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Constituents of the Root Bark of *Ailanthus altissima* SWINGLE. Isolation and X-Ray Crystal Structures of Shinjudilactone and Shinjulactone C and Conversion of Ailanthone into Shinjudilactone[1]

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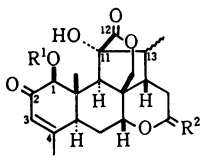
Two new quassinoids, shinjudilactone and shinjulactone C were isolated from the root bark of *Ailanthus altissima* SWINGLE and their structures were established to be 1β,11α-dihydroxy-2,16-dioxo-13(12→11α)*abeo*-picras-3-en-12,20-olide and 1α,12α : 5α,13α-dicyclo-1β,12β,20-trihydroxy-9β*H*-picras-3-ene-2,11,16-trione, respectively, by X-ray diffraction analysis. Shinjudilactone was prepared from ailanthone by benzilic acid rearrangement.

Quassinoids, bitter principles isolated from Simaroubaceous plants, have been extensively investigated from the interest in anti-tumor activity and structure determination,[2] and some of them have been shown to exhibit useful biological activities.[3] Recently these quassinoids have attracted much attention as synthetic target molecules.[4]

In Japan there grow two species of plants belonging to Simaroubaceae, *Picrasma ailanthoides* PLANCHON (=*P. quassioides* BENN, Japanese name : Nigaki) and *Ailanthus altissima* SWINGLE (=*A. glandulosa* DESF., Japanese name: Shinju or Niwaurushi) and these plants are known to contain bitter principles in leaves, barks, trunks, and roots. The bitter principles of *P. ailanthoides* have been investigated by us[2b] and by Takemoto *et al.*[5] and more than twenty quassinoids have been isolated. As a continuation of our work on bitter principles of Simaroubaceous plants in Japan, we examined the bitter principles of *A. altissima*. We wish to report on the X-ray crystal structures of new quassinoids, shinjudilactone (**1**) and shinjulactone C (**2**) isolated from root barks of the plant.

The half-dried root bark of *A. altissima*, defatted with petroleum ether, was continuously extracted with ethyl acetate and the extract was separated to afford seven



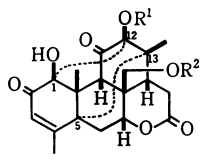
1 R^1=H, R^2=O; 13α-CH_3

5 R^1=CH_3, R^2=O; 13α-CH_3

6 R^1=Ac, R^2=O; 13α-CH_3

7 R^1=H, R^2=H,OH; 13α-CH_3

12 R^1=H, R^2=O; 13β-CH_3

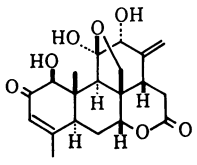


2 R^1=R^2=H

8 R^1=H, R^2=Ac

9 R^1=R^2=Ac

10 R^1=H, R^2=C(=O)H



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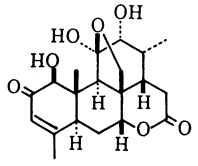

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constituents, which were however found to be all known quassinoids, amarolide,[6,7] amarolide 11-acetate,[6,7] ailanthone (**3**),[8-10] glaucarubinone,[11] $\Delta^{13(18)}$-dehydroglaucarubinone,[12] $\Delta^{13(18)}$-dehydroglaucarubolone,[13] and shinjulactone A.[14]

Concentrated aqueous extract of the root bark of this plant was continuously extracted with dichloromethane. The organic layer was evaporated to give a residue, which was subjected to separation by silica-gel column chromatography to afford two new quassinoids, shinjudilactone (**1**) and shinjulactone C (**2**) in 0.01% and 0.001% yields, respectively, together with known chaparrolide,[15] chaparrinone (**4**),[16] shinjulactone B,[17] amarolide, ailanthone (**3**), glaucarubinone, and $\Delta^{13(18)}$-dehydroglaucarubolone.

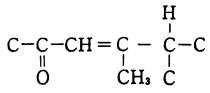
Shinjudilactone (**1**), a bitter quassinoid, crystallized from ethyl acetate-methanol as colorless needles, mp 274—276 °C and $[\alpha]_D^{23}$ +102° (pyridine). Elemental analysis and high-resolution mass spectrum indicate the formula $C_{20}H_{24}O_7$. The spectral examination showed the presence of hydroxyl(s) (IR 3250 cm^{-1}), two carbonyls (ester or lactone moieties) (IR 1745 and 1735 cm^{-1}; ^{13}C NMR δ 170.6 and 173.5), a proton at the lactone terminus (^1H NMR δ 4.808, t), an α,β-unsaturated ketone (IR 1670 cm^{-1}; UV 238 nm; ^{13}C NMR δ 196.9), a tertiary methyl, a secondary methyl, and a vinyl methyl (^1H NMR δ 1.235, s, δ 1.240, d, and δ 1.798, br s, respectively).

On methylation with diazomethane, shinjudilactone (**1**) gave *O*-methylshinjudilactone (**5**), mp 291—294 °C, which still showed an absorption band at 3400 cm^{-1} due to a hydroxyl group, indicating the presence of two hydroxyl groups for **1**. Treatment of **1** with acetic anhydride and pyridine at room temperature gave a monoacetate (**6**), which showed a singlet signal at δ 5.78 due to a proton attached to the acetoxy-bearing carbon atom and an IR absorption band due to a hydroxyl group at 3480 cm^{-1}. The hydroxyl group was shown to be tertiary, because no diacetate was produced by acetylation under drastic conditions. Shinjudilactone (**1**) was reduced with sodium borohydride to afford a hemiacetal (**7**), which showed a multiplet signal due to a hemiacetal-methine proton at δ 5.68. The IR spectrum (1740 cm^{-1}) of **7** showed a lactone grouping still remained intact, indicating that **1** possesses two lactone groupings. Seven oxygen atoms of **1** were thus

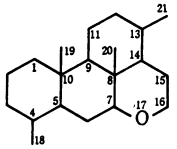
Table 1. ^{13}C NMR Spectra of shinjudilactone (**1**)[a] and chaparrinone (**4**)[b]

Position number of carbon	1	4	Position number of carbon	1	4
1	83.8d	82.5	11	78.7s	108.9
2	196.9s	197.1	12	173.5s	77.9
3	126.3d	124.7	13	45.6d	30.4
4	162.0s	162.3	14	53.6d	41.1
5	42.2d	43.1	15	32.9t	29.4
6	27.0t	25.0	16	170.6s	167.6
7	73.9d	77.6	18	22.1q	22.1
8	48.4s	44.9	19	10.6q	9.4
9	55.0d	41.1	20	76.2t	70.1
10	43.0s	44.3	21	13.8q	12.5

a) Measured in a pyridine-d_5 solution. b) Measured in a dimethyl-d_6 sulfoxide solution (Ref. 16b).



A



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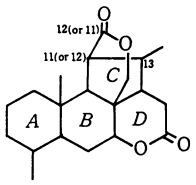


C

characterized. These findings indicate pentacyclic skeleton for **1**.

^1H NMR spectrum of shinjudilactone (**1**) showed that an olefinic proton resonating at δ 6.095 is coupled with a vinyl methyl and also with a methine proton at an allylic position with a coupling constant J=2.5 Hz, the presence of the same partial structure (**A**) as that of chaparrinone (**4**) being suggested for **1**. The assignment of signals in the ^{13}C NMR spectrum of **1** was carried out by comparison with signals of **4**[16b] (Table 1). It is inferred that the easily reducible lactone grouping should be located in the D ring[18] and the other one in the C ring. Shinjudilactone (**1**) could not be formulated based on the normal picrasane skeleton (**B**),[19] but should possess a migrated picrasane skeleton, a 13(12→11α) or 9(11→12)*abeo*-picrasane dilactone structure (**C**). Formation of **1** from ailanthone (**3**) could be reasonably explained by biogenetic consideration (*vide infra*).

Unambiguous proof for the proposed structure (**1**) of shinjudilactone was provided by X-ray diffraction analysis. The crystal of **1** belongs to a monoclinic space group $P2_1$ with the cell parameters of a=7.446(2), b=18.241(8), c=6.679(2) Å, and β=109.39(6)°. There are two molecules in the unit cell. Intensity data were collected on a Philips PW1100 automatic four-circle diffractometer using monochromated Cu $K\alpha$ radiation. A total of 1739 independent structure factors with $F_o \geq 2.5\ \sigma(F_o)$ within 2θ=156° were obtained by the 2θ-θ scanning mode. The structure was solved by the direct method using MULTAN program. An E-map revealed the positions of all the non-hydrogen atoms, and the hydrogen atoms were located in a difference electron density map. The structure was refined by the block-diagonal least-squares calculations

Table 2. Atomic positional parameters ($\times 10^4$) and isotropic temperature factor ($\times 10^2$) for non-hydrogen atoms of shinjudilactone (**1**) with estimated standard deviations in parentheses

Atom	x	y	z	B_{eq}[a]
C(1)	2375(4)	2285(0)	957(4)	357(4)
C(2)	2273(4)	1485(2)	1613(5)	478(4)
C(3)	4040(4)	1143(2)	2949(5)	514(4)
C(4)	5764(4)	1455(1)	3356(4)	432(4)
C(5)	5930(4)	2220(1)	2545(4)	311(3)
C(6)	7903(4)	2394(1)	2383(4)	347(4)
C(7)	8119(3)	3201(1)	1976(4)	245(3)
C(8)	6500(3)	3494(1)	99(4)	246(3)
C(9)	4557(3)	3274(1)	297(3)	212(3)
C(10)	4245(3)	2429(1)	485(4)	280(3)
C(11)	3300(3)	3804(1)	-1355(3)	278(3)
C(12)	3402(3)	3667(2)	-3586(4)	289(4)
C(13)	4313(3)	4555(1)	-585(4)	339(3)
C(14)	6454(3)	4350(1)	-38(4)	271(3)
C(15)	7911(4)	4701(2)	1918(4)	270(4)
C(16)	8154(3)	4306(1)	3957(4)	261(4)
C(18)	7536(5)	1083(2)	4739(5)	555(5)
C(19)	4179(4)	1952(2)	-1456(4)	307(4)
C(20)	6687(3)	3223(2)	-1980(4)	304(4)
C(21)	3723(5)	4893(2)	1197(5)	484(5)
O(1)	714(3)	2409(1)	-810(4)	428(3)
O(2)	764(3)	1150(1)	1024(5)	650(5)
O(3)	1378(2)	3802(1)	-1423(3)	365(2)
O(4)	2095(3)	3809(1)	-5172(3)	407(3)
O(5)	8458(3)	4611(1)	5659(3)	360(3)
O(6)	8092(2)	3576(1)	3903(2)	243(2)
O(7)	5031(2)	3422(1)	-3794(3)	349(3)

a) $B_{eq}=8\pi^2(u_1^2+u_2^2+u_3^2)/3$.

Tbale 3. Bond lengths of shinjudilactone (**1**) with estimated standard deviations in parentheses

Bond length		l/Å	Bond length		l/Å
Atom 1	Atom 2		Atom 1	Atom 2	
C(1)	–C(2)	1.534(3)	C(9)	–C(10)	1.570(3)
C(1)	–C(10)	1.549(4)	C(9)	–C(11)	1.530(3)
C(1)	–O(1)	1.416(3)	C(10)	–C(19)	1.549(4)
C(2)	–C(3)	1.461(4)	C(11)	–C(12)	1.537(4)
C(2)	–O(2)	1.223(4)	C(11)	–C(13)	1.567(4)
C(3)	–C(4)	1.347(4)	C(11)	–O(3)	1.416(3)
C(4)	–C(5)	1.517(4)	C(12)	–O(4)	1.205(3)
C(4)	–C(18)	1.498(4)	C(12)	–O(7)	1.343(3)
C(5)	–C(6)	1.541(4)	C(13)	–C(14)	1.558(4)
C(5)	–C(10)	1.570(3)	C(13)	–C(21)	1.529(5)
C(6)	–C(7)	1.516(4)	C(14)	–C(15)	1.534(3)
C(7)	–C(8)	1.519(3)	C(15)	–C(16)	1.497(4)
C(7)	–O(6)	1.464(3)	C(16)	–O(5)	1.217(3)
C(8)	–C(9)	1.548(4)	C(16)	–O(6)	1.332(3)
C(8)	–C(14)	1.564(4)	C(20)	–O(7)	1.459(3)
C(8)	–C(20)	1.523(4)			

TABLE 4. BOND ANGLES OF SHINJUDILACTONE (1) WITH ESTIMATED STANDARD DEVIATIONS IN PARENTHESES

Bond angle			ϕ/°	Bond angle			ϕ/°
Atom 1	Atom 2	Atom 3		Atom 1	Atom 2	Atom 3	
C(2)	–C(1)	–C(10)	110.6(2)	C(19)	–C(10)	–C(5)	113.0(2)
C(2)	–C(1)	–O(1)	106.1(2)	C(19)	–C(10)	–C(9)	116.7(2)
C(10)	–C(1)	–O(1)	113.5(2)	C(1)	–C(10)	–C(5)	106.9(2)
C(3)	–C(2)	–C(1)	117.4(3)	C(1)	–C(10)	–C(9)	110.5(2)
C(3)	–C(2)	–O(2)	121.9(3)	C(5)	–C(10)	–C(9)	102.3(2)
C(1)	–C(2)	–O(2)	120.7(3)	C(12)	–C(11)	–C(9)	112.4(2)
C(4)	–C(3)	–C(2)	123.2(3)	C(12)	–C(11)	–C(13)	106.7(2)
C(5)	–C(4)	–C(3)	120.1(3)	C(12)	–C(11)	–O(3)	110.1(2)
C(5)	–C(4)	–C(18)	118.5(2)	C(9)	–C(11)	–C(13)	101.7(2)
C(3)	–C(4)	–C(18)	121.3(3)	C(9)	–C(11)	–O(3)	113.1(2)
C(6)	–C(5)	–C(4)	114.0(2)	C(13)	–C(11)	–O(3)	112.6(2)
C(6)	–C(5)	–C(10)	113.0(2)	O(4)	–C(12)	–C(11)	122.1(2)
C(4)	–C(5)	–C(10)	113.6(2)	O(4)	–C(12)	–O(7)	118.3(2)
C(7)	–C(6)	–C(5)	111.9(2)	C(11)	–C(12)	–O(7)	119.5(2)
C(8)	–C(7)	–C(6)	112.8(2)	C(14)	–C(13)	–C(11)	102.2(2)
C(8)	–C(7)	–O(6)	108.8(2)	C(14)	–C(13)	–C(21)	116.8(2)
C(6)	–C(7)	–O(6)	105.3(2)	C(11)	–C(13)	–C(21)	112.1(2)
C(9)	–C(8)	–C(7)	110.3(2)	C(15)	–C(14)	–C(8)	111.8(2)
C(9)	–C(8)	–C(14)	105.1(2)	C(15)	–C(14)	–C(13)	118.6(2)
C(9)	–C(8)	–C(20)	111.4(2)	C(8)	–C(14)	–C 13)	104.7(2)
C(7)	–C(8)	–C(14)	113.3(2)	C(16)	–C(15)	–C(14)	114.3(2)
C(7)	–C(8)	–C(20)	110.5(2)	O(5)	–C(16)	–C(15)	123.9(2)
C(14)	–C(8)	–C(20)	106.1(2)	O(5)	–C(16)	–O(6)	118.4(2)
C(10)	–C(9)	–C(8)	115.3(2)	C(15)	–C(16)	–O(6)	117.6(2)
C(10)	–C(9)	–C(11)	127.3(2)	O(7)	–C(20)	–C(8)	111.6(2)
C(8)	–C(9)	–C(11)	98.1(2)	C(7)	–O(6)	–C(16)	118.7(2)
C(19)	–C(10)	–C(1)	107.1(2)	C(12)	–O(7)	–C(20)	122.7(2)

assuming anisotropic thermal motions for non-hydronge atoms and isotropic ones for hydrogen atoms. The final *R*-factor was 0.036. The final atomic coordinates are listed in Table 2 and bond lengths and bond angles are listed in Tables 3 and 4.[20] The computer-generated perspective drawing of molecule **1** is shown in Fig. 1.

Thus the structure of shinjudilactone (**1**) is shown to be formulated as 1β,11α-dihydroxy-2,16-dioxo-13(12→11α)*abeo*-picras-3-en-12,20-olide. The same rearranged skeleton could be derived by a 9(11→12)*abeo*-type rearrangement (*vide infra*).

Shinjulactone C (**2**), mp 292 °C (decomp), $[\alpha]_D^{23}$ −344° (pyridine), exhibited no bitter taste and the molecular formula, $C_{20}H_{22}O_7$, was determined by high resolution mass spectrum. The IR (*ca.* 3480, 1775, 1720, and 1650 cm^{-1}) and UV (λ_{max} 248 nm) spectra reveal the presence of hydroxyl(s) and three carbonyls, one of which is assigned to be an α,β-unsaturated ketone. The unsaturated carbonyl group is inferred to be located in the A ring; the mass spectrum of **2** afforded a prominent fragment peak at *m/e* 151 $(C_9H_{11}O_2)^+$ probably due to a tropylium ion (**D**), suggesting the presence of a partial structure (**E**), because the fragment ion **D** is observed in the mass spectrum of ailanthone (**3**).[8b] ^{1}H NMR spectrum (Table 5) of **2** showed the presence of two tertiary methyls (δ 1.092 and δ 1.306, each s), a vinyl methyl (δ 2.019, d), two methine protons (δ 2.900, s and δ 2.170, ddd), a lactone-terminus proton (δ 5.235, ddd),

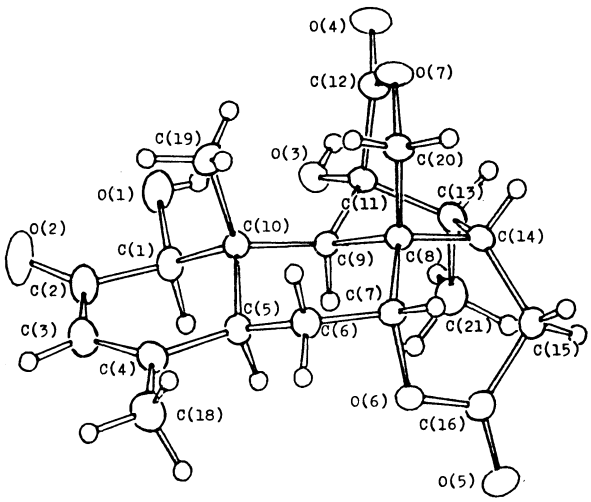


Fig. 1. Perspective view of shinjudilactone (**1**).[a]
a) For clarity hydrogen atoms are represented by spheres of arbitrary radius.

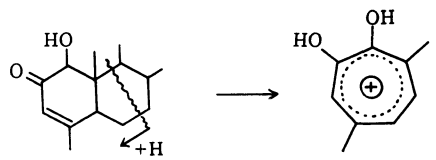
and an olefinic proton (δ 6.497, d). The lactone-terminus proton was shown to couple with the methine proton at δ 2.170 with a coupling constant J=2.5 Hz.

Four oxygen atoms were thus explained by the presence of a lactone, an α,β-unsaturated ketone, and an isolate ketone. The remaining three oxygen atoms were shown to be hydroxyl groups, one of which was shown to be primary by the following evidence. ^{1}H NMR (δ 4.052

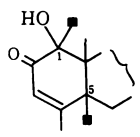
Table 5. ^{1}H NMR Spectra of shinjudilactone (**1**) and shinjulactone C (**2**) (400 MHz, pyridine-d_5)[a,b]

	1		**2**	
1-H	4.229 s			
3-H	6.095 br s		6.497 br s	
5-H	3.224 br d	J=13		
6α-H	2.308 ddd	J=15, 3, 2.5	2.402 dd	J=15.5, 10
6β-H	2.082 ddd	J=15, 13, 2.5	2.699 dd	J=15.5, 5
7-H	4.808 t	J=2.5	5.235 ddd	J=10, 5, 2.5
9-H	2.723 s		2.900 s	
13-H	2.182 quin	J=7		
14-H	2.284 ddd	J=10.5, 7, <1	2.170 ddd	J=11, 3, 2.5
15α-H	3.125 dd	J=16, 10.5	2.969 dd	J=19.5, 11
15β-H	2.702 dd	J=16, <1	3.252 dd	J=19.5, 3
4-CH_3	1.798 br s		2.019 br s	
10-CH_3	1.235 s		1.092 s	
13-CH_3	1.240 d	J=7	1.306 s	
20-H_2	4.307 d	J=12	4.052 d	J=12
	4.793 d	J=12	4.090 d	J=12

a) Coupling constants are expressed in Hz. b) s: singlet, d: doublet, t: triplet, quin: quintet, br: broad.



E **D** (*m/e* 151)



F

■ denotes a carbon atom.

and δ 4.090, each d) and ^{13}C NMR (δ 60.2, t) spectra and a fragment ion at *m/e* 343 due to $(M-CH_2OH)^+$ suggest the presence of a primary hydroxyl group. Acetylation of shinjulactone C (**2**) gave a monoacetate (**8**) and a diacetate (**9**). The primary hydroxyl group of **2** easily reacts with formic acid at room temperature to afford a formate (**10**), which, on refluxing with 50% formic acid, gave the starting shinjulactone C (**2**). In the ^{1}H NMR spectrum of monoacetate (**8**), an AB quartet signal (δ_A 4.47 and δ_B 4.59, J_{AB}=12 Hz) was observed, suggesting that the $-CH_2OH$ group had been acetylated. The diacetate (**9**), yield of which increased by prolonged reaction time, showed that an absorption band at *ca.* 3450 cm^{-1} due to a hydroxyl group still remained in the IR spectrum. In our recent study,[21] the diacetate (**9**) was prepared from ailanthone (**3**) and was shown to be a 12,20-di-*O*-acetyl derivative. Two signals (δ 88.3 and δ 93.6, each s) due to carbon atoms bearing a tertiary hydroxyl group were observed in the ^{13}C NMR spectrum of **2**. The absence of coupling between olefinic and allylic protons due to the structure moiety (**A**) was shown for **2**. From these observations, a partial structure (**F**) was suggested for shinjulactone C.

^{13}C NMR spectrum (Table. 6) and discussion developed above indicating that shinjulactone C (**2**) possesses a hexacyclic skeleton, two carbon atoms at C-1 and C-5 in the partial structure (**F**) must connect with different carbon atoms respectively. The following

Table 6. ^{13}C NMR Spectrum of shinjulactone C (**2**)

Assignment of carbon atom		Number of carbon atom	δ-value (pyridine-d_5)
>C=O	(isolated)	1	209.8 s
	(conjugated)	1	195.2 s
	(lactone or ester)	1	170.8 s
>C=C<	(tetrasubstituted)	1	165.9 s
>C=CH-	(trisubstituted)	1	127.8 d
-C(-)-O		2	93.6 s, 88.3 s
-CH-O		1	72.6 d
$-CH_2-O$		1	60.2 t
-C(-)-		4	55.5 s, 55.3 s, 50.7 s, 45.4 s
-CH-		2	51.7 d, 36.2 d
$-CH_2-$		2	30.2 t, 30.0 t
$-CH_3$		3	22.7 q, 14.5 q, 12.7 q

difference NOE experiment proved that these bond-formation resulted in a remarkable deformation of the molecule of shinjulactone C; on saturation of a singlet signal due to $C_{(9)}$–H at δ 2.900, signals at δ 1.092 ($C_{(10)}$–CH_3), δ 5.235 (–CH), and δ 4.052 (one of $-C\underline{H}_2OH$) caused increase in area, and on saturation

Table 7. Atomic positional parameters ($\times 10^4$) and isotropic temperature factors ($\times 10^2$) for non-hydrogen atoms of shinjulactone C (**2**) with estimated standard deviations in parentheses

Atom	x	y	z	B_{eq}[a]
C(1)	2839(3)	2904(3)	-94(4)	245(5)
C(2)	1965(3)	3510(3)	-681(5)	293(6)
C(3)	1338(4)	4016(3)	331(5)	378(6)
C(4)	1478(3)	3914(3)	1689(5)	361(6)
C(5)	2322(3)	3231(3)	2233(4)	252(5)
C(6)	2611(3)	3476(3)	3735(5)	287(5)
C(7)	3515(3)	2838(3)	4220(4)	236(5)
C(8)	3665(3)	1951(3)	3231(4)	209(5)
C(9)	3946(3)	2348(3)	1763(4)	203(5)
C(10)	3274(3)	3270(3)	1300(4)	212(5)
C(11)	3578(3)	1522(3)	818(4)	261(5)
C(12)	2498(3)	1862(3)	503(4)	181(5)
C(13)	2020(3)	2085(3)	1998(4)	226(5)
C(14)	2618(3)	1458(3)	3095(4)	242(5)
C(15)	2097(4)	1364(3)	4550(5)	383(6)
C(16)	2699(4)	1680(4)	5786(5)	449(7)
C(18)	787(5)	4423(5)	2702(7)	686(9)
C(19)	3850(4)	4244(3)	1250(5)	282(6)
C(20)	4474(3)	1229(3)	3746(5)	319(6)
C(21)	894(3)	1832(4)	2011(5)	336(6)
O(1)	3602(2)	2799(2)	-1097(3)	269(4)
O(2)	1830(3)	3534(3)	-1934(4)	424(5)
O(3)	3992(2)	757(2)	442(4)	323(4)
O(4)	1914(2)	1224(2)	-322(3)	178(4)
O(5)	2612(4)	1335(3)	6924(4)	618(7)
O(6)	3359(3)	2452(2)	5628(3)	290(5)
O(7)	5396(2)	1725(3)	4052(4)	334(5)

a) $B_{eq}=8\pi^2(u_1^2+u_2^2+u_3^2)/3$.

of a singlet signal due to a tertiary methyl at δ 1.306, signals at δ 6.497 ($>C=C_{(3)}-H$) and δ 2.019 ($C=\overset{|}{C}_{(4)}-CH_3$) showed increase in area. These enhancement in area due to NOE had never been observed in the usual picrasane derivatives. However, since further information for the structure elucidation of shinjulactone C (**2**) could be obtainable by neither spectral nor chemical investigation, single crystal X-ray diffraction analysis was carried out. Shinjulactone C (**2**) crystallized from acetone in orthorhombic space group $P2_12_12_1$ with the cell parameters of $a=13.247(6)$, $b=13.331(6)$, and $c=9.596(4)$ Å. Four molecules are contained in the unit cell. Intensity data were measured and the structure was solved and refined in the same manner with shinjudilactone (**1**) as described before. The 1831 independent reflections with $F_o \geq 2.5\ \sigma(F_o)$ were used for structure determination. The structure was refined to give the R-factor of 0.073 including all hydrogen atoms. Final atomic coordinates are listed in Table 7 and bond lengths and bond angles are listed in Tables 8 and 9.[20] Figure 2 shows a computer-generated drawing of the molecule **2**, showing to be formulated as 1α,12α : 5α,13α-dicyclo-1β,12β,20-trihydroxy-9βH-picras-3-ene-2,11,16-trione.

The structure elucidation of shinjudilactone (**1**) and shinjulactone C (**2**) has revealed that these new quassinoids possess modified picrasane skeletons. Since it seems possible that these modified quassinoids are biogenetically derived from ailanthone (**3**), conversion

Table 8. Bond lengths of shinjulactone C (**2**) with estimated standard deviations in parentheses

Bond length		l/Å	Bond length		l/Å
Atom 1	Atom 2		Atom 1	Atom 2	
O(1)	-C(1)	1.402(5)	C(5)	-C(10)	1.548(6)
O(2)	-C(2)	1.216(6)	C(5)	-C(13)	1.596(5)
O(3)	-C(11)	1.213(5)	C(6)	-C(7)	1.540(6)
O(4)	-C(12)	1.395(5)	C(7)	-C(8)	1.529(6)
O(5)	-C(16)	1.191(6)	C(8)	-C(9)	1.550(6)
O(6)	-C(7)	1.460(5)	C(8)	-C(14)	1.540(6)
O(6)	-C(16)	1.360(6)	C(8)	-C(20)	1.523(6)
O(7)	-C(20)	1.418(6)	C(9)	-C(10)	1.581(5)
C(1)	-C(2)	1.520(6)	C(9)	-C(11)	1.507(5)
C(1)	-C(10)	1.536(6)	C(10)	-C(19)	1.507(6)
C(1)	-C(12)	1.569(5)	C(11)	-C(12)	1.531(6)
C(2)	-C(3)	1.446(7)	C(12)	-C(13)	1.596(6)
C(3)	-C(4)	1.323(7)	C(13)	-C(14)	1.560(6)
C(4)	-C(5)	1.533(6)	C(13)	-C(21)	1.529(6)
C(4)	-C(18)	1.497(8)	C(14)	-C(15)	1.563(6)
C(5)	-C(6)	1.526(6)	C(15)	-C(16)	1.490(7)

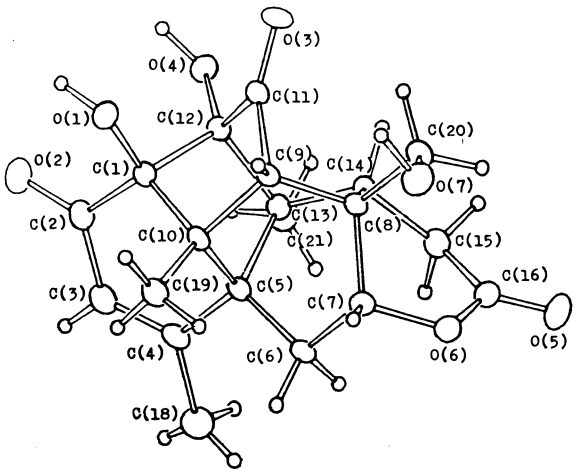


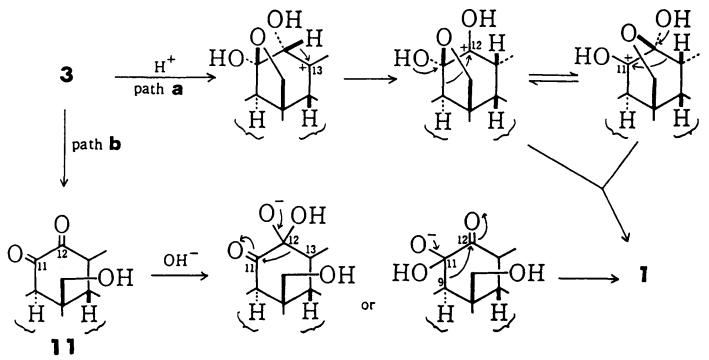
Fig. 2. Perspective view of shinjulactone C (**2**).[a]
a) For clarity hydrogen atoms are represented by spheres of arbitrary radius.

of **3** into shinjudilactone (**1**) was then investigated. The skeletal rearrangement of C ring of ailanthone (**3**) would be possible through two pathways *in vivo* (Scheme 1). Path **a** is initiated by protonation to $\Delta^{13(21)}$-double bond of **3**, followed by hydride shift to provide a cation at C-12. An *O*-terminus of a hemiacetal-bridge may shift from C-11 to the C-12 cationic center to give a cation at C-11. Each one of these cations could undergo ring-contraction followed by deprotonation to give **1**. The other path **b** comprises benzilic acid rearrangement of an intermediate α-diketone (**11**). Since a hydroxide ion is accessible to either C-12 or C-11 of the α-diketone (**11**), 13(12→11α)*abeo*-type or 9(11→12α)*abeo*-type rearrangement similar to those in the path **a** is considered. The resulting hydroxy carboxylic acid undergoes lactonization to furnish shinjudilactone (**1**).

According to these considerations, chemical conversion of ailanthone (**3**) into shinjudilactone (**1**) was investigated. The reaction did not occur under acidic conditions using *p*-toluenesulfonic acid, hydrochloric

Table 9. Bond angles of shinjulactone C (2) with estimated standard deviations in parentheses

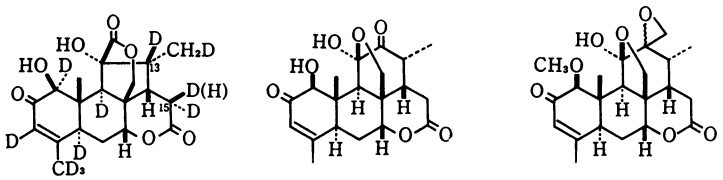
Bond angle			ϕ/°	Bond angle			ϕ/°
Atom 1	Atom 2	Atom 3		Atom 1	Atom 2	Atom 3	
C(2)	-C(1)	-O(1)	110.3(3)	C(8)	-C(9)	-C(11)	102.7(3)
C(2)	-C(1)	-C(10)	116.1(3)	C(19)	-C(10)	-C(1)	115.8(3)
C(2)	-C(1)	-C(12)	112.7(3)	C(19)	-C(10)	-C(5)	117.3(3)
O(1)	-C(1)	-C(10)	111.0(3)	C(19)	-C(10)	-C(9)	113.2(3)
O(1)	-C(1)	-C(12)	111.7(3)	C(1)	-C(10)	-C(5)	100.8(3)
C(10)	-C(1)	-C(12)	94.1(3)	C(1)	-C(10)	-C(9)	102.1(3)
C(3)	-C(2)	-O(2)	124.6(4)	C(5)	-C(10)	-C(9)	105.7(3)
C(3)	-C(2)	-C(1)	115.9(4)	C(12)	-C(11)	-O(3)	127.8(4)
O(2)	-C(2)	-C(1)	119.5(4)	C(12)	-C(11)	-C(9)	101.8(3)
C(4)	-C(3)	-C(2)	122.2(4)	O(3)	-C(11)	-C(9)	130.3(4)
C(5)	-C(4)	-C(3)	119.9(4)	C(13)	-C(12)	-O(4)	113.8(3)
C(5)	-C(4)	-C(18)	119.5(4)	C(13)	-C(12)	-C(1)	106.1(3)
C(3)	-C(4)	-C(18)	120.5(5)	C(13)	-C(12)	-C(11)	104.4(3)
C(6)	-C(5)	-C(4)	112.2(3)	O(4)	-C(12)	-C(1)	119.5(3)
C(6)	-C(5)	-C(10)	109.5(3)	O(4)	-C(12)	-C(11)	116.7(3)
C(6)	-C(5)	-C(13)	113.6(3)	C(1)	-C(12)	-C(11)	93.7(3)
C(4)	-C(5)	-C(10)	112.2(3)	C(14)	-C(13)	-C(5)	106.9(3)
C(4)	-C(5)	-C(13)	109.7(3)	C(14)	-C(13)	-C(12)	107.7(3)
C(10)	-C(5)	-C(13)	98.9(3)	C(14)	-C(13)	-C(21)	111.8(3)
C(7)	-C(6)	-C(5)	111.3(3)	C(5)	-C(13)	-C(12)	101.9(3)
C(8)	-C(7)	-O(6)	108.7(3)	C(5)	-C(13)	-C(21)	117.0(3)
C(8)	-C(7)	-C(6)	109.9(3)	C(12)	-C(13)	-C(21)	110.7(3)
O(6)	-C(7)	-C(6)	111.3(3)	C(15)	-C(14)	-C(8)	110.9(3)
C(9)	-C(8)	-C(7)	109.3(3)	C(15)	-C(14)	-C(13)	114.9(3)
C(9)	-C(8)	-C(14)	106.6(3)	C(8)	-C(14)	-C(13)	106.6(3)
C(9)	-C(8)	-C(20)	110.0(3)	C(16)	-C(15)	-C(14)	116.9(4)
C(7)	-C(8)	-C(14)	105.4(3)	O(5)	-C(16)	-O(6)	117.2(5)
C(7)	-C(8)	-C(20)	112.2(3)	O(5)	-C(16)	-C(15)	124.7(5)
C(14)	-C(8)	-C(20)	113.1(3)	O(6)	-C(16)	-C(15)	118.0(4)
C(10)	-C(9)	-C(8)	112.7(3)	O(7)	-C(20)	-C(8)	112.3(4)
C(10)	-C(9)	-C(11)	102.5(3)	C(7)	-O(6)	-C(16)	117.4(4)



Scheme 1.

acid, acetic acid–hydrochloric acid, or iron(III) chloride–hydrochloric acid, while a very complex mixture was obtained in the reaction of **3** with boron trifluoride etherate in benzene or dichloromethane, no shinjudilactone (**1**) being detected in the reaction mixture by TLC examination.

Reactions under alkaline conditions such as sodium hydroxide in water, potassium hydroxide in methanol, and barium hydroxide in pyridine, gave extremely polar products, structures of which could not be identified. However, ailanthone (**3**) was treated with sodium hydrogencarbonate in boiling aqueous methanol and then the reaction mixture was acidified with hydrochloric acid to give a reaction mixture nearly quantitatively, showing two spots on TLC. Separation of the mixture afforded two compounds in a ratio of 1 : 1, one of which was found to be shinjudilactone (**1**) and the other with a lower R_f value on TLC was determined to be a 13β-epimer (**12**) of **1** by spectral investigation (see Experimental). Reaction of **3** with sodium carbonate under the same conditions as above gave the same reaction mixture, but accompanied by a



13 14 15

small amount of by-products.

Formation of shinjudilactone (**1**) from ailanthone (**3**) has been thus demonstrated, although it remained unresolved whether the reaction proceeds through 13(12→11)*abeo*-type or 9(11→12)*abeo*-type rearrangement. The pathway through benzilic acid rearrangement is also supported by i) labeling experiment and ii) isolation of an intermediate.

i) Treatment of ailanthone (**3**) with $NaDCO_3$ in boiling D_2O–CH_3OD and the reaction product was treated with dilute hydrochloric acid to afford labeled shinjudilactone and its 13-epimer. The labeled shinjudilactone was shown to be an undecadeuterio derivative (**1**-d_{11}) containing a decadeuterio derivative (**1**-d_{10}). The labeled positions were determined by ^1H NMR measurement at 400 MHz and shown in the structure **13**. Ten hydrogen atoms were completely replaced with deuterium atoms and a multiplet signal at δ 2.70 due to the $C_{(15\beta)}$–H was observed, accounting for the presence of **1**-d_{10}. The presence of a deuterium atom at C-9 implies the formation of a carbonyl group at C-11 followed by enolization, which is favorable to the path **b**, during the reaction. The location of a deuterium atom at C-13β of **1**-d_{11} would reject a direct hydride transfer mechanism from C-12β to a cationic center at C-13 as depicted in the path **a**. ii) Ailanthone (**3**) was isomerized by heating in pyridine for 10 h to afford a hemiacetal, for which the structure (**14**) could be assigned by ^1H and ^{13}C NMR measurement. The structure of hemiacetal moiety of **14** was confirmed by ^{13}C–^1H long range selective decoupling experiment measured at 90 MHz. When the ^1H signal due to $C_{(9)}$–H at δ 2.88 was irradiated, the ^{13}C signal at δ 108.15 became sharp, but ^{13}C signal at δ 207.46 still remained broad, being coupled with a proton at C-13. This observation leads to the conclusion that the hemiacetal carbon resonating at δ 108.15 and the carbonyl carbon at δ 207.46 are located in C-11 and C-12 positions, respectively. The fact that $C_{(9)}$–H kept α-configuration intact[22] was demonstrated by NOE experiment measured at 400 MHz. On irradiation at δ 2.88 due to $C_{(9)}$–H, signal due to $C_{(1)}$–H (δ 4.42) increased in area by 15%, while neither signal due to $C_{(7)}$–H (δ 4.79) nor due to $C_{(20)}$–H_2 (δ 4.15 and δ 4.46) showed NOE enhancement.

The structure (**14**), which is equivalent to the hypothetical α-diketone (**11**), has been proposed for isoailanthone by Polonsky *et al.*[8b] Isoailanthone was prepared by treatment of **3** with dilute alkali, but neither detailed description nor spectral data of isoailanthone was given. Only spectral data of its 1-*O*-methyl derivative prepared by methylation with diazomethane were registered.[8b] The hemiacetal (**14**) was then treated with diazomethane to yield a product, which however was suggested to be a 12-spirooxirane-derivative (**15**) from the spectral examination (see Experimental). This compound (**15**) is not identical with 1-*O*-methylisoailanthone. The reason why the disagreement occurred is obscure and further investigation is now in progress. On treatment with sodium hydrogencarbonate in boiling aqueous methanol, the hemiacetal (**14**) gave shinjudilactone (**1**) and its 13-epimer (**12**).

It would be suggestive that shinjudilactone (**1**) is synthesized biogenetically from ailanthone (**3**) or its equivalent through a path similar to the benzilic acid rearrangement. Recently Ochi *et al.*[23] have isolated a 6-epi-*ent*-gibberellane derivative, rabdoepigibberellolide, from *Rabdosia shinkokianus* HARA and suggested its biogenetic pathway from rabdosianin A through benzilic acid rearrangement.

Although biogenesis of shinjulactone C (**2**) with an unusual hexacyclic 1α,12α : 5α,13α-dicyclo-9βH-picrasane skeleton, is still unknown, a biogenetic precursor with a normal picrasane skeleton, such as ailanthone (**3**), would undergo an inversion of a chiral center at C-9 position prior to the bond-formation between C-1 and C-12 and between C-5 and C-13. Further investigation is now in progress.

Experimental

General Procedures. All melting points were measured on a Mel-temp capillary melting point apparatus (Laboratory Devices) and uncorrected. Optical rotations were determined on a JASCO polarimeter DIP-181. Ultraviolet absorption (UV) spectra and infrared (IR) spectra were measured on a Hitachi 340 and a Hitachi 260-30 spectrometer, respectively. Mass (MS) spectra were run on a Hitachi RMU-6 Tokugata mass spectrometer and high-resolution mass spectra on a JEOL JMS-D300 mass spectrometer operating at 70 eV. Proton nuclear magnetic resonance (^1H NMR) spectra (90 MHz) were taken using a Varian EM 390 and carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra (22.5 MHz) JEOL FX 90Q unless otherwise stated. Measurement of ^1H NMR spectra at 400 MHz and ^{13}C NMR spectra at 100 MHz was carried out on a JMN GX 400 (JEOL) spectrometer. Chemical shifts were expressed in ppm downfield from tetramethylsilane as an internal standard (δ value) and coupling constants in Hz. Thin-layer chromatography (TLC) was carried out on Kieselgel 60 GF_{254} coated in 0.25 mm- or 0.5 mm-thickness or on TLC plates Silica Gel F_{254} with Concentration Zone (E. Merck). Wakogel C-200 (Wako), Silicic acid AR (Mallinckrodt) or Celite No. 545 (Wako) was used for column chromatography.

Plant Materials. Roots of *Ailanthus altissima* SWINGLE were collected twice at the Botanical Gardens, Faculty of Science, the University of Tokyo in January 1980 and 1981. Bark was stripped off from the root, air-dried, and chipped to afford 3.2 and 10 kg of materials, respectively.

Extraction and Separation. *i) Extraction with Ethyl Acetate*: The root bark (3.2 kg), defatted with petroleum ether (18 l) for 6 h, was extracted twice with ethyl acetate (18 l) for 6 h and then with methanol (18 l) for 6 h. Since the bitter taste was mainly exhibited in the ethyl acetate-extract, which was subjected to further separation. Non-bitter solids, precipitated from the extract on standing, were filtered off and the filtrate was concentrated to give a residue (30 g), which was partitioned between dichloromethane and aqueous methanol.

Column A: The aqueous methanol layer, on evaporation, gave a bitter residue (*ca.* 11 g), 3.5 g of which was subjected to column chromatographic separation (C-200, 180 g), eluted with chloroform (each 360 ml) containing following percentage of methanol: 1, 5, 10, 20, 40, 60, and 100%, and 28 fractions (each 90 ml) were collected. Elution with chloroform containing *ca.* 5% methanol afforded a small quantity of bitter principles, which were inferred to be a mixture of amarolide and amarolide 11-acetate by TLC examination (developed with 5% methanol–chloroform). Further confirmation was carried out by comparison with authentic samples, both of which were isolated from methanol extract of the root bark of the plant in *ca.* 0.01% yield, respectively.

Column B: Fraction 13 (2.1 g) of Column A was further separated by dry column chromatography (C-200, 420 g). A mixture (2 : 1) of benzene–acetone was passed through the column and 16 fractions (each 420 ml) were collected. Recrystallization of fractions 7—16 from ethyl acetate gave ailanthone (**3**; 1.2 g).

Column C: Fractions 3—6 (450 mg) of Column B were combined and separated by dry column chromatography (C-200, 140 g), eluting with 5% methanol–containing chloroform. Ten fractions (each 70 ml) were collected and a small quantity of ailanthone (**3**) was obtained from fractions 6—10. Fractions 3—5 were combined and separated by preparative TLC developed with benzene–acetone (1 : 1) and then with methanol–chloroform (1 : 9) to give ailanthone (**3**; trace), glaucarubinone (27 mg), and $\Delta^{13(18)}$-dehydroglaucarubinone (40 mg).

Column D: The dichloromethane layer obtained by the partition was evaporated to afford a bitter residue (19 g), 17 g of which was subjected to separation by column chromatography (C-200, 900 g). After elution with chloroform–benzene (1 : 1, 1.8 l) and chloroform (1.8 l), following solvents were successively passed through the column: 1%-, 2%-, 4%-, 8%-, 16%-, and 32%-methanol in chloroform (each 1.8 l) and 18 fractions (each 900 ml) were collected.

Column E: Fraction 15 (3.5 g) of Column D was chromatographed over silica gel (C-200, 300 g) eluting with benzene–acetone (3 : 2) to give 20 fractions (each 300 ml).

Column F: Fraction 16 (0.5 g) of Column A was chromatographed over silica gel (C-200, 100 g) eluting with benzene–acetone (1 : 1) to 10 fractions (each 100 ml).

Column G: Fractions 5—17 of Column E and fractions 7—14 of Column F were combined to afford a residue (450 mg) on evaporation, which was dissolved in chloroform, passed though a column packed with a mixture of silicic acid (23 g) and Celite (23 g). Elution with chloroform (92 ml) and 1%-, 2%-, 5%-, 10%-, 20%-, and 50%-methanol in chloroform (each 92 ml) afforded 25 fractions (each 23 ml). Recrystallization of fraction 20 from methanol gave shinjulactone A (7 mg). Fractions 17—19 were purified by preparative TLC developed with 10% methanol in chloroform to give $\Delta^{13(18)}$-glaucarubolone (20 mg).

ii) Extraction with Water: The air-dried root bark (10 kg) was extracted with hot water (90 °C, 20 l) overnight. The extraction was repeated twice and the aqueous extracts were combined and evaporated *in vacuo* to give a concentrated extract (*ca.* 5 l). The extract was divided into three portions, each of which was extracted continuously with dichloromethane (1 l) overnight and the extraction was repeated four times. Evaporation of the combined dichloromethane extract gave a residue (45 g).

Column H: The residue (40 g) above obtained, was chromatographed over silica gel (C-200, 1.3 kg) and eluted with 1%-, 2%-, 4%-, 8%-, 16%-, 32%-, and 64%-methanol in chloroform (each 2.6 l). Eighteen fractions (each 1.3 l) were collected and following residues were obtained on evaporation; fr 7 (5.6 g), fr 8 (4.0 g), fr 9 (1.8 g), fr 10 (4.4 g), fr 11 (3.2 g), fr 12 (3.7 g), fr 13 (3.0 g), fr 14 (3.3 g), fr 15 (5.3 g), and fr 16 (2.4 g).

Column I: Fraction 7 of Column H was subjected to separation by dry column chromatography (C-200, 560 g) and a mixture of benzene–acetone (4 : 1) was passed to afford 46 fractions (each 140 ml). Fractions 12 and 13 gave amarolide. Recrystallization of fractions 27—35 from methanol afforded shinjudilactone (**1**; 70 mg).

Column J: The mother liquor obtained from the recrystallization of shinjudilactone (**1**) afforded a residue (500 mg), which was chromatographed over silica gel (C-200, 100 g, eluted with 5% methanol in chloroform) and then silicic acid (70 g, eluted with 2.5% methanol in dichloromethane) to afford chaparrinone (**4**; 18 mg).

Column K: Recrystallization of fraction 8 (4.0 g) of Column H from methanol–chloroform afforded shinjudilactone (**1**; 200 mg) in needles and mother liquor, which gave a residue (3.8 g) on evaporation. The residue was chromatographed over silica gel (C-200, 600 g) and a mixture of benzene and ethanol (9 : 1) was passed to afford 12 fractions (each 400 ml). From fractions 7—12, shinjudilactone (**1**; 900 mg) was obtained by crystallization from methanol.

Column L: Fraction 10 of Column H was chromatographed over silica gel (C-200, 500 g, dry; elution with benzene–acetone (3 : 1)) and 36 fractions (each 200 ml) were obtained. Fractions 22—29 afforded ailanthone (**3**; *ca.* 1 g).

Column M: Fraction 14 of Column H was separated by column chromatography (C-200, 350 g) eluted with a lower phase of a mixture, chloroform–methanol–water (150 : 25 : 6) to give 27 fractions (each 100 ml). From fractions 13—16, $\Delta^{13(18)}$-dehydroglaucarubolone (100 mg) was obtained by crystallization from acetone.

Column N: Fractions 18—21 (380 mg) of Column L were dissolved in chloroform and the solution was passed through a column of silica gel (C-200, 200 g) and the following solvents were passed: chloroform (200 ml), 1%-methanol in chloroform (400 ml), 3%- (400 ml), and 5%- (800 ml). Eighteen fractions (each 100 ml) were collected and fractions 11—14 gave shinjudilactone (**1**; 50 mg) and fraction 16 afforded glaucarubinone (50 mg) after purification by preparative TLC developed with 3% methanol in ethyl acetate.

Column O: Fraction 11 of Column H was separated by column chromatography (C-200, 400 g) eluted with 1%-methanol in ethyl acetate (800 ml) and then with 2%- (1600 ml) to give 15 fractions (each 160 ml). Fractions 8—14 were dissolved in chloroform and passed through a dry column of silica gel (C-200, 300 g). Chloroform (300 ml), 2%-methanol in chloroform (600 ml), and 4%-(2050 ml) were successively passed to afford 39 fractions (each 75 ml). Fractions 17—22 consisted of mainly ailanthone (**3**) and fractions 31—36 afforded shinjulactone B (11 mg) after purification by preparative TLC developed with 5% methanol in chloroform.

Column P: Fraction 13 of Column H was subjected to partition chromatography over silica gel (C-200, 500 g, dry). Eluting solvent consisted of a 1 : 1 (v/v) mixture of a lower layer of dichloromethane–methanol–water (100 : 25 : 6) and

dichloromethane. Eighteen fractions (each 200 ml) were collected. Recrystallization of fractions 6 and 7 from acetone gave chaparrolide (*ca.* 200 mg). Shinjulactone C (**2**; *ca.* 20 mg) was obtained from the mother liquor by recrystallization from acetone.

Since separation of quassinoids in the root bark of *A. altissima* was difficult and therefore separation procedures were very complicated, it is impossible to describe all procedures carried out in this experiment. The contents of each quassinoids are estimated by summing up amounts obtained in various separation routes and are shown in Table 10.

*Shinjudilactone (**1**).* Colorless needles crystallized from ethyl acetate–methanol, mp 274—276 °C; $[\alpha]_D^{23}$ +102° (*c* 0.76, C_5H_5N); IR (KBr) *ca.* 3250, 1745, 1735, 1670, and 1620 cm^{-1}; UV (EtOH) 238 nm (ε 10800); ^1H NMR (Table 5); ^{13}C NMR (Table 1); MS *m/e* (%) 376 (M^+; 80), 358 (20), 347 (30), 332 (60), 303 (98), 288 (75), and 95 (100); Found: *m/e* 376.1509. Calcd for $C_{20}H_{24}O_7$: M 376.1520. Found: C, 62.03; H, 6.74; Calcd for $C_{20}H_{24}O_7 \cdot 1/2\ H_2O$: C, 62.33; H, 6.54%.

*1-O-Methylshinjudilactone (**5**).* Shinjudilactone (**1**; 30 mg) in methanol (10 ml) was treated with diazomethane in ether and the reaction mixture was allowed to stand overnight. After the usual work-up, the reaction product was purified by preparative TLC developed with 3% methanol–chloroform to give 1-*O*-methylshinjudilactone (**5**; 15 mg); mp 291—294 °C (from methanol); $[\alpha]_D^{23}$ +53.5° (*c* 0.27, $CHCl_3$); IR (Nujol) 3400, 1745, 1720, 1680, and 1630 cm^{-1}; UV (EtOH) 239.5 nm (ε 5400); ^1H NMR ($CDCl_3$) δ 1.05 (3H, s; $C_{(10)}$–CH_3), 1.11 (3H, d, J=7 Hz; $C_{(13)}$–CH_3), 1.95 (3H, br s; $C_{(4)}$–CH_3), 3.63 (1H, s; $C_{(1)}$–H), 3.75 (3H, s; CH_3O), 4.00 and 4.52 (each 1H, d, J=11.5 Hz; $C_{(20)}$–H), 4.52 (1H, t, J=2.5 Hz; $C_{(7)}$–H), 5.98 (1H, m; $C_{(3)}$–H), and 6.08 (1H, s; OH); MS *m/e* (%) 390 (M^+; 60), 360 (100), 345 (50), 330 (20), 301 (10), and 288 (45); Found: *m/e* 390.1659. Calcd for $C_{21}H_{26}O_7$: M 390.1677.

*1-O-Acetylshijudilactone (**6**).* Shinjudilactone (**1**; 20 mg) was acetylated with acetic anhydride (2 ml) in pyridine (2 ml) at room temperature for 9 h. Addition of methanol and the usual work-up afforded 1-*O*-acetylshinjudilactone quantitatively, mp 269—272 °C (from methanol); IR (Nujol) 3480, 1730, 1680, and 1630 cm^{-1}; UV (EtOH) 240 nm (ε 8000); ^1H NMR (C_5D_5N) δ 1.12 (3H, d, J=7 Hz; $C_{(13)}$–CH_3), 1.36 (3H, s; $C_{(10)}$–CH_3), 1.77 (3H, br s; $C_{(4)}$–CH_3), 2.25 (3H, s; –$OCOCH_3$), 4.26 and 4.73 (each 1H, d, J=12 Hz; $C_{(20)}$–H), 4.64 (1H, t, J=3 Hz; $C_{(7)}$–H), 5.78 (1H, s; $C_{(1)}$–H), and 6.05 (1H, m; $C_{(3)}$–H); MS *m/e* (%) 418 (M^+; 30), 400 (25), 358 (95), 330 (40), and 60 (100); Found: *m/e* 418.1678. Calcd for $C_{22}H_{26}O_8$: M 418.1628.

*Reduction of **1** with Sodium Borohydride.* To a solution of shinjudilactone (**1**; 30 mg) in ethanol (10 ml) kept at 0 °C, sodium borohydride (6 mg) in ethanol (2 ml) was added and the mixture was stirred for 4 h at 0 °C. Acetic acid (1 ml) was added and the solvents were evaporated *in vacuo* to afford a residue, which was dissolved in a mixture of dichloromethane (10 ml) and brine (10 ml). Extraction with dichloromethane (10 ml × 3), evaporation *in vacuo*, and crystallization from methanol gave a hemiacetal (**7**; 20 mg), mp 276—277.5 °C; IR (Nujol) *ca.* 3300, 1740, 1660, and 1610 cm^{-1}; UV (EtOH) 240 nm (ε 11500); ^1H NMR (C_5D_5N) δ 1.13 (3H, d, J=6 Hz; $C_{(13)}$–CH_3), 1.17 (3H, s; $C_{(10)}$–CH_3), 1.76 (3H, br s; $C_{(4)}$–CH_3), 4.20 and 4.43 (each 1H, d, J=12 Hz; $C_{(20)}$–H), 4.26 (1H, t, J=3 Hz; $C_{(7)}$–H), 4.35 (1H, s; $C_{(1)}$–H), 5.68 (1H, m; $C_{(16)}$–H), and 6.04 (1H, m; $C_{(3)}$–H); MS *m/e* (%) 378 (M^+; 20), 360 (70), 345 (40), 334 (40), and 316 (100); Found: *m/e* 378.1681. Calcd for $C_{20}H_{26}O_7$: M 378.1679.

*Shinjulactone C (**2**).* Colorless prisms crystallized from acetone, mp 292 °C (decomp); $[\alpha]_D^{23}$ −344° (*c* 0.46, C_5H_5N); IR (KBr) *ca.* 3480, 1775, 1720, 1650, 1620 (sh), 1390, and 1190 cm^{-1}; UV (MeOH) 248 nm (ε 10600); ^1H NMR (Table 5); ^{13}C NMR (Table 6); MS *m/e* (%) 374 (M^+; 100), 356 (5), 343 (20), 315 (10), and 151 (60); Found: *m/e* 374.1379. Calcd for $C_{20}H_{22}O_7$: M 374.1366.

*Acetylation of Shinjulactone C (**2**).* *i)* Shinjulactone C (**2**; 20 mg) was treated with acetic anhydride (5 ml) and pyridine (5 ml) at room temperature overnight. After methanol (5 ml) was added, the reaction mixture was evaporated *in vacuo* to give a residue, which was shown to be a 7 : 3 mixture of a monoacetate (**8**) and a diacetate (**9**) by TLC examination. Acetylation of the mixture was repeated under the same conditions as above and the acetylation product was separated by preparative TLC developed with 10% methanol–chloroform to give the monoacetate (**8**; 1 mg) and the diacetate (**9**; 20 mg). *ii)* A mixture of shinjulactone C (**2**; 10 mg) and acetic acid (5 ml) was heated under reflux for 15 h to afford the monoacetate (**8**) quantitatively. 20-*O*-Acetylshinjulactone C (**8**): mp 131—134 °C (from acetone–hexane); $[\alpha]_D^{22}$ −222° (*c* 0.13, $CHCl_3$); IR (Nujol) *ca.* 3450, 1770, 1740 (br), 1660, 1620 (sh), and 1240 cm^{-1}; UV (EtOH) 245 nm (ε 14000); ^1H NMR (C_5D_5N) δ 1.11 (3H, s; $C_{(13)}$– or $C_{(10)}$–CH_3), 1.30 (3H, s; $C_{(10)}$– or $C_{(13)}$–CH_3), 1.96 (3H, s; –$OCOCH_3$), 2.03 (3H, br s; $C_{(4)}$–CH_3), 2.49 (1H, s; $C_{(9)}$–H), 4.47 and 4.59 (each 1H, d, J=12 Hz; $C_{(20)}$–H), 5.02 (1H, m; $C_{(7)}$–H), and 6.47 (1H, br s; $C_{(3)}$–H); ^1H NMR ($CDCl_3$) δ 0.99 (3H, s; $C_{(13)}$– or $C_{(10)}$–CH_3), 1.03 (3H, s; $C_{(10)}$– or $C_{(13)}$–CH_3), 2.08 (6H, s; $C_{(4)}$–CH_3 and –$OCOCH_3$), 4.07 (2H, s; $C_{(20)}$–H_2), 4.63 (1H, m; $C_{(7)}$–H), and 6.35 (1H, br s; $C_{(3)}$–H); MS *m/e* (%) 416 (M^+; 25), 398 (10), 388 (8), 374 (8), 356 (100), 193 (30), and 151 (10); Found: *m/e* 416.1464. Calcd for $C_{22}H_{24}O_8$: M 416.1469. 12,20-Di-*O*-acetylshinjulactone C (**9**): mp 152—154 °C (from acetone–hexane); $[\alpha]_D^{21}$ −200° (*c* 0.24, $CHCl_3$); IR (Nujol) *ca.* 3450, 1780, 1740 (br), 1665, 1620 (sh), and 1220 cm^{-1}; UV (EtOH) 245.5 nm (ε 9600); ^1H NMR (C_5D_5N) δ 1.14 (6H, s; $C_{(13)}$– and $C_{(10)}$–CH_3), 1.71 (3H, br s; $C_{(4)}$–CH_3), 1.94 and 2.06 (each 3H, s; –$OCOCH_3$), 2.57 (1H, s; $C_{(9)}$–H), 4.42 and 4.51 (each 1H, d, J=12 Hz; $C_{(20)}$–H), and 6.52 (1H, br s; $C_{(3)}$–H); ^1H NMR ($CDCl_3$) δ 0.99 (3H, s, $C_{(13)}$– or $C_{(10)}$–CH_3), 1.00 (3H, s; $C_{(10)}$– or $C_{(13)}$–CH_3), 2.06 and 2.13 (each 3H, s; –$OCOCH_3$), 2.10 (3H, br s; $C_{(4)}$–CH_3), 4.10 (2H, s; $C_{(20)}$–H_2), 4.63 (1H, m; $C_{(7)}$–H), and 6.37 (1H, br s; $C_{(3)}$–H); ^{13}C NMR (C_5D_5N) δ 12.3 q, 13.3 q, 20.0 q, 20.3 q, 22.6 q, 29.8 t, 29.8 t, 35.4 d, 42.4 s, 51.0 s, 52.7 d, 55.0 s, 56.2 s, 63.5 t, 72.6 d, 86.4 s, 97.5 s, 128.4 d, 165.5 s, 169.7 s, 170.0 s, 170.0 s, 193.2 s, and 201.0 s; MS *m/e* (%) 458 (M^+; 12), 430 (10), 416 (100), 398 (20), 193 (60), and 151 (58); Found: *m/e* 458.1590. Calcd for $C_{24}H_{26}O_9$: M 458.1587.

*Formylation of Shinjulactone C (**2**).* A solution of shin-

Table 10.

Compound	Yield/%	
	AcOEt-extract	H_2O-extract
Ailanthone (**3**)	0.1	0.05
Amarolide	0.01	0.01
Amarolide 11-acetate	0.01	—
Glaucarubinone	0.001	0.001
$\Delta^{13(18)}$-Dehydroglaucarubinone	0.001	—
$\Delta^{13(18)}$-Dehydroglaucarubolone	0.0005	0.001
Shinjulactone A	0.001	—
Shinjulactone B	—	0.0005
Chaparrolide	—	0.005
Chaparrinone (**4**)	—	0.001
Shinjudilactone (**1**)	—	0.01
Shinjulactone C (**2**)	—	0.001

julactone C (**2**; 12 mg) in formic acid (5 ml) was stirred at room temperature for 2 h. Evaporation of the solvent *in vacuo* afforded 20-*O*-formylshinjulactone C (**10**) quantitatively, mp 268—271 °C (from acetone); IR (KBr) *ca.* 3450, 1770, 1730 (br), 1660, and 1180 cm^{-1}; ^1H NMR (C_5D_5N) δ 1.10 (3H, s; $C_{(13)}$- or $C_{(10)}$-CH_3), 1.27 (3H, s; $C_{(10)}$- or $C_{(13)}$-CH_3), 2.00 (3H, br s; $C_{(4)}$-CH_3), 2.49 (1H, s; $C_{(9)}$-H), 4.44 and 4.57 (each 1H, d, J=12 Hz; $C_{(20)}$-H), 4.96 (1H, m; $C_{(7)}$-H), 6.45 (1H, br s; $C_{(3)}$-H), and 8.25 (1H, s; H-CO); MS *m/e* (%) 402 (M^+; 100), 374 (10), 359 (10), 343 (15), 297 (20), and 151 (40); Found: *m/e* 402.1293. Calcd for $C_{21}H_{22}O_8$: M 402.1313.

Hydrolysis of 20-O-Formylshinjulactone C (10). The formate (**10**; 12 mg) was heated under reflux with a mixture of formic acid (3 ml) and water (3 ml) for 5 h to afford shinjulactone C (**2**) quantitatively.

Conversion of Ailanthone (3) into Shinjudilactone (1). *i)* Ailanthone (**3**; 21 mg) in a mixture of methanol (2 ml) and water (2 ml) was heated with sodium hydrogencarbonate (5 mg) under reflux for 30 min. The reaction mixture was acidified with concd hydrochloric acid (2 drops), evaporated to concentrated solution (*ca.* 1 ml) under reduced pressure, and extracted with dichloromethane. After usual work-up, a residue (20 mg) was subjected to separation by preparative TLC developed with chloroform–methanol (19 : 1) to afford shinjudilactone (**1**; 10 mg) and 13-epishinjudilactone (**12**; 10 mg), mp 263—266 °C (from methanol–ethyl acetate); $[\alpha]_D^{23}$ +48° (*c* 0.57, C_5H_5N); IR (KBr) *ca.* 3300, 1745, 1675, 1620, 1250, and 1180 cm^{-1}; UV (EtOH) 239 nm (ε 10300); ^1H NMR (C_5D_5N) δ 1.19 (3H, d, J=6 Hz; $C_{(13)}$-CH_3), 1.20 (3H, s; $C_{(10)}$-CH_3), 1.77 (3H, br s; $C_{(4)}$-CH_3), 4.22 (1H, s; $C_{(1)}$-H) 4.25 and 4.66 (each 1H, d, J=12 Hz; $C_{(20)}$-H), 4.65 (1H, t, J=2 Hz; $C_{(7)}$-H), and 6.06 (1H, m; $C_{(3)}$-H); ^{13}C NMR (C_5D_5N) δ 9.8, 11.4, 22.2, 27.0, 29.3, 41.9, 42.5, 42.8, 44.5, 48.3, 51.0, 74.3, 76.0, 76.6, 83.5, 126.3, 161.8, 170.9, 175.7, and 196.7; MS *m/e* (%) 376 (M^+; 8), 358 (6), 347 (8), 340 (10), 312 (45), 294 (40), 268 (100), and 253 (60); Found: *m/e* 376.1532. Calcd for $C_{20}H_{24}O_7$: M 376.1520.

ii) Reaction of ailanthone (**3**) with sodium carbonate in boiling aqueous methanol afforded the same reaction mixture of **1** and **12**, but accompanied with a formation of a small amount of by-products.

iii) Reactions of ailanthone (**3**) under following conditions were carried out, but all attempts were not successful; a) *p*-toluenesulfonic acid in tetrahydrofuran, reflux for 48 h, b) 2 M† hydrochloric acid in methanol, room temperature for 12 h and then reflux for 12 h, c) acetic acid-2 M hydrochloric acid in water, room temperature overnight, and then reflux overnight, d) 2 M hydrochloric acid–iron (III) chloride in water, reflux overnight, e) boron trifluoride etherate in benzene or dichloromethane, room temperature overnight, and f) sodium hydroxide in water, potassium hydroxide in methanol, or barium hydroxide in pyridine, reflux overnight.

Conversion of Ailanthone (3) into Undecadeuterioshinjudilactone (1-d_{11}). A mixture of ailanthone (**3**; 21 mg), $NaDCO_3$ (5 mg), D_2O (2 ml), and CH_3OD (2 ml) was heated under reflux for 30 min. The reaction mixture was acidified with concd hydrochloric acid (2 drops) and worked-up as usual to give a crude deuteriated product (20 mg), from which undecadeuterioshinjudilactone (**1**-d_{11}; 10 mg) was separated by preparative TLC. **1**-d_{11}: ^1H NMR (400 MHz, C_5D_5N) δ 1.22 (2H, br s; $C_{(13)}$-CH_2D), 1.23 (3H, s; $C_{(10)}$-CH_3), 2.06 (1H, br d, J=14 Hz; $C_{(6\beta)}$-H), 2.26 (1H, br s; $C_{(14)}$-H), 2.28 (1H, dd, J=14 Hz and 2.5 Hz; $C_{(6\alpha)}$-H), 2.70(0.5 H, m; $C_{(15\beta)}$-H), 4.28 and 4.78 (each 1H, d, J=11.5 Hz; $C_{(20)}$-H), and 4.78 (1H, t, J=2.5 Hz; $C_{(7)}$-H); MS *m/e* 387, 386, 367, 342, 100, and 68.

† 1 M = 1 mol dm^{-3}.

Isomerization of Ailanthone (3) into Hemiacetal (14). Ailanthone (**3**; 30 mg) in pyridine (5 ml) was refluxed for 10 h and the reaction product was separated by preparative TLC to give a hemiacetal (**14**; 20 mg), mp 166—169 °C (from acetone–benzene); IR (KBr) 3450, 1740, 1680, 1240, and 1050 cm^{-1}; UV (EtOH) 238 nm (ε 8100); ^1H NMR (C_5D_5N) δ 1.03 (3H, d, J=8 Hz), 1.58 (3H, s), 1.76 (3H, br s), 2.83 (1H, s), 4.12 and 4.43 (each 1H, d, J=9 Hz), 4.76 (1H, t, J=2.5 Hz), and 6.06 (1H, m); ^{13}C NMR (C_5D_5N) δ 10.21, 10.40, 22.30, 26.14, 28.80, 40.64, 42.07, 43.51, 46.05, 46.73, 51.20, 72.82, 77.64, 84.11, 108.15, 126.35, 161.46, 169.12, 196.79, and 207.41; MS *m/e* (%) 376 (M^+; 15), 358 (16), 332 (29), 303 (46), and 95 (100); Found: *m/e* 376.1514. Calcd for $C_{20}H_{24}O_7$: M 376.1520.

Methylation of hemiacetal (**14**; 20 mg) in tetrahydrofuran (5 ml) with an excess of diazomethane in ether at room temperature overnight gave a reaction mixture, which was subjected to separation by preparative TLC to afford an *O*-methyl oxirane derivative (**15**; 7 mg), mp 274—277 °C (from acetone–hexane), $[\alpha]_D^{22}$ −65° (*c* 0.46, $CHCl_3$); IR (Nujol) 3220, 1730, 1680, and 1240 cm^{-1}; UV (EtOH) 238 nm (ε 9500); ^1H NMR ($CDCl_3$) δ 0.81 (3H, d, J=7 Hz; $C_{(13)}$-CH_3), 1.29 (3H, s; $C_{(10)}$-CH_3), 1.95 (3H, br s; $C_{(4)}$-CH_3), 2.63 (1H, s; $C_{(9)}$-H), 2.57 and 3.26 (each 1H, d, J=5.5 Hz; $-CH_2-$), 3.56 (1H, s; $C_{(1)}$-H), 3.70 (3H, s; $-OCH_3$), 3.80 and 4.07 (each 1H, d, J=9 Hz; $C_{(20)}$-H), 4.49 (1H, t, J=2.5 Hz; $C_{(7)}$-H), 6.00 (1H m; $C_{(3)}$-H), and 7.45 (1H, s; -OH); ^{13}C NMR ($CDCl_3$) δ 9.8 q, 10.3 q, 22.5 q, 25.7 t, 28.7 t, 29.3 d, 42.8 d, 43.3 d, 44.7 s, 45.5 t, 46.3 s, 49.3 d, 61.5 q, 64.5 s, 72.1 t, 78.0 d, 93.4 d, 106.7 s, 127.0 d, 160.4 s, 169.8 s, and 195.0 s; MS *m/e* (%) 404 (M^+; 100), 374 (60), and 165 (80); Found: *m/e* 404.1855. Calcd for $C_{22}H_{28}O_7$: M 404.1835.

Conversion of Hemiacetal (14) into Shinjudilactone (1) and Its 13-Epimer (12). Hemiacetal (**14**; 16 mg) was heated with sodium hydrogencarbonate (10 mg) in aqueous methanol (4 ml) for 30 min to afford a mixture (11 mg) of shinjudilactone (**1**) and its 13-epimer (**12**). The physical and spectral data of these compounds, after separation by preparative TLC, were completely identical with those of authentic samples, respectively.

Inhibitory Activities. Inhibitory effects (ID_{50}) against HeLa cells were >10 μg/ml, >10 μg/ml, and 0.01—0.1 μg/ml for shinjudilactone (**1**), shinjulactone C (**2**), and ailanthone (**3**), respectively.

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