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THE STRUCTURE OF YUZURINE

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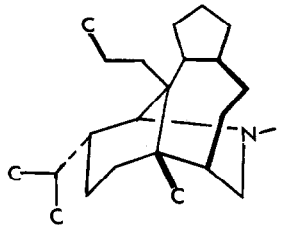
The plant Daphniphyllum macropodum Miquel ("Yuzuriha" in Japanese) contains a great variety of related alkaloids, which can be regarded as a triterpene alkaloid.[1] From a structural point of view, they are divided into five types of nitrogen heterocyclic skeleton. However, all of them possess in common the 2-azabicyclo[3.3.1]nonane system [A], a part of which constitutes a part of the bicyclo[5.3.0]decane system. Thus, these daphniphyllum alkaloids are formally related to one another by bond formation or fission.[2] In the present paper, we wish to describe the novel structure of a new daphniphyllum alkaloid, named "Yuzurine",[3] which has no 2-azabicyclo[3.3.1]nonane system and differes from the other structurally known alkaloids that have been isolated from the plant Daphniphyllum macropodum Miquel.

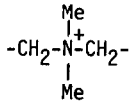
Yuzurine (I), which has been isolated from the bark and leaves of the same plant,[3] is a colourless viscous liquid with a molecular formula [$C_{24}H_{37}O_4N$; ν_{max}(KBr) 1740cm^{-1}; m/e 403 (M^+); δ($CDCl_3$) 0.85(3H, t, J= 7.4Hz), 2.17(3H, s), 3.21(3H, s), 3.64(3H, s) and 3.93ppm(2H, s)], and characterized as the corresponding methiodide (II) [m.p. 229-230°; $C_{25}H_{40}O_4NI$; ν_{max}(Nujol) 1740cm^{-1}; m/e 403 (M^+), 388, 371, 314 and 287; δ($CDCl_3$) 0.88 (3H, t, J= 7.5Hz), 3.20(3H, s), 3.35(1H, br.d, J= 13.5Hz), 3.57(3H, s), 3.64(3H, s), 3.67 (3H, s), 3.70-3.85(1H, overlapped at δ3.67 and 3.85ppm), 3.85(2H, br.s), 4.06(1H, d, J= 12.0Hz) and 4.10ppm(1H, d, J= 13.5Hz).

From the above spectral data, yuzurine (I) seems to be quite different from the other daphniphyllum alkaloids, whose structures have been already established. Firstly, this new

alkaloid has CH_3CH_2- grouping [δ 0.85ppm(3H, d, J= 7.4Hz)]. Furthermore, the NMR spectrum of the free base indicates the presence of each one MeN and MeO group (δ 2.17 and 3.21ppm) in addition to a carbomethoxyl group (ν_{max} 1740cm^{-1} and δ 3.64ppm). As expected, two methyl groups attached to the nitrogen atom (δ 3.57 and 3.64ppm (or 3.67)) were found in the case of the corresponding methiodide (II). Secondly, three doublets with geminal coupling constants (12 - 13.5Hz) were newly observed at δ3.35, 4.06 and 4.10ppm in the NMR spectrum of II. In addition, the NMR signal corresponding to the geminal doublet at δ4.06ppm is present at δ3.67 - 3.85ppm. From these data, the methiodide (II) must have a partial structure [B]. Finally, the complex structure of yuzurine (I) was elucidated by an X-ray crystallographic analysis of the corresponding methiodide (II).

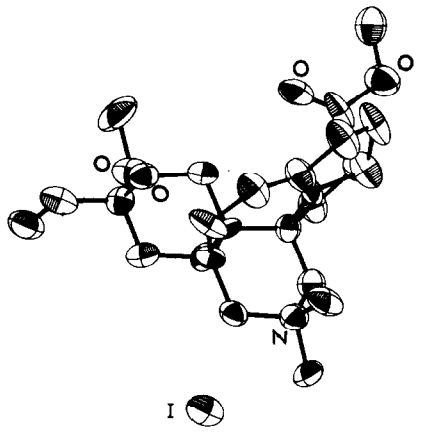


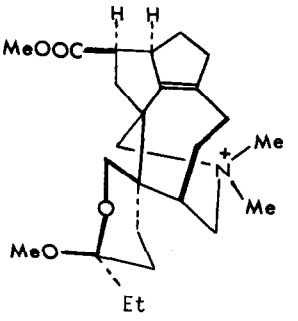
[A]



[B]

Recrystallization of II from benzene - MeOH afforded pale yellow needles, which were shown to be orthorhombic with unit cell dimensions of a = 16.403, b = 9.549, c = 16.612Å and belong to space group $P_{2_12_12}$. The density measured by the flotation method using a mixed solvent of n-hexane - CCl_4 is 1.39g·cm^{-3}, which agreed with the calculated value of 1.392g·cm^{-3} based on the presence of four molecules in a unit cell. Lattice constant and intensities were measured on a Hilger and Watts four-circle automatic diffractometer Y-290 with Cu - K_α radiation. A total 1733 independent non-zero intensities were collected in the range, $\theta \leq 68°$. The structure was solved by heavy-atom method using our programs. Refinement of the structural parameters was carried out by the block-diagonal least-squares calculation with anisotropic thermal parameters, and the R factor was 0.080. The molecular shape of II is shown in Fig. 1. The structure (II) so far obtained is in good agreement with the physical data of yuzurine methiodide. Therefore, the structure of yuzurine should be represented by I.





(II)

Fig. 1. Three-dimensional view of yuzurine methiodide (II) with spheres of arbitrary radius.

From a structural point of view, yuzurine (I) can be included in the yuzurimine group of alkaloids, although it lacks the 2-azabicyclo[3.3.1]nonane system, which is found in the cases of the other hitherto known daphniphyllum alkaloids.

Biogenetically, this alkaloid may be derived from yuzurimine-B (III), whose stereostructure has been already established[4], as shown in the next page (see Fig. 2).

REFERENCES

1. K. T. Suzuki, S. Okuda, H. Niwa, M. Toda, Y. Hirata and S. Yamamura, Tetrahedron Letters, 799 (1973).

2. M. Toda, H. Niwa, H. Irikawa, Y. Hirata and S. Yamamura, Tetrahedron in press (1974).

3. Yuzurine has been cited as the Alkaloid-A_2 (M. Toda, Y. Hirata and S. Yamamura, Tetrahedron, 28, 1477 (1972)).

4. H. Irikawa, S. Yamamura and Y. Hirata, ibid., 28, 3727 (1972).

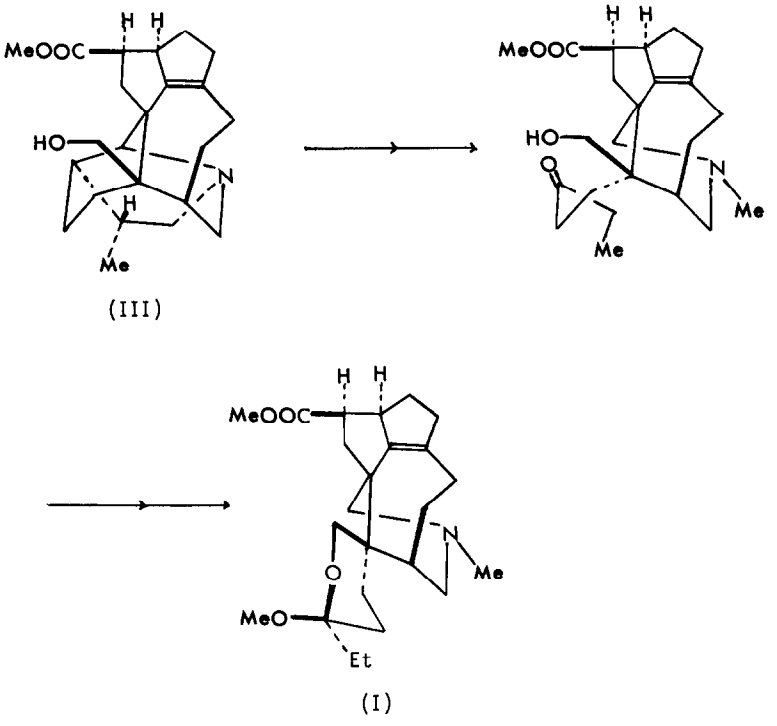


Fig. 2. A plausible pathway from yuzurimine-B to yuzurine.