## THE STRUCTURES OF TWO NEW ZWITTERIONIC ALKALOIDS

FROM ANODENDRON AFFINE DRUCE.

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Two new water-soluble pyrrolizidine alkaloids were isolated from <u>Anodendron affine</u> Druce (Apocyanaceae ; Japanese name "Sakaki-kazura" ).

In this communication we wish to report structures of anodendrine (I) and alloanodendrine (II), both of which contain the quarternary ammonium moiety.

Anodendrine picrate forms yellow needles ( $C_{13}H_{21}O_2N - C_6H_3O_7N_3$ , m.p. 123 - 124°). Physical properties of anodendrine (I) are as follows:  $v \frac{CHC1}{max}$  1606 (carbonyl), 1665 cm<sup>-1</sup> (double bond); end absorption,  $\varepsilon$  (212 mµ) = 645 in methanol;  $[\alpha]_D^{25^\circ}$  = 9.5°(in ethanol) ; pKa' = 3.7 (50% methanol); Rf = 0.37 on paper chromatography (ethyl acetate : ethanol : water = 5 : 3 : 2 V/V).

Anodendrine (I) shows a strong absorption at 1606 cm<sup>-1</sup> assigned to a carbonyl group in its IR spectrum, while the corresponding band appeared at 1712 cm<sup>-1</sup> in its picrate spectrum. The difference between these two spectra indicates that I contains a carbonyl group. Further anodendrine (I) must be a quarternary amine, since it shows only pKa' value at 3.7.





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On catalytic hydrogenolysis of anodendrine (I) with 10% palladium-charcoal in methanol, a crystalline product was obtained.

This compound (III), ( $C_8H_{13}O_2N - C_6H_3O_7N_3$ , m.p. 175 - 176°, as picrate; [a]  $\frac{25^\circ}{D}$  = 44.2° (water); pKa' = 3.95, 10.55 (50% methanol)), was identical with laburninic acid (1) by comparison with the authentic sample.

The 100 Mc NMR spectrum ( in  $CDCl_3$  ) of anodendrine (I) shows signals attributable to: two olefinic methyls at 1.86 and 1.90 ppm; two allylic protons 3.9 - 4.5 ppm; an olefinic proton at 5.43 ppm ( br. t, 1H ); and twelve protons at 1.7 - 2.2 ( 6H ), 2.93 ( m, 1H ), 3.3 -3.9 ( 4H ), and 4.55 ppm ( m, 1H ), arising from laburninic acid (III).

Irradiation of two methyl signals at 1.86 and 1.90 ppm converted the broad olefinic signal at 5.43 ppm (br. t, J = 7.5, 1H) to a sharp triplet. On irradiation of the olefinic signal at 5.43 ppm, the complex signal at 3.9 - 4.5 ppm (2H) was changed to two pair doublets. These observation indicate the presence of group IV.

From these results, we can conclude the structure I for anodendrine.



Alloanodendrine p-bromophenacyl ester bromide ( $C_{13}H_{21}O_2N - C_8H_6OBr_2 \cdot 4/5$  CHCl<sub>3</sub>, m.p. 82 - 84°) resembles the corresponding derivative of anodendrine in their IR spectra. Physical properties of alloanodendrine (II) are shown below;  $v \frac{CHCl_3}{max}$  1597 (carbonyl), 1665 cm<sup>-1</sup> (double bond); end absorption,  $\varepsilon$  (212 mµ) = 640 im methanol;  $[\alpha] \frac{25^{\circ}}{D} = 18^{\circ}$  (in ethanol); pKa' = 3.2 (water); Rf = 0.37 on paper chromatography (ethyl acetate : ethanol : water = 5 : 3 : 2 V/V ).

Alloanodendrine (II) is very similar to anodendrine (I) in NMR spectral behaviors.

From these findings, II is expected to be the epimer of I at C-1.

Hydrogenolysis of II gave (+)-isoretronecanolic acid (V) (2) ( $C_8H_{13}O_2N - C_6H_3O_7N_3$ , m.p. 219 - 220° (dec.), as picrate;  $[\alpha]_D^{25°} = 72°$  (in ethanol)), whic was confirmed by comparison with the authentic sample. The results of these physical data and hydrogenolysis suggest that alloanodendrine has the structure II.

Further we confirmed the structures of anodendrine (I) and alloanodendrine (II) by synthesis.

Laburninic acid (III) was chosen as the starting material for the synthesis of I, which was esterified with hydrogen chloride - methanol. Treatment of the ester with isopropenyl bromide in chloroform - benzene (2:1) at 50° followed by hydrolysis of the product gave an amino acid, which was identified as anodendrine (I). Also alloanodendrine (II) was synthesized from (+)isoretronecanolic acid (V), following the same procedure as employed for the synthesis of I. Each synthetic sample was found to be completely identical with natural anodendrine (I) and alloanodendrine (II) in spectral (IR, UV, and NMR ) behaviors and by mixed melting points determination.

The complete structure, including the absolute configuration can now be established: anodendrine, I, and alloanodendrine, II.

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