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NEOLIGNANS AND ALKALOIDS FROM LICARIA ARMINIACA (NEES) KOSTERM

PART: 1

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ABSTRACT

Two neolignans 3a-allyl-5-methoxy and dimethoxy-2-(3,4-methylenedioxy phenyl)-3-methyl-2,3,3a,4,5,6-hexahydro-6-oxobenzofurans and four minor alkaloids (bracteoline, o-methyl bracteoline, α-dehydroreticuline and unknown alkaloid) have been isolated from the wood stem and stem bark of Licaria arminiaca F. Lauraceae. These alkaloids although known were isolated for the first time from the genus Licaria. The structures of three of them were deduced from spectral and chemical evidence.

INTRODUCTION

Licaria arminiaca (Nees) kosterm is one of the most widely distributed lauraceous plant. It is a tree which grows in the Amazon region[1]. A previous study of the trunk wood of the plant revealed the presence of sitosterol, two poroson -

type neolignans (For nomenclature see Pages, 3 &4), 7-dimethoxycoumarin, magnolin and 7-oxoaporphine(tri-O-methylmoschatoline)[1,2].

The other licaria species were the subject of interest for many researchers. Gottlieb et al[3] stated that the wood of Licaria species contains eusiderin and aurin-neolignans. Silva and Maia[4] isolated safrol, sitosterol, eugenol, 3,4-methylenedioxy alcohol, and syringic aldhyde from the trunk wood of Licaria Puchury-Major. Aiba et al[5] reported the presence of Licaria-A and Licaria-B in the wood of Licaria aritu. Giesbrecht et al[6] isolated canellin-A, canellin-B, canellin-C, dillapiol, elemicin and sitosterol from the trunk wood of Licaria canella. Braz Fo et al[7] examined the trunk wood of Licaria rigida and isolated the neolignan, eusiderin-B, canellin-A, canellin-C. and sitosterol.

From the above, it is clear that little was reported about the neolignans, while one alkaloid only was isolated from the trunk wood of the titled plant. Therefore, the following work deals with the isolation and identification of the neolignans and alkaloids of Licaria arminiaca.

EXPERIMENTAL

Material:

The plant material used in this work consists of dried stem wood and stem bark of Licaria arminiaca (Lauraceae) obtained from US Dept. of Agriculture, NA ✱2158, South America, where it is identified.

Extraction:

Air dried powdered plant material (16 kg) was exhaustively extracted with ethanol (40 liters) at room temperature. The solvent from the percolate was removed under reduced pressure below 40° to give a viscous mass (320 g) which was extracted with 1% hydrochloric acid. The aqueous acidic solution was extracted with ether (5 x 300 ml) (F_1, 10.816 g) and then basified with aqueous NH_4OH to pH_9. The liberated bases were extracted with ethyl acetate (F_2, 9.169 g). The remaining aqueous alkaline solution gave positive test for alkaloids (F_3).

Chromatography of Ether Extract (F_1):

The concentrated ether extract (10.816 g) was chromatographed on silicic acid. The column (60 cm x 3 cm) was successively eluted with pet. ether, pet. ether-chloroform (1:1), chloroform and chloroform-methanol with an increasing proportions of methanol. Elution was monitored by TLC. A total of 5 fractions, 500 ml each collected (E_1 - E_5).

Fraction (E_3): (elution with pet. ether-chloroform, 4:1)gave a crude compound which was subjected to preparative TLC (plate: Silica gel G, solvent: chloroform-methanol 9:1). The major band was removed and extracted with chloroform. Removal of the solvent furnished compound I (700 mg), viscous oil, R_f 0.5 (TLC, Silica gel G, chloroform-methanol-NH_4OH, 97:3:2 drops). $\{\alpha\}_D^{25}$ (Methanol) + 90. λ_{max} (MeOH, nm) 218, 252 and 285, not changed in methanolic KOH.

IR_{max} (K Br, cm^{-1}): 1665,1635, 1510, 1495, 1450, 1235 and 1185.

Neolignans and alkaloids from Licaria arminiaca (Ness) Kosterm Part: 1

NMR (60 MHz, $CDCl_3$, PPM) 6.8 (br.S, 3 Ar.H.), 5.96 (S,O_2CH_2), 5.5-5.7 (m,CH=) 5.4 (S,H-7), 5.2(d, J=2Hz, H-2), 5.1 (m,CH_2=), 4.0 (dd, J=5,12 Hz, H-5), 3.6 (S, OMe-5), 2.2(d, J=8Hz,Me-3) and 2.6 (m, H-3).

The mass spectrum shows peaks at m/e 342.04 (M^+), 162 $(Pi\ CH\ CHMe)^+$ and 149 $(Pico)^+$.

This compound was found identical (U.V, I.R, NMR and MS) to that reported for the benzofuranoid neolignan: (3-a-allyl-5-methoxy-2-(3,4-methylenedioxyphenyl)-3-methyl-2,3,3a,4,5,6-hexahydro-6-oxobenzofuran(Fig. 1)[1] .

Fraction (E_4): (elution with chloroform) gave a crude compound which was applied to preparative TLC analysis: Silica gel G; Solvent: chloroform-methanol, 9:1). The major band, when removed and extracted with chloroform, gave compound II (44 mg), chromatographically pure viscous oil, R_f 0.43(TLC, Silica gel G, solvent: chloroform-methanol-NH_4OH, 97:3:2

λ_{max} (MeOH, nm) 211, 239 and 275. ν_{max} (KBr, cm^{-1}):1670, 1630, 1500, 1490, 1440, 1240 and 1200. NMR shows an additional OMe, singlet at δ 3.8 instead of the H-7 signal at 5.6 in the spectrum of compound I. The mass spectrum shows peaks at m/e 372 (M^+), 162 $(PIÇH.CHMe)^+$ and 149 $(Pico)^+$.

The compound remained unchanged on treatment with AC_2O/ pyridine.

The physical constants, chemical properties and spectroscopic data of the separated compound were identical with reported data for the benzofuranoid neolignan:3a-allyl-5-7-dimethoxy-2-(3,4-methylenedioxyphenyl)-3-methyl-2,3,3a,4,5,6-

hexahydro-6-oxobenzofuran(Fig. 1)[1] .

Chromatography of Ethyl Acetate Extract (F_2):

The ethyl acetate alkaloid mixture (F_2, 9.169 g) was fractionated over silica gel. The column (60 cm x3 cm) was successively eluted with petroleum ether, pet. ether-chloroform(1:2) , chloroform and chloroform-methanol with an increasing proportions of methanol. The effluent was collected in fractions each 300 ml. A total of 26 fractions were collected (A $\longrightarrow$ z).

Fraction K: Fraction eluted with chloroform-methanol(84:16) were mixed and the solvent removed. The residue was crystallised from methanol-ethyl acetate to afford a white powder (40.2 mg). R_f 0.41 (TLC, silica gel G, chlorofor-methanol-NH_4OH, 90:10:2 drops) m.p. 213-15°C. $[\alpha]_D^{25}$ = + 35(MeOH) .

λ_{max} (MeOH, nm) 222, 280, 304 and 313, changed in methanolic KOH.

ν_{max} 1080, 1110, 1250, 1280, 1315, 1335, 1415, 1515,1585, 1608 and 3300-3500 cm^{-1}.

The NMR spectrum of the base integrated for 24 protons. A signal at δ 2.5 (S, 3H) was assigned to one N-methyl group. The signal for two aromatic methoxyl groups was at 3.8 (S, 6H). In the aromatic region there were three protons; a singlet at 6.58 was assigned to C-3 proton. A singlet at 6.85 was due to the proton at C-8. The characteristic low field signal for the C-11 proton appeared as a singlet at 8.1.

Neolignans and alkaloids from Licaria arminiaca (Ness) kosterm Part: 1

In the mass spectrum of the base the molecular ion peak appeared at m/e 327 (M^+), other significant peaks in the mass spectrum were at m/e 326 (M^+-1), 312 (M^+-15), 296 (M^+-31), 284 (M^+-43). The mass fragmentation pattern of the base was that of aporphine alkaloid type[8].

The base gave a monoacetate (M^+-368) and diacetate(M^+411) on treatment with AC_2O/pyridine indicate the presence of two hydroxyl groups.

The physical, chemical and spectroscopic properties of the base were very close to that of Bracteoline[9,10](Fig. 1).

Fraction H: elution with chloroform-methanol, 90% 10) gave a crude base (254.4 mg) which was subjected to preparative TLC (plate: silica gel-G; solvent: chloroform-methanol, 10%). The major band was removed and extracted with methanol to give the pure base (52 mg). R_f0.56 (silica gel G; chloroform-methanol, 10%).

λ_{max}(MeOH, nm) 227, 280 and 315, changed in methanolic KOH.

ν_{max} 1110, 1230, 1280, 1320, 1370, 1420, 1460, 1515,1608 and 3300-3500 cm^{-1}.

The IR spectrum of the base in conjunction with its UV spectrum suggested the presence of an aporphine system in the molecule.

The NMR (60 mHz, $CDCl_3$) showed the presence of three aromatic methoxyl groups at δ 3.62 , 3.75 and 3.86 and an N-methyl group at 2.5. The aromatic protons appear at δ 6.33 (S,C_3 -H), 6.80 (S,C_8-H) and 8.03 (S,C_{11}-H).

In the mass spectrum of the base, the molecular ion peak appeared at m/e 341(M^+). Other significant peaks in the spectrum were at m/e 340 (M^+-1), 326 (M^+-15), 310 (M^+-31) and 281 (M^+-60).

The mass fragmentation pattern of the base was that of aporphine type alkaloid[8]. The base gave the monoacetate(M^+: 382) on treatment with AC_2O/pyridine to indicate the presence of one hydroxyl group.

The structure 3-(O-methylbracteoline), (Fig. 1), for the base emerged from the data given above.

Fraction M: Fractions eluted with chloroform-methanol(80:20) were mixed and the solvent was removed. The residue (937.7 mg) was transferred to a SiO_2 column (50 g). Elution with chloroform-methanol (80:20) yielded a pure base(40 mg). R_f 0.41 (plate: SiO_2, solvent: chloroform-methanol-NH_4OH, 50: 15:5 drops).

λ_{max} (MeOH) nm, 227 and 283 (changed in methanolic KOH indicating the presence of phenolic hydroxyl groups). ν_{max} (KBr); 1020, 1130, 1280, 1440, 1515, 1660 and 3300-3500 cm^{-1}

The NMR (60 mHz, $CDCl_3$) showed the presence of two aromatic methoxyl groups at 3.85 (S, 6H). The aromatic protons appear at δ 6.65 (S,C_5-H), 6.2 (S, H-8), 7.3 (S,H-10), 7.0 (d, J=8.5 Hz, H-13) and 6.75 (d, J=8.5 Hz, H-14), A signal at δ 2.8 (S, 3H) was assigned to one N-methyl group.

In the mass spectrum of the isolated compound, the molecular ion peak appeared at m/e 327 (M^+). Other significant peaks in the spectrum were at m/e 312 (M^+ -15), 297

(M^+-30), 162 (2.6%), 149(11.17%), 148 (14.67), 137 (8.13%), 91 (8.7%) and 77 (7.58%).

The fragmentation pattern of the base was that of benzylisoquinoline type alkaloid[11].

From the spectral data (IR, UV, NMR and MS) given above, the possible structure is ∝-dehydroreticuline (Fig. 1).

Fraction C: The fractions which eluted from chloroform-methanol, 70:22, were mixed and the solvent ramoved to give a mixture (590.1 mg).

The concentrated extract was chromatographed on a column (1 cm x 30 cm), silica gel (30 g), elution with chloroform-methanol (78:22) gave a crude product (50 mg) that was subjected to preparative TLC (plate: SiO_2, solvent: chloroform-methanol, 45:5), the major band on the plates was scraped, extracted with methanol and the slovent removed to give the pure base (30 gm).

The isolated compound exhibited the following data: R_f0.58 (plate: SiO_2, solvent: chloroform-methanol (45:5).

λ_{max}(MeOH) nm 227 and 280 (changed in methanolic KOH) indicating the presence of phenolic hydroxyl group (s).

ν_{max}(KBr): 1050, 1100, 1250, 1290, 1450, 1610, 2970 and 3300-3500 cm^{-1}.

The NMR spectrum (60Hz, $CDCl_3$) shows the presence of two aromatic methoxyl groups at δ 3.9 (S, 6H), and aromatic protons appear at δ 6.6 (S, 1H), 6.85 (d, J=8.5 Hz, 1H). 5.6 (S, 1H), and 7.15 (d, J=8.5 Hz, 1H).

In the mass spectrum, the characteristic peaks were at 178 (100%), 163 (27.92%), 148 (2.05%). 134 (467%), 107 (16.33%), 91 (5.05%) and 71 (11. 99%).

The fragmentation pattern of the base was that of benzylisoquinoline type alkaloid[11].

The data indicate that the isolated alkaloid does not coincide with or come near to any alkaloid previously reported from this type. Owing to the limited quantity of the alkaloid, it was not possible to proceed further towards determination of its structure.

CONCLUSION

The study of the alcohol extract of wood stem and stem bark of Licaria arminiaca (Ness) kosterm revealed the presence of neolignans and alkaloids. Chromatographing the ether extract over silicic acid column followed by praparative TLC succeeded in the isolation of two neolignans . By physical, chemical and spectral analysis the structures of the isolated neolignans were proved to be:

1) 3a-allyl-5-methoxy-2-(3',4'-methylenedioxyphenyl)-3-methyl-2,3,3a,4,5,6-hexahydro-6-oxobenzofuran (Fig. 1).

2) 3a-allyl-5,7-dimethoxy-2-(3',4'-methylenedioxyphenyl)-3-methyl-2,3,3a,4,5,6-hexahydro-6-oxobenzofuran (Fig. 1).

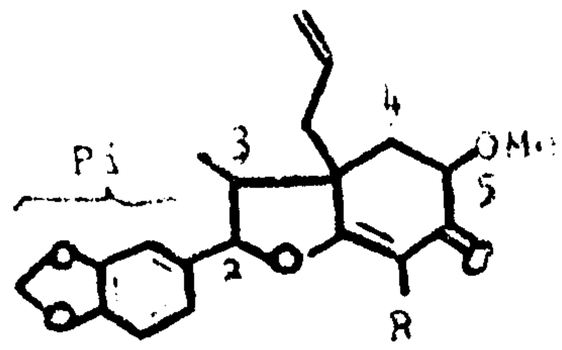
Fractionation of ethyl acetate extract yielded four alkaloids.

ALKALOIDS (1) and (2): Aprophine type alkaloids, their structures were established by physical, chemical and spectral methods (UV., IR, NMR and MS) and proved to be Bracteoline and O-methylbracteoline.

ALKALOID (3): Benzylisoquinoline alkaloid. From UV.,IR, NMR and MS its possible structure was proved to be α-dehydroreticuline.

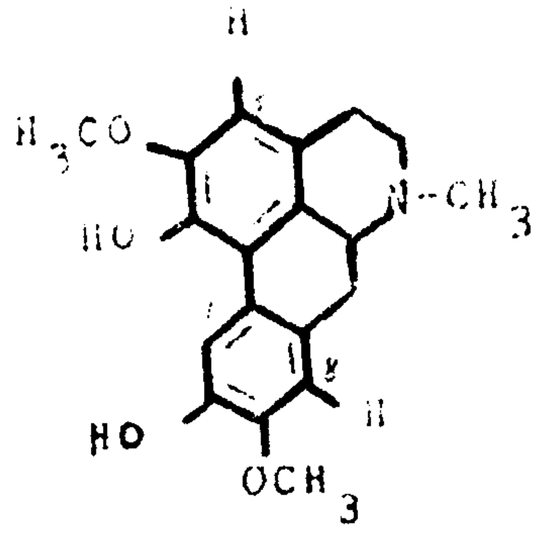
According to the available literature the three alkaloids are reported for the first time in genus Licaria,

ALKALOID (4): Available in minute quantity , its spectroscopic data are given, it is benzylisoquinoline alkaloid containing phenolic hydroxyl group (s) and two aromatic methoxyl groups.



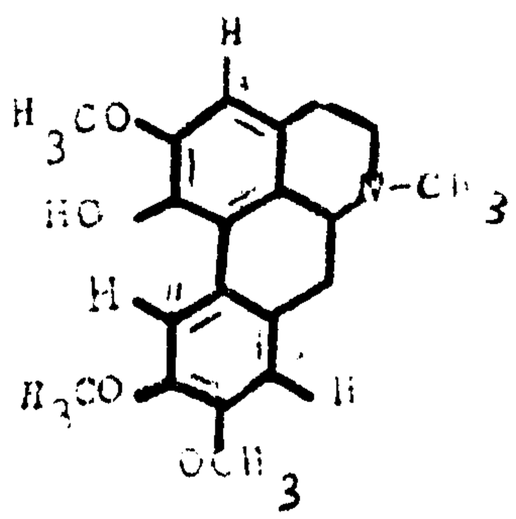
Neolignan I R=H
Neolignan II R=OMe
Pi=Pipronyl group.

(1)



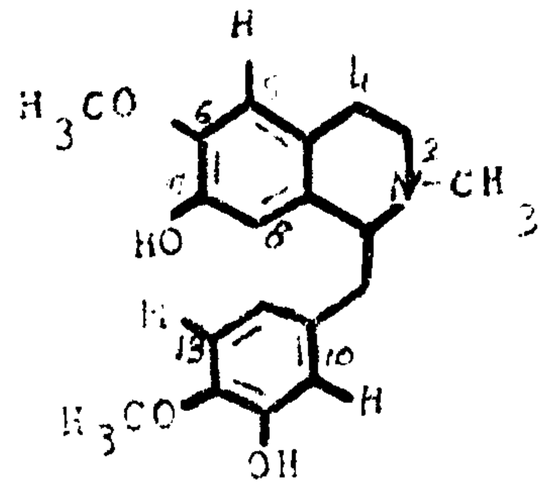
Bracteoline

(2)



O-methylbracteoline

(3)



α-dehydroreticuline

(4)

Fig.1

Neolignans and alkaloids from Licaria arminiaca (Ness)kosterm
Part: 1

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مركبات النيوليقنان و القلويدات الموجودة فى نبات الليكاريا أرمنياكا (نييس) كوسترم

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بدراسة الخلاصة الكحولية لسيقان وقلف سيقان نبات الليكاريا أرمنياكا أمكن فصل مادتين نيوليقنان وبدراسة خواصهما الطبيعية والكيميائية والتحليل الالى لهما امكن التعرف عليهما.

كما امكن فصل اربعة قلويدات موجودة بكميات ضئيلة وبدراسة خواصهم الطبيعية والكيميائية والتحليل الالى لهم تبين ان القلويد الاول والثانى يتبع مجموعة الابورفين بينما القلويد الثالث والرابع يتبع مجموعة البنزيل أيزوكينولين . وقد أمكن التعرف على التركيب الكيميائى لثلاثة منهم ولم يمكن التعرف على القلويد الرابع لقلة الكمية المفصولة منه وهذه القلويدات الاربعة قد تم فصلها لاول مرة من جنس النبات.

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