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BITTER PRINCIPLES OF *PICRASMA AILANTHOIDES* PLANCHON

NIGAKILACTONES J, K, L, M AND N[1]

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Abstract—Five new crystalline bitter principles were isolated from the stem-chips of *Picrasma ailanthoides* Planchon (Simaroubaceae). Structures of nigakilactones J, K, L, M and N were shown to be **1a**, **2a**, **3d**, **4c** and **4b**, respectively.

The isolation and determination of the structures of bitter principles (nigakilactones A, B, C, D, E, F, G, H and I and nigakihemiacetals A, B and C) of *Picrasma ailanthoides* Planchon (= *P. quassioides* Bennett, Japanese name: nigaki, Simaroubaceae) have already been reported.[2a-g] We have further examined minor components in the bitter principles of the plant and isolated additional five new bitter substances which were named as nigakilactones J, K, L, M and N. Evidence establishing structures **1a**, **2a**, **3d**, **4c** and **4b** for nigakilactones J, K, L, M and N, respectively, are reported in the present paper.[1] Recently, isolation of picrasins A,[3a] B,[3b] C,[3c] D,[3d] E,[3d] F,[3e] and G[3f] from the same plant together with their structural studies were recorded by Hikino *et al.*

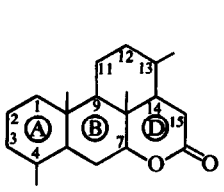
Nigakilactone J (**1a**)

Nigakilactone J crystallized from chloroform-light petroleum as colorless needles, m.p. 240–241° and $[\alpha]_D$ +42° (EtOH). The mass spectrum indicates the formula $C_{23}H_{34}O_7$ (M^+ at *m/e* 422). The IR spectrum in nujol shows OH absorptions at 3550 and 3450 cm^{-1}. The IR (1735 and 1250 cm^{-1}), PMR (δ 1·93, 3H, s) and mass [$(M-AcOH)^+$ at *m/e* 362] spectra suggest the presence of an acetoxyl group. An IR absorption at 1722 cm^{-1} (sh) is indicative of the presence of a lactone grouping in a 6-membered or larger ring. This received support from the PMR signal at δ 4·22 (1H, m) due to a proton at the lactone terminus (—C<u>H</u>—O—CO—). The IR spectrum also shows an absorption at 1704 cm^{-1} due to a saturated ketone function. The UV spectrum shows no absorption maximum due to a conjugated system. The presence of a OMe group, two secondary and two tertiary Me groups is shown in the PMR spectrum (Table 1). No signal due to an olefinic proton is observed.

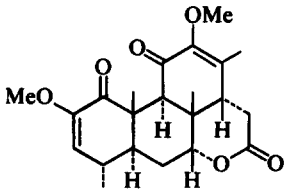
A monoacetate (**1b**), $C_{25}H_{36}O_8$ (M^+ at *m/e* 464), m.p. 275–276°, PMR (Table 1), obtained by acetylation of nigakilactone J (**1a**), shows no IR absorption due to an OH group. Therefore, one OH group must be present in nigakilactone J.

The nature of seven O atoms involved in nigakilactone J is thus clarified. The molecular formula of nigakilactone J along with the above spectral data are best interpreted on the basis of the saturated skeletal structure (**A**) related to quassin (**6**).[4] The PMR spectrum of nigakilactone J shows a quartet (1H, δ 5·28, J = 12 and 9 Hz; C<u>H</u>—OAc) and a quartet (1H, δ 3·18, J = 9 and 11 Hz; C<u>H</u>—OMe), whose signal patterns are closely similar to those of nigakilactone C (**8c**)[2a,c] (Table 1). This suggests the location of an acetoxyl group on C-11 and a OMe group on C-12 for nigakilactone J as that for nigakilactone C (**8c**). As all bitter substances hitherto isolated from the same plant[1-3] have a CO and a OMe (or an OH) groups at C-1 and C-2, respectively, the location of a CO group on C-1 and of an OH group on C-2 is suggested for nigakilactone J. With this information, nigakilactone J could be formulated as **1a**. This was confirmed by the following transformations.

Nigakilactone B (**8a**)[2a,c] was treated with hydrochloric acid to give nornigakilactone B (**8b**),[2c] $C_{21}H_{30}O_6$ (M^+ at *m/e* 378). The presence of a diosphenol moiety in **8b** was shown by the shift of UV max in EtOH from 280 nm to 335 nm on addition of alkali. Treatment of nornigakilactone B (**8b**) in acetic acid under reflux with zinc powder yielded a mixture of the dihydro derivatives (epimers at C-2; **7a** and **7b**), which was separated by preparative TLC to afford **7a** (major product), $C_{21}H_{32}O_6$ (M^+ at *m/e* 380), m.p. 210–211°, PMR (Table 1), and **7b** (minor product), $C_{21}H_{32}O_6$ (M^+ at *m/e* 380), m.p. 231–232·5°. On treatment of **1a** with hydrochloric acid in acetic acid, the same mixture (**7a** and **7b**) was obtained. The absence of the UV max due to a conjugated system was shown for **7a**. The mass spectra of **7a** and **7b** are essentially identical, although their IR spectra are different. These facts



A



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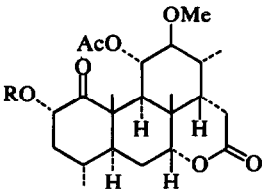
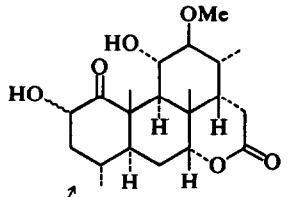
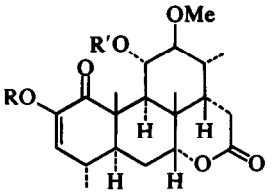


1a: R = H
1b: R = Ac



7a: 2α-OH
7b: 2β-OH



8a: R = Me, R′ = H
8b: R = H, R′ = H
8c: R = Me, R′ = Ac

suggest that **7b** is an epimer at C-2 of **7a**. The major product (**7a**) was acetylated to give an acetyl derivative which was shown to be identical with **1b**. The structure (**1a**) is thus given for nigakilactone J.*

In the PMR spectrum of **1b** a quartet due to a proton on C-2 appears at δ 5·58 (Table 1). The observed coupling constants ($J = 13$ and 7 Hz) suggest that this proton is in axial conformation (2β-H configuration). This leads to the stereochemistry (**1a**) for nigakilactone J.

Nigakilactone K (**2a**)

The molecular formula of nigakilactone K, $C_{22}H_{30}O_7$, m.p. 226–227°, $[\alpha]_D$ −26° (EtOH), was determined by the appearance of the M^+ peak at *m/e* 406 in the mass spectrum. The IR absorptions at 3400, 1674 and 1634 cm^{-1} along with the UV absorption maximum at 270 nm (ε 5900) show the presence of an α,β-unsaturated ketone and the OH group. In the PMR spectrum the presence of one secondary and three tertiary Me groups, two OMe groups and two olefinic protons is observed (Table 1). The PMR signals at δ 6·02 (1H, s, proton at C-15) and δ 4·25 (1H, m, proton at C-7), an IR absorption at 1700 cm^{-1} and an UV absorption at 238 nm (ε 6700 sh) are indicative of the presence of an α,β-unsaturated δ-lactone.

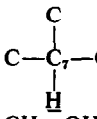
Nigakilactone K was acetylated to give a monoacetate (**2b**), $C_{24}H_{32}O_8$ (M^+ 448), which still shows an IR absorption due to an OH group. Therefore, the nature of all seven O atoms involved in nigakilactone K is characterized, showing the presence of two OH groups in its molecule.

Oxidation of nigakilactone K with sodium dichromate in acetic acid yielded a ketone (**2c**), $C_{22}H_{28}O_7$ (M^+ at *m/e* 404), which was then treated with thionyl chloride in pyridine to afford known dehydroquassin (**9**).[4] The skeletal structure of nigakilactone K is thus shown.

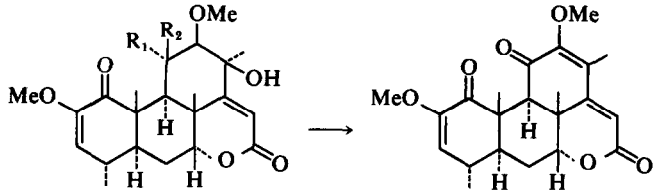
The PMR signals due to the protons on C-11 and C-12 of the monoacetate (**2b**) resonate as a quartet (1H, H—C(OAc)—, δ 5·67, $J = 12$ and 9 Hz) and a doublet (1H, H—C(OMe)—, δ 3·13, $J = 9$ Hz), respectively. As no proton is attached to C-13, one

*Picrasin C was later shown to be identical with nigakilactone J by Hikino *et al.*[3c]

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

Compounds	1a	1b	2a	2b	3a	3b	3b[d]	3d	4a	4b	4c	7a	8c	10a
s-CH_3	0·90d $J=6$ 1·04d $J=7$	0·96d $J=6$ 1·03d $J=7$	1·18d $J=7$	1·10d $J=7$	1·10d $J=7$ 1·10d $J=7$	1·10d $J=7$ 1·10d $J=7$	0·91d $J=7$ 1·33d $J=7$	1·12d $J=7$	1·01d $J=6·5$ 1·10d $J=6$	1·16d $J=7$	1·10d $J=6$ 1·17d $J=6$	0·92d $J=6$ 1·04d $J=6$	1·01d $J=6$ 1·06d $J=7$	1·11d $J=7$
t-CH_3	1·26s 1·28s	1·27s 1·32s	1·45s 1·48s 1·50s	1·25s 1·51s 1·51s	1·28s 1·43s	1·22s 1·45s	1·37s 1·50s	1·36s 1·47s 1·53s	1·24s 1·42s	1·28s 1·50s 1·53s	1·20s 1·50s	1·22s 1·40s	1·27s 1·27s	1·22s 1·46s 1·46s
—O—CO—CH_3	1·93s	2·02s 2·11s	—	2·00s	—	—	—	—	—	—	—	—	1·95s	—
CH—OCH_3	3·18q $J=9$ $J=11$	3·11q $J=9$ $J=11$	*e*	3·13d $J=9$	—	—	—	—	—	—	—	*e*	3·20q $J=9$ $J=11$	*e*
—OCH_3	3·45s	3·40s	3·60s 3·77s	3·56s 3·56s	3·55s	3·55s	3·50s	3·56s	3·54s	3·65s	3·64s	3·58s	3·42s 3·54s	3·58s 3·73s
	4·22m	4·16m	4·25m	4·24m	4·23m	4·55m	4·88m	4·20m	4·10m	4·20m	4·67m	4·11m	4·14m	4·13m
CH—OH	4·74m	—	*e*	—	—	—	—	—	*e*	*e*	*e*	4·72m	—	*e*
O—CH_2—O	—	—	—	—	4·99d $J=1$ 5·15d $J=1$	5·00d $J=1$ 5·16d $J=1$	5·20d $J=1$ 5·36d $J=1$	5·00d $J=1$ 5·22d $J=1$	—	—	—	—	—	—
CH—OAc	5·28q $J=12$ $J=9$	5·28q $J=12$ $J=9$ 5·58q[b] $J=13$ $J=7$	—	5·67q $J=12$ $J=9$	—	—	—	—	—	—	—	—	5·22q $J=11$ $J=9$	—
C=CH	—	—	5·43d $J=2·5$ 6·02s[c]	5·14d $J=2·5$ 6·02s[c]	5·25d $J=2·5$	5·24d $J=2·5$	5·23d $J=2·5$	5·25d $J=2·5$	5·35d $J=2·5$	5·55d $J=2·5$	5·56d $J=2·5$	—	5·10d $J=2·5$	5·43d $J=2·5$

[a]Determined in $CDCl_3$ at 60 MHz. Coupling constants are expressed in Hz. s: singlet, d: doublet, q: quartet, m: multiplet.
[b]Signal due to proton at C-2; the others due to proton at C-11.
[c]Signal due to proton at C-15; the others due to proton at C-3.
[d]Determined in pyridine at 60 MHz.
[e]Not assigned.



2a: $R_1 = OH, R_2 = H$
2b: $R_1 = OAc, R_2 = H$
2c: $R_1, R_2 = O$

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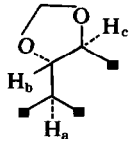
OH group must be located on this carbon (C-13), and the observed coupling constants indicate that the three adjacent protons (at C-9, C-11 and C-12) are in axial–axial relationships for the monoacetate (**2b**). Thus, the structure including stereochemistry of nigakilactone K should be represented by **2a**. The structures **2b** and **2c** follow for its monoacetate and ketone, respectively.

Nigakilactone L (**3d**)

The molecular formula of $C_{22}H_{30}O_7$ (M^+ at *m/e* 406) was given for nigakilactone L, m.p. 296°, $[\alpha]_D$ +65° (EtOH). The IR (3560, 3430, 3180, 1710 and 1635 cm^{-1}) and the UV (263·5 nm, ϵ 4500) spectra show characteristic absorption bands for an α,β-unsaturated ketone and the OH group. An IR absorption at 1730 cm^{-1} suggests the presence of a lactone grouping in a 6-membered or larger ring. The PMR signal at δ 4·20 (1H, m) due to a proton at the lactone terminus (—CH—O—CO—) was observed. The presence of one secondary and three tertiary Me groups, one OMe group and an olefinic proton is shown in the PMR spectra. These spectral data are best interpreted on the basis of a skeletal structure of known nigakilactone F (**10a**).[2b,c] The significant difference between the PMR spectra of nigakilactones L and F is that in the former spectrum signals due to a methylene dioxy moiety (δ 5·00, 1H, d, J = 1 Hz and δ 5·22, 1H, d, J = 1 Hz) appear and no signal due to a OMe group on C-12 is observed. The presence of an olefinic proton (δ 5·25, 1H, d, J = 2·5 Hz, proton at C-3) in the PMR spectrum and the absence of the shift of the UV absorption max on addition of alkali suggest the presence of the methylated diosphenol moiety in the ring A.[2c] Therefore, the OMe group must be located on C-2.

The presence of the partial structure (**B**) is shown



■: indicates carbon with no proton

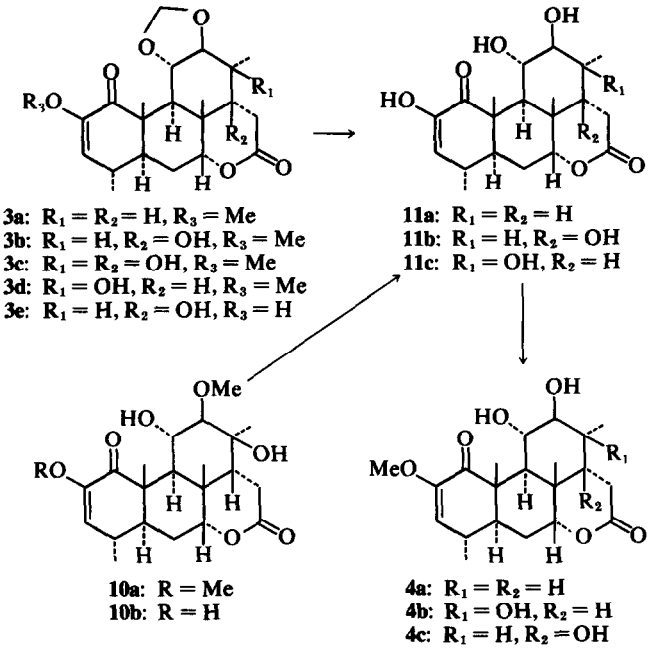
B

for nigakilactone L as follows. In the PMR spectrum 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 seven oxygen atoms involved in nigakilactone L is characterized, indicating the presence of one OH group in the molecule.

The signal due to a proton at the lactone terminus (—CH—O—CO—) appears at δ 4·20.[4] This suggests that no OH group is attached to C-14 for nigakilactone L. The UV maximum at 263·5 nm showing the absence of H-bond between the OH at C-11 and the CO group at C-1,[2c] provides evidence for nigakilactone L that no OH group is located on C-11. An appearance of an olefinic proton on C-3 resonates at δ 5·25 as a doublet shows the presence of a proton (and absence of OH group) on C-4 for nigakilactone L. Recently, Hikino *et al* isolated from the same plant three bitter principles, picrasins D (**3a**),[3d] E (**3b**),[3d] and F (**3c**),[3e] which have a methylene dioxy moiety in the C ring. 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 Me groups should lead to the location of an OH group on C-13 as in the case of nigakilactone F (**10a**). This was confirmed as follows. Nigakilactone L was treated with BCl_3 in CH_2Cl_2, and then with aqueous MeOH to give a diosphenol (**11c**), which on treatment with diazomethane gave nigakilactone N (**4b**), of which structure elucidation will be described below. Thus the structure **3d** including stereochemistry is given for nigakilactone L.

Picrasins D (**3a**) *and E* (**3b**)

During the isolation of nigakilactones, we have also isolated picrasins D (**3a**)[3d] and E (**3b**)[3d] which were identified with the authentic specimens by a direct comparison. **3a** was cleft with BCl_3 and the reaction product (**11a**) was methylated with CH_2N_2 to give nigakilactone A (**4a**). Thus, the structure of picrasin D (**3a**) including the stereochemistry was confirmed.



3a: $R_1 = R_2 = H, R_3 = Me$
3b: $R_1 = H, R_2 = OH, R_3 = Me$
3c: $R_1 = R_2 = OH, R_3 = Me$
3d: $R_1 = OH, R_2 = H, R_3 = Me$
3e: $R_1 = H, R_2 = OH, R_3 = H$

11a: $R_1 = R_2 = H$
11b: $R_1 = H, R_2 = OH$
11c: $R_1 = OH, R_2 = H$

10a: R = Me
10b: R = H

4a: $R_1 = R_2 = H$
4b: $R_1 = OH, R_2 = H$
4c: $R_1 = H, R_2 = OH$

Nigakilactone M (**4c**)

The molecular formula of $C_{21}H_{30}O_7$ (M^+ at *m/e* 394) was given for nigakilactone M, m.p. 173–178°, $[\alpha]_D$ +39° (EtOH). The IR (ν_{max} 1680 and 1635 cm^{-1}) and the UV (λ_{max} 271 nm) spectra show characteristic absorptions for an α,β-unsaturated ketone. The IR absorption at 1735 cm^{-1} along with the PMR signal at δ 4·67 (1H, m) suggests the presence of a δ-lactone. The IR spectrum (ν_{max} 3580, 3460 and 3350 cm^{-1}) also shows the presence of an OH group. The presence of two secondary and two tertiary Me groups, a OMe group and an olefinic proton is shown by the PMR spectrum (Table 1).

The above spectral data of nigakilactone M and those of nigakilactone A (**4a**) are closely related. As nigakilactone M contains one O atom more than nigakilactone A, the presence of an extra OH group is suggested for nigakilactone M (**4c**). The PMR spectrum of nigakilactone A shows a signal at δ 4·10 due to a proton at the lactone terminus (—CH—O—CO—),[4] while the spectrum of nigakilactone M indicates a signal at δ 4·67 due to the corresponding proton. This downfield shift[2f] suggests that the extra OH group may be located on C-14 (with β-orientation) for nigakilactone M.

This received support from the following transformation. A methylene dioxy ring of known picrasin E (**3b**)[3d] was cleft with BCl_3 and then hydrolysed with aqueous MeOH. The resulting product was a mixture of four compounds (TLC) which were considered to be **3b**, **4c**, **3e** and **11b**. The latter two products gave blue color with ferric chloride suggesting the presence of a diosphenol moiety. Without isolation of each component, this mixture was methylated with diazomethane and separated by preparative TLC to afford nigakilactone M and the starting picrasin E. Thus the structure including stereostructure of nigakilactone M is established as **4c**.

Nigakilactone N (**4b**)

Mass spectrometry (M^+ at *m/e* 394) indicated $C_{21}H_{30}O_7$ as a molecular formula of nigakilactone N, m.p. 207–211°, $[\alpha]_D$ +36° (EtOH). The IR (ν_{max} 3570, 3550, 3495 and 3350 cm^{-1}) spectrum shows characteristic absorptions for the OH group. The IR (1680 and 1635 cm^{-1}) and the UV (λ_{max} 270 nm) spectra show characteristic absorptions for an α,β-unsaturated ketone. The IR absorption at 1718 cm^{-1} along with the PMR signal at δ 4·20 (1H, m) shows the presence of a δ-lactone. The PMR spectrum shows also the presence of one secondary and three tertiary Me groups, a OMe group and an olefinic proton (Table 1).

These spectral data are best interpreted on the basis of the skeletal structure of known nigakilactone F (**10a**, $C_{22}H_{32}O_7$).[2b,c] The marked difference between the PMR spectra of nigakilactones N and F is that the latter spectrum shows signals due to two OMe groups at C-2 and C-12, while the former only one. These observations suggest that nigakilactone N may be a monodemethyl derivative of nigakilactone F.

Nigakilactone F (**10a**) was treated with BCl_3, aqueous MeOH and in turn with diazomethane to give nigakilactone N. Thus, the structure **4b** including stereochemistry is given for nigakilactone N.

EXPERIMENTAL

IR, UV and mass spectra were measured using Hitachi EPI-G2, Hitachi EPS-3 and Hitachi RMU-6 spectrometers, respectively. PMR spectra were taken on a JEOL JNM-C-60 spectrometer at 60 MHz in $CDCl_3$ soln containing TMS as an internal standard. Chemical shifts are expressed in δ (ppm downfield from TMS). Optical rotations were measured with a YANACO OR-50 polarimeter. All m.ps were determined on a hot block and reported uncorrected. Silica gel column and TLC were carried out on Wakogel C-200 and Kieselgel G, respectively.

Isolation. Extraction of crude material (200 g) from the stem-chips (160 kg) of *Picrasma ailanthoides* Planchon was described elsewhere.[2c,f] A part of the residue (70 g)[2f] was dissolved in benzene and chromatographed on alumina (2 kg, Showa Chemical Co., treated with dilute HCl, washed with water and dried at 110° for 6 hr). The elutions (each 3 l.) were carried out successively with benzene (fr 1), benzene–ether (1 : 1, frs 2–9), ether (frs 10–32), ether–AcOEt (4 : 1, frs 33–34), ether–AcOEt (1 : 1, frs 35–38) and AcOEt (frs 39–54). Each fraction was examined by TLC and the fractions which showed the same chromatograms were combined.

Fractions 22–26 were combined and the solvent was distilled off. The residue (2·0 g) was further chromatographed on silica gel (dry column, 200 g, eluent: ether, each fraction 50 ml). The fractions 22–26 gave a residue (540 mg), which was further chromatographed on silica gel (dry column, 70 g, eluent: acetone–benzene, 1 : 2, each fraction 30 ml). The fractions 2 and 3 were combined and crystallized from $CHCl_3$-light petroleum and then from AcOEt to afford *picrasin D* as colorless needles (30 mg), m.p. 272·5–273·0°, which was identified by a direct comparison with an authentic specimen of *picrasin D*.[3d]

Fraction 39 gave a residue (1·5 g) which was chromatographed on silica gel (dry column, 150 g, eluent: AcOEt–benzene, 1 : 1, each fraction 50 ml). The fractions 7–9 were combined and evaporation of the solvents gave a residue (residue A, 0·7 g). The fractions 11–16 gave a residue (residue B, 0·6 g). The residue A was chromatographed on silica gel (dry column, 150 g, eluent: AcOEt–ether, 1 : 1, each fraction 30 ml). The fractions 8–10 gave a residue (156 mg), which was crystallized from acetone–ether and then from AcOEt to give colorless needles (55 mg). This was identified by a direct comparison with an authentic specimen of *picrasin E*.[3d] The fractions 11–13 were combined and evaporated to give a residue (200 mg), which was further chromatographed on silica gel (dry column, 30 g, eluent: benzene–acetone, 2 : 1, each fraction 10 ml). The fractions 2–5 gave a solid, which was crystallized from acetone–ether to give *nigakilactone J* (**1a**) as colorless needles (15 mg), m.p. 240–241°, $[\alpha]_D$ +42° (*c* 0·20, EtOH); IR (Nujol) ν_{max} 3550, 3450, 1735, 1722(sh), 1704 and 1250 cm^{-1}; PMR (Table 1); Mol. wt. 422 (by mass spectrum). $C_{23}H_{34}O_7$ requires Mol. wt. 422. The residue B was crystallized from acetone to give *nigakihemiacetal C*[2e] and the mother liquor gave a residue (73 mg), which was further chromatographed on silica gel (dry column, 15 g, eluent: benzene–acetone, 2 : 1, each fraction 5 ml). The fraction 2 gave a residue which was crystallized from benzene–light petroleum to give *nigakilactone K* (**2a**) as colorless needles (10 mg), m.p. 226–227°, $[\alpha]_D$ −26° (*c* 0·32, EtOH); UV (MeOH) λ_{max} 270 nm (ε 5900), 238 nm (ε 6700 sh); IR (Nujol) ν_{max} 3400, 1700, 1674 and 1634 cm^{-1}; PMR (Table 1); Mol. wt. 406 (by mass spectrum). $C_{22}H_{30}O_7$ requires mol. wt. 406.

Fractions 40 and 41 were combined and the solvent was removed. The residue (2·2 g) was further chromatographed on silica gel (dry column, 250 g, eluent: AcOEt–benzene, 1 : 1, each fraction 50 ml). The fractions 17–26 gave a residue (250 mg), which was dissolved in hot $CHCl_3$. After the soln had been cooled, ppts appeared, which was shown to be identical with *nigakihemiacetal C*[2e] by a direct comparison with an authentic sample. The ppts were filtered off and the filtrate was evaporated to afford a residue, which was chromatographed on silica gel (dry column, 50 g, eluent: benzene–acetone, 3 : 1, each fraction 30 ml). The fractions 5–7 gave a solid, which was crystallized from acetone to give *nigakilactone L* (**3d**) as colorless needles (10 mg), m.p. 296°, $[\alpha]_D$ +65° (*c* 0·07, EtOH); UV (MeOH) λ_{max} 263·5 nm (ε 4500); IR (Nujol) ν_{max} 3560, 3430, 3180, 1730, 1710 and 1635 cm^{-1}; PMR (Table 1), mol. wt. 406 (by mass spectrum). $C_{22}H_{30}O_7$ requires mol. wt. 406.

Fractions 48–51 gave a residue (1·99 g), which was chromatographed on silica gel (dry column, 250 g, eluent: benzene–aceton, 2 : 1, each fraction 50 ml). The fractions 27–50 gave a residue (245 mg), which was further chromatographed on silica gel (dry column, 60 g, eluent: acetone–AcOEt, 1 : 5, each fraction 25 ml). The fractions 7–15 gave a residue (30 mg) containing two components which were separated by preparative silica gel TLC (developed with $CHCl_3$–EtOH, 20 : 1) into *nigakilactone M* (**4c**, 10 mg) and *nigakilactone N* (**4b**, 10 mg). Nigakilactone M (**4c**) showed m.p. 173–178°, $[\alpha]_D^*$ +39° (*c* 0·54, EtOH); UV (MeOH) λ_{max} 271 nm (ε 2660); IR (Nujol) ν_{max} 3580, 3460, 3350, 1735, 1680 and 1635 cm^{-1}; mol. wt. 394 (by mass spectrum). $C_{21}H_{30}O_7$ requires mol. wt. 394; PMR (Table 1). Nigakilactone N (**4b**) showed m.p. 207–211°; $[\alpha]_D^*$ +36° (*c* 0·44, EtOH); UV (MeOH) λ_{max} 270 nm (ε 2800); mol. wt. 394 (by mass spectrum). $C_{21}H_{30}O_7$ requires mol. wt. 394; PMR (Table 1).

Acetylation of nigakilactone J (**1a**). A mixture of nigakilactone J (6·3 mg), Ac_2O (1 ml) and pyridine (1 ml) was allowed to stand overnight at room temp. After addition of MeOH, the solvents were removed to give **1b**, IR (Nujol) ν_{max} 1738 and 1262 cm^{-1}, absence of OH absorption; PMR (Table 1); mass spectrum *m/e* 464 (M^+; $C_{25}H_{36}O_8$), 404 (M–AcOH)$^+$ and 344 (M–2 × AcOH)$^+$.

Reduction of nornigakilactone B (**8b**). Nigakilactone B (**8a**,[2a,c] 30 mg) was heated with 2N HCl (6 ml) and AcOH (2 ml) on a steam bath for 1 hr. After the mixture had been cooled, it was neutralized with 2N KOH (26 ml), extracted with $CHCl_3$ and evaporated to give **8b** (27 mg). The crude **8b** (24 mg), without further purification, was heated in AcOH (5 ml) under reflux, to which Zn dust was added portionwise during 2 hr. After cooling, the mixture was filtered and the filtrate was concentrated under reduced pressure. Neutralization with $NaHCO_3$, extraction with $CHCl_3$ and evaporation of the solvent afforded a mixture containing three components, which was chromatographed on silica gel (dry column, 10 g, eluent: AcOEt–ether, 1 : 1, each fraction 10 ml). The fractions 5–8 were combined and further separated by preparative TLC (developed with acetone–benzene, 1 : 2). A component with a higher R_f value was discarded and a component with a lower R_f value was extracted and crystallized from benzene-light petroleum to give colorless needles (**7b**), m.p. 231–232·5°; mass spectrum *m/e* 380 (M^+; $C_{21}H_{32}O_6$); IR (Nujol) ν_{max} 3460, 1724 and 1700 cm^{-1}.

*The previously reported values (ref. 1*c*) were corrected by reinvestigation of $[\alpha]_D$ measurement.

The fractions 9–13 were crystallized from benzene-light petroleum to afford colorless needles (**7a**), m.p. 210–211°; mass spectrum *m/e* 380 (M^+; $C_{21}H_{32}O_6$); IR (Nujol) ν_{max} 3500, 1725 and 1700 cm^{-1}; PMR (Table 1).

Acetylation of **7a**. A mixture of **7a** (3·7 mg), Ac_2O (2 ml) and pyridine (2 ml) was heated on a water bath for 12 hr and MeOH was added. On removal of the solvents, the residue giving two spots on TLC, was separated into each component by preparative TLC. A component with a higher R_f value was extracted and crystallized from $CHCl_3$-light petroleum to give colorless needles, which was shown to be identical with **1b** in respects to MS, IR, TLC and mixed m.p. Another component with a lower R_f value was purified by the same treatment and found to be the starting material (**7a**).

Acetylation of nigakilactone K (**2a**). Nigakilactone K (**2a**, 9·0 mg), Ac_2O (2 ml) and pyridine (2 ml) were heated at 110° for 23 hr and then at 60° for 26 hr. MeOH was added to the mixture and the solvents were removed. The residue was subjected to purification by preparative TLC (developed with AcOEt–ether, 1 : 1) to give **2b** (about 2 mg) as colorless solids, IR (Nujol) ν_{max} 3420, 1730, 1715, 1700(sh), 1640 and 1242 cm^{-1}; mass spectrum *m/e* 448 (M^+; $C_{24}H_{32}O_8$); PMR (Table 1).

Oxidation of nigakilactone K (**2a**). Nigakilactone K (**2a**, 5·5 mg) in AcOH (2 ml) was treated with $Na_2Cr_2O_7$ (8·7 mg) in AcOH (2 ml), neutralized with aq $NaHCO_3$ and extracted with $CHCl_3$. The extract was distilled to give a solid, which was crystallized from benzene-light petroleum. The oxidized product (**2c**) was obtained as colorless crystals, IR (Nujol) ν_{max} 3430, 1720(br) and 1630 cm^{-1}; mass spectrum *m/e* 404 (M^+; $C_{22}H_{28}O_7$).

Dehydration of **2c** *to dehydroquassin* (**9**). **2c** (3 mg) was dissolved in pyridine (0·3 ml) and treated with $SOCl_2$ (0·03 ml) at room temp for 1 hr. The mixture was poured into ice water, extracted with $CHCl_3$ and worked up as usual. Recrystallization from $CHCl_3$-light petroleum gave a pale yellow solid, whose IR, UV, MS and TLC data were identical with those of known dehydroquassin (**9**)[4] prepared from quassin (**6**).[4]

Treatment of nigakilactone L (**3d**) *with* BCl_3. A soln of **3d** (7·4 mg) in CH_2Cl_2 (1 ml) was kept at −80°. To this soln BCl_3 (1·5 ml) in CH_2Cl_2 (1·5 ml) was added during 20 min. The resulting soln was stirred at 0° for 4 hr and allowed to stand overnight at room temp. After the solvent had been removed under reduced pressure, aqueous MeOH was added. The reaction products (**11c** and **4b**) were methylated with diazomethane in ether to afford a single product (**4b**), which was found to be identical with nigakilactone N (**4b**).

Treatment of picrasin D (**3a**) *with* BCl_3. Picrasin D (**3a**, 23 mg) in CH_2Cl_2 (1 ml) was kept at −80° and BCl_3 (1 ml) in CH_2Cl_2 (1 ml) was added. The mixture was stirred at 0° for 2 hr and then at room temp for 1 hr. The mixture, after work up as usual, was methylated with diazomethane and purified by passing through a column (Al_2O_3, 3 g, eluent: EtOH) to afford nigakilactone A (**4a**, about 5 mg), whose IR, PMR, MS and TLC were identical with those of **4a**.

Treatment of picrasin E (**3b**) *with* BCl_3. Picrasin E (**3b**, 18·6 mg) was dissolved in CH_2Cl_2 (2 ml) and kept at −80°. To this soln BCl_3 in CH_2Cl_2 (1·5 ml) was added during 5 min and the resulting soln was stirred at 0° for 30 min and then at room temp for 2 hr. After addition of MeOH, the mixture, giving 4 spots on TLC, was mentylated with diazomethane, and purified by silica gel column (eluent: acetone–benzene, 1 : 1) followed by preparative TLC. Nigakilactone M (10·6 mg) and the starting picrasin E were obtained. The resulting nigakilactone M was identical with the natural product in respects of IR, UV, PMR, MS and TLC.

Demethylation of nigakilactone F (**10a**) *with* BCl_3. A soln of **10a** (64 mg) in CH_2Cl_2 (2 ml) was kept at −80°. BCl_3 (0·3 ml) in CH_2Cl_2 (1·5 ml) was added to this soln dropwise during 10 min. After the soln was stirred for 3 hr at room temp, CH_2Cl_2 and BCl_3 were removed *in vacuo* to give a pale yellow residue. In order to remove HCl in the residue, MeOH (10 ml) containing 0·05% H_2O was added to it and the solvents were distilled off. Four-times repetition of the procedure gave HCl-free pale yellow material, which was dissolved in MeOH (2 ml) and treated with diazomethane in ether. The reaction product showed 4 spots on TLC. The components with the highest and the third R_f values were negative for $FeCl_3$-test. These two compounds were separated by preparative TLC (developed with benzene–acetone, 3 : 2). The compound with the highest R_f value was identical with the starting material. The compound with the third R_f value was obtained as a colorless solid (8 mg), which was identified with nigakilactone N (**4b**) by MS, PMR, IR and TLC.

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