[Chem. Pharm. Bull. 21(4) 837—839 (1973)]

UDC 547.94.02 : 581.192

The Structure of a New β-Carboline Alkaloid from *Picrasma ailanthoides* Planchon

Yoshikazu Kondo and Tsunematsu Takemoto

Pharmaceutical Institute, Tohoku University[1]

(Received September 21, 1972)

A new alkaloid, 1-hydroxymethyl-β-carboline (V) has been isolated from the stems of *Picrasma ailanthoides* Planchon (Simaroubaceae) along with methyl β-carboline-1-carboxylate. The structure of V has been established by physical and chemical means.

Extracts of *Picrasma ailanthoides* Planchon (=*P. quassioides* Bennett) (Simaroubaceae) are extensively used as a bitter stomachic. The main principles reported were the quassolidan derivatives.[2] Earlier chemical investigations on the alkaloid showed the presence of two canthine alkaloids, 4,5-dimethoxycanthin-6-one[3] and 5-hydroxy-4-methoxycanthin-6-one (nigakinone).[4] Now the presence of two additional alkaloids, methyl β-carboline-1-carboxylate (I) and a new alkaloid, 1-hydroxymethyl-β-carboline (V) was proved.

The aqueous extract of the stem-chips of *P. ailanthoides* Planchon was thoroughly extracted with chloroform. The chloroform extract was fractionated by chromatography on a silica gel column. Two alkaloids whose *Rf* values were close to each other were obtained from the eluates with chloroform (see Experimental). Fractional recrystallization and purification *via* the picrate gave pure 4,5-dimethoxycanthin-6-one (II), mp 145—146°, and compound I, mp 163°.

Elemental analysis of I was in good agreement with $C_{13}H_{10}O_2N_2$. The mass spectrum also confirmed this formula showing molecular peak at *m/e* 226. The ultraviolet (UV) absorption spectrum showed maxima at 246 (log ε 4.26), 257.5 (log ε 4.26), 275 (log ε 4.31), 301 (log ε 4.07) and 350 nm (log ε 3.83). The nuclear magnetic resonance (NMR) spectrum of I displayed signals due to a carbomethoxy group at 4.08 ppm, aromatic ring protons and a broad imino proton at 9.89 ppm disappearing on addition of D_2O.

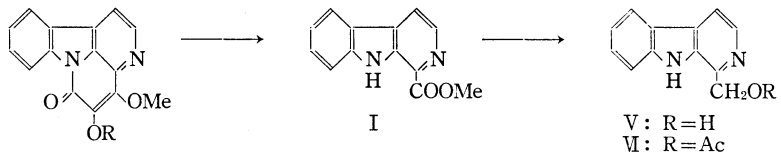
These observations led to methyl β-carboline-1-carboxylate[5] as the structure of I. The structure was also confirmed by the oxidation of 5-hydroxy-4-methoxycanthin-6-one (III) with potassium permanganate yielding methyl β-carboline-1-carboxylate[4] which was identical with the natural product.

Subsequent elution of the column with a mixture of chloroform–methanol gave 5-hydroxy-4-methoxycanthin-6-one (III) (nigakinone) and compound V, mp 228—230° (decomp). Elemental analysis combined with mass spectrometric result indicated a molecular formula $C_{12}H_{10}ON_2$ for V. The UV spectrum of V showed maxima at 212.5 (log ε 4.40), 235 (log ε 4.58), 240 (infl) (log ε 4.56), 250 (infl) (log ε 4.40), 282 (infl) (log ε 4.07), 289 (log ε 4.24), 338 (log ε 3.71) and 347 nm (log ε 3.70) which were very similar to those of harman derivatives.[6] The NMR spectrum of V showed a singlet at 4.94 ppm integrating two protons which was assignable to

1) Location: *Aobayama, Sendai.*
2) T. Murae, T. Tsuyuki, T. Ikeda, T. Mishihama, S. Masuda, and T. Takahashi, *Tetrahedron*, **27**, 5147 (1971) and references cited therein.
3) N. Inamoto, S. Masuda, O. Shimamura, and T. Tsuyuki, *Bull. Chem. Soc. Japan*, **34**, 888 (1961).
4) Y. Kimura, M. Takido, and S. Koizumi, *Yakugaku Zasshi*, **87**, 1371 (1967).
5) E. Sanchez and J. Comin, *Phytochem.*, **10**, 2155 (1971).
6) H. Bickel, H. Schmid, and P. Karrer, *Helv. Chim. Acta*, **78**, 649 (1955); N. J. Leonard and R.C. Elderfield, *J. Org. Chem.*, **7**, 556 (1942).

the hydroxymethyl group. V gave a monoacetate VI, mp 113—113.5° whose α-methylene protons showed the predictable downfield shift[7] in the NMR. From these findings the structure of V was concluded as 1-hydroxymethyl-β-carboline. Moreover the structure of V was evidenced by the synthetic manner. Reduction of I with lithium alanate in tetrahydrofuran gave 1-hydroxymethyl-β-carboline whose spectral data and melting point were identical with those of natural product.

Recent studies of alkaloids from the genus *Picrasma* showed the presence of three new β-carboline derivatives, 1-ethyl-4-methoxy-β-carboline (crenatine),[8] 1-ethyl-4,8-dimethoxy-β-carboline (crenatidine)[5,8] and 1-vinyl-4-methoxy-β-carboline.[9]



II: R=Me
III: R=H
IV: R=Ac

I

V: R=H
VI: R=Ac

Experimental[10]

Isolation of Alkaloids I, II, III, and V——32 kg of the stem-chips of *Picrasma ailanthoides* PLANCHON was extracted with aq. MeOH. Aqueous MeOH extract was concentrated under reduced pressure until removal of MeOH. The aqueous residue was thoroughly shaken with $CHCl_3$ using a shaking machine. The combined $CHCl_3$ extract was evapolated *in vacuo* to afford the brown viscous residue. Half of the residue was chromatographed on a silica gel column (55×600 mm), and the column was eluted with $CHCl_3$. 200 ml of fractions were collected and monitored by thin-layer chromatography (TLC). The first few fractions of the $CHCl_3$ eluates gave a semi-crystalline residue which showed two spots on TLC. Crystallization from MeOH gave 4,5-dimethoxycanthin-6-one (II), mp 144—145° (lit.[3] 147.3—147.5°) as pale yellow needles. Yield: total 3.86 g. *Anal.* Calcd. for $C_{16}H_{12}O_3N_2$: C, 68.56; H, 4.32; N, 10.00. Found: C, 68.34; H, 4.33; N, 10.06. NMR ($CDCl_3$) ppm: 4.04 (3H, s, $-OCH_3$), 4.42 (3H, s, $-OCH_3$), 7.83 (1H, d, J=5.1 Hz, C-1), 7.28—8.65 (4H, m, C-7, 8, 9, 10), 8.77 (1H, d, J=5.1 Hz, C-2).

II Picrate: The picrate was prepared by the usual procedure. Recrystallization from EtOH gave bright yellow prisms, mp 185—186° (decomp). *Anal.* Calcd. for $C_{22}H_{15}O_{10}N_5$: C, 51.87; H, 2.97; N, 13.75. Found: C, 51.71; H, 2.86; N, 13.59.

The mother liquor of II left an oily residue which gave a crystalline picrate. The picrate was recrystallized from MeOH to afford bright yellow needles, mp 193—195° (decomp). Yield: total 3.5 g. *Anal.* Calcd. for $C_{19}H_{13}O_9N_5$: C, 50.12; H, 2.88; N, 15.38. Found: C, 50.29; H, 2.58; N, 15.30. The picrate was dissolved in acetone and the acetone solution was put on an Al_2O_3 (Brockmann, activity 2—3) column. The column was eluted with acetone to give a crystalline mass. Recrystallization from ether afforded I as colorless needles, mp 163°. *Anal.* Calcd. for $C_{13}H_{10}O_2N_2$: C, 69.01; H, 4.46; N, 12.38. Found: C, 68.91; H, 4.56; N, 12.19. M^+ 226. UV λ_{max}^{EtOH} nm (log ε): 246 (4.26), 257.5 (4.26), 275 (4.31), 301 (4.07), 370 (3.83). NMR ($CDCl_3$) ppm: 4.08 (3H, s, –COOMe), 7.15—8.16 (4H, m, C-5, 6, 7, 8), 8.06 (1H, d, J=4.7 Hz, C-4), 8.55 (1H, d, J=4.7 Hz, C-3), 9.89 (1H, br. s, >NH).

The subsequent eluates with $CHCl_3$–MeOH (95: 5) was evaporated under reduced pressure to leave a yellow crystalline mass. Recrystallization from MeOH gave 5-hydroxy-4-methoxycanthin-6-one (nigakinone) (III) as yellow needles, mp 223—224° (decomp). Yield: total 7.7 g. *Anal.* Calcd. for $C_{15}H_{10}O_3N_2$: C, 67.66; H, 3.79; N, 10.52. Found: C, 67.65; H, 4.05; N, 10.27. NMR (DMSO-d_6) ppm: 4.27 (3H, s, $-OCH_3$), 7.37—8.50 (4H, m, C-7, 8, 9, 10), 8.02 (1H, d, J=5.1 Hz, C-1), 8.74 (1H, d, J=5.1 Hz, C-5).

7) L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," 2nd Ed., Pergamon press, Oxford, 1969, p. 179.
8) E. Sanchez and J. Comin, *Ann. Asoc. Quim. Argent.*, **57**, 57 (1969).
9) S. R. Johns, J. A. Lamberton, and A. A. Sioumis, *Aust. J. Chem.*, **23**, 629 (1970).
10) Melting points were taken on a Yamato melting point apparatus and uncorrected. The UV spectra were measured in 95% EtOH on a Hitachi 124 spectrophotometer. The NMR spectra were recorded on a Hitachi H-60 spectrometer with tetramethylsilane (TMS) as internal standard. The mass spectra were recorded on a Hitachi mass spectrometer RMU-7 at 80 eV. Thin-layer chromatography (TLC) was carried out on silica gel HF_{254} (Merk AG) in the solvent system, $CHCl_3$: MeOH (95: 5).

III Acetate (IV): The acetate was prepared by the usual procedure. Recrystallization from MeOH gave colorless needles, mp 194° (decomp.). (lit.[4] mp 193—194°). *Anal.* Calcd. for $C_{17}H_{12}O_4N_2$: C, 66.23; H, 3.92; N, 9.09. Found: C, 65.82; H, 3.92; N, 9.27.

The $CHCl_3$–MeOH (9: 1) eluates gave a yellow crystalline mass. Recrystallization from MeOH afforded yellow needles (V), mp 228—230° (decomp.). Yield: total 815 mg. *Anal.* Calcd. for $C_{12}H_{10}ON_2$: C, 72.71; H, 5.09; N, 14.13. Found: C, 72.70; H, 5.21; N, 14.20. M^+ 198. UV λ_{max}^{EtOH} nm (log ε): 212.5 (4.40), 235 (4.58), 240 (infl) (4.56), 250 (infl) (4.40), 282 (infl) (4.07), 289 (4.24), 338 (3.71), 347 (3.70). NMR (DMSO-d_6) ppm: 4.20 (2H, br. s, >NH and –OH), 4.95 (2H, s, $-CH_2OH$), 6.99—8.15 (4H, m, C–5, 6, 8), 7.89 (1H, d, J= 5.3 Hz, C–4), 8.15 (1H, d, J=5.3 Hz, C–3).

V HCl Salt: To a MeOH solution of V was added 2 ml of conc. HCl and evapolated under reduced pressure. The crystalline residue was recrystallized from MeOH to afford yellow needles, mp 240° (decomp.). *Anal.* Calcd. for $C_{12}H_{11}ON_2Cl$: C, 61.41; H, 4.72; N, 11.94. Found: C, 61.36; H, 5.18; N, 12.10.

V Acetate (VI): The acetate was prepared by the usual manner. Recrystallization from ether gave pale yellow needles, mp 113—113.5°. *Anal.* Calcd. for $C_{14}H_{12}O_2N_2$: C, 69.99; H, 5.03; N, 11.66. Found: C, 69.92; H, 5.00; N, 11.35. NMR ($CDCl_3$) ppm: 1.09 (3H, s, –COMe), 5.62 (2H, s, $-CH_2-OAc$), 7.10—8.15 (4H, m, C–5, 6, 7, 8), 7.91 (1H, d, J=5.6 Hz, C–4), 8.41 (1H, d, J=5.6 Hz, C–3), 9.45 (1H, br. s, >NH).

Conversion of 5-Hydroxy-4-methoxycanthin-6-one (III) to Methyl β-Carboline-1-carboxylate (I)——1.0 g of III was oxidazed with $KMnO_4$ as described by Kimura, *et al.*[4] The resulting product, methyl β-carboline-1-carboxylate was recrystallized from benzene to give pale yellow needles, mp 168°. Yield: 500 mg. This synthetic product was identical with the natural one by direct comparison.

Conversion of Methyl β-Carboline-1-carboxylate (I) to 1-Hydroxymethyl-β-carboline (V)——A stirred solution of 500 mg of I in 10 ml of anhydrous THF was treated with $LiAlH_4$. After stirring for 5 hr at room temperature, excess $LiAlH_4$ was destroyed by the addition of moist EtOAc. The resulting solution was shaken with four 100 ml portions of $CHCl_3$. The organic solvent layer was evaporated *in vacuo*. The residue was recrystallized from MeOH to give 1-hydroxymethyl-β-carboline as yellow needles which was identical with the natural product by direct comparison.