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Studies on the Alkaloids from *Picrasma quassioides* BENNET. VI.[1] Structures of Picrasidines N, O, and Q

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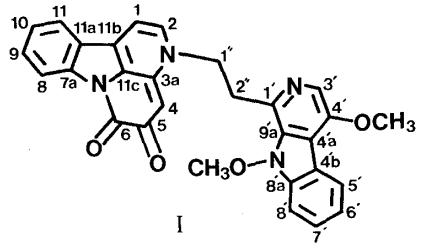
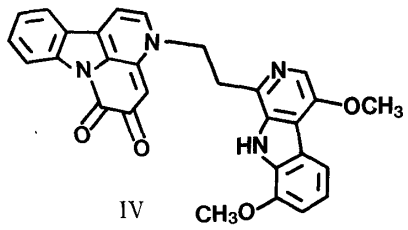
Three new alkaloids, picrasidines N (I), O (II), and Q (III), have been isolated from the root wood of *Picrasma quassioides* BENNET (Simaroubaceae). The structures were determined on the basis of spectral analysis and chemical evidence.

Keywords——*Picrasma quassioides*; Simaroubaceae; root wood; alkaloid; picrasidine N; picrasidine O; picrasidine Q; canthine-5,6-dione; β-carboline

In the previous paper,[1] we reported the structural elucidation of three new alkaloids, two of them having a canthine-5,6-dione structure, isolated from *Picrasma quassioides* BENNET (Simaroubaceae, Japanese name "Nigaki"). This paper deals with the structural elucidation of three new alkaloids, picrasidines N (I), O (II), and Q (III), having a canthin-6-one or canthine-5,6-dione structure, isolated from the root wood of the plant.



I



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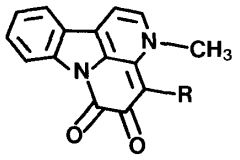
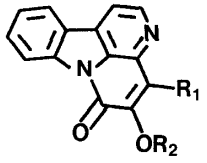
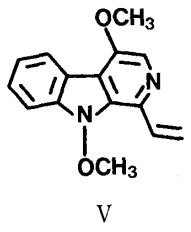


II: R = OCH_3
VII: R = H



III: R_1 = OH, R_2 = CH_3
VI: R_1 = H, R_2 = $COCH_3$
VIII: R_1 = OCH_3, R_2 = H
IX: R_1 = OCH_3, R_2 = CH_3



V

Chart 1

Picrasidine N (I) was isolated as orange needles, and its molecular formula was determined to be $C_{29}H_{22}N_4O_4$ by elemental analysis. Its infrared (IR) spectrum showed carbonyl absorption bands at 1655 and 1695 cm^{-1}. However, the IR spectrum provided no evidence of the presence of an amino group or hydroxyl group. The presence of two carbonyl carbons was indicated by the signals at δ 156.35 and 169.90 in the carbon-13 nuclear magnetic

resonance (^{13}C-NMR) spectrum (Table I). The ultraviolet (UV) spectrum of I was similar to that of picrasidine M (IV),[1] which suggested that I contains the canthine-5,6-dione and β-carboline chromophores in the molecule (Fig. 1). The mass spectral (MS) fragmentation of I, studied with the aid of field desorption (FD)-MS and electron ionization (EI)-MS, was particularly informative. The FD-MS exhibited a molecular ion at *m/z* 490 and FD- and EI-MS exhibited significant ions at *m/z* 236 and 254, which represented the canthine-5,6-dione unit and β-carboline unit having one ethylene and two methoxyl functions. In the proton nuclear magnetic resonance (^{1}H-NMR) and ^{13}C-NMR spectra of I, the proton and carbon atoms of the canthine-5,6-dione unit showed chemical shift values similar to those of IV, suggesting that I is unsubstituted except for the N(3)-position. On the other hand, subtraction of the canthine-5,6-dione unit formula $C_{14}H_7N_2O_2$ from the molecular formula gave the β-carboline unit formula $C_{15}H_{15}N_2O_2$. The ^{1}H-NMR spectrum of the β-carboline unit of I showed A_2B_2 pattern signals at δ 3.78 and 4.85 (each 2H, t, J=7.0 Hz), attributable to a CH_2–CH_2 unit, and three singlets at δ 4.06 (3H, s), 4.13 (3H, s), and 8.17 (1H, s) assigned to the two methoxyl signals and a lone aromatic proton, respectively, as well as four aromatic signals at δ 8.20 (dd), 7.32 (td), 7.59 (td), and 7.62 (dd) (each 1H, J=7.8 and 2.0 Hz). However, the NH

Table I. ^{13}C-NMR Spectral Data[a] for Compounds I, II and IV

Carbon	I	IV	II
C-1	103.65	103.29	103.97
C-2	135.50	135.44	138.11
C-3a	124.50	124.39	121.86
C-4	92.95	93.08	132.91
C-5	169.90	169.83	164.56
C-6	156.35	156.29	156.77
C-7a	138.95	138.90	138.91
C-8	115.64	115.60	115.49
C-9	129.40	129.29	129.43
C-10	125.02	124.92	125.26
C-11	122.35	122.24	122.04
C-11a	124.02	123.99	124.19
C-11b	124.31	124.15	125.19
C-11c	139.55	139.46	132.51
C-1″	52.10	51.74	44.06
C-2″	31.38	31.44	(3-CH_3)
C-1′	137.01	134.72	59.50
C-3′	120.82	119.62	(4-OCH_3)
C-4	149.73	149.81	
C-4′a	116.59	117.02	
C-4′b	123.23	121.07	
C-5′	122.35	115.08	
C-6′	127.47	120.21	
C-7′	122.60	107.23	
C-8′	108.82	145.44	
C-8′a	131.81	129.57	
C-9′a	132.66	134.27	
4′-OCH_3	56.31	55.96	
8′-OCH_3		55.32	
9′-OCH_3	64.73		

a) Solvent: all compounds in DMSO-d_6 at 80 °C. The signal assignments were based on comparisons with structurally related compounds.[4]

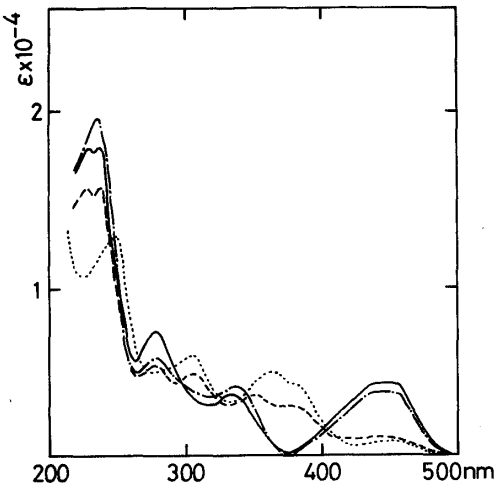


Fig. 1. UV Spectra of Compounds I and IV

——, I in EtOH; – – –, I in EtOH+HCl; – · – · –, IV in EtOH; ------, IV in EtOH+HCl.

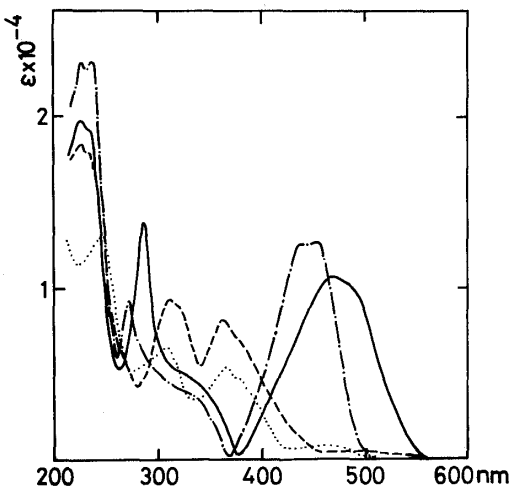


Fig. 2. UV Spectra of Compounds II and VII

——, II in EtOH; – – –, II in EtOH+HCl; – · – · –, VII in EtOH; ------, VII in EtOH+HCl.

TABLE II. ^{1}H-NMR Spectral Data[a] for Compounds I, II, III, IV, and V

Proton	I	IV	II	III	V
H-1	7.37 (d, J=6.9)	7.34 (d, J=6.9)	7.43 (d, J=7.0)	8.29 (d, J=5.0)	
H-2	7.89 (d, J=6.9)	7.87 (d, J=6.9)	7.91 (d, J=7.0)	8.83 (d, J=5.0)	
H-4	6.13 (s)	6.15 (s)			
H-8	8.47 (dd, J=8.2, 1.7)	8.47 (dd, J=8.2, 1.5)	8.44 (dd, J=8.2, 1.1)	8.49 (dd, J=7.7, 1.2)	
H-9	7.68 (td, J=8.2, 1.7)	7.68 (td, J=8.2, 1.5)	7.66 (td, J=8.2, 1.1)	7.75 (td, J=7.7, 1.2)	
H-10	7.51 (td, J=8.2, 1.7)	7.52 (td, J=8.2, 1.5)	7.50 (td, J=8.2, 1.1)	7.51 (td, J=7.7, 1.2)	
H-11	8.17 (dd, J=8.2, 1.7)	8.15 (dd, J=8.2, 1.5)	8.15 (dd, J=8.2, 1.1)	8.35 (dd, J=7.7, 1.2)	
H-1''	4.85 (t, J=7.0)	4.77 (t, J=7.0)	3.82 (s, 3-CH_3)	3.89 (s, 5-OCH_3)	
H-2''	3.78 (t, J=7.0)	3.72 (t, J=7.0)	4.26 (s, 4-OCH_3)		
H-3′	8.17 (s)	7.99 (s)			8.15 (s)
H-5′	8.20 (dd, J=7.8, 2.0)	7.76 (d, J=7.9)			8.25 (d, J=8.0)
H-6′	7.32 (td, J=7.8, 2.0)	7.15 (t, J=7.9)			7.30 (t, J=8.0)
H-7′	7.59 (td, J=7.8, 2.0)	7.05 (d, J=7.9)			7.50 (t, J=8.0)
H-8′	7.62 (dd, J=7.8, 2.0)				7.53 (d, J=8.0)
H-9′		11.42 (s)[b]			
4′-OCH_3	4.13 (s)	4.08 (s)			4.13 (s)
8′-OCH_3		3.97 (s)			
9′-OCH_3	4.06 (s)				4.00 (s)
				H_A>C=C<H_M / H_X	7.15 J_{AM}=17.5 6.22 J_{AX}=11.0 5.48 J_{MX}=2.0

a) Solvent: I, II, III, and IV in DMSO-d_6 at 80 °C and V in $CDCl_3$. b) Disappeared on addition of D_2O.

proton of the indole moiety of the β-carboline structure was not observed. The pattern and location of the signals of the β-carboline unit of I were essentially similar to those of picrasidine D (4,9-dimethoxy-1-vinyl-β-carboline, V).[2] Thus, picrasidine N is composed of the canthine-5,6-dione and the β-carboline subunits linked through N(3) and C(1′′). Chemical evidence for the structure was obtained as follows. The cleavage of the N(3)–C(1′′) bond of I with acetic anhydride gave 4,9-dimethoxy-1-vinyl-β-carboline (V) and 5-acethoxycanthin-6-one (VI).[1] All the spectral data for V and VI were in good agreement with those of corresponding authentic samples.[1,2] Thus, the structure of picrasidine N was determined as formula I.

Picrasidine O (II) was isolated as red needles and its molecular formula was determined to be $C_{16}H_{12}N_2O_3$ by high-resolution mass spectrometry. Its IR spectrum showed carbonyl absorption bands at 1642 and 1682 cm^{-1}. The presence of two carbonyl carbons in the structure was indicated by the signals at δ 156.77 and 164.56 in the ^{13}C-NMR spectrum. Its UV spectrum was similar to picrasidine L (VII),[1] and showed a hypochromic shift on the addition of acid, but was unchanged by base (Fig. 2). Based on the above results, picrasidine O has the canthine-5,6-dione chromophore. The ^{1}H-NMR spectrum of II showed two three-proton singlets at δ 3.82 and 4.26 attributable to methyl and methoxyl signals, respectively, and a pair of *ortho* coupled signals at δ 7.43 and 7.91 (each d, J=7.0 Hz) assigned to H-1 and H-2, respectively, as well as four aromatic signals at δ 7.50 (td), 7.66 (td), 8.15 (dd), and 8.44 (dd) (each J=8.2 and 1.1 Hz) assigned to H-8 to H-11. Based on the above results, the structure of picrasidine O is proposed to be 4-methoxy-3-methylcanthine-5,6-dione (II). Chemical evidence for the structure was obtained by the methylation of 5-hydroxy-4-methoxycanthin-6-one (VIII)[3] with dimethyl sulfate to give synthetic compound II. All the spectral data of natural picrasidine O were in good agreement with those of the synthetic compound. Thus, the structure of picrasidine O was determined as 4-methoxy-3-methylcanthine-5,6-dione (II).

Picrasidine Q (III) was isolated as pale yellow needles and its molecular formula was determined to be $C_{15}H_{10}N_2O_3$ by elemental analysis. Its IR spectrum showed hydroxyl and carbonyl absorption bands at 3350 and 1680 cm^{-1} and its UV spectrum exhibited the typical absorption of the canthin-6-one chromophore.[3] The ^{1}H-NMR spectrum of III showed a methoxyl signal at δ 3.89 (3H, s), and a pair of *ortho* coupled signals at δ 8.29 and 8.83 (each J=5.0 Hz) assigned to H-1 and H-2, respectively, as well as four aromatic signals at δ 8.49 (dd), 7.75 (td), 7.51 (td), and 8.35 (dd) (each 1H, J=7.7 and 1.2 Hz) assigned to H-8 and H-11. Methylation of III with diazomethane gave 4,5-dimethoxycanthin-6-one (IX).[3] Based on the above results, the structure of picrasidine Q is proposed to be III or VIII. The data of picrasidine Q were inconsistent with those of authentic 5-hydroxy-4-methoxy-canthin-6-one (VIII).[3] From the above results, the structure of picrasidine Q was determined as 4-hydroxy-5-methoxycanthin-6-one (III).

Experimental

All melting points were determined on a Yanagimoto micro-melting point apparatus and are uncorrected. The UV and IR spectra were recorded with Hitachi 340 and Hitachi 260-30 spectrophotometers, respectively. The ^{1}H-NMR and ^{13}C-NMR spectra were recorded with JEOL GX-400 (^{1}H 400 MHz and ^{13}C 100 MHz) and Hitachi R-900 (^{1}H 90 MHz) Fourier-transform spectrometers. Chemical shifts are given on the δ scale (ppm) with tetramethylsilane as an internal standard, and coupling constants are given in Hz. The following abbreviations are used: s=singlet, d=doublet, dd=double doublet, t=triplet, td=triplet doublet, and sh=shoulder. Mass spectra were measured with a JEOL JMS D-300 mass spectrometer. Column chromatography was carried out on silica gel (BW-820MH, Fuji Devison Co., Ltd.). Thin layer chromatography (TLC) and preparative TLC were performed on silica gel 60 GF_{254} (Merck), and the spots were detected with Dragendorff's reagent or by UV illumination.

Extraction and Isolation——Dried root wood (30 kg) of *Picrasma quassioides* collected at Chiba city, Chiba prefecture in August, 1983, was extracted with MeOH (100 l) at 35 °C for 48 h. The MeOH extract was evaporated to dryness and the residue was partitioned between water and $CHCl_3$. The $CHCl_3$ solution was dried over Na_2SO_4 and

concentrated to give a $CHCl_3$-soluble fraction (250 g) which was applied to a column of silica gel (1.5 kg). The column was eluted successively with $CHCl_3$, $CHCl_3$–MeOH (19 : 1, 9 : 1, 4 : 1, and 1 : 1), and MeOH. The $CHCl_3$–MeOH (9 : 1) fraction was repeatedly chromatographed on silica gel to give picrasidines N (26 mg) and O (20 mg), and Q (5 mg).

Picrasidine N (I)——Orange needles ($CHCl_3$: MeOH = 1 : 1), mp 171—172 °C (dec.). UV λ_{max}^{EtOH} nm (log ε): 232 (4.25), 241 (4.25), 284 (3.87), 342 (3.52), 442 (3.59), 466 (3.59). UV $\lambda_{max}^{EtOH+HCl}$ nm (log ε): 232 (4.20), 241 (4.20), 284 (3.73), 314 (3.56), 342 (3.56), 356 (sh, 3.50), 442 (3.03), 466 (3.03). UV $\lambda_{max}^{EtOH+NaOH}$ nm (log ε): 232 (4.25), 241 (4.25), 284 (3.87), 342 (3.52), 442 (3.59), 466 (3.59). IR ν_{max}^{KBr} cm^{-1}: 1695, 1655, 1600, 1285, 1250, 1150, 1050. ^{13}C-NMR and ^{1}H-NMR: Tables I and II, respectively. FD-MS *m/z*: 513 $(M+Na)^+$, 490 (M^+), 254, 236. EI-MS *m/z* (%): 254 (54), 236 (20), 224 (100), 169 (30). *Anal.* Calcd for $C_{29}H_{22}N_4O_4$: C, 71.01; H, 4.52; N, 11.42. Found: C, 71.10; H, 4.51; N, 11.30.

Reaction of I with Acetic Anhydride——A solution of I (10 mg) in acetic anhydride (5 ml) was refluxed for 2 h. The reaction mixture was poured into ice-water, basified with 5% Na_2CO_3 solution and extracted with $CHCl_3$. The $CHCl_3$ solution was dried over Na_2SO_4 and concentrated to give a mixture of V and VI, which was separated by preparative TLC to give V (3 mg) and VI (3 mg).[1] Compound V, colorless needles, mp 191—192 °C. MS *m/z* (%): 254 (M^+, 60), 226 (12), 223 (100), 208 (65), 197 (18). IR ν_{max}^{KBr} cm^{-1}: 1610, 1550, 1270, 1250, 1050. ^{1}H-NMR (90 MHz, $CDCl_3$) δ: Table II. This compound was identified by direct comparison (TLC, IR, ^{1}H-NMR spectra, and mixed melting point determination) with an authentic sample.[2] Compound VI, pale yellow plates, mp 210 °C. MS *m/z* (%): 278 (M^+, 10), 236 (100), 207 (13), 180 (40). IR ν_{max}^{KBr} cm^{-1}: 1775, 1677, 1636, 1605, 1437, 1380, 1200,1165, 1140, 1030. ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 2.44 (3H, s, 5-$OCOCH_3$), 7.46 (1H, td, J=8.0, 1.2 Hz, H-10), 7.58 (1H, d, J=5.0 Hz, H-1), 7.64 (1H, td, J=8.0, 1.2 Hz, H-9), 7.77 (1H, s, H-4), 8.04 (1H, dd, J=8.0, 1.2 Hz, H-11), 8.54 (1H, dd, J=8.0, 1.2 Hz, H-8), 8.78 (1H, d, J=5.0 Hz, H-2). This compound was identified by direct comparison (TLC, IR, ^{1}H-NMR spectra, and mixed melting point determination) with an authentic sample.[1]

Picrasidine O (II)——Red needles, mp 274 °C (dec.). UV λ_{max}^{EtOH} nm (log ε): 242 (4.28), 250 (sh, 4.27) 290 (4.20), 360 (3.54), 480 (4.04), 500 (4.00). UV $\lambda_{max}^{EtOH+HCl}$ nm (log ε): 242 (4.14), 258 (sh, 4.11), 320 (3.84), 328 (sh, 3.81), 378 (3.76), 416 (sh, 3.52). UV $\lambda_{max}^{EtOH+NaOH}$ nm (log ε): 242 (4.18), 250 (sh, 4.14), 294 (4.00), 383 (3.39), 484 (3.79), 500 (3.78). IR ν_{max}^{KBr} cm^{-1}: 1682, 1642, 1549, 1500, 1450, 1408, 1282, 1108. ^{13}C-NMR and ^{1}H-NMR: Tables I and II, respectively. MS *m/z* (%): 280 (M^+, 70), 265 (93), 250 (11), 209 (44), 182 (100), 181 (90). High-resolution MS: Calcd for $C_{16}H_{12}N_2O_3$, *m/z* 280.0848. Found *m/z* 280.0871.

Synthesis of II——A stirred solution of 5-hydroxy-4-methoxycanthin-6-one (VIII, 1.0 g)[3] in acetone (60 ml) containing K_2CO_3 (3 g) was treated with dimethyl sulfate (4 ml). The reaction mixture was refluxed with stirring for 5 h. After the usual work-up, the crude product was recrystallized from $CHCl_3$–MeOH (1 : 1) to give II (660 mg), red needles, mp 274 °C (dec.). MS *m/z* (%): 288 (M^+, 70), 265 (94), 250 (13), 209 (50), 182 (100). IR ν_{max}^{KBr} cm^{-1}: 1682, 1642, 1540, 1500, 1450, 1280, 1110. *Anal.* Calcd for $C_{16}H_{12}N_2O_3$: C, 68.59; H, 4.32; N, 9.99. Found: C, 68.35; H, 4.18; N, 9.93.

Picrasidine Q (III)——Pale yellow needles ($CHCl_3$: MeOH = 1 : 1), mp 286—289 °C. UV λ_{max}^{EtOH} nm (log ε): 247 (4.24), 270 (sh, 3.97), 288 (3.98), 299 (sh, 3.95), 340 (sh, 3.82), 358 (3.98), 370 (sh, 3.85). UV $\lambda_{max}^{EtOH+HCl}$ nm (log ε): 247 (4.24), 270 (sh, 3.97), 188 (3.98), 199 (sh, 3.95), 340 (sh, 3.82), 358 (3.98), 370 (sh, 3.85). UV $\lambda_{max}^{EtOH+NaOH}$ nm (log ε): 245 (4.25), 280 (4.23), 340 (3.91), 400 (3.25). IR ν_{max}^{KBr} cm^{-1}: 1682, 1642, 1549, 1500, 1450, 1408, 1282, 1108. ^{1}H-NMR: Table II. MS *m/z* (%): 266 (M^+, 98), 251 (68), 237 (49), 195 (59), 167 (100), 140 (53). High-resolution MS: Calcd for $C_{15}H_{10}N_2O_3$, *m/z* 266.0692. Found *m/z* 266.0748.

Methylation of III—Methylation of III (3 mg) with diazomethane in ether–MeOH at room temperature for 15 h gave 4,5-dimethoxycanthin-6-one (3 mg), mp 146 °C. MS *m/z* (%): 280 (M^+, 100), 250 (50), 220 (60), 192 (62), 167 (67). IR ν_{max}^{KBr} cm^{-1}: 1670, 1635, 1270, 1110, 1090. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 4.04 (3H, s, 5-OCH_3), 4.40 (3H, s, 4-OCH_3), 7.19 (1H, t, J=7.7 Hz, H-10), 7.37 (1H, t, J=7.7 Hz, H-9), 7.47 (1H, d, J=5.0 Hz, H-1), 7.59 (1H, d, J=7.7 Hz, H-11), 8.16 (1H, d, J=7.7 Hz, H-8), 8.54 (1H, d, J=5.0, H-2). This compound was identified by direct comparison (TLC, IR, ^{1}H-NMR spectra, and mixed melting point determination) with an authentic sample.[3]

References and Notes

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