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BITTER PRINCIPLES OF PICRASMA AILANTHOIDES PLANCHON

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The bitter principles of various genera of the family Simaroubaceae have been studied by several groups of workers in recent years (1). We now wish to report the isolation and the determination of the structures of three new bitter substances, nigakilactone A, B and C, from Picrasma ailanthoides Planchon (2) (Japanese name : nigaki, Simaroubaceae). A fourth constituent, nigakilactone D, is identical with quassin.

The concentrated aqueous extract of the stem-chips of the plant was further extracted with benzene and the extract was purified by repetition of chromatography and recrystallization giving rise to four bitter principles, nigakilactone A, B, C and D.

Nigakilactone A, B and C were shown to be closely related lactones in the following way. Methylation of nigakilactone A (I) $\left[\text{m.p. } 237.5\text{-}238^\circ, C_{21}H_{30}O_6, M^+ 378, [\alpha]_D + 35^\circ (c=0.26, \text{ in EtOH}), \lambda_{max}^{EtOH} 271 \text{ nm } (\varepsilon\ 4{,}800); \text{IR (nujol)}, 3570, 3490, 1720, 1680, 1635 \text{ cm}^{-1}\right]$ with CH_3I-Ag_2O-dimethylformamide gave nigakilactone B (II) $\left[\text{m.p. } 278.5^\circ, C_{22}H_{32}O_6, M^+ 392, [\alpha]_D + 17^\circ (c=0.19, \text{ in EtOH}), \lambda_{max}^{EtOH} 272 \text{ nm } (\varepsilon\ 6{,}700); \text{IR (nujol)}, 3460, 1725, 1675, 1630 \text{ cm}^{-1}\right]$, which was formed by alkaline hydrolysis of nigakilactone C (III) $\left[\text{m.p. } 252.5\text{-}253^\circ, C_{24}H_{34}O_7, [\alpha]_D + 9^\circ (c=0.28, \text{ in EtOH}), \lambda_{max}^{MeOH} 265 \text{ nm } (\varepsilon\ 4{,}300); \text{IR (nujol)}, 1735, 1730, 1700, 1625 \text{ cm}^{-1}\right]$. The latter compound (III) was obtained on acetylation of II with Ac_2O-pyridine.

Nigakilactone A (I) afforded a monoacetate (IV) (3) $\left[\text{m.p. } 224\text{-}225^\circ, C_{23}H_{32}O_7, M^+ 420, \lambda_{max}^{MeOH} 273 \text{ nm } (\varepsilon\ 4{,}000); \text{IR (nujol)}, 3430, 1740, 1720, 1685, 1630 \text{ cm}^{-1}\right]$

TABLE 1. PMR spectral data (δ in ppm)[a]

Compounds	I	II	III	IV	V	VI	VIII
$C-\overset{C}{\underset{C}{C}}-C\underline{H}_3$	1.24 s 1.42 s	1.21 s 1.45 s	1.27 s 1.27 s	1.25 s 1.42 s	1.18 s 1.63 s	1.05 s 1.64 s	1.18 s 1.54 s
$C-\overset{C}{\underset{H}{C}}-C\underline{H}_3$	1.01 d J=6.5 1.10 d J=6	1.00 d J=6.5 1.13 d J=6.5	1.01 d J=6 1.06 d J=7	0.89 d J=6 1.11 d J=6.5	1.06 d J=6.5 1.12 d J=7	1.10 d J=6 1.17 d J=6.5	1.11 d J=7
$C=C-C\underline{H}_3$	-	-	-	-	-	-	1.85 s
$-O-CO-C\underline{H}_3$	-	-	1.95 s	2.06 s	2.17 s	-	-
$-O-C\underline{H}_3$	3.54 s	3.60 s 3.65 s	3.42 s 3.54 s	3.51 s	3.56 s	3.55 s	3.54 s 3.65 s
$C-\overset{C}{\underset{\underline{H}}{C}}-O-$	4.10 m	4.15 m	4.14 m	4.10 m	4.37 m	4.30 m	4.36 m
$C\underline{H}-OAc$	-	-	5.22 q J=11 J=9	4.80 q J=11 J=9	5.23 d J=12	-	-
$C=C\underline{H}$	5.35 d J=2.5	5.45 d J=2.5	5.10 d J=2.5	5.31 d J=2	5.38 d J=2.5	5.37 d J=2.5	5.29 d J=2

[a] Determined in $CDCl_3$ at 60 MHz. Coupling constants are expressed in Hz. s: singlet, d: doublet, q: quartet, m: multiplet.

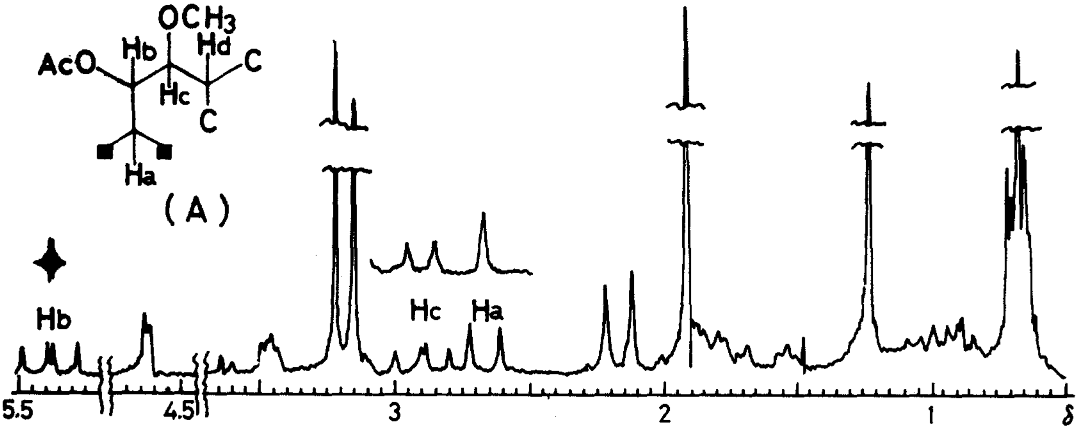


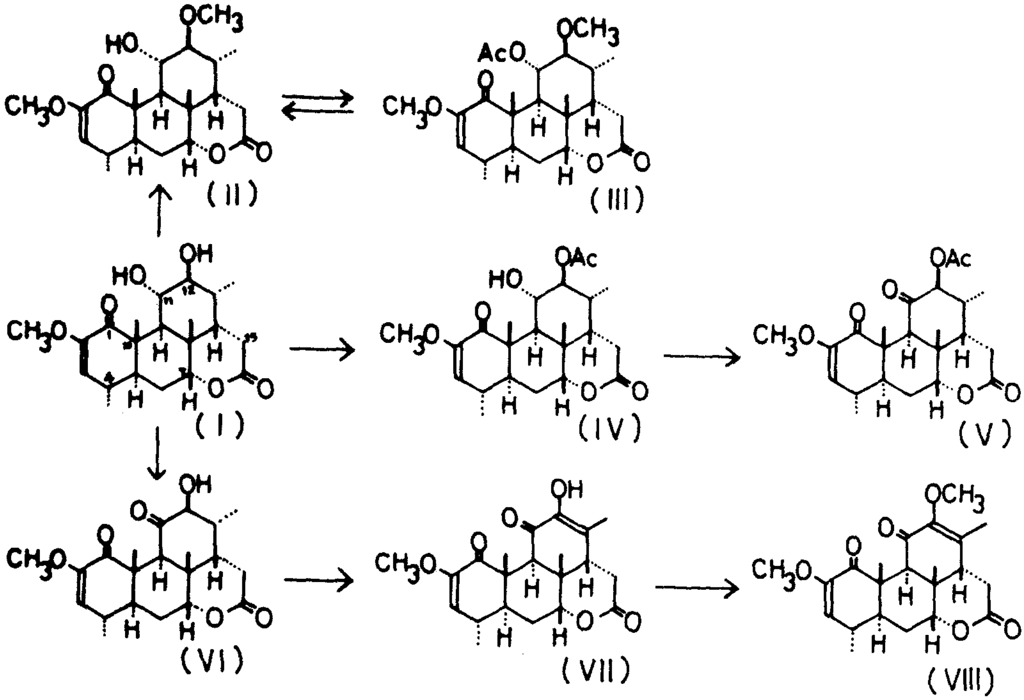
FIGURE 1. PMR spectra of nigakilactone C (III) in C_6D_6 at 100 MHz. (■ indicates carbon with no proton)

by acetylation with Ac_2O-pyridine. On oxidation with $Na_2Cr_2O_7$ in acetic acid, IV yielded a keto-acetate (V) [m.p. 230-231.5°, λ_{max}^{EtOH} 264 nm (ε 5,000) ; IR (nujol), 1740, 1730, 1700, 1635 cm^{-1}, absence of ν_{O-H}]. This evidence indicates the presence in I of two hydroxyl groups. In the PMR spectrum of IV (Table 1) a quartet (1H, $\underline{H}-\overset{|}{\underset{|}{C}}-OAc$, δ 4.80 , J = 11 and 9 Hz) appears, and in the spectrum of V (Table 1) this quartet is changed to a doublet and shifted to down field (δ 5.23 , J = 12 Hz), thus suggesting that the two hydroxyl groups are both secondary and in a relationship of α,β-diequatorial each other.

Oxidation of I with CrO_3-pyridine at room temperature gave an α-ketol (VI) [λ_{max}^{EtOH} 263 nm ; IR (nujol), 3450, 1720-1730, 1685, 1630 cm^{-1} ; PMR (Table 1)]. Oxidation of VI with Bi_2O_3 afforded a diosphenol (VII) [λ_{max}^{MeOH} 270 nm (ε 11,200), shifted to 313 and 263 nm in alkaline solution ; IR (nujol), 3420, 1730, 1700, 1630 cm^{-1}]. On methylation with dimethyl sulfate and alkali, VII gave a methylated diosphenol which was shown to be identical (IR, UV, PMR, ORD, MS and TLC) with quassin (VIII)(4,5,6). These findings, along with the observation that the PMR spectrum of nigakilactone A (I)(Table 1) shows the presence of one olefinic proton and the absence of vinyl methyl, are best accommodated by a unique expression I for nigakilactone A. Thus the structure of nigakilactone A is established as I.

PMDR experiment on nigakilactone C (III)(Figure 1 ; cf. Table 1) afforded the evidence for the presence of a partial structure (A). Irradiation on the proton quartet at δ 5.37 (H_b) causes a collapse of the other proton quartet at δ 2.90 (H_c) into a doublet and changes the proton doublet at δ 2.66 (H_a) into a singlet. The coupling constants of H_a-H_b (J = 11 Hz), H_b-H_c (J = 9 Hz) and H_c-H_d (J = 11 Hz) indicate that the three adjacent protons are in axial-axial relationships. These observations lead to the structure III for nigakilactone C. The structure II follows for nigakilactone B.

Nigakilactone D [m.p. 219-220°, $C_{22}H_{28}O_6$, M^+ 388] was found to be identical (m.p., mixed m.p., IR, ORD, PMR and TLC) with quassin (VIII).



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