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The Structures of Nigakilactones K and L

The isolation of a number of bitter principles from *Picrasma ailanthoides* PLANCHON (=*P. quassioides* BENNETT; Simaroubaceae) together with their structural studies have been described.[1-8] Two additional new bitter principles, nigakilactones K and L, have now been isolated from the same plant. In this communication, we wish to report evidence leading to structures Ia and IVd for nigakilactones K and L, respectively.

The molecular formula of nigakilactone K, $C_{22}H_{30}O_7$, mp 226—227°, $[\alpha]_D$—26° (*c* 0.32 in EtOH), was determined by mass spectroscopy (M^+ at *m/e* 406). The IR (3400, 1700, 1674, 1634 cm^{-1}) and UV (λ_{max} 270 nm, ε 5900; 238 nm, ε 6700 (sh) in MeOH) spectra show characteristic absorption bands for an α,β-unsaturated ketone, an α,β-unsaturated δ-lactone and the hydroxyl group. In the proton magnetic resonance (PMR) spectrum the presence of one secondary and three tertiary methyls, two methoxyl groups and two olefinic protons is observed (Table I).

TABLE I. PMR Spectral Data (δ in ppm)[a]

Compounds	*sec*-CH_3	*t*-CH_3	$-OCH_3$	$-O-CH_2-O-$	C–CH–O– (7)	C=CH
Nigakilactone K	1.18d *J*=7	1.45s 1.48s 1.50s	3.60s 3.77s	—	4.25m	5.43d *J*=2.5 6.02s[b]
Nigakilactone L	1.12d *J*=7	1.36s 1.47s 1.53s	3.56s	5.00d *J*=1 5.22d *J*=1	4.20m	5.25d *J*=2.5
Nigakilactone F	1.11d *J*=7	1.22s 1.46s 1.46s	3.58s 3.73s	—	4.13m	5.43d *J*=2

a) Determined in $CDCl_3$ at 60 MHz.
b) Signal due to $C_{(15)}$-H; the others due to $C_{(3)}$-H.

Acetylation of nigakilactone K gave a monoacetate (Ib), $C_{24}H_{32}O_8$ (M^+ at *m/e* 448), which still shows an infrared (IR) absorption due to hydroxyl group. Therefore, the nature of all seven oxygen atoms involved in nigakilactone K is characterized, showing the presence of two hydroxyl groups in its molecule.

1) *a*) T. Murae, T. Tsuyuki, T. Nishihama, S. Masuda and T. Takahashi, *Tetrahedron Letters*, **1969**, 3013; *b*) T. Murae, T. Tsuyuki, T. Ikeda, T. Nishihama, S. Masuda and T. Takahashi, *Tetrahedron*, **27**, 1545 (1971).
2) H. Hikino, T. Ohta and T. Takemoto, *Chem. Pharm. Bull.* (Tokyo), **18**, 219 (1970).
3) T. Murae, T. Ikeda, T. Tsuyuki, T. Nishihama and T. Takahashi, *Bull. Chem. Soc. Japan*, **43**, 969 (1970).
4) H. Hikino, T. Ohta and T. Takemoto, *Chem. Pharm. Bull.* (Tokyo), **18**, 1082 (1970).
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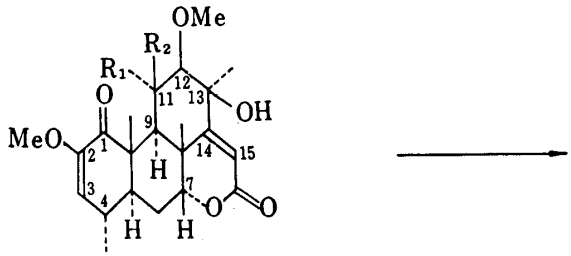
7) H. Hikino, T. Ohta and T. Takemoto, *Chem. Pharm. Bull.* (Tokyo), **19**, 212 (1971).
8) T. Murae, T. Tsuyuki and T. Takahashi, *Chem. Pharm. Bull.* (Tokyo), **19**, 1747 (1971).

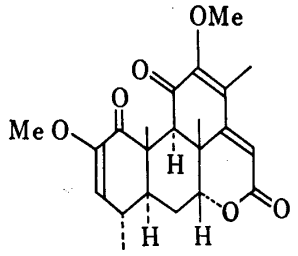
On oxidation with sodium dichromate in acetic acid, nigakilactone K yielded a ketone (Ic), $C_{22}H_{28}O_7$ (M^+ at *m/e* 404), which was then treated with thionyl chloride in pyridine to afford known dehydroquassin (II).[9] The skeletal structure of nigakilactone K is thus clarified.

In the PMR spectrum of the monoacetate (Ib) the protons on C-11 and C-12 resonate as a quartet (1H, H-C-OAc, δ 5.67, J=12 and 9 Hz) and a doublet (1H, H-C-OMe, δ 3.13, J=9 Hz), respectively. As the carbon (C-13) bears no proton, a hydroxyl group must be located on this carbon (C-13) ,and the observed coupling constants indicate that the three adjacent protons (C-9, C-11 and C-12) are in axial-axial relationships for the monoacetate (Ib). The sturcture including stereochemistry of nigakilactone K is thus established as Ia. The structures Ib and Ic follows for its monoacetate and ketone, respectively.

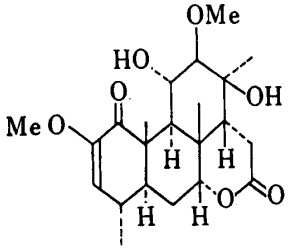
The molecular formula of $C_{22}H_{30}O_7$ (M^+ at *m/e* 406) was given for nigakilactone L, mp 296°, $[\alpha]_D$ +65° (*c*=0.07, EtOH). The IR (3560, 3430, 3180, 1730, 1710, 1635 cm^{-1}) and UV (λ_{max} 263.5 nm, ε 4500, in MeOH) spectra indicate the presence of an α,β-unsaturated ketone, a δ-lactone and the hydroxyl group. The PMR spectrum (Table I) showing the presence of one secondary and three tertiary methyls, one methoxyl group and an olefinic proton is best interpreted on the basis of skeletal structure of known nigakilactone F (III).[3] The marked difference between the PMR spectra of nigakilactones L and F is that in the former spectrum signals due to a methylene dioxy moiety (Table I) appear and no signal due to methoxyl group on C-12 is observed. The presence of partial structure (A) is shown for nigakilactone L as follows. The protons, H_b and H_c, resonate as a quartet (δ 4.02, J=12 and 9 Hz) and a doublet (δ 3.65, J=9 Hz), respectively. The observed coupling constants show that the three adjacent protons (H_a, H_b and H_c) are in axial-axial relationships. Therefore, the nature of



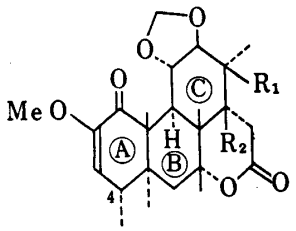
Ia : R_1=OH, R_2=H
Ib : R_1=OAc, R_2=H
Ic : R_1, R_2=O



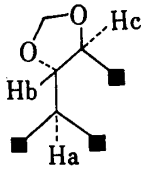
II



III



IVa : R_1=H , R_2=H
IVb : R_1=H , R_2=OH
IVc : R_1=OH, R_2=OH
IVd : R_1=OH, R_2=H



A

■: indicates carbon with no proton

9) Z. Valenta, S. Papadopoulos and C. Podešva, *Tetrahedron*, **15**, 100 (1961).

seven oxgen atoms involved in nigakilactone L is clarified, indicating the presence of one hydroxyl group in the molecule.

An appearance of signal due to a proton at the lactone terminus (-CH-O-CO-) at δ 4.20[1,3,5] shows that no hydroxyl group is attached to C-14 for nigakilactone L. The ultraviolet (UV) maximum at 263.5 nm showing the absence of hydrogen bond between the hydroxyl at C-11 and the carbonyl group at C-1,[1b] provides evidence for nigakilactone L that no hydroxyl group is located on C-11. An olefinic proton on C-3 resonates at δ 5.25 as a doublet. This shows the presence of a proton (and the absence of hydroxyl group) on C-4 for nigakilactone L. Recently, Hikino, *et al.* isolated from the same plant three bitter principles, picrasin D (IVa), E (IVb)[7] and F (IVc),[10] which have a methylene dioxy moiety in the C ring. Optical rotatory dispersion (ORD) and circular dichroism (CD) data of nigakilactone L agree with those of picrasin E.[7] None of these picrasins, however, is found to be identical with nigakilactone L.

These data along with the observation that nigakilactone L contains three tertiary and one secondary methyl groups should lead to the location of a hydroxyl group on C-13 as in the case of nigakilactone F. Nigakilactone L is considered to be formed biogenetically by oxidation of nigakilactone F (III). The structure IVd is thus given for nigakilactone L.

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Structure of Kinamycin C, and the Structural Relationship among Kinamycin A, B, C, and D

In previous papers,[1] we reported fermentation, isolation, and purification of a new quinone antibiotic, kinamycin, which was isolated from the culture broth of *Streptomyces murayamaensis sp. nov.* Hata *et* Ohtani. In this paper we wish to describe the structure of kinamycin C and the structural relationship among kinamycin A, B, C, and D. The infrared (IR) spectra of kinamycins show a sharp absorption of nitrile or isonitrile group at 2155 cm^{-1}. The ultraviolet (UV) and visible spectra of each component show a maximum absorption in the range of 240—260 and 380—450 nm, which are a characteristic absorption in naphthoquinone-type compounds.[2] The presence of phenolic OH is established with a red shift of their absorption in alkaline solution. In the nuclear magnetic resonance (NMR) spectra, three aromatic protons of kinamycins are signaled at 7.02—7.7 δ by a typical absorption of

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2) I. Singh, R.T. Ogata, R.E. Moore, C.W. Chang, and P.J. Scheuer, *Tetrahedron*, **24**, 6053 (1968).