New Des-4-methylpicrasane Quassinoids from Picrasma javanica

Kazuo Koike, Kiyoshi Ishii, Katsuyoshi Mitsunaga, and Taichi Ohmoto

J. Nat. Prod., **1991**, 54 (3), 837-843• DOI:
10.1021/np50075a013 • Publication Date (Web): 01 July 2004

Journal of Natural Products
Vol. 54, No. 3, pp. 837-843, May-Jun 1991

NEW DES-4-METHYLPICRASANE QUASSINOIDS FROM *PICRASMA JAVANICA*

KAZUO KOIKE, KIYOSHI ISHII, KATSUYOSHI MITSUNAGA, and TAICHI OHMOTO*

School of Pharmaceutical Sciences, Toho University, 2-2-1 Miyama, Funabashi, Chiba 274, Japan

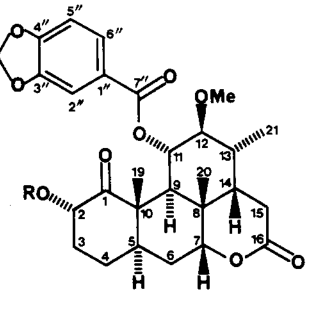
ABSTRACT.—Six new des-4-methylpicrasane-type quassinoids, javanicins K [**1**], L [**2**], O [**3**], R [**4**], S [**5**], and T [**6**], were isolated from Indonesian *Picrasma javanica*. In addition, two known picrasane quassinoids, nigakilactones B and F, were isolated. The structures have been determined by spectral means and by comparison with authentic samples.

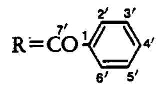
Quassinoids, bitter principles of Simaroubaceae plants, have been extensively investigated from the standpoint of structure determination and their useful biological activities (1,2). Particularly, recent studies of this family have received renewed attention because of antimalarial (3) and antitumor (1,4) activities shown by some quassinoids. In previous papers (5–10), we isolated 17 new des-4-methylpicrasane-type quassinoids from Indonesian *Picrasma javanica* Bl. In a continuation of our work on the isolation and characterization of bitter principles of *P. javanica*, we report the isolation and structure elucidation of six new des-4-methylpicrasane quassinoids from this plant.

RESULTS AND DISCUSSION

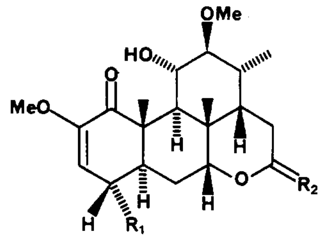
Javanicin K [**1**], $C_{35}H_{38}O_{10}$ ($[M]^+$ *m/z* 618.2441, calcd 618.2454), was obtained as colorless needles, mp 275–276°, $[\alpha]^{21}D$ −30.1°. Its ir spectrum showed absorption bands due to δ-lactone (ν max 1724 cm^{-1}), ester (ν max 1720, 1280, and 1260 cm^{-1}), and benzene (ν max 1628 and 1500 cm^{-1}) moieties, and the uv spectrum (λ max 220, 262, and 298 nm) was similar to that of javanicin N [**7**] (10). The ^{1}H-nmr spectrum of **1** showed signals due to one methoxyl at δ 3.26 (3H, s), nonequivalent methylene protons at δ 5.81 and 5.98 (each 1H, d, J = 1 Hz), and two sets of aromatic protons at δ 7.45 (2H, t, J = 8 Hz), 7.54 (1H, t, J = 8 Hz), and 8.02 (2H, d, J = 8 Hz) and 6.83 (1H, d, J = 8 Hz), 7.80 (1H, d, J = 2 Hz), and 7.98 (1H, dd, J = 8 and 2 Hz). In the ^{13}C-nmr spectrum, two sets of sp^2-carbon signals for two phenyl groups were observed. The long-range ^{1}H-^{13}C COSY spectrum revealed long-range couplings between carbonyl carbon at C-7′ (δ 164.94) and aromatic protons at H-2′/H-6′ (δ 8.02), between carbonyl carbon at C-7″ (δ 165.51) and aromatic proton at H-6″ (δ 7.98) and between oxygen-bearing carbons at C-3″ (δ 148.2)/C-4″ (δ 151.76) and nonequivalent protons at H-8″ (δ 5.81 and 5.98), thus suggesting that javanicin K has a benzoyl and a 3,4-methylenedioxybenzoyl groups. Mass spectral fragment ions at *m/z* 149 and 105 substantiated these assignments. The ^{1}H-^{1}H COSY revealed the presence of two isolated structure units, -CH-$(CH_2)_2$-CH-CH_2-CH- and -CH-$(CH)_4$-CH_2- groups in the formula. The features of ^{1}H- and ^{13}C-nmr spectra of **1** were very similar to those of **7** except that the acetoxyl group in **7** was replaced by the benzoyl group in **1**. The locations of the benzoyl and the 3,4-methylenedioxybenzoyl groups were determined from the long-range ^{1}H-^{13}C COSY spectrum. Thus, couplings were observed between C-7′ and H-2 and between C-7″ and H-11. The relative stereochemistry of **1** was established through a series of difference nOe experiments. Irradiation of Me-8 at δ 1.17 induced nOe's at H-7 (9%), H-11 (18%), H-13 (15%), H-14 (13%), and Me-10 (25%). Irradiation of Me-10 at δ 1.53 induced nOe's at H-2 (11%), H-11 (6%), and Me-8 (8%). Irradiation of Me-13 at δ 0.96 induced 5% nOe at H-12. On the basis of the above results, the structure of javanicin K was determined to be **1**.

Javanicin L [**2**], $C_{21}H_{32}O_6$ ($[M]^+$ *m/z* 380.2225, calcd 380.2190), was obtained as

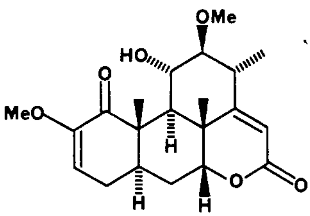


1 R= 

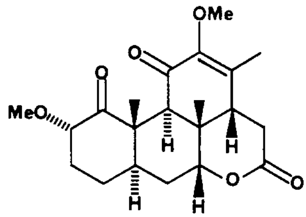
5 R=H
7 R=Ac



	R_1	R_2
2	H	<OH, H
4	OH	O
8	H	O-glc, H
9	H	O
10	OAc	O



3



6
11 2,3-dehydro

colorless prisms, mp 228–230°, $[\alpha]^{26}$D +38.3°. The ir and uv spectra of **2** indicated the presence of hydroxyl (ν max 3480 and 3400 cm^{-1}) and α,β-unsaturated carbonyl (ν max 1670, 1637 cm^{-1} and λ max 267 nm) groups. The ^1H nmr of **2** showed hemiacetal protons at δ 4.71 (1H, dd, $J=9$ and 2 Hz) and 5.33 (1H, brd, $J=2$ Hz), suggesting hemiacetal epimers at C-16 (7,8). Other proton signals were also doubled. Enzymatic hydrolysis of javanicinoside A [**8**] (5) with β-glucosidase afforded javanicin L [**2**]. On the basis of the above results, the structure of javanicin L was determined to be **2**.

Javanicin O [**3**], $C_{21}H_{28}O_6$ ($[M]^+$ *m/z* 376.1907, calcd 376.1878), was obtained as colorless needles, mp 254–256°, $[\alpha]^{20}$D +50.2°. The ir and uv spectra showed the presence of α,β-unsaturated carbonyl (ν max 1725, 1670, and 1635 cm^{-1} and λ max 268 nm) groups. In the ^1H-nmr spectrum, an olefinic proton signal at δ 5.78 (1H, d, $J=1$ Hz) showed long-range coupling with the C-13 proton at δ 2.73 in the ^1H-^1H COSY spectrum of **3**. The lack of a signal for H-14 indicated the quarternary nature of C-14. Comparing the chemical shifts of **3** with those of javanicin A [**9**] (6) revealed pronounced downfield shifts for H-13 and Me-13 in **3** ($\Delta\delta=0.4$ and 0.7 ppm, respectively). On the other hand, a similar comparison of carbon signals for both compounds revealed downfield shifts of C-12 and C-13 (each $\Delta\delta=4$ ppm) in **3**. These results suggested that javanicin O has a double bond at C-14–C-15 in the molecule. The relative stereochemistry of **3** was determined by difference nOe experiments as follows. Irradiation of OMe-12 protons at δ 3.69 produced nOe's on H-11 (3%) and H-13 (7%). Irradiation of H-11 at δ 4.00 produced nOe's on H-8 (10%) and Me-10 (5%). Irradia-

TABLE 1. ^{1}H-nmr Spectral Data of Quassinoids.[a]

Proton	Compound					
	1[b]	**2**[c]	**3**[c]	**4**[c]	**5**[c]	**6**[c]
H-2	5.93 dd (12,7)				4.47 dt (12,7)	4.45 dd (12,7)
H-3	1.73 m	5.61 dd (6,2)	5.68 dd (6,3)	5.66 d (2)	1.31 m	1.51 m
	2.21 m				2.42 m	2.37 m
H-4	1.31 m	2.09 m	2.25 m	4.34 dd (9,2)	1.37 m	1.51 m
	1.75 m	2.13 m	2.33 dd (10,3)		1.72 m	1.82 m
		2.27 m[d]				
		2.37 m[d]				
H-5	1.95 m	2.45 m	2.42 m	2.07 m	1.81 m	1.79 m
H-6	1.63 ddd (14,3,3)	1.53 m	1.84 ddd (15,3,3)	1.96 dd (14,12)	1.74 ddd (14,3,3)	1.76 m
	1.91 m	1.96 m	2.08 ddd (15,12,3)	2.42 ddd (14,3,3)	1.95 ddd (14,12,3)	1.96 ddd (14,12,3)
		1.38 m[d]				
		2.00 m[d]				
H-7	4.19 brt (3)	3.26 t (3)	4.18 t (3)	4.20 dd (3,2)	4.19 t (3)	4.26 t (3)
		3.81 t[d] (3)				
H-9	3.17 d (12)	2.50 d (11)	2.02 d (11)	2.19 d (11)	2.92 d (12)	3.27 s
		2.52 d[d] (11)				
H-11	5.82 dd (12,9)	3.68 dd (11,8)	4.00 ddd (11,9,8)	3.76 bt (11)	5.51 dd (12,9)	
H-12	3.43 dd (12,9)	2.84 m	2.66 dd (10,8)	2.89 dd (11,9)	3.23 dd (12,9)	
H-13	2.21 m	2.07 m	2.73 m	2.10 m	2.26 m	
H-14	1.75 m	1.67 m		1.74 m	1.83 m	2.46 dd (12,7)
H-15	2.74 dd (19,7)	1.44 m	5.78 d (1)	2.46 dd (19,12)	2.60 dd (20,12)	2.64 dd (19,12)
	2.93 dd (19,12)	1.75 m		2.65 dd (19,8)	2.69 dd (20,8)	3.00 dd (19,7)
H-16		4.71 dd[d] (9,2)				
		5.33 brd (2)				
8-Me	1.17 s	1.10 s	1.26 s	1.24 s	1.22 s	1.21 s
		1.13 s[d]				
10-Me	1.53 s	1.38 s (2 × Me)	1.38 s	1.45 s	1.34 s	1.44 s
13-Me	0.96 d (6)	0.97 d (8)	1.24 d (6)	1.02 d (7)	1.05 d (7)	1.92 s
		0.99 d[d] (8)				
2-OH					3.42 d (7)	
11-OH			4.42 d (9)			
2-OMe		3.59 s (2 × OMe)	3.60 s	3.64 s		3.40 s
12-OMe	3.26 s	3.62 s (2 × OMe)	3.69 s	3.64 s	3.29 s	3.65 s
H-2′,-6′	8.02 d (8)					
H-3′, -5′	7.45 t (8)					
H-4′	7.54 t (8)					
H-2″	7.80 d (2)				7.41 d (2)	
H-5″	6.83 d (8)				6.82 d (8)	
H-6″	7.98 dd (8,2)				7.59 dd (8,2)	
H-8″	5.81 d (1)				6.02 d (1)	
	5.98 d (1)				6.03 d (1)	

[a]Coupling constants (J in Hz) are given in parentheses.
[b]In C_5D_5N.
[c]In $CDCl_3$.
[d]Signals due to another isomer at C-16.

tion of H-7 at δ 4.18 produced 6% nOe at Me-8. On the basis of the above results, the structure of javanicin O was determined to be **3**.

Javanicin R [**4**], $C_{21}H_{30}O_7$ ([M]$^+$ *m/z* 394.1997, calcd 394.1983), was obtained as colorless needles, mp 239–241°, $[\alpha]^{26}D$ +17.4°. Its ir and uv spectra indicated the presence of hydroxyl (ν max 3480 and 3440 cm^{-1}), δ-lactone (ν max 1730 cm^{-1}), and α,β-unsaturated ketone (ν max 1680, 1640 cm^{-1} and λ max 262 nm) groups. The ^{1}H- and ^{13}C-nmr spectra of **4** were very similar to those of javanicin A [**9**] (6) as shown in Tables 1 and 2. The mol wt of **4** was 16 mass units higher than that of **9**, suggesting one more hydroxyl group than in **9**. Comparing the ^{1}H- and ^{13}C-nmr chemical shifts of **4** with those of **9** revealed a ^{1}H downfield shift for H-4β (Δδ = 2.2 ppm) and ^{13}C downfield shifts (β effect) for C-3 (Δδ = 1.9 ppm) and C-5 (Δδ = 7.9 ppm) and a ^{13}C upfield shift (γ effect) for C-6 (Δδ = 5.5 ppm) in **4**, when compared with the corresponding signals in **9**. Furthermore, in the ^{1}H-nmr spectrum of the acetyl derivative **10**, H-4β

TABLE 2. ^{13}C-nmr Spectral Data of Quassinoids.

Carbon	Compound				
	1[a]	**3**[b]	**4**[b]	**5**[b]	**6**[b]
C-1	207.89	203.63	203.98	214.32	209.69
C-2	73.47	149.29	149.44	73.22[c]	79.34
C-3	33.71	111.96	114.39	39.19	34.59
C-4	25.20	28.09	68.55	24.97	24.87
C-5	42.86	36.16	44.57	42.56	41.51
C-6	28.25	28.72	24.14	29.03	29.10
C-7	82.37	78.02	82.12	82.52	82.17
C-8	35.96	39.17	36.08	35.07[d]	36.76
C-9	36.17	43.08	37.49	35.80[d]	47.23
C-10	51.36	47.27	49.17	49.83	49.38
C-11	73.88	73.21	73.75	70.28[c]	190.83
C-12	85.83	92.78	88.41	85.62	148.27
C-13	34.88	39.20	34.76	35.98[d]	139.98
C-14	45.30	149.24	45.99	45.22	47.27
C-15	29.45	110.90	28.22	27.96	31.45
C-16	169.89	168.25	170.13	169.96	168.81
C-19	12.35	10.62	12.50	12.57	13.86
C-20	21.83	20.12	21.51	22.02	23.06
C-21	14.39	13.47	14.42	14.32	15.68
2-OMe		55.25	55.52		57.72
12-OMe	60.29	61.87	61.78	60.98	59.69
C-1′	125.44				
C-2′, -6′	130.09				
C-3′, -5′	128.55				
C-4′	133.28				
C-7′	164.94				
C-1″	125.84			123.55	
C-2″	110.61			109.70	
C-3″	148.02			147.88	
C-4″	151.76			151.97	
C-5″	108.02			108.08	
C-6″	126.45			125.91	
C-7″	165.51			165.34	
C-8″	102.19			101.83	

[a]In C_5D_5N.
[b]In $CDCl_3$.
[c,d]May be interchanged.

gave a clear downfield shift ($\Delta\delta = 1.2$ ppm). These data indicated that an extra hydroxyl group is located at C-4 with an α orientation. Difference nOe experiments indicated that the relative stereochemistry of javanicin R [**4**] was identical to that of javanicin A [**9**] except for H-4β. An nOe was observed for H-4β (10%) when Me-10 was irradiated, suggesting that the H-4β was β axial. On the basis of the above results, the structure of javanicin R was determined to be **4**.

Javanicin S [**5**], $C_{28}H_{34}O_9$ ($[M]^+$ *m/z* 514.2196, calcd 514.2193), was obtained as colorless needles, mp 265–267°, $[\alpha]^{26}D$ +1.1°. Javanicin S [**5**] was identified as the free C-2 hydroxyl derivative of javanicin N [**7**] (10), as the acetate of **5** had mp, [α]D, ir and ^{1}H-nmr spectra identical to those of **7**.

Javanicin T [**6**], $C_{21}H_{28}O_6$ ($[M]^+$ *m/z* 376.1898, calcd 376.1878), was obtained as colorless needles, mp 106–108°, $[\alpha]^{26}D$ −18.1°. The ir and uv spectra of **6** indicated the presence of δ lactone (ν max 1730 cm^{-1}) and α,β-unsaturated ketone (ν max 1685, 1640 cm^{-1}, and λ max 250 nm) groups. The ^{1}H- and ^{13}C-nmr spectra of **6** were very similar to those of javanicin F [**11**] (8); however, the difference between **6** and **11** indicated that **6** has no olefinic proton signal at C-3. From hrms, an unsaturation number of **6** was 1 unit lower than that of **11**, suggesting that one of the α,β-unsaturated ketone groups in **11** was replaced by a saturated ketone group in **6**. The ^{1}H-^{1}H COSY further suggested the presence of the isolated structure unit, -CH-$(CH_2)_2$-CH-CH_2-CH-, in the formula. These data indicated that the structure of **6** is that of 2,3-dihydrojavanicin F. The stereochemistry of javanicin T [**6**] was established by difference nOe spectra. A strong nOe observed for H-2β-axial (14%) when Me-10 was irradiated showed that the methoxyl group (δ 3.40) at C-2 was located at an α equatorial positon. Likewise, irradiation of Me-8 resulted in nOe's of Me-10 (9%), H-7 (11%), and H-14 (11%). On the basis of the above results, the structure of javanicin T was determined to be **6**.

In addition to **1**–**6**, the known picrasane quassinoids nigakilactones B and F were isolated and identified by direct comparison with authentic samples (11).

EXPERIMENTAL

PLANT MATERIAL.—The leaves (6.4 kg) and stems (3.7 kg) of *P. javanica* were collected in Bogar, Indonesia in July 1986, and identified by the members of Botanical Garden of Bogor. A voucher specimen has been deposited in the Department of Pharmacognosy, Toho University.

GENERAL EXPERIMENTAL PROCEDURES.—Melting points were measured with a Yanagimoto micro-melting point apparatus (hot-stage type) and are uncorrected. Uv spectra were recorded on a Hitachi 340 uv-vis spectrometer and ir spectra on a Hitachi 260-30 ir spectrometer. Optical rotations were measured on a JASCO DIP-4 polarimeter. Eims and hrms were determined on a JEOL D-300 and DX-303 mass spectrometers. ^{1}H-nmr (400 MHz), ^{13}C-nmr (100 MHz), and 2D nmr were recorded on a JEOL GX-400 FT-NMR spectrometer. TMS was used as an internal standard.

ISOLATION OF JAVANICINS K [**1**], L [**2**], O [**3**], R [**4**], AND S [**5**].—The dried leaves (6.4 kg) of *P. javanica* were extracted with MeOH (110 liters). The extract was concentrated under reduced pressure to give a residue (1.7 kg), to which an equal volume of H_2O was added. The aqueous solution was extracted with $CHCl_3$ (10 liters) followed by *n*-BuOH (10 liters). The $CHCl_3$-soluble fraction (200 g) was chromatographed on Si gel (2 kg) column and eluted with C_6H_6, C_6H_6/$CHCl_3$, $CHCl_3$, $CHCl_3$/MeOH, and MeOH. The fraction obtained by eluting with C_6H_6-$CHCl_3$ (1:4) was further purified by preparative hplc [column Senshu Pak SSC-Silica gel 3251-N, 8 mm i.d. × 250 mm, solvent system CH_2Cl_2-MeOH (99:1), detect 254 nm] to afford javanicin K [**1**] (50 mg). Similar treatment of the fraction eluting with $CHCl_3$ afforded javanicin L [**2**] (50 mg), javanicin O [**3**] (50 mg), javanicin R [**4**] (8 mg), and javanicin S [**5**] (9 mg).

ISOLATION OF JAVANICIN T [**6**].—The fractionation of MeOH extract from the stems of *P. javanica* was described in a previous report (10). The $CHCl_3$-soluble fraction (73 g) was subjected to repeated cc on Diaion HP-20 (Mitsubishi Kasei) and further purification by low-pressure lc [column CQ-3, 24 mm i.d. × 250 mm, Fuji Gel, solvent system CH_2Cl_2-MeOH (100:1), detect 254 nm] and hplc [column Senshu Pak SSC Silica 3251-N, 8 mm i.d. × 250 mm, solvent system CH_2Cl_2-MeOH (100:1), detect 254 nm] to give javanicin T [**6**] (80 mg).

JAVANICIN K [**1**].—Colorless needles (MeOH); mp 275–276°; $[\alpha]^{21}D$ −30.1° (c = 2.7, $CHCl_3$); uv λ max (MeOH) 220 (4.27), 262 (3.81), 298 (3.71) nm; ir ν max (KBr) 2940, 1724, 1720, 1628, 1607, 1500, 1487, 1444, 1280, 1260, 1230, 1160, 1110, 1080, 1040, 760 cm^{-1}; hrms *m/z* $[M]^+$ 618.2441 (calcd for $C_{35}H_{38}O_{10}$, 618.2454); eims (70 eV) *m/z* (rel. int.) $[M]^+$ 618 (11), 452 (3), 330 (25), 274 (5), 243 (2), 166 (10), 149 (100), 105 (75); ^1H nmr see Table 1; ^{13}C nmr see Table 2.

JAVANICIN L [**2**].—Colorless prisms (MeOH); mp 228–230°; $[\alpha]^{26}D$ +38.3° (c = 1.7, $CHCl_3$); uv λ max ($CHCl_3$) 267 (3.57) nm; ir ν max (KBr) 3480, 3400 (br), 2900, 1670, 1637, 1453, 1245, 1105, 1085, 1060, 1040 cm^{-1}; hrms *m/z* $[M]^+$ 380.2225 (calcd for $C_{21}H_{32}O_6$, 380.2190); eims (70 eV) *m/z* (rel. int.) $[M]^+$ 380 (9), 348 (30), 333 (21), 314 (100), 299 (61), 270 (18), 252 (17), 237 (24), 227 (9), 219 (18), 203 (30), 191 (11), 163 (13); ^1H nmr see Table 1.

ENZYMATIC HYDROLYSIS OF JAVANICINOSIDE A [**8**].—Javanicinoside A [**8**] (5 mg) and β-glucosidase (20 mg, from Almond, Sigma) were dissolved in H_2O (3 ml) and incubated at 37° for 2 weeks. After cooling, the aglycone was extracted with $CHCl_3$ and afforded javanicin L [**2**] (2 mg). This compound was identical with natural javanicin L on the basis of the comparison of the tlc, ir, ^1H-nmr, and ms spectra.

JAVANICIN O [**3**].—Colorless needles (MeOH): mp 254–256°; $[\alpha]^{20}D$ +50.2° (c = 2.1, $CHCl_3$); uv λ max ($CHCl_3$) 268 (3.42) nm; ir ν max (KBr) 3520, 2940, 1725, 1670, 1635, 1445, 1268, 1235, 1120, 1082, 1063, 1038 cm^{-1}; hrms $[M]^+$ *m/z* 376.1907 (calcd for $C_{21}H_{28}O_6$, 376.1878); eims (70 eV) *m/z* (rel. int.) $[M]^+$ 376 (100), 361 (11), 344 (46), 331 (24), 313 (27), 289 (62), 269 (6), 255 (9), 205 (9), 195 (13); ^1H nmr see Table 1; ^{13}C nmr see Table 2.

JAVANICIN R [**4**].—Colorless needles (MeOH): mp 239–241°; $[\alpha]^{26}D$ +17.4° (c = 0.8, $CHCl_3$); uv λ max ($CHCl_3$) 262 (3.53) nm; ir ν max (KBr) 3480, 3440, 1730, 1680, 1640, 1450, 1350, 1260, 1240, 1110, 1040 cm^{-1}; hrms $[M]^+$ *m/z* 394.1997 (calcd for $C_{21}H_{30}O_7$, 394.1983); eims (70 eV) *m/z* (rel. int.) $[M]^+$ 394 (20), 376 (11), 362 (25), 328 (55), 269 (17), 234 (30), 219 (51), 167 (20), 143 (35), 98 (100); ^1H nmr see Table 1; ^{13}C nmr see Table 2.

ACETYLATION OF JAVANICIN R [**4**].—Javanicin R [**4**] (7 mg) was acetylated with Ac_2O (0.5 ml) and pyridine (0.5 ml) at room temperature for 6 h. After MeOH (15 ml) was added, the reaction mixture was evaporated in vacuo to give monoacetyljavanicin R [**10**] (8 mg): $[\alpha]^{25}D$ +4.0° (c = 0.9, $CHCl_3$) ir ν max (KBr) 3460, 2918, 1733, 1685, 1637, 1455, 1325, 1230, 1110, 1040 cm^{-1}; eims (70 eV) *m/z* (rel. int.) $[M]^+$ 436 (98), 394 (50), 376 (28), 344 (17), 328 (27), 43 (100); ^1H-nmr δ (400 MHz, $CDCl_3$) 5.58 (1H, dd, J = 9, 2 Hz, H-4), 5.51 (1H, d, J = 2 Hz, H-3), 4.16 (1H, dd, J = 4, 2 Hz, H-7), 3.640 (3H, s, OMe-2), 3.635 (3H, s, OMe-12), 2.89 (1H, dd, J = 11, 9 Hz, H-12), 2.66 (1H, dd, J = 20, 7 Hz, H-15), 2.46 (1H, dd, J = 20, 12 Hz, H-15), 2.24 (1H, d, J = 11 Hz, H-9), 2.11 (3H, s, OAc-4), 1.50 (3H, s, Me-10), 1.23 (3H, s, Me-8), 1.02 (3H, d, J = 7 Hz, Me-13).

JAVANICIN S [**5**].—Colorless needles (MeOH): mp 265–267°; $[\alpha]^{26}D$ +1.1° (c = 0.8, $CHCl_3$); uv λ max (MeOH) 220 (3.56), 264 (3.04), 296 (3.04) nm; ir ν max (KBr) 3440, 1722, 1630, 1503, 1440, 1370, 1292, 1270, 1167, 1110, 1082, 1042, 990 cm^{-1}; hrms *m/z* $[M]^+$ 514.2196 (calcd for $C_{28}H_{34}O_9$, 514.2193); eims (70 eV) *m/z* (rel. int.) $[M]^+$ 514 (40), 365 (22), 348 (100), 287 (32), 259 (11), 227 (9), 166 (20), 149 (79), 121 (10), 105 (2); ^1H nmr see Table 1; ^{13}C nmr see Table 2.

ACETYLATION OF JAVANICIN S [**5**].—Javanicin S [**5**] (2.5 mg) was acetylated with Ac_2O (0.5 ml) and pyridine (0.5 ml) at room temperature for 3 h. After MeOH (15 ml) was added, the reaction mixture was evaporated in vacuo to give javanicin N [**7**] (2.6 mg). This compound was identical with the authentic sample (10) on the basis of comparison of the $[\alpha]D$ (−46.8°, c = 0.3, $CHCl_3$), ir, ^1H nmr, ms, and mmp.

JAVANICIN T [**6**].—Colorless needles (MeOH): mp 106–108°; $[\alpha]^{26}D$ −18.1° (c = 0.8, $CHCl_3$); uv λ max ($CHCl_3$) 250 (3.64) nm; ir ν max (KBr) 1730, 1685, 1640, 1450, 1275, 1250, 1200, 1140, 1115, cm^{-1}; hrms *m/z* $[M]^+$ 376.1898 (calcd for $C_{21}H_{28}O_6$, 376.1878); eims (70 eV) *m/z* (rel. int.) $[M]^+$ 376 (92), 362 (11), 348 (17), 333 (95), 301 (46), 288 (23), 273 (30), 243 (29), 215 (21), 205 (31), 152 (21); ^1H nmr see Table 1; ^{13}C nmr see Table 2.

ACKNOWLEDGMENTS

We are grateful to Dr. T. Tsuyuki, The University of Tokyo, for the generous gift of authentic nigakilactones Brand F, and to Eisai Co., Ltd., and P.T. Eisai Indonesia Co., Ltd., for their kind supply of the plant material. We thank the member of the Botanical Garden of Bogor, Indonesia, for identification of plant material.

LITERATURE CITED

1. J. Polonsky, *Fortschr. Chem. Org. Naturst.*, **30**, 101 (1973).

2. J. Polonsky, *Fortschr. Chem. Org. Naturst.*, **43**, 221 (1986).
3. J.D. Phillipson and M.J. O'Neill, in: "Biologically Active Natural Products." Ed. by K. Hostettmann and P.J. Lea, Oxford University Press, England, 1989, pp. 49–64.
4. P.D. Gillin, D.S. Reiner and M. Suffness, *Antimicrob. Agents Chemother.*, **22**, 342 (1982).
5. T. Ohmoto, K. Koike, K. Mitsunaga, H. Fukuda, K. Kagei, K. Kawai, and T. Sato, *Chem. Pharm. Bull.*, **37**, 993 (1989).
6. T. Ohmoto, K. Koike, K. Mitsunaga, H. Fukuda, and K. Kagei, *Chem. Pharm. Bull.*, **37**, 2991 (1989).
7. K. Koike and T. Ohmoto, *Phytochemistry*, **29**, 2617 (1990).
8. K. Koike, K. Mitsunaga, and T. Ohmoto, *Chem. Pharm. Bull.*, **38**, 2746 (1990).
9. K. Koike, K. Ishii, K. Mitsunaga, and T. Ohmoto, *Phytochemistry*, **30**, 933 (1991).
10. K. Koike, K. Ishii, K. Mitsunaga, and T. Ohmoto, *Chem. Pharm. Bull.*, **39**, 939 (1991).
11. T. Murae, T. Tsuyuki, T. Ikeda, T. Nishihama, S. Masuda, and T. Takahashi, *Tetrahedron*, **27**, 1545 (1971).

Received 16 October 1990