New Alkaloids, Picrasidines W, X and Y, from *Picrasma quassioides* and X-Ray Crystallographic Analysis of Picrasidine Q

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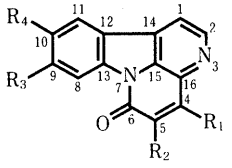
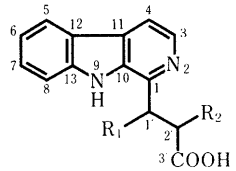
Three new alkaloids, picrasidines W (1), X (2) and Y (3), were isolated from the wood of *Picrasma quassioides* Bennet (Simaroubaceae). Their structures were determined by spectral and chemical evidence. Previously isolated picrasidine Q (4) was unambiguously determined by X-ray crystallographic analysis.

Keywords *Picrasma quassioides*; Simaroubaceae; picrasidine W; picrasidine X; picrasidine Y; picrasidine Q

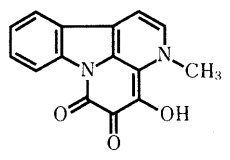
The wood of *Picrasma quassioides* Bennet (Simaroubaceae; Japanese name: nigaki, and Chinese name; Kumu) is a well-known crude drug used as a bitter stomachic in Japan and China. In previous papers, we reported the structures of many indole alkaloids of β-carboline, canthin-6-one and β-carboline dimer types.[1–11] Studied of the canthin-6-one alkaloids of various natural origins were recently reviewed by Ohmoto and Koike.[12] Previously, we reported that canthin-6-one had an antifungal effect on mycotoxin-producing fungi.[13] β-Carboline and canthin-6-one alkaloids has strong inhibitory effects on cyclic AMP phosphodiesterase.[14,15] In addition, they increased of the blood flow rate in the intestine and stomach of rabbits[16] and exhibited antiviral activity on the Herpes simplex virus.[17] Continuing the search for new biologically active natural products of this plant, we have isolated three new alkaloids, named picrasidines W (**1**), X (**2**) and Y (**3**). Additionally, we previously reported the structure of 4-hydroxy-5-methoxycanthin-6-one (picrasidine Q, **4**)[6] as a new natural product on the basis of spectral and chemical evidence. However, Verpoorte co-workers recently isolated the same compound from *P. quassioides* collected in China and reassigned our picrasidine Q (**4**) as 4-hydroxy-3-methylcanthin-5,6-dione (**5**).[18] Therefore, we examined the X-ray crystallographic analysis of **4**, and the results indicate that our picrasidine Q was correctly determined to be 4-hydroxy-5-methoxycanthin-6-one, where as the compound isolated by Verpoorte's group should be reassigned as 5-hydroxy-4-methoxycanthin-6-one (**6**).[3,19]



	R_1	R_2	R_3	R_4
1	OH	OMe	H	OH
4	OH	OMe	H	H
6	OMe	OH	H	H
7	OMe	OMe	H	H
8	OH	OMe	H	OAc
9	OMe	OMe	H	OMe
10	H	H	OMe	H



	R_1	R_2
2	H	OH
3	OH	OH
13	H	H
14	H	OAc



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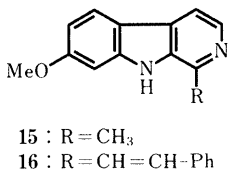

15 : R = CH_3
16 : R = CH=CH-Ph
17 : R = CHO

Chart 1

Results and Discussion

The wood of *P. quassioides* collected in Japan was extracted with methanol and then successively partitioned with chloroform, ethyl acetate, *n*-butanol and water. The *n*-butanol extract was chromatographed on Diaion HP-20, and Dragendorff's reagent positive fractions were further separated by ODS medium pressure liquid chromatography (MPLC) to give picrasidines W (**1**), X (**2**) and Y (**3**) as new compounds.

The first compound, picrasidine W (**1**), was obtained as pale yellow needles. The molecular formula, $C_{15}H_{10}N_2O_4$, was determined by high-resolution mass measurement (HRMS). The infrared (IR) spectrum of **1** indicated bands at 3306 (OH) and 1651 (lactam) cm^{-1}. The ultraviolet (UV) absorption behavior was similar to those of canthin-6-one alkaloids, which suggested that **1** has a canthin-6-one chromophore.[1,3,6,20] The proton nuclear magnetic resonance (^{1}H-NMR) spectrum of **1** showed a methoxyl signal at δ 3.89 (3H, s), a pair of *ortho* coupled signals at δ 8.21 (1H, d, J=5.2 Hz, H-1) and 8.78 (1H, d, J=5.2 Hz, H-2), and ABX type signals at δ 7.17 (1H, dd, J=8.8 and 2.5 Hz), 7.65 (1H, d, J=2.5 Hz) and 8.29 (1H, d, J=8.8 Hz) corresponding to the three aromatic protons of the mono-substituted indolic part. From the HRMS, **1** contains one more oxygen atom more than picrasidine Q (**4**), and the presence of an extra hydroxyl group was also suggested for **1**. The ^{1}H- and carbon-13 (^{13}C)-NMR spectra of **1** were very similar to those of **4**, except that the indolic part of **1** was replaced by an oxygen function. Acetylation of **1** with acetic anhydride–pyridine gave the monoacetate (**8**) with the ABX protons resonating downfield *ca.* 0.2—0.5 ppm with repect to those of **1**. Methylation of **1** with excess methyl iodide in acetone with K_2CO_3 afforded dimethyl ether (**9**) as shown in its ^{1}H-NMR spectrum in $CDCl_3$, where two methoxyl resonances at δ 4.08 and 4.46 (each 3H, s) were observed. These results suggested a hydroxyl group and a methoxyl group located at the C-4 and C-5 positions, respecively. The splitting pattern in the ^{1}H-NMR spectrum for the three aromatic protons of the indolic part of **1** clearly revealed that the remaining hydroxyl group is located at either the C-9 or C-10 position. Measurement of

TABLE I. ^{1}H-NMR Spectral Data for Compounds **1**, **4**, **6** and **8** in DMSO-d_6

Position	**1**[a]	**8**[b]	**4**[b]	**6**[b]	Verpoorte's **4**[c]
H-1	8.21 d (5.2)	8.27 d (5.0)	8.29 d (5.0)	7.95 d (5.0)	8.18 d (5)
H-2	8.78 d (5.2)	8.83 d (5.0)	8.83 d (5.0)	8.71 d (5.0)	8.78 d (5)
H-8	8.29 d (8.8)	8.51 d (8.8)	8.49 dd (7.7, 1.2)	8.38 d (7.7)	8.50 d (8.5)
H-9	7.17 dd (8.8, 2.5)	7.51 dd (8.8, 2.4)	7.75 td (7.7, 1.2)	7.67 t (7.7)	7.76 t (15)
H-10			7.51 td (7.7, 1.2)	7.49 t (7.7)	7.58 t (15)
H-11	7.65 d (2.5)	8.17 d (2.4)	8.35 dd (7.7, 1.2)	8.14 d (7.7)	8.38 d (8.5)
OMe-4				4.28 s	
OMe-5	3.89 s	3.88 s	3.89 s		4.21 s
OAc-10		2.35 s			

a) Measured at 500 MHz. *b*) Measured at 400 MHz. *c*) Ref. 18.

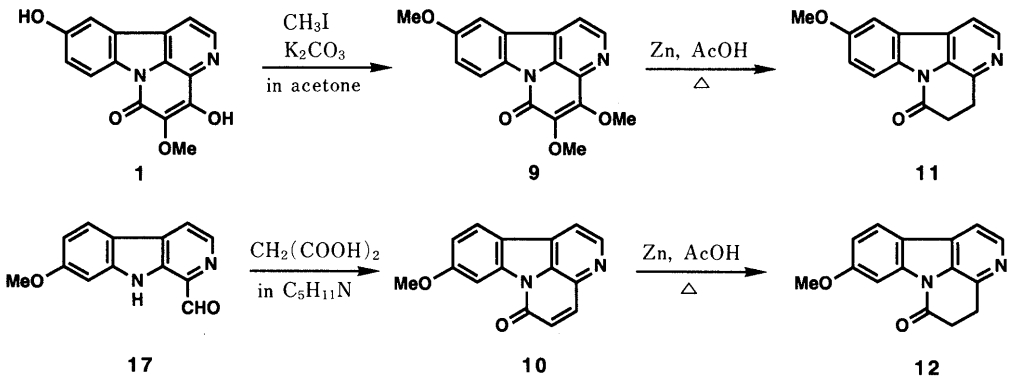

Fig. 1

the ^{1}H–^{1}H shift correlation (COSY), proton-detected heteronuclear chemical shift correlation (HMQC) and long-range proton-detected heteronuclear chemical shift correlation (HMBC) spectra of **1**, and subsequent comparison with the reported ^{1}H- and ^{13}C-NMR assignments for canthin-6-one alkaloids[12] led us to favor the C-10 position. In order to determine the location of the hydroxyl group of the indolic part, the hydrogenation of **9** with zinc and acetic acid gave a 4,5-dihydro derivative (**11**) (Fig. 1). Also, we synthesized 9-methoxycanthin-6-one (**10**) from 7-methoxy-1-methyl-β-carboline (harmine, **15**), and the hydrogenation of **10** afforded 9-methoxy-4,5-dihydrocanthin-6-one (**12**). The data of **11** were inconsistent with those of **12**. From the above results, the remaining hydroxyl group was determined to be located at C-10, and the structure of picrasidine W (**1**) was determined to be 4,10-dihydroxy-5-methoxycanthin-6-one.

The second and third compounds, picrasidine X (**2**) and picrasidine Y (**3**) were obtained as amorphous solids. Picrasidines X (**2**) and Y (**3**) were determined to have the molecular formulae $C_{14}H_{12}N_2O_3$ and $C_{14}H_{12}N_2O_4$, respectively, by HRMS and a combination of fast atom bombardment mass spectrometry (FABMS) and ^{13}C-NMR spectra. The UV spectra of **2** and **3** were characteristic of β-carboline chromophores.[1,3,4] The IR spectra of **2** and **3** showed absorption bands at 3355 (br, OH) and 1630 (C=O) cm^{-1} for **2** and 3421 (br, OH) and 1634 (C=O) cm^{-1} for **3**. The presence of a carbonyl carbon in the structure was indicated by the signal at δ 175.07 for **3** and at δ 173.79 for **4** in the ^{13}C-NMR spectra. The ^{1}H- and ^{13}C-NMR spectra of **2** and **3** were similar to those of β-carboline-1-propionic acid (**13**).[3] The major differences between **2** and **3** were in the spectral features arising from the C-1 functional group. In picrasidine X (**2**), a methylene signal [δ_H 3.46 (1H, dd, J=14.7 and 7.1 Hz) and 3.50 (1H, dd, J=14.7 and 5.9 Hz) and δ_C 37.44], a methine signal [δ_H 4.65 (1H, dd, J=7.1 and 5.9 Hz) and δ_C 69.42] and a carbonyl carbon signal (δ_C 175.07) were observed. The methine proton at δ 4.65 was determined to be the proton in the hydroxy-bearing carbon because the signal shifted to δ 5.70 upon acetylation. In the HMBC spectrum of **2**, the methylene signals showed $^3J_{CH}$ cross-peaks with a quaternary carbon at C-10 (δ 134.84) and a carbonyl carbon at C-3′ (δ 175.07). These results suggested that picrasidine

TABLE II. ^{13}C-NMR Spectral Data for Compounds **1**, **4**, and **6** in DMSO-d_6[a]

Position	**1**[b]	**4**[c]	**6**[c]	Verpoorte's **4**[d]
C-1	116.29	116.61	113.70	114.79
C-2	144.18	144.69	144.11	145.22
C-4	151.71	152.65	142.68	143.59
C-5	135.61	135.62	139.60	140.52
C-6	157.01	157.65	156.27	157.32
C-8	116.39	115.61	115.22	116.14
C-9	118.39	130.75	129.62	130.71
C-10	154.97	125.03	124.65	125.65
C-11	108.76	123.50	122.39	123.59
C-12	125.48	124.34	124.20	125.16
C-13	131.91	138.68	137.38	138.42
C-14	129.05	129.11	127.96	128.97
C-15	128.28	128.25	124.82	125.77
C-16	131.88	132.17	133.46	134.39
OMe-4			60.51	
OMe-5	59.68	59.92		60.95

a) Signal assignments were carried out by HMQC and HMBC spectra. *b*) Measured at 125 MHz. *c*) Measured at 100 MHz. *d*) Ref. 18.

TABLE III. ^{1}H-NMR Spectral Data for Compounds **2**, **3**, and **13** in DMSO-d_6[a]

Position	2	3	13
H-3	8.28 d (5.5)	8.27 d (5.1)	8.25 d (5.1)
H-4	7.99 d (5.5)	8.03 d (5.1)	7.92 d (5.1)
H-5	8.21 dd (7.7, 1.1)	8.21 d (7.9)	8.15 dd (7.8, 1.2)
H-6	7.24 ddd (7.7, 7.0, 1.0)	7.24 dd (7.9, 7.1)	7.23 ddd (7.8, 7.0, 1.1)
H-7	7.55 ddd (8.1, 7.0, 1.1)	7.55 dd (8.1, 7.1)	7.54 ddd (8.2, 7.0, 1.2)
H-8	7.62 dd (8.1, 1.0)	7.67 d (8.1)	7.61 dd (8.2, 1.1)
NH	11.57 br s	11.10 br s	11.49 br s
H-1′	3.46 dd (14.7, 7.1)	5.40 d (3.0)	3.38 t (7.3)
	3.50 dd (14.7, 5.9)		
H-2′	4.65 dd (7.1, 5.9)	4.48 d (3.0)	2.89 t (7.3)

a) Measured at 400 MHz.

TABLE IV. ^{13}C-NMR Spectral Data for Compounds **2**, **3**, and **13** in DMSO-d_6[a]

Position	2	3	13
C-1	142.26	145.11	143.87
C-3	136.61	136.31	137.12
C-4	111.94	112.24	112.47
C-5	121.65	121.54	121.30
C-6	119.27	119.24	118.96
C-7	128.07	128.21	127.56
C-8	113.20	113.78	111.70
C-10	134.84	133.83	133.87
C-11	127.74	128.69	127.03
C-12	120.85	120.31	120.88
C-13	140.67	140.75	140.29
C-1′	37.44	74.24	27.94
C-2′	69.42	75.27	31.31
C-3′	175.07	173.79	173.70

a) Signal assignments were carried out by HMQC and HMBC spectra and measured at 100 MHz.

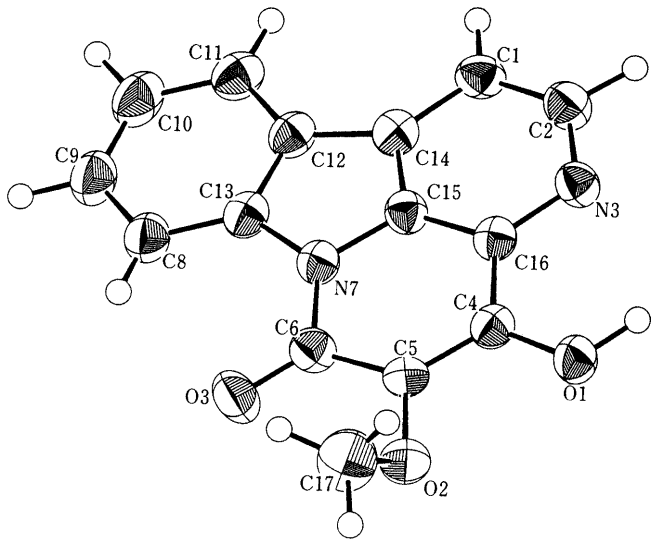

Fig. 2. ORTEP Drawing of Picrasidine Q (**4**)

X (**2**) has a $-CH_2CH(OH)COOH$ group. In picrasidine Y (**3**), the molecular weight of **3** was 16 mass units higher than that of **2**, suggesting the presence of one more hydroxyl group than in **2**. The ^{1}H- and ^{13}C-NMR spectra of **3** showed two methine signals [δ_H 4.48 (1H, d, J=3.0 Hz) and 5.40 (1H, d, J=3.0 Hz) and δ_C 74.24 and 75.27] and a carbonyl carbon signal at δ 173.79, was determined to be a

TABLE V. Final Positional Parameters ($\times 10^4$) and Equivalent Isotropic Thermal Parameters with Estimated Standard Deviations in Parentheses for Picrasidine Q (**4**)

Atom	x	y	z	B_{eq}
O(1)	5001.4 (7)	3531 (1)	−3994 (3)	3.83 (6)
O(2)	4550.8 (8)	1904 (1)	−1748 (3)	4.27 (7)
O(3)	3380.7 (8)	1922 (1)	1742 (3)	4.44 (7)
N(3)	4238.7 (8)	5247 (1)	−2768 (3)	3.21 (7)
N(7)	3286.5 (8)	3514 (1)	1382 (3)	3.08 (7)
C(1)	3238 (1)	5945 (2)	322 (5)	3.5 (1)
C(2)	3825 (1)	5981 (2)	−2061 (5)	3.6 (1)
C(4)	4445 (1)	3544 (1)	−2245 (4)	2.96 (8)
C(5)	4224 (1)	2733 (1)	−1061 (4)	3.21 (9)
C(6)	3608 (1)	2656 (1)	783 (4)	3.4 (1)
C(8)	2259 (1)	3137 (2)	4570 (5)	3.8 (1)
C(9)	1670 (1)	3544 (2)	5867 (5)	4.4 (1)
C(10)	1507 (1)	4491 (2)	5541 (5)	4.6 (1)
C(11)	1925 (1)	5080 (2)	3933 (5)	4.0 (1)
C(12)	2517 (1)	4692 (1)	2640 (4)	3.18 (8)
C(13)	2670 (1)	3728 (1)	2964 (4)	3.18 (9)
C(14)	3062 (1)	5086 (1)	836 (4)	3.07 (9)
C(15)	3504 (1)	4335 (1)	142 (4)	2.90 (8)
C(16)	4073 (1)	4405 (1)	−1653 (4)	2.85 (8)
C(17)	4967 (2)	1451 (2)	718 (6)	5.7 (1)
H(0)	5120 (1)	4150 (2)	−4870 (5)	7.7 (7)
H(1)	2970 (1)	6490 (1)	130 (4)	3.9 (4)
H(2)	3970 (1)	6610 (1)	−3070 (4)	4.0 (5)
H(8)	2370 (1)	2490 (1)	4740 (4)	4.1 (5)
H(9)	1340 (1)	3110 (1)	7000 (4)	4.9 (5)
H(10)	1100 (1)	4780 (1)	6620 (4)	5.6 (6)
H(11)	1810 (1)	5760 (1)	3660 (4)	4.9 (5)
H(17)	5410 (2)	1830 (3)	1070 (9)	18 (2)
H(17A)	5150 (1)	880 (2)	−10 (9)	8.8 (8)
H(17B)	4700 (2)	1430 (2)	2610 (7)	12 (1)

$-CH(OH)CH(OH)COOH$ group. On the basis of the above data, the structure of picrasidine X and Y were proposed to be the structures **2** and **3**, except for the configuration at the C-1′ and/or C-2′ positions, respectively.

Picrasidine Q (**4**) is a crystalline compound isolated by us from *P. quassioides*.[6] In order to establish a definitive structure, X-ray crystallographic analysis of a single crystal was carried out. An ORTEP drawing of the X-ray model of picrasidine Q (**4**) is presented in Fig. 2. Our X-ray analysis showed that picrasidine Q has the structure (**4**). On the other hand, compound **4** has been isolated from *P. quassioides* collected in China, and elucidated as a new compound by Verpoote's group.[18] However, their ^{1}H–^{1}H COSY, ^{1}H–^{13}C HETCOR and 1D difference decoupling experiments were misassigned as 4-hydroxy-5-methoxy-canthin-6-one (**4**). The reported ^{1}H- and ^{13}C-NMR data are in good agreement with those of 5-hydroxy-4-methoxy-canthin-6-one (**6**).[20] These results strongly suggest that Verpoorte's **4** is in fact **6**, which was already isolated as a main compound, nigakinone[3,19] as was 4,5-dimethoxy-canthin-6-one (**7**)[21] from *P. quassioides*.

Experimental

General Experimental Procedures Melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. IR spectra were recorded as KBr pellets on a JASCO 7300 FTIR spectrometer. UV spectra were recorded on a Hitachi 340 spectrometer in MeOH. Optical rotations were determined on a JASCO DIP-4 digital polarimeter. EIMS and FABMS were measured on JEOL D-300 and JEOL DX-303 mass spectrometers, respectively. ^{1}H-, ^{13}C- and 2D- NMR spectra were recorded with JEOL A-500 (500 MHz for ^{1}H-NMR and 125 MHz for ^{13}C-NMR)

or JEOL EX-400 (400 MHz for ^{1}H-NMR and 100 MHz for ^{13}C-NMR) spectrometers. Chemical shifts are expressed in δ (ppm) downfield from tetramethylsilane as an internal standard, and coupling constants in hertz (Hz). Silica gel (BW-820 MH, Fuji Davison) and Diaion HP-20 (Mitsubishi Kasei) were used for column chromatography. MPLC was carried out on an ODS [Chromatorex C_{18}, Fuji Davison, 24 mm i.d. × 300 mm, detector UV 254 nm, solvent system MeOH–H_2O (1 : 1)].

Plant Material The wood sample of *Picrasma quassioides* was collected at Funabashi, Chiba, Japan, in September 1985. It was identified by Dr. N. Sahashi (Department of Biology, Toho University, Japan). A voucher specimen is deposited at Department of Pharmacognosy, School of Pharmaceutical Sciences, Toho University.

Extraction and Isolation of Alkaloids Dried wood (50 kg) of the plant was powdered and extracted with MeOH (100 l) at 60 °C for 24 h. 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 successively extracted with $CHCl_3$ (15 l), EtOAc (15 l) and then *n*-BuOH (15 l). The *n*-BuOH extract (175 g) was applied to a column of Diaion HP-20 (3 kg), using H_2O–MeOH as the eluent, with an increasing MeOH content: H_2O–MeOH (9 : 1, 7 : 3, 1 : 1, 3 : 7) and then MeOH. Dragendorff's reagent positive fractions (32 g) were combined and chromatographed on a silica gel (1 kg) column. Elution was performed with 1, 2, 5, 10, 20, 40, 50% MeOH in $CHCl_3$, and then MeOH. The 20—50% MeOH in $CHCl_3$ fractions was subjected to MPLC using reversed phase C_{18} to give picrasidines W (**1**, 35 mg), X (**2**, 15 mg) and Y (**3**, 5 mg).

Picrasidine W (1) Yellow needles (MeOH), mp 225—227 °C. IR ν_{max} cm^{-1}: 3306, 1651, 1636, 1323, 1291, 1247, 1217, 1136, 1100, 1070, 1013, 955. UV λ_{max}^{MeOH} nm (log ε): 230 (4.53), 242 (4.50), 254 (sh, 4.44), 282 (4.40), 304 (sh, 4.13), 355 (4.21), 370 (4.21). UV $\lambda_{max}^{MeOH+HCl}$ nm (log ε): 230 (4.54), 242 (4.48), 254 (sh, 4.39), 282 (4.39), 304 (sh, 4.09), 3.30 (sh, 3.93), 355 (4.17), 370 (4.21), 395 (sh, 3.75). UV $\lambda_{max}^{MeOH+NaOH}$ nm (log ε): 238 (4.57), 260 (4.57), 282 (sh, 4.38), 294 (4.38), 306 (4.27), 346 (sh, 4.18), 362 (4.27), 400 (sh, 3.45). EIMS *m/z* (rel. int.): 282 (M^+, 97), 267 (64), 253 (42), 236 (3), 211 (23), 183 (100), 156 (13), 127 (10). HMBC correlations (500 MHz, DMSO-d_6): H-1→C-2, C-12, C-15; H-2→C-1, C-12, C-14, C-16; H-8→C-10, C-12, C-13; H-9→C-10, C-11, C-13; H-11→C-9, C-10, C-13, C-14; OMe-5→C-5. HRMS: Calcd for $C_{15}H_{10}N_2O_4$, *m/z* 282.0641, Found *m/z* 282.0643.

Acetylation of 1 Picrasidine W (**1**, 5 mg) was acetylated with Ac_2O (0.2 ml) and pyridine (0.2 ml) for 15 h at room temperature. After MeOH (5 ml) was added, the reaction mixture was evaporated under reduced pressure to give monoacetate (**8**, 5 mg). Compound **8**: Pale yellow needles, mp 258—260 °C. IR ν_{max} cm^{-1}: 1752, 1670, 1650, 1619, 1598, 1226, 1174, 1141, 1073, 1020. EIMS *m/z* (rel. int.): 324 (M^+, 100), 309 (50), 295 (38), 282 (34), 267 (69), 253 (58), 255 (16), 211 (20), 183 (68).

Methylation of 1 Picrasidine W (**1**, 5 mg) was suspended in acetone and methylated with excess methyl iodide and K_2CO_3 (20 mg). The reaction mixture was refluxed with stirring for 2 h, after the usual work-up, to give dimethyl ether (**9**, 5 mg). Compound **9**: Pale yellow needles, mp 258—260 °C. EIMS *m/z* (rel. int.): 340 (M^+, 1), 310 (100), 295 (89), 267 (50), 251 (21), 238 (13), 224 (14), 196 (56). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 3.98 (3H, s, OMe-5), 4.08 (3H, s, OMe-10), 4.46 (3H, s, OMe-4), 7.26 (1H, dd, *J* = 9.2, 2.2 Hz, H-9), 7.55 (1H, d, *J* = 2.2 Hz, H-11), 7.91 (1H, d, *J* = 5.2 Hz, H-1), 8.54 (1H, d, *J* = 9.2 Hz, H-8), 8.83 (1H, d, *J* = 5.2 Hz, H-2).

Hydrogenation of 9 Compound **9** (3 mg) in acetic acid (1 ml) was boiled with granulated zinc for 15 min, then solution was diluted with water, neutralized by the addition of 5% Na_2CO_3 solution, and extracted with $CHCl_3$. Evaporation of the $CHCl_3$ solution gave 4,5-dihydro-10-methoxycanthin-6-one (**11**, 2 mg). Compound **11**: Amorphous powder. EIMS *m/z* (rel. int): 252 (M^+, 100), 238 (58), 223 (74), 209 (62), 195 (18). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 3.21 (2H, t, *J* = 7.7 Hz, H-5), 3.49 (1H, t, *J* = 7.7 Hz, H-4), 3.95 (3H, s, OMe-10), 7.26 (1H, dd, *J* = 9.2, 2.5 Hz, H-9), 7.49 (1H, d, *J* = 2.5 Hz, H-11), 7.69 (1H, d, *J* = 5.1 Hz, H-1), 8.43 (1H, d, *J* = 9.2 Hz, H-8), 8.50 (1H, d, *J* = 5.1 Hz, H-2).

Benzylidene Harmine (16) Harmine (**15**, 500 mg, purchased from Sigma) was refluxed with distilled benzaldehyde (3 ml) for 4 h. After cooling, the reaction mixture yield a yellow precipitate. It was separated, washed with ether and $CHCl_3$, and recrystallized from MeOH to give bulky yellow needles (**16**, 380 mg). Compound **16**: mp 144—145 °C. IR ν_{max} cm^{-1}: 3480, 1640, 1585, 1370, 1230, 1155. EIMS *m/z* (rel. int.): 300 (M^+, 45), 299 (100), 284 (16), 256 (11), 150 (4), 128 (11). ^{1}H-NMR (DMSO-d_6, 400 MHz) δ: 3.91 (3H, s, OMe-7), 6.88 (1H, dd, *J* = 8.4, 2.2 Hz, H-6), 7.06 (1H, d, *J* = 2.2 Hz, H-8), 7.85 (1H, d, *J* = 5.1 Hz, H-4), 8.07 (1H, d, *J* = 8.4 Hz, H-5), 8.31 (1H, d, *J* = 5.1 Hz, H-3), 7.84, 7.89 (each 1H, d, *J* = 15.8 Hz, H-1′, H-2′), 7.34 (1H, t, *J* = 7.3 Hz, H-3″), 7.46 (1H, m, H-4″), 7.60 (1H, t, *J* = 7.3 Hz, H-5″), 7.74 (1H, d, *J* = 7.3 Hz, H-2″), 7.94 (1H, d, *J* = 7.3 Hz, H-6″). *Anal.* Calcd for $C_{20}H_{16}N_2O \cdot H_2O$: C, 75.33; H, 5.15; N, 6.50. Found: C, 75.26; H, 5.21; N, 6.61.

1-Formyl-7-methoxy-β-carboline (17) Benzylidene harmine (**16**, 300 mg) was dissolved in AcOH–H_2O (4 : 1), osmium tetraoxide (40 mg) and sodium paraperiodate (0.8 g). The reaction mixture was stirred for 72 h. The aqueous acetic acid was removed under reduced pressure, the residue was suspended in a 10% $NaHCO_3$ solution (30 ml), extracted with $CHCl_3$ and dried over $MgSO_4$, and the solvent was removed under reduced pressure to give a yellow solid. This was then recrystallized from acetone to give yellow prisms (**17**, 180 mg). Compound **17**: mp 203—204 °C. IR ν_{max} cm^{-1}: 3410, 1675, 1625, 1580, 1305, 1250, 1220, 1150, 1125. EIMS *m/z* (rel. int.): 226 (M^+, 100), 198 (51), 183 (40), 155 (31). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 3.94 (3H, s, OMe-7), 6.96 (1H, dd, *J* = 8.3, 2.4 Hz, H-6), 7.03 (1H, d, *J* = 2.4 Hz, H-8), 8.02 (1H, d, *J* = 8.3 Hz, H-5), 8.05 (1H, d, *J* = 4.9 Hz, H-4), 8.60 (1H, d, *J* = 4.9 Hz, H-3), 9.99 (1H, br s, NH), 10.32 (1H, s, CHO-1). *Anal.* Calcd for $C_{13}H_{10}N_2O_2 \cdot H_2O$: C, 66.38; H, 4.71; N, 11.91. Found: C, 66.91; H, 4.33; N, 11.62.

9-Methoxycanthin-6-one (10) 1-Formyl-7-methoxy-β-carboline (**17**, 100 mg) was condensed with malonic acid (200 mg) in piperidine to give a pale yellow solid. Column chromatography of the solid on silica gel provided pale yellow needles (**10**, 35 mg) upon elution with $CHCl_3$–MeOH (19 : 1). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 3.97 (3H, s, OMe-9), 6.92 (1H, d, *J* = 9.9 Hz, H-5), 7.03 (1H, dd, *J* = 8.6, 2.4 Hz, H-10), 7.79 (1H, d, *J* = 4.9 Hz, H-1), 7.88 (1H, *J* = 8.6 Hz, H-11), 7.98 (1H, d, *J* = 9.9 Hz, H-4), 8.13 (1H, d, *J* = 2.4 Hz, H-8), 8.74 (1H, d, *J* = 4.9 Hz, H-2). Compound **10**: mp 177—179 °C. IR ν_{max} cm^{-1}: 1665, 1630, 1610, 1330, 1270, 1220, 1150, 1030. EIMS *m/z* (rel. int.): 250 (M^+, 100), 235 (9), 221 (21), 207 (35), 192 (13), 179 (29). *Anal.* Calcd for $C_{15}H_{10}N_2O_2$: C, 71.99; H, 4.00; N, 11.91. Found: C, 72.05; H, 4.12; N, 11.31.

Hydrogenation of 10 Compound **10** (3 mg) in acetic acid (1 ml) was boiled with granulated zinc for 15 min, then the solution was diluted with water, neutralized by the addition of 5% Na_2CO_3 solution, and extracted with $CHCl_3$. Evaporation of the $CHCl_3$ solution gave 4,5-dihydro-9-methoxycanthin-6-one (**12**, 2 mg). Compound **12**: Amorphous powder. EIMS *m/z* (rel. int.): 252 (M^+, 100), 236 (5), 224 (60), 208 (8), 181 (18). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 3.21 (2H, t, *J* = 7.7 Hz, H-5), 3.48 (1H, t, *J* = 7.7 Hz, H-4), 3.97 (3H, s, OMe-9), 7.06 (^{1}H, dd, *J* = 8.6, 2.2 Hz, H-10), 7.62 (1H, d, *J* = 5.5 Hz, H-1), 7.91 (1H, d, *J* = 8.6 Hz, H-11), 8.06 (1H, d, *J* = 2.2 Hz, H-8), 8.47 (1H, d, *J* = 5.5 Hz, H-2).

Picrasidine X (2) Pale yellow solid (MeOH), mp 180—181 °C. $[\alpha]_D^{22}$ −37.0° (*c* = 0.4, pyridine). IR ν_{max} cm^{-1}: 3355 (br), 3191 (br), 1630, 1594, 1505, 1448, 1372, 1340, 1295, 1216, 1108, 1082. UV λ_{max}^{MeOH} nm (log ε): 250 (4.58), 290 (4.23), 303 (sh, 4.27), 352 (3.79), 370 (sh, 3.71). UV $\lambda_{max}^{MeOH+HCl}$ nm (log ε): 250 (4.60), 303 (4.39), 368 (3.86). UV $\lambda_{max}^{MeOH+NaOH}$ nm (log ε): 236 (4.60), 300 (sh, 4.42), 280 (sh, 4.09), 289 (4.29), 335 (3.75), 350 (3.75). EIMS *m/z* (rel. int.): 256 (M^+, 2), 238 (14), 220 (100), 192 (78), 182 (18), 154 (4). HMBC correlations (400 MHz, DMSO-d_6): H-3→C-4, C-11; H-4→C-10, C-12; H-5→C-7, C-13; H-6→C-8, C-12; H-7→C-5, C-8; H-8→C-12, C-7; H-1′→C-1, C-10, C-3′; H-2′→C-1. HRMS: Calcd for $C_{14}H_{12}N_2O_3$, *m/z* 256.0848, Found *m/z* 282.0820.

Acetylation of 2 Picrasidine X (**1**, 1 mg) was acetylated with Ac_2O (0.1 ml) and pyridine (0.1 ml) for 15 h at room temperature. After MeOH (5 ml) was added, the reaction mixture was evaporated under reduced pressure to give a monoacetate (**14**, 0.5 mg). Compound **14**: ^{1}H-NMR (DMSO-d_6, 400 MHz) δ: 1.93 (3H, s, OAc-2′), 3.59 (1H, dd, *J* = 15.0, 5.1 Hz), 3.68 (1H, dd, *J* = 15.0, 8.4 Hz) (each H-1′), 5.70 (1H, dd, *J* = 8.4, 5.1 Hz, H-2′), 7.23 (1H, t, *J* = 7.7 Hz, H-6), 7.54 (1H, t, *J* = 7.7 Hz, H-7), 7.61 (1H, d, *J* = 7.7 Hz, H-8), 7.96 (1H, d, *J* = 5.0 Hz, H-4), 8.19 (1H, d, *J* = 7.7 Hz, H-5), 8.25 (1H, d, *J* = 5.0 Hz, H-3).

Picrasidine Y (3) Pale yellow solid (MeOH), mp 184—185 °C. $[\alpha]_D^{22}$ −33.2° (*c* = 0.5, pyridine). IR ν_{max} cm^{-1}: 3421 (br), 2925, 1634, 1538, 1506, 1455, 1332, 1230, 1127, 1055. UV λ_{max}^{MeOH} nm (log ε): 250 (4.51), 290 (4.21), 302 (4.27), 352 (3.60), 370 (sh, 3.51). EIMS *m/z* (rel. int.): 236 ($[M-2\times H_2O]^+$, 100), 208 (16), 194 (8), 180 (29), 168 (50), 153 (12). FABMS *m/z*: 295 $[M+Na]^+$, 273 $[M+H]^+$.

X-Ray Analysis of Picrasidine Q (4) Crystallized from MeOH, $C_{15}H_{10}N_2O_3$, M_r = 266.26, yellow needles having approximate dimensions of 0.100 × 0.100 × 0.400 mm were mounted on a glass fiber. All measurements were made on a Rigaku AFC5R diffractometer with graphite monochromated CuK_α radiation (λ = 1.54178 Å), μ(CuK_α) = 9.06 cm^{-1} and a 12 kW rotating anode generator using ω-2θ scan technique to a maximum 2θ value of 120.2°. Cell constants and an orientation matrix for data collection, obtained from a least-squares refinement using the setting an-

gles of 18 carefully centered reflections in the range $47.00 < 2\theta < 56.53°$ corresponded to a monoclinic cell with dimensions: $a = 18.090$ (2) Å, $b = 14.243$ (2) Å, $c = 4.512$ (2) Å; $\beta = 96.31$ (2)°; $V = 1155.5$ (4) Å^3. Calculated density = 1.530 g/cm^3 for $Z = 4$. Base on the systematic absence of $h01$: $h \neq 2n$, $0k0$: $k \neq 2n$ and the successful solution and refinement of the structure, the space group was determined to be $P2_1/a$ (#14). Of the 2051 reflections which were collected, 1795 were unique ($R_{int} = 0.016$). The molecular structure of 4 was solved by a direct method (SHELXS-86[21]) and refined by using the full-matrix least-squares technique. The final refinement cycle gave $R = 0.032$ ($R_w = 0.030$). The final Fourier difference synthesis showed a maximum and minimum of $+0.14\,e^-$/Å^3 and $-0.21\,e^-$/Å^3, respectively. Atomic coordinates, bond angles, thermal parameters and structure factors are deposited at the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, U.K.

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