Chem. Pharm. Bull.
34(5)2090—2093(1986)

Studies on the Alkaloids from *Picrasma quassioides* BENNET. VII.[1] Structures of β-Carboline Dimer Alkaloids, Picrasidines-H and -R

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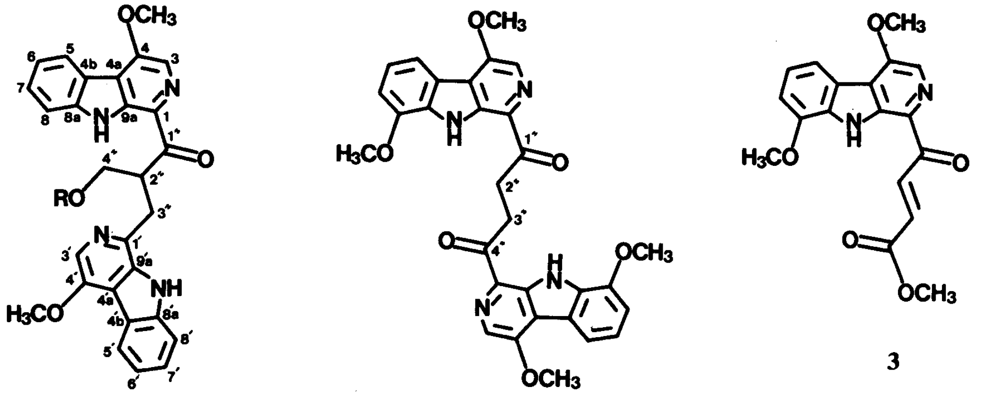
(Received October 7, 1985)

Two new β-carboline dimer alkaloids, picrasidines-H (**1**) and -R (**2**), have been isolated from the root bark of *Picrasma quassioides* BENNET (Simaroubaceae). The structures were determined on the basis of spectral analysis.

Keywords——*Picrasma quassioides*; Simaroubaceae; root bark; β-carboline dimer alkaloid; picrasidine-H; picrasidine-R

In the previous papers,[2] we reported the structural elucidation of β-carboline dimer alkaloids isolated from the methanol extract of the root bark and wood of *Picrasma quassioides* BENNET (Simaroubaceae, Japanese name "Nigaki"). We now report the structure of two new β-carboline dimer alkaloids, picrasidines-H (**1**) and -R (**2**) from the root bark of the plant.



1: R=H
1a: R=$COCH_3$

2

3

Chart 1

Picrasidine-H (**1**) was isolated as colorless needles, mp 218—220 °C (dec.) and $[\alpha]_D^{25}$ $-63.1°$ ($c=1.3$, dimethylsulfoxide (DMSO)). The electron-ionization mass spectrum (EI-MS) of **1** showed the molecular ion peak at m/z 480, and the molecular formula was determined to be $C_{28}H_{24}N_4O_4$ from the high-resolution MS. The infrared (IR) spectrum of **1** showed a conjugated carbonyl absorption at $1660\,cm^{-1}$. The presence of a carbonyl carbon was also indicated by the signal at δ 200.4 in the carbon-13 nuclear magnetic resonance (^{13}C-NMR) spectrum (Table I). The ultraviolet (UV) spectrum of **1** exhibited maxima at 228, 240, 286, 346, and 368 nm (characteristic of the β-carboline chromophore) and showed an extra absorption at 368 nm (log ε 3.46) due to a conjugated carbonyl grouping.[2,3] The proton nuclear magnetic resonance (^1H-NMR) spectrum of **1** showed eleven aliphatic proton signals at δ 3.82 (1H, dd, $J=18$, 4 Hz), 3.84 (2H, dd, $J=8$, 5 Hz), 4.02 (3H, s), 4.23 (1H, ddd, $J=9$, 8, 4 Hz), 4.26 (3H, s), 4.37 (1H, dd, $J=18$, 9 Hz), and one hydroxyl proton at δ 4.83 (1H, t, $J=5$ Hz, disappeared on addition of deuterium oxide). Extensive spin decoupling and pseudo-internuclear double resonance experiments on the ^{1}H-NMR spectrum of **1** indicated that **1** had the partial structure A (Fig. 1). The methylene protons at δ 3.84 were assigned to protons on a hydroxyl-bearing carbon because they coupled with the hydroxyl proton at δ 4.83 and shifted to δ 4.40 and 4.55 (each 1H) upon acetylation. In the long-range selective proton decoupling (LSPD) experiments on **1**, irradiation of either the H-3'' protons at δ 3.82 and 4.37 (triple irradiation experiment) or the H-4'' protons at δ 3.84 reduced the multiplet signals of

A

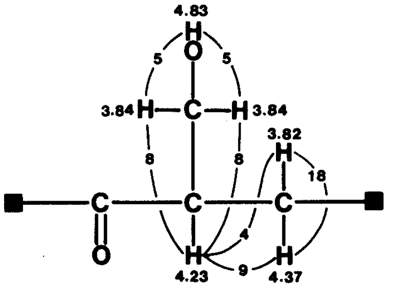


Fig. 1. Partial Structure A and ^{1}H-NMR Spectral Data

Chemical shifts (δ) and coupling constants (Hz).

TABLE I. ^{13}C-NMR Spectral Data[a)] for Compounds **1**, **1a**, and **2**

Carbon	**1**	$^1J_{CH}$ (Hz)	**1a**	**2** (Carbon)
1	135.5		134.8	130.8 (=1')
3	121.4	179	120.7	120.7 (=3')
4	153.9		153.4	154.0 (=4')
4a	117.4		117.1	118.4 (=4'a)
4b	120.2		119.8	120.6 (=4'b)
5	122.9	160	122.4	115.5 (=5')
6	120.3	160	119.8	121.0 (=6')
7	127.4	160	126.8	107.2 (=7')
8	112.6	160	112.1	145.5 (=8')
8a	140.8		139.1	128.2 (=8'a)
9a	130.9		130.0	130.3 (=9'a)
1'	139.9		137.4	
3'	119.7	179	119.7	
4'	149.7		149.4	
4'a	116.1		116.1	
4'b	119.0		118.6	
5'	123.1	160	118.7	
6'	119.1	160	122.6	
7'	126.7	160	126.2	
8'	111.5	160	111.5	
8'a	139.6		139.9	
9'a	135.6		135.1	
1''	200.4		198.6	200.8 (=1'')
2''	40.1		38.1	38.6 (=2'')
3''	38.3		36.6	
4''	65.6		66.1	
4-OCH_3	56.6		56.7	56.1 (=4'-OCH_3)
8-OCH_3				55.3 (=8'-OCH_3)
4'-OCH_3	55.8		55.7	

a) Compounds **1** and **1a** in DMSO-d_6 solution and compound **2** in $CDCl_3$ solution. *b)* The signal assignments were based on spectral analysis of ^{1}H–^{13}C shift correlation spectra, LSPD experiments and comparisons with the spectra of structurally related compounds.[1-4)]

TABLE II. ^{1}H-NMR Spectral Data[a] for Compounds **1**, **1a**, and **2**

Proton	**1**	**1a**	**2**	(Proton)	**3**
3	8.30 (s)	8.29 (s)	8.21 (s)	(=3′)	8.22 (s)
5	8.18 (dd, 8, 1)	8.18 (dd, 8, 1)	7.89 (d, 8)	(=5′)	7.87 (d, 8)
6	7.25 (td, 8, 1)	7.24 (td, 8, 1)	7.23 (t, 8)	(=6′)	7.26 (t, 8)
7	7.47 (td, 8, 1)	7.47 (td, 8, 1)	6.98 (d, 8)	(=7′)	7.02 (d, 8)
8	7.66 (dd, 8, 1)	7.64 (dd, 8, 1)			
9 (NH)	11.69 (s)[b]	11.62 (s)[b]	10.38 (s)[b]	(=9′)	10.42 (s)[b]
3′	7.90 (s)	7.93 (s)			
5′	8.18 (dd, 8, 1)	8.18 (dd, 8, 1)			
6′	7.23 (td, 8, 1)	7.23 (td, 8, 1)			
7′	7.52 (td, 8, 1)	7.52 (td, 8, 1)			
8′	7.65 (dd, 8, 1)	7.68 (dd, 8, 1)			
9′ (NH)	11.73 (s)[b]	11.68 (s)[b]			
2″	4.23 (ddd, 9, 8, 4)	4.41 (m, 9, 9, 6, 5, 4)	3.91 (s)	(=3″)	7.04 (d, 16)
3″ H×1	3.82 (dd, 18, 4)	3.77 (dd, 17, 4)			
H×1	4.37 (dd, 18, 9)	4.34 (dd, 17, 9)			
4″ H×2	3.84 (dd, 8, 5)	4.55 (dd, 9, 5) 4.40 (dd, 9, 6)			
4-OCH_3	4.26 (s)	4.26 (s)	4.26 (s)	(4′-OCH_3)	4.27 (s)
8-OCH_3			3.96 (s)	(8′-OCH_3)	4.04 (s)
4′-OCH_3	4.02 (s)	4.04 (s)			
4″-OH	4.83 (t, 5)[b]				
4″-$OCOCH_3$		1.86 (s)			
4″-$COOCH_3$					3.88 (s)

a) Compounds **1** and **1a** in DMSO-d_6 solution, **2** and **3** in $CDCl_3$ solution. *b*) Disappeared on addition of D_2O.

the carbonyl carbon at δ200.4 to a triplet, revealing three-bond couplings between the carbonyl carbon and the H-3″ and H-4″ protons. The ^{1}H-NMR, ^{13}C-NMR, and MS spectra of **1** indicated the presence of two β-carboline subunits. The locations of two methoxyl groups and the partial structure A in the structure **1** were obtained as follows. The chemical shifts and splitting patterns of a pair of four adjacent aromatic protons, the two lone aromatic protons, and the two lowest field singlets were similar. In the proton coupled ^{13}C-NMR spectra of **1**, the values of the one-bond ^{13}C–^{1}H coupling constant ($^1J_{CH}$) of C-5—C-8 and C-5′—C-8′ were observed to be in the range of 160 Hz. The $^1J_{C3\text{-}H}$ and $^1J_{C3'\text{-}H}$ values of 179 Hz were larger than those of the other carbons because of the effect of the neighboring N atom. In order to determine the location of two methoxyl groups, nuclear Overhauser effect (NOE) experiments were carried out; irradiation of the methoxyl signals at δ4.26 and 4.02 produced 22% enhancement of H-3 and H-3′, respectively. Therefore, the two methoxyl groups (δ4.26 and 4.02) were unambiguously placed at C-4 and C-4′, respectively, and the two β-carboline subunits are linked through C (1) and C(1′).

From these results, the structure of picrasidine-H, except for the configuration at C-2″, was concluded to be represented by formula **1**.

Picrasidine-R (**2**) was isolated as colorless needles. The EI-MS of **2** showed the molecular ion peak at m/z 538, and the molecular formula was determined to be $C_{30}H_{24}N_4O_6$ from the high-resolution MS. The IR spectrum of **2** showed a conjugated carbonyl group at 1660 cm^{-1}. The presence of a carbonyl carbon was also indicated by the signal at δ200.8 in the ^{13}C-NMR spectrum of **2** (Table I). The UV characteristic was similar to that of **1**, which suggested that **2** has a conjugated carbonyl function at the C-1 position on the β-carboline skeleton. The ^{13}C-NMR spectrum of **2** indicated the presence of fifteen carbons; three aliphatic carbons (CH_3– × 2, –CH_2– × 1), eleven aromatic carbons (=CH– × 4, =C< × 7), and one carbonyl carbon (Table I). In the ^{1}H-NMR spectrum of **2**, some signals are readily assigned to two methoxyl protons (δ 3.96 and 4.26, each 3H, s), methylene protons (δ 3.91, 2H, s) three aromatic protons [ABX pattern, δ 6.98 (1H, d, J=8 Hz), 7.23 (1H, t, J=8 Hz), and 7.89 (1H, d, J=8 Hz)], a lone aromatic proton (δ 8.21, 1H, s), and the NH proton (δ 10.38, 1H, s), disappeared on addition of deuterium oxide). The pattern and location of signals of the β-carboline unit were essentially similar to those of picrasidine-E (**3**). Therefore the two methoxyl groups were unambiguously placed at C-4 and C-8. Thus, picrasidine-R is composed of two β-carboline subunits linked through C (1) and C (1′) in a four carbon-unit to form a symmetric molecule. Besides the molecular ion at m/z 538, the MS shows intense peaks at m/z 283 (base ion peak), 253, 228, and 198.

From these results, the structure of picrasidine-R was concluded to be represented by formula **2**.

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 a JEOL GX-400 (^{1}H 400 MHz and ^{13}C 100 MHz) spectrometer. Chemical shifts are given on the δ scale with tetramethylsilane as 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, sh = shoulder. MS were measured with a JEOL JMS DX-300 mass spectrometer. Column chromatography was carried out on silica gel (BW-820 MH, Fuji Devison). Optical rotation was measured with a JASCO DIP-4 digital polarimeter. Thin layer chromatography (TLC) was performed on Silica gel 60 GF$_{254}$ (Merck), and the spots were detected by Dragendorff's reagent or by UV illumination.

Isolation of Picrasidine-H (1)——The air-dried root bark (3.6 kg) of *Picrasma quassioides* BENNET collected in August, 1983 at Chiba city, Chiba prefecture, was extracted with methanol (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 chromatographed on silica gel using CHCl$_3$ and MeOH as eluents to give picrasidine-H (29 mg).

Isolation of Picrasidine-R (2)——The air-dried root bark (5.5 kg) of *P. quassioides* collected in August, 1984 at Funabashi city, Chiba prefecture, was extracted with MeOH (72 l) at 40 °C for 48 h. The MeOH extract was treated in the same way as described for the isolation of picrasidine-H to give picrasidine-R (1.5 mg).

Picrasidine-H (1)——Colorless needles (MeOH), mp 218—220 °C (dec.), $[\alpha]^{25}_{D}$ $-63.1°$ (c=1.3, dimethyl sulfoxide). UV λ^{EtOH}_{max} nm (log ε): 228 (4.29), 240 (4.31), 276 (sh, 3.99), 286 (4.06), 334 (sh, 3.33), 346 (3.61), 368 (3.46). IR ν^{KBr}_{max} cm^{-1}: 3420, 3200, 1660, 1620, 1590, 1487, 1450, 1300, 1272, 1230, 1150, 1115. ^{13}C-NMR and ^{1}H-NMR: Table I and Table II, respectively. MS m/z (%): 480 (M^{+}, 52), 462 (65), 269 (83), 255 (100), 197 (52), 169 (43). High-resolution MS: Calcd for $C_{28}H_{24}N_4O_4$, m/z 480.1798. Found: m/z 480.1862.

Acetylation of Picrasidine-H (1)——Picrasidine-H (**1**, 10 mg) was acetylated with acetic anhydride (0.2 ml) in pyridine (0.5 ml) at room temperature for 10 h. The product (10 mg) was crystallized from MeOH to give monoacetylpicrasidine-H (**1a**) as colorless needles, mp 158—159 °C. MS m/z (%): 552 (11), 463 (54), 462 (73), 446 (21), 444 (15), 431 (11), 297 (69), 264 (87), 251 (82), 249 (100), 237 (73), 225 (29), 212 (25), 198 (93), 169 (18), 155 (60). ^{13}C-NMR and ^{1}H-NMR: Table I and II, respectively. IR ν^{KBr}_{max} cm^{-1}: 1740, 1660, 1610, 1450, 1370, 1250, 1140.

Picrasidine-R (2)——Colorless needles (MeOH), mp 297—300 °C (dec.). UV λ^{EtOH}_{max} nm (log ε): 234 (4.22), 254 (3.97), 276 (4.11), 310 (sh, 3.27), 372 (3.68). IR ν^{KBr}_{max} cm^{-1}: 3420, 1660, 1610, 1470, 1380, 1260, 1150, 1060. ^{13}C-NMR and ^{1}H-NMR: Table I and II, respectively. MS m/z (%): 538 (M^{+}, 17), 508 (29), 283 (100), 253 (78), 228 (43), 198 (33). High-resolution MS: Calcd for $C_{29}H_{24}N_4O_5$ (M^{+}$-$OCH$_2$), m/z 508.1747, Found: m/z 508.1758; Calcd for $C_{16}H_{15}N_2O_3$, m/z 283.1183, Found: m/z 283.1106; Calcd for $C_{15}H_{13}N_2O_2$, m/z 253.0977, Found: m/z 253.0943; Calcd for $C_{13}H_{12}N_2O_2$, m/z 228.0902, Found: m/z 228.0902; Calcd for $C_{12}H_{10}N_2O$, m/z 198.0821, Found: m/z 198.0793.

Acknowledgement We are grateful to Mr. Keiji Ikeda, Nippon Flour Mills Co., Ltd. for high-resolution MS measurements. We thank Miss Yohko Sakamoto for measuring NMR spectra and Mr. Mitsuo Takayama for MS.

References and Notes

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