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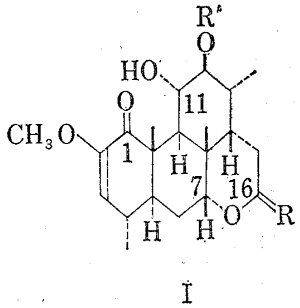
Bitter Principle of *Picrasma ailanthoides* PLANCHON. Nigakihemiacetal C

A number of bitter principles have been isolated from *Picrasma ailanthoides* PLANCHON (=*P. quassioides* BENNETT), and their structures have been determined.1–5) In addition to the previously reported nigakilactones A, B, C, D (=quassin),1) E, F,3) G (=picrasin A4)) and H5) along with nigakihemiacetals A and B (=neoquassin),5) we have recently isolated a new bitter substance, nigakihemiacetal C. The evidence establishing structure I (R=OH, H; R′=H) for nigakihemiacetal C is reported in the present paper.

Nigakihemiacetal C6) crystallized as colourless needles from ethanol, with mp 265—265.5° and $[\alpha]_D$ +49° (MeOH). The mass spectrum indicates the formula $C_{21}H_{32}O_6$ (M^+ at *m/e* 380). The infrared (IR) (ν_{max}^{Nujol} 3520, 3280, 3200, 1658, 1634 cm^{-1}) and ultraviolet (UV) (λ_{max}^{MeOH} 272 nm, ε 4600) spectra reveal characteristic absorptions for hydroxyl group and an α,β-unsaturated ketone. No absorption was observed in the region which would be expected for a lactone grouping. The proton magnetic resonance (PMR) spectrum of nigakihemiacetal C showing the presence of two secondary and two tertiary methyls, a methoxyl group and an olefinic proton, is closely related to the spectrum of known nigakilactone A,1) I (R=O, R′=H) (Table I).

TABLE I. PMR Spectral Data (δ in ppm, in $CDCl_3$)

Compounds	*sec*-CH_3	*t*-CH_3	$-O-C\underline{H}_3$	$\overset{C}{\overset{\mid}{C-C\underline{H}-O-}}$ (7)	$C=C\underline{H}$
Nigakihemiacetal C	1.05 d *J*=7	1.16 s	3.53 s		5.48 d *J*=2
	1.13 d *J*=6	1.45 s			
Nigaklilactone A	1.01 d *J*=6.5	1.24 s	3.54 s	4.10 m	5.35 d *J*=2.5
	1.10 d *J*=6	1.42 s			



I

Nigakihemiacetal C, when treated with Ac_2O-pyridine at room temperature, afforded a diacetate ($C_{25}H_{36}O_8$, M^+ at *m/e* 464, ν_{max}^{Nujol} 3450, 1740, 1672, 1630, 1240 cm^{-1}; λ_{max}^{MeOH} 272 nm, ε 5300), which still shows hydroxyl bands in its IR spectrum. In the PMR spectrum (in $CDCl_3$), signals due to proton 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, I (R=OH, H; R′=H), related to nigakilactone

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6) The hemiacetals of this type exist as mixture of isomers at C_{16}. Separation on preparative thin-layer chromatogram followed by elution of each component with acetone resulted in formation of the same mixture.

A. Indeed, nigakihemiacetal C gave nigakilactone A,[1] I (R=O, R'=H), on oxidation with Ag_2O. Thus, nigakihemiacetal C should be represented by I (R=OH, H; R'=H). The presence of hydrogen bond between carbonyl at C_1 and hydroxyl group at C_{11} leads to structure I (R=OAc, H; R'=Ac) for the diacetate.

Spectral data of nigakilactone I, mp 255—256°, $C_{21}H_{28}O_6$ (M^+ at *m/e* 376), suggest that this bitter substance would be identical with picrasin B.[2] This was confirmed by direct comparison with the authentic specimen.[2]

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Total Synthesis of Optically Active Natural O-Methylthalicberine

O-Methylthalicberine is the first bisbenzylisoquinoline alkaloid isolated from a Ranunculaceous plant, that is, *Thalictrum Thunbergii* DC (Japanese name "Akikaramatsu") by Fujita and Tomimatsu.[1] Its structure[2] and absolute configuration[2,3] has been clarified and its unique 19-membered macro-ring system was the first example[4] in the bisbenzylisoquinoline alkaloids. We describe here the total synthesis of optically active natural O-methylthalicberine, which confirms its structure and absolute configuration **1b**.

An important intermediate, (*S*)-(+)-O-benzyl-8-bromo-N-nor-laudanidine (**2a**), mp 98—99°, $[\alpha]_D$ +38.7° ($CHCl_3$), was yielded by the optical resolution of the synthetic racemate of **2a** *via* its (−)-tartaric acid salt. N-Methylation of the resolved base **2a** gave (+)-O-benzyl-8-bromolaudanidine (**2b**). The structure and optical purity of the compounds **2a** and **2b** was assured by the comparison of the melting point and the specific rotation with those of their enantiomers which have been synthesized by Inubushi, *et al.*,[5] respectively.

The Ullmann condensation of the base **2b** with N-*t*-butoxycarbonyl-3-hydroxy-4-methoxyphenethyl amine (**3**), mp 101—102°, $C_{14}H_{21}O_4N$, synthesized from O-benzylisovanillin *via* a usual pathway afforded the compound **4a** as an oily product[6] in 39% yield. Hydrogenolysis

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[5] Y. Inubushi, Y. Masaki, S. Matsumoto, and F. Takami, *Tetrahedron Letters*, **1968**, 3399; *idem*, *J. Chem. Soc.* (*C*), **1969**, 1547.

[6] The infrared (IR) and nuclear magnetic resonance (NMR) spectra of the amorphous or oily substance marked with this symbol showed reasonable patterns for the corresponding structure to each compound and homogeneity was also verified by thin-layer chromatography and NMR spectrum measurements.