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Studies on the Alkaloids from *Picrasma quassioides* BENNET. V.[1] Structures of Picrasidines L, M, and P

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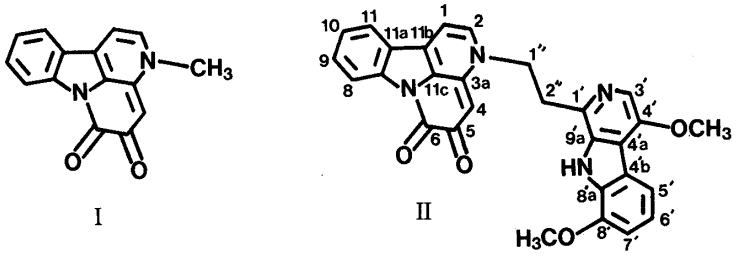
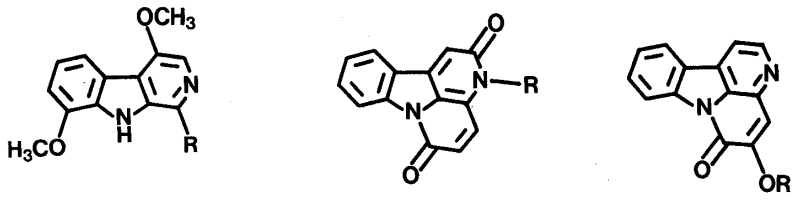
Two new alkaloids, picrasidines M (II) and P (III), have been isolated from the root-bark of *Picrasma quassioides* BENNET. The structure of picrasidine L has been revised from 3-methylcanthin-2,6-dione to 3-methylcanthin-5,6-dione (I). The structures were determined on the basis of spectral analysis and chemical evidence.

Keywords——*Picrasma quassioides*; Simaroubaceae; root-bark; alkaloid; picrasidine L; picrasidine M; picrasidine P; canthin-5,6-dione; β-carboline

In earlier studies on the alkaloids from *Picrasma quassioises* BENNET (Simaroubaceae, Japanese name "Nigaki") grown in Japan, we isolated several new alkaloids.[1-4] This paper deals with the structural elucidation of two new alkaloids, picrasidines M (II) and P (III), isolated from the root-bark of the plant. A revised structure of picrasidine L (I), which has already been isolated from the wood of the plant,[2] is also reported.



I II



III: R=H
IX: R=CH_2CH_3
X: R=CH=CH_2

IV: R=CH_3
V: R=OCH_3

VI: R=H
VII: R=Ac
VIII: R=CH_3

Chart 1

Picrasidine L (I) was obtained as orange-red needles and its molecular formula was determined to be $C_{15}H_{10}N_2O_2$ by high resolution mass spectrometry (MS). Its infrared (IR) spectrum showed carbonyl absorption bands at 1695 and 1655 cm^{-1}. The presence of two carbonyl carbons in its structure was confirmed by the signals at δ 156.34 and 169.79 in the carbon-13 nuclear magnetic resonance (^{13}C-NMR, 100 MHz) spectrum (Table I). Its ultraviolet (UV) absorption spectrum was similar to that of 3-methoxycanthin-2,6-dione (V) (Fig. 1).[5] However, the UV absorption of V was not altered by the addition of acid or base. On the

other hand, the UV absorption of I showed a hypochromic shift on the addition of acid, but was unchanged by base (Fig. 1). The hypochromic shift of the absorption maxima in the presence of acid was very similar to that of 5-hydroxycanthin-6-one (VI) (Fig. 2),[6,7] indicating that picrasidine L has the canthin-5,6-dione chromophore. The proton nuclear magnetic resonance (^{1}H-NMR, 400 MHz) spectrum of I in deuteriodimethylsulfoxide at 80 °C showed four aromatic signals at δ 8.46 (1H, dd), 7.68 (1H, td), 7.52 (1H, td), and 8.18 (1H, dd), (each J=8.2, 1.2 Hz) assigned to H-8 to H-11, a pair of *ortho*-coupled signals at δ 7.40 (1H, d, J= 7.0 Hz) and 7.97 (1H, d, J=7.0) assigned to H-1 and H-2, respectively, and two singlets at δ 3.89 (3H, s) and 5.98 (1H, s) attributable to methyl protons and an olefinic proton (H-4), respectively. Based on the above results, it is considered that the structure of picrasidine L should be 3-methylcanthin-5,6-dione (I). Chemical evidence for the structure was obtained by the methylation of 5-hydroxycanthin-6-one (VI)[6] with dimethyl sulfate to give synthetic compound I. All the spectral data of natural picrasidine L were in good agreement with those of the synthetic compound. Thus, the structure of picrasidine L was revised from the previously reported 3-methylcanthin-2,6-dione to 3-methylcanthin-5,6-dione (I).

Picrasidine M (II) was isolated as orange needles and its molecular formula was determined to be $C_{29}H_{22}N_4O_4$ by elemental analysis. Its IR spectrum showed an amino absorption band at 3420 cm^{-1} and carbonyl absorption bands at 1688 and 1650 cm^{-1}. The presence of two carbonyl carbons in its structure was proved by the signals at δ 156.29 and

TABLE I. ^{13}C-NMR Spectral Data for Compounds I, II, and IX

Carbon	I	II	IX
C-1	103.42	103.29	
C-2	135.80	135.44	
C-3a	124.24	124.39	
C-4	92.78	93.08	
C-5	169.79	169.83	
C-6	156.34	156.29	
C-7a	138.89	138.90	
C-8	115.62	115.60	
C-9	129.26	129.29	
C-10	124.94	124.92	
C-11	122.29	122.24	
C-11a	124.07	123.99	
C-11b	124.11	124.15	
C-11c	140.15	139.46	
C-1″	40.66	51.74	13.13
C-2″		31.44	25.92
C-1′		134.72	140.99
C-3′		119.62	119.84
C-4′		149.81	149.99
C-4′a		117.02	116.68
C-4′b		121.07	121.69
C-5′		115.08	114.53
C-6′		120.21	120.00
C-7′		107.23	107.09
C-8′		145.44	146.08
C-8′a		129.57	129.82
C-9′a		134.27	134.56
4′-OCH$_3$		55.96	55.89
8′-OCH$_3$		55.32	55.36

Solvent: I and II in DMSO-d_6 at 80 °C, IX in $CDCl_3$.

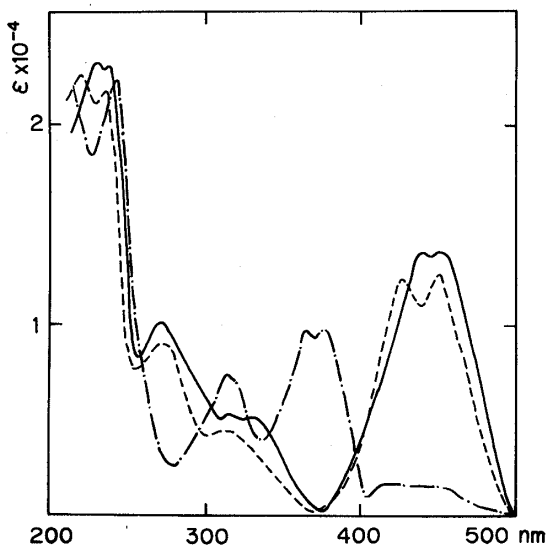


Fig. 1. UV Spectra of Compounds I and V

——, I in EtOH; - - - - -, I in EtOH + HCl; – – – –, V in EtOH.

TABLE II. ^{1}H-NMR Spectral Data for I, II, III, and IX

Proton	I	II	III	IX
H-1	7.40 (d, J=7.0)	7.34 (d, J=6.9)		
H-2	7.97 (d, J=7.0)	7.87 (d, J=6.9)		
H-4	5.98 (s)	6.15 (s)		
H-8	8.46 (dd, J=8.2, 1.2)	8.47 (dd, J=8.2, 1.5)		
H-9	7.68 (td, J=8.2, 1.2)	7.68 (td, J=8.2, 1.5)		
H-10	7.52 (td, J=8.2, 1.2)	7.52 (td, J=8.2, 1.5)		
H-11	8.18 (dd, J=8.2, 1.2)	8.15 (dd, J=8.2, 1.5)		
H-1''	3.89 (s, N-CH_3)	4.77 (t, J=7.1)		1.37 (t, J=8.0)
H-2''		3.72 (t, J=7.1)		3.10 (q, J=8.0)
H-1'			8.61 (s)	
H-3'		7.99 (s)	8.07 (s)	7.95 (s)
H-5'		7.76 (d, J=7.9)	7.91 (dd, J=7.8, 1.0)	7.90 (d, J=8.0)
H-6'		7.15 (t, J=7.9)	7.22 (t, J=7.8)	7.14 (t, J=8.0)
H-7'		7.05 (d, J=7.9)	6.99 (dd, J=7.8, 1.0)	6.83 (d, J=8.0)
N(9')-H		11.42 (s)[a]	8.49 (s)[a]	9.64 (s)[a]
C(4')-OCH_3		4.08 (s)	4.15 (s)	4.02 (s)
C(8')-OCH_3		3.97 (s)	4.03 (s)	3.85 (s)

Solvent: I and II in DMSO-d_6 at 80 °C, III and IX in $CDCl_3$. Coupling constants in Hz. *a*) Disappeared with D_2O.

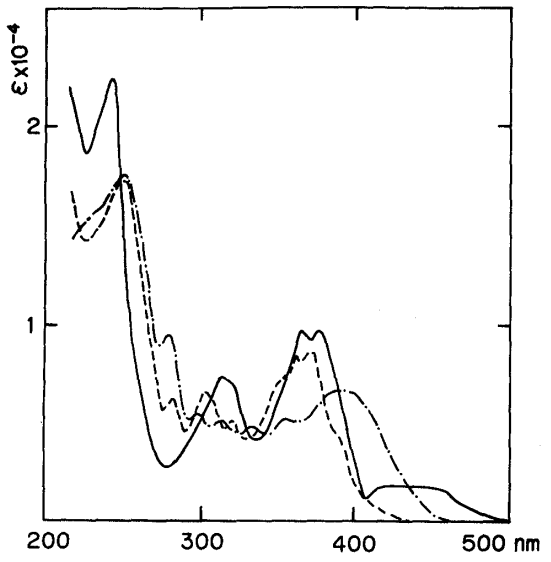


Fig. 2. UV Spectra of Compounds I and VI

——, I in EtOH+HCl; – – – –, VI in EtOH; – – – –, VI in EtOH+HCl.

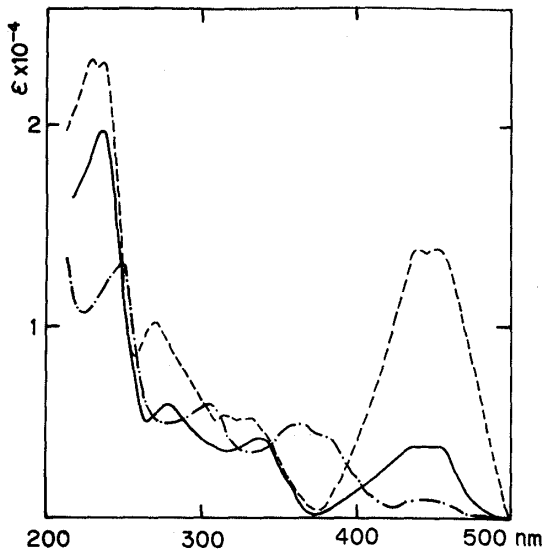


Fig. 3. UV Spectra of Compounds I and II

——, II in EtOH; – – – –, II in EtOH+HCl; – – – –, I in EtOH.

169.83 in the ^{13}C-NMR spectrum (Table I, 100 MHz). The UV absorption behavior was similar to that of picrasidine L, which suggested that the molecule possessed canthin-5,6-dione chromophore (Fig. 3). The assignment of structure II to picrasidine M was based on its spectral and chemical properties. The mass spectral fragmentation of II studied with the aid of field desorption (FD)-MS and electron ionization (EI)-MS were particularly informative. The FD-MS exhibited a molecular ion at m/z 490 and FD- and EI-MS showed significant ions at m/z 236 and 254. The prominent ion at m/z 236 represents the canthin-5,6-dione moiety of II. In the ^{1}H-NMR (Table II, 400 MHz) and ^{13}C-NMR spectra (Table I) of II in deuteriodimethylsulfoxide at 80 °C, the proton and carbon atoms of the canthin-5,6-dione moiety showed similar chemical shift values to those of I, suggesting that II is unsubstituted

except for the N(3)-position. On the other hand, subtraction of the canthin-5,6-dione formula $C_{14}H_7N_2O_2$ from the molecular formula gave a partial formula $C_{15}H_{15}N_2O_2$. The ^{1}H-NMR spectrum of the $C_{15}H_{15}N_2O_2$ moiety of II showed A_2B_2 pattern signals at δ 3.72 (2H, t, J= 7.1 Hz) and 4.77 (2H, t, J=7.1 Hz) attributed to a CH_2–CH_2 unit and three singlets at δ 3.97 (3H, s), 4.13 (3H, s), and 7.99 (1H, s) assigned to two methoxyl signals and a lone aromatic proton, respectively, as well as ABX-pattern signals at δ 7.05 (1H, d, J=7.9), 7.15 (1H, t, J= 7.9 Hz), and 7.76 (1H, d, J=7.9 Hz), and the lowest field singlet at δ 11.42 (1H, s, exchangeable on deuteration) assigned to the NH proton. The pattern and location of the signals of the partial structure $C_{15}H_{15}N_2O_2$ of II were essentially similar to those of crenatidine (1-ethyl-4,8-dimethoxy-β-carboline, IX).[8] Thus, picrasidine M is composed of canthin-5,6-dione and β-carboline subunits linked through the N(3) and C(1′′). Chemical evidence for the structure was obtained as follows. The cleavage of N(3)–C(1′′) bond of II with acetic anhydride gave 5-acetoxycanthin-6-one (VII) and 4,8-dimethoxy-1-vinyl-β-carboline (X). Methylation of VII with diazomethane by the Scheuer method[9] gave 5-methoxycanthin-6-one (VIII). All the spectral data of VIII and X were in good agreement with those of corresponding authentic samples. Thus, the structure of picrasidine M was proposed to be II.

This is the first report of the isolation of a dimeric alkaloid which consists of canthinone and β-carboline derivatives.

Picrasidine P was obtained as colorless needles and its molecular formula was determined to be $C_{13}H_{12}N_2O_2$ by high-resolution MS. Its UV spectrum [λ_{max}^{EtOH} nm (log ε) 240 (4.33), 266 (3.50), 284 (3.47), 332 (3.31), 348 (3.31)] was characteristics of β-carboline type alkaloid,[1-3] and its IR spectrum showed an amino absorption band at 3440 cm^{-1}. The ^{1}H-NMR spectrum (400 MHz) of picrasidine P in deuteriochloroform showed two methoxyl signals at δ 4.03 (3H, s) and 4.15 (3H, s) and two singlets at δ 8.07 (1H, s) and 8.61 (1H, s) assigned to lone aromatic protons at H-3 and H-1, respectively, as well as ABX-pattern signals at δ 7.91 (1H, dd, J=7.8, 1.0 Hz), 7.22 (1H, t, J=7.8 Hz), and 6.99 (1H, dd, J=7.8, 1.0 Hz) assigned to H-5 to H-7, and a lower field singlet at δ 8.49 (1H, s, exchangeable on deuteration) attributable to the NH proton of the indole moiety. On the basis of the above data, picrasidine P should be represented by formula 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) 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. MS 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 by Dragendorff's reagent or by UV illumination.

Extraction and Isolation——Dried root-bark (3.6 kg) of *Picrasma quassioides* collected at Chiba city, Chiba prefecture in August, 1983, was extracted with MeOH (60 l) at 35 °C for 48 h. The 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 (125 g) which was passed through a column of silica gel (1.5 kg) and eluted successively with $CHCl_3$–MeOH (4 : 1), $CHCl_3$–MeOH (1 : 1), and MeOH. The $CHCl_3$ fraction was repeatedly chromatographed on silica gel to afford picrasidine P (2 mg). The $CHCl_3$–MeOH (1 : 1) fraction was repeatedly chromatographed on silica gel to afford picrasidine L (35 mg) and picrasidine M (55 mg).

Picrasidine L (I)——Orange-red needles, mp 330 °C<. UV λ_{max}^{EtOH} nm (log ε): 242 (4.33), 250 (4.30), 287 (3.87), 345 (3.55), 444 (4.10), 462 (4.10). UV $\lambda_{max}^{EtOH+HCl}$ nm (log ε): 252 (4.30), 316 (3.83), 330 (sh, 3.75), 376 (3.97), 394 (4.00), 444 (3.18), 462 (3.19). UV $\lambda_{max}^{EtOH+NaOH}$ nm (log ε): 242 (4.33), 250 (4.30), 287 (3.87), 345 (3.55), 444 (4.10), 462 (4.10). IR ν_{max}^{KBr} cm^{-1}: 1695, 1655, 1540, 1445, 1330, 1215. ^{1}H-NMR and ^{13}C-NMR: Tables I and II, respectively. MS *m/z*:

250 (M^+, 69%), 222 (87), 193 (100), 179 (5), 168 (33), 152 (8), 140 (14). High-resolution MS: Calcd for $C_{15}H_{10}N_2O_2$, *m/z* 250.0715. Found *m/z* 250.0715.

Synthesis of I——A stirred solution of 5-hydroxycanthin-6-one (VI, 10 mg) in acetone (30 ml) and K_2CO_3 (2 g) was treated with dimethyl sulfate (0.2 ml). The reaction mixture was refluxed with stirring for 5 h. After the usual work-up, the crude product was purified by preparative TLC on silica gel to give I (3 mg), orange-red needles, mp 330 °<. MS *m/z*: 250 (M^+). IR ν_{max}^{KBr} cm^{-1}: 1695, 1655, 1540, 1445, 1330, 1215. *Anal.* Calcd for $C_{15}H_{10}N_2O_2$: C, 71.99; H, 4.03; N, 11.19. Found: C, 71.85; H, 4.05; N, 11.27.

Picrasidine M (II)——Orange needles (dimethylsulfoxide), mp 294—295 °C (dec.). UV λ_{max}^{EtOH} nm (log ε): 240 (4.30), 284 (3.65), 338 (3.42), 444 (3.52), 464 (3.52). UV $\lambda_{max}^{EtOH+HCl}$ nm (log ε): 250 (4.10), 316 (3.63), 374 (3.50), 396 (3.43), 444 (3.05), 464 (3.05). UV $\lambda_{max}^{EtOH+NaOH}$ nm (log ε): 240 (4.30), 284 (3.65), 338 (3.42), 442 (3.52), 464 (3.52). IR ν_{max}^{KBr} cm^{-1}: 3420, 1688, 1650, 1550, 1510, 1450, 1280, 1210, 1150, 1065. ^{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 (61%), 236 (21), 224 (28), 182 (100), 154 (19), 83 (55). *Anal.* Calcd for $C_{29}H_{22}N_4O_4$: C, 71.01; H, 4.52; N, 11.42. Found: C, 71.12; H, 4.50; N, 11.22.

Reaction of II with Acetic Anhydride——A solution of II (50 mg) in acetic anhydride (5 ml) was refluxed for 2 h. The reaction mixture of II 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 VII and X, which was separated by preparative TLC on silica gel to give VII (23 mg) and X (23 mg). Recrystallization of VII from acetone gave pale yellow plates, mp 209—210 °C. MS *m/z*: 278 (M^+). 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, 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). Methylation of VII (10 mg) with diazomethane in dioxane–moist ether was carried out at room temperature for 15 h by the Scheuer method.[9] The solvent was removed *in vacuo*, and recrystallization of the residue from methanol gave colorless prisms, mp 240 °C (lit.[3] mp 239—240 °C). MS *m/z*: 250 (M^+). IR ν_{max}^{KBr} cm^{-1}: 1680, 1640, 1440, 1290, 1250, 1050. This compound was identified by direct comparison (TLC, IR spectra, and mixed mp) with an authentic sample.[3]

Recrystallization of X from acetone gave pale yellow prisms, mp 158 °C (lit.[3] mp 158 °C). MS *m/z*: 254 (M^+). IR ν_{max}^{KBr} cm^{-1}: 3440, 1630, 1575, 1290, 1270, 1050. This compound was identified by direct comparison (TLC, IR spectra, and mixed mp) with an authentic sample.[3]

Picrasidine P (III)——Colorless needles (acetone), mp 198 °C. UV λ_{max}^{EtOH} nm (log ε): 240 (4.33), 266 (3.50), 284 (3.47), 332 (3.31), 348 (3.31). UV $\lambda_{max}^{EtOH+HCl}$ nm (log ε): 250 (4.06), 315 (3.48), 370 (3.20). UV $\lambda_{max}^{EtOH+NaOH}$ nm (log ε): 240 (4.33), 266 (3.50), 284 (3.47), 332 (3.31), 348 (3.31). IR ν_{max}^{KBr} cm^{-1}: 3440, 1630, 1650, 1570, 1445, 1322, 1250, 1114, 1029. ^{1}H-NMR: Table I. MS *m/z*: 228 (M^+, 100%), 213 (53), 185 (52), 183 (30), 170 (20), 155 (22), 142 (26). High-resolution MS, Calcd for $C_{13}H_{12}N_2O_2$: *m/z* 228.0899. Found: *m/z* 228.0885.

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References and Notes

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7) 5-Hydroxycanthin-6-one——UV λ_{max}^{EtOH} nm (log ε): 242 (sh, 4.21), 252 (4.25), 280 (3.97), 306 (sh, 3.80), 321 (3.68), 336 (3.67), 374 (3.67), 394 (3.70). UV $\lambda_{max}^{EtOH+HCl}$ nm (log ε): 248 (4.22), 280 (sh, 3.84), 310 (3.84), 324 (sh, 3.81), 340 (sh, 3.80), 358 (3.98), 375 (3.91), 390 (sh, 3.77). UV $\lambda_{max}^{EtOH+NaOH}$ nm (log ε): 242 (4.24), 258 (4.24), 284 (4.04), 321 (3.62), 336 (3.62), 420 (3.84).
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