

THE ISOLATION AND STRUCTURES OF DAPHNITEIJSMINE, DAPHNIJSMINE AND DESACETYLDAPHNIJSMINE

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The plant Daphniphyllum macropodum Miquel contains a great variety of related alkaloids, that have been structurally divided into five types of nitrogen heterocyclic skeleton.¹ In the light of the biosynthetic studies on the daphniphyllum alkaloids,² further great efforts have been made to search for an important key intermediate such as I. In the present paper, we wish to describe the isolation and structures of three biogenetically important alkaloids, two of which have an interesting N-oxide structure.

Previously, we reported the isolation of six alkaloids, including daphnilactone-B as a main component, from the fruits of Daphniphyllum teijsmanni Zollinger collected at Irako Cape.¹ We further examined the alkaloidal components of the fruits of the same plant, which were collected in Yakushima (in early November). According to the similar procedure as reported earlier, the MeOH extracts were chromatographed on alumina and eluted, in the following order, with n-hexane, n-hexane-benzene (10 : 1), benzene, EtOAc and EtOAc-MeOH (9 : 1).¹ From the fraction eluted with n-hexane-benzene (10 : 1), daphnilactone-B, which was easily crystallized from n-hexane-benzene, was collected by filtration. The filtrates were further chromatographed on silica gel (Mallinckrodt, 100 mesh), and eluted with EtOAc to give a small amount of daphniteijsmine (II), m.p. 187-188° (from n-hexane-EtOAc); C₃₂H₄₉O₅N; m/e 527 (M⁺), 286 and 216; ν_{\max} (Nujol) 3380br., 1735 and 1700cm⁻¹. On the basis of the above data, daphniteijsmine can be regarded as an isomer of daphniphylline (III)³. The different point is that the mass spectrum of the former has a prominent peak only at m/e 286, whereas a pair of the remarkable peaks are observed at m/e 286 and 272 in the case of III. Furthermore, as known in the case of secodaphniphylline (IV)⁴, daphniteijsmine was readily acetylated with

Ac₂O-pyridine to give the corresponding N-acetyl derivative (V), C₃₄H₅₁O₆N; m/e 569 (M⁺) and 328; γ_{\max} (film) 1735, 1705 and 1640cm⁻¹. From these data coupled with an exhaustive comparison of the NMR spectra between daphniteijsmine and secodaphniphylline, the former should be regarded as acetoxyscodaphniphylline (II) (see Table 1): the multiplets at δ 2.6-2.9, which can be assigned to the methylene protons adjacent to the carbonyl group, is observed in IV, whereas II has the signal at δ 5.77(dd, J= 12, 2.5Hz) due to O=C-CH(OAc) as found in the case of daphniphylline (III) [δ 5.52(1H, dd, J= 12, 3Hz)]³.

The isolation of daphniteijsmine (II) suggests that daphniphylline (III) is not necessarily derived from codaphniphylline (VI) by acetoxylation *in vivo*².

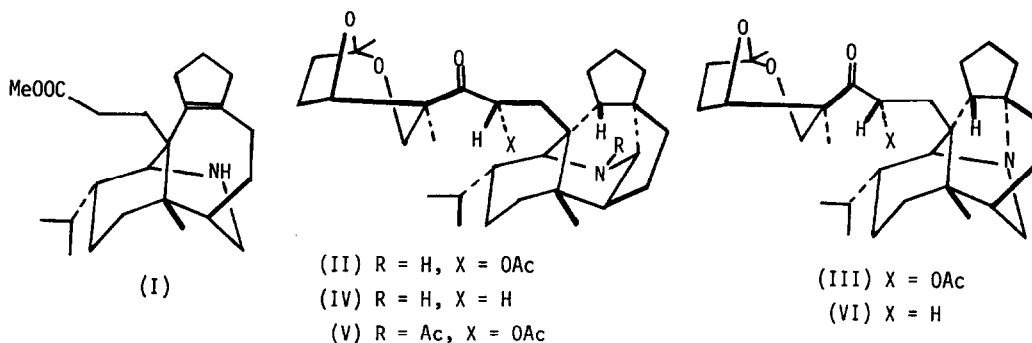


Table 1. The NMR spectra of secodaphniphylline and daphniteijsmine*

Secodaphniphylline (IV)	Daphniteijsmine (II)
0.77 (3H, s)	0.94 (6H, br.s)
0.89 (3H, s)	
0.89 (3H, d, J= 6Hz)	0.96 (6H, d, J= <u>ca.</u> 6.5Hz)
0.90 (3H, d, J= 6Hz)	
1.42 (3H, s)	1.50 (3H, s)
2.51 (1H, d, J= 4.2Hz)	2.53 (1H, d, J= 4.0Hz)
2.6 - 2.9 (2H, m)	
3.01 (1H, br.s)	3.24 (1H, br.s)
3.49 (1H, d, J= 12Hz)	3.67 (1H, d, J= 12.5Hz)
4.23 (1H, dd, J= 12, 2Hz)	4.50 (1H, dd, J= 12.5, 2Hz)
4.62 (1H, m)	4.66 (1H, m)
	5.77 (1H, dd, J= 12, 2.5Hz)

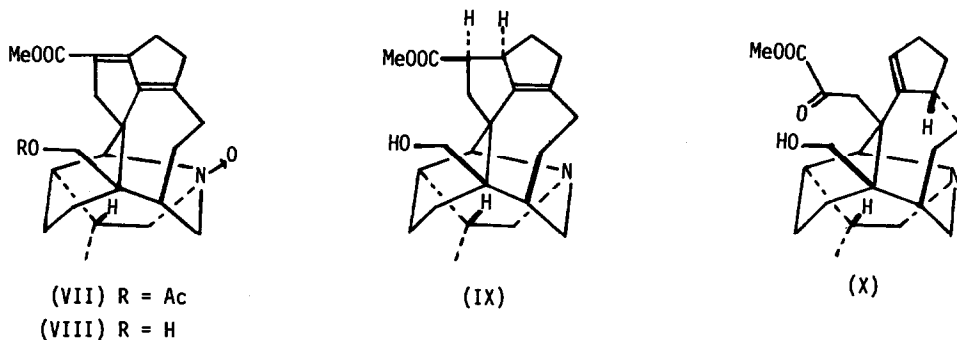
* In CDCl₃.

Elution of the MeOH extracts on alumina with EtOAc afforded a viscous oil, which was further separated by preparative TLC [Kieselgel 60 PF₂₅₄ in n-hexane-Et₂O-Et₂NH (20 : 20 : 1)] to give two crystalline compounds as a minor component.

Daphnijsmine (VII): m.p. 205-207° (from n-hexane-EtOAc); C₂₅H₃₃O₅N; m/e 427 (M⁺), 411, 410, 409, 396 (M⁺-31, m* = 366), 395 and 394; ν_{\max} (Nujol) 1745, 1680br., 1650, 1628 and 1255cm⁻¹; λ_{\max} (MeOH) 300nm (ϵ , 16300); δ (CDCl₃) 1.10(3H, d, J = 7.0Hz), 2.06(3H, s), 3.05-3.75(5H, complex), 3.73(3H, s), 3.92(1H, d, J = 12Hz) and 4.16(1H, d, J = 12Hz).

Desacetyldaphnijsmine (VIII): m.p. (dec) ca. 200° (from n-hexane-EtOAc); C₂₃H₃₁O₄N; m/e 385 (M⁺), 369, 368, 367, 354, 353 and 352; ν_{\max} (CHCl₃) 3400br., 1690br., 1650 and 1625cm⁻¹; λ_{\max} (MeOH) 301nm (ϵ , 15000); δ (CDCl₃) 1.10(3H, d, J = 7.0Hz), 3.20(1H, d, J = 11Hz), 3.56(1H, d, J = 11Hz), 3.00-3.75(5H, complex) and 3.72(3H, s).

From the above physical data of both alkaloids, the only different point is that VII has an acetoxy-methyl group, whereas a hydroxy-methyl group is present in VIII. The presence of an amine oxide in VII (or VIII) can be confirmed by the mass spectrum with three characteristic fragment peaks [M⁺ - 16, M⁺ - 17 and M⁺ - 18], as found in that of macrodaphnine, whose structure has been determined by an X-ray crystallographic analysis⁵. Both alkaloids have a secondary methyl group as well as a carbomethoxyl group as found in the case of the yuzurimine group of alkaloids. However, the IR and UV spectra of VII (or VIII) indicate that the carbomethoxyl group must be conjugated with two double bonds. From these data together with co-occurrence of yuzurimine-B (IX), the structures of daphnijsmine and desacetyldaphnijsmine can be represented by VII and VIII, respectively.



Biogenetically, these two new alkaloids belong to the yuzurimine group of alkaloids, but differ from them in the following point: daphnijsmine and desacetyldaphnijsmine both have the $\Delta^{1,2,3,4}$ -unsaturated carbomethoxyl chromophore, which suggests that these new alkaloids may be produced from a precursor (X) similar to daphnilactone-B^{1,6}.

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