

N-terminal amino acids are characterized as DNP-derivatives simultaneously in the C-terminal determination procedure.

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### 2-(2-Heptenyl)-3-methyl-4-quinolinol from a *Pseudomonas*

Recently K. Arima and others have established the structure of pyrrolnitrin (I),<sup>1)</sup> a metabolite of a *Pseudomonas*. From the same strain, the authors have isolated isopyrrolnitrin (II)<sup>2)</sup> and oxypyrrolnitrin (III).<sup>3)</sup> In the course of our investigation, the fourth metabolite was isolated from the acetone extract of the bacterial cells.

This substance, m.p. 255° (decomp.), possesses an empirical formula of C<sub>17</sub>H<sub>21</sub>ON (Anal. Calcd.: C, 79.96; H, 8.29; N, 5.49. Found: C, 80.27; H, 8.57; N, 5.45. mol. wt. 255 by mass spectrometry).

The UV spectrum (Fig. 1) has a bifurcation at the 320~340 μm region in the neutral medium, which is characteristic in 4-quinolinol derivatives. The absorption of hydroxy group in the IR spectrum appears broad at 3200~2500 cm<sup>-1</sup>. The NMR spectrum (60 Mc) in CF<sub>3</sub>COOH exhibits the following signals: δ=8.48 p.p.m. (1H, broad doublet), ca. 8.0 p.p.m. (3H, multiplet), ca. 5.8 p.p.m. (2H, multiplet), 3.72 p.p.m. (2H, doublet), 2.53 p.p.m. (3H, singlet), ca. 2.2 p.p.m. (2H, broad quartet), ca. 1.4 p.p.m. (4H, broad multiplet) and 0.95 p.p.m. (3H, destroyed triplet). Suitable structure for the metabolite is represented by VI. The presence of 2-heptenyl group is supported by the appearance of the base peak at m/e (M-43) on the mass spectrum.

Catalytic reduction in EtOH in the presence of Adams' platinum oxide gave dihydro derivative (V), m.p. 231~233° (C<sub>17</sub>H<sub>23</sub>ON, Anal. Calcd.: C, 79.33; H, 9.01; N, 5.44. Found: C, 79.62; H, 9.22; N, 5.36). On the other hand, the reduction in glacial AcOH in the presence of the same catalyst afforded hexahydro derivative (VI), m.p. 268~270° (C<sub>17</sub>H<sub>27</sub>ON, Anal. Calcd.: C, 78.11; H, 10.41; N, 5.36. Found: C, 78.26; H, 10.21; N, 5.36). The UV spectrum, λ<sub>max</sub><sup>EtOH</sup>

- 1) K. Arima, H. Imanaka, M. Kousaka, A. Fukuta, G. Tamura: J. Antibiotic, Ser. A, 18, 201 (1965).
- 2) M. Hashimoto, K. Hattori: Bull. Chem. Soc. Jap., 39, 410 (1966).
- 3) *Idem*: This Bulletin, 14, 1314 (1966).

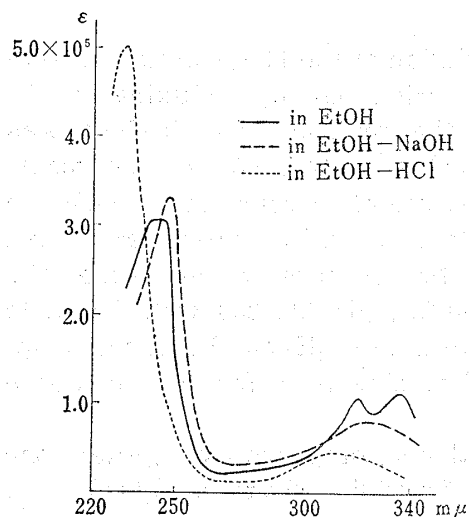
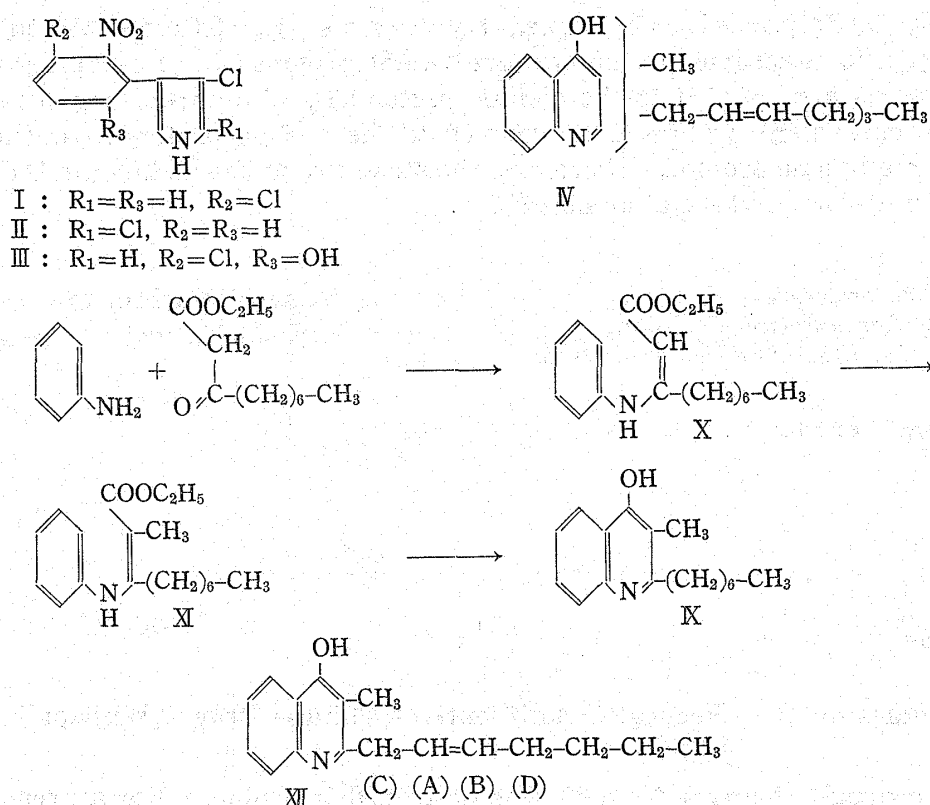


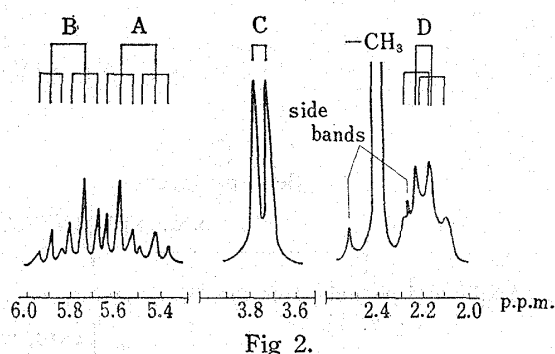
Fig. 1.



$m\mu$  ( $\epsilon$ ): 224 (20,200), 268 (14,300) (the addition of HCl moves the maxima to 244  $m\mu$ ), indicates that the 4-hydroxypyridine nucleus has not been changed during the reduction. VI has no aromatic proton signal in the NMR spectrum (60 Mc) in  $CF_3COOH$ : ca.  $\delta=2.9$  p.p.m. (6H, multiplet), 2.40 p.p.m. (3H, singlet), ca. 2.0 p.p.m. (4H, multiplet), ca. 1.4 p.p.m. (10H, broad multiplet) and 0.92 p.p.m. (3H, destroyed triplet). This fact shows that the methyl and the heptyl groups are attached to the pyridine nucleus. The structure of the metabolite can be extended from IV to 2-(2-heptenyl)-3-methyl-4-quinolinol (VII) or 2-methyl-3-(2-heptenyl)-4-quinolinol (VIII). And the fact that some 2-*n*-alkyl-4-quinolinol\*<sup>1</sup> have been isolated from certain strains of *Pseudomonas*<sup>4)</sup> may explain VII to be preferable to VIII.

2-Heptyl-3-methyl-4-quinolinol (IX) was synthesized as follows. Ethyl 3-ketodecanoate and aniline were condensed and the product (X) was converted to methylated derivative (XI) by metal sodium and methyl iodide in dry benzene. XI was cyclized by reflux in diphenylether to give IX, which was identical with V derived from the natural metabolite.

The position of the double bond is established by NMR (100 Mc) spectrum\*<sup>2</sup> in  $CF_3COOH$  (Fig. 2). Two olefinic protons form the AB component of an  $ABX_2V_2$  system:  $\delta_A=$



\*<sup>1</sup> 2-Heptyl-4-quinolinol (Pyo Ib), 2-nonyl-4-quinolinol (Pyo Ic), 2-(1-nonenyl)-4-quinolinol (Pyo III), 2-undecyl-4-quinolinol, 2-heptyl-4-quinolinol N-oxide, 2-octyl-4-quinolinol N-oxide, 2-nonyl-4-quinolinol N-oxide and 2-undecyl-4-quinolinol N-oxide.

\*<sup>2</sup> We thank M. C. Woods, Tohoku University, for measurement of 100 Mc. NMR spectrum.

4) E. E. Hays, I. C. Wells, P. A. Katzman, C. K. Cain, F. A. Jacobs, S. A. Thayer, E. A. Daisy, W. L. Gaby, E. C. Roberts, R. D. Muir, C. J. Carroll, L. R. Jones, N. J. Wade: *J. Biol. Chem.*, **196**, 331 (1952). J. W. Lightbown: *Nature London*, **166**, 356 (1950). *Idem*: *J. Gen. Microbiol.*, **11**, 477 (1954). J. W. Cornforth, A. T. James: *Biochem. J.*, **63**, 124 (1956).

5.66 p.p.m.,  $\delta_B = 5.85$  p.p.m.,  $J_{AB} = 15.5$  c.p.s.,  $J_{AC} = 6.0$  c.p.s.,  $J_{BD} = 6.0$  c.p.s. A doublet ( $J = 6.0$  c.p.s) at 3.72 p.p.m. is assigned to the two equivalent protons (C). Decoupling shows that these two protons are coupled to the clefinic proton (A). A quartet (doublet of triplets) from the two equivalent protons (D) is coupled to the clefinic proton (B) and also to the two adjacent methylene protons. Therefore, the structure of the metabolite is determined as 2-(2-heptenyl)-3-methyl-4-quinolinol (XII).

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### Studies on the Chemical Constituents of Chinese Drug "Wujiapi"

A Chinese drug "Wujiapi" (五加皮) was described in Chinese literatures since two thousand years ago and widely employed as a tonic. As the original plants of this drug, more than seventeen plants are recorded, most of which belong to Araliaceae, but only one, *Periploca sepium* BGE. (北五加皮), belongs to Asclepiadaceae.<sup>1a, b)</sup>

It should be noted that the plants of different families are employed under the same name for the same purpose. The drug material, "Wujiapi," which was imported from China was extracted with hot ethanol. After evaporation of the solvents in vacuum, the syrupy brown residue was dissolved in water and extracted with benzene. The benzene-soluble fraction was washed with 2N NaOH [Fr. I] and then 2N HCl [Fr. II].

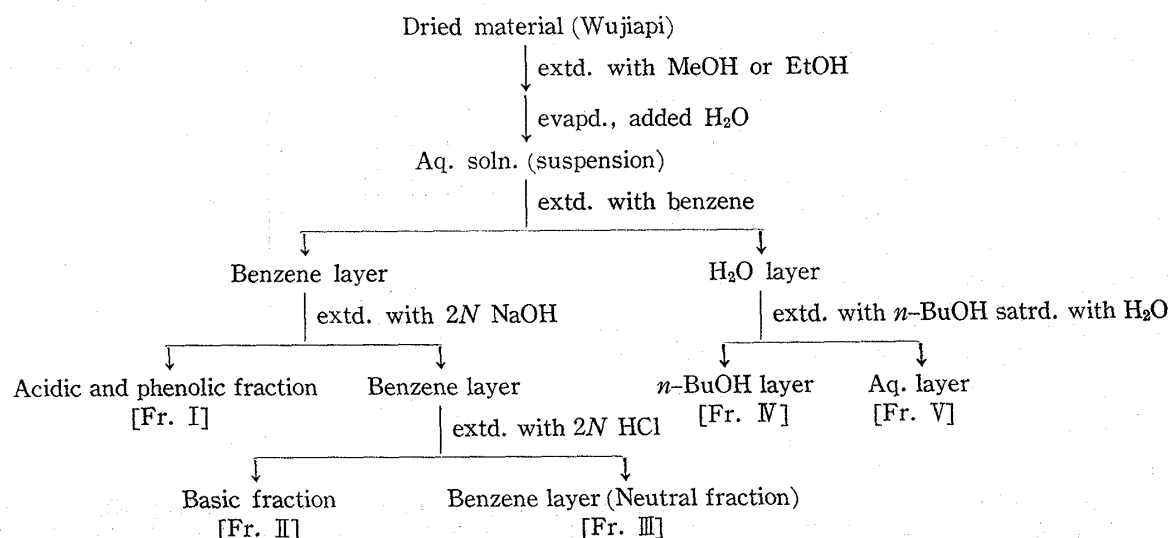


Chart 1. Extraction and Isolation

1a) "Zhong Yao Zhi" (中藥志), Vol. III, p. 402 (Pharmaceutical Institute, Chinese Academy of Medical Science, Peking (1961)). 1b) J. Sato; On the Chinese Medicinal Plants (漢藥の原植物), p. 34 (Japan Society for Promotion of Science, Tokyo (1959)).