PHENYLPENTENYLAMINES FROM *CATHA EDULIS*

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Khat, the young leaves of *Catha edulis* Forsk. (Celastraceae), is widely used in East Africa and the Arabian peninsula as an amphetamine-like stimulant due to its content of cathinone, norpseudoephedrine, and norephedrine (1,2). Merucathine, the pentenyl-analogue of norephedrine, has recently been found (3). Further chemical and spectroscopic studies (4) have shown the (3*R*,4*S*)- instead of the originally postulated (3*S*,4*S*)-configuration. Merucathinone and pseudomerucathine, the analogues of cathinone and norpseudoephedrine, have only been identified by gc/ms and hplc with photodiode array detection until now (2).

In this report we describe the isolation and structure elucidation of the phenylpentenylamines merucathinone, pseudomerucathine, and merucathine as their acetyl derivatives. Considering the low concentration in khat (5) and the known instability of keto-khatamines, particularly as free bases (2), the phenylpentenylamines were extracted as oxalates and separated as acetyl derivatives. Recent in vitro studies showed their pharmacological activity (6,7), but they play only a minor role concerning the psychoactive effects of khat.

EXPERIMENTAL

PLANT MATERIAL.—Fresh leaves of *C. edulis* were bought in January 1983, at the streetmarket of Nairobi, Kenya, originating from the khat cultivation areas of Meru, North Kenya. The plant material was deep-frozen within 24 h and transported by air in a cooler to the laboratory. A voucher specimen has been deposited at the Institute of Pharmacy, University of Berne.

EXTRACTION AND ISOLATION.—The extraction of the plant material (540 g) and the precipitation of the khatamines as oxalates were performed as reported earlier (5,8). After dissolving the oxalates (700 mg) in CH_2Cl_2 and treating with NH_3 gas, Ac_2O and pyridine were added and the mixture stirred at room temperature for 24 h. The reaction mixture was diluted with CH_2Cl_2, poured into ice-saturated aqueous $NaHCO_3$, and stirred. After separation of the organic layer, the aqueous phase was washed with CH_2Cl_2. The combined organic phases were washed with 1N HCl and saturated aqueous $NaHCO_3$, dried (Na_2SO_4), and evaporated. The khatamine acetyl derivatives (500 mg) were dissolved in MeOH and separated by mplc on Merck Lichroprep RP-18 15-25 μm (460×26 mm i.d.) using MeOH-H_2O (60:40) as mobile phase. Each fraction was monitored (254 nm) by hplc on a Spherisorb ODS-1 5 μm column (250×4.6 mm i.d.), using MeOH-H_2O (57:43, 0.8 ml/min) as mobile phase. Fractions 15-63 were combined and again separated by mplc (MeOH-H_2O, 50:50). The final purification was done by semi-preparative hplc on Spherisorb ODS-1 5 μm (250×10 mm i.d.) with MeOH-H_2O (65:35, 3 ml/min) to give, after evaporation, 4.3 mg acetylmerucathinone, 0.8 mg diacetylpseudomerucathine, and 5.7 mg diacetylmerucathine.

IDENTIFICATION.—Acetylmerucathinone: uv λ max (photodiode array detector) 297 nm; ir ν max (CCl_4) 3430, 2990, 1680, 1665, 1630, 1500, 1455, 1375, 910, 690 cm^{-1}; ^1H nmr ($CDCl_3$) ppm 1.44 (d, J=7.1 Hz, 3H, H-5), 2.05 (s, 3H, N-Ac), 4.99 (qd, J=7.1, 1H, H-4), 6.53 (br d, J=5.7, 1H, H-N), 6.80 (d, J=16.1, 1H, H-2), 7.40 and 7.58 (m, 5H, H-arom.), 7.74 (d, J= 16.1, 1H, H-1); eims *m/z* 217 (1%, M^+), 189 (4), 158 (4), 131 (14), 103 (8), 86 (48), 77 (6), 44 (100). Diacetylpseudomerucathine: uv λ max 251, 282, 292 nm; ir ν max 3450, 2980, 1745, 1690, 1500, 1450, 1370, 1230, 970, 690 cm^{-1}; ^1H nmr ppm 1.18 (d, J=7.1, 3H, H-5), 1.98 (s, 3H, N-Ac), 2.13 (s, 3H, O-Ac), 4.35 (m, 1H, H-4), 5.42 (ddd, J=7.0, 5.4 and 0.7, 1H, H-3), 5.52 (br d, J=8.2, 1H, H-N), 6.10 (dd, J=15.8 and 7.3, 1H, H-2), 6.63 (d, J=15.9, 1H, H-1), 7.32 (m, 5H, H-arom); eims *m/z* 261 (1%, M^+), 202 (11), 160 (3), 133 (7), 115 (2), 103 (1), 91 (2), 86 (65), 77 (2), 55 (4), 44 (100). Diacetylmerucathine: uv, ir, and eims identical to diacetylpseudomerucathine; ^1H nmr ppm 1.19 (d, J=6.9, 3H, H-5), 1.97 (s, 3H, N-Ac), 2.13 (s, 3H, O-Ac), 4.35 (m, 1H, H-4), 5.44 (ddd, J=6.8, 4.0 and 1.3, 1H, H-3), 5.56 (br d, J=8.6, 1H, H-N), 6.12 (dd, J=16.0 and 6.8, 1H, H-2), 6.65 (dd, J=16.0 and 0.96, 1H, H-1), 7.32 (m, 5H, H-arom).

Full details of the isolation and identification of the compounds are available on request to the authors.

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A NEW DIHYDROSTILBENE IN *DENDROBIUM CHRYSANTHUM*

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Many phenanthrene stilbenoids have been isolated from plants of the Orchidaceae (1). These compounds are considered to play important roles in such plants as phytoalexins (2). Our present work describes the occurrence and structural elucidation of a new stilbenoid from *Dendrobium chrysanthum* Wall. ex Lindl.

The new compound was isolated from an EtOH extract after Si gel chromatography and exhibited $C_{17}H_{20}O_5$ (M^+ 304). Its ^{1}H-nmr spectrum indicated two singlets [2.80 (4H), 6.36 (2H) ppm] and an ABX system [6.60 (d, J=1.8 Hz), 6.67 (dd, J=7.9, 1.8 Hz), and 6.82 (d, J=7.9 Hz)], in addition to three methoxy and two hydroxy groups. The singlet at 2.80 ppm was assigned to two pairs of methylene protons of a bibenzyl system. The ms showed two conspicuous fragments at *m/z* 167 and 137. The former corresponds to a benzyl fragment bearing a hydroxy and two methoxy groups, and the latter to a benzyl fragment bearing one hydroxy and one methoxy group. By comparison with a synthetic stilbenoid (4,3′-dihydroxy-3,5,5′-trimethoxydihydrostilbene) (3), two protons at 6.36 ppm were attributed to those at C-2 and C-6, indicating that one moiety of the compound is a 4-hydroxy-3,5-dimethoxybenzyl residue. On the other hand, the ABX system was assignable to the protons at carbons-2′, 5′, and 6′. The nOe experiments supported these proposed oxygenation patterns, because a 21% nOe for the protons at 6.36 ppm and a 20.7% nOe of the protons at 6.60 ppm on irradiation of a methoxy at 3.84 ppm were observed. Therefore, the structure was concluded to be 4,4′-dihydroxy-3,3′,5-trimethoxybibenzyl.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—The mp was determined on a Büchi melting point apparatus and is uncorrected. Mass spectrum was obtained on a Jeol-D300 spectrometer at 70 eV. ^{1}H-nmr spectrum was determined on a Varian XL-300 spectrometer and chemical shifts were referenced to internal TMS.

PLANT MATERIAL.—The whole plant of *D. chrysanthum* was collected in May 1983, in Guangxi Province, China. The voucher specimen is kept at the Herbarium, China Pharmaceutical University.

EXTRACTION AND ISOLATION.—Whole plants (200 kg) of *D. chrysanthum* were extracted with EtOH. The extract was concentrated to give a brown residue, diluted with H_2O, and then the suspended solution was extracted with $CHCl_3$. The organic phase was subjected to chromatography on Si gel using C_6H_6-EtOAc (10:1) as solvent to give the compound (10 mg), which was crystallized from Et_2O, mp 87-89°. ^{1}H nmr ($CDCl_3$) δ 2.80 (4H, s, 2×CH_2), 3.83 (3H, s, OCH_3), 3.84 (6H, s, 2×OCH_3), 5.36, 5.46 (1H, each s, OH), 6.36 (2H, s, H-2,6), 6.60 (1H, d, J=1.8 Hz, H-2′), 6.67 (1H, dd, J=7.9, 1.8 Hz, H-6′), 6.82 (1H, d, J=7.9 Hz, H-5′); ms *m/z* (rel. int.) 304 [M^+] (22), 167 (100), 137 (34), 122 (12).

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