Albaconol, A Novel Prenylated Resorcinol (= Benzene-1,3-diol) from Basidiomycetes *Albatrellus confluens*

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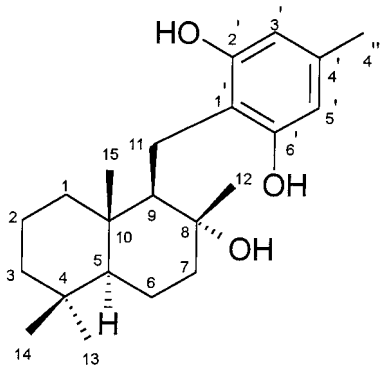
The new substance albaconol (**1**) was isolated along with grifolin (**2**), emeheterone (**3**), and the pyrazinol derivative **4** from the fresh fruiting bodies of the basidiomycetes *Albatrellus confluens*. Structures were established by spectral analysis, including 2D NMR spectroscopy. Albaconol (**1**) possesses the skeleton of a drimane-type sesquiterpenoid, which is directly connected to a resorcinol (= benzene-1,3-diol) moiety; this prenylated resorcinol represents a new C skeleton.

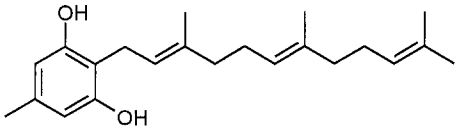
Introduction. – Rapid progress is being made in the area of therapeutic vanilloids in recent years, including the discovery of compounds that are recognized by vannilloid receptors but do not have the homovanillyl moiety. These achievements should provide even more tools for further understanding pain at the molecular level and for the design of new painkillers [1]. The compound scutigeral (**5**), a non-pungent triprenylphenol from *Albatrellus ovinus*, was reported to stimulate rat dorsal-root-ganglion neurons by interaction at vanilloid receptors and to act as an orally active, nonpainful painkiller targeting vanilloid receptors [2]. We have been interested in the biologically active substances present in inedible mushrooms since many of these show bitter and pungent tastes, and especially those belonging to Polyporaceae have been used as medicinal drugs in China from ancient times [3]. Little attention has been paid to the chemical constituents of inedible mushrooms in China. As part of a search for naturally occurring bioactive metabolites of the higher fungi in the Yunnan Province and for analogues of the scutigeral type, the chemical composition of *Albatrellus confluens*, collected at Wudin county, Yunnan Province, was investigated. It was found that the fruiting bodies of the inedible mushroom *Albatrellus confluens* contained high concentrations of albaconol (**1**), a new prenylated resorcinol (= benzene-1,3-diol). The isolation, structure characterization, and biological activity of albaconol (**1**)[1]) are discussed in this report, as well as the isolation of the known compounds grifolin (**2**), emeheterone (**3**), and pyrazinol **4**.

Results and Discussion. – *A. confluens* (dry weight 0.715 kg) was collected at Wudin county, Yunnan Province. Freshly collected entire fruiting bodies were immersed in EtOH and left at room temperature for several days. The extract was then decanted and evaporated and the residue extracted with CH_2Cl_2/MeOH 1:1 (6 times). Repeated chromatography afforded albaconol (**1**; 2.463 g) as colorless crystals and as the major component of the *A. confluens* extracts. The spectral data of **1** resemble those of

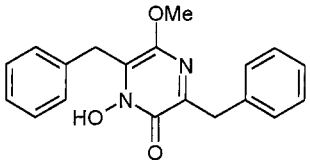
[1]) Trivial numbering; for the systematic name of **1**, see *Exper. Part.*



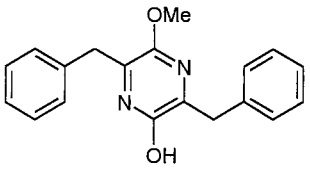
1 albaconal[1])



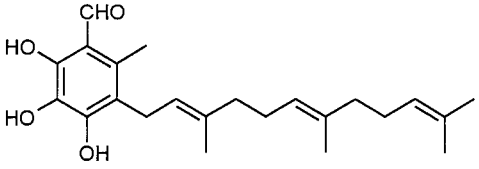
2 grifolin



3 emeheterone



4



5 scutigeral

drimane [4–6], suggesting that it possesses the skeleton of a drimane-type sesquiterpenoid connected directly to a resorcinol moiety. This was confirmed by ^{1}H,^{1}H COSY, HMBC, and HMQC experiments (*Table*).

The high-resolution MS of **1** indicated a molecular formula of $C_{22}H_{34}O_3$ (M^+ 346.2502, calc. 346.2508) and showed a significant peak at *m/z* 328 suggesting loss of H_2O. The ^{1}H-NMR spectrum exhibited 1 D_2O-exchangeable *s* at 8.61 ppm assigned to two phenolic OH groups, 1 *s* of two aromatic protons at 6.09 ppm, and the *s* of an aromatic Me group at 2.08 ppm. The aromatic ring of **1** is thus anchored *via* a methylene moiety, as shown by two benzylic methylene protons resonating at 3.00 (*dd*) and 2.42 ppm (*d*). The presence of a 2-substituted 5-methylbenzene-1,3-diol structure, as suggested by the ^{1}H-NMR spectrum, was confirmed by the ^{13}C-NMR data (see *Table*). In addition to the signals of this partial structure, the ^{13}C-NMR spectrum of **1** showed fifteen signals (3 C, 2 CH, 6 CH_2, 4 Me), including that of a tertiary methyl alcohol moiety (*s* at 75.5 ppm). The latter gave rise to a *s* at 1.28 ppm in the ^{1}H-NMR spectrum and an IR absorption at 3425 cm^{-1}. Three *s* for Me groups at 0.80, 0.84, and 0.96 were also observed, and with no evidence for unsaturation, these results indicated a bicyclic structure. The proton systems, one at C(1) through C(3), one at C(5) through C(7), and another at C(9) through C(11), were established by ^{1}H,^{1}H-COSY and HMQC. The connectivity of these

Table. *^{1}H- and ^{13}C-NMR Data* ((D_6)acetone) *of* **1**. δ in ppm, J in Hz.

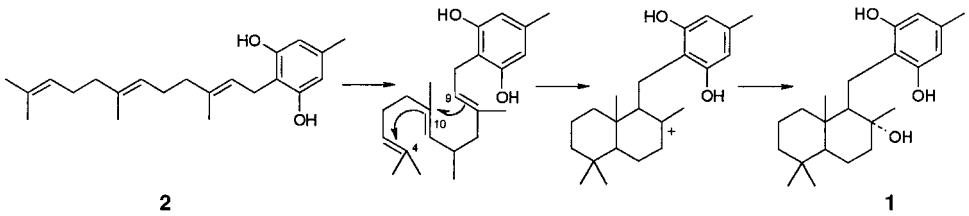
	δ(c) (DEPT)	δ(H)	^{1}H,^{1}H-COSY	HMBC (selected)
CH_2(1)	38.6(CH_2)	2.15 (*m*), 0.55 (*m*)	CH_2(2)	
CH_2(2)	19.0(CH_2)	1.18 (*m*), 1.50 (*m*)	CH_2(1), CH_2(3)	
CH_2(3)	42.7(CH_2)	1.30 (*m*), 1.05 (*m*)	CH_2(2)	
C(4)	30.1(C)			
H–C(5)	57.1(CH)	0.90 (*dd*, J = 12, 1.8)	CH_2(6)	CH_2(3), CH_2(7), H–C(9), Me(13), Me(14), Me(15)
CH_2(6)	21.1(CH_2)	1.63 (*m*), 1.33 (*m*)	H–C(5), CH_2(7)	
CH_2(7)	44.7(CH_2)	1.90 (*m*), 1.62 (*m*)	CH_2(6)	
C(8)	75.5(C)			OH–C(8), H–C(9), CH_2(11), Me(12)
H–C(9)	61.5(CH)	1.60 (*m*)	CH_2(11)	OH–C(8), CH_2(11), Me(12), Me(15)
C(10)	40.0(C)			CH_2(11)
CH_2(11)	18.7(CH_2)	3.00 (*dd*, J = 15, 7.5) 2.42 (*d*, J = 15)	H–C(9)	
Me(12)	24.3(Me)	1.28 (*s*)		
Me(13)	33.8(Me)	0.84 (*s*)		
Me(14)	21.9(Me)	0.80 (*s*)		
Me(15)	15.4(Me)	0.96 (*s*)		
C(1′)	114.2(C)			arom. OH, arom. H, CH_2(11), H–C(9)
C(2′), C(6′)	156.6(C)			arom. OH, arom. H, CH_2(11)
H–C(3′), H–C(5′)	108.6(CH)	6.09 (*s*)		arom. OH, arom. H, Me(4″)
C(4′)	136.6(C)			Me(4″)
Me(4″)	21.1(Me)			
OH–C(2′), OH–C(6′)		8.61 (*s*)		
OH–C(8)		5.07 (*s*)		

three units and the position of the C–C linkage between C(11) and C(1′) as well as the OH group at C(8) were confirmed by a HMBC experiment (*Table*).

Albaconol (**1**), an interesting analogue of the vanilloid-receptor modulators of the scutigeral/grifolin type, was tested in the vanilloid-receptor type 1 models. Unfortunately, no modulation was observed, and further investigations are not planned.

The new compound **1** belongs to a group of prenylated resorcinols, of which most probably arise from rearrangements of the isoprene units of grifolin (**2**) by formation of the ring structure at C(9) and C(10) and at C(4) and C(5) (*Scheme*).

Scheme. *Proposed Biosynthetic Route to Albaconol* (**1**)



2 **1**

Comparison of the physicochemical properties with the reported data allowed to identify compounds **2**–**4**, isolated from same fungus, as grifolin [7][8], emeheterone [9], and a pyrazinol derivative [10], respectively. Compound **4** was reported to promote melanin synthesis by B16 melanoma cells [10].

Experimental Part

General. M.p.: uncorrected. IR: KBr pellets; in cm^{-1}. ^1H- and ^{13}C-NMR: *Bruker AM-400* and *-DRX-500* spectrometers; δ in ppm, J in Hz. MS: *VG Autospec-3000* spectrometer; m/z (rel. int.).

Mushroom Material. The Basidiomycetes *Albatrellus confluens* were collected at Wudin county in Yunnan province, China, in July, 1999. The voucher specimen was deposited at the herbarium of the Kunming Institute of Botany, Chinese Academy of Sciences.

Extraction and Isolation. The entire freshly collected fruiting bodies of *A. confluens* (dry weight 0.715 kg) were immersed in 95% EtOH and left at r.t. for several days. Then the EtOH extract was decanted and evaporated and the residue extracted with CH_2Cl_2/MeOH 1:1 (6 times). The extract (285 g) was fractionated by column chromatography (silica gel, $CHCl_3$/AcOEt 8:2). The combined *Frs. 1–4* were purified by repeated column chromatography (silica gel, petroleum ether/AcOEt 19:1, 9:1) or recrystallization to give pure pyrazinol derivative **4** (20 mg), albaconol (**1**; 2.463 g), emeheterone (**3**; 690 mg), and grifolin (**2**; 14.761 g).

Albaconol (=*2-[[*rel-*(1*R,*2*R,*4a*S,*8a*S)-Decahydro-2-hydroxy-2,5,5,8a-tetramethylnaphthalen-1-yl]methyl]-4-methylbenzene-1,3-diol*; **1**). Colorless crystals. M.p. 212–214° (petroleum ether/acetone) $[\alpha]_D = +63.8$ (c = 0.4, MeOH). IR (KBr): 3425, 3248, 1629, 1580. ^1H- and ^{13}C-NMR: *Table*. HR-EI-MS: 346.2508 ($C_{22}H_{34}O_3^+$, M^+; calc. 346.2502). EI-MS: 346 (10), 328 (80), 313 (12), 191 (80), 175 (55), 137 (100), 109 (20), 95 (30).

Grifolin (=*5-methyl-2-[(2*E,*6*E*)-3,7,11-trimethyldodeca-2,6,10-trienyl]benzene-1,3-diol*; **2**). Colorless needles after recrystallization from hexane. UV, IR, ^1H- and ^{13}C-NMR: identical with those of an authentic specimen.

Emeheterone (=*1-Hydroxy-5-methoxy-3,6-bis(phenylmethyl)pyrazin-2-(1*H*)-one*; **3**). Colorless needles. M.p. 207.5–209° (acetone). IR (KBr): 3400, 1650. ^1H-NMR ($CDCl_3$): 3.93 (*s*, MeO); 3.94 (*s*, CH_2); 4.25 (*s*, CH_2);7.20–7.50 (*m*, 10 H). EI-MS: 322 (3), 305 (92), 290 (10), 277 (12), 117 (40), 91 (100).

5-Methoxy-3,6-bis(phenylmethyl)pyrazin-2-ol (**4**). Yellow needles. M.p. 164–165° (acetone). IR (KBr). 3400, 1650. ^1H-NMR ($CDCl_3$): 4.00 (*s*, MeO); 4.08 (*s*, CH_2); 4.16 (*s*, CH_2); 7.20–7.50 (*m*, 10 H). ^{13}C-NMR ($CDCl_3$): 36.2 (CH_2); 38.3 (CH_2); 54.0 (Me); 126.2 (CH); 126.5 (CH); 128.3 (2 CH); 128.5 (2 CH); 129.1 (2 CH); 129.3 (2 CH); 134.6 (C); 138.1 (C); 138.7 (C); 140.5 (C); 151.3 (C); 153.0 (C). EI-MS (rel. int.): m/z 306 (100), 291 (25), 277 (18), 263 (15), 201 (25), 118 (50), 91 (95).

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