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DAPHNILACTONE-B, A MAJOR ALKALOID, FROM THE FRUITS OF DAPHNIPHYLLACEAE[*]

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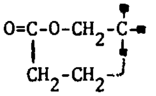
Studies on daphniphyllum alkaloids have been carried out mainly by two groups.[1] We further examined alkaloidal components of the fruits of three kinds of plants growing in Japan [Daphniphyllum macropodum Miquel (yuzuriha), Daphniphyllum teijsmanni Zollinger (Himeyuzuriha) and Daphniphyllum humile Maxim (Ezoyuzuriha)], and could isolate a new major alkaloid, daphnilactone-B (I), from all of them.[2] In the present paper, we describe the isolation and structure of daphnilactone-B, a biogenetically important substance, and the chemical transformation of it to a daphniphylline-type compound.

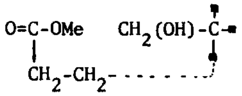
The fruits of Daphniphyllum teijsmanni Zollinger were pulverized and extracted with large amounts of MeOH. According to essentially the same procedure as already described,[3] an oily material containing alkaloidal components was obtained from the methanol extracts, and then chromatographed on basic alumina (Nakarai Chemical Co. Ltd., 300 mesh) and eluted, in the following order, with n-hexane, n-hexane - benzene (1 : 1), benzene and $CHCl_3$ to give six alkaloids [1, methyl homosecodaphniphyllate in 0.00013% yield (with n-hexane).[3] 2, methyl homodaphniphyllate (II) and daphniphylline in 0.00006 and 0.00031% yields, respectively (with n-hexane - benzene (1 : 1).[4,5] 3, daphnilactone-B in 0.033% yield (with benzene). 4, yuzurimine and yuzurimine-B (III) in each 0.0006% yield ($CHCl_3$)[6]].[7]

Daphnilactone-B (I), m.p. 92-94°, has a molecular formula $C_{22}H_{31}O_2N$ [m/e 341 (M^+)], ν_{max} ($CHCl_3$) 1726cm^{-1} and no NH; δ($CDCl_3$) 1.00 (3H, d, J= 6.0Hz), 3.63 (1H, d, J= 13Hz), 4.73 (1H, d, J= 13Hz) and 5.67ppm (1H, br.s, Wh= 5.5Hz). The presence of a lactone ring (A) is confirmed by its spectral data [ν_{max} 1726cm^{-1}; δ 3.63 (1H, d, J= 13Hz) and 4.73ppm

(1H, d, J= 13Hz)] coupled with the chemical evidences, as follows. When treated with NaOMe-MeOH (room temp., overnight), daphnilactone-B (I) was converted into the corresponding methyl ester (B) having a hydroxy-methyl group, m/e 373 (M^+); ν_{max} ($CHCl_3$) 3600, 3400 and 1730cm^{-1}; δ($CDCl_3$) 3.60 (1H, d, J= 9.5Hz), 3.62 (3H, s) and 4.22ppm (1H, d, J= 9.5Hz).[8]



(A)



(B)

In the mass spectrum of the ester, a pair of the remarkable peaks are observed at m/e 300 and 286, indicating the presence of $-CH_2CH_2COOMe$ in (B). Furthermore, only one methyl doublet at δ1.04ppm (or 1.00ppm) is observed in the NMR spectrum of the ester (or I), which is similar to that of yuzurimine-B (III). In conclusion, when considered in the light of co-occurrence of methyl homodaphniphyllate (II) and yuzurimine-B (III) (or yuzurimine), the structure (I) of daphnilactone-B can be derived from a common intermediate (IV)[3,9] except for a biogenetically expected position of the trisubstituted double bond [δ 5.67ppm (1H, br.s, Wh= 5.5Hz)], which has recently been established by X-ray analysis of the free base (I).[10]

From a biogenetic point of view, daphnilactone-B (I) is regarded as one of the important intermediates between methyl homodaphniphyllate (II) and yuzurimine-B (III) (or yuzurimine). Finally, I was successfully converted into a daphniphylline-type compound, as follows. When treated with BrCN - K_2CO_3 in benzene (room temp., overnight), I afforded in 90% yield a bromo-cyanamide (V) [m.p. 210° (decomp.); ν_{max} ($CHCl_3$) 2240cm^{-1}; δ ($CDCl_3$) 3.58ppm (2H, br.s); m/e 448 and 446 (M^+)], in which a position of the bromine atom was determined by dehydrobromination with AgF - pyridine giving an olefin (VI), m.p. 198-200°; m/e 366 (M^+); ν_{max} ($CHCl_3$) 1645cm^{-1}; δ ($CDCl_3$) 1.92 (3H, s), 4.96 (1H, br.s) and 5.10ppm (1H, br.s). Further treatment of V with $NaBH_4$ in dimethylsulfoxide (room temp., overnight) afforded the corresponding debromo-cyanamide (VII) in 50% yield, m.p. 208-212°; m/e 368 (M^+); ν_{max} ($CHCl_3$) 2240 and 1735cm^{-1}; δ($CDCl_3$) 0.98 (3H, d, J= 5.5Hz), 1.06 (3H, d, J= 5.5Hz), 3.05 (1H, br.d, J= 13.5Hz), 3.41 (1H, br.s), 3.75 (1H,d, J= 13.0Hz), 4.11 (1H, q, J= 13.5, 7.2Hz), 4.85 (1H, d, J= 13.0Hz) and 5.85ppm (1H, br.m, Wh= 5.4Hz). Finally, when treated with 90% HCOOH (under reflux, overnight), VII afforded a daphniphylline-type compound (VIII) in 55% yield, m.p. 166-168°, the structure of which was supported by its physical data [$C_{22}H_{33}O_2N$ (m/e 343 (M^+)); ν_{max} ($CHCl_3$) 1730cm^{-1} and no NH; δ($CDCl_3$) 0.92 (3H, d, J= 6.2Hz), 1.00 (3H, d, J= 6.2Hz), 2.50-2.90 (4H, complex),[11] 3.38 (1H, br.d, J= 12.5Hz), 3.52 (1H, d, J= 12.5Hz) and 4.67ppm (1H, d, J= 12.5Hz)] coupled with von Brown degradation of VIII, as follows: VIII reacted with BrCN - K_2CO_3 in benzene (room temp., overnight) to give in 90% yield a cyanamide (IX), an isomer of VII, m.p. 233-235°; m/e 368 (M^+); ν_{max} ($CHCl_3$) 2240 and 1735cm^{-1}; δ($CDCl_3$) 0.98 (3H, d, J= 6.0Hz), 1.06 (3H, d, J= 6.0Hz), 3.02 (1H, br.d, J= 14.0Hz), 3.28 (1H, d, J= *ca*. 2Hz), 3.70 (1H, d, J= 13.0Hz), 4.12 (1H, q, J= 14.0, 7.0Hz), 5.08 (1H, d, J= 13.0Hz) and 5.72ppm (1H, br.m, Wh= 15Hz). In particular, the Wh-value (15Hz) of the NMR signal at δ5.72ppm indicates that the newly formed trisubstituted double bond must be included in the seven-membered ring in contrast with those of I and VII [δ5.67 (1H, br.s, Wh=5.5Hz) and 5.87ppm (1H, br.s, Wh= 5.4Hz), respectively].[12]

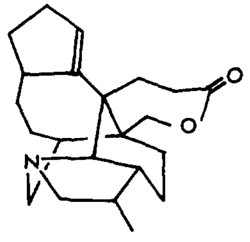
All compounds gave satisfactory physical data and elemental analyses.

REFERENCES AND FOOTNOTE

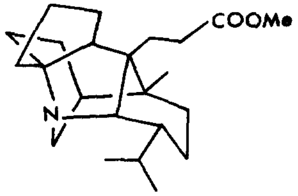
* Daphniphyllaceae has often been included in Euphorbiaceae.

1. O.E. Edwards in "The Alkaloids Vol. 1", The Chemical Society, London, 1971, p. 375 and references cited therein; M. Toda, H. Irikawa, S. Yamamura and Y. Hirata, *Nippon Kagaku Zasshi*, **91**, 103 (1970).
2. Each alkaloidal component is pretty similar to each other on analytical TLC plate (Kieselgel GF_{254}) using n-hexane-Et_2O-Et_2NH (20 : 20 : 3) as solvent.
3. M. Toda, Y. Hirata and S. Yamamura, *Tetrahedron*, **28**, 1477 (1972).
4. M. Toda, S. Yamamura and Y. Hirata, *Tetrahedron Letters*, 2585 (1969).
5. H. Irikawa, N. Sakabe, S. Yamamura and Y. Hirata, *Tetrahedron*, **24**, 5691 (1968).
6. H. Sakurai, H. Irikawa, S. Yamamura and Y. Hirata, *Tetrahedron Letters*, 2883 (1967); H. Irikawa, S. Yamamura and Y. Hirata, *Tetrahedron* in press (1972).
7. Daphnilactone-B and methyl homodaphniphyllate have been found only in the fruits.
8. The methyl ester (B) was easily reconverted into the original lactone, when allowed to stand at room temperature.
9. Probably, C_{22}-compounds are not derived from four mevalonates and one acetate,[1] but formed by an oxidative removal of eight carbon atoms from C_{30}-compounds (daphniphylline or secodaphniphylline).
10. K. Sasaki and Y. Hirata, To be published.

11. The signals corresponding to two protons attached to the carbon atoms bearing the nitrogen atom are shifted to lower field in the NMR spectrum of the hydrochloride.
12. Von Brown degradation of daphniphylline-type compounds have already been known to give the corresponding cyanamides, which have the same trisubstituted double bond as that of IX.



(I)



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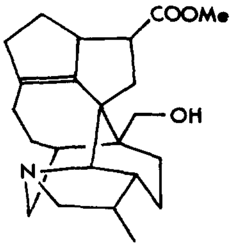

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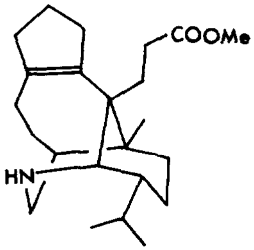

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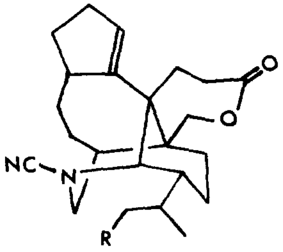
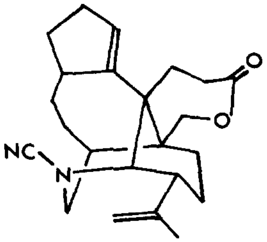
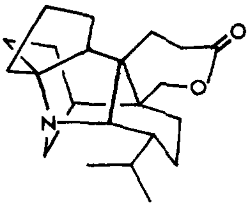


(V) R = Br

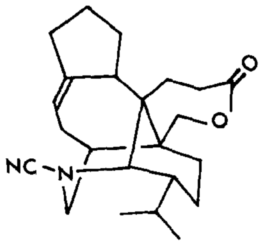
(VII) R = H



(VI)



(VIII)



(IX)