A New Pericarbonyl Lignan from *Amauroderma rude*

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Abstract: A new pericarbonyl lignan (1), named amaurolignan A was isolated from an ethanol extract of the fruiting bodies in *Amauroderma rude* of family *Ganodermataceae*, together with two known lignans, 4-methoxymatairesinol 4′-β-D-glucoside (2) and lappaol F (3). The structures of compounds (1-3) were elucidated using NMR and MS spectroscopic methods.

Keywords: Pericarbonyl lignan; amaurolignan A; *Amauroderma rude*. © 2018 ACG Publications. All rights reserved.

1. Introduction

“Lingzhi” is a mushroom that has been renowned in China for more than 2000 years because of its claimed medicinal properties and symbolic fortune, which translates as ‘Ganodermataceae’ in a broad sense, and in a narrow sense it represents the highly prized medicinal Ganoderma species distributed in East Asia [1]. Its medicinal properties include anti-aging, lowering blood pressure, improving immunity, and preventing and treating various cancers, chronic bronchitis, gastric ulcers, hepatitis, neurasthenia and thrombosis [2-4]. The medicinal effects of many mushrooms such as *Ganoderma lucidum*, *Lentinula edodes*, *Agaricus blazei*, *Antrodia camphorate* and *Grifola frondosa* come from their metabolites including polysaccharides, triterpenes, lucidenic acids, adenosine, ergosterol, glucosamine and cerebrosides [5-8]. This caused us to look further into another mushroom, *Amauroderma rude* (Berk.) Torrend, which called ‘Xuezhi’ in China and some species in this genus have been newly recognized as medicinal fungus [9-10]. The genus *Amauroderma* contains approximately 30 species and most of the species are widespread in tropical areas and rarely studied [11].

In an attempt to look for potential active substances from the *Amauroderma rude*, the isolation and chemical identification of one new pericarbonyl lignan (1) and two known lignans, 4-methoxymatairesinol 4′-β-D-glucoside (2) [12] and lappaol F (3) [13] (Figure 1) from the ethanol extract of *A. rude* were taken. Details of the isolation and identification of compound 1 are presented herein and the known compounds 2-3 were compared of spectroscopic data with those reported.

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2. Materials and Methods

2.1. Instrumentation and Reagents

The UV data was detected by Shimadzu UV-2401A. Mass spectra were performed on a VG Autospec-3000 spectrometer under 70 eV. 1D and 2D NMR spectra were recorded on Bruker AV-400 spectrometer with TMS as the internal standard (Bruker BioSpin Group). SiO2 (100–200 mesh, Qingdao Marine Chemical Inc., China). Lichroprep RP-18 gel (40–63 μm, Merck, Darmstadt, Germany), and MCI gel (75–150 μm, Mitsubishi Chemical Corporation, Tokyo, Japan) were used for column chromatography. Semi-preparative HPLC was performed on an Agilent 1100 liquid chromatography with a Welch Ultimate XB-Phenyl or Ultimate XB-C18 (10 μm, 4.6 mm × 25 cm). Preparative HPLC was performed on a Shimadzu LC-8A preparative liquid chromatograph with a Shimadzu PRC-ODS (K) column. Fractions were monitored by TLC and spots were visualized by heating silica gel plates sprayed with 8% H2SO4 in EtOH. All solvents including petroleum ether (60-90 °C) were distilled prior to use.

2.2 Plant Materials

The fruiting bodies of Amauroderma rude were collected in January 2017 from Ruili State, Yunnan Province, China, and were authenticated by Prof. Min Zhou (Key Laboratory of Chemistry in Ethnic Medicinal Resources, Yunnan Minzu University). A sample (201701A) was preserved in Yunnan Minzu University, Kunming.

2.3. Extraction

The chopped, dried fruiting bodies of A. rude (40 kg) was extracted with 95% ethanol solution heated under reflux (2 times/60 min), at 20 °C to give a residue (3 kg). The extract was suspended in pure water with EtOAc. The EtOAc fraction (1.3 kg) was partitioned with a silica gel column (dichloromethane: methanol, from 1:0~80:1~20:1~10:1~8:1~5:1~2:1, each 5 L) and separated over YMC ODS (MeOH/H2O 30%~55%~90%~100%, each 2 L) to a residue (3 kg). The extract was suspended in pure water (from 80:1~20:1~10:1~8:1~5:1~2:1, each 5 L) and partitioned with EtOAc. The EtOAc fraction (1.3 kg) was partitioned with a silica gel column (dichloromethane: methanol, from 1:0~80:1~20:1~10:1~8:1~5:1~2:1, each 5 L) to afford six subfractions (Fr. A-F). Fr. D (110 g) was further eluted with MCI column using a stepwise gradient of MeOH/H2O (from 30%~55%~90%~100%, each 4 L) to afford three fractions (Fr. D1-D3). Fr. D2 (45.0 g) was loaded onto ODS (MeOH/H2O 40%~60%~80%~100%, each 2 L) to give four fractions (Fr. D2-1~4). Fr. D2-2 (15.5 g) was separated over YMC-Pack ODS-A (20×250 mml. D.S. 5 μm) prep. HPLC (68% MeOH/H2O), yielding 2 (25.0 mg) and 3 (30.6 mg). Fr. D2-3 (10.0 g) was further eluted with a silica gel (dichloromethane/acetone, from 80:1~20:1~10:1~8:1~2:1, each 2 L) and separated over semi-prep. HPLC (50% MeOH/H2O) to yield 1 (22.0 mg).

Amaurolignan A (1): yellow oil; UV λmax 230, 280 and 330 nm; 1H NMR (CD3OD) and 13C NMR (CD3OD) see Table 1; HR-ESIMS m/z 329.0669 [M-H] (calculated for C17H14O7, 329.0667).

4-Methoxymatairesinol 4′-β-D-Glucoside (2): White oily liquid; 1H NMR (400 MHz, CD3OD): δH 7.07 (1H, d, J = 8.2 Hz, H-5′), 6.83 (1H, d, J = 8.6 Hz, H-5), 6.76 (1H, s, H-2), 6.66 (1H, d, J = 8.2 Hz, H-6), 6.61 (2H, d, J = 5.9 Hz, H-2′/6′), 4.19 (1H, t, J = 8.2 Hz, H-9′a), 3.94 (1H, t, J = 8.2 Hz, H-9′b), 3.87 (1H, d, J = 12.0 Hz, H-Glc-6a), 3.80 (1H, s, H-OCH3), 3.76 (6H, s, H-3/3′), 3.70 (1H, d, J = 11.3 Hz, H-Glc-6b), 3.50 (2H, d, J = 6.7 Hz, H-Glc-2, 3), 3.42 (2H, s, H-Glc-4, 5), 2.92 (1H, dd, J = 13.9, 5.3 Hz, H-7a), 2.82 (1H, dd, J = 13.9, 7.2 Hz, H-7b), 2.68 (1H, dd, J = 13.2, 7.2 Hz, H-8), 2.56 (2H, d, J = 6.3 Hz, H-7a/7b′), 2.49 (1H, dd, J = 14.6, 7.5 Hz, H-8′). 13C NMR (400 MHz, CD3OD): δC 132.7 (C-1), 114.8 (C-2), 149.1 (C-3), 150.4 (C-4), 113.1 (C-5), 123.0 (C-6), 35.4 (C-7), 47.6 (C-8), 134.2 (C-1′), 113.6 (C-2′), 150.6 (C-3′), 146.8 (C-4′), 117.8 (C-5′), 122.1 (C-6′), 38.9 (C-7′), 42.5 (C-8′), 72.9 (C-9′), 102.9 (Glc-1′), 74.9 (Glc-2′), 77.8 (Glc-3′), 71.3 (Glc-4), 78.1 (Glc-5), 62.5 (Glc-6), 56.7 (OCH3), 56.5 (OCH3-3′/3′).

Lappaol F (3): 1H NMR (400 MHz, CD3OD): δH 6.63 (1H, br s, H-2), 6.57 (2H, d, J = 2.0 Hz, H-6/6′), 2.76 (1H, dd, J = 12.0, 8.0 Hz, H-7a), 2.92 (1H, dd, J = 16.0, 8.0 Hz,H-7b), 2.65 (1H, m, H-8), 6.50 (1H, br s, H-2′), 2.55 (1H, m, H-8′), 3.94 (1H, dd, J = 8.0, 4.0 Hz, H-9′a), 4.25 (1H, dd, J = 8.0, 4.0 Hz, H-9′b),
6.98 (1H, d, J = 2.0 Hz, H-2′”), 6.74 (2H, t, J = 8.0 Hz, H-5′”, H-5’’”), 6.80 (1H, dd, J = 8.0, 4.0 Hz, H-6′”, H-6’’”), 5.46 (1H, t, J = 7.0 Hz, H-7′′/7’′”), 3.48 (2H, dd, J = 12.0, 4.0 Hz, H-8′”, H-8’’”).

13C NMR (400 MHz, CD3OD): δC 130.2 (C-1), 113.8 (C-2), 147.5 (C-3), 145.3 (C-4), 132.7 (C-5), 114.8 (C-6), 35.8 (C-7), 47.8 (C-8), 181.6 (C-9), 130.4 (C-1′), 116.0 (C-2′), 147.5 (C-3′), 133.3 (C-5′), 116.1 (C-6′), 39.3 (C-7′), 42.6 (C-8′), 73.0 (C-9′), 134.3 (C-1″), 110.6 (C-2″), 148.0 (C-3″), 141.8 (C-4″), 118.3 (C-5″), 120.0 (C-6″), 89.1 (C-7″), 55.0 (C-8″), 64.6 (C-9″), 134.3 (C-1″), 110.5 (C-2″), 149.1 (C-3″), 134.5 (C-4″), 118.9 (C-5″), 119.9 (C-6″), 89.2 (C-7″), 55.0 (C-8″), 64.6 (C-9″), 56.4, 56.4, 56.6, 56.7 (OCH3).

Figure 1. Key HMBC correlations of compound 1 and the structures of compounds 1-3

Figure 2. Key ROESY correlations (arrows) for compound 1

3. Results and Discussion

Compound 1, yellow oil, showed a molecular formula of C17H14O7, as deduced from HRESI (-) MS at m/z 329.0669 ([M-H]-, calcld 329.0667). Its 1H NMR spectra (Table 1) showed feature signals for one methylene at δH 4.10 (br s, 2H), six aromatic proton signals at δH 6.58 (d, J = 8.2, 1H), 6.63 (d, J = 8.2, 1H), 6.70 (br s, 1H), 6.75 (d, J = 8.2, 1H), 7.38 (br s, 1H) and 7.41 (d, J = 8.4, 1H) assigned to two trisubstituted benzene rings, and one olefinic proton at δH 7.74 (s, 1H). Preliminary investigation of 13C-NMR and DEPT spectra (Table 1) revealed a total of 17 carbon signals, consisting of nine quaternary carbons (including one olefinic, six aromatics, one ketone carbonyl and a carboxyl), seven methines (including one olefinic and six aromatics) and one methylene, indicating that compound 1 is a lignan. The NMR data is very closely related to β-(3,4-dimethoxybenzoyl)-α-(3,4-dimethoxybenzylidene) propionic acid [14] except for missing methoxys in 1. This change indicated that the methoxys in β-(3,4-dimethoxybenzoyl)-α-(3,4-dimethoxybenzylidene) propionic acid was reduced to the hydroxyls in 1, which can be observed in 13C-NMR and DEPT spectrum. The key HMBC correlations from H-8 to C-1, C-7, C-9, C-10 and C-11, and from H-10 to C-1’ confirmed the connection between the straight chain fragment and the two benzene rings (Figure 1). The cis-trans isomerism of double bond at Δ9(10) was trans can be confirmed by the cross-peaks
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of H-8/H-2/H-6 and H-10/H-5'/H-6' in ROESY spectrum (Figure 2). Thus, 1 was elucidated to be amaurolignan A.

These skeleton type of pericarbonyl lignans were rare in nature, most of them are intermediates in organic synthesis reactions, like the Perkin condensation product α-arylidine-β-benzoyl propionic acid [15-18]. To be best of our knowledge, this is the first report of natural compound with this skeleton from the fungus and the first time from Ganodermataceae.

Table 1. $^1$H NMR and $^{13}$C NMR data for compound 1 (at 400 MHz in CD$_3$OD, $\delta$ in ppm, J in Hz)

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Supporting Information


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References


