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BITTER PRINCIPLES OF *PICRASMA AILANTHOIDES* PLANCHON

NIGAKIHEMIACETALS A, B AND C, AND NIGAKILACTONES G, H AND I[1]

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Abstract—Three new crystalline bitter principles, nigakihemiacetal A (I), nigakihemiacetal C (IIIa) and nigakilactone H (V), have been isolated from the stem-chips of *Picrasma ailanthoides* Planchon (Simaroubaceae), and their structures determined. The other three bitter constituents, nigakihemiacetal B, nigakilactone G and nigakilactone I proved to be identical with neoquassin (II), picrasin A (IVa) and picrasin B (VI), respectively.

THE isolation and determination of the structures of bitter principles (nigakilactones A, B, C, D, E and F) of *Picrasma ailanthoides* Planchon (= *P. quassioides* Bennett) (Japanese name: nigaki, Simaroubaceae) have already been reported.[2] The concentrated aqueous extract of the stem-chips of the same plant was further extracted with benzene and the extract was purified by repetition of chromatography giving rise to the other six bitter substances, which we have named nigakihemiacetals A, B and C, and nigakilactones G, H and I. Evidence establishing structures I, III and V for nigakihemiacetal A, nigakihemiacetal C and nigakilactone H, respectively, are reported in the present paper.[1] Recently, isolation of picrasins A,[3b] B,[3a] D and E[3c] from the same plant together with their structural studies were recorded by Hikino *et al.*[3] Nigakihemiacetal B, nigakilactone G and nigakilactone I are shown to be identical with neoquassin (II),[4] picrasin A (IVa)[3b] and picrasin B (VI),[3a] respectively.

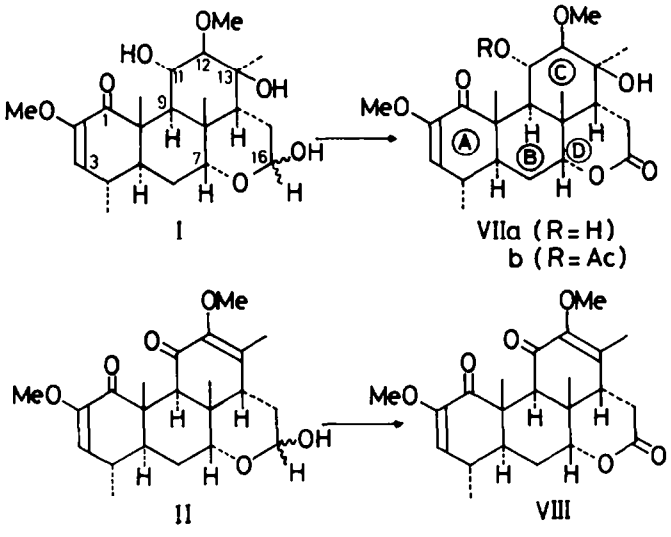
Nigakihemiacetals A (I), *B* (II) *and C* (IIIa)*

Nigakihemiacetal A crystallized from aqueous EtOH as colourless needles, m.p. 262–263° and $[\alpha]_D$ + 20° (EtOH). Elemental analysis and the mass spectrum indicate the formula $C_{22}H_{34}O_7$ (M^+ at *m/e* 410). The IR spectrum in nujol shows OH absorptions at 3560, 3470 and 3360 cm^{-1}. The UV absorption at 272 nm (ε 5800) and IR absorptions at 1668 and 1634 cm^{-1} indicate the presence of an α,β-unsaturated ketone function. No absorption was observed in the region which would be expected for a lactone grouping. The PMR spectrum showing the presence of one secondary and three tertiary Me's and two OMe groups (Table 1), is closely related to the spectrum of known nigakilactone F (VIIa).[2b] A doublet (1H, δ 2·51, *J* = 11 Hz), a quartet (1H, δ 3·52, *J* = 11 and 9 Hz), a doublet (1H, δ 2·98, *J* = 9 Hz) and an olefinic proton doublet (δ 5·40, *J* = 2·5 Hz) are considered to be due to protons at C-9, C-11, C-12 and C-3, respectively, if the presence of the same skeletal structure of rings A, B and C

* The hemiacetals of this type exist as a mixture of isomers at C-16. Separation on preparative TLC followed by elution of each component with solvent such as acetone and MeOH resulted in formation of the same mixture.

is assumed for nigakihemiacetal A and nigakilactone F. The marked difference between the PMR spectra of nigakihemiacetal A and nigakilactone F is that in the former spectrum a multiplet at δ 3·88 (1H) appears and no signal due to a proton at the lactone terminus ($-\underset{|}{CH}-O-CO-$) is observed. These observations suggest that nigakihemiacetal A is a hemiacetal related to nigakilactone F. The signal at δ 3·88 could be due to a proton at the hemiacetal terminus ($-\underset{|}{CH}-O-CH(OH)-$). On oxidation with Ag_2O, nigakihemiacetal A gave nigakilactone F (VIIa).[2b] Thus, the structure of nigakihemiacetal A is established as I.

The molecular formula of $C_{22}H_{30}O_6$ (M^+ at *m/e* 390) was given for nigakihemiacetal B, m.p. 230·5–231°, $[\alpha]_D$ + 20° (EtOH). The IR, UV and PMR spectral data (Table 1) suggest that this bitter substance would be identical with neoquassin (II),[4] a hemiacetal isolated from *Quassia amara* (Simaroubaceae). This was confirmed by the formation of quassin (VIII)[4] on oxidation of this hemiacetal with Ag_2O.



The molecular formula of nigakihemiacetal C, $C_{21}H_{32}O_6$, m.p. 265–265·5°, $[\alpha]_D$ + 49° (MeOH), was determined by elemental analysis and the appearance of the M^+ peak at *m/e* 380 in the mass spectrum. The IR (3520, 3280, 3200, 1658 and 1634 cm^{-1}) and UV (λ_{max} 272 nm; ε 4600; in MeOH) spectra reveal characteristic absorptions for OH and an α,β-unsaturated ketone. No absorption was observed in the region which would be expected for a lactone grouping. The presence of two secondary and two tertiary Me's, a OMe group and an olefinic proton is shown in the PMR spectrum (Table 1) which is closely related to that of known nigakilactone A (IXa).[2a] This provides convincing support for the presence in nigakihemiacetal C of the same skeletal structure as that of nigakilactone A.

Nigakihemiacetal C, when treated with Ac_2O-pyridine at room temperature, afforded a diacetate (IIIb), $C_{25}H_{36}O_8$ (M^+ at *m/e* 464), which still shows OH bands in

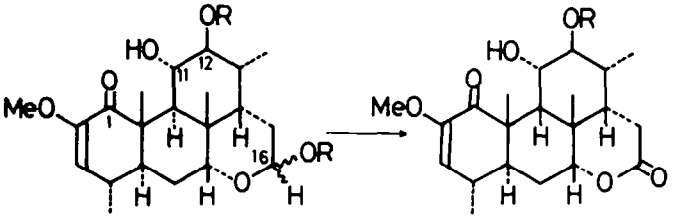
TABLE 1. PMR SPECTRAL DATA (δ in ppm)[a]

Compounds	I	II	IIIa	IVa[b]	IVb	V	VI	VIIa	VIII	IXa	XI	XII	XIIIb
t-CH_3	1·20s 1·34s 1·44s	1·05s 1·49s	1·16s 1·45s	0·97s 1·00s 1·41s	0·91s 1·02s 1·20s	1·27s 1·35s 1·50s	1·20s 1·45s	1·22s 1 46s 1·46s	1·18s 1·54s	1·24s 1·42s	1·17s 1·19s 1·71s	1·27s 1·53s	0·92s 0·98s 1·31s
s-CH_3	1·11d $J = 7$	1·07d $J = 6$	1·05d $J = 7$ 1·13d $J = 6$	0·89d $J = 7$	1·08d $J = 7$	1·15d $J = 7·5$	0·93d $J = 6$	1·11d $J = 7$	1·11d $J = 7$	1·01d $J = 6·5$ 1·10d $J = 6$	1·03d $J = 6$	1·15d $J = 6$	1·13d $J = 7$
C=C−CH_3	—	1·83s	—	—	—	—	1·91s	—	1·85s	—	—	2·00s	—
−O−CO−CH_3	—	—	—	—	1·97s	—	—	—		—	—	—	1·99s 2·15s
CH−OCH_3	2·98d $J = 9$	—	—	—	—	3·02d $J = 9$		3·03d $J = 9$	—	—	3·83s		—
−OCH_3	3·58s 3·69s	3·55s 3·61s	3·53s	3·49s	3·57s	3·63s 3·77s	3·65s	3·58s 3·73s	3·54s 3·65s	3·54s	3·58s 3·58s	3·55s 3·78s	—
CH−OH[c]	3·52q $J = 11$ $J = 9$	-			—	3·96q $J = 11$ $J = 9$		4·00q $J = 11$ $J = 9$	—		—	–	—
C | C−C_7−O− | H	3·88m	3·95m		4·24m	4·20m	4·56m	4·30m	4·13m	4·36m	4·10m	4·53m	4·28m	4·18m
C=CH	5·40d $J = 2·5$	5·25d $J = 2·5$	5·48d $J = 2$	5·32d $J = 2·5$	5·16d $J = 2·5$	5·51d $J = 2·5$	—	5·43d $J = 2$	5·29d $J = 2$	5·35d $J = 2·5$	5·42d $J = 2·5$	5·28d $J = 2·5$	5·95d $J = 2·5$

[a] Determined in $CDCl_3$ at 60 MHz.
[b] Determined in Pyr-d_5 at 60 MHz.
[c] Other than hemiacetal structure. Coupling constants are expressed in Hz. s: singlet, d: doublet, q: quartet, m: multiplet.

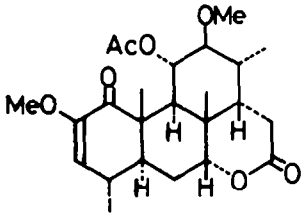
its IR spectrum. In the PMR spectrum, signals due to protons on acetoxyl-bearing carbon appear at δ 4·95 (1H), δ 5·72 (0·5H) and δ 6·33 (0·5H). These observations suggest that nigakihemiacetal C is a hemiacetal related to nigakilactone A. In fact, oxidation of nigakihemiacetal C with Ag_2O gave nigakilactone A (IXa).[2a] Thus, nigakihemiacetal C should be represented by IIIa.

The presence of H-bond between the OH group at C-11 and the CO group at C-1 has been shown[2c] for nigakilactone A (IXa), nigakilactone B (IXb)[2a] and nigakilactone F (VIIa),[2b] which exhibit the UV maximum at 272 nm (in MeOH or EtOH). This absorption maximum is shifted to 263–265 nm (in MeOH or EtOH) for nigakilactone C (X),[2a] nigakilactone E (VIIb)[2b] and for 11-keto derivatives,[2c] which are lacking such an OH group.[2c] The above diacetate showing the UV maximum at 272 nm can be formulated as 12, 16-diacetate (IIIb). The absorption maximum at 272 nm of nigakihemiacetal A is compatible with the structure I.



IIIa (R=H)
b (R=Ac)

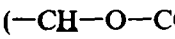
IXa (R=H)
b (R=Me)



X

Nigakilactone H (V)

The analysis of nigakilactone H, m.p. 274·5–275·5°, $[\alpha]_D$ + 67° (EtOH), fitted best for molecular formula $C_{22}H_{32}O_8$ (M^+ at *m/e* 424). The IR (3450, 1675, 1640 cm^{-1}) and UV (λ_{max} 271 nm; ε, 4260; in MeOH) spectra show characteristic absorption bands for an α,β-unsaturated ketone and the OH group. An IR absorption at 1725 cm^{-1} 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 4·56 (1H, m) due to proton

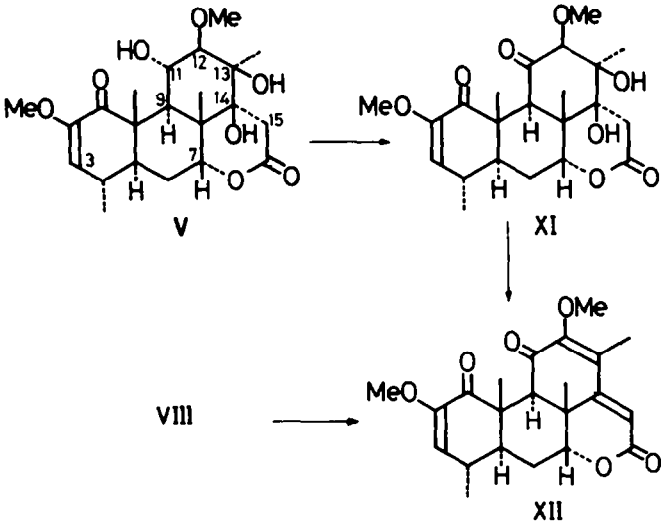


at the lactone terminus (—CH—O—CO—). The presence of one secondary and three tertiary Me's and two OMe groups is shown in the PMR spectra, which is best interpreted on the basis of skeletal structure (rings A, B and C) of known nigakilactone F (VIIa)[2b] (Table 1). The protons on C-9, C-11, C-12 and C-3 of nigakilactone H resonate as a doublet (1H, δ 2·05, J = 11 Hz), a quartet (1H, δ 3·96, J = 11 and 9 Hz), a doublet (1H, δ 3·02, J = 9 Hz) and as a doublet (1H, δ 5·51, J = 2·5 Hz), respectively.

Oxidation of nigakilactone H with sodium dichromate in acetic acid gave a ketone (XI), m.p. 161–163°, $C_{22}H_{30}O_8$. In the PMR spectrum, signals due to protons on C-9 and C-12 appear as a singlet at δ 2·61 (1H) and a singlet at δ 3·38 (1H), respectively. No signal due to proton on C-11 is observed.

These observations along with the molecular formula of nigakilactone H suggest that this lactone contains one OH group more than nigakilactone F (VIIa). Furthermore, in the PMR spectra of nigakilactone H and its ketone (XI), a signal due to two protons on C-15 appears as *singlet* at δ 2·67 and at δ 2·89, respectively. This shows that the C-14 is tertiary, and leads to the location of an extra OH group on C-14 for nigakilactone H. Thus, nigakilactone H and its ketone should be represented by V and XI, respectively.

On treatment with thionyl chloride in pyridine at room temperature, the ketone (XI) afforded a dehydrated product, whose IR, UV, PMR, MS and $[\alpha]_D$ data were identical with those of known dehydroquassin (XII)[4] prepared from quassin (VIII).[4] The skeletal structure of nigakilactone H is thus confirmed. In the PMR spectrum of nigakilactone H, the coupling constants between protons on C-9 and C-11 (J = 11 Hz) and between protons on C-11 and C-12 (J = 9 Hz) show that the three adjacent protons are in axial-axial relationships. The signal due to proton on C-7 of nigakilactone F (VIIa) appears at δ 4·13 (1H, m), and the corresponding proton of nigakilactone H resonates at downfield δ 4·56 (1H, m). This shows that the OH group on C-14 of nigakilactone H is in β-configuration. The facile dehydration of the ketone (XI) to yield XII suggests that the OH group at C-13 is in axial conformation. Therefore the stereostructure of nigakilactone H can be represented by V. The UV maximum at 271 nm provides support for the location of the OH group on C-11 for nigakilactone H (V), while the ketone (XI) shows an absorption maximum at shorter wave length (264 nm).



Nigakilactones G (IVa) *and I* (VI)

Nigakilactone G, $C_{26}H_{34}O_8$ (M^+ at *m/e* 474), m.p. 305–305·5°, $[\alpha]_D$ + 41° (EtOH), is shown to be identical with picrasin A (IVa)[3b] reported by Hikino *et al.* Our work

described below includes some different transformations from that reported by Hikino *et al.* Spectral data are also presented (Table 1).

The IR and UV spectra of nigakilactone G show the presence of an α,β-unsaturated ketone function, a ketone, a δ-lactone, a γ-lactone and the OH group. In the PMR spectrum the presence of one secondary and three tertiary Me's, a OMe group and an olefinic proton is observed.

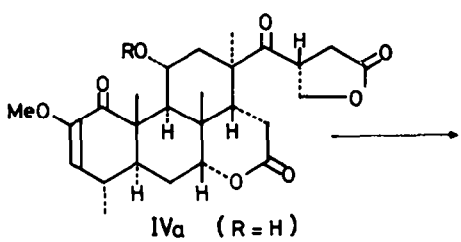
Acetylation of nigakilactone G gave a monoacetate (IVb), $C_{28}H_{36}O_9$ (M^+ at *m/e* 516), m.p. 295–296°, which shows no IR absorption due to OH group. Therefore one OH group should be present in nigakilactone G.

The nature of eight O atoms involved in nigakilactone G is thus characterized. The above spectral data along with the molecular formula suggest that nigakilactone G is related to known simarolide (XIV).[5] Nigakilactone G shows the UV maximum at 271 nm while the maximum at 263 nm is observed for IVb. This suggests the presence of H-bonding between the OH group (at C-11) and the CO group (at C-1) for nigakilactone G.

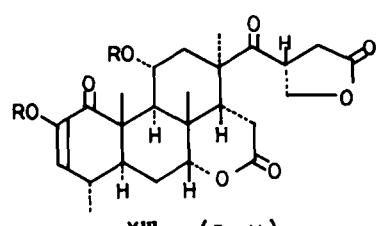
Treatment of nigakilactone G with hydrochloric acid in acetic acid afforded nornigakilactone G (XIIIa), $C_{25}H_{32}O_8$ (M^+ at *m/e* 460), m.p. 280·5–282°, whose UV maximum in MeOH shifted from 279 nm to 321 nm on addition of alkali. This shows the presence of a diosphenol moiety in XIIIa and in turn a methylated diosphenol grouping in nigakilactone G (most probably in the A ring).

On acetylation, nornigakilactone G (XIIIa) gave its diacetate (XIIIb), $C_{29}H_{36}O_{10}$ (M^+ at *m/e* 544), m.p. 308–309°, whose olefinic proton (on C-3) resonates at downfield δ 5·95 (1H, d, J = 2·5 Hz) while the corresponding proton of IVb appears at δ 5·16 (1H, d, J = 2·5 Hz) (Table 1).

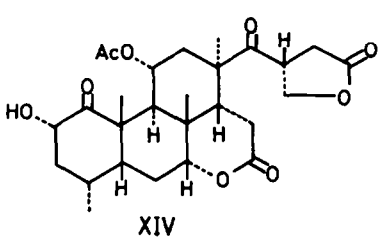
These observations lead to a location of an OH group on C-11, and of methylated diosphenol grouping in the ring A as shown in IVa for nigakilactone G. Furthermore, the spectral data of nornigakilactone G (XIIIa) and the diacetate (XIIIb) are in accord



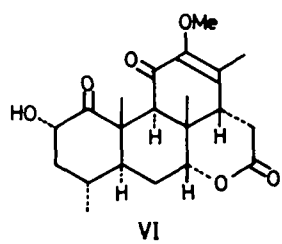
IVa (R = H)
b (R = Ac)



XIIIa (R = H)
b (R = Ac)



XIV



VI

with those of the simarolide derivatives XIIIa[5a] and XIIIb,[5a] respectively, described by Polonsky. Thus, the structure IVa is suggested for nigakilactone G. The identity of nigakilactone G with picrasin A (IVa)[3b] was confirmed by direct comparison.

Finally, spectral data of nigakilactone I, $C_{21}H_{28}O_6$ (M^+ at *m/e* 376), m.p. 255–256°, $[\alpha]_D$ + 3° (in EtOH), suggest that this substance would be identical with picrasin B (VI).[3a] This was confirmed by direct comparison with the authentic specimen.

A number of bitter principles have been isolated from plants of the family Simaroubaceae.[6] Neoquassin (II) is the only bitter substance which has a hemiacetal moiety in the D ring, although several bitter substances are known to have the same moiety in the C ring.[6] Nigakihemiacetals A (I) and C (IIIa) constitute the second and the third examples of the former type.

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 $CDCl_3$ solution containing TMS as an internal standard, unless otherwise stated. Chemical shifts are expressed in δ (ppm downfield from TMS). All melting points were determined on a hot block and are reported uncorrected.

Isolation. The stem-chips (160 kg) of *Picrasma ailanthoides* Planchon were ground into powder and extracted three times with boiling water. The aqueous extract was concentrated under reduced pressure and extracted with benzene. Evaporation of the solvent gave a dark brown residue (70 g) which tasted considerably bitter. The residue was chromatographed on alumina (2 Kg, Showa Chemical Co.; treated with dil HCl, washed with water and dried at 110° for 6 hr). The eluted fractions (each 3 l) were collected and examined by TLC (silica gel).

Fractions 14–18 (eluent: ether) were combined and the solvent was distilled off. The residue (2·3 g) was further chromatographed on silica gel dry column (250 g, Wako-gel C-200). Each fraction eluted with AcOEt-ether (1 : 2) (each 50 ml) was tested for TLC (silica gel). The fractions 5–9 thus obtained were combined and the solvent distilled off. The residue was crystallized from benzene-light petroleum to give *nigakihemiacetal B* (II) (0·8 g) as colourless plates, m.p. 230·5–231°; $[\alpha]_D$ + 20° (*c* 0·21, in EtOH); UV (MeOH) λ_{max} 256 nm (ε 11,400); IR (Nujol) γ_{max} 3400, 1690, 1674, 1640, 1621 cm^{-1}. (Found: C, 68·14; H, 7·44. Mol. wt. by mass spectrum 390. Calc. for $C_{22}H_{30}O_6$: C, 67·67; H, 7·74%. Mol. wt. 390). PMR data are registered in the Table 1.

Fractions 27–34 (eluent: AcOEt–ether, 1 : 1) gave a residue (4·9 g) which was chromatographed on silica gel dry column (400 g) (eluent: AcOEt–ether, 1 : 1; each fraction 150 ml) to give the fractions 7–9. These fractions were combined and evaporation of the solvent gave a residue (4·1 g) which was further chromatographed on silica gel dry column (200 g) (eluent: AcOEt-ether, 1 : 1; each fraction 50 ml). The fractions 8–12 gave a residue which was chromatographed on silica gel dry column (eluent: AcOEt-benzene, 1 : 1). Fractional crystallization of this residue from acetone gave nigakilactone E (VIIb)[2b] and *nigakihemiacetal A* (I). The latter compound (I) was crystallized from aqueous EtOH as colourless needles (200 mg), m.p. 262–263°, $[\alpha]_D$ + 20° (*c*, 0·22, in EtOH); UV (MeOH) λ_{max} 272 nm (ε 5800), IR (Nujol) γ_{max} 3560, 3470, 3360, 1668, 1634 cm^{-1}; PMR (Table 1). (Found: C, 63·76; H, 8·20. Mol wt. by mass spectrum 410. Calc. for $C_{22}H_{34}O_7$: C, 64·37; H, 8·35%. Mol. wt. 410).

Fraction 39 (eluent: AcOEt) 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 solvent gave a residue (0·7 g) which was further chromatographed on silica gel dry column (150 g) (eluent: AcOEt-ether, 1 : 1, each fraction 30 ml). The fractions 11–13 were combined and evaporation of the solvent gave a residue (200 mg) which was chromatographed on silica gel dry column (30 g) (eluent: benzene-acetone, 2 : 1; each fraction 10 ml). The fractions 8–11 gave a solid which was crystallized from $CHCl_3$-light petroleum to give *nigakilactone H* (V) as colourless needles (20 mg), m.p. 274·5–275·5°; $[\alpha]_D$ + 67° (*c*, 0·14, in EtOH), UV (MeOH) λ_{max} 271 nm (ε 4260) : IR (Nujol) γ_{max} 3450, 1725, 1675, 1640 cm^{-1}; PMR (Table 1). (Found: C, 62·46; H, 7·62. Mol. wt. by mass spectrum 424. Calc. for $C_{22}H_{32}O_8$: C, 62·25; H, 7·60%. Mo. wt. 424).

Fractions 40–41 (eluent : AcOEt) gave a residue (2·2 g) which was chromatographed on silica gel dry column (250 g) (eluent : AcOEt-benzene. 1 : 1 : each fraction 50 ml). The fractions 10–16 gave a residue (500 mg) which was further chromatographed on silica gel dry column (100 g) (eluent acetone-benzene. 1 : 2) to afford *nigakilactone I* (VI) which was crystallized from AcOEt as colourless needles (300 mg), m.p. 255–256°, $[\alpha]_D$ + 3° (*c*, 0·22, in EtOH), UV (MeOH) λ_{max} 253 nm (ε 9100); IR (Nujol) ν_{max} 3480, 1732, 1722, 1674, 1636 cm^{-1}; PMR (Table 1). Mol. wt. by mass spectrum 376. $C_{21}H_{28}O_6$ requires Mol. wt. 376. This substance was shown to be identical with authentic specimen of picrasin B[3a] in all respects. The fractions 17–26 gave a residue (2·2 g) which was dissolved in $CHCl_3$. After cooling there appeared precipitated material which was crystallized from acetone and aqueous MeOH to give *nigakihemiacetal C* (IIIa) as colourless needles (100 mg), m.p. 265–265·5°; $[\alpha]_D$ + 49° (*c*, 0·13, in MeOH); UV (MeOH) λ_{max} 272 nm (ε 4600); IR (Nujol) ν_{max} 3520, 3280, 3200, 1658, 1634 cm^{-1}; PMR (Table 1). (Found: C, 65·95; H, 8·48. Mol. wt. by mass spectrum 380. $C_{21}H_{32}O_6$ requires; C, 66·30; H, 8·48%. Mol. wt. 380).

Fractions 52–59 (eluent: AcOEt-acetone, 1 : 1) gave a residue (3·5 g) which was chromatographed on silica gel dry coloumn (500 g) (eluent: benzene-acetone, 3 : 1; each fraction 100 ml). The fractions 17–21 gave *nigakilactone G* (IVa) which crystallized from acetone-benzene as colourless needles (300 mg), m.p. 305–305·5°; $[\alpha]_D$ + 41° (*c*, 0·29. in EtOH); UV (MeOH) λ_{max} 271 nm (ε 5300); IR (Nujol) ν_{max} 3430, 1778, 1734, 1690, 1678, 1640 cm^{-1}; PMR (Table 1). (Mol. wt. by mass spectrum 474. $C_{26}H_{34}O_8$ requires Mol. wt. 474). This substance was shown to be identical with authentic specimen of picrasin A[3b] in all respects.

Oxidation of nigakihemiacetal A. Compound I (18 mg) was dissolved in 10 ml EtOH and 8 ml water, and treated with freshly prepared Ag_2O (from 1 g $AgNO_3$) for 17 hr under reflux. The warm mixture was filtered through Celite, the filtrate was diluted with water and extracted with $CHCl_3$. Evaporation of the solvent yielded a residue which was purified by silica gel dry column chromatography followed by crystallization from aqueous MeOH to afford colourless needles (14 mg), which were shown to be identical with nigakilactone F (VIIa)[2b] by IR, UV, NMR, $[\alpha]_D$, TLC, mass spectrum and mixed m.p.

Oxidation of nigakihemiacetal B. Compound II (22 mg), treated with Ag_2O, gave a crude reaction product. This was crystallized from benzene-light petroleum to afford a lactone as colourless needles. This lactone was shown to be identical with the authentic specimen of quassin (VIII)[4] in all respects.

Acetylation of nigakihemiacetal C. Compound IIIa (10 mg) was treated with Ac_2O (2 ml) in pyridine (2 ml) for 15 hr at room temp. The mixture was treated as usual to give a residue. Crystallization from $CHCl_3$-light petroleum afforded IIIb as colourless crystals, m.p. 157–163°; UV (MeOH) λ_{max} 272 nm (ε 5300); IR (Nujol) ν_{max} 3450, 1740, 1672, 1630, 1240 cm^{-1}. (Mol. wt. by mass spectrum 464. $C_{25}H_{36}O_8$ requires Mol. wt. 464).

Oxidation of nigakihemiacetal C. Compound IIIa (32 mg), treated with Ag_2O, gave a residue which, on crystallization from benzene-light petroleum, afforded IXa[2a] as colourless needles (24 mg). The identity was confirmed by direct comparison with an authentic specimen.

Oxidation of nigakilactone H. To a soln of V (17 mg) in AcOH (1 ml), $Na_2Cr_2O_7$ (100 mg) in AcOH (1 ml) was added and the mixture was kept for 2 hr at room temp, neutralized with $NaHCO_3$ and extracted with $CHCl_3$. Evaporation of the solvent gave a residue which was crystallized from benzene-light petroleum to afford XI as colourless needles, m.p. 161–163°; UV (MeOH) λ_{max} 264 nm (ε 5920); IR (Nujol) ν_{max} 3450, 1720, 1690, 1625 cm^{-1}; PMR (Table 1). (Mol. wt. by mass spectrum 422. $C_{22}H_{30}O_8$ requires Mol. wt. 422).

Dehydration of the ketone (XI). To a soln of XI (13 mg) in pyridine (0·5 ml) was added $SOCl_2$ (0·1 ml), and the mixture kept for 40 min at room temp. The soln was poured on ice-water and extracted with $CHCl_3$. The extract was purified by preparative silica gel TLC followed by crystallization from aqueous MeOH to afford XII whose identity with dehydroquassin[4] was confirmed by TLC, IR, UV, $[\alpha]_D$ and mass spectrum.

Dehydroquassin (XII). A soln of VIII[4] (451 mg), DDQ (271 mg) and benzoic acid (146 mg) in benzene (15 ml) was heated under reflux for 16 hr. The cooled mixture was filtered and the filtrate was chromatographed on alumina column (70 g, Showa Chemical Co.) (eluent: benzene-acetone, 2 : 1; each fraction 50 ml). The fraction 4 gave a residue (235 mg) which was further chromatographed on silica gel dry column (eluent: ether) followed by crystallization from aqueous MeOH to afford XII as pale yellow needles (17 mg), m.p. 214–216°; $[\alpha]_D$ + 200° (*c*, 0·05, in EtOH); UV (MeOH) λ_{max} 228 nm (ε 8500), 269 nm (ε 9200), 303 nm (ε 11000); IR (Nujol) 1727, 1701, 1686, 1632, 1614, 1588 cm^{-1}; PMR (Table1). (Mol. wt. by mass spectrum 386. $C_{22}H_{26}O_6$ requires Mol. wt. 386). These data are in good agreement with those of dehydroquassin reported.[4]

Acetylation of nigakilactone G. A mixture of IVa (29 mg), Ac_2O (4 ml) and pyridine (4 ml) was heated on steam bath for 17 hr, and after addition of MeOH the solvent was evaporated *in vacuo* to afford a residue (28 mg). This was chromatographed on silica gel dry column (8 g) (eluent: benzene-acetone, 3 : 1) followed

by crystallization from benzene-light petroleum to give IVb as colourless prisms, m.p. 295–296°; Mol. wt. by mass spectrum 516, $C_{28}C_{36}O_9$ requires Mol. wt. 516; UV (MeOH) λ_{max} 263 nm (ε 4100); IR (Nujol) ν_{max} 1782, 1737, 1718, 1697, 1640, 1255 cm^{-1}, absence of ν_{O-H}; PMR (Table 1).

Demethylation of nigakilactone G. A mixture of IVa (28 mg), 2N HCl (12 ml) and AcOH (4 ml) was heated on steam bath for 1·5 hr, cooled and, after addition of 2N NH_4OH (12 ml), alkalined with $NaHCO_3$. Extraction with $CHCl_3$ and chromatography on silica gel dry column (6 g) (eluent: benzene-acetone, 3:1) followed by crystallization from acetone–benzene–light petroleum gave XIIIa, m.p. 280·5–282°; Mol. wt. by mass spectrum 460, $C_{25}H_{32}O_8$ requires Mol. wt. 460; UV (MeOH) λ_{max} 279 nm (ε 5250), shifted to 321 nm (ε 3400) in alcoholic alkali; IR (Nujol) ν_{max} 3400, 1778, 1728, 1690, 1667, 1652 cm^{-1}.

Acetylation of nornigakilactone G (XIIIa). A mixture of XIIIa (20 mg), NaOAc (30 mg) and Ac_2O (2 ml) was heated under reflux for 2 hr. Evaporation of Ac_2O under reduced pressure gave a residue which was dissolved in $CHCl_3$. Insoluble materials were filtered off and the filtrate was evaporated to dryness. The residue was chromatographed on silica gel dry column followed by crystallization from MeOH to afford XIIIb as colourless crystals, m.p. 308–309°; Mol. wt. by mass spectrum 544, $C_{29}H_{36}O_{10}$ requires Mol. wt. 544; UV (MeOH) λ_{max} 234 nm (ε 5950); IR (Nujol) ν_{max} 1769, 1731, 1716, 1696, 1252 cm^{-1}, absence of ν_{O-H}; PMR (Table 1).

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