A New Dimeric Alkaloid from the Leaf of *Psychotria calocarpa*

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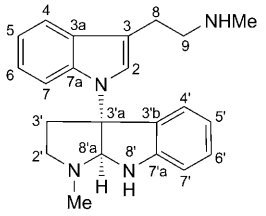
Psychotriasine was isolated from the leaves of *Psychotria calocarpa* (Rubiaceae). The structure was established by spectroscopic methods including 2D-NMR analysis. To the best of our knowledge, psychotriasine is the first example of a dimeric tryptamine-related alkaloid that contains a free N^{α}-methyltryptamine unit in the molecule.

Introduction. – Plants of the genus *Psychotria* have been used in folk medicine for the treatment of constipation in Malaysia [1]. Several polymeric indole alkaloids have been isolated from related plants [2–3], but there has been no previous work on chemical components of *Psychotria calocarpa*. In our continuing chemical and pharmacological studies on indole alkloids possessing biological activity [4–6], we have been interested in compounds of this type for some time. To discover the active principles from this species, studies on the alkaloids of *Psychotria calocarpa* were carried out. The present article deals with the isolation and the structure elucidation of a novel dimeric indole alkaloid, namely of psychotriasine[1]).



Psychotriasine[1])

Results and Discussion. – Psychotriasine, obtained as an amorphous, optically active powder, had the molecular formula $C_{22}H_{26}N_4$, as established by HR-ESI-MS analysis (*m*/*z* 347.2188 ($[M+H]^+$)), which is identical with that of the known dimeric alkaloid calycanthine. The ^{13}C-NMR spectrum (*Table*) disclosed 14 aromatic C-atoms and eight sp^3 C-atoms including one characteristic aminal C-atom (δ(C) 87.0), which suggested that psychotriasine is composed of two tryptamine-related moieties containing one indoline (=2,3-dihydro-1*H*-indole) and one 1*H*-indole chromophore. The structures of the two individual parts in psychotriasine were revealed by detailed

[1]) Arbitrary atom numbering; for the systematic name, see *Exper. Part.*

analysis of one- and two-dimensional NMR spectra, as follows. The ^{1}H- and ^{13}C-NMR, and ^{1}H,^{1}H-COSY plot suggested that unit A has a 1*H*-indole moiety, and no substituents at C(4), C(5), C(6), and C(7). In addition, the characteristic signal of H–C(2) of unit A (δ(H) 7.38 (*s*, 1 H)) was observed. The HMBCs shown in the *Figure* suggested that each unit possessed a fragment $MeNCH_2CH_2$, connected to C(3) of each indole moiety. Taken together, psychotriasine has one N^{α}-methyltryptamine (= *N*-methyl-1*H*-indole-3-ethanamine) unit A which is connected to another unit, at N(1) and/or N^{α}. The ^{13}C-NMR spectrum revealed that unit B has six aromatic C-atoms and five sp^3 C-atoms. The characteristic NMR signals ascribable to C(8′a) (δ(H) 5.20 (*s*, 1 H) and δ(C) 87.0) implied that unit B possessed a 'pyrrolidinoindoline' skeleton. The ^{1}H-NMR spectrum indicated the presence of an *N*-methyl group (δ(H) 2.39 (*s*)). There was a downfield quaternary C-atom signal at δ(C) 79.4 (C(3′a)) indicating C(3′a) being adjacent to an N-atom. This connection was supported by the presence of HMBC cross-peaks between δ(C) 79.4 (C(3′a)) and δ(H) 7.13 (H–C(8a)). Therefore, the structure of the new alkaloid, named psychotriasine, was established. To the best of our knowledge, psychotriasine is the first example of a dimeric tryptamine-related alkaloid that contains a free *N*-methyltryptamine unit in the molecule.

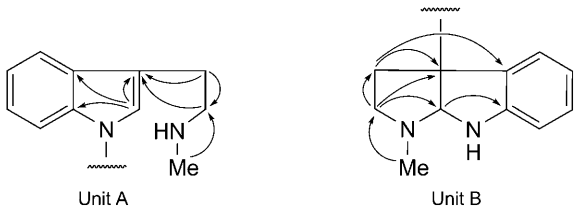


Figure. *HMBCs for units A and B in psychotriasine*

Table. *^{1}H- and ^{13}C-NMR Data* (500 and 125 MHz, resp.; CD_3OD) *of Psychotriasine*[1]). δ in ppm, *J* in Hz.

Unit		δ(C)	δ(H)	Unit		δ(C)	δ(H)
A	H–C(2)	125.0	7.38 (*s*)	B	CH_2(2′)	52.0	2.93–2.96, 2.54–2.57 (2*m*)
	C(3)	112.7	–		CH_2(3′)	39.9	3.28–3.30, 2.46–2.49 (2*m*)
	C(3a)	130.4	–		C(3′a)	79.4	–
	H–C(4)	124.7	6.85 (*dd*, *J* = 7.8, 1.0)		C(4′a)	131.3	–
	H–C(5)	120.1	6.97 (*dt*, *J* = 7.8, 1.0)		H–C(4′)	112.2	7.12 (*dd*, *J* = 7.8, 1.0)
	H–C(6)	130.7	7.04 (*dt*, *J* = 7.8, 1.0)		H–C(5′)	122.4	6.94 (*dt*, *J* = 7.8, 1.0)
	H–C(7)	120.1	7.52 (*dd*, *J* = 7.8, 1.0)		H–C(6′)	119.6	6.56 (*dt*, *J* = 7.8, 1.0)
	C(7a)	137.7	–		H–C(7′)	110.0	6.68 (*dd*, *J* = 7.8, 1.0)
	CH_2(8)	25.6	2.91–2.94 (*m*)		C(7′a)	152.5	–
	CH_2(9)	52.0	2.85–2.88 (*m*)		C(8′a)	87.0	5.20 (*s*)
	MeN	36.3	2.44 (*s*)		MeN	35.7	2.39 (*s*)

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Experimental Part

General. Solvents were distilled before use. TLC and columm chromatography (CC): plates precoated with silica gel F_{254} and silica gel *H* (SiO_2; *Qingdao Haiyang Chemical CO., Ltd.*, Qingdao, P. R. China). Semi-prep. HPLC: *Agilent-1100* (*Zorbax-SB-C*$_{18}$ column, 9.4 × 250 mm, 5 μm). Optical rotation: *Horiba-SEAP-300* spectropolarimeter. UV Spectra: *Shimadzu-210A* double-beam spectrometer; λ_{max} (log ε) in nm. IR Spectra: *Bio-Rad-FTS-135* spectrometer; KBr pellets; $\tilde{\nu}$ in cm^{-1}. 1D- and 2D-NMR Spectra: *Bruker-AM-500* spectrometer; δ in ppm rel. to Me_4Si as internal standard, *J* in Hz. EI- and HR-ESI-MS: *VG-AUTO-spec-3000* spectrometer; *m*/*z* (rel. %).

Plant Material. The leaves of *Psychotria calocarpa* were collected in Xishuangbanna (Yunnan Province of China) in February 2005 and were air-dried. The plant was identified by Prof. *De-Ding Tao*, Chinese Academy of Sciences. A specimen of this plant was deposited with the Kunming Institute of Botany, Kunming, P. R. China.

Extraction and Isolation. The dried leaves of *Psychotria calocarpa* (4.0 kg) were ground and extracted under reflux with 95% EtOH (3 ×). After evaporation of the solvent, the residue was extracted with 2% HCl soln. The acid-soluble fraction was washed with $CHCl_3$, then basified to pH 10 with 25% aq. NH_3 soln., and extracted with $CHCl_3$ to give the crude alkaloid fraction (4.0 g). The crude alkaloid fraction was isolated by initial CC (SiO_2, increasing proportions of MeOH in $CHCl_3$) and then subjected to reversed-phase HPLC (*RP-18*, gradient 10 → 60% H_2O/MeOH), and finally H_2O/MeOH 65 :35) to yield psychotriasine.

Psychotriasine (= rel-N-*Methyl-1-[(3a*R,*8a*S*)-2,3,8,8a-tetrahydro-1-methylpyrrolo[2,3*-b*]indol-3a(1*H*)-yl]-1*H*-indole-3-ethanamine):* Colorless, amorphous powder. $[\alpha]_D^{19.2} = +104.2$ ($c = 0.1$, MeOH). UV (MeOH): 208, 245, 295. IR (KBr): 3012, 2820, 2780, 1489, 1433, 810, 780. ^{1}H- and ^{13}C-NMR: *Table.* EI-MS: 346 (100, M^+), 314 (25), 280 (43), 173 (21). HR-ESI-MS: 347.2188 ($[M+H]^+$, $C_{22}H_{27}N_4^+$; calc. 347.2236).

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