Tetrahedron Letters No. 14, pp 1201 - 1204, 1975. Pergamon Press. Printed in Great Britain.

LAURIFONINE, LAURIFINE AND LAURIFININE, THREE NEW DIBENZ(d,f)AZONINE ALKALOIDS FROM COCCULUS LAURIFOLIA DC*

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(Received in UK 14 February 1975; accepted for publication 26 February 1975)

In the course of our continuing chemical study of plants with biological activity we have isolated three new dibenz(d,f)azonine alkaloids, laurifonine (1), laurifine (2) and laurifinine (13) from the leaves of Cocculus laurifolia DC[1-4].

Laurifonine (1) $C_{20}H_{25}O_3N$ (M^+ 327), $(\alpha)_D \pm 0^\circ$ (EtOH), perchlorate, mp 182-85° (MeOH-ether); ν_{max}^{KBr} 2900, 1600, 1240, 1030 cm^{-1}; λ_{max}^{MeOH} 221 and 283 nm (logε, 4.30 and 3.90); ms m/e 327 (M^+, base peak), 312 (M-15), 270 (M-57), 256 (M-71), 255 (M-72), 227 (M-100), 226 (M-101) and 163.5 (M^{++}). Its nmr spectrum ($CDCl_3$) had signals at τ 7.68 (NCH_3), 6.10 (OCH_3), 6.20 (OCH_3), 6.24 (OCH_3), 7.30-7.50 (8 H). Of the 5 protons in the aromatic region 2 para oriented protons were at τ 3.28 and 3.22 respectively. The remaining 2 ortho and 1 meta coupled protons giving an ABC pattern, appeared between τ 2.83-3.20 (J_{AB}, AC and BC = 0.2, 2.5 and 9.5 Hz).

I when subjected to Zn dust distillation yielded 7, R=H, mp 132-33° (C_6H_6-hexane), ν_{max}^{KBr} 1606, 1600, 1540, 1230 and 1040 cm^{-1}; ms m/e 268 (M^+), 267 (M-1), 253 (M-15), 225 (M-43), 195 (M-73), 182 (M-86). The structure 7, R=H, of the phenanthrene derivative was confirmed by its synthesis. Decarboxylation of 2,3,6-trimethoxyphenanthrene-9-carboxylic acid (7, R=COOH)[6] with quinoline - Cu powder yielded 7, R=H.

Treatment of 1 with CH_3I gave the corresponding methiodide, which on Hofmann degradation afforded 3 and 4. Second Hofman elimination of 3 and 4 afforded 5. Cleavage of 5 with OsO_4-$NaIO_4$ gave 6 mp 150-51° (MeOH), ν_{max}^{KBr} 1689 (CHO) cm^{-1}, λ_{max}^{MeOH} 227 and 281 nm; ms m/e 300 (M^+), 271 (M-29, base peak), 246 (M-54), 232 (M-68), 220 (M-80), 206 (M-94). The structure 6 for the aldehyde was confirmed by its synthesis from 7, R=H. Treatment of 7, R=H, with OsO_4

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*CDRI Communication No.1995

gave the diol which was cleaved with $NaIO_4$ to yield 6.

Laurifine (2), $C_{19}H_{23}O_3N$ (M^+ 313), $(\alpha)_D \pm 0$ (EtOH) was obtained as an amorphous base; ν^{KBr}_{max} 3450 indicated the presence of NH function. Its UV spectrum had λ^{MeOH}_{max} 221 and 284 ($\log\epsilon$ 4.34 and 3.96) and remained unchanged in base. In its nmr ($CDCl_3$) spectrum, there was no signal for N-methyl group. However, 3 OMe signals were at τ 6.06, 6.10 and 6.18, and 8 methylene protons were between τ 6.80 to 7.70. Of the 5 aromatic protons, 2 *para* coupled protons were at τ 3.28 and 3.30 respectively. The remaining 3 protons were between τ 2.84 to 3.28. In its mass spectrum the ions were m/e 313 (M^+, base peak), 298 (M-15), 270 (M-43), 255 (M-58), 239 (M-74) and 156.5 (M^{++}).

Treatment of 2 with HCHO-$NaBH_4$ gave N-methyl derivative which was found identical with 1 in terms of the Rf value, uv, ir, nmr and mass.

Laurifinine (13), $C_{19}H_{23}O_3N$ (M^+ 313), $(\alpha)_D \pm 0$ (EtOH); perchlorate mp 243-45°, had ν^{KBr}_{max} 3400 (OH), 1610, 1500, 1450 (aromatic ring) cm^{-1}; λ^{MeOH}_{max} 223 and 284 ($\log\epsilon$ 4.24 and 3.84) nm. In its nmr ($CDCl_3$) spectrum 1 N-methyl and 2 O-methyl groups were at τ 7.68, 6.18 and 6.20 respectively. Of the 8 methylene protons 2 protons multiplet was centred at τ 6.75 and the remaining 6 protons were at about τ 7.42. A broad signal at τ 5.18, which disappeared on D_2O shake, was due to OH. In the aromatic region 2 *para* coupled protons were at τ 3.24 and 3.34 respectively and 2 *meta* and 1 *para* coupled protons were between τ 2.76 to 3.26. In its mass spectrum the ion were m/e 313 (M^+, base peak), 255 (M-58), 256 (M-59), 298 (M-15), 270 (M-43), 225 (M-88), 195 (M-118) and 156.5 (M^{++}).

Treatment of 13 with ethereal CH_2N_2 furnished the O-methyl derivative which was found identical with 1 in terms of tlc, Rf value, uv, ir, nmr and mass. The presence of hydroxyl group in ring C in 13 was located by base catalysed deuterium exchange[5]. In the mass spectrum of the deuterated laurifinine the molecular ion was at m/e 314 and the other ions were at m/e 299, 271, 259 and 258. The position of OH group at C_{11} in 13 was assigned on biogenetic considerations.

The occurrence of laurifonine (1), laurifine (2) and laurifinine (13) in *Cocculus laurifolia* DC is of biogenetic importance, in view of the fact that recently a new group of *Erythrina* alkaloids such as cocculidine (14) and cocculine (15) which could be named as 'Abnormal *Erythrina* alkaloids', have been isolated from this plant. The trisubstituted dibenz(d,f)azonine alkaloids, to which these new bases belong, are most probably the key intermediates in the biosynthesis of the abnormal *Erythrina* alkaloids. The biosynthesis of 1,2 and 13 could be envisaged from nor-protosinomenine (8) as follows: Oxidative coupling of 8 could give the neo-proaporphine 9. Reduction of the carbonyl function followed by elimination of OH as shown in 10 would afford 11. Reduction of C=N bond in 11 could furnish 12 from which 1,2 and 13 would be formed by unexceptional steps.

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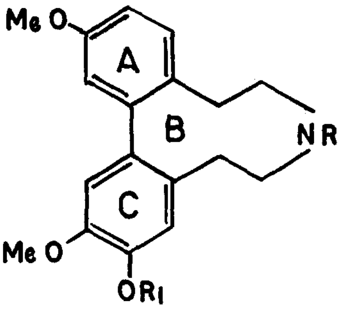
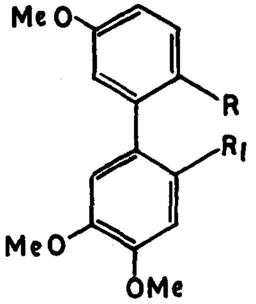
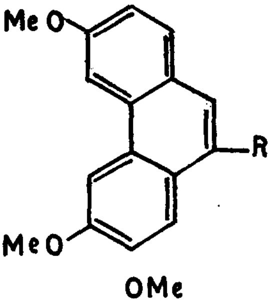


1, R = R_1 = Me
2, R = H, R_1 = Me



3, R = $CH{=}CH_2$; R_1 = $-(CH_2)_2N(Me)_2$
4, R_1 = $CH{=}CH_2$; R = $-(CH_2)_2N(Me)_2$
5, R = R_1 = $CH{=}CH_2$
6, R = R_1 = CHO



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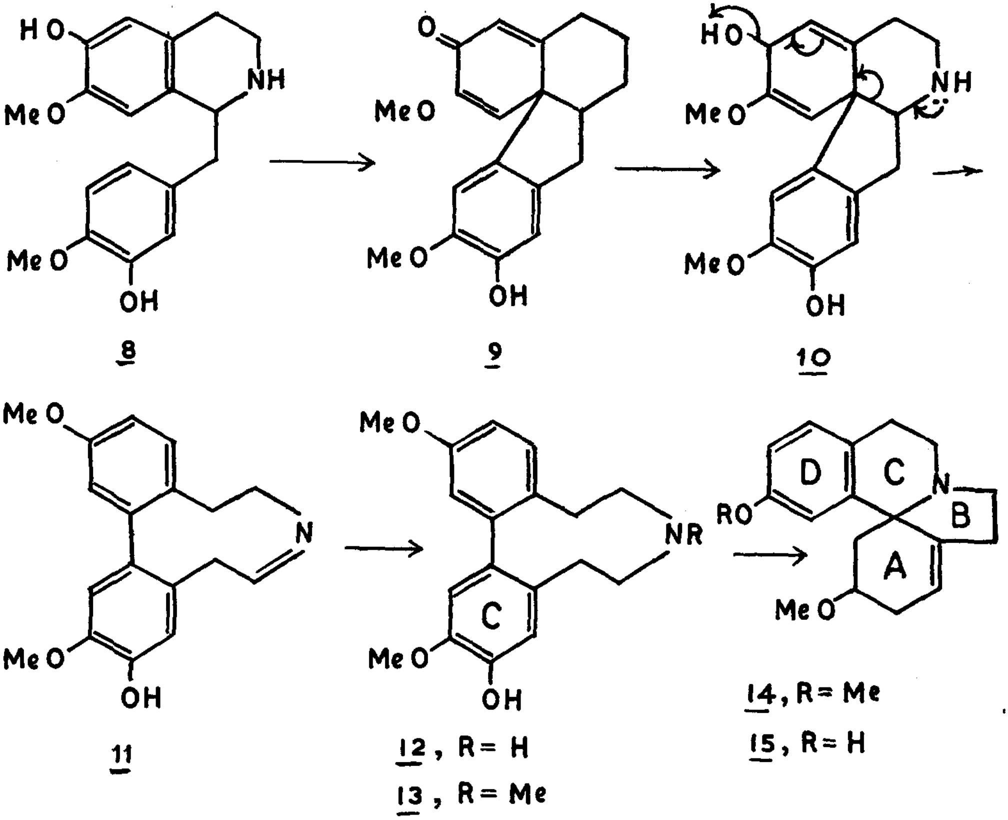

12, R = H
13, R = Me
14, R = Me
15, R = H