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New Indole Derivatives from the Fruit Bodies of *Tricholoma Sciodes* and *T. Virgatum*

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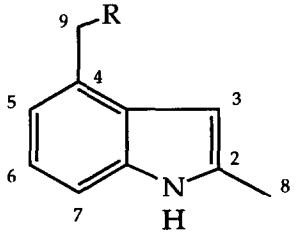
Abstract: The indole derivatives **1-3** were isolated from the fruit bodies of *Tricholoma sciodes* and *T. virgatum*, and their structures were determined by spectroscopy. The compounds are new natural products, although 2,4-dimethylindole (**1**) previously has been prepared synthetically.

Despite their wide occurrence in Nature, species belonging to the genus *Tricholoma* (Basidiomycetes) have been poorly studied in respect to their contents of secondary metabolites.[1] In the course of our respective screening programs of European Basidiomycetes we have investigated the fruit bodies of *T. sciodes* Mart. and *T. virgatum* Kummer, two species that both are considered inedible because of their bitter and acrid taste.[2] TLC analyses of ethyl acetate extracts revealed the presence of several compounds that were not present in other *Tricholoma* species investigated recently.[3,4] Silica gel column and centrifugal radial chromatography afforded the three indole derivatives **1-3** shown in Figure 1.

Figure 1



1 R=H
2 R=OH
3 R=OCH_3

The structure determination of the compounds was based on high resolution mass spectroscopy data, which suggested the elemental composition of the compounds, and on the NMR data which

are summarized in Table 1 (^{1}H NMR and ^{13}C NMR data), as well as in Figure 2 [^{1}H-^{13}C long-range and NOESY correlations for 4-methoxymethyl-2-methylindole (**3**)]. The indoles reported here are new as natural products, although 2,4-dimethylindole (**1**) has been prepared synthetically.[5, 6, 7] However, the spectroscopic data given previously are insufficient for an identification, and a full set of data is therefore given here.

Table 1. ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR data for 2,4-dimethylindole (**1**), 4-hydroxymethyl-2-methylindole (**2**) and 4-methoxymethyl-2-methylindole (**3**). The spectra were recorded in $CDCl_3$, and the solvent signals (7.26 and 77.0 ppm) were used as reference. The coupling constants *J* are given in Hz.

	^{1}H (δ; multiplicity; *J*)			^{13}C (δ; multiplicity)		
	1	**2**	**3**	**1**	**2**	**3**
1	7.82; brs	8.18; brs	7.91; brs	-	-	-
2	-	-	-	134.3; s	135.6; s	135.2; s
3	6.24; m	6.32; m	6.34; m	98.9; d	98.4; d	98.9; d
3a	-	-	-	128.9; s	127.4; s	128.0; s
4	-	-	-	129.1; s	131.4; s	128.8; s
5	6.88; d; 7.2	7.08; d; 7	7.04; d; 7.1	119.8; d	118.3; d	119.3; d
6	7.03; dd; 7, 8	7.12; dd; 7,7	7.08; dd; 7, 8	121.0; d	120.9; d	120.7; d
7	7.13; d; 8.1	7.21; d; 7	7.24; d; 7.8	107.8; d	110.2; d	110.0; d
7a	-	-	-	135.7; s	136.3; s	136.2; s
8	2.45; s	2.38; s	2.45; d; 0.6	13.7; q	13.7; q	13.7; q
9	2.52; s	4.90; s	4.72; s	18.8; q	64.1; t	73.4; t
OCH_3	-	-	3.41; s	-	-	58.0; q

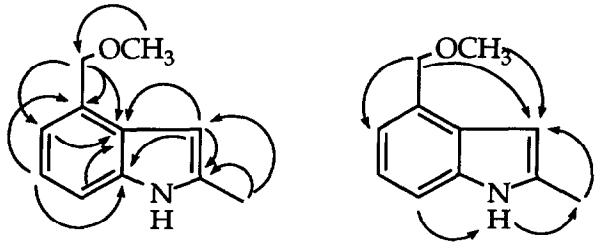
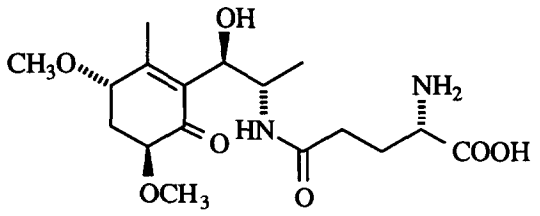


Figure 2. Significant ^{1}H-^{13}C long-range (left) and NOESY (right) correlations for 4-methoxymethyl-2-methylindole (**3**). The corresponding correlations were also observed for 2,4-dimethylindole (**1**) and 4-hydroxymethyl-2-methylindole (**2**).

The indole derivatives found in Basidiomycetes are shikimate metabolites whose biosyntheses involves tryptophan,[1] and they consequently have alkyl substituents on C-3 instead of on C-2 as compounds **1-3**. A possible precursor of the indoles **1-3** is lascivol (**4**), isolated as the bitter principle of the fruit bodies of *T. lascivum*,[8] as lascivol (**4**) yields the 2,4-dimethylindole derivative **5** upon treatment with strong acid.[8]



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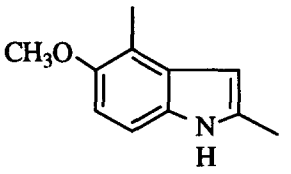

5

Figure 3

The carbon skeleton of compounds **1-3** suggest that they have a unprecedented polyketide origin.

EXPERIMENTAL

Fruit bodies of *Tricholoma sciodes* (Secr.) Mart. were collected in the vicinity of Lund, and extracted on the same day. The fruit bodies were ground in a meat grinder, and the mush was extracted with ethyl acetate (approximately 2 liters per kg fresh mushroom). The organic phase was separated, dried with Na_2SO_4, and the solvent was evaporated. From 1 kg of fresh mushrooms approximately 8 mg of 2,4-dimethylindole (**1**), 38 mg of 4-hydroxymethyl-2-methylindole (**2**), and 80 mg of 4-methoxymethyl-2-methylindole (**3**) were obtained. The fresh fruit bodies of *T. virgatum* were frozen at -20°C, rapidly broken with a hammer and extracted at -20°C with ethyl acetate (4 l/kg). The organic phase was dried with $MgSO_4$ and filtered through a short Al_2O_3 column to remove free fatty acids. Compound **1** was identified by GCMS analysis of the extract, while compounds **2** and **3** were isolated (6 and 8 mg from 1 kg fresh fruit bodies, respectively). The NMR spectra (see Table 1) were recorded with a Bruker ARX500 spectrometer, the UV spectra with a Cary 219, the IR spectra with a Perkin Elmer 257, and the mass spectra with a Jeol SX102 spectrometer.

2,4-Dimethylindole (**1**) was obtained as a yellow oil. UV (ethanol) λ_{max} (ε): 223 nm (19200), 268 nm (4400), 271 nm (4400), 273 nm (4300), 278 nm (2900). IR (KBr): 3380, 2920, 1690, 1610, 1160 and 770 cm^{-1}. For NMR data, see Tables 1 and 2. MS (EI, 70 eV), m/z: 145.0892 (M^+, 67 %, $C_{10}H_{11}N$ requires 145.0891), 144 (100 %), 130 (15 %).

4-Hydroxymethyl-2-methylindole (**2**) was obtained as a yellow oil. UV (ethanol) λ_{max} (ε): 219 nm (22500), 266 nm (4700), 274 nm (5600). IR (KBr): 3360, 2920, 1440, 1420, 1390, 1340, 1290, 1220, 1060, 1000 and 780 cm^{-1}. For NMR data, see Tables 1 and 2. MS (EI, 70 eV), m/z: 161.0842 (M^+, 100 %, $C_{10}H_{11}ON$ requires 161.0840), 144 (71 %), 132 (58 %), 117 (23 %), 101 (33 %), 84 (50 %), 59 (63 %).

4-Methoxymethyl-2-methylindole (**3**) was obtained as a yellow oil. UV (ethanol) λ_{max} (ε): 222 nm (25400), 279 nm (6100). IR (KBr): 3380, 2920, 1620, 1570, 1450, 1420, 1400, 1360, 1300, 1200, 1170, 1100 and 780 cm^{-1}. For NMR data, see Tables 1 and 2. MS (EI, 70 eV), m/z: 175.0999 (M^+, 38 %, $C_{11}H_{13}ON$ requires 175.0997), 159 (10 %), 144 (100 %), 132 (17 %), 130 (21 %).

Acknowledgements

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