Handbook of Secondary Fungal Metabolites

VOLUME I
Handbook of Secondary Fungal Metabolites

VOLUME I

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Preface

The "Handbook of Secondary Fungal Metabolites" is presented in three volumes and is comprehensive to the extent that all major groups of secondary fungal metabolites are included. The format is similar to that presented in the "Handbook of Toxic Fungal Metabolites" with the major exception that actual spectra are not included; however, spectral data are included where available. Also included in these volumes are the methods used by the authors to isolate and purify metabolites. Another major difference is that the appropriate references are presented with each metabolite, negating the need to turn to the end of each group to find the appropriate references. Each volume contains four indexes: secondary metabolite index, molecular formula index, molecular weight index, and fungal/plant source index. In a few instances, plant sources are included when the metabolites are closely related to fungal metabolites or the source of precursors may be fungal; i.e., the baccharins, which are found in extracts from *Baccharis megapotamica*. These metabolites are closely related to the macrocyclic trichotheccenes found in extracts of fungi such as *Myrothecium* spp. and *Stachybotrys* spp. Also, metabolites from the fungal symbiont of lichens are sometimes presented. To aid in the interpretation of NMR data, the numbering system presented in the literature is included for the major representative fungal metabolite and, at times, for several related metabolites. Fungal sources are given as reported in the original references. It is recognized that the taxonomy in several cases has been revised, perhaps more than once. It is beyond the scope of these volumes to deal with what is "currently accepted taxonomy" because this is a dynamic science that, in many cases, is as yet undefined.

The "Handbook" has been divided into sections, and the placement of metabolites is based on chemical relationships. One section of each volume contains a miscellaneous section to accommodate metabolites difficult to place into one of the sections. The miscellaneous section of Volume III contains some metabolites related to those that appear in Volumes I and II. This occurred when related metabolites were discovered after Volumes I and II were completed.
It is hoped that this compilation of data on secondary fungal metabolites will aid investigators in the identification of known or related fungal metabolites. Because fungal metabolites represent a wide diversity of chemical species, these volumes will be useful to scientists interested in correlations of structural features with various spectral and biological characteristics. The known biological activity of metabolites is presented, which may aid in future studies related to the identification of new uses for fungal metabolites.

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Indole Alkaloids

3-(3-Indolyl)propane-1,2,3-triol
3-(3,3-Diindolyl)propane-1,2-diol
4-(3-Indolyl)butane-1,2,3-triol
N-Methyl-4-dimethylallyltryptophan
Lysergic Acid
Ergine; Lysergic acid amide
8-Hydroxyergine
Erginine; Isolysergic acid amide
8-Hydroxyerginine
Lysergol
Lysergene
Lysergine
Ergonovine; Ergometrine; Ergobasine
Ergonovinine; Ergometrmine; Ergobasinine
Agroclavine
6,7-seco-Agroclavine
Dihydroagroclavine
Festuclavine
Elymoclavine
Elymoclavine-O-β-fructofuranoside
Elymoclavine-O-β-fructofuranosyl-(2-1)-O-β-D-fructofuranoside
Chanoclavine-I; Chanoclavine
Isochanoclavine-I
Chanoclavine-II
N-Demethylchanoclavine-II; Norchanoclavine II
Setoclavine
Isosetoclavine
Costaclavine
Pyroclavine
Molliclavine
Pennclavine
Cycloclavine
Ergotamine
Ergotaminine
8-Hydroxyergotamine
Ergosine
Ergosinine
Ergostine
Ergostinine
Ergonine
Ergovaline
Ergoptine
Ergocornine
Ergocorninine
O-12'-Methylergoeornine
Ergocristine
Ergocristinine
Ergosecaline
Ergosecalinine
Ergobalansine
Ergobalansinine
α-Ergocryptine
O-12'-Methyl-α-ergocryptine
β-Ergocryptine
5'-epimer of β-Ergocryptine
β-Ergocryptam
β,β-Ergoannam
Ergobutine
Ergobutyrine
Rugulovasine A
8-Chlororugulovasine A
Rugulovasine B
8-Chlororugulovasine B
Fumigaclavine A; 9β-Acetoxy-6,8α-dimethylergoline
Roquefortine A; Isofumigaclavine A; 9-Acetoxy-6,8-dimethylergoline
Fumigaclavine B; 9-Hydroxy-6,8-dimethylergoline
Roquefortine B; Isofumigaclavine B; 9-Hydroxy-6,8-dimethylergoline
Fumigaclavine C; 2-Dimethylallyl-9-acetoxy-6,8-dimethylergoline
1. Indole Alkaloids

Common/Systematic Name
3-(3-Indolyl)propane-1,2,3-triol

Molecular Formula/Molecular Weight
C_{11}H_{13}NO_{3}, MW = 207.08954

![Chemical Structure]

General Characteristics
Red-violet color reaction with p-dimethylanisocinnamaldehyde.

Fungal Source
*Balansia epichloë*

Isolation/Purification
Purification was achieved by column chromatography on Porapak Q and preparative TLC on silica gel GF_{254} [TLC developing systems were chloroform-methanol (80:20, v/v) and benzene-dimethylformamide (86.5:13.5)].

Biological Activity
Toxic to fertile Leghorn chicken eggs: 23μg/egg = 80%; 68μg/egg = 100% mortality.

Spectral Data
UV:
\[ \lambda_{\text{max}}^{\text{MeOH}} = 220(\log e=4.95), 273(4.00), 280(4.02), \text{and} 289\text{nm} (3.95). \]

IR:
\((\text{KBr}) 1550, 1420, 1410, 1335, 1065, 1050, 740, \text{and} 780 \text{cm}^{-1}.\)

Mass Spectrum:
207.08, 189.07, 188.06, 186.05, 172.07, 171.06, 170.05, 160.07, 159.06, 146.05, 145.05, 144.08, 144.04, 142.06, 130.06, 118.06, 117.05, 116.05, 103.05, 91.05, 90.04, \text{and} 89.03 m/e.

Reference
Common/Systematic Name
3-(3,3-Diindolyl)propane-1,2-diol

Molecular Formula/Molecular Weight
\[ \text{C}_{19}\text{H}_{18}\text{N}_{2}\text{O}_{2}; \text{MW} = 306.13683 \]

General Characteristics
Red-violet color reaction with \( p \)-dimethylaminocinnamaldehyde.

Fungal Source
\textit{Balansia epichloë}

Isolation/Purification
Purification was achieved by column chromatography on Porapak Q and preparative TLC on silica gel GF\textsubscript{254} \[ \text{TLC developing systems were chloroform-methanol (80:20, \text{v/v}) and benzene-dimethylformamide (86.5:13.5, \text{v/v})}. \]

Biological Activity
Toxic to fertile Leghorn chicken eggs: 20\( \mu \text{g/egg} = 20\% \); 60\( \mu \text{g/egg} = 55\% \) mortality; 99\( \mu \text{g/egg} = 100\% \) mortality.

Spectral Data
UV:
\[ \lambda_{\text{max}}^{\text{MeOH}} = 221(\log \varepsilon = 4.88), 275(3.97), 282(4.01), \text{and} 291\text{nm (3.96)}. \]

IR:
(KBr) 1550, 1410, 1335, 1080, 1050, and 780cm\(^{-1}\).

Mass Spectrum:
306.1368(M\(^{+}\)), 272.1326, 270.1145, 258.1132, 257.1049, 256.0993, 245.1069, 218.0958, 217.0887, 188.0671, 171.0675, 170.06, 160.07, 159.06, 144.04, 142.06, 130.06, 118.06, 117.05, 116.05, 103.05, 91.05, 90.04, and 89.03m/z.

Reference
1. Indole Alkaloids

Common/Systematic Name
4-(3-Indolyl)butane-1,2,3-triol

Molecular Formula/Molecular Weight
C₁₂H₁₅NO₃, MW = 221.10519

General Characteristics
Red-violet color reaction with p-dimethylaminocinnamaldehyde.

Fungal Source
*Balansia epichloë*

Isolation/Purification
Purification was achieved by column chromatography on Porapak Q and preparative TLC on silica gel GF₂₅₄ [TLC developing systems were chloroform-methanol (80:20, v/v) and benzene-dimethylformamide (86.5:13.5, v/v)].

Biological Activity
Toxic to fertile Leghorn chicken eggs: 57µg/egg = 53% mortality; 113µg/egg = 100% mortality.

Spectral Data

UV:
\[ \lambda_{\text{max}}^{\text{MeOH}} = 221(\log \epsilon = 4.65), 272(3.78), 279(3.8), \text{ and } 288\text{nm (3.73).} \]

IR:
(KBr) 1550, 1410, 1340 1080, 1030, and 780cm⁻¹.

Mass Spectrum:
221.10(M⁺), 203.09, 201.08, 189.07, 188.07, 186.05, 172.07, 171.06, 170.06, 160.07, 159.06, 146.05, 145.05, 144.08, 144.04, 142.06, 130.06, 118.06, 117.05, 116.05, 103.05, 91.04, 91.05, 90.04, and 89.08m/e.

Reference
Common/Systematic Name

N-Methyl-4-dimethylallyltryptophan

Molecular Formula/Molecular Weight

C_{17}H_{22}N_{2}O_{2}; MW = 286.16813

\[
\begin{align*}
\text{Me} & \quad \text{Me} \\
\text{CO}_2\text{H} & \\
\text{NH} & \quad \text{Me} \\
\end{align*}
\]

General Characteristics

N-Methyl-4-dimethylallyltryptophan crystallized from methanol as needles; mp., 232°C.

Fungal Source

*Claviceps fusiformis*.

Isolation/Purification

*Claviceps fusiformis* was grown aerobically in submerged cultures in both shaken flasks and stirred fermenters. When alkaloid production began, anaerobic conditions were imposed and the cultures stood for three days. Clavine alkaloids were extracted with chloroform at alkaline pH and then the amphoteric metabolites extracted with *n*-butanol at neutral pH. The butanol extract, which contained considerable quantities of chanoclavines and other oxygenated clavine alkaloids, was chromatographed on silica gel with chloroform/methanol/ammonia as the eluant.

Biological Activity

All natural ergot alkaloids possess to a greater or lesser degree, biological effects that can be classified as direct peripheral effects on smooth muscle (uterine contraction and vasoconstriction), indirect peripheral effects (humoral, serotonin antagonism, and adrenergic blockage), and central nervous system effects (bulbomedullary and mesodiencephalic components).

Spectral Data

UV:

\[\lambda_{\text{max}}^\text{MeOH} = 274, 280, \text{ and } 295\text{nm}.\]
1. Indole Alkaloids

IR:
(KBr) 3580, 3250(broad) 1640, 1400, and 770cm⁻¹.

¹H NMR:
(CD₂COOD) _inter alia_ 8.64(s, 6H), 7.64(s, 3H), 5.06(t, 1H, J=-7.0Hz), and 6.3-7.0ppm (complex, 4H).

Mass Spectrum:
286, 198, 156, 155, and 154m/e. The fragmentation under electron-impact was very similar to bis-seco-dehydrocyclopiazonic acid with allylic cleavage of the amino acid side chain giving the ion of m/e 198, followed by cyclization to a series of tricyclic ions m/e 156, 155, and 154 with elimination of a C-3 unit. Cyclization of this type is only possible if the two side chains are located in the peri-position of the indole nucleus, i.e. at positions 3 and 4.

TLC Purification
Silica gel plates developed with methylene chloride-isopropyl alcohol (92:8, v/v) three times which results in the separation of alkaloids into the isolysergic acid group, the ergotoxine group, the ergoxine group and a mixture of the ergotamine and clavine groups. Extraction of the alkaloids from the silica using methanol-chloroform (1:4 or 1:1, v/v) followed by rechromatography in chloroform-methanol (9:1 or 4:1, v/v) separates ergovaline from the clavine alkaloids (agroclavine and chanoclavines).

TLC Solvent systems for silica gel chromatography (v/v):

a) Methylene chloride-isopropyl alcohol (92:8; 90:10; 75:25).
b) Chloroform-methanol (90:10; 80:20; 90:10 in saturated NH₃ atmosphere).
c) Chloroform-methanol-NH₃ (94:5:1).
d) Chloroform-ethylamine (90:10).
e) Benzene-dimethylformamide (86.5:13.5).

References


1. Indole Alkaloids

Common/Systematic Name
Lysergic acid

Molecular Formula/Molecular Weight
\( C_{16}H_{16}N_{2}O_{2}; \text{MW} = 268.12118 \)

General Characteristics
Hexagonal scales, plates from water (associated with one or two moles water); mp., 240°C (dec.); \([\alpha]_{D}^{20} +40^\circ (c=0.5, \text{in pyridine}); pK_{a} = 3.44/pK_{a} = 7.68. Moderately soluble in pyridine; sparingly soluble in water and neutral organic solvents; soluble in NaOH, \( \text{NH}_4\text{OH}, \text{Na}_2\text{CO}_3, \text{and } \text{HCl solutions}; \text{and slightly soluble in dilute } \text{H}_2\text{SO}_4. \) Methyl ester derivative, thin leaflets from benzene; mp., 168°C.

Fungal Source
Sclerotia and saprophytic culture of \textit{Claviceps purpurea}.

Biological Activity
All natural ergot alkaloids possess to a greater or lesser degree, biological effects that can be classified as direct peripheral effects on smooth muscle (uterine contraction and vasoconstriction), indirect peripheral effects (humoral, serotonin antagonism, and adrenergic blockage), and central nervous system effects (bulbomedullary and mesodiencephalic components).

Spectral Data

IR:

\(^{13}\text{C NMR:}\)
\((\text{CDCl}_3)\) (methyl lysergate) C-2, 118.2; C-3, 110.2; C-4, 26.9; C-5, 62.6; C-7, 54.6; C-8, 41.8; C-9, 117.6; C-10, 136.0; C-11, 127.6; C-12, 112.0; C-13, 122.9; C-14, 109.4; C-15, 133.7; C-16, 125.9; C-17, 172.4; Me, 51.9; and NMe, 43.4 ppm.
1. Indole Alkaloids

Mass Spectrum:
LREIMS: 268(M⁺, 100%), 224, 221, 207, 192, 180, 167, and 154m/e.

References

B. Berde and H. O. Scheld (eds.); Ergot Alkaloids and Related Compounds; In Handbook of Experimental Pharmacology; Springer-Verlag, New York (1978).

A. Hofmann; Die Mutterkorn Alkaloide; Enke Verlag, Stuttgart, 218 pp., 1964.
Common/Systematic Name
Ergine; Lysergic acid amide

Molecular Formula/Molecular Weight
C_{16}H_{17}N_{3}O; \text{MW} = 267.13716

\[
\begin{align*}
\text{O} & \\
\text{H}_2\text{N} & \text{C} \\
& \text{Me} \\
\end{align*}
\]

General Characteristics
Crystallized from acetone as massive colorless prisms; m.p. 196°C; \([\alpha]_D^{20} + 414^\circ\), \([\alpha]_{546}^{20} + 520^\circ\) (c=1.0, in CHCl$_3$); pK = 6.2 (in 80% methylcellosolve); blue color with Keller's reagent.

Fungal Source
Ergot of Claviceps purpurea and Paspalum distichum L. (also isolated from seeds of Rivea corymbosa (L.) and Ipomoea tricolor, Convolvulaceae).

Biological Activity
The ergopeptine alkaloids produce a wide range of biological activities and some are used routinely in medical practice. All natural ergot alkaloids possess to a greater or lesser degree, biological effects that can be classified as direct peripheral effects on smooth muscle (uterine contraction and vasoconstriction), indirect peripheral effects (humoral, serotonin antagonism, and adrenergic blockage), and central nervous system effects (bulbomedullary and mesodiencephalic components). Some ergopeptine alkaloids are used routinely in medical practice. Central American Indians used seeds of Rivea corymbosa and Ipomoea tricolor as a magic drug called "Ololiuqui".

Spectral Data

IR:

UV:
UV spectrum identical to that of lysergic acid or isolysergic acid.
Mass Spectrum:
LREIMS: 267(M⁺, 100%), 249, 224, 221, 207, 192, 180, 167, and 154 m/e.

**TLC Purification**
Silica gel plates developed with methylene chloride-isopropyl alcohol (92:8, v/v) three times which results in the separation of alkaloids into the isolysergic acid group, the ergotoxine group, the ergoxine group and a mixture of the ergotamine and clavine groups. Extraction of the alkaloids from the silica using methanol-chloroform (1:4 or 1:1, v/v) followed by rechromatography in chloroform-methanol (9:1 or 4:1, v/v) separates ergovaline from the clavine alkaloids (agroclavine and chanoclavines).

**TLC Solvent systems for silica gel chromatography (v/v):**

a) Methylene chloride-isopropyl alcohol (92:8; 90:10; 75:25).
b) Chloroform-methanol (90:10; 80:20; 90:10 in saturated NH₃ atmosphere).
c) Chloroform-methanol-NH₃ (94:5:1).
d) Chloroform-ethylamine (90:10).
e) Benzene-dimethylformamide (86.5:13.5).

**HPLC Data**
Extract with alkaline methanol, filter, followed by direct HPLC analysis with fluorescence detection; mobile phase, either 60% or 70% alkaline methanol. This technique works well for ergopeptide alkaloids.

**References**

A. Hofmann; Die Mutterkorn Alkaloid; Enke Verlag, Stuttgart, 218 pp., 1964.
Common/Systematic Name
8-Hydroxyergine

Molecular Formula/Molecular Weight
C_{16}H_{17}N_{3}O_{2}; MW = 283.13208

\[\text{Structure Image}\]

Fungal Source
*Claviceps paspali* (strain MG-6).

Isolation/Purification
The strain *C. paspali* MG-6 was isolated from the grass *Paspalum dilatatum* in the vicinity of Rome. Alkaloids were separated by adsorption on bentonite (Flieger et al., 1989b). A crude alkaloid mixture was chromatographed on Kieselgel 60 F_{254}, Merck preparative TLC plates and eluted with chloroform-isopropyl alcohol-ammonia (90:10:0.036, v/v/v); Rf values of 8-hydroxyergine and 8-hydroxyerginine were 0.50 and 0.91, respectively. Prepurified alkaloids were chromatographed on a Separon SGX C_{18} column (Tessek, Czechoslovakia) particle size 7μm. The mobile phase consisted of (A) MeOH-H_{2}O-NH_{3} (90:10:0.036, v/v/v) and (B) MeOH-H_{2}O-NH_{3} (20:80:0.036, v/v/v). The column was equilibrated with 4% A in B and subsequently eluted with a linear gradient up to 54% A in B.

Biological Activity
The ergopeptine alkaloids produce a wide range of biological activities and some are used routinely in medical practice. All natural ergot alkaloids possess to a greater or lesser degree, biological effects that can be classified as direct peripheral effects on smooth muscle (uterine contraction and vasoconstriction), indirect peripheral effects (humoral, serotonin antagonism, and adrenergic blockage), and central nervous system effects (bulbomedullary and mesodiencephalic components). The ergopeptine alkaloids produce a wide range of biological activities and some are used routinely in medicine.
1. Indole Alkaloids

Spectral Data

$^1$H NMR: 
(CD$_3$OD) H-2, 6.984(J$_{2,4a}$=1.8Hz); H-4a, 2.749; H-4b, 3.569(J$_{4a,4b}$=14.5Hz); H-5, 3.265(J$_{4a,5}$=11.8Hz, J$_{4b,5}$=5.9Hz); H-7a, 2.936(J$_{7a,7b}$=11.7Hz, J$_{7a,8}$=1.0Hz); H-7b, 2.965; H-9, 6.358(J$_{9a,9}$=0, J$_{5,9}$=2.1Hz); H-12, 7.193(J$_{12,13}$=7.4Hz, J$_{12,14}$=0.7Hz); H-13, 7.107(J$_{13,14}$=7.9Hz); H14, 7.231; and N-Me, 2.590ppm.

$^{13}$C NMR: 
(CD$_3$OD) C-2, 120.66; C-3, 110.52; C-4, 27.15; C-5, 64.20; C-6, 62.71; C-7, 73.84; C-8, 121.00; C-9, 139.91; C-10, 128.13; C-11, 113.43; C-12, 123.93; C-13, 111.95; C-14, 136.02; C-15, 128.13; C-16, 177.92, and N-Me, 43.75ppm.

Mass Spectrum: 
EIMS: 283(M$^+$, C$_{16}$H$_{17}$N$_3$O$_2$, 61%), 266(C$_{16}$H$_{16}$N$_3$O, 27), 265(C$_{16}$H$_{15}$N$_3$O, 37), 248(C$_{16}$H$_{15}$N$_2$O, 59), 240(C$_{14}$H$_{12}$N$_2$O$_2$, 86), 223(C$_{14}$H$_{12}$N$_2$O$_2$, 86), 221(C$_{13}$H$_{13}$N$_2$, 42), 206(C$_{14}$H$_{10}$N$_2$, 19), 195(C$_{13}$H$_{9}$NO, 36), 194(C$_{13}$H$_{8}$NO, 32), 181(C$_{13}$H$_{11}$N, 26), 180(C$_{13}$H$_{10}$N, 26), 167(C$_{12}$H$_6$N, 83), and 154(C$_{11}$H$_4$N, 100).

TLC Purification
Silica gel plates developed with methylene chloride-isopropyl alcohol (92:8, v/v) three times which results in the separation of alkaloids into the isolysergic acid group, the ergotoxine group, the ergoxine group and a mixture of the ergotamine and clavine groups. Extraction of the alkaloids from the silica using methanol-chloroform (1:4 or 1:1, v/v) followed by rechromatography in chloroform-methanol (9:1 or 4:1, v/v) separates ergovaline from the clavine alkaloids (agroclavine and chanoclavines).

TLC Solvent systems for silica gel chromatography (v/v):
- b) Chloroform-methanol (90:10; 80:20; 90:10 in saturated NH$_3$ atmosphere).
- c) Chloroform-methanol-NH$_3$ (94:5:1).
- d) Chloroform-ethylamine (90:10).
- e) Benzene-dimethylformamide (86.5:13.5).

References

Common/Systematic Name
Erginine; Isolysergic acid amide

Molecular Formula/Molecular Weight
C_{16}H_{17}N_{3}O; MW = 267.13716

\[
\begin{array}{c}
\text{O} \\
\text{H}_{2}\text{N-} \\
\text{C} \\
\text{N-Me} \\
\end{array}
\]

General Characteristics
Crystallized from methanol as solvated prisms; mp., 132-134°C; [\alpha]_D^{20} + 480°, [\alpha]_54612^{20} + 608° (c=0.5, in pyridine); pK=6.1 (in 80% methylcellosolve).

Fungal Source
Ergot and saprophytic culture of *Claviceps purpurea*. Epimers are not considered as naturally occurring, but as products formed during extraction and purification; epimerization at C-8 occurs in either acid or base.

Biological Activity
The ergopeptine alkaloids produce a wide range of biological activities and some are used routinely in medical practice. All natural ergot alkaloids possess to a greater or lesser degree, biological effects that can be classified as direct peripheral effects on smooth muscle (uterine contraction and vasoconstriction), indirect peripheral effects (humoral, serotonin antagonism, and adrenergic blockage), and central nervous system effects (bulbomedullary and mesodiencephalic components). Some ergopeptine alkaloids are used routinely in medical practice. Central American Indians used seeds of *Rivea corymbosa* and *Ipomoea tricolor* as a magic drug called "Ololiuqui".

Spectral Data
IR:
1. Indole Alkaloids

**TLC Purification**

Silica gel plates developed with methylene chloride-isopropyl alcohol (92:8, v/v) three times which results in the separation of alkaloids into the isolysergic acid group, the ergotoxine group, the ergoxine group and a mixture of the ergotamine and clavine groups. Extraction of the alkaloids from the silica using methanol-chloroform (1:4 or 1:1, v/v) followed by rechromatography in chloroform-methanol (9:1 or 4:1, v/v) separates ergovaline from the clavine alkaloids (agroclavine and chanoclavines).

**TLC Solvent systems for silica gel chromatography (v/v):**

a) Methylene chloride-isopropyl alcohol (92:8; 90:10; 75:25).

b) Chloroform-methanol (90:10; 80:20; 90:10 in saturated NH₃ atmosphere).

c) Chloroform-methanol-NH₃ (94:5:1).

d) Chloroform-ethylamine (90:10).

e) Benzene-dimethylformamide (86.5:13.5).

**HPLC Data**

Extract with alkaline methanol, filter, followed by direct HPLC analysis with fluorescence detection; mobile phase, either 60% or 70% alkaline methanol. This technique works well for ergopeptide alkaloids.

**References**

B. Berde and H. O. Scheld (eds.); Ergot Alkaloids and Related Compounds; In Handbook of Experimental Pharmacology; Springer-Verlag, New York (1978).

A. Hofmann; Die Mutterkorn Alkaloide; Enke Verlag, Stuttgart, 218 pp., 1964.

1. Indole Alkaloids

Common/Systematic Name
8-Hydroxyerginine

Molecular Formula/Molecular Weight
C₁₆H₁₇N₃O₂; MW = 283.13208

Fungal Source
Claviceps paspali MG-6.
Epimers are not considered as naturally occurring but as products formed during extraction and purification; epimerization at C-8 occurs in either acid or base.

Isolation/Purification
The strain C. paspali MG-6 was isolated from the grass Paspalum dilatatum in the vicinity of Rome. Alkaloids were separated by adsorption on bentonite (Flieger et al., 1989b). A crude alkaloid mixture was chromatographed on Kieselgel 60 F₂₅₄, Merck preparative TLC plates, and eluted with chloroform-isopropyl alcohol-ammonia (90:10:0.036, v/v/v); Rf values of 8-hydroxyergine and 8-hydroxyerginine were 0.50 and 0.91, respectively. Prepurified alkaloids were chromatographed on a Separon SGX C₁₈ column (Tessek, Czechoslovakia) of particle size 7μ. The mobile phase consisted of (A) MeOH-H₂O-NH₃ (90:10:0.036, v/v/v) and (B) MeOH-H₂O-NH₃ (20:80:0.036, v/v/v). The column was equilibrated with 4% A in B and subsequently eluted with a linear gradient up to 54% A in B.

Spectral Data
¹H NMR:
(CD₃OD) H-2, 6.974(J₂-₄a=1.6Hz); H-4a, 2.649; H-4b, 3.606(J₂₄b=<>0, J₄₄b₉=-14.6Hz); H-5, 3.150(J₄₄₅=11.5Hz, J₄₅₉=5.9Hz); H-7a, 3.080(J₇₈₉=-11.3Hz, J₇₉₉=1.5Hz); H-7b, 2.626; H-9, 6.268(J₉₉₉=0.8Hz, J₉₉=2.2Hz); H-12, 7.118(J₁₂₁₃=7.0Hz, J₁₂₁₄=1.7Hz); H-13, 7.090(J₃₄₁₄=7.2Hz); H-14, 7.219ppm; and N-Me, 2.614ppm.
\[ ^{13}\text{C} \text{ NMR:} \]

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\begin{align*}
& (\text{CD}_3\text{OD}) \text{ C-2, 120.53; C-3, 110.55; C-4, 28.27; C-5, 64.11; C-6, 63.06; C-7, 71.87; C-8, 124.30; C-9, 139.13; C-10, 128.04; C-11, 113.15; C-12, 123.96; C-13, 111.72; C-14, 135.95; C-15, 127.99; C-16, 179.59; \text{and N-Me, 43.39ppm.}
\end{align*}
\]

\[ \text{Mass Spectrum:} \]

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\begin{align*}
& \text{EIMS: } 283(M^+, \text{C}_{16}\text{H}_{17}\text{N}_3\text{O}_2, \text{100}), 266(\text{C}_{16}\text{H}_{16}\text{N}_3\text{O}, \text{14}), 265(\text{C}_{16}\text{H}_{15}\text{N}_3\text{O}, \text{29}), 248(\text{C}_{16}\text{H}_{12}\text{N}_2\text{O}_2, \text{35}), 240(\text{C}_{16}\text{H}_{12}\text{N}_2\text{O}_2, \text{31}), 223(\text{C}_{16}\text{H}_{12}\text{N}_2\text{O}_2, \text{31}), 221(\text{C}_{15}\text{H}_{13}\text{N}_2, \text{42}), 206(\text{C}_{14}\text{H}_{10}\text{N}_2, \text{12}), 195(\text{C}_{13}\text{H}_9\text{N}, \text{60}), 194(\text{C}_{13}\text{H}_9\text{N}, \text{61}), 181(\text{C}_{13}\text{H}_11\text{N}, \text{50}), 180(\text{C}_{13}\text{H}_10\text{N}, \text{20}), 167(\text{C}_{12}\text{H}_9\text{N}, \text{94}), \text{and } 154(\text{C}_{11}\text{H}_9\text{N}, \text{96%}).
\end{align*}
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**Reference**