Identification and Synthesis of Novel Chlorinated *p*-Anisylpropanoid Metabolites from *Bjerkandera* Species

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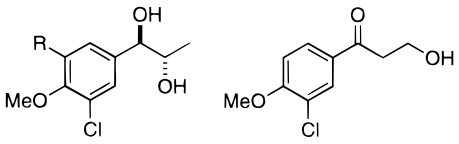
Received April 24, 1998

Analysis of the EtOAc extracts from the culture medium of *Bjerkandera* sp. BOS55 and *B. fumosa* revealed the presence of two novel chlorinated metabolites. Their structures were unambiguously established as *erythro*-1-(3′,5′-dichloro-4′-methoxyphenyl)-1,2-propanediol (**2**) and 1-(3′-chloro-4′-methoxyphenyl)-3-hydroxy-1-propanone (**3**) through synthesis of authentic samples and comparison of retention times and mass spectral data. The production of trametol (**1**) by *Bjerkandera* sp. BOS55 was also a new finding.

Although the majority of the natural organohalogens are metabolites from organisms living in marine environments,[1] several strains of different genera of wood- and forest litter-degrading basidiomycetes are also known to produce a wide variety of organohalogens.[2] White-rot fungi belonging to the genus *Bjerkandera*, for instance, produce in addition to the commonly occurring chlorinated *p*-anisyl metabolites (CAM aldehydes and alcohols),[3−7] also chlorinated 4-hydroxybenzoic acid derivatives,[8] chlorinated hydroquinone derivatives,[6,9] and veratryl chloride.[10]

As part of our continuing search for novel halometabolites from basidiomycetes, a further study on *Bjerkandera* species has recently resulted in the characterization of three other chlorinated compounds not previously reported as metabolites from *Bjerkandera*. In the present paper, we describe the structure elucidation of these compounds and their synthesis. The first chlorinated compound, trametol (**1**), was isolated recently from a fungal strain belonging to the genus *Trametes*.[11] The two other compounds, *erythro*-1-(3′,5′-dichloro-4′-methoxyphenyl)-1,2-propanediol (**2**) and 1-(3′-chloro-4′-methoxyphenyl)-3-hydroxypropan-1-one (**3**), are new organohalogens that have not been previously reported as de novo metabolites, from basidiomycetes or any other living organism.



1: R = H
2: R = Cl

3

Results and Discussion

The two fungal strains studied by us, *Bjerkandera* sp. BOS55 and *B. fumosa*, were cultivated as previously described.[8] When the culture fluid was completely covered by the mycelium (ca. 3 weeks), the culture fluid was filtered and extracted with EtOAc. In addition to the already known halometabolites, GC/MS analysis revealed the presence of two unknown chlorinated compounds in *Bjerkandera* sp. BOS55 and another one in that of *B. fumosa*.

The EIMS of the first unknown compound in the EtOAc extract of *Bjerkandera* sp. BOS55 displayed a molecular ion peak and an isotope peak at *m/z* 216 and 218, respectively, and prominent fragment ion peaks at *m/z* 173, 171, 143, 128, and 108. Thus, the structure of the unknown compound was tentatively assigned as **1** (trametol), a monochlorinated metabolite previously isolated from *Trametes* sp. IPV-F640.[11]

The EIMS of the other unknown compound from *Bjerkandera* sp. BOS55 exhibited a very weak molecular ion peak at *m/z* 250. The prominent fragment ion and two isotope ions at *m/z* 205, 207, and 209, respectively, pointed to the presence of two Cl atoms in the molecule. As with **1**, the main fragmentation sequence was $[M]^{\bullet+} \rightarrow [M - C_2H_5O]^+ \rightarrow [M - C_2H_5O - CO]^+ \rightarrow [M - C_2H_5O - CO - Cl]^{\bullet+}$ resulting in ion peaks at *m/z* 205, 177, and 142, respectively. These mass spectral data suggested that **1** and the unknown metabolite differed only by the presence of an additional aromatic Cl atom in the latter compound. Since metabolites containing the 3,5-dichloro-4-methoxyphenyl unit are commonly produced by *Bjerkandera* species,[5,6,8] the unknown dichlorinated compound was formulated as 1-(3′,5′-dichloro-4′-methoxyphenyl)-1,2-propanediol (**2**).

The appearance of a molecular ion and an isotope ion at *m/z* 214 and 216, respectively, in the EIMS of the unknown metabolite from *B. fumosa* indicated a monochlorinated compound. The fragmentation pattern strongly resembled that of **1**, on the understanding that most of the prominent fragment ion peaks appeared at *m/z* values that were two lower than in the spectrum of **1**. These mass spectral data suggested a trametol-like compound in which the alcohol function at C-1 is oxidized. The loss of H_2O and CH_2O resulting in fragment ions at *m/z* 196 and 184, respectively, further indicated the presence of a primary OH group at C-3.[12] On the basis of these considerations, 1-(3′-chloro-4′-

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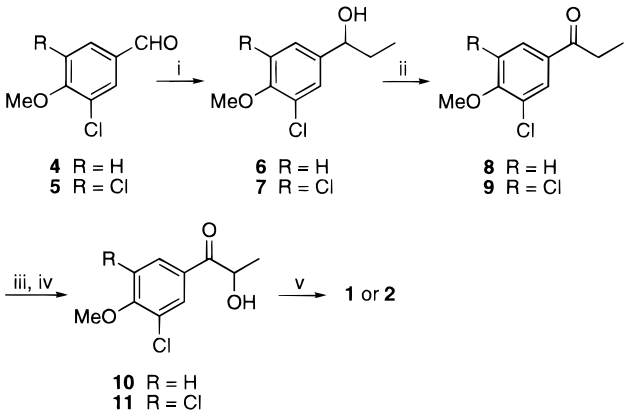
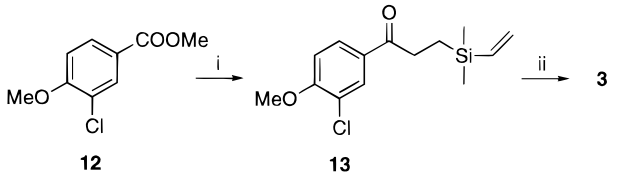
S0163-3864(98)00164-5 CCC: $15.00 © 1998 American Chemical Society and American Society of Pharmacognosy
Published on Web 08/07/1998

Scheme 1[a]



[a] Key: (i) EtMgBr, ether, 0 °C; (ii) PDC, CH_2Cl_2, rt; (iii) TMSCl, Et_3N, rt; (iv) cat. OsO_4, NMMO, acetone, 0 °C; (v) $Zn(BH_4)_2$, ether, 0 °C.

Scheme 2[a]



[a] Key: (i) Mg, I_2, dimethylvinylchlorosilane, *N*-methylpyrrolidinone, rt; (ii) KHF_2, CF_3COOH, CH_2Cl_2, Δ; KF, H_2O_2, MeOH, rt.

methoxyphenyl)-3-hydroxy-1-propanone (**3**) was proposed as the most likely structure for this metabolite.

To establish unambiguously the proposed structures of **1**−**3**, samples of reference material were needed, and this prompted us to prepare the authentic compounds. The reaction sequence outlined in Scheme 1 was followed for the synthesis of **1** and **2**. Treatment of the readily available aldehydes **4**[3] and **5**[5] with EtMgBr followed by oxidation of the adducts (**6** and **7**) with PDC afforded the corresponding 1-aryl-1-propanone derivatives **8** and **9** in overall yields of 68 and 82%, respectively. After oxidation of the trimethylsilyl enol ether of **8** and **9** with OsO_4 in the presence of the *N*-methylmorpholine *N*-oxide (NMMO),[13] the respective α-ketols **10** and **11** were obtained in yields higher than 70%. Reduction of the two α-ketols completed the synthesis of **1** and **2**. In contrast to $NaBH_4$, which gave both the erythro and threo forms,[14] the use of $Zn(BH_4)_2$[15] resulted in the erythro-selective formation of **1** and **2**.[16] GC/MS analysis revealed that these erythro compounds were identical with natural **1** and **2** from *Bjerkandera* sp. BOS55. The erythro configuration has also been reported for trametol isolated from *Trametes* sp. IPV-F640.[11] The possibility that both natural diols possess the threo configuration could be ruled out because GC/MS analysis of the erythro/threo mixtures revealed that the retention times of the threo isomers clearly differed from those of the erythro isomers.

A three-step procedure, recently developed by Prakash et al.,[17] was employed for the synthesis of **3** (Scheme 2). The first step involved a Grignard addition of chlorodimethylvinylsilane to the commercially available methyl 3-chloro-4-methoxybenzoate (**12**) to afford the corresponding vinylsilane **13** in 57% yield. Treatment of **13** with KHF_2 in CF_3COOH and oxidation of the resulting crude silyl fluoride with 30% H_2O_2 in the presence of KF and $KHCO_3$ gave **3** in 70% overall yield, identical in retention time (co-injection) and mass spectral data with the natural product. With the reference compounds available, the concentrations of these natural compounds in the culture fluid were determined by GC analysis using the internal standard quantitation method[18] and were found to be 14, 9, and 16 mg/L for **1**, **2**, and **3**, respectively.

As far as we know, this is the first report of the de novo biosynthesis of **2** and **3** by a fungus or any other living organism. The production of **1** by a *Bjerkandera* species is also a new finding. These chlorinated *p*-anisylpropanoid compounds may undergo cleavage of the C(1)−C(2) bond to give the corresponding CAM aldehydes and alcohols, the most common type of halometabolites produced by *Bjerkandera* species. A similar cleavage has been found during fungal metabolism of lignin model compounds by the white-rot fungi *T. versicolor*[19] and *Phanerochaete chrysosporium*.[20] CAM alcohols play an important role in the ligninolytic system of white-rot fungi as oxidase substrates.[20] Inhibitory,[22] cytostatic, and antifungal activities[23] have been observed for both the dichlorinated aldehyde and alcohol.

Experimental Section

General Experimental Procedures. Melting points were determined on an Olympus HSA melting point apparatus and are uncorrected. All ^1H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Bruker AC-E 200 spectrometer at 200 and 50 MHz, respectively. The chemical shifts are reported in δ (ppm) using TMS as internal standard. ^{13}C NMR assignments marked with an asterisk may be reversed. GC/MS analyses were carried out on an HP5970B quadrupole MS coupled to an HP5890 gas chromatograph equipped with a fused silica capillary column (DB-17, 30 m × 0.25 mm i.d., film thickness: 0.25 μm). Carrier gas and flow: He at 1.1 mL/min. Injector temperature: 220 °C; temperature program: 70−250 °C at 7 °C/min, hold 20 min. Injection volume: 10 μL, split ratio 1:100. EIMS were obtained at 70 eV. HREIMS data of synthesized compounds were determined on a Finnigan EI-MAT95 spectrometer. Elemental analyses were determined on a Carlo Erba elemental analyzer 1106. Chemical reagents were obtained from commercial sources and used directly without further purification. Solvents were dried and freshly distilled by common practice. For all dry reactions, flasks were dried at 150 °C and flushed with dry N_2 just before use, and reactions were carried out under an atmosphere of dry N_2. Product solutions were dried over anhydrous $MgSO_4$, prior to evaporation of the solvent under reduced pressure by using a rotary evaporator. A 0.14 M solution of $Zn(BH_4)_2$ in ether was prepared from 14.0 mL of $ZnCl_2$ (1.0 M in ether) and 1.35 g of $NaBH_4$ according to a previously described procedure.[15]

Starting Materials. 3-Chloro-4-methoxybenzaldehyde (**4**)[3] and 3,5-dichloro-4-methoxybenzaldehyde (**5**)[5] were prepared as described. Methyl 3-chloro-4-methoxybenzoate (**12**) was purchased from Lancaster Synthesis (Mühlheim am Main, Germany).

Biological Material. *Bjerkandera* sp. strain BOS55 was obtained from the Culture Collection of Industrial

Microbiology (CIMW), Agricultural University Wageningen, The Netherlands. *B. fumosa* CBS152.79 was obtained from the Centraalbureau voor Schimmelcultures (CBS), Baarn, The Netherlands. Both fungal strains were cultivated on a defined medium as described.[8]

Extraction and Sample Preparation. Filtration and extraction of the culture fluid were performed as described.[8] After removal of EtOAc under reduced pressure, the remaining residue was redissolved in 0.5 mL of freshly distilled EtOAc containing 52 μg of 4-bromoanisole as the internal standard and then subjected to GC/MS analysis.

Quantitation of Chlorometabolites. After having synthesized **1**−**3** (see below), the concentration of the natural products in the culture fluids was determined by GC analysis using the internal standard quantitation method.[18]

(±)-1-(3′-Chloro-4′-methoxyphenyl)-1-propanol (6). To a stirred solution of 5.1 g (30.0 mmol) of **4** in 100 mL of ether was added dropwise 15 mL (45 mmol) of EtMgBr (3 M in ether) at 0 °C. The reaction mixture was stirred at 0 °C for 30 min and then carefully quenched with 1 M aqueous HCl. After addition of water, the two-phase mixture was separated, and the aqueous layer was extracted with ether. The combined organic layers were washed successively with water, saturated aqueous $NaHCO_3$, and brine. After drying and evaporation, the remaining residue was flash chromatographed [3:1 petroleum ether (bp 40−60 °C)/EtOAc)] to give 5.0 g (83%) of **6** as a colorless oil: ^{1}H NMR δ 7.32 (1H, d, J = 2.1 Hz, H-2′), 7.14 (1H, dd, J = 8.4, 2.1 Hz, H-6′), 6.86 (1H, d, J = 8.4 Hz, H-5′), 4.47 (1H, t, J = 6.6 Hz, H-1), 3.86 (3H, s, COCH_3), 2.14 (1H, br, OH), 1.83−1.59 (2H, m, H_2-2), 0.86 (3H, t, J = 7.4 Hz, H_3-3); ^{13}C NMR δ 154.2 (s, C-4′), 137.8 (s, C-1′), 127.9 (d, C-2′),* 125.3 (d, C-6′),* 122.2 (s, C-3′), 111.8 (d, C-5′), 75.0 (d, C-1), 56.1 (q, COCH$_3$), 31.8 (t, C-2), 10.0 (q, C-3); EIMS m/z 202 $[M + 2]^+$ (2.7), 200 $[M]^+$ (8), 173 (33), 171 (100), 145 (6), 143 (19), 128 (12), 108 (37), 77 (11), 65 (8); HREIMS m/z $[M]^+$ 200.0604 (calcd for $C_{10}H_{13}ClO_2$, 200.0604); *anal.* C 60.03%, H 6.74%, calcd for $C_{10}H_{13}ClO_2$, C 59.85%, H 6.53%.

(±)-1-(3′,5′-Dichloro-4′-methoxyphenyl)-1-propanol (7). The same procedure applied on 9.4 g (46.1 mmol) of **5** afforded 9.14 g (85%) of **7** as a colorless oil: ^{1}H NMR δ 7.22 (2H, s, H-2′, H-6′), 4.48 (1H, dt, J = 6.6, 3.0 Hz, H-1), 3.85 (3H, s, COCH_3), 2.36 (1H, d, J = 3.0 Hz, OH), 1.80−1.58 (2H, m, H_2-2), 0.89 (3H, t, J = 7.4 Hz, H_3-3); ^{13}C NMR δ 151.0 (s, C-4′), 142.3 (s, C-1′), 129.1 (s, C-3′, C-5′), 126.4 (d, C-2′, C-6′), 74.5 (d, C-1), 60.7 (q, COCH$_3$), 31.8 (t, C-2), 9.9 (q, C-3); EIMS m/z 238 $[M + 4]^+$ (1.3), 236 $[M + 2]^+$ (7.5), 234 $[M]^+$ (12), 209 (11), 207 (63), 205 (100), 177 (12), 162 (17), 142 (78), 99 (17); HREIMS m/z $[M]^+$ 234.0212 (calcd for $C_{10}H_{12}Cl_2O_2$, 234.0214); *anal.* C 51.47%, H 5.44%, calcd for $C_{10}H_{12}Cl_2O_2$, C 51.08%, H 5.14%.

1-(3′-Chloro-4′-methoxyphenyl)-1-propanone (8). To a stirred solution of 4.5 g (22.5 mmol) of **6** in 100 mL of CH_2Cl_2 was added 9.3 g (24.8 mmol) of PDC. After being stirred at 25 °C overnight, the reaction mixture was filtered over a short pad of Hyflo. The filtrate was concentrated under reduced pressure and flash chromatographed [9:1 petroleum ether (bp 40−60 °C)/EtOAc)] to give 3.65 g (82%) of **8** as a white solid: mp 91−92 °C (lit.[24] mp 88−90 °C); ^{1}H NMR δ 7.99 (1H, d, J = 2.2 Hz, H-2′), 7.87 (1H, dd, J = 8.6, 2.2 Hz, H-6′), 6.95 (1H, d, J = 8.6 Hz, H-5′), 3.95 (3H, s, COCH_3), 2.93 (2H, q, J = 7.2 Hz, H_2-2), 1.20 (3H, t, J = 7.2 Hz, H_3-3); ^{13}C NMR δ 198.5 (s, C-1), 158.6 (s, C-4′), 130.5 (s, C-1′), 130.4 (d, C-2′),* 128.4 (d, C-6′),* 122.8 (s, C-3′), 111.2 (d, C-5′), 56.4 (q, COCH$_3$), 31.5 (t, C-2), 8.3 (q, C-3); EIMS m/z 200 $[M + 2]^+$ (3.4), 198 $[M]^+$ (11), 171 (31), 169 (100), 141 (7), 126 (12), 111 (8), 98 (4), 77 (10) 63 (9); HREIMS m/z $[M]^+$ 198.0446 (calcd for $C_{10}H_{11}ClO_2$, 198.0448); *anal.* C 60.42%, H 5.54%, calcd for $C_{10}H_{11}ClO_2$, C 60.46%, H 5.58%.

1-(3′,5′-Dichloro-4′-methoxyphenyl)-1-propanone (9). The same procedure applied on 8.5 g (36.3 mmol) of **7** afforded 8.2 g (97%) of **9** as a white solid: mp 65−66 °C (lit.[25] mp 90 °C); ^{1}H NMR δ 7.87 (2H, s, H-2′, H-6′), 3.94 (3H, s, COCH_3), 2.92 (2H, q, J = 7.2 Hz, H_2-2), 1.20 (3H, t, J = 7.2 Hz, H_3-3); ^{13}C NMR δ 197.5 (s, C-1), 155.9 (s, C-4′), 133.7 (s, C-1′), 129.8 (s, C-3′, C-5′), 128.7 (d, C-2′, C-6′), 60.9 (q, COCH$_3$), 31.7 (t, C-2), 8.0 (q, C-3); EIMS m/z 236 $[M + 4]^+$ (1.5), 234 $[M + 2]^+$ (9), 232 $[M]^+$ (15), 207 (11), 205 (64), 203 (100), 160 (10), 145 (8), 111 (15), 97 (13); HREIMS m/z $[M]^+$ 232.0052 (calcd for $C_{10}H_{10}Cl_2O_2$, 232.0058); *anal.* C 51.26%; H 4.30%, calcd for $C_{10}H_{10}Cl_2O_2$, C 51.52%, H 4.32%.

(±)-1-(3′-Chloro-4′-methoxyphenyl)-2-hydroxy-1-propanone (10). To a stirred solution of 400 mg (2.0 mmol) of **8** in 5 mL of MeCN was added successively 1.12 mL (8.0 mmol) of Et_3N, 1.02 mL (8.0 mmol) of TMSCl, and 1.20 g (8.0 mmol) of NaI. After being stirred at 25 °C overnight, the reaction mixture was diluted with 50 mL of petroleum ether (bp 40−60 °C), and then 4 mL of pyridine was added. The organic layer was washed with saturated aqueous $NaHCO_3$, dried, and evaporated to give 480 mg of a yellow oil. A solution of this oil in 3 mL of Me_2CO was added dropwise to an ice-cold mixture of 4 mL of water and 9 mL of Me_2CO containing 0.5 mL (0.04 mmol) of OsO_4 (2.5 wt % solution in 2-methyl-2-propanol) and 258 mg (2.2 mmol) of *N*-methylmorpholine *N*-oxide. The reaction mixture was stirred at 0 °C for 2 h, and then $NaHSO_3$ (0.35 g) and Florisil (1.35 g) were added. The resulting mixture was stirred for an additional 5 min and filtered. The pH of the filtrate was adjusted to 7 with 1 M aqueous H_2SO_4, and then Me_2CO was removed under reduced pressure. The remaining aqueous layer was acidified to pH 2, saturated with NaCl, and extracted with EtOAc. The combined organic layers were dried and evaporated, and the remaining residue was flash chromatographed [5:1 petroleum ether (bp 40−60 °C)/EtOAc)] to give 333 mg (78%) of **10** as a colorless oil that solidified on standing: mp 70−71 °C; ^{1}H NMR δ 7.97 (1H, d, J = 2.2 Hz, H-2′), 7.84 (1H, dd, J = 8.6, 2.2 Hz, H-6′), 6.99 (1H, d, J = 8.6 Hz, H-5′), 5.07 (1H, dq, J = 7.0, 6.5 Hz, H-2), 3.98 (3H, s, COCH_3), 3.73 (1H, d, J = 6.5 Hz, OH), 1.43 (3H, d, J = 7.0 Hz, H_3-3); ^{13}C NMR δ 200.0 (s, C-1), 159.4 (s, C-4′), 130.9 (d, C-2′),* 129.2 (d, C-6′),* 126.7 (s, C-1′), 123.3 (s, C-3′), 111.5 (d, C-5′), 69.0 (d, C-2), 56.5 (q, COCH$_3$), 22.5 (q, C-3); EIMS m/z 216 $[M + 2]^+$ (0.6), 214 $[M]^+$ (1.8), 171 (40), 169 (100), 141 (6), 126 (11), 111 (7), 77 (10), 63 (9), 45 (9); HREIMS m/z $[M]^+$ 214.0397 (calcd for $C_{10}H_{11}ClO_3$, 214.0397);

anal. C 55.71%; H 5.09%, calcd for $C_{10}H_{11}ClO_3$, C 55.95%, H 5.17%.

(±)-1-(3′,5′-Dichloro-4′-methoxyphenyl)-2-hydroxy-1-propanone (11). The same procedure applied on 232 mg (1.0 mmol) of **9** afforded 175 mg (71%) of **11** as a colorless oil that solidified on standing: mp 48−49 °C; ^{1}H NMR δ 7.84 (2H, s, H-2′, H-6′), 5.04 (1H, q, J = 7.0 Hz, H-2), 3.95 (3H, s, COCH_3), 3.61 (1H, br, OH), 1.42 (3H, d, J = 7.0 Hz, H_3-3); ^{13}C NMR δ 199.5 (s, C-1), 156.8 (s, C-4′), 130.3 (s, C-1′),* 130.2 (s, C-3′, C-5′),* 129.4 (d, C-2′, C-6′), 69.4 (d, C-2), 61.0 (q, COCH$_3$), 22.1 (q, C-3); EIMS m/z 250 [M + 2]$^+$ (0.7), 248 [M]$^+$ (1.2), 207 (29), 205 (96), 203 (100), 162 (14), 142 (31), 111 (19), 97 (21), 45 (29); HREIMS m/z [M]$^+$ 248.0001 (calcd for $C_{10}H_{10}Cl_2O_3$, 248.0007); *anal*. C 48.35%; H 4.06%, calcd for $C_{10}H_{10}Cl_2O_3$, C 48.21%, H 4.05%.

(±)-*erythro*-1-(3′-Chloro-4′-methoxyphenyl)-1,2-propanediol [(±)-Trametol] (1). To a stirred solution of 54 mg (0.25 mmol) of **10** in 4 mL of ether was added dropwise 1.0 mL (0.14 mmol) of $Zn(BH_4)_2$ (0.14 M in ether) at 0 °C. After being stirred at 0 °C for 30 min, the reaction mixture was quenched with a few drops of water. Stirring was continued for an additional 30 min, and then anhydrous $MgSO_4$ was added. After filtration and evaporation of the solvent under reduced pressure, the remaining residue was flash chromatographed [1:1 petroleum ether (bp 40−60 °C)/EtOAc)] to give 52 mg (95%) of **1** as a white solid: mp 117−118 °C (lit.[11] (−)-**1** mp 74 °C); ^{1}H NMR spectrum was as previously reported for (−)-**1**;[11] ^{13}C NMR δ 154.5 (s, C-4′), 133.4 (s, C-1′), 128.5 (d, C-2′),* 126.1 (d, C-6′),* 122.3 (s, C-3′), 111.7 (d, C-5′), 76.4 (d, C-1), 71.1 (d, C-2), 56.2 (q, COCH$_3$), 17.2 (q, C-3); EIMS m/z 218 [M + 2]$^+$ (0.7), 216 [M]$^+$ (2), 173 (34), 171 (100), 143 (16), 128 (9), 108 (32), 77 (11), 65 (9), 45 (7); HREIMS m/z [M]$^+$ 216.0552 (calcd for $C_{10}H_{13}ClO_3$, 216.0553).

(±)-*erythro*-1-(3′,5′-Dichloro-4′-methoxyphenyl)-1,2-propanediol (2). The same procedure applied on 54 mg (0.22 mmol) of **11** afforded 53 mg (97%) of **2** as a white solid: mp 100−102 °C; ^{1}H NMR δ 7.25 (2H, s, H-2′, H-6′), 4.56 (1H, d, J = 4.0 Hz, H-1), 3.94 (1H, dq, J = 6.3, 4.0 Hz, H-2), 3.85 (3H, s, COCH_3), 2.78 (2H, br, 2 × OH), 1.02 (3H, d, J = 6.3 Hz, H_3-3); ^{13}C NMR δ 151.3 (s, C-4′), 138.0 (s, C-1′), 129.1 (s, C-3′, C-5′), 127.0 (d, C-2′, C-6′), 75.9 (d, C-1), 70.9 (d, C-2), 60.7 (q, COCH$_3$), 17.1 (q, C-3); EIMS m/z 252 [M + 2]$^+$ (0.4), 250 [M]$^+$ (0.7), 209 (11), 207 (54), 205 (87), 191 (37), 177 (18), 142 (100), 99 (36), 45 (40); HREIMS m/z [M]$^+$ 250.0158 (calcd for $C_{10}H_{12}Cl_2O_3$, 250.0164); *anal*. C 47.55%; H 4.72%, calcd for $C_{10}H_{12}Cl_2O_3$, C 47.83%, H 4.82%.

[3-(3′-Chloro-4′-methoxyphenyl)-3-oxo]propyldimethylvinylsilane (13). A mixture of 1.21 g (50.0 mmol) of Mg powder, 0.2 g (0.8 mmol) of I_2, and 23.5 g (200 mmol) of chlorodimethylvinylsilane in 50 mL of *N*-methylpyrrolidinone was stirred at 25 °C for 5 min, after which time 5.0 g (25.0 mmol) of methyl 3-chloro-4-methoxybenzoate (**12**) was added in small portions. The reaction mixture was stirred at 25 °C overnight and then quenched with diluted aqueous NH_4Cl. After extraction with EtOAc, the combined organic layers were washed with saturated aqueous $NaHCO_3$, dried, and evaporated. The remaining residue was flash chromatographed [30:1 petroleum ether (bp 40−60 °C)/EtOAc)] to give 4.02 g (57%) of **13** as a light yellow oil: ^{1}H NMR δ 7.94 (1H, d, J = 2.1 Hz, C-2′), 7.82 (1H, J = 8.6, 2.1 Hz, H-6′), 6.94 (1H, J = 8.6 Hz, C-5′), 6.14 (1H, dd, J = 19.4, 14.6 Hz, Si−CH=CH$_2$), 5.95 (1H, dd, J = 14.6, 4.8 Hz, Si−CH=CH_{cis}), 5.69 (1H, dd, J = 19.4, 4.8 Hz, Si−CH=CH_{trans}), 3.93 (3H, s, COCH_3), 2.88−2.80 (2H, m, H_2-2), 0.97−0.89 (2H, m, H_2-3), 0.09 (6H, s, Si(CH_3)$_2$); ^{13}C NMR δ 198.7 (s, C-1), 158.5 (s, C-4′), 138.1 (d, SiCH=C), 132.4 (t, SiC=CH$_2$), 130.4 (d, C-2′),* 130.3 (s, C-1′), 128.4 (d, C-6′),* 122.7 (s, C-3′), 111.2 (d, C-5′), 56.3 (q, COCH$_3$), 32.7 (t, C-2), 9.6 (t, C-3), −3.5 (q, Si(CH$_3$)$_2$); EIMS m/z 284 [M + 2]$^+$ (1.7), 282 [M]$^+$ (4.9), 281 (13), 267 (93), 255 (84), 169 (97), 146 (34), 85 (100), 75 (29), 59 (77); HREIMS m/z [M]$^+$ 282.0841 (calcd for $C_{14}H_{19}ClO_2Si$, 282.0843); *anal*. C 59.39%; H 7.08%, calcd for $C_{14}H_{19}ClO_2Si$, C 59.47%, H 6.77%.

1-(3′-Chloro-4′-methoxyphenyl)-3-hydroxy-1-propanone (3). To a solution of 3.63 g (12.9 mmol) of **13** in a mixture of 25 mL of CH_2Cl_2 and 16 mL of CF_3COOH was added 2.0 g (25.3 mmol) of KHF_2. The reaction mixture was refluxed for 2.5 h, allowed to come to 25 °C, and then poured into ice−water. After extraction with petroleum ether (bp 40−60 °C), the combined organic layers were washed with saturated aqueous $NaHCO_3$, dried, and evaporated to give 3.1 g of the crude silyl fluoride as a yellow oil: HREIMS m/z [M − 15]$^+$ 259.0348 (calcd for $C_{11}H_{13}ClFO_2Si$, 259.0357). To a stirred solution of this crude silyl fluoride in 50 mL of a 1:1 mixture of MeOH and THF were added successively 1.27 g (21.9 mmol) of KF, 1.0 g (11.9 mmol) of $NaHCO_3$, and 2.86 mL (32.7 mmol) of 35% H_2O_2. After being stirred at 25 °C overnight, the reaction mixture was cooled to 0 °C and quenched with diluted aqueous $NaHSO_3$. After filtration, the aqueous mixture was extracted with ether, and the combined organic layers were washed with saturated aqueous $NaHCO_3$, dried, and evaporated. The remaining residue was crystallized from a 9:1 mixture of petroleum ether (bp 40−60 °C) and EtOAc, respectively, to give 1.93 g (70%) of **3** as white needles: mp 77−78 °C; ^{1}H NMR δ 7.98 (1H, d, J = 2.2 Hz, H-2′), 7.86 (1H, dd, J = 8.6, 2.2 Hz, H-6′), 6.96 (1H, d, J = 8.6 Hz, H-5′), 3.99 (2H, t, J = 5.2 Hz, H_2-2), 3.96 (3H, s, COCH_3), 3.14 (2H, t, J = 5.2 Hz, H_2-3), 2.63 (1H, br, OH); ^{13}C NMR δ 198.1 (s, C-1), 159.1 (s, C-4′), 130.4 (d, C-2′),* 130.2 (s, C-1′), 128.6 (d, C-6′),* 123.0 (s, C-3′), 111.3 (d, C-5′), 58.1 (t, C-3), 56.4 (q, COCH$_3$), 40.0 (t, C-2); EIMS m/z 216 [M + 2]$^+$ (2.4), 214 [M]$^+$ (7.7), 196 (12), 184 (5), 169 (100), 141 (7), 126 (12), 111 (8), 77 (17), 63 (14); HREIMS m/z [M]$^+$ 214.0399 (calcd for $C_{10}H_{11}ClO_3$, 214.0397); *anal*. C 55.77%; H 5.17%, calcd for $C_{10}H_{11}ClO_3$, C 55.95%, H 5.17%.

Acknowledgment. This project was financially supported by the Technology Foundation, Utrecht, The Netherlands, under project no. WLM33.3127, entitled "Fungal Chlorinated Aromatic Metabolites: Natural Priority Pollutants and Dioxin Precursors in the Environment". The authors are grateful to Dr. O. Vajna de Pava from the Dipartimento di Chimica del Politecnico di Milano, Italy, for the gift of a sample of (−)-trametol (**1**).

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NP980164H