DEHYDROPUNTARENINE AND DEHYDROSAULATINE TO NEW ISOQUINOLINE ALKALOIDS FROM ROOTS OF BERBERIS ACTINACANTHA

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Abstract

The isolation and characterization of two new isoquinoline alkaloids, *Dehydropuntarenine* and *Dehydrosaulatine*, obtained during the column chromatography of an alkaloidal fraction from the roots of B. Actinacantha (Berberidaceae) are described.

Introduction

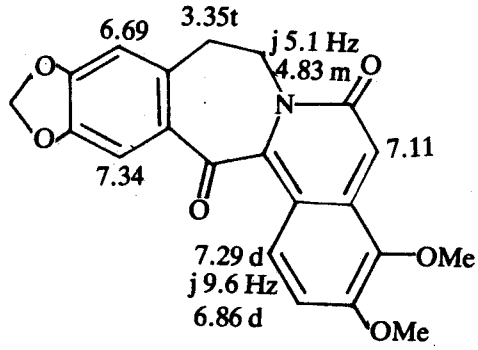
Berberis actinacantha Mart. (Berberidaceae) has proven to be a rich source of isoquinoline derived alkaloids. One of the more interesting of these is the ketolactam (±)- puntarenine (1) independently isolated and characterized by two different research groups [1, 2]. At a slightly later date, the alkaloid saulatine (2), which is the tetramethoxy analog of (1) was obtained from *Abuta bullata* Moldenke (Menispermaceae) [3]. However there is only one report on the chemical constituent of the roots of B. actinacantha.

Results and Discussion

In the present paper we report on the study of an alkaloidal fraction from the *roots* of *B. actinacantha.* Besides reisolating puntarenine two new compounds structurally related to puntarenine and saulatine were obtained.

These two new alkaloids we describe are the red ketolactam dehydropuntarenine (3), $C_{21}H_{17}NO_6$, and its tetramethoxy analog dehydrosaulatine (4), $C_{22}H_{21}NO_6$. The 360 MHz ^{1}H NMR spectrum ($CDCl_3$) of dehydropuntarenine is given in figure 3. Three aromatic proton singlets were in evidence at δ 6.69, 7.34, together with two doublets at δ 6.86 and 7.29, J_o 9.6 Hz, representing H-12 and H-13. Two methoxyl singlets were present at δ 3.85 and 3.96, and a methylenedioxy singlet was at δ 6.05.

The mass spectrum of dehydropuntarenine (3) exhibited molecular ion m/z 379, which was also the base peak. The UV spectrum, λ max (MeOH) 246, 266 and 462 nm, indicated a highly conjugated system: while the IR spectrum showed ν max ($CHCl_3$) 1626, 1637 and 1710 cm^{-1}.



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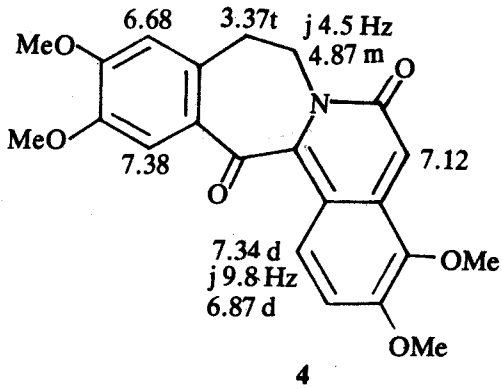

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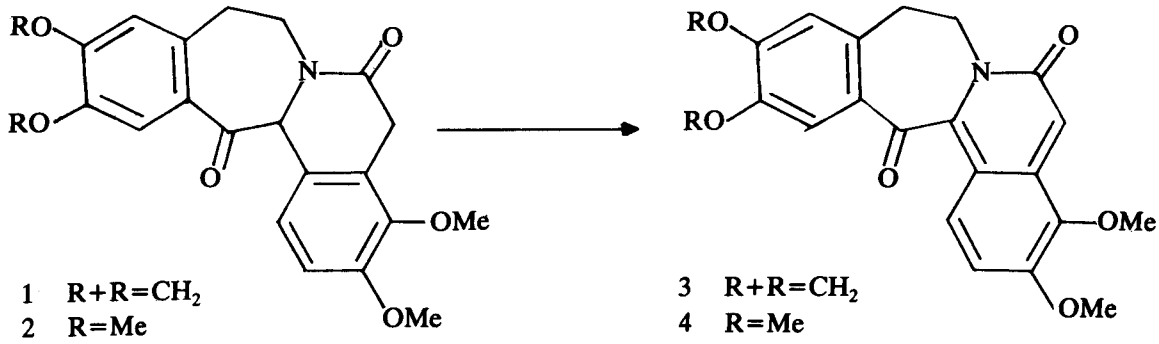
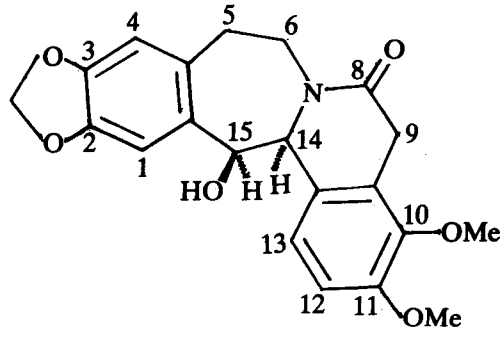
Key words: Berberis Actinacantha, Dehydropuntarenine, Dehydrosaulatine

Proof of structure for dehydropuntarenine (3) was forthcoming from chemical evidence. Platinum black dehydrogenation of puntarenine in refluxing mesitylene furnished dehydropuntarenine (3).



Furthermore, the sodium borohydride reduction of the deep red dehydropuntarenine (3) in methanol led mostly to alcohol (5) already described in the literature [2], obtained from sodium reduction of puntarenine together with the alcohol (6) in 10% yield.

The NMR spectrum of (6) is noteworthy since the H_1 and H_{13} absorptions appear further downfield than in the spectrum of alcohol (5), namely at δ 6.91 and 7.06 respectively. This reflects the fact that C_{15} in alcohol (6) is quasi eqasi equatorial and is close to H_1 and H_{13}. Additionally, $J_{14,15}$ in (6) is 8 Hz, corresponding to a dihedral angle approximating 145°.



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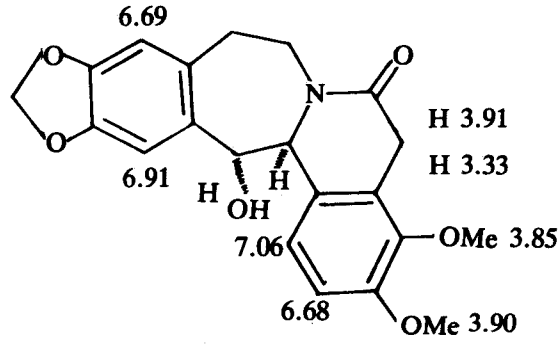

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The spectral characteristics of dehydrosaulatine (4) paralleled those for (3), except that in the NMR spectrum of the former four methoxyl singlets were in evidence at δ 3.85, 3.93, 3.96, and 3.97. The mass spectral molecular ion and base peak, **m/z** 395, was 16 mass units greater than for dehydropuntarenine.

It has been reported that puntarenine and saulatine are artifacts of isolation [4]. By extension dehydropuntarenine (3) and dehydrosaulatine (4) could also be artifact of isolation formed from oxidation of puntarenine and saulatine during column chromatography. This sort of oxidation on a chromatographic column is possible since silica gel is an active surface where O_2 and H_2O from the atmosphere are adsorbed and from the other hand, over several weeks or months, the column is continuously flushed with solvents which are, themselves, saturated or nearly saturated with O_2 and H_2O.

Experimental Section

Plant collection. B. actinacantha was collected in Locurr Hill, immediately east of Santiago, in the spring of 1985. A voucher specimen was deposited in the herbarium of the Natural History Museum in Santigo.

The dried, powdered plant was first defatted with petroleum ether. Extraction was with cold ethanol, and the evaporation of the solvent was carried out with the minimun application of heat. The extracts were fractionated using 3NHCI and then dil. ammonium hydroxide. The alkaloidal fraction was subjected to extensive column chromatography on silica gel, and to thin layer chromatography onpre-prepared Merck Silica, gel G glass plates.

Conversion of Puntarinine to *Dehydropuntarenine.* Puntarenine (5 mg) was dissolved in mesitylene (6 mi). A small amount of platinum black was added to the solution and the mixture was refluxed for 3 hrs. and then filtered. The filtrate which was deep red evaporated under reduced pressure to afford Dehydropuntarenine (4.2 mg) which was fairly pure.

Reduction of *Dehydropuntarenine.* Dehydropuntarenine (3 mg), methanol (16 ml), and sodium borohydride (20 mg) were mixed to gether and stirred for 3 hr. Then the solvent was removed and the reside was dissolved in saturated solution of sodium sulphate (20 ml) and extracted four times with chloroform (20 ml).

The combined chloroform layer was dried over (Na_2SO_4) for an hour, filtered, and evaporated. The residue was checked on tlc. Two compounds were observed which were in fact *cis* and *trans* dihydropuntarenine. By repeating the experiment with a larger amount of starting material (120 mg), the ratio of about 9/1 was founded for the two alcohols.

Table: Spectral Characteristics of the Alkaloids

Dehydropuntarenine (3):
IR($CHCl_3$): δ_{max} 1626, 1637 and 1710 cm^{-1}
NMR($CDCl_3$, 360 MHz): δ 3.35 (2H, t, J 5.1 Hz., H-5), 3.85 (3H, s, CH_3O- at 10), 3.96 (3H, s, CH_3O- at 11), 4.83 (2H, m, H-6), 6.05 (2H, s, $CH_2<^{O}_{O}$), 6.69 (1H, s, H-4), 6.86 (1H, d, J_o = 9.6 Hz, H-12), 7.11 (1H, s, H-9), 7.29 (1H, d, J_o 9.6 Hz, H-13), 7.34 (1H, s, H-1); MS: m/z 380 (M^+, 1, 25), 379 (M^+, 100), 365 (18), 364 (70), 366 (26), 220 (20), 190 (20), 176 (35), 175 (34), 184 (44), 147 (32), 137 (26), 89 (28), 86 (39), 84 (61), 51 (36), 49 (94), 28 (64).
UV(CH_3OH): λ_{max} 246, 266 and 462 nm

Dehydrosaulatine (4):
IR($CHCl_3$): δ_{max} 1637 and 1710 cm^{-1}
NMR($CDCl_3$), 200 MHz): δ 3.37 (2H, t, J 4.5 Hz, H_5), Four methoxy at 3.85 (s), 3.93 (s), 3.96 (s), 8.97 (s), 4.87 (2H, m, H-6), 6.68 (1H, s, H-4), 6.87 (1H, d, J_o 9.8 Hz, H-12), 7.12 (1H, s, H-9), 7.34 (1H, d, J_o 9.8 Hz, H-13), 7.38 (1H, s, H-1)
MS: m/z 396 (M^+ + 1, 26), 395 (M^+, 100), 381 (17), 380 (70), 352 (28) 192 (22), 191 (21), 91 (15), 77 (15)

Dihydropuntarenine (6):
IR($CHCl_3$): δ_{max} 1634 nd 3605 cm^{-1}
NMR ($CDCl_3$, 200 MHz): δ 3.33 (1H, d, J 20.09 Hz, H-9), 3.85 (3H, s, CH_3O- at 10), 3.90 (3H, s, CH_3-O- at 11), 3.91 (1H, d, J 20.09 Hz, H-9), 4.51 (1H, d, J 8 Hz, H-15), 4.59 (1H, d, J 8 Hz, H-14), 6,69 (1H, s, H-4), 6.88 (1H, d, J_o 8.4 Hz, H-12), 6.91 (1H, s, H-1), 7.06 (1H, d, J_o 8.4 Hz, H-13)
MS: m/z 384 (M^+ + 1, 20), 383 (M^+, 87), 354 (15), 220 (20), 207 (70), 206 (86) 205 (84), 193 (13), 192 (100), 191 (41), 190 (27), 178 (35), 177 (72), 176 (51), 163 (17), 149 (25), 148 (32), 147 (20), 135 (14), 119 (15), 91 (26), 77 (14),

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