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FORMATION OF METHYL HOMODAPHNIPHYLLATE, A PLAUSIBLE INTERMEDIATE BETWEEN DAPHNIPHYLLINE AND YUZURIMINE, AND ISOLATION OF TWO NEW ALKALOIDS

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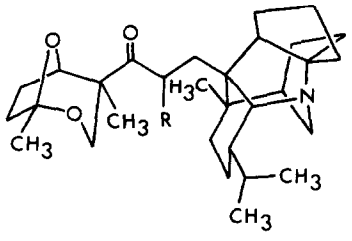
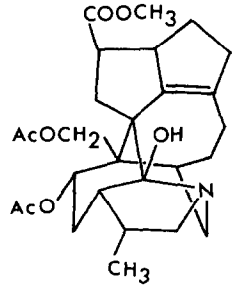
Daphniphyllum alkaloids are structurally divided into two groups, daphniphylline (I) (or codaphniphylline (II)) and yuzurimine (III), the main carbon skeleton of which consists of four isoprene units and an acetate (1). From a biogenetic point of view, methyl homodaphniphyllate (IV) is regarded as one of plausible intermediates between daphniphylline (I) and yuzurimine (III).



(I) R = OAc

(II) R = H

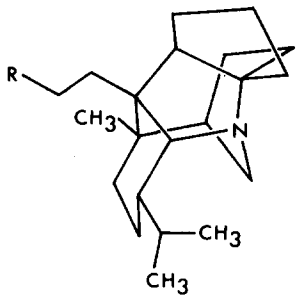
(V) R = OH

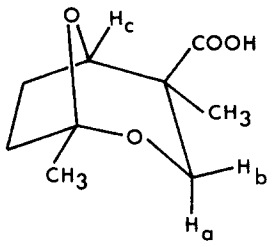


(III)

Oxidation of desacetyl daphniphylline (V) with sodium metaperiodate in aqueous methanol has been known to afford a ketal-acid (VI) and an unstable aldehyde which was reduced with sodium borohydride to an amino-alcohol (VII) (1). Treatment of VII with tosyl chloride in dry pyridine (at room temperature, overnight) afforded a tosylate (VIII), m.p. 107.5°, in 53 % yield, which reacted

with potassium cyanide in aqueous methanol (under reflux for 100 hr.) to give a mixture of two products, an amide (IX), m.p. 281° (in a sealed tube), and a cyano-compound (X), m.p. 156°, in 21 and 35 % yields, respectively. The above mixture was hydrolyzed with 6N HCl (under reflux for 6 hr.), and then treated again with 20% HCl - MeOH (at room temperature overnight) to give methyl homodaphniphyllate hydrochloride (IV), m.p. 234°; m/e 359 (M^+), 286 and 272; ν_{max}^{KBr} 2750 - 2400 br. and 1735 cm^{-1}; NMR spectrum: 0.93 (3H, d, J=6 cps), 1.04 (3H, s), 1.12 (3H, d, J=6 cps), 1.2 - 2.7 (22H, m), 3.1 - 3.5 (3H, m) and 3.63 ppm (3H, s), in 52 % yield. IV was also obtained, in about 20 % yield, by Beckmann rearrengement of codaphniphylline (II) followed by esterification





(VI)

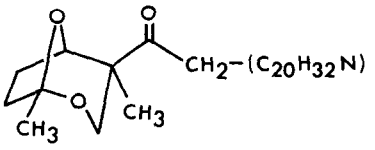
(IV) R = $COOCH_3$; (VII) R = OH

(VIII) R = OTs; (IX) R = $CONH_2$; (X) R = CN

with 6N HCl - MeOH. However, we have not yet found methyl homodaphniphyllate (IV) in Daphniphyllum Macropodium Miquel, from which seventeen alkaloids have been isolated in our laboratory (2).

Recently, we could isolate two new alkaloids (secodaphniphylline (XI), m.p. 130°; $C_{30}H_{47}O_3N$; m/e 469 (M^+), 344, 328, 316, 286 and 216; ν_{max}^{KBr} 1704 cm^{-1}, and methyl homosecodaphniphyllate (XII), m.p. 103°; $C_{23}H_{37}O_2N$; m/e 359 (M^+), 344, 328, 316, 286 and 216; ν_{max}^{KBr} 1735 cm^{-1}) from the same plant (3). The relationship between them was proved to be the same as that of daphniphylline - methyl homodaphniphyllate by the followings. In the comparison of NMR spectra between

The Scheme.



(XI)

$H_3COOC-CH_2-(C_{20}H_{32}N)$

(XII)

1)

1)

2),3),4)

N-Acetyl Secodaphniphylline (XIII) → N-Acetyl Homoseco-daphniphyllate (XIV)

1) Ac_2O - Pyridine, at room temperature overnight. 2) $NH_2OH \cdot HCl$ - Pyridine, at 90° for 24 hr. 3) MsCl - Pyridine, at 80° for 24 hr. 4) 6N HCl - MeOH, under reflux for 24 hr.

The Table.

VI	XI	XII
	0.77 (3H, s)	0.79 (3H, s)
1.03 (3H, s)	0.89 (3H, s)	
	0.89 (3H, d, J=6 cps)	0.89 (6H, d, J=6 cps)
	0.90 (3H, d, J=6 cps)	
1.50 (3H, s)	1.42 (3H, s)	
	2.51 (1H, d, J=4.2 cps)	2.53 (1H, d, J=4.2 cps)
	2.6 - 2.9 (2H, m)	2.1 - 2.5 (2H, m)
	3.01 (1H, br. s)	2.98 (1H, br. s)
3.63 ($1H^a$, d, J=12 cps)	3.49 (1H, d, J=12 cps)	
4.30 ($1H^b$, q, J=12, 2 cps)	4.23 (1H, q, J=12, 2 cps)	
4.77 ($1H^c$, m)	4.62 (1H, m)	
		3.67 (3H, s)

XI and XII, the former has each signal corresponding to protons of the ketal-acid (VI), a degradation product of daphniphylline (I). On the other hand, these signals are not found in the latter, but instead a methyl signal of the ester group is observed at 3.67 ppm. The remaining signals are nearly identical in both compounds (see the Table). Finally, the N-acetyl compound (XIII), which was obtained by acetylation of XI with acetic anhydride - pyridine, was converted into methyl N-acetyl homosecodaphniphyllate (XIV), m.p. 106.5°; $C_{25}H_{39}O_3N$; ν_{max}^{KBr} 1750 and 1650 cm^{-1}, which was also obtained by treatment of XII with acetic anhydride - pyridine, as described in the Scheme.

Structural studies on methyl homosecodaphniphyllate (XII) and other alkaloids isolated from Daphniphyllum Macropodium Miquel are now in progress.

Melting points are uncorrected. All compounds gave satisfactory physical data. Chemical shifts of all NMR spectra are given in ppm from an internal TMS standard using $CDCl_3$ as a solvent.

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REFERENCES

1. H. Irikawa, N. Sakabe, S. Yamamura and Y. Hirata, Tetrahedron, 24, 5691 (1968), and other references are cited therein.
2. To be published.
3. Secodaphniphylline (XI) and methyl homosecodaphniphyllate (XII) are isomers of codaphniphylline (II) and methyl homodaphniphyllate (IV), respectively. These alkaloids were isolated from methanol extracts of Daphniphyllum Macropodium Miquel by repeated coloumn chromatography using alumina (Nakarai Co. Ltd.) - n-hexane and then silica gel (Mallinckrodt, 100 Mesh) - Et_2O-Et_2NH (100 : 0.5).