Two New Aromatic Compounds from *Hericium erinaceum* (Bull.: Fr.) Pers.[1)]

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Two new aromatic compounds, erinacerins A (1) and B (2), were isolated from the fruiting bodies of *Hericium erinaceum* (Bull.: Fr.) Pers. (Hericiaceae) together with a known compound, hericenone A (3). The structures of the new compounds were elucidated on the basis of their spectral data. It was found that 1 occurred as a racemate.

Key words *Hericium erinaceum*; Hericiaceae; aromatic compound; mushroom

The fruiting bodies of *Hericium erinaceum* (Bull.: Fr.) Pers. (Yamabushitake in Japanese, Hericiaceae) are known as an edible mushroom. The constituents of *H. erinaceum* have been previously investigated and shown to contain aromatic compounds,[2—5)] fatty acids,[6)] sterols[7)] and polysaccharides.[8)] Some aromatic compounds, including hericenone A (**3**), were found to have significant cytotoxicity against HeLa cells[2)] and stimulating activity of the synthesis of the nerve growth factor.[3)] In a continuation of our investigation of chemical constituents from mushrooms, we describe here the isolation and structural elucidation of two new aromatic compounds, erinacerins A (**1**) and B (**2**), together with a known compound (**3**) from the fruiting bodies of *H. erinaceum*. Compound **3** was identified as hericenone A by comparison of its spectroscopic data with those previously described in the literature.[2,4)]

Compound **1**, called erinacerin A, was obtained as a colorless oil. The molecular formula was determined to be $C_{27}H_{31}NO_4$ by high-resolution (HR)-electron ionization (EI)-MS. The IR spectrum showed the presence of a γ-lactam (1705 cm^{-1}), an α,β-unsaturated ketone (1680 cm^{-1}) and phenyl groups (1614 cm^{-1}). The ^{1}H-NMR spectrum (*vide* Experimental) showed signals due to a tertiary methyl group [δ_H 1.41 (3H, CH_3-9′)], two olefinic methyl groups [δ_H 1.85 (3H, CH_3-8′), 2.14 (3H, CH_3-10′)], six methylenes [δ_H 1.90 (1H, H-2′a), 2.02 (1H, H-2′b), 2.64 (1H, H-4′a), 2.68 (1H, H-1′a), 2.69 (1H, H-1′b), 2.76 (1H, H-4′b), 2.98 (2H, H_2-2″), 3.83 (1H, H-1″a), 3.84 (1H, H-1″b), 4.11 (1H, H-3a), 4.17 (1H, H-3b)], a methoxyl group [δ_H 3.87 (3H)], a trisubstituted double bond [δ_H 6.05 (1H, H-6′)] and six aromatic protons [δ_H 6.90 (1H, H-7), 7.20—7.32 (5H, H-4″—H-8″)]. The ^{13}C-NMR spectrum (*vide* Experimental), obtained with the aid of a distortionless enhancement by polarization transfer (DEPT) spectrum, showed characteristic signals appearing to be due to a carbonyl [δ_C 198.1 (C-5′)], a carbonyl of γ-lactam [δ_C 168.9 (C-1)],[9)] two methylene carbons linked to γ-lactam nitrogen [δ_C 44.4 (C-1″), 48.0 (C-3)][9)] and an oxygenated quaternary carbon [δ_C 75.9 (C-3′)]. There were thirteen degrees of unsaturation in the molecule according to the molecular formula. Two benzene rings, a γ-lactam and an α,β-unsaturated ketone accounted for twelve of those. One degree of unsaturation remained, implying that there was one more ring in this structure. The ^{1}H–^{1}H shift correlation spectroscopy (^{1}H–^{1}H COSY) spectrum of **1** implied connectivities for H_2-1′–H_2-2′ and H_2-1″–H_2-2″. Interpretation of the ^{1}H-detected heteronuclear multiple-bond coherence (HMBC) spectrum revealed correlations from H_2-3 to C-1, C-3a and C-7a; H-7 to C-1 and C-6; H_2-1′ to C-4, C-5 and C-6; H-4′ and H-6′ to C-5′; CH_3-8′ and CH_3-10′ to C-6′; CH_3-9′ to C-2′, C-3′ and C-4′; H_2-1″ to C-3; H_2-2″ to C-4″ and C-8″; and CH_3O-6 to C-6. As a result, C-3′ carbon is linked to an oxygen atom at C-4 to establish a dihydropyran ring. Therefore, the structure of **1** was deduced to be as shown in Fig. 1. Despite the presence of an asymmetric carbon at C-3′, the specific rotation of **1** was almost zero, suggesting its racemic nature. This was proved by chiral reverse-phase HPLC, in which **1** was separated into two peaks in a ratio of 1 : 1 [peak A, (−)-**1**: $[\alpha]_D^{25}$ −16.8° (MeOH); peak B, (+)-**1**: $[\alpha]_D^{26}$ +16.1° (MeOH)], both of which gave ^{1}H-NMR spectra identical to those of the starting material. The circular dichroism (CD) spectra of (+)-**1** and (−)-**1** exhibited mirror images [(+)-**1**: 261.5 nm ($\Delta\varepsilon$ +4.6), 224.0 nm ($\Delta\varepsilon$ −5.2), (−)-**1**: 260.5 nm ($\Delta\varepsilon$ −5.4), 223.1 nm ($\Delta\varepsilon$ +5.2)], confirming their enantiomeric relationship or, in other words, the racemic na-

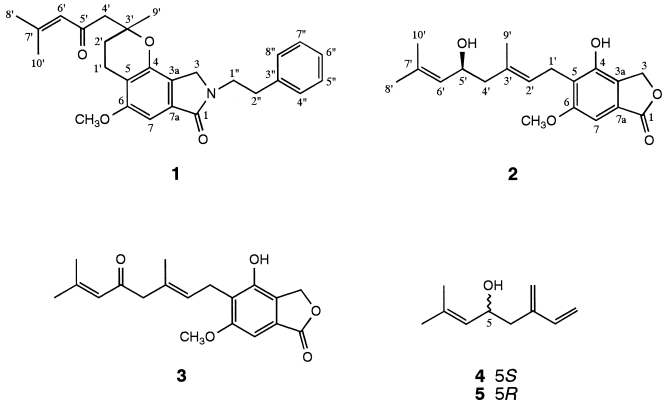

Chart 1

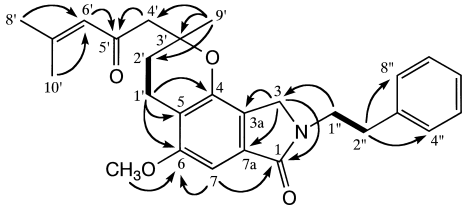

Fig. 1. ^{1}H–^{1}H COSY (Bold Line) and HMBC (Full-Line Arrows) Correlations for **1**

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ture of our initial preparation.

Compound **2**, called erinacerin B, was obtained as an amorphous powder, $[\alpha]_D$ +12.7°. The molecular formula was determined to be $C_{19}H_{24}O_5$ by HR-EI-MS [*m/z* 314 (M^+-H_2O)] and ^{13}C-NMR data. The IR spectrum showed the presence of hydroxyl groups (3383 cm^{-1}), a phthalide (1763 cm^{-1}) and a benzene ring (1603 cm^{-1}). The ^{1}H- and ^{13}C-NMR spectra of **2** were similar to those of **3**, except that the C-5′ carbonyl group in **3** was replaced by a hydroxyl group [δ_H 4.54 (H-5′), δ_C 66.0 (C-5′)][10] in **2**. The position of this hydroxyl group was confirmed by the ^{1}H–^{1}H COSY spectrum, in which H-5′ showed connectivity to H_2-4′ and H-6′. The absolute configuration of the hydroxyl group at C-5′ was determined as *S* by comparing the specific rotation values of **2** [$[\alpha]_D$ +12.7° (MeOH)], (*S*)-(+)-ipsdienol [**4**, $[\alpha]_D$ +15.7° (MeOH)][11] and (*R*)-(−)-ipsdienol [**5**, $[\alpha]_D$ −15.3° (MeOH)].[11] On the basis of the above data, the structure of **2** was represented as shown in the formula.

Experimental

General Procedures Optical rotations were determined using a JASCO DIP-360 digital polarimeter. CD spectra were measured on a JASCO J-720 spectropolarimeter. IR spectra were recorded with a Perkin-Elmer Spectrum One FT-IR spectrophotometer and UV spectra with a Beckman DU-64 spectrophotometer. ^{1}H- and ^{13}C-NMR spectra were recorded on JEOL JNM-LA 600 (600 and 150 MHz, respectively) and JEOL JNM-LA 400 (400 and 100 MHz, respectively) spectrometers. Chemical shifts are given on a δ (ppm) scale, with tetramethylsilane as internal standard. HR-EI-MS were recorded on a JEOL JMS-DX 303 mass spectrometer. Column chromatography was carried out on a Kieselgel 60 (230—400 mesh, Merck). HPLC was carried out on a Tosoh HPLC system (pump, CCPD; detector, RI-8010).

Fungal Material The fresh fruiting bodies of *Hericium erinaceum* (from Sendai, Miyagi Prefecture, Japan) were purchased in a food market.

Extraction and Isolation The fresh fruiting bodies of *H. erinaceum* (1.3 kg) were extracted three times with Et_2O at room temperature for 2 weeks. The Et_2O extract (6.8 g) was chromatographed on a silica gel column using *n*-hexane–EtOAc (7 : 3—1 : 7), EtOAc, and MeOH to afford 32 fractions. Fraction 14 was purified by preparative HPLC [column, TSKgel ODS-120T (7.8 mm i.d.×30 cm, Tosoh), column temperature, 40 °C; mobile phase, MeOH–H_2O (7 : 1); flow rate, 1.0 ml/min] to give **1** (3.6 mg) and **3** (5.0 mg). The separation of **1** into its enantiomers [(−)-**1** (1.2 mg, t_R 14.4 min), (+)-**1** (1.2 mg, t_R 19.2 min)] was achieved by HPLC using a chiral column chromatograph [column, Chiralpak AD-RH (4.6 mm i.d.×15 cm, Daicel Chemical Industries, Ltd.); mobile phase, CH_3CN–H_2O (7 : 3); flow rate, 0.5 ml/min]. Fraction 16 was purified by preparative HPLC [column, TSKgel ODS-120T (7.8 mm i.d.×30 cm, Tosoh), column temperature, 40 °C; mobile phase, MeOH–H_2O (7 : 1); flow rate, 1.0 ml/min] to give **2** (1.6 mg).

Erinacerin A (**1**): Colorless oil. $[\alpha]_D^{21}$ ±0° (*c*=0.4, MeOH). IR ν_{max} ($CHCl_3$) cm^{-1}: 1705, 1680, 1614. UV λ_{max} (MeOH) nm (log ε): 215 (4.6), 244 (4.2), 292 (3.4). HR-EI-MS *m/z*: 433.2237 (M^+, Calcd for $C_{27}H_{31}NO_4$: 433.2253). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.41 (3H, s, CH_3-9′), 1.85 (3H, d, *J*=1.2 Hz, CH_3-8′), 1.90 (1H, ddd, *J*=13.9, 7.1, 6.8 Hz, H-2′a), 2.02 (1H, ddd, *J*=13.9, 6.6, 6.6 Hz, H-2′b), 2.14 (3H, d, *J*=1.2 Hz, CH_3-10′), 2.64 (1H, d, *J*=14.1 Hz, H-4′a), 2.68 (1H, dd, *J*=7.1, 6.6 Hz, H-1′a), 2.69 (1H, dd, *J*=6.8, 6.6 Hz, H-1′b), 2.76 (1H, d, *J*=14.1 Hz, H-4′b), 2.98 (2H, t, *J*=7.6 Hz, H_2-2″), 3.83 (1H, t, *J*=7.6 Hz, H-1″a), 3.84 (1H, t, *J*=7.6 Hz, H-1″b), 3.87 (3H, s, CH_3O-6), 4.11 (1H, d, *J*=16.8 Hz, H-3a), 4.17 (1H, d, *J*=16.8 Hz, H-3b), 6.05 (1H, br s, H-6′), 6.90 (1H, s, H-7), 7.20—7.32 (5H, m, H-4″—H-8″). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 17.4 (C-1′), 20.8 (C-10′), 24.8 (C-9′), 27.8 (C-8′), 30.6 (C-2′), 34.9 (C-2″), 44.4 (C-1″), 48.0 (C-3), 52.3 (C-4′), 55.9 (CH_3O-6), 75.9 (C-3′), 96.2 (C-7), 113.5 (C-5), 121.9 (C-3a), 125.0 (C-6′), 126.5 (C-6″), 128.6, 128.7 (C-4″, C-5″, C-7″, C-8″), 132.2 (C-7a), 138.8 (C-3″), 148.6 (C-4), 155.6 (C-7′), 158.5 (C-6), 168.9 (C-1), 198.1 (C-5′).

(+)-**1**: Colorless oil. $[\alpha]_D^{26}$ +16.1° (*c*=0.1, MeOH). CD λ_{ext} (*c*=2.15×10^{-5} M, MeOH) (nm) ($\Delta\varepsilon$): 261.5 (+4.6), 224.0 (−5.2).

(−)-**1**: Colorless oil. $[\alpha]_D^{25}$ −16.8° (*c*=0.1, MeOH). CD λ_{ext} (*c*=2.06×10^{-5} M, MeOH) (nm) ($\Delta\varepsilon$): 260.5 (−5.4), 223.1 (+5.2).

Erinacerin B (**2**): Amorphous powder. $[\alpha]_D^{24}$ +12.7° (*c*=0.2, MeOH). IR ν_{max} ($CHCl_3$) cm^{-1}: 3383, 1763, 1603. UV λ_{max} (MeOH) nm (log ε): 212 (4.5), 259 (4.0), 296 (3.5). HR-EI-MS *m/z*: 314.1526 (M^+-H_2O, Calcd for $C_{19}H_{22}O_4$: 314.1518). ^{1}H-NMR (600 MHz, $CDCl_3$) δ: 1.71 (3H, d, *J*=1.1 Hz, CH_3-10′), 1.72 (3H, d, *J*=1.5 Hz, CH_3-8′), 1.87 (3H, s, CH_3-9′), 2.21 (1H, dd, *J*=13.6, 4.8 Hz, H-4′a), 2.26 (1H, dd, *J*=13.6, 8.8 Hz, H-4′b), 3.51 (1H, dd, *J*=16.5, 7.7 Hz, H-1′a), 3.58 (1H, dd, *J*=16.5, 6.2 Hz, H-1′b), 3.87 (3H, s, CH_3O-6), 4.54 (1H, dt, *J*=4.8, 8.8 Hz, H-5′), 5.16 (1H, br d, *J*=8.8 Hz, H-6′), 5.20 (2H, s, H_2-3), 5.37 (1H, m, H-2′), 6.97 (1H, s, H-7). ^{13}C-NMR (150 MHz, $CDCl_3$) δ: 16.4 (C-9′), 18.2 (C-10′), 23.3 (C-1′), 25.8 (C-8′), 47.7 (C-4′), 56.2 (CH_3O-6), 66.0 (C-5′), 68.0 (C-3), 98.5 (C-7), 121.1 (C-5), 123.6 (C-2′), 125.1 (C-3a), 127.4 (C-6′), 127.8 (C-7a), 136.1 (C-7′), 137.1 (C-3′), 150.4 (C-4), 159.2 (C-6), 171.7 (C-1).

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References and Notes

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