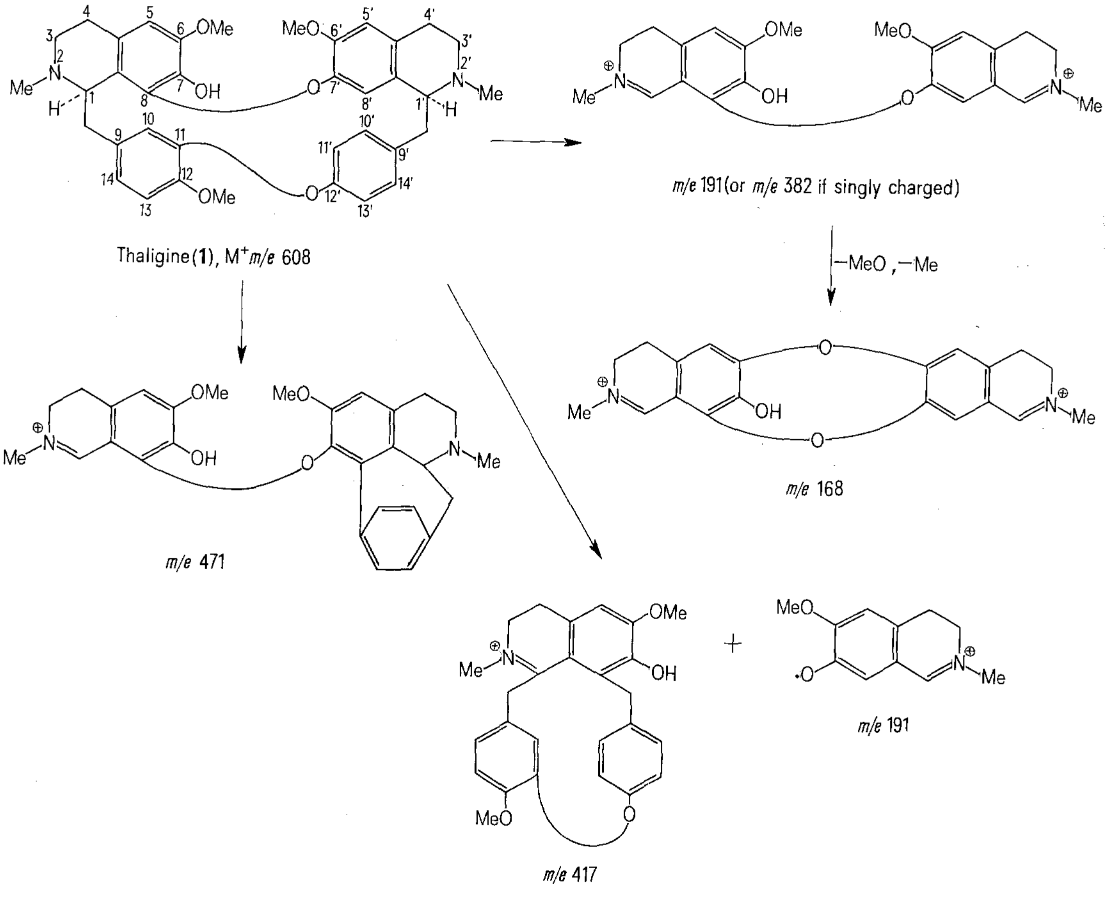
SPECIALIA

Thaligine, a New *Bis*benzylisoquinoline Alkaloid from *Thalictrum polygamum* Muhl. (Ranunculaceae)

The new dimeric base thaligine (**1**), $C_{37}H_{40}N_2O_6$, has been obtained from the basic, non-water soluble extracts of the giant meadow rue, *Thalictrum polygamum* Muhl. (Ranunculaceae)[1,2]. Recrystallization from methanol gave colorless needles; mp 153°; $[\alpha]_D^{25}$ + 87° (c 0.33, MeOH); ord (c 0.049, MeOH) $[\alpha]_{310}$ + 61°, $[\alpha]_{288}$ + 1061° (pk), $[\alpha]_{270}$ + 490° (tr), $[\alpha]_{240}$ 7960°; λ_{max}^{EtOH} 282 nm (log ε 3.94) and λ_{min}^{EtOH} 259 nm (log ε 3.65), with a bathochromic shift in base due to the presence of a phenolic function.

The major peaks in the low resolution mass spectrum of thaligine were *m/e* 608 (M^+, 70%), 471 (2%), 417 (9%), 382 (27%), 381 (19%), 367 (38%), 191 (100%), 174 (28%) and 168 (21%). The diagnostic doubly charged base ion *m/e* 191 showed the further loss of methoxyl and methyl radicals to furnish the doubly charged ion *m/e* 168. The abundant fragment *m/e* 382 lost a hydrogen atom to give ion *m/e* 381, or alternatively lost a methyl group to supply *m/e* 367. The observation that *m/e* 417 was much more intense than *m/e* 471 suggested that thaligine was a *bis*benzylisoquinoline alkaloid of the berbamine type (Scheme)[3].

The 60 MHz NMR-spectrum ($CDCl_3$) confirmed that thaligine (**1**) belonged to the berbamine series since two N-methyl singlets were present at δ2.34 and 2.53, separated by 0.19 ppm. If the alkaloid had been of the oxyacanthine type, these peaks would have appeared within a distance of 0.03 to 0.1 ppm from each other[3].



Mass spectral fragmentation of Thaligine (1). (The structures of the fragmentation products are hypothetical).

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[1] Thalphenine, thalphenine methine (≡ thaliglucine), and N-methylpalaudine are other new isoquinoline alkaloids found in *T. polygamum*: M. Shamma, J. L. Moniot, S. Y. Yao and J. A. Stanko, Chem. Commun., *1972*, 408. – M. Shamma and J. L. Moniot, J. Pharm. Sci. *61*, 295 (1972).

[2] The plant was collected in the vicinity of University Park, Pennsylvania. Elemental analysis was by high resolution mass spectroscopy.

[3] For a discussion of the NMR- and mass spectra of *bis*benzylisoquinoline alkaloids, as well as for the appropriate lead references, see M. Shamma, *The Isoquinoline Alkaloids* (Academic Press, New York 1972), p. 146.

The spectrum also contained 3 methoxyl singlets at $\delta 3.76$ (C–6′), 3.92 and 3.94 (C–6 and C–12), 12 methylene protons centered around $\delta 2.90$, 2 methine protons at $\delta 3.59$ and 3.62 (C–1 and C–1′), a high field aromatic proton singlet at $\delta 6.10$ (C–8′), and 9 other aromatic protons between $\delta 6.25$ and 7.20. The absence of a high field methoxyl resonance between $\delta 3.02$ and 3.20 confirmed that a hydroxyl function was present at C–7. Since the C–6′ methoxyl appears at $\delta 3.76$, the existence of thaligine in either the (+ –) or (– +) form was suggested[4]; and indeed *O*-methylation with diazomethane afforded (+)-isotetrandrine of known absolute configuration[5]. The two samples of isotetrandrine were identical in terms of Rf values, UV-, NMR- and mass spectra, and ord curves.

Résumé. Le nouvel alcaloïde thaligine (**1**) a été tiré du *Thalictrum polygamum* Mulh. (Ranunculaceae).

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[4] I. R. C. BICK, J. HARLEY-MASON, N. SHEPPARD and M. J. VERNENGO, J. chem. Soc. *1961*, 1896.

[5] M. TOMITA, M. KOZUKA and M. SATOMI, J. Pharm. Soc. Japan *87*, 1012 (1967).

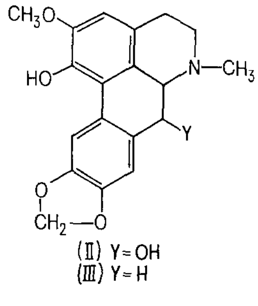
[6] The authors are grateful to the National Institutes of Health for grant No. HL-12971, and to Professor J. L. BEAL for alkaloidal samples.

Structure of Nandazurine, from *Nandina domestica* Thumb.

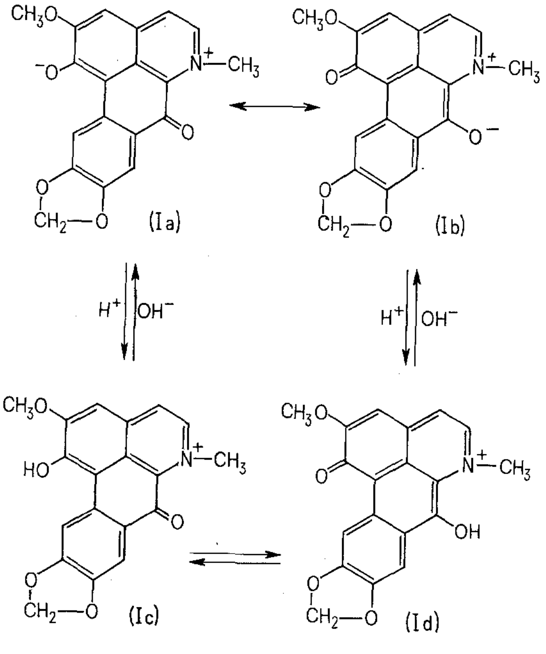
Nandazurine, a green colored alkaloid, was first isolated in 1925 from the bark of *Nandina domestica* Thumb. (Berberidaceae) by KITAZATO[1], however its structure has long been unknown. Recently, we isolated nandazurine from the same plant along with several other alkaloids. In this communication we wish to present a report on the structure elucidation of nandazurine.

Nandazurine (I), amorphous dark green powder showing a single spot on TLC, $C_{19}H_{13}O_5N$ (elemental analyses, molecular ion peak at m/e 335), $[\alpha]_D \pm 0°$ (C_5H_5N). It is sparingly soluble in common organic solvents and insoluble in aqueous alkali, and gives a positive ferric chloride test. The IR-spectrum (KBr) of nandazurine (I) showed absorptions at 1625 (weak) and 1575 cm^{-1} (medium) (conjugated $>C=O$ and $-\overset{|}{C}=\overset{|}{N^+}-$). Its NMR-spectrum (in trifluoroacetic acid) revealed an N-methyl group (at 4.98δ), a methoxyl group (at 4.43δ), a methylenedioxy group (at 6.22δ), 3 aromatic protons (at 7.62, 7.89, 8.85δ) and one AB quartet (J = 7 Hz, at 8.43, 8.67δ). Its UV-spectrum in ethanol or aqueous ethanolic alkali exhibited λ_{max} 221, 230(sh), 260, 324, 394, 426, 450(sh) and 606 nm (log ε; 4.41, 4.43, 4.38, 4.58, 3.84, 3.78, 3.73 and 3.53), which showed a hypsochromic shift on addition of acid solution.

Treatment of nandazurine (I) with sodium borohydride in aqueous methanol gave hexahydronandazurine (II), light green needles, mp 230 ~234°, $C_{19}H_{19}O_5N$, $[\alpha]_D \pm 0°$ ($CHCl_3$); NMR (δ, C_5D_5N): 2.58 (3H, s., N–CH_3), 3.67 (3H, s., OCH_3), 5.00 (2H, broad s., 2×OH), 5.92, 6.01 (2H, 2×d., J = 1.5Hz, –OCH_2O–), 6.61, 7.17, 7.29 (each 1H, s., aromatic proton), 5.10 (1H, d., J=2.5Hz, $-\overset{|}{C}H(OH)$). Its UV-spectrum showed [λ_{max} 221 nm (log ε, 4.86), 239 (sh., 4.11), 288 (4.08) and 310 (4.16)] which is characteristic to 1,2,9,10-tetrasubstituted phenolic aporphine alkaloids and exhibits a bathochromic shift on addition of alkali ethanolic solution[2]. These spectral data suggested that hexahydronandazurine (II) should have a 7-hydroxy-1,2,9,10-tetrasubstituted aporphine structure as in II.



(II) Y=OH
(III) Y=H



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[1] Z. KITAZATO, J. pharm. Soc. Japan *45*, 695 (1925).

[2] M. SHAMMA, Experientia *16*, 484 (1960).