Tetrahedron Letters No.27, pp. 2591-2596, 1967. Pergamon Press Ltd. Printed in Great Britain.

CHEMOTAXONOMICAL ALKALOID STUDIES I .

STRUCTURE OF NERVOSINE

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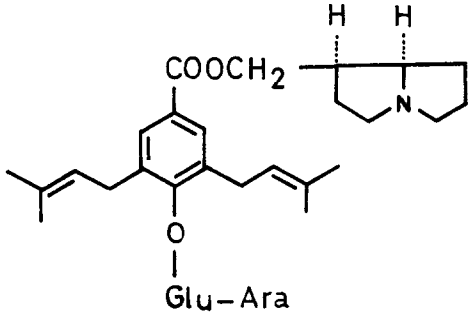
(Received 6 April 1967; in revised form 4 May 1967)

On the basis of morphorogy, it is very difficult to classify some plants in the Liparis species of Orchidaceae. We have examined the possibility of chemotaxonomical classification in several plants of the Liparis species.

From our observation, it is clear that some Liparis species of the Orchidaceae family contain new types of alkaloids which are similar to each other.

In this communication, we wish to report the structure of Nervosine (I), named by us, which was isolated from Liparis nervosa Lindl.*.



(I)

Nervosine (I), ($C_{36}H_{53}O_{12}N \cdot H_2O$ - $C_6H_3O_7N_3$, m.p. 130 - 131°, as picrate; $[\alpha]_D^{20°}$=+12.8° as HCl salt (methanol); pKá: 10.0 (66 % methanol); Rf: 0.62 (n-BuOH : AcOH : H_2O = 4 : 1 : 1); negative Tollens test), shows strong bands at 3400 and 1120 - 980 cm^{-1} in its IR spectrum and a positive Benzidine - HIO_4 test which indicate that Nervosine (I) is a glycoside.

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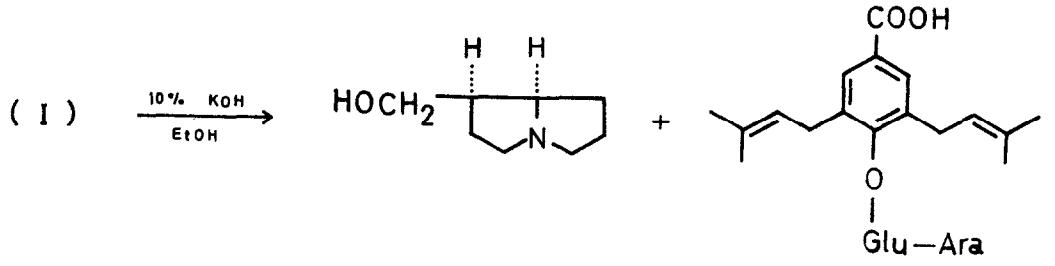
* Japanese name is Kokuran.

Other physical properties of Nervosine are as follow: ν_{max}^{KBr} (cm^{-1}) 1715 (carbonyl), 1605 (benzene ring); λ_{max} (ε) 243, 280, 289 mμ (15000, 2300, 2000) in neutral and alkaline methanol; NMR*(in D_2O - D_2SO_4): 1.63 (12H, singlet, ($C=C-CH_3 \times 4$)), 7.60 ppm (2H, singlet, (benzene proton)).

On alkaline hydrolysis of I, two products were obtained.



(II) (III)

One is a basic compound (II), ($C_8H_{15}ON$ - $C_6H_3O_7N_3$, m.p. 193 - 194°, as picrate; $[\alpha]_D^{20°}$=+73° (methanol)), which is identical to Lindelofidine (d-isoretronecanol)(1).

It was confirmed by the following physical data: pKá: 10.5 (50 % methanol); m/e: 141 (M^+), 124 (M^+-OH), 110 (M^+-CH_2OH), 83 (base peak, M^+-CH_2=CH-CH_2OH); NMR (in pyridine): 1.90 -2.50 (7H, multiplet), 2.65 - 4.10 (4H, multiplet), 3.95 (2H, doublet, J=7 cps), 4.54 ppm (1H, multiplet) from internal TMS.

Further additional supporting data were obtained by oxidation of II with chromic acid in dil-H_2SO_4. The physical properties of the oxidation product, ($C_8H_{13}O_2N$ - $C_6H_3O_7N_3$, m.p. 219 - 220°, as picrate)(2); pKá: 4.05, 10.5 (50 % methanol); m/e: 155 (M^+), 127 (M^+-CO), 110 (M^+-COOH), 83 (M^+-CH_2=CH-COOH, base peak)), are in full agreement with the corresponding amino acid.

The IR spectrum of the acidic compound (III), Nervosinic acid, ($C_{28}H_{40}O_{12}\cdot H_2O$, m.p. 168 - 169; pKá: 5.80 (66 % methanol); $[\alpha]_D^{20°}$=-14° (methanol)), has absorption bands at 3400 (strong) and 1130 - 980 cm^{-1} (strong) indicating to be a glycoside.

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* Only sharp signals are described.

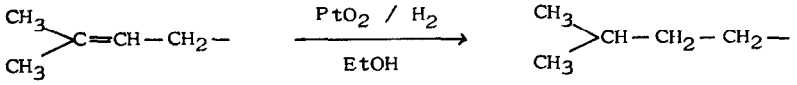
The UV spectrum of III in neutral methanol is very similar to that of Nervosine (I) indicating the presence of the same chromophore as I .

However, the hypsochromic shift in alkaline methanol solution (8 mμ) suggests the presence of a new carboxylic function in conjugation with the chromophore. When hydrogenated with platinum dioxide in ethanol, III was transformed to tetrahydro derivative (IV), ($C_{28}H_{44}O_{12}.H_2O$, m.p. 187 - 189°).

Its UV spectrum was almost identical with that of III. This fact indicates that III contains two isolated double bonds. Comparison of the NMR spectra of III and IV, showed a doublet at 0.97 ppm (12H, J=5 cps) in IV, instead of two singlets at 1.66 and 1.73 ppm (both 6H) in III.

Furthermore, a doublet at 3.92 ppm (4H, J=7 cps) and a triplet at 5.56 ppm (2H, J=7 cps) in III disappeared in IV, while a broad multiplet at 1.71 ppm (6H, multiplet) and a broad triplet at 3.17 ppm (4H, J=7.5 cps) appeared in IV.

This is interpreted as follows:



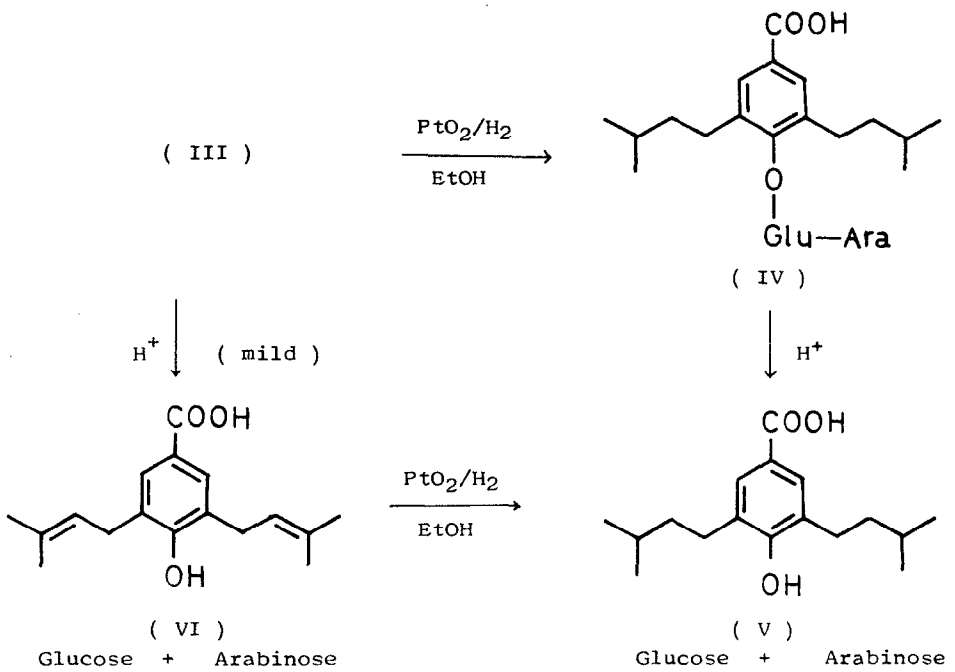
(IIIa) (IVa)

When IV was treated with 2N hydrochloric acid, it gave D-glucose, L-arabinose and a dibasic acid (V), ($C_{17}H_{26}O_3$, m.p. 138 - 139°). Physical properties: pKa': 6.3, 11.8 (66% methanol), ν_{max}^{KBr} (cm^{-1}) 3500 (- OH), 3200 - 2400, 1673 (conjugated -COOH), 1605 (benzene ring), 1390 and 1375 (gem-dimethyl group); λ_{max} (ε) 258 mμ (11500) in neutral methanol, 291 mμ (17000) in alkaline methanol, suggest that this compound has a hydroxybenzoic acid chromophore.

Furthermore from the NMR spectrum in $CDCl_3$: (0.97 (12H, doublet, J=5.1 cps), 1.2 - 1.8 (6H, multiplet), 2.66 (4H, triplet, J=7 5 cps), 7.79 ppm (2H, singlet)), we assigned the structure V to this acidic compound.

On the other hand, the acid hydrolysis of Nervosinic acid (III) under mild conditions afforded Nervogenic acid (VI), ($C_{17}H_{22}O_3$, m.p. 96 - 97°), the UV spectrum of which was in good agreement with that of V.

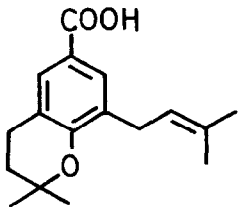
The catalytic hydrogenation of VI also afforded compound V. From the above results, the structure of Nervogenic acid can be assigned as VI.



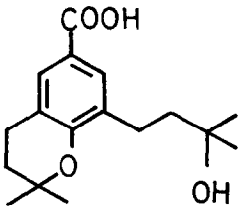
The NMR spectrum of VI, (1.80 (12H, singlet), 3.40 (4H, doublet, J=7.5 cps), 5.36 (2H, triplet, J=7.5 cps), 7.80 ppm (2H, singlet)), is in agreement with this structure. Supporting data were obtained by further acid treatment of VI which afforded two 2,2-dimethyl-6-carboxychroman derivatives VII, ($C_{17}H_{22}O_3$, m.p. 120 - 121°; ν_{max}^{KBr} (cm^{-1}) 3200 - 2400, 1670, 1605, 1595, 1205, 1155, 1120; λ_{max} (ε) 265 mμ (13000) in methanol, 255 mμ (11500) in alkaline methanol; NMR: (in $CDCl_3$) 1.38 (6H, singlet), 1.76 (6H, singlet), 1.83 (2H, triplet, J=7.0 cps), 2.84 (2H, triplet, J=7 cps), 3.32 (2H, doublet, J=7.5 cps), 5.32 (1H, triplet, J=7.5 cps), 7.76 ppm (2H, singlet), and VIII, ($C_{17}H_{24}O_4$, m.p. 170 - 171°; ν_{max}^{KBr} (cm^{-1}) 3300, 3200 - 2400, 1675, 1605, 1388, 1375, 1205,

1155, 1120; λ_{max} (ε) 265 mμ (14000) in methanol, 255 mμ (11700) in alkaline methanol; NMR: (in CD_3COCD_3) 1.25 (6H, singlet), 1.37 (6H, singlet), 1.50 - 1.95 (4H, multiplet), 2.50 - 3.0 (4H, multiplet), 7.64 ppm (2H, singlet)).

Both were also obtained directly by acid hydrolysis of I and III under drastic conditions. A small amount of the compound VIII was obtained from VII on further treatment with acid.



(VII)



(VIII)

The structure of the sugar moiety is disucussed below. The disaccaride obtained from III by acid hydrolysis under mild conditions, was reduced by sodium borohydride followed by acid hydrolysis to give arabinose which was confirmed by the paper chromatography. A spot corresponding to glucose could not be detected. This indicates that in the disaccaride, the aldehyde group of glucose was reduced indicating that C_1 of glucose must have been in glycoside linkage with the phenolic hydroxyl group of the aglycone (VI).

From these results, the structure of Nervosinic acid could be assigned as III. Since Nervosine must be constructed with the alkaline degradation products II and III, the structure of Nervosine could be assigned as I.

Acknowledgements: This work was supported by the Grant-in-Aid of Scientific Research from the Ministry of Education of Japan and the United States Public Health Service, National Institute of Health, through grant GM-7969.

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