Javanicins N, P and Q, New Quassinoids from *Picrasma javanica*

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A new quassinoid, javanicin N, was isolated from the woods of *Picrasma javanica* (Simaroubaceae) collected in Indonesia, and two new quassinoids, javanicins P and Q, were also isolated from the leaves of the same plant. Their structures were determined by spectroscopic data.

Keywords *Picrasma javanica*; Simaroubaceae; javanicin N; javanicin P; javanicin Q; des-4-methylpicrasane; quassinoid

We have recently reported on several novel des-4-methylpicrasane type quassinoids^{1–5)} and quassinoid glucosides^{2,6)} from *Picrasma javanica* BL. collected in Indonesia. Continuing to examine *P. javanica* extracts, we have now isolated three new quassinoids, javanicins N (**1**), P (**2**) and Q (**3**), which are reported here.

Results and Discussion

Javanicin N (**1**), mp 222–224 °C, was obtained as colorless needles, and its molecular formula was C₃₀H₃₆O₁₀ as determined by high-resolution mass spectrometry (HRMS). The infrared (IR) spectrum of **1** indicated the presence of δ -lactone ($\nu_{\max}$ 1735 cm⁻¹), aromatic ($\nu_{\max}$ 1610, 1490 and 762 cm⁻¹) and ester ($\nu_{\max}$ 1700 and 1290 cm⁻¹) groups. Its ultraviolet (UV) spectrum ($\lambda_{\max}$ 220, 262 and 296 nm) was similar to that of javanicin G (**4**),³⁾ indicating that **1** has an aromatic ring in the molecule. Comparison of the proton and carbon-13 nuclear magnetic resonance (¹H- and ¹³C-NMR) spectral data (Tables I and II) with those of **4** indicated that a methoxyl group (δ 2.84, s) at C-2 in **4** was replaced by an acetoxyl group (δ 1.97, s) in **1**. The relative downfield shift ($\Delta\delta$ = 1.59 ppm) of the H-2 proton in **1** may be attributed to the relief from anisotropic shielding due to the acetyl carbonyl group. The position of the acetoxyl, 3,4-methylenedioxybenzoyloxyl and methoxyl groups were assigned to be C-2, C-11 and C-12, respectively, based on the ¹³C-¹H long-range

correlation spectroscopy (COSY) of **1**. A carbonyl carbon at δ 169.89 correlated with H-2 (δ 5.71) and acetyl protons (δ 1.97). A carbonyl carbon at δ 165.58 correlated with H-11 (δ 5.80) and *ortho* protons (δ 7.83 and 8.00, each 1H) of the 3,4-methylenedioxybenzoyl group. A methine carbon at δ 85.85 (C-12) correlated with a methoxyl proton (δ 3.29). The relative stereochemistry of **1** was examined through an extensive series of nuclear Overhauser effect (NOE) experiments. Irradiation of Me-8 at δ 1.15 induced NOEs at H-7 (14%), Me-10 (11%), H-11 (11%), H-13 (10%) and H-14 (7%). Irradiation of Me-10 at δ 1.43 induced NOEs at H-2 (15%), OMe-12 (3%), Me-8 (8%) and H-11 (8%). Irradiation of Me-13 at δ 0.97 induced 7% NOE at H-12. Thus, the proton at C-2 (δ 5.71) was assigned as the β -axial from the coupling constants (J = 12 and 7 Hz), and this was confirmed by the presence of an NOE with C-10 β -axial methyl protons. On the basis of the above data, the structure of javanicin N is proposed to be **1**.

Javanicin P (**2**), mp 150–152 °C, was obtained as colorless needles, and its molecular formula was C₂₁H₃₀O₇ as determined by HRMS. The IR and UV spectra of **2** indicated the presence of hydroxyl ($\nu_{\max}$ 3440 cm⁻¹), δ -lactone ($\nu_{\max}$ 1725 cm⁻¹) and α,β -unsaturated ketone ($\nu_{\max}$ 1670, 1633 cm⁻¹ and $\lambda_{\max}$ 266 nm) groups. The ¹H-NMR spectrum of **2** showed signals due to one secondary methyl at δ 1.09 (d, J = 7 Hz, Me-13), two tertiary methyls at δ 1.15 (s, Me-8) and 1.45 (s, Me-10), two methoxys at δ 3.60 (s, OMe-2) and 3.65 (s, OMe-12) and an olefinic proton at δ 5.67 (dd, J = 5 and 2 Hz). The ¹H- and ¹³C-NMR spectral data of javanicin P (**2**) and those of javanicin A (**5**)¹⁾ were closely related. From HRMS, **2** contains one oxygen atom more than **5**, and the presence of an extra hydroxyl group was suggested for **2**. The downfield shift of the lactone terminus proton at δ 4.58 (H-7, δ 4.10) revealed the extra hydroxyl group was located on C-14 with a β -orientation in **2**, as it had been established for the nigakilactone M (**8**) (H-7, δ 4.76) and nigakilactone A (**9**) (H-7, δ 4.10).⁷⁾ A downfield shift (β -effect) was observed for the C-8 ($\Delta\delta$ = 2.9 ppm) and C-15 ($\Delta\delta$ = 7.5 ppm) resonances, and an upfield shift (γ -effect) was experienced by the C-7 ($\Delta\delta$ = 3.7 ppm) resonance in javanicin P (**2**), as compared with the corresponding signals in javanicin A (**5**), which also suggested that the extra hydroxyl group is attached at C-14. The relative stereochemistry of **2** was determined by NOE measurements as follows. Irradiation of H-7 at δ 4.58 induced 12% NOE at Me-8. Irradiation of H-11 at δ 3.77 induced NOEs at Me-8 (9%) and Me-10 (6%). Irradiation of Me-13 at δ 1.09 induced 5% NOE at H-12. Based on the above data, the structure of javanicin P is proposed to be **2**.

Javanicin Q (**3**), mp 243–245 °C, was obtained as

Chart 1

TABLE I. ¹H-NMR Spectral Data for Compounds 1–6

Proton	1 ^{b)}	4 ^{a)}	2 ^{a)}	5 ^{b)}	3 ^{b)}	6 ^{b)}
H-2	5.71 dd (12, 7)	4.12 dd (11, 7)				
H-3	1.53 m, 2.10 m	1.49 m, 2.26 m	5.67 dd (5, 2)	5.49 dd (6, 2)	5.51 dd (6, 2)	5.56 dd (5, 2)
H-4	1.25 m, 1.66 m	1.44 m, 1.78 m	2.18 m, 2.37 m	1.86 ddd (18, 6, 4), 2.16 ddd (18, 11, 2)	1.90 m, 2.16 m	1.99 ddd (18, 5, 4), 2.20 ddd (18, 10, 2)
H-5	1.92 m	1.80 m	2.35 m	2.28 m	2.66 m	2.53 m
H-6	1.60 m, 1.88 m	1.73 ddd (14, 3, 3), 1.92 ddd (14, 13, 3)	1.76 ddd (14, 4, 4), 1.93 m	1.55 ddd (14, 3, 3), 1.96 ddd (14, 11, 3)	1.51 ddd (14, 3, 3), 2.04 m	1.38 ddd (14, 5, 3), 2.03 ddd (14, 11, 3)
H-7	4.18 t (3)	4.17 t (3)	4.58 dd (4, 2)	4.10 t (3)	3.31 t (3)	3.96 t (3)
H-9	3.14 d (12)	2.92 d (12)	2.03 d (12)	2.43 d (11)	2.94 d (11)	2.81 d (10)
H-11	5.80 dd (12, 9)	5.50 dd (12, 9)	3.77 ddd (12, 9, 7)	3.96 ddd (11, 9, 8)	4.41 ddd (11, 9, 4)	4.37 dd (10, 9)
H-12	3.43 dd (12, 9)	3.26 dd (11, 9)	2.72 dd (10, 7)	3.08 dd (10, 8)	3.15 d (9)	3.16 d (9)
H-13	2.21 m	2.24 m	1.92 m	2.08 m		
H-14	1.76 m	1.82 m		1.66 ddd (12, 8, 5)	1.85 m	2.16 m
H-15	2.73 dd (19, 7), 2.91 dd (19, 12)	2.62 dd (20, 12), 2.68 dd (20, 8)	2.58 d (19), 2.73 d (19)	2.67 dd (20, 8), 2.76 dd (20, 12)	1.95 m, 2.08 m	1.74 (2H, m)
H-16					5.06 dd (9, 2)	4.82 d (2)
Me-8	1.15 s	1.34 s	1.15 s	1.07 s	1.53 s	1.55 s
Me-10	1.43 s	1.27 s	1.45 s	1.35 s	1.44 s	1.45 s
Me-13	0.97 d (7)	1.05 d (7)	1.09 d (7)	0.99 d (8)	1.34 s	1.23 s
OMe-2		2.84 s	3.60 s	3.45 s	3.48 s	3.48 s
OMe-12	3.29 s	3.30 s	3.65 s	3.71 s		3.72 s
OMe-16					3.67 s	3.33 s
OH-11			4.01 d (9)	4.60 d (9)	4.39 d (4)	
OAc-2	1.97 s					
H-2'	7.83 d (2)	7.53 d (2)				
H-5'	7.03 d (8)	6.82 d (8)				
H-6'	8.00 dd (8, 2)	7.72 dd (8, 2)				
H-8'	6.05 d (1), 6.09 d (1)	6.01 d (1), 6.02 d (1)				

Coupling constants (*J* in Hz) are given in parentheses. a) In CDCl₃. b) In C₅D₅N.TABLE II. ¹³C-NMR Spectral Data for Compounds 1–6

Carbon	1 ^{b)}	4 ^{a)}	2 ^{a)}	5 ^{b)}	3 ^{b)}	6 ^{b)}
C-1	208.21	211.01	204.48	204.75	206.26	206.37
C-2	72.89	79.99	149.16	149.72	149.63	149.61
C-3	33.69	35.32	112.35	112.47	112.35	112.24
C-4	25.16	25.26	27.77	28.08	28.50 ^{c)}	28.49
C-5	42.72	42.04	36.06	36.72	37.69 ^{d)}	37.52
C-6	29.42	29.19	28.67	29.61	29.89 ^{c)}	29.42
C-7	82.40	82.61	78.77	82.42	72.01	69.98
C-8	36.18	34.92	40.86	37.96	39.89 ^{d)}	38.98
C-9	36.04	35.80	38.92	37.96	38.84 ^{d)}	38.91
C-10	51.26	50.70	47.53	48.16	52.70	48.73
C-11	73.81	73.57	73.07	74.05	76.61	71.94
C-12	85.85	85.74	88.94	88.78	90.88	90.62
C-13	34.94	35.58	42.58	34.95	78.07	76.62
C-14	45.26	45.49	74.27	44.85	48.89	47.18
C-15	28.29	27.93	36.13	28.64	28.87 ^{c)}	29.31
C-16	169.16	169.91	170.02	169.99	97.25	98.22
C-19	12.32	12.64	11.24	11.27	11.56	11.45
C-20	21.78	22.24	15.33	21.38	26.87	26.74
C-21	14.36	14.42	10.41	14.68	23.97	24.37
OMe-2		57.44	55.24	55.08	55.05	55.04
OMe-12	60.28	61.00	61.51	61.28		62.36
OMe-16					61.37	54.22
OCOMe-2	20.26					
OCOMe-2	169.89					
C-1'	125.36	123.75				
C-2'	110.81	110.01				
C-3'	148.04	147.73				
C-4'	151.91	151.83				
C-5'	108.05	107.96				
C-6'	126.58	126.16				
C-7'	165.58	165.26				
C-8'	102.33	101.80				

a) In CDCl₃. b) In C₅D₅N. c, d) Values may be interchanged.

colorless prisms, and its molecular formula was C₂₁H₃₂O₇ as determined by HRMS. The IR and UV spectra of **3** indicated the presence of hydroxyls ($\nu_{\max}$ 3557, 3480 and 3420 cm⁻¹) and α,β -unsaturated ketone ($\nu_{\max}$ 1672, 1628 cm⁻¹ and $\lambda_{\max}$ 268 nm) groups. The ¹H-NMR spectrum of **3** showed signals due to three tertiary methyls at δ 1.34 (s, Me-13), 1.44 (s, Me-10) and 1.53 (s, Me-8), two methoxyls at δ 3.48 (s, OMe-2) and 3.67 (s, OMe-16), an olefinic proton at δ 5.51 (dd, *J* = 6 and 2 Hz) and a hemiacetal proton at δ 5.06 (dd, *J* = 9 and 2 Hz). The ¹H- and ¹³C-NMR signals of javanicin Q (**3**) showed close correspondence with those of javanicin C (**6**),¹⁾ except that a methoxyl signal was missing at C-12 and replaced by a hydroxyl group. The couplings between the hemiacetal proton at C-16 and methylene protons at C-15 were increased to coupling constants 9 and 2 Hz, suggesting that the hemiacetal proton at C-16 had a β -orientation in **3**, as had been established earlier for the javanicinoside A (**7**) (H-16, *J* = 9 and 2 Hz).⁶⁾ The relative upfield shift ($\Delta\delta$ = 0.65 ppm) of a proton at the lactone terminus (H-7, δ 3.31) in **3** compared with that of the corresponding proton at δ 3.96 in **6**, suggests that methoxyl may be located on C-16 with an α -configuration. The relative stereochemistry of **3** was determined by NOE measurements as follows. Irradiation of H-11 proton at δ 4.41 induced NOEs at Me-8 (5%) and Me-10 (5%). Irradiation of H-7 at δ 3.31 induced NOEs at Me-8 (14%), H-14 (6%) and H-16 (20%). Irradiation of Me-13 protons at δ 1.34 induced 3% NOE at H-12. On the basis of above data, the structure of javanicin Q is proposed to be **3**.

Experimental

All melting points were determined on a Yanagimoto micromelting point

apparatus and are uncorrected. The UV and IR spectra were recorded on Hitachi 340 and Hitachi 260-30 spectrophotometers, respectively. The ^1H - and ^{13}C -NMR spectra were recorded with a JEOL JNM GX-400 (^1H , 400 MHz; ^{13}C , 100 MHz) spectrometer. Chemical shifts are given on the δ -scale (with ppm downfield from tetramethylsilane as an internal standard) and coupling constants (J) in hertz (Hz). Electron-impact (EI) MS and HRMS were run on JEOL JMS D-300 and JEOL JMS DX-303 mass spectrometers, respectively. Optical rotations were determined on a JASCO DIP-4 digital polarimeter. Column chromatography was carried out on silica gel (BW-820MH, Fuji Davison) and the Diaion HP-20 (Mitsubishi Kasei). Low-pressure liquid chromatography (LC) and high performance LC (HPLC) were carried out on silica gel (CQ-3, 24 mm i.d. $\times$ 360 mm, Fuji gel, detector: 254 nm) and silica gel (Senshu Pak SSC-Silica 3251-N, 8 mm i.d. $\times$ 250 mm, detector: 254 nm), respectively.

Isolation of Javanicin N (1) The dried stems (3.7 kg) of *Picrasma javanica* collected in Bogor, Indonesia, in July, 1986, were extracted with MeOH (49 l). The MeOH extract was concentrated under reduced pressure to give a residue, to which an equal volume of H_2O was added. The aqueous solution was extracted with CHCl_3 (12 l) and then *n*-BuOH (3.6 l). The CHCl_3 soluble fraction (73 g) was subjected to repeated column chromatography on silica gel and further purified by low-pressure LC and HPLC to give javanicin N (1, 30 mg).

Isolation of Javanicins P (2) and Q (3) The fractionation of the MeOH extract from the leaves of *P. javanica* was described in a previous report.⁴⁾ The CHCl_3 soluble fraction (200 g) was subjected to repeated column chromatography on a Diaion HP-20 and further purified by low-pressure LC on silica gel with CH_2Cl_2 -MeOH (20:1, v/v) and HPLC on silica gel with CH_2Cl_2 -MeOH (20:1, v/v) to give javanicin P (2, 13 mg) and javanicin Q (3, 11 mg).

Javanicin N (1): Colorless needles (MeOH), mp 222–224 °C, $[\alpha]_{\text{D}}^{27} -48.0^\circ$ ($c=3.0$, CHCl_3). UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 220 (4.03), 262 (3.60), 296 (3.54). IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 1735, 1700, 1610, 1490, 1290, 1260, 1100, 1040, 762. ^1H - and ^{13}C -NMR data are given in Tables I and II, respectively. MS m/z : 556 (M^+ , 30%), 390 (19), 365 (11), 330 (54), 261 (11), 166 (14), 149 (100), 121 (9). HRMS m/z 556.2271 $[\text{M}]^+$ (Calcd for $\text{C}_{30}\text{H}_{36}\text{O}_{10}$:

556.2298).

Javanicin P (2): Colorless needles (MeOH), mp 150–152 °C, $[\alpha]_{\text{D}}^{22} +52.0^\circ$ ($c=1.2$, MeOH). UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 266 (3.54). IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3440, 1725, 1670, 1633, 1460, 1445, 1265, 1237, 1120, 1038. ^1H - and ^{13}C -NMR data are given in Tables I and II, respectively. MS m/z : 394 (M^+ , 8%), 376 (9), 331 (36), 287 (22), 269 (100), 155 (30), 234 (78), 203 (37), 191 (24), 159 (37), 151 (28), 139 (52). HRMS m/z : 394.1997 $[\text{M}]^+$ (Calcd for $\text{C}_{21}\text{H}_{30}\text{O}_7$: 394.1983).

Javanicin Q (3): Colorless prisms (MeOH), mp 243–245 °C, $[\alpha]_{\text{D}}^{21} +102.7^\circ$ ($c=1.1$, MeOH). UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 268 (3.79). IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3557, 3480, 3420, 1672, 1628, 1430, 1270, 1240, 1100, 1065. ^1H - and ^{13}C -NMR are given in Tables I and II, respectively. MS m/z : 396 (M^+ , 9%), 378 (64), 360 (67), 290 (66), 262 (32), 232 (52), 205 (40), 191 (56), 180 (40), 163 (63), 139 (76), 127 (40). HRMS m/z 396.2119 $[\text{M}]^+$ (Calcd for $\text{C}_{21}\text{H}_{32}\text{O}_7$: 396.2139).

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