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A PYRIDINE-TYPE ALKALOID FROM *MALLOTUS APELTA*

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Key Word Index—*Mallotus apelta*; Euphorbiaceae; anti-HIV; malloapeltine; 4,5,4′-trimethyl-ellagic acid.

Abstract—Malloapeltine, 4-methoxy-3-cyano-pyridine 1-oxide was isolated, along with 4,5,4′-trimethyl-ellagic acid, from the roots of *Mallotus apelta*, which showed significant anti-HIV activity in a previous screening experiment. Their structures were identified by spectral methods.

INTRODUCTION

Roots of *Mallotus apelta* have been widely used in traditional Chinese medicine for the treatment of chronic hepatitis [1]. Recently, in an extensive screen for effective anti-HIV natural products, extracts of these roots also showed significant activity [2]. However, only four triterpenic compounds have been described as its constitutions [1]. The wide occurrence of the species and its biological activities prompted us to make a detailed chemical investigation of *M. apelta*. This paper reports the structural elucidation of a new pyridine type alkaloid from this species.

RESULTS AND DISCUSSION

The alcoholic extract of the roots was fractionated with petrol and ethyl acetate. The ethyl acetate portion was chromatographed on a silica gel column to yield compounds **1** and **2** subsequently. Compound **2** was identified as the known compound 4, 5, 4′-trimethyl-ellagic acid by comparison of its physical and spectral data with authentic material [3]. It was first purified from *M. apelta*.

Compound **1** was obtained as white powder, m.p. 204–206°C. EI and HREI-mass spectrometry provided the $[M]^+$ at m/z 150.0430 and the molecular formula, $C_7H_6N_2O_2$. A strong absorption at 2220 cm^{-1} in the IR spectrum indicated the presence of a triple bond. The ^{13}C NMR spectrum exhibited a quaternary carbon signal at δ100.6, which was consistent with the shift of a cyano group. There were no signals between δ80–90; therefore, the triple bond is not ethynyl.

The ^{13}C NMR and DEPT spectra displayed five aromatic carbon signals between δ111.3 and 157.0 and there are two quaternary carbon signals among them. While the ^1H NMR gave only three aromatic hydrogen signals between δ7.40 and 8.76, combined with the given molecular formula, the parent ring was determined as pyridine with two substituents, one is cyano, the other is methoxyl [δ_H 3.98 (*s*) and δ_C 57.87].

The ^1H NMR spectrum exhibited signals for H-2 and H-6 at δ8.76 (*d*, J = 2.5 Hz) and δ8.48 (*dd*, J = 2.5, 7.5 Hz), respectively, their *meta*-coupling constant value is 2.5 Hz. The H-2 signal is 0.31 ppm lower than that of H-6 because of the deshielding effect of the cyano group *ortho* to it. Thus, the cyano group is substituted at C-3. H-6 also couples with another hydrogen at δ7.34 (*d*, J = 7.5 Hz). The coupling constant value proves that the two protons are *ortho* to each other. Therefore, the methoxyl group is at C-4. The 2D NOE experiment exhibited the spatial correlation of the methoxyl group with H-5 at δ7.34 (*d*, J = 7.5 Hz). According to HMQC, the carbon signals were all assigned.

The EI-mass spectrum of compound **1** showed a basepeak at m/z 150 and an intense ion at m/z 134 corresponding with $[M–O]^+$. The IR spectrum exhibited strong absorption at 1250 cm^{-1}, consistent with that of an N → O bond. Thus, the last oxygen

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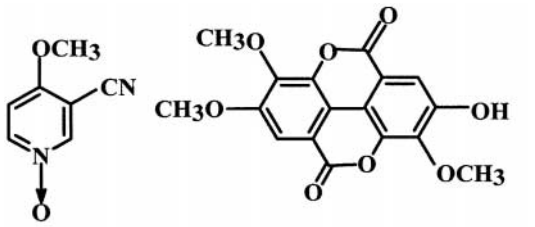
must combine with the nitrogen [4]. Compound **1** was named **malloapeltine** and it was also isolated from the most anti-HIV part of the extracts.



EXPERIMENTAL

General

M.p.s are uncorr. ^{1}H NMR, ^{13}C NMR and HMQC were recorded on Bruker ACF-300 type NMR instrument at 300 and 75 MHz, respectively, in DMSO-d_6.

Plant material

Roots of *Mallotus apelta* Muell. Arg. were collected in Guangxi Province in August 1990. A voucher specimen is deposited in the herbarium of the Guilin Institute of Medicinal Control.

Extraction and isolation

Dried roots were extracted with 95% EtOH. The combined extracts were concd almost to dryness under red. pres. Hot petrol was then added and insol. materials removed by filtration. The filtrate was concd to obtain part 1. Then, hot EtOAc was added to the insol. materials to obtain part 2. Part 2 was subjected to silica gel CC eluting first with petrol EtOAc and then with $CHCl_3$–MeOH to obtain compounds **1** and **2** subsequently using $CHCl_3$–MeOH (4:1).

Table 1. ^{1}H and ^{13}C NMR spectral data of malloapeltine (^{1}H 300 MHz and ^{13}C 75 MHz, δ, DMSO-d_6)

Carbon	H	C
2	8.76 (*d*, *J* = 2.5 Hz)	141.8
3	–	157.7
4	–	112.6
5	7.34 (*d*, *J* = 7.5 Hz)	111.1
6	8.45 (*dd*, *J* = 2.5, 7.5 Hz)	144.3
-OCH_3	3.98 (*s*)	57.9
-CN	–	100.6

Compound **1**

Amorphous powder, m.p. 204–206°. UV γ_{max}^{MeOH} nm: (*c*, 0.06, MeOH): 220.0 (log ε, 1.93), 280 (log ε, 1.53). IR ν_{Max}^{KBr} (cm^{-1}): 3010, 3000, 2960, 2220 (CN-), 1620, 1500, 1475, 1300, 1250 (N → O), 1000, 770. EI-MS: *m*/*z* (rel. int.): 150 (100), 134 (85.3), 105 (33.7), 77 (28.5), 64 (48.3), 51 (28.8). ^{1}H and ^{13}C NMR: Table 1.

Compound **2**, *4,5,4′-trimethyl-ellagic acid*

Yellow needles (pyridine), m.p. 248–250°. UV, IR and ^{1}H NMR in agreement with the reported data [3]. IR ν_{Max}^{KBr} (cm^{-1}): 3410 (–OH), 1750, 1720 (two C=O), 1600, 1500, 1360, 1120, 1090, 980. ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.99 (3H, *s*), 4.04 (3H, *s*), 4.05 (3H, *s*), 7.48 (1H, *s*), 7.57 (1H, *s*), 10.81 (–OH, *s*). EI-MS *m*/*z* (rel. int.): 344 (100), 329 (13.9), 286 (35.9), 241 (9.8).

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