EtOH for another 4 days. The EtOH was evaporated and the residue taken up in dil. HCl. The soln. was extracted with $CHCl_3$. The aq layer was basified to pH 8 with 10% NaOH, and then re-extracted with $CHCl_3$. The latter $CHCl_3$ extract was dried over K_2CO_3, filtered, and evaporated. Residue was column chromatographed on neutral alumina, activity 1, 80–200 mesh (Fisher Scientific Co.). The initial solvent was $CHCl_3$. The major alkaloid obtained with $CHCl_3$ was protopine (**8**) whose identity was confirmed by spectral comparison with an authentic sample. The fraction collected using 20% MeOH in $CHCl_3$ as solvent contained pallidine (**7**) and norpallidine (**6**); R_f's 0.58 and 0.31, respectively. Pallidine (**7**) was characterized through spectral comparisons with an authentic sample. In a separate series of experiments, the $CHCl_3$ extracts from the aerial parts of the plant were chromatographed on Brockmann alumina. The first few fractions collected from hexane yielded protopine (**8**), while the subsequent fractions gathered using hexane–benzene (9:1) provided (−)-bicuculline (**9**) [7] identified by spectral comparisons.

Norpallidine (**6**). λ_{max}^{EtOH} 238 and 281 nm (log ε 3.93 and 3.75); CD (MeOH, 9.3×10^{-5} g/ml) $[\theta]_{328}$ −1,346°, $[\theta]_{294}$ +7,068°, $[\theta]_{282}$ +6,058° and $[\theta]_{262}$ +33,656°. Mass spectrum

m/e 313 (M^+, base), 298, 285 and 270. High resolution MS, M^+, calcd. 313.1313, found 313.1295.

N-*Methylation of norpallidine.* A soln of 2 mg of **6** in 2 ml 85% HCOOH and 1 ml 40% HCHO was heated on a steam-bath for 10 hr. Solvent was evaporated under *vacuo*, the residue diluted with 10 ml H_2O, basified with 1N NaOH to pH 8, and thoroughly extracted with $CHCl_3$. TLC gave a major spot which was collected and shown to be spectrally identical with an authentic sample of pallidine (**7**).

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APORPHINE AND TETRAHYDROBENZYLISOQUINOLINE ALKALOIDS IN *SASSAFRAS ALBIDUM*§

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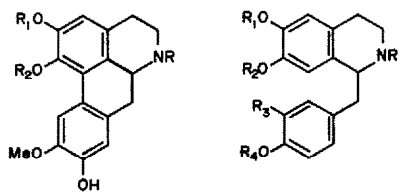
Key Word Index—*Sassafras albidum*; Lauraceae; alkaloids; boldine; norboldine; isoboldine; norcinnamolaurine; cinnamolaurine; reticuline.

Several volatile compounds [1–4] namely safrole, eugenol, α-pinene, camphor, α-phellandrene, β-phellandrene, coniferaldehyde, piperonylacrolein have been identified in the root of *Sassafras albidum*. Besides these, sesamin and desmethoxyaschantin, the two lignans, sitosterol and 2,3-dihydroxy-1-[3,4-methylenedioxy phenyl]-propane have also been isolated from the root [2]. Recently we have identified eleven more volatile compounds in the petroleum ether extract [5]. We now report on the alkaloids of the root bark.‡

The alkaloidal fraction, separated by treatment with 5% aqueous HCl, showed the presence of at least six Dragendroff positive compounds by TLC. The six alkaloids were separated by preparative TLC. The compounds (A–C) showed UV spectra characteristic of 1,2,9,10-tetraoxygenated aporphine alkaloids [6,7]. The IR spectra showed bands for OH/NH function and aromatic system. The mass spectral fragmentation patterns and the relative intensities of the peaks especially those of M^+ and the base peaks $(M-1)^+$ were in agreement with the presence of 1,2,9,10-tetraoxygenated aporphine nucleus [8] in these compounds. The relative intensities of M^+ and $(M-31)^+$ peaks in the mass spectra, suggested [9] that only compounds A and B have a methoxyl group at position 1 of the aporphine nucleus whereas compound C does not. The presence of intense $(M-43)^+$ peaks in compounds A and C and a $(M-29)^+$ peak in compound B indicated [9] that A and C are N-Me aporphines while B is a N-unsubstituted (NH) aporphine. From spectral properties and other available data A and C were identified as boldine (**1**) [11], and isoboldine (**3**) [11] respectively. The identities were confirmed by direct comparison with authentic samples. Compound B was identified as norboldine (**2**) [11], this was confirmed by conversion to the corresponding N–Me derivative and comparison to a pure specimen of boldine (**1**).

The UV spectra of compounds (D–F) suggested that they were 1-benzyl 1,2,3,4-tetrahydroisoquinoline alkaloids. The mass spectra of the compounds which showed



	R	R_1	R_2
(1) Boldine;	Me	H	Me
(2) Norboldine;	H	H	Me
(3) Isoboldine;	Me	Me	H

	R	R_1	R_2	R_3	R_4
(4) Norcinnamolaurine;	H	$-CH_2-$		H	H
(5) Cinnamolaurine;	Me	$-CH_2-$		H	H
(6) Reticuline;	Me	Me	H	OH	Me

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‡ While this work was in progress presence of unidentified alkaloids has been suggested [10].

§ Part 6 in the series "Potential Carcinogens".