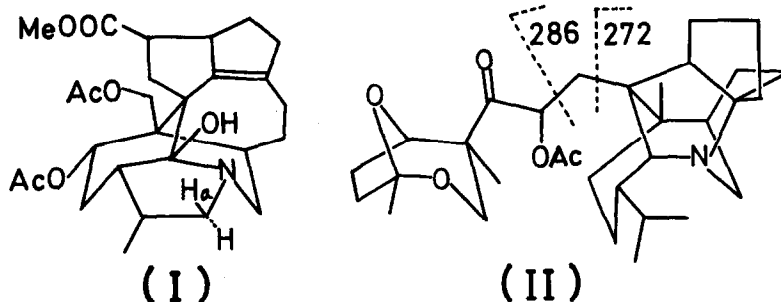


ISOLATION OF YUZURIMINES A AND B
FROM DAPHNIPHYLLUM MACROPODUM MIQUEL

Hiroshi Sakurai, Hajime Irikawa, Shosuke Yamamura and Yoshimasa Hirata
Chemical Institute, Faculty of Science, Nagoya University, Nagoya, Japan
(Received 1 May 1967; in revised form 17 May 1967)

In the previous paper (1, 2), we reported the isolation of five new alkaloids from Daphniphyllum macropodum Miquel. These alkaloids are structurally divided into two groups, yuzurimine (I) and daphniphylline (II)(3, 4, 5). The former has a secondary methyl group, a tertiary acetoxy-methyl group and a carbomethoxyl group, and there are no typical fragmentation peaks in its mass spectrum. On the other hand, in addition to the presence of five methyl groups, the latter has characteristic peaks at m/e 286 and 272 in its mass spectrum (2).



We further examined alkaloidal components of the above plant and could isolate two new alkaloids, yuzurimines A (m.p. 249 - 252°C (dec.) as hydrochloride) and B (m.p. 282 - 284.5°C as hydrochloride).

Extraction of the bark and leaves of the above plant by the previously reported method (1) gave a resinous substance, from which yuzurimines A and B were isolated by column chromatography on silica gel using the mixed solvent (hexane : ethyl ether : diethyl amine = 25 : 25 : 1). Yuzurimine A hydrochloride was recrystallized from methanol - ethyl ether to give colorless needles, m.p. 249 - 252°C (dec.)(in a sealed tube), having a molecular formula $C_{25}H_{35}O_5N \cdot HCl$ (UV spectrum: ϵ_{210}^{EtOH} 6250; IR spectrum: ν_{max}^{KBr} 3430, 2600 br.).

1732 br., 1240, 1164 and 1030 cm^{-1} ; mass spectrum: m/e 429 (M^+), 418 and 352). The IR spectrum of yuzurimine A hydrochloride is very similar to that of yuzurimine hydrochloride, as shown in Fig. 1. On the basis of careful comparison of the NMR spectra of yuzurimine and yuzurimine A coupled with the difference

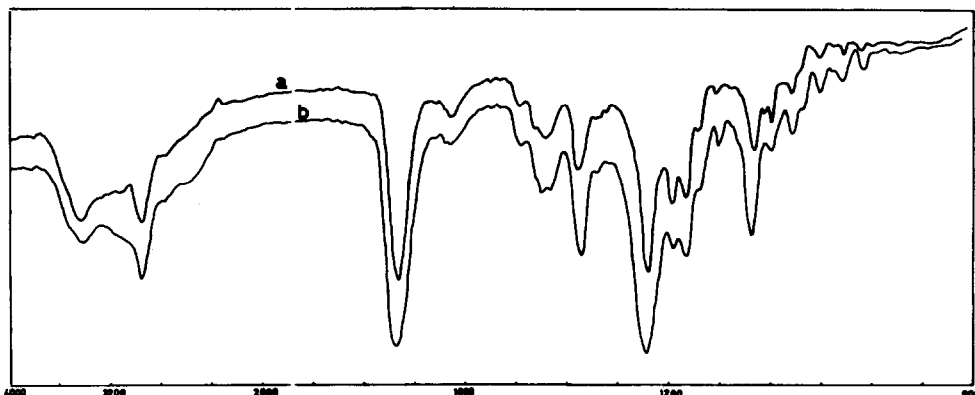


Fig. 1. The IR spectrum of yuzurimine A (a), and the IR spectrum of yuzurimine (b).

of mass number ($C_2H_2O_2 = 58$) between them, the structure of the latter can be deduced, as discussed below. The NMR spectra of yuzurimine and yuzurimine A are shown in Fig. 2 and 3, respectively (6). The significant differences

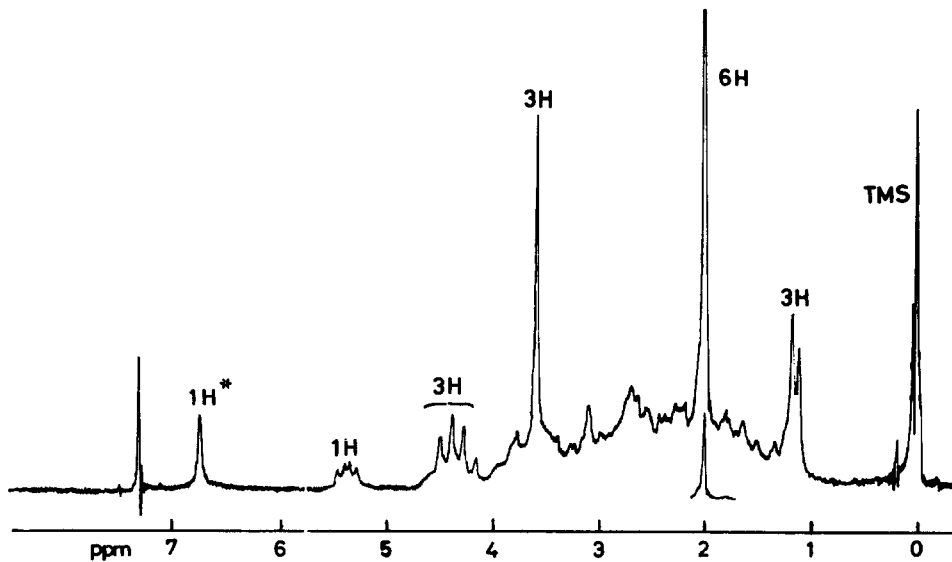


Fig. 2. The NMR spectrum of yuzurimine

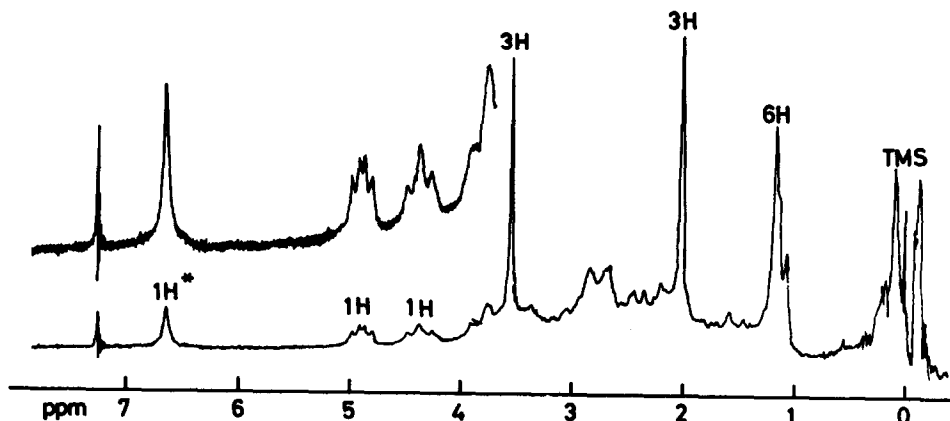


Fig. 3. The NMR spectrum of yuzurimine A

* Disappeared on addition of D₂O

between them are discussed below. The NMR signals at 1.98 ppm (6H, s) and an AB quartet centered at 4.32 ppm (2H, q, $J = 11$ cps) are assigned to acetoxy and acetoxy-methyl groups, respectively. On the other hand, yuzurimine A has tertiary methyl signals at 1.17 ppm instead of the acetoxy-methyl signals in yuzurimine. The remaining signals are nearly identical in both compounds. Each peak in the NMR spectra can be assigned, as described in Table I.

Table I

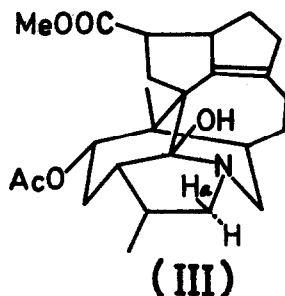
Yuzurimine	Yuzurimine A	Assignment
1.11 (3H, d, $J=7$ cps)	1.07 (3H, d, $J=7$ cps)	$\overset{ }{\text{C}}\text{H}-\text{Me}$
	1.17 (3H, s)	$\text{C}^{\dagger}-\text{Me}$
1.98 (6H, s)	2.01 (3H, s)	-CAc
3.53 (3H, s)	3.55 (3H, s)	-COOMe
3.20 - 4.00 (4H, br)*	3.20 - 4.00 (4H, br)*	
4.00 - 4.60 (1H, br)**	4.20 - 4.60 (1H, br)**	
4.32 (2H, q, $J=11$ cps)		$-\text{CH}_2\text{OAc}$
5.36 (1H, q, $J=7, 12$ cps)	4.89 (1H, q, $J=7, 12$ cps)	$-\text{CH}_2-\overset{ }{\text{C}}\text{H}-\text{CAc}$
6.66 (1H, s)	6.66 (1H, s)	$-\text{CH}$

Abbreviations: br, broad; d, doublet; q, quartet; s, singlet.

* Broad peaks in the 3.20 - 4.00 ppm region will be assigned to three of four protons on the carbon atoms attached to a nitrogen atom and an α -proton of carbomethoxyl group.

** A broad peak can be assigned to the proton (a) (in I and III). The lowering is due to the shielding effect of the nearby hydroxyl group.

Therefore, yuzurimine A can be regarded as desacetoxy-yuzurimine (III).



Yuzurimine B hydrochloride was recrystallized from methanol to afford white crystals, m.p. 282 - 284.5°C (in a sealed tube), having a molecular formula $C_{23}H_{33}O_3N \cdot HCl$ (UV spectrum: ϵ_{210}^{EtOH} 7230; IR spectrum: ν_{max}^{KBr} 3440, 2600 br., 1735, 1067 and 1028 cm^{-1} ; mass spectrum: m/e 371 (M^+), 354 and 340).

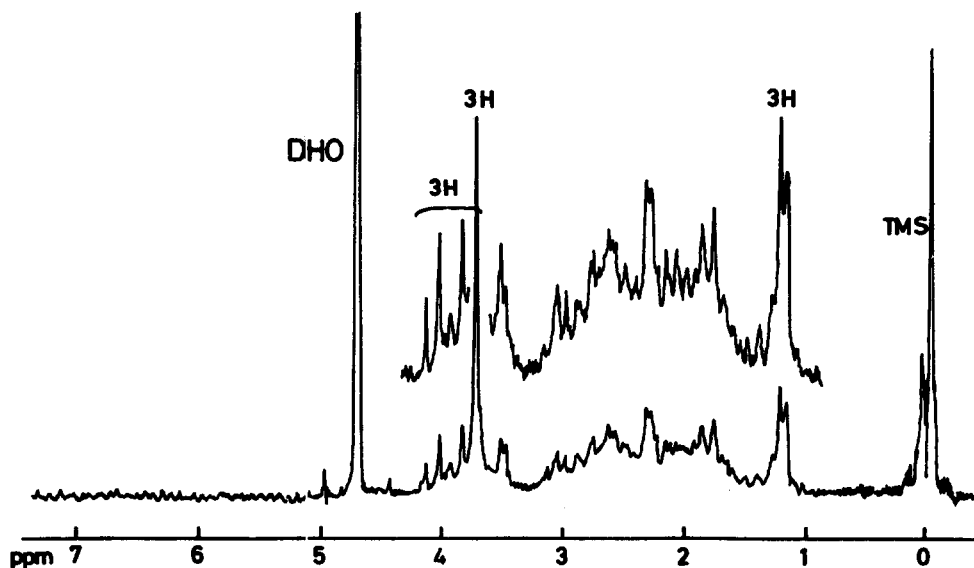
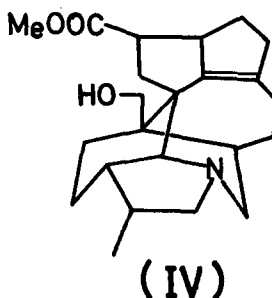


Fig. 4. The NMR spectrum of yuzurimine B

* Disappeared on addition of D_2O

The NMR spectrum of yuzurimine B hydrochloride in deuterium oxide is shown in Fig. 4. NMR signals at 1.22 (3H, doublet, $J = 6$ cps) and 3.72 ppm (3H, singlet) are due to secondary methyl and carbomethoxyl groups, respectively. Furthermore, the AB quartet centered at 3.94 ppm (2H, q, $J = 11.5$ cps) indicates the presence of a tertiary hydroxy-methyl group. This fact was supported by acetylation of yuzurimine B hydrochloride, which afforded a monoacetate hydrochloride, m.p. 266 - 267.5°C (m/e 413 (M^+), 370, 353 and 340; IR spectrum: $\nu_{\text{max}}^{\text{KBr}}$ 2600 br., 1737, 1240 and 1032 cm^{-1} (no hydroxy absorpction band)). In its NMR spectrum, the new signals at 2.08 (3H, singlet) and 4.47 ppm (2H, singlet) are observed instead of the AB quartet at 3.94 ppm in yuzurimine B.

Finally, comparison of the NMR spectra (Fig. 2 and 4) between yuzurimine and yuzurimine B coupled with the difference of molecular weight ($\text{C}_{44}\text{H}_{44}\text{O}_4 = 116$) and absence of the acetoxy group in the latter suggests the structure IV for yuzurimine B. Studies are now in progress to transform yuzurimine (I) into yuzurimines A and B.



All m.ps are uncorrected. Satisfactory analyses were obtained for all new compounds described herein.

Acknowledgements: The authors are grateful to Takeda Chemical Industries, LTD. for measurement of NMR spectra. They are also indebted to the National Institutes of Health, U.S.A., which supported this work through Grant RG-7969 and GM-7969.

REFERENCES

1. N. Sakabe, H. Irikawa, H. Sakurai and Y. Hirata, Tetrahedron Letters, 9, 963 (1966).
2. H. Irikawa, H. Sakurai, N. Sakabe and Y. Hirata, Tetrahedron Letters, 44,

5363 (1966).

3. N. Sakabe and Y. Hirata, Tetrahedron Letters, 9, 965 (1966).
4. H. Sakurai, N. Sakabe and Y. Hirata, Tetrahedron Letters, 50, 6309 (1966).
5. H. Irikawa, S. Yamamura, N. Sakabe and Y. Hirata, Tetrahedron Letters, 6, 553 (1967).
6. Chemical shifts of all NMR spectra are given in ppm from an internal TMS standard using CDCl_3 as a solvent unless otherwise stated.