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DAPHNITEIJSMANINE, THE DAPHNIPHYLLUM ALKALOID WITH A NEW KETAL MOIETY

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Our biosynthetic studies on the daphniphyllum alkaloids have revealed that they are biosynthesized from six molecules of mevalonic acid via a squalene-like intermediate, and let us demonstrate a possible biosynthetic pathway from squalene to daphniphylline, one of the C_{30}-alkaloids.[1] Further efforts have been made to search for the important intermediates estimated from the above idea. In the present paper, we wish to describe the isolation and structure of daphniteijsmanine (I) with a new ketal moiety together with chemical conversion of secodaphniphylline (II) into N-acetyldaphniteijsmanine acetate (III).

According to essentially the same procedure as reported earlier, the alkaloidal components were obtained from the MeOH extracts of the fruits of the plant Daphniphyllum teijsmanii Zollinger collected in Yakushima[2], and chromatographed on alumina. Elution with AcOEt gave a viscous oil, whose analytical TLC showed several spots. This oil was further separated by repeated preparative TLC [Kieselgel 60 PF_{254} in n-hexane-Et_2O-Et_2NH (10 : 10 : 1)] to afford a small amount of crystalline solid of daphniteijsmanine (I), m.p. 228-232° (from n-hexane-EtOAc); $C_{30}H_{49}O_3N$; m/e 471(M^+), 456, 454, 440, 428, 286 and 216; ν_{max}(Nujol) 3450br.cm^{-1} and no C=O.

From the NMR (see The Table) and mass spectra (δ 0.76, 0.92, 0.94, 2.54 and 3.06; m/e 286), daphniteijsmanine (I) must have the same nitrogen heterocyclic skeleton as that of secodaphniphylline (II)[3]. However, the remarkable difference is seen in the non-nitrogen containing moiety of the structure, as follows. Although the alkaloids (I) and (II) both have two methyl singlets (I, δ1.12 and 1.48; II, δ0.89 and 1.42), the former has the NMR

signal at δ3.42(2H, s) due to a hydroxymethyl group, which is shifted to δ3.80(2H, br.s) on acetylation with Ac_2O-pyridine (room temp., overnight) giving N-acetyldaphniteijsmanine acetate (III), $C_{34}H_{53}O_5N$; m/e 555(M^+) and 328; ν_{max}(film) 1745 and 1643cm^{-1}; $\delta(CDCl_3)$[4] o.77(3H, d, J= 6Hz), 0.80(3H, s), 1.14(3H, s), 1.15(3H, d, J= 6Hz), 1.48(3H, s), 2.07(3H, s), 2.14(3H, s), 3.38(1H, dd, J= 8,5Hz), 3.80(2H, br.s), 3.53(1H, d, J= 4.5Hz), 4.08(1H, m) and 4.36(1H, m). In the NMR spectrum of I (or III), two signals at δ3.37 and 4.22 (δ3.38 and 4.08) are due to two protons (-C<u>H</u>-O-). From the above data coupled with a biogenetic consideration, daphniteijsmanine (I) seems to have a ketal grouping similar to that of the degradation product (IV) of daphniphylline[5] except for its stereochemistry (see The Table).

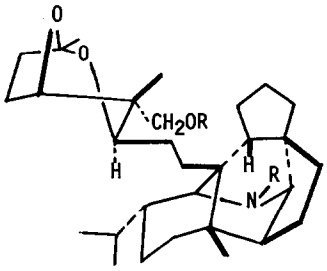
The Table. The NMR spectra of I and IV.*

(I)	(IV)
0.76 (3H, s)	
0.92 (3H, d, J = 6.2Hz)	
0.94 (3H, d, J = 6.2Hz)	
1.12 (3H, s)	0.74 (3H, s)
1.48 (3H, s)	1.46 (3H, s)
2.54 (1H, d, J = 4.4Hz)	
3.06 (1H, br.s)	
3.37 (1H, dd, J = 8.0, 5.0Hz)	3.40 (1H, d, J = 12Hz)
	3.65 (1H, d, J = 12Hz)
3.42 (2H, s)	3.78 (2H, br.s)
4.22 (1H, m)	4.18 (1H, m)

* In $CDCl_3$.

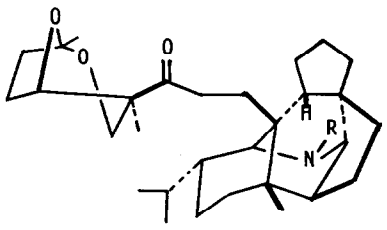
From a comparison of the NMR spectra between I and IV, it is clear that the stereochemistry at the carbon atom bearing both methyl and hydroxyl groups is different to each other. In addition, the proton corresponding to the NMR signal at δ3.37 is in an α-configuration, as shown in the structure (I) with the most stable conformation. Finally, the structure (I) thus obtained was confirmed by the following chemical evidences.

N-Acetylsecodaphniphylline (V)[3] was reduced with $NaBH_4$ in THF (room temp., overnight) to give the corresponding hydroxy-compound (VI) as a main product (in 72% yield), m.p. 216-217°; $C_{32}H_{51}O_4N$ (m/e 513(M^+)); ν_{max}(Nujol) 3480 and 1640cm^{-1}; $\delta(CDCl_3)$ 4.06(1H, m). When heated in AcOH at 110° for 4.5hr, the compound (VI) was recovered in spite of a vigourous condition enough to cleave a ketal ring in VI. This fact may be attributable to an un-



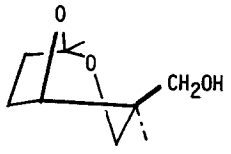
(I) R = H

(III) R = Ac

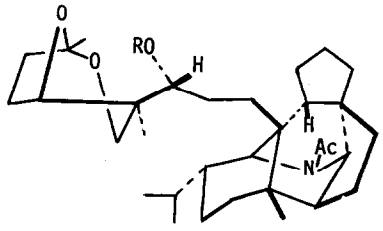


(II) R = H

(V) R = Ac



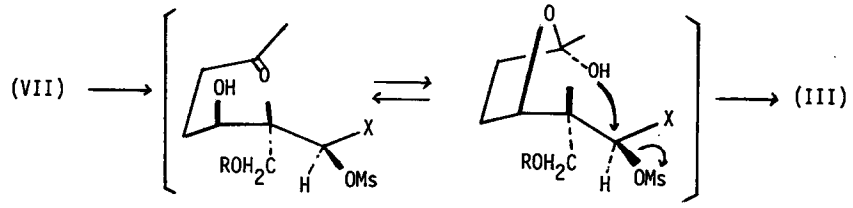
(IV)



(VI) R = H

(VII) R = Ms

favourable configuration of the newly formed hydroxyl group. Thus, VI was further treated with mesyl chloride-pyridine (room temp., 2.5hr) to give a viscous oil of the corresponding mesylate (VII), m/e 495(M^+- $MeSO_3H$); ν_{max}(film) 1640, 1360br. and 1335sh.cm^{-1}; $\delta(CDCl_3)$ 3.10(3H, s) and 5.47(1H, m). When treated with AcOH under the same condition as described above (110°, 4.5hr),[6] the mesylate (VII) was converted into N-acetyldaphniteijsmanine acetate (III), via a plausible intermediate (VIII), in 28% yield (TLC, IR, NMR and mass spectra).

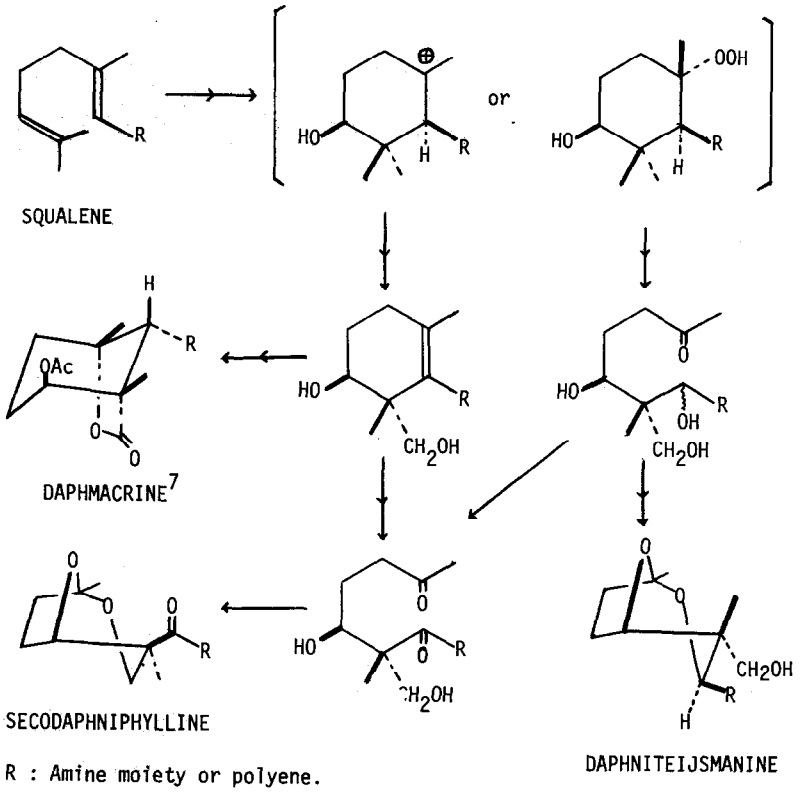


(VIII)

R = H or Ac; X: Amine moiety.

From a biogenetic point of view, the present studies showed a novel example in the field of triterpenoids as well as of triterpene alkaloids (see The Scheme)[1].

The Scheme. Biogenesis of the non-nitrogen containing moiety of the alkaloids.



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REFERENCES AND FOOTNOTES

1. K.T. Suzuki, S. Okuda, H. Niwa, M. Toda, Y. Hirata and S. Yamamura, Tetrahedron Letters 799 (1973).
2. S. Yamamura and Y. Hirata, Tetrahedron Letters in press (1974).
3. M. Toda, Y. Hirata and S. Yamamura, Tetrahedron 28, 1477 (1972).
4. Two signals at δ3.53 and 4.36 can be assigned to two protons attached to the carbon atoms bearing the N-Ac group, as found in the case of N-acetylsecodaphniphylline (V).
5. The ketal acid, an oxidation product of daphniphylline, was treated with excess diazomethane in Et_2O, and then reduced with $LiAlH_4$ in THF to give IV (H. Irikawa, N. Sakabe, S. Yamamura and Y. Hirata, Tetrahedron 24, 5691 (1968).
6. An olefin [$C_{32}H_{49}O_3N$; m/e 495(M^+); ν_{max}(Nujol) 1645cm^{-1}; δ($CDCl_3$) 5.42-5.96(2H, complex)] has been also obtained in 27% yield.
7. T. Nakano, Y. Saeki, C.S. Gibbons and J. Trotter, Chem. Commun. 600 (1968).