

The metabolites of *Trichoderma longibrachiatum*. Part II. The structures of trichodermolide and sorbiquinol

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Abstract: *Trichoderma longibrachiatum* Rifai aggr. is a fungus reported to be antagonistic to the fungus *Mycena citricolor*, the causative agent of the American leaf spot disease of coffee. We have investigated the metabolites produced when *T. longibrachiatum* is grown in liquid culture and have isolated several new compounds. The structures of trichodermolide (**2**) and sorbiquinol (**3**) were determined by a combination of spectroscopic techniques, including ^1H and ^{13}C NMR, IR, UV, CD, ORD, and mass spectrometry, and by preparation of derivatives.

Key words: *Trichoderma longibrachiatum*, leaf spot disease, coffee, fungal metabolites.

Résumé : Le *Trichoderma longibrachiatum* Rifai aggr. est un champignon qui serait l'antagoniste du champignon *Mycena citricolor*, l'agent qui serait la cause de la maladie des taches sur les feuilles du café américain. On a étudié les métabolites produits lorsqu'on fait une culture liquide du *T. longibrachiatum* et on a isolé plusieurs nouveaux composés. On a déterminé les structures du trichodermolide (**2**) et du sorbiquinol (**3**) par une combinaison de techniques spectroscopiques, y compris la RMN du ^1H et du ^{13}C , l'IR, l'UV, le DC, la DRO et la spectrométrie de masse, ainsi que par la préparation de dérivés.

Mots clés : *Trichoderma longibrachiatum*, maladie des taches sur les feuilles, café, métabolites de champignons.

[Traduit par la rédaction]

Introduction

In part 1 of this series (1), we described the isolation of several metabolites from liquid cultures of *Trichoderma longibrachiatum*, Rifai aggr. The studies leading to the assignment of structure **1** to trichodimerol, an intrinsically interesting natural product that possesses an axis of symmetry, were described. In this article we present evidence for the structural assignment of two other interesting new natural products produced by the fungus, the pale yellow compounds trichodermolide (**2**) and sorbiquinol (**3**).

Results and discussion

Trichodermolide (**2**) is a pale yellow, optically active glass showing maximum ultraviolet (UV) absorption at 280 nm. The molecular formula $\text{C}_{24}\text{H}_{28}\text{O}_5$ was determined by high-resolution mass spectrometry (HREIMS) and the molecular weight was confirmed by chemical ionization mass spectrometry (CIMS). The base peak in the electron impact mass spectrum (m/z 95) arises from fragmentation of the sorbyl chains ($\text{H}_7\text{C}_5\text{CO}^+$). The spectrum also shows a $M^+ - 95$ peak and a peak at m/z 352 corresponding to the loss of CO_2 (lactone carbon and oxygens). The infrared spectrum (IR) shows absorption at 1781 cm^{-1} (γ -lactone) and at 1687 and 1637 cm^{-1} (α,β -unsaturated ketone).

The ^1H NMR spectrum of trichodermolide (**2**) in CDCl_3 shows three methyl singlets (δ 1.78, 1.45, and 1.24), and an AB quartet at δ 3.66 ($J = 19\text{ Hz}$) arising from the C-7 methylene group, an isolated three-hydrogen spin system at δ 2.45 (dd, 18.5 and 4 Hz), 3.26 (dd, 18.5 and 6 Hz), and 3.34 (dd, 4 and 6 Hz) for the C-14 methylene hydrogens and the C-5 methine hydrogen, respectively. Signals for the two *E,E*-sorbyl chains are readily apparent. When the spectrum is recorded in benzene the C-7 methylene signals split into clear doublets at δ 3.02 and 3.19 ($J = 17\text{ Hz}$). The large geminal coupling constants observed for the C-7 and C-14 methylene hydrogens are consistent with their location α to carbonyl groups (**2**).

The ^{13}C NMR spectrum of trichodermolide (**2**) (Table 1) shows 24 carbons: 5 methyl carbons, 2 methylene carbons, 1 sp^3 methine carbon (C-5, δ 56.0), 1 sp^3 quaternary carbon (C-4, δ 51.8), a tertiary carbon bearing oxygen (C-6, δ 87.2), 8 sp^2 carbons as doublets, 2 olefinic carbons as singlets, and 4 carbonyl carbons (δ 176.1 (lactone), 191.2, 195.5, and 196.6).

The molecular formula for trichodermolide indicates 11 unsaturations. Two sorbyl chains account for six, the lactone for two, the unsaturated ketone for two, and thus there is only one carbocyclic ring. The functionality described accounts for all five oxygens. A series of NOE experiments (in CDCl_3) served to further define structure **2**. The methine hydrogen at C-5 (δ 3.34) shows strong NOE enhancement with the methylene hydrogen at δ 2.45 (one H-14) and the methyls at δ 1.45 and 1.24. The methyl hydrogens at δ 1.24 (H-22) also show NOE enhancement with the methylene hydrogen at δ 3.26 (an H-14) and the methylene at δ 3.66 (H-7). The methylene at δ 3.66 in turn gives reciprocal enhancement with the alkenic methyl (H-21) at δ 1.76 as well as with two hydrogens (δ 6.15 and 7.24) of one of the sorbyl chains. The C-14 methylene

Received November 14, 1995.

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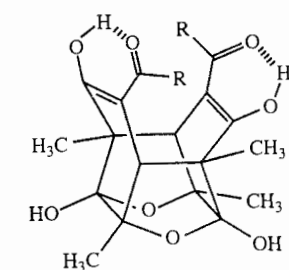
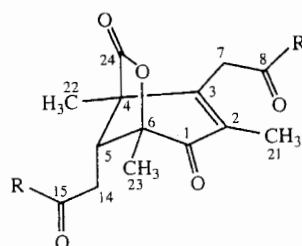
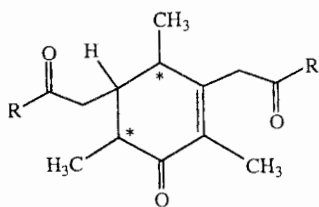
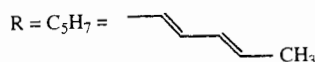
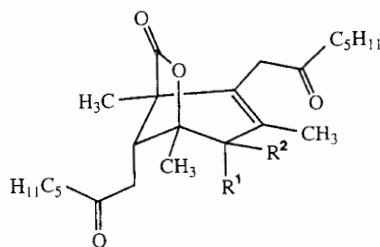
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hydrogens (δ 3.26 and 2.45) give strong mutual enhancement as well as enhancement of hydrogens of the other sorbyl chain (δ 6.10 and 7.20).

These data define the constitution of trichodermolide as shown in structure **4** where the starred carbon atoms indicate the points of attachment of the lactone ring. It was now necessary to determine the orientation of the lactone ring, i.e., whether the lactone carbonyl carbon is attached to C-4 or to C-6. The selective INEPT technique (3) was used to locate the carbonyl carbon. The NOE results above indicate that the methyl group at C-4 resonates at δ 1.24, that at C-6 at δ 1.45. Selective Irradiation of the δ 1.24 hydrogens (CH_3 at C-4) gives rise to signals for the carbons at δ 51.8 (C-4), 148.6 (C-3), and the lactone carbonyl carbon (δ 176.1). Irradiation of the

methyl hydrogens at δ 1.45 (CH_3 at C-6) gives signals for the carbons at δ 87.2 (C-6) and δ 191.2 (C-1). The carbon at δ 56.0 (C-5) was not enhanced in either experiment although it should be coupled ($^3J_{\text{CH}}$) to both methyls. The absence of enhancement may be due to the passive modulation of the carbon by the one-bond C—H coupling (4). Final confirmation of the ring substructure of trichodermolide was obtained from the HMBC spectrum, which showed the correlations (C/H's): 1/21, 23; 2/7, 21; 3/7, 21, 22; 4/7, 14, 22; 5/14, 22, 23; 6/5, 14, 23. The HMBC correlations 8/7, and 15/5, 14 assigned the carbonyl signals at 195.5 and 196.6 to C-8 and C-15, respectively. These results establish structure **2** (other than the stereochemistry at C-5) for trichodermolide.

Additional information on the stereochemistry of trichoder-

**1****2** R = C₅H₇**5** R = *n*-C₅H₁₁**4****6a** R¹ = OH, R² = H**6b** R¹ = H, R² = OH**7a** R¹ = OAc, R² = H**7b** R¹ = H, R² = OAc

molide was obtained by the preparation of several derivatives. Hydrogenation over palladium on carbon produced an octahydro derivative (**5**), as confirmed by the HREIMS and CIMS. The IR (1782, 1715, and 1688 cm⁻¹) and UV (272 nm) spectra of octahydrotrichodermolide (**5**) indicated that the enone had resisted reduction.

Octahydrotrichodermolide (**5**) was selectively reduced with excess sodium borohydride in methanol for a short time to produce a mixture of epimeric alcohols, **6a** and **6b**. These could be separated through careful column chromatography. Neither epimer shows strong absorption in their UV spectra, indicating the enone was reduced. The IR spectra of both epimers show absorption for an alcohol (3460 and 3450 cm⁻¹)

while their ¹H NMR spectra show the presence of two hexanoyl side chains.

α -Decahydrotrichodermolide (**6a**) was acetylated by treatment with acetic anhydride to give the corresponding *O*-acetyl- α -decahydrotrichodermolide (**7a**). The introduction of an acetyl group in **7a** caused the expected shifts in its ¹H NMR spectrum when compared to the ¹H NMR spectrum of **6a**. Comparison of the ¹H NMR chemical shifts reveals that H-1 is shifted downfield from δ 3.71 in **6a** to δ 5.55 in **7a**, which is expected for a secondary alcohol (5), and that Me-23 and Me-21 are shifted upfield from δ 1.46 and 1.69 in **6a** to δ 1.35 and 1.53 in **7a** (0.11 and 0.16 ppm, respectively). Similarly, β -decahydrotrichodermolide (**6b**) was acetylated with acetic

Table 1. ^{13}C NMR data of trichodermolide (**2**), octahydrotrichodermolide (**5**), α -decahydrotrichodermolide (**6a**), *O*-acetyl- α -decahydrotrichodermolide (**7a**), anhydrodecahydrotrichodermolide (**9**), and compound **10** (CDCl_3 , 75.5 MHz).

Carbon	Chemical shift in δ (ppm ^{a,b})					
	2 ^c	5 ^c	6a ^c	7a ^c	9 ^c	10
1	191.2	191.1	73.7	72.5	130.2a	
2	134.2	134.1	132.2	132.0	132.0	131.0a
3	148.6	149.6	128.0	129.6	130.5	135.4a
4	51.8	51.5	48.8	48.5	52.9	135.8a
5	56.0	55.6	46.6	46.6	49.6	—
6	87.2	86.9	84.3	83.4	77.1	—
7	35.1	37.1	37.2	37.1	33.1	44.9
8	195.5	206.9 ^a	208.2 ^a	208.2 ^a	206.9	208.9
9	129.9 ^a	43.0 ^b	42.4 ^b	42.4 ^b	42.1	42.0
10	144.1 ^b	23.6 ^c	23.4	23.3 ^c	23.4	23.4
11	124.4 ^c	29.7 ^d	31.4	31.3	31.3 ^a	31.4
12	141.5 ^b	22.4 ^e	22.5	22.4	22.5	22.4
13	18.9	13.9	14.0	13.9	13.9 ^b	13.9
14	42.0	44.3	43.2	43.2	92.9	—
15	196.6	207.5 ^a	209.7 ^a	209.9 ^a	153.8	—
16	130.2 ^a	43.2 ^b	42.7 ^b	42.7 ^b	49.6	—
17	144.8 ^b	23.4 ^c	23.4	23.6 ^c	26.8	—
18	126.9 ^c	31.3 ^d	31.4	31.4	31.4 ^a	—
19	142.4 ^b	22.4 ^e	22.5	22.5	22.5	—
20	18.9	13.9	13.9	13.9	14.1 ^b	—
21	11.6	11.5	20.4	20.8 ^d	20.2	20.6
22	16.2	16.1 ^f	16.2 ^c	15.7	17.2 ^c	16.7
23	16.2	16.3 ^f	15.7 ^c	15.6	15.6 ^c	—
24	176.1	176.0	177.7	177.0	178.5	—
CO	—	—	—	169.6	—	—
Me	—	—	—	19.7 ^d	—	—

^aThe assignments of the signals with the same superscript in the same column are interchangeable.

^bRelative to the carbon of the solvent (77.0 for CDCl_3).

^cMultiplicity from APT.

^dNot observed.

anhydride to give *O*-acetyl- β -decahydrotrichodermolide (**7b**). The introduction of the acetyl group causes shifts similar to the shifts in the ^1H NMR spectrum of **6a** discussed above. These results are consistent with these methyls being α to the alcohol (for a similar example in aromatic systems, see ref. 6) in **6a** and **6b** and show that the enone is reduced selectively.

To determine the relative stereochemistry of the two isomers formed we attempted acid-catalyzed formation of the cyclic acetal **8**.

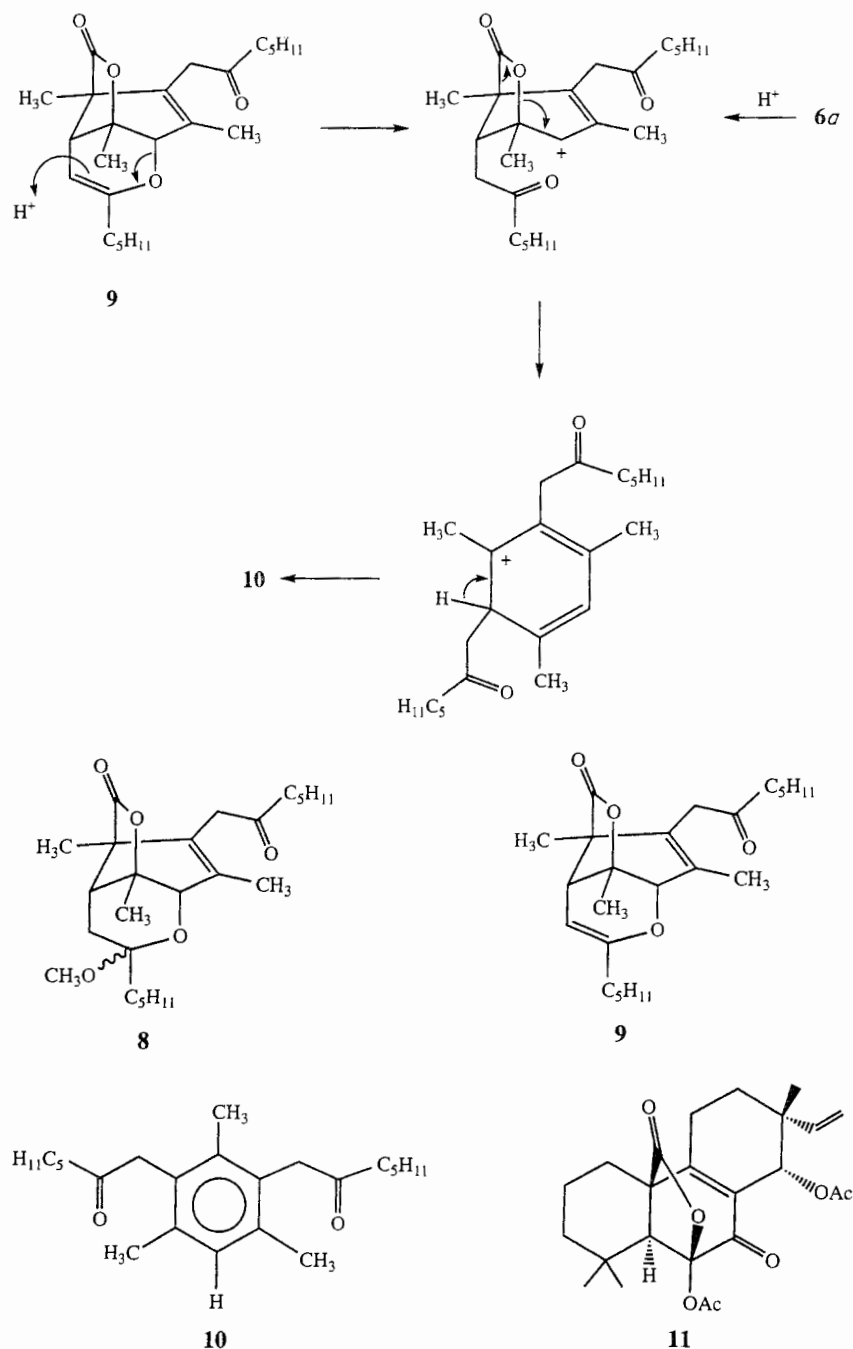
Compound **8** was not produced upon treatment with *p*-toluenesulphonic acid in methanol; instead this resulted in dehydration of the major epimer **6a**, and simplified the isolation of the minor isomer **6b**, which did not undergo reaction. The dehydration product **9** was easily separated from **6b** by column chromatography. Mass spectrometry (HREIMS and CIMS) confirmed the molecular formula of **9** as $\text{C}_{24}\text{H}_{36}\text{O}_4$. The IR spectrum of **9** shows absorptions corresponding to lactone (1779 cm^{-1}) and ketone (1715 cm^{-1}) but no OH absorption. Comparison of the ^{13}C NMR spectra of anhydro derivative **9** with that of alcohol **6a** indicates the presence of an additional double bond the alkenic carbons of which form part of an enol

ether double bond (Table 1). Further comparison of the ^1H NMR spectra of the compounds shows that the three-hydrogen spin system in **6a** is absent in **9** and has been replaced by two mutually coupled hydrogens at δ 4.56 and 2.19 ($J = 6\text{ Hz}$). The COSY spectrum of anhydrodecahydrotrichodermolide shows the expected correlations Me-21/H-1, H-7; H-5/H-1, H-14; and H-7/H-1, thus confirming the structure as shown in **9**.

The formation of anhydrodecahydrotrichodermolide (**9**) from the major reduction product, α -decahydrotrichodermolide (**6a**), confirmed the stereochemistry shown and established the relative stereochemistry at C-5 in trichodermolide.

Prolonged exposure of compound **9** or **6a** to strongly acidic conditions resulted in the formation of the aromatic compound **10**. Mass spectrometry of compound **10** shows a molecular formula $\text{C}_{23}\text{H}_{36}\text{O}_2$. Its IR spectrum shows the presence of a ketone (1704 cm^{-1}) and an aromatic ring ($1450, 1418\text{ cm}^{-1}$). The UV spectrum of compound **10** confirmed the presence of the aromatic group with low-intensity maxima at 205, 210, and 269 nm, indicating that the aromatic ring is unconjugated (**7**). Compound **10** displays a very simple ^1H NMR spectrum. It shows absorptions for one aromatic hydrogen (δ 6.92), four

Scheme 1.



methylene benzylic hydrogens (δ 3.76), three aromatic methyls as singlets at δ 2.20 (6H) and δ 2.04 (3H), and two equivalent hexanoyl side chains. The simplicity of the 1H NMR spectrum indicates that **10** possesses an element of symmetry.

To establish the relative distribution of the aromatic substituents a series of NOE experiments was performed on **10**. The methyl at δ 2.04 ppm gives NOE enhancement to the methylene hydrogens at δ 3.76, while the latter give enhancement to both aromatic methyls.

The aromatization of anhydrodecahydrotrichodermolide (**9**) is not surprising since compounds containing similar functional groups are known to aromatize. For example, the acid-catalyzed decarboxylation of gibberellic acid (**8**) and the aro-

matization of 2β -hydroxy-19-oxo-4-androstene-3,17-dione to estrone (**9**) are known to occur in the presence of acid. A possible mechanistic pathway for the formation of **10** is shown in Scheme 1.

The determination of the absolute stereochemistry of trichodermolide (**2**) by analysis of its CD spectrum is complicated since it shows a series of Cotton effects. However the CD spectrum of octahydrotrichodermolide (**5**) is simpler. It displays a split Cotton effect with extrema of opposite sign at 270 and 222 nm ($A = +28$, positive chirality) due to the inherently dissymmetric α,β -unsaturated ketone chromophore, which shows homoconjugation to the lactone carbonyl (**10**). Examination of molecular models reveals that the π bond of

the lactone carbonyl of octahydrotrichodimerol is in a favourable position to homoconjugate with the double bond of the α,β -unsaturated ketone.

The UV spectrum of octahydrotrichodermolide displays characteristics in accordance with this assumption. These are: longer absorption wavelength and lower intensity than expected for the charge transfer band ($\epsilon = 5600$ vs. 10 000, 272 vs. 237 nm) and a stronger $n-\pi^*$ absorption ($\epsilon = 1200$ vs. 100). These shifts and intensity changes confirm the homoconjugative effect (11).

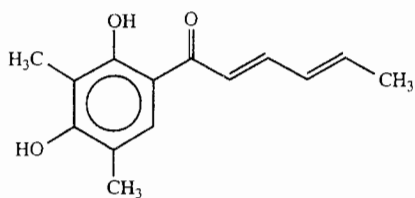
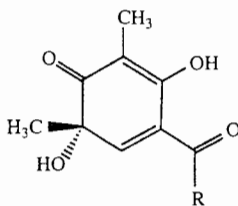
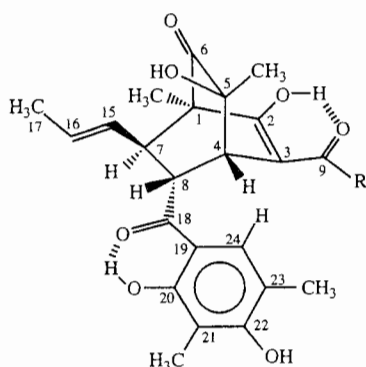
Homoconjugation of lactone carbonyls with enones has been documented. Ellestad et al. (12) reported the UV and CD spectra of compound **11**. The UV spectrum of compound **11** shows maxima at longer wavelengths (260–265 nm) than other abietane derivatives with similar structure and a C-10 methyl (13). The CD spectrum of compound **11** shows a split Cotton effect, with extrema at 262 and 230 nm ($A = +74.4$, positive chirality) and its absolute stereochemistry is known (14). Since octahydrotrichodermolide (**5**) and compound **11** possess virtually the same chromophore and the same chirality in their CD spectra, we assign the absolute stereochemistry of trichodermolide as shown in 2.

Sorbiquinol was obtained as a pale yellow amorphous solid, $[\alpha]_D^{25} +234$ (MeOH). The molecular formula $C_{28}H_{32}O_7$ is based on HREIMS and CIMS data. The EIMS spectrum of sorbiquinol shows fragment ions at m/z 95 corresponding to a sor-

byl side chain and a base peak at m/z 165 corresponding to the substituted benzoyl ion derived from sorbicillin (**12**), also isolated from this fungus (1). The CIMS shows fragment ions at m/z 233 (protonated sorbicillin) and at m/z 249, which could be derived from a sorbicillin *o*-quinol (**13**). Diels–Alder reaction between **12** and **13** gives rise to the bicyclo[2.2.2] adduct **3**. This structure nicely explains all the properties of sorbiquinol (**3**).

The UV spectrum shows base-induced shifts consistent with the enolic-phenol chromophores (see Experimental). The IR spectrum shows absorption for hydroxyl groups (3450 cm^{-1}), saturated ketone (1730 cm^{-1}), strongly chelated carbonyl (1627 cm^{-1}), and aromatic ring(s) (1606 cm^{-1}).

The ^1H NMR spectrum of sorbiquinol shows methyl singlets (δ 1.20, 1.16), two aromatic methyls (δ 2.26, 2.12), an aromatic methine (δ 7.59), two chelated hydroxyl groups (δ 13.98, 12.58), one *E,E*-sorbyl chain (δ 5.53, 7.17, 5.93, 6.08, and 1.82), a three-hydrogen spin system (δ 4.28 (dd, 6.5, 1.5), 3.26 (dd, 10, 6.5 Hz), and 3.32 (d, 1.5 Hz)), and an *E*-1-propenyl (δ 5.45 (dq, 15, 6.5 Hz, 1H), 5.02 (ddq, 15, 10, 1.5 Hz, 1H), and 1.60 (dd, 6.5, 1.5 Hz, 3H)) group. Decoupling experiments carried out in acetone allow us to connect the latter two fragments and build up the fragment $\text{H}_3\text{C}-\text{CH}=\text{CH}-\text{CH}-\text{CH}-\text{CH}$ present between C-4 and C-17. The hydrogen at δ 5.02 (H-15) shows *trans* coupling (15 Hz) to the hydrogen at δ 5.45 (H-16) and is also coupled to the hydrogen at δ 3.26 (10 Hz, H-7),

**12****13** R = C_3H_7 **16** R = C_5H_{11} **3** R = C_5H_7 **14** R = C_5H_{11} **15** R = C_5H_{11} , 15,16-dihydro

which in turn is coupled to the hydrogen at δ 4.28 (6.5 Hz, H-8). The latter hydrogen is also coupled to the methine hydrogen at δ 3.32 (1.5 Hz, H-4).

The ^{13}C NMR spectrum of sorbiquinol (Table 2) shows 28 carbons. Six signals are assigned to methyl groups, three to aliphatic methines, six to sp^2 methines, one to a tertiary carbon bearing oxygen (δ 75.7), three to carbonyl groups (δ 211.5, 202.1, 198.0), three to oxygen-bearing sp^2 carbons (δ 168.8, 161.9, 159.0) that are not carbonyls, and four to non-hydro-

gen-bearing sp^2 carbons. A comparison of the ^1H and ^{13}C NMR spectra of sorbiquinol and sorbicillin (**12**) revealed that both compounds have the fragment $(\text{HO})_2(\text{H}_3\text{C})_2\text{C}_6\text{HCO}$. The presence of this fragment is also supported by the mass spectra of sorbiquinol (vide supra). An NOE experiment shows strong enhancement (26%) of the methine hydrogen at δ 4.48 (H-8) and an enhancement of the aromatic methyl at δ 2.24 upon irradiation of the aromatic hydrogen at δ 7.69 (H-24). This information locates the aromatic ring relative to C-8 and is in

Table 2. ^{13}C NMR data of sorbiquinol (**3**), tetrahydrosorbiquinol (**14**), and hexahydrosorbiquinol (**15**).

Carbon	Chemical shifts in δ (ppm ^{a,b})		
	3 ^c	14 ^{c,d}	15 ^{c,d}
1	63.2	62.6	63.1
2	168.8	180.7	180.4
3	106.8	106.3	106.4
4	47.0 ^b	47.0 ^b	46.9 ^b
5	75.7	75.4	75.4
6	211.5	211.4	211.6
7	46.5 ^b	46.5 ^b	42.7 ^b
8	46.7 ^b	47.0 ^b	46.4 ^b
9	198.0	196.9	197.5
10	117.2	31.7	32.7
11	142.4	26.1	26.1
12	130.8	31.5	31.6
13	139.4	22.1	21.1
14	18.9	13.9	13.8
15	128.6	127.2	33.3
16	130.6	130.5	20.7
17	17.8	17.8	14.0
18	202.1	202.2	202.9
19	112.0 ^a	111.9 ^a	111.3 ^a
20	161.9	162.0	162.3
21	110.7	110.6	110.8 ^a
22	159.0	159.0	159.0
23	115.0 ^a	115.0 ^a	115.2 ^a
24	129.0	129.0	128.7
CH ₃ -C-1	10.0	9.7	9.7
CH ₃ -C-5	24.3	24.3	24.4
CH ₃ -C-21	7.5	7.5	7.5
CH ₃ -C-23	16.0	15.7	16.0

^aSignals with the same superscript in the same column are interchangeable.

^bRelative to the carbon of the solvent (77.0 for CDCl₃).

^cMultiplicity from APT.

^dAlso obtained from [1- ^{13}C]acetate-incorporated sorbiquinol.

agreement with the Diels–Alder hypothesis and the resulting structure **3**.

This structure is supported by further NOE experiments, carried out in acetone. The methine hydrogen at C-4 shows NOE with the methyl group on C-5 (δ 1.20). Similarly, the methyl at C-1 (δ 1.07) shows an NOE enhancement to the methine at δ 3.19 (H-7). In addition, the hydrogen at C-4 shows a strong NOE enhancement (25%) with the α -hydrogen of the sorbyl chain (δ 5.82). The NOE experiments proved very useful in determining the relative stereochemistry of sorbiquinol. The hydrogen at C-8 (δ 4.48) shows strong NOE enhancement (14%) with H-15 (δ 5.16), thus establishing that the 1-propenyl group is *cis* to H-8. The absence of enhancement between the methyl at C-5 (δ 1.20) and H-8 suggests that these two groups are in an *anti* arrangement. Conclusive results, however, were obtained from the ^1H NMR pyridine solvent shift study. Addition of ca. 20% of pyridine-*d*₅ to the CDCl₃ solution of sorbiquinol results in the signals for H-8 and H-15 being shifted downfield by 0.37 and 0.24 ppm, respectively, indicating that the C-5 hydroxyl group is *syn* to

H-8 and H-15. Additional support of this assignment is provided by the relatively high-field signals of the C-5 methyl group (δ 1.20; usually ca. 1.50 ppm), which may be attributed to the shielding effect of the adjacent sorbyl enol system.

Catalytic hydrogenation of sorbiquinol over Pd/C for 1 h afforded the tetrahydro derivative **14** while reduction for 2 days gave the hexahydro derivative **15**. Compound **14** has the molecular formula C₂₈H₃₆O₇ as determined by HREIMS. The EIMS shows a hexanoyl chain (*m/z* 99) and a base peak at *m/z* 165, corresponding to (HO)₂(H₃C)₂C₆HCO⁺. The ^1H and ^{13}C NMR spectra confirm that the sorbyl chain is replaced by a hexanoyl chain (Table 2). Under these conditions the C-15, C-16 double bond is not hydrogenated.

Hexahydrosorbiquinol (**15**) has molecular formula C₂₈H₃₈O₇ obtained from the HREIMS and confirmed by CIMS. All ^1H and ^{13}C NMR signals of compound **15** are similar to those of compound **14**, except those of the *E*-1-propenyl chain, which are replaced by the signals of an *n*-propyl group (Table 2). Similar to the parent compound sorbiquinol, the chemical ionization spectra of the hydrogenated derivatives **14** and **15** show retro-Diels–Alder fragment ions corresponding to sorbicillin (for **14**, at *m/z* 233) or dihydrosorbicillin (for **15**, at *m/z* 235) and tetrahydrosorbicillin-*o*-quinol **16** (for **14** and **15**).

The CD spectra of sorbiquinol, tetrahydrosorbiquinol, and hexahydrosorbiquinol all display a split Cotton effect with positive chirality. The absolute configuration of these compounds, however, cannot be unambiguously deduced from the CD spectra since the direction of the electric transition dipole moment vector of the aromatic chromophore cannot be readily determined. The similarity between the oxygenated sorbicillin subunits present in sorbiquinol, trichodimerol, and the very closely related metabolites of *Verticillium intertextum* (**15**) suggests that they all may have the (*S*) configuration of the oxygen-bearing tertiary carbon atom (C-5 in sorbiquinol), present also in the key intermediate **13**.

Both trichodermolide (**2**) and sorbiquinol (**3**) proved to be inactive against *Mycena citricolor*, but they do represent new structural types of natural products.

Experimental

The general experimental section and the isolation and purification of trichodermolide and sorbiquinol are described in the first part of this series (1). The nuclear Overhauser enhancement determinations (NOE) are from difference spectra and are reported as enhanced area over the irradiated signal area in the difference spectrum. Trichodermolide and sorbiquinol showed the following characteristics:

Trichodermolide (**2**): [α]_D +97 (c 0.98, EtOH); FTIR ν_{max} (cm⁻¹): 3015, 2920, 1781, 1687, 1637, 1595, 1375, 1320, 1188, 997; UV (MeOH) λ_{max} nm (log ϵ): 280 (4.72), 217 (4.15); no change upon addition of NaOH or HCl; CD (EtOH) $\lambda_{\text{extremum}}$ nm ($\Delta\epsilon$): 224 (-15.4), 260 (+5.4), 273 (+2.9), 289 (+9); ORD (EtOH) $\lambda_{\text{extremum}}$ nm ($[\phi]$): 240 (-49 000), 278 (-30 000), 300 (+15 000); ^1H NMR (CDCl₃) δ : 1.24 (s, 3H, H-22), 1.45 (s, 3H, H-23), 1.78 (s, 3H, H-21), 1.87 (d, 6 Hz, 3H, H-13), 1.89 (d, 6 Hz, 3H, H-20), 2.45 (dd, 18.5, 4 Hz, 1H, H-14), 3.26 (dd, 18.5, 6 Hz, 1H, H-14), 3.34 (dd, 6, 4 Hz, 1H, H-5), 3.66 (AB, 19 Hz, 2H, H-7), 6.10 (d, 15.5 Hz, 1H, H-9), 6.15 (d, 15.5 Hz, 1H, H-16), 6.20–6.25 (m, 4H, H-11, 12, 18, 19), 7.20 (dd, 15.5, 9.5 Hz, 1H,

H-17), 7.24 (dd, 15.5, 9.5 Hz, 1H, H-10); NOE δ : [1.24] (H-22): 3.66 (H-7) (4%), 3.34 (H-5) (10%), 3.26 (H-14) (3%); [1.45] (H-23): 2.45 (H-14) (6%), 3.34 (H-5) (9%); [1.78] (H-21): 3.66 (H-7) (7%); [2.45] (H-14): 3.34 (H-5) (8%), 3.26 (H-14) (20%), 6.15 (H-16) (3%), 7.20 (H-17) (3.5%); [3.34] (H-5): 1.24 (H-22) (2%), 1.45 (H-23) (3%), 2.45 (H-14) (10%); [3.66] (H-7): 1.78 (H-21) (11%), 1.24 (H-22) (3%), 6.10 (H-9) (15%), 7.24 (H-10) (19%); [3.26] (H-14): 2.45 (H-14) (27%), 6.15 (H-16) (6%), 7.20 (H-17) (7%); HMBC (C/H's): 1/21, 23; 2/7, 21; 3/7, 21, 22; 4/7, 14, 22; 5/14, 22, 23; 6/5, 14, 23; 8/7; 15/5, 14; ^{13}C NMR spectrum: see Table 1; HREIMS: 396.1936 (calcd. for $\text{C}_{24}\text{H}_{28}\text{O}_5$: 396.1937, 0.7%), 352 ($\text{C}_{23}\text{H}_{28}\text{O}_3$, 0.2%), 340 (0.2), 301 (0.2), 258 (0.3), 257 (0.7), 248 (1), 191 (2.8), 95 (100); CIMS (NH_3): 414 (M + 18, 15%), 397 (M + 1, 100%); TLC: R_f 0.45 (petroleum ether / EtOAc 5:2).

Sorbiquinol (3): [α] $_D$ +234 (c 0.36, MeOH); FTIR ν_{max} (cm^{-1}): 3450, 3020, 2960, 2920, 2850, 1730, 1627, 1606, 1562, 1380, 1166, 995; UV (MeOH) λ_{max} nm (ϵ): 292 (23 000), 359 (22 500), 374 (19 500); NaOH: 252 (18 200), 283 (18 300), 352 (27 000); HCl regenerated the original spectrum; CD (MeOH) $\lambda_{\text{extremum}}$ nm ($\Delta\epsilon$): 343 (+25), 296 (-28); A = +53; ORD (MeOH) $\lambda_{\text{extremum}}$ nm ($[\phi]$): 362 (+38 000), 323 (-85 000), 272 (+73 000), 252 (+85 000); ^1H NMR (CDCl_3) δ : 1.16 (s, 3H, CH_3 -C-1), 1.20 (s, 3H, CH_3 -C-5), 1.60 (dd, 6.5, 1.5 Hz, 3H, H-17), 1.82 (dd, 7, 1.5 Hz, 1H, H-14), 2.12 (s, 3H, CH_3 -C-21), 2.26 (s, 3H, CH_3 -C-23), 3.26 (dd, 10, 6.5 Hz, 1H, H-7), 3.32 (d, 1.5 Hz, 1H, H-4), 4.28 (dd, 6.5, 1.5 Hz, 1H, H-8), 5.02 (ddq, 15, 10, 1.5 Hz, 1H, H-15), 5.45 (dq, 15, 6.5 Hz, 1H, H-16), 5.53 (d, 15 Hz, 1H, H-10), 5.93 (ddq, 15, 10, 1.5 Hz, 1H, H-12), 6.08 (dq, 15, 7 Hz, 1H, H-13), 7.17 (dd, 15, 10.5 Hz, 1H, H-11), 7.59 (s, 1H, H-24), 12.58 (s, 1H, OH-20), 13.98 (s, 1H, OH-2); (acetone- d_6) δ : 1.07 (s, 3H, CH_3 -C-1), 1.20 (s, 3H, CH_3 -C-5), 1.58 (dd, 7, 1.5 Hz, 3H, H-17), 2.24 (s, 3H, CH_3 -C-23), 3.19 (dd, 10, 6.5 Hz, 1H, H-7), 3.50 (d, 1.5 Hz, 1H, H-4), 3.79 (br s, 1H, OH-5), 4.48 (dd, 6.5, 1.5 Hz, 1H, H-8), 5.16 (ddq, 15, 10, 1.5 Hz, 1H, H-15), 5.45 (dq, 15, 7 Hz, 1H, H-16), 5.82 (d, 15 Hz, 1H, H-10), 5.95 (ddq, 15, 10, 1.5 Hz, 1H, H-12), 6.13 (dq, 15, 7 Hz, 1H, H-13), 7.12 (dd, 10, 15 Hz, 1H, H-11), 7.69 (s, 1H, H-24), and 8.05 (br s, 1H, OH-22); NOE (acetone- d_6) δ : [1.07] (CH_3 -C-1): 3.19 (H-7) (4%), 5.16 (H-15) (2%); [1.20] (H-27): 3.50 (H-4) (2%), 3.79 (OH-5) (0.7%); [1.58] (H-17): 5.16 (H-15) (2.5%), 5.45 (H-16) (4%); [3.19] (H-7): 4.48 (H-8) (2%), 5.16 (H-15) (2%); [3.50] (H-4): 1.20 (CH_3 -C-5) (4%), 4.48 (H-8) (5%), 5.82 (H-10) (25%), 5.95 (H-12) (-2%), 7.69 (H-24) (16%); [4.48] (H-8): 3.19 (H-7) (4%), 3.50 (H-4) (5%), 5.16 (H-15) (14%), 5.45 (H-16) (-2%), 7.69 (H-24) (26%); [5.16] (H-15): 4.48 (H-8) (7%), 3.19 (H-7) (4%), 1.58 (H-17) (6%); [5.45] (H-16): 3.19 (H-7) (9%); [5.82] (H-10): 3.50 (H-4) (19%); [7.12] (H-11): 5.82 (H-10) (2%), 5.95 (H-12) (5%), 6.13 (H-13) (16%); [7.69] (H-24): 2.24 (CH_3 -C-23) (9%), 4.48 (H-8) (24%), 3.50 (H-4) (5%), 5.82 (H-10) (-1%), 5.16 (H-15) (-2%), 5.45 (H-16) (-2%); ^{13}C spectrum: see Table 2; HREIMS: 480.2132 (calcd. for $\text{C}_{28}\text{H}_{32}\text{O}_7$: 480.2149, 17%), 452 (2), 434 (1), 248 (2), 233 (18), 232 (32), 217 (22), 191 (8), 165 (100), 95 (31); CIMS: 481 (M + 1, 12%), 249 (24), 233 (100); TLC: R_f 0.28 (2% EtOH - CHCl_3), 0.50 (6%).

Preparation of derivatives

Hydrogenation of trichodermolide

Trichodermolide (**2**) (58 mg) in ethyl acetate (10 mL) was hydrogenated over excess 5% palladium on carbon for 1 h at

room temperature. The reaction mixture was filtered, concentrated, and purified by column chromatography (silica gel, C_6H_6 : Et_2O 3:1, R_f 0.74) to give pure octahydrotrichodermolide (**5**) (30.1 mg, 51% yield): [α] $_D$ +119 (c 0.55, CHCl_3); FTIR ν_{max} (cm^{-1}): 2956, 2923, 2872, 2850, 1782, 1715, 1688, 1618, 1463, 1379, 1304, 1184, 1052, 920; UV (MeOH) λ_{max} nm (ϵ): 219 (5600), 272 (5700), 325 (1200), 329 (1200); CD (MeOH) $\lambda_{\text{extremum}}$ nm ($\Delta\epsilon$): 270 (+13), 222 (-15); ORD (MeOH) $\lambda_{\text{extremum}}$ nm ($[\phi]$): 288 (+24 000), 242 (-58 000); ^1H NMR (CDCl_3) δ : 0.89 (t, 7 Hz, 3H, H-13), 0.91 (t, 7 Hz, 3H, H-20), 1.22 (s, 3H, H-22), 1.30 (m, 8H, H-11,12,18,19), 1.46 (s, 3H, H-23), 1.60 (m, 4H, H-10,17), 1.75 (s, 3H, H-21), 2.30 (dd, 19, 3.5 Hz, 1H, H-14), 2.45 (m, 2H, H-16), 2.52 (t, 7 Hz, 2H, H-9), 3.12 (dd, 19, 7.5 Hz, 1H, H-14), 3.24 (dd, 7.5, 3.5 Hz, 1H, H-5), 3.48 (AB, 17.5 Hz, 2H, H-7); NOE (CDCl_3) δ : [1.22] (H-22): 3.24 (H-5) (13%), 3.48 (H-7) (8%); [1.46] (H-23): 2.30 (H-14) (8%), 3.24 (H-5) (10%); [1.75] (H-21): 3.48 (H-7) (6%); [3.24] (H-5): 1.22 (H-22) (1%), 1.46 (H-23) (1%), 2.30 (H-14) (3.5%); ^{13}C NMR spectrum: see Table 1; HREIMS: 404.2552 (calcd. for $\text{C}_{24}\text{H}_{36}\text{O}_5$: 404.2564, 0.8%), 262 (33), 163 (19), 99 (100), 85 (20), 71 (79); CIMS: 405 (M + 1, 100%).

Reduction of octahydrotrichodermolide (5)

Octahydrotrichodermolide (**5**) (22 mg) was dissolved in benzene-ethanol (2 mL), cooled to 0°C, and excess sodium borohydride in ethanol was added. The reaction was quenched after 1.5 min by addition of saturated aqueous ammonium chloride (0.5 mL). The reaction mixture was diluted with water (8 mL), and extracted with ethyl acetate (3 \times 15 mL). The ethyl acetate extract was concentrated and purified by column chromatography (silica gel, 2% EtOH - CHCl_3 R_f 0.24) to give α -decahydrotrichodermolide (**6a**) (10.0 mg, 45% yield): FTIR ν_{max} (cm^{-1}): 3460, 2956, 2932, 2872, 2860, 1773, 1756, 1713, 1379, 1043, 925; ^1H NMR (CDCl_3) δ : 0.87 (t, 7 Hz, 3H, H-20), 0.88 (t, 7 Hz, 3H, H-13), 1.06 (s, 3H, H-22), 1.30 (m, 8H, H-11,12,18,19), 1.46 (s, 3H, H-23), 1.55 (m, 4H, H-10,17), 1.68 (s, 3H, H-21), 2.22 (br, 1H, OH-1), 2.44 (t, 7 Hz, 2H, H-9), 2.50 (m, 2H, H-16), 2.71 (dd, 6.5, 5 Hz, 1H, H-5), 2.83 (dd, 18.5, 5 Hz, 1H, H-14), 2.99 (dd, 18.5, 6.5 Hz, 1H, H-14), 3.27 (s, 2H, H-7), 3.71 (d, 6 Hz, 1H, H-1); NOE (CDCl_3) δ : [1.06] (H-22): 2.71 (H-5) (2.3%), 3.27 (H-7) (3.8%); [1.46] (H-23): 2.71 (H-5) (3.1%), 2.83 (H-14) (1%), 3.71 (H-1) (2.7%); [1.68] (H-21): 3.27 (H-7) (1.5%), 3.71 (H-1) (1.5%); [3.27] (H-7): 2.44 (H-9) (5%), 1.68 (H-21) (7%), 1.06 (H-22) (4%); [3.71] (H-1): 2.22 (OH-1) (6%), 1.68 (H-21) (4%), 1.46 (H-23) (4%), 1.06 (H-22) (4%); ^{13}C NMR spectrum: see Table 1; HREIMS: 406.2730 (calcd. for $\text{C}_{24}\text{H}_{38}\text{O}_5$: 406.2720, 0.8%), 150 (19), 149 (22), 147 (37), 133 (28), 121 (50), 99 (100), 71 (70), and traces of starting material.

Formation of anhydrodecahydrotrichodermolide (9)

Octahydrotrichodermolide (**5**) (21.5 mg) was dissolved in benzene-ethanol (1 mL), and sodium borohydride (14.1 mg) in ethanol (1 mL) was added at 0°C. After 2 min the reaction was quenched by addition of saturated aqueous ammonium

² This signal is present as a multiplet, indicating that these hydrogens are diastereotopic and magnetically similar, forming an AA'BB'-like system.

³ This signal is present as a multiplet, indicating that these hydrogens are diastereotopic (vide supra).

chloride (0.5 mL), diluted with water (5 mL), and extracted with chloroform (3 × 5 mL). The chloroform extract was evaporated, and the crude mixture was treated with *p*-toluenesulphonic acid (10 mg) in methanol (4 mL) for 2 weeks at room temperature. The methanol was removed under reduced pressure and the mixture purified by column chromatography (silica gel, 2% EtOH – CHCl₃) to afford β-decahydrotrichodermolide (**6b**) (2.8 mg): FTIR ν_{\max} (cm⁻¹): 3450, 2956, 2929, 2872, 2858, 1770, 1714, 1457, 1379, 1049; UV (MeOH): no absorptions detected; ¹H NMR (CDCl₃) δ : 0.89 (t, 7 Hz, 3H, H-20), 0.90 (t, 7 Hz, 3H, H-13), 1.03 (s, 3H, H-22), 1.30 (m, 8H, H-11,12,18,19), 1.49 (s, 3H, H-23), 1.56 (m, 4H, H-10,17), 1.68 (s, 3H, H-21), 2.32 (dd, 18, 3 Hz, 1H, H-14), 2.43 (t, 7 Hz, 2H, H-9), 2.53 (m, ³2H, H-16), 2.89 (dd, 7, 3 Hz, 1H, H-5), 3.19 (dd, 18, 7 Hz, 1H, H-14), 3.25 (AB, 18 Hz, 2H, H-7), 3.70 (br s, 1H, H-1); NOE (CDCl₃) δ : [1.03] (H-22): 3.25 (H-7) (1%), 2.89 (H-5) (5%); [1.49] (H-23): 3.70 (H-1) (3%), 2.89 (H-5) (3%); [1.68] (H-21): 3.70 (H-1) (2%), 3.25 (H-7) (0.8%); HREIMS: 406.2737 (calcd. for C₂₄H₃₈O₅: 406.2720, 0.8%), 361 (29), 248 (19), 245 (22), 149 (54), 147 (26), 133 (20), 121 (38), 99 (100), 71 (66); CIMS: 424 (M + 18, 100%), 407 (M + 1, 12%). Further chromatography with 3% Et₂O – C₆H₆ as eluant afforded aromatic compound **10** (2.6 mg): FTIR ν_{\max} (cm⁻¹): 2958, 2928, 2871, 2858, 1704, 1450, 1418; UV (MeOH) λ_{\max} nm (ϵ): 205 (13 000), 210 (15 000), 269 (400); no change upon addition of NaOH or HCl; ¹H NMR (CDCl₃) δ : 0.87 (t, 7 Hz, 6H), 1.26 (m, 8H), 1.56 (m, 4H), 2.04 (s, 3H, CH₃Ar), 2.20 (s, 6H, 2 × CH₃Ar), 2.40 (t, 7 Hz, 4H, COCH₂), 3.76 (s, 4H, 2 × CH₂Ar), 6.92 (s, 1H, ArH); ¹³C NMR spectrum: see Table 1; HREIMS: 344.2714 (calcd. for C₂₃H₃₆O₂: 344.2715, 5%), 326 (21), 245 (C₁₇H₂₅O, 100%), 227 (24), 147 (23), 99 (44); CIMS: 362 (M + 18, 100%), 345 (M + 1, 1%), 245 (7); NOE δ : [2.04] (CH₃Ar): 3.76 (CH₂Ar) (4.3%), 2.20 (CH₃Ar) (-3.2%); [2.20] (CH₃Ar): 3.76 (CH₂Ar) (1.5%), 6.92 (ArH) (3.6%); [3.76] (CH₂Ar): 2.20 (CH₃Ar) (5%), 2.40 (COCH₂) (4%), 2.04 (CH₃Ar) (7.3%); [6.92] (ArH): 2.20 (CH₃Ar) (13.5%); and anhydrodecahydrotrichodermolide (**9**) (2.4 mg): FTIR ν_{\max} (cm⁻¹): 2955, 2930, 2872, 2859, 1779, 1715, 1687, 1381, 1180, 1070; UV (MeOH) λ_{\max} nm (ϵ): 202 (6000), 232 (2000); no change upon addition of NaOH or HCl; ¹H NMR (CDCl₃) δ : 0.86 (t, 7 Hz, 6H, H-13,20), 1.04 (m, 4H, H-18,19), 1.17 (s, 3H, H-22), 1.20 (m, 4H, H-11,12), 1.43 (s, 3H, H-23), 1.43 (m, 2H, H-17), 1.53 (m, 2H, H-10), 1.68 (s, 3H, H-21), 2.04 (m, ³2H, H-16), 2.19 (d, 6 Hz, 1H, H-5), 2.37 (m, 2H, H-9), 3.21 (s, 2H, H-7), 4.08 (br s, 1H, H-1), 4.56 (d, 6 Hz, 1H, H-14); COSY (CDCl₃): Me-21 (δ 1.68)/H-1 (δ 4.08), H-7 (δ 3.21); H-5 (δ 2.19)/H-1 (δ 4.08), H-14 (δ 4.56); H-7 (δ 3.21)/H-1 (δ 4.08); NOE (CDCl₃) δ : [1.17] (H-22): 2.19 (H-5) (3.3%), 3.21 (H-7) (2%), 4.56 (H-14) (1%); [1.43] (H-23): 2.04 (H-16) (1%), 2.19 (H-5) (2.5%), 4.08 (H-1) (3.3%); [1.68] (H-21): 3.21 (H-7) (2%), 4.08 (H-1) (3.5%); [2.19] (H-5): 1.17 (H-22) (6%), 1.43 (H-23) (8%), 4.56 (H-14) (10%); [3.21] (H-7): 1.17 (H-22) (4%), 1.68 (H-21) (5.4%), 2.37 (H-9) (1%); [4.08] (H-1): 1.43 (H-23) (7%), 1.68 (H-21) (5.4%); [4.56] (H-14): 2.04 (H-16) (5%), 2.19 (H-5) (11%), 2.37 (H-9) (1%); ¹³C NMR spectrum: see Table 1; HREIMS: 388.2611 (calcd. for C₂₄H₃₆O₄: 388.2615, 0.6%), 277 (C₁₈H₂₉O₂, 100%), 245 (21), 99 (55); CIMS: 406 (M + 18, 100%), 390 (M + 2, 36%).

α -Decahydrotrichodermolide (**6a**) (4.5 mg) was treated with 1% methanolic *p*-toluenesulphonic acid (2 mL), at room

temperature for 2 h. The reaction mixture was concentrated and purified by column chromatography (silica gel, 2% EtOH – CHCl₃), to give the enol ether anhydrodecahydrotrichodermolide (**9**) (3.5 mg, *R*_f 0.71).

α -Decahydrotrichodermolide (**6a**) (3 mg) was acetylated by overnight reaction with acetic anhydride (1 mL) and pyridine (0.5 mL) at room temperature. The excess pyridine and acetic anhydride were removed azeotropically with toluene to give pure *O*-acetyl- α -decahydrotrichodermolide (**7a**) (2.5 mg): FTIR ν_{\max} (cm⁻¹): 2956, 2928, 2872, 2857, 1780, 1748, 1715, 1457, 1417, 1380, 1371, 1258, 1022, 931, 804; UV (MeOH): no UV absorptions detected; ¹H NMR (CDCl₃) δ : 0.89 (t, 7 Hz, 3H, H-20), 0.90 (t, 7 Hz, 3H, H-13), 1.10 (s, 3H, H-22), 1.30 (m, 8H, H-11, 12, 18, 19), 1.35 (s, 3H, H-23), 1.53 (s, 3H, H-21), 1.58 (m, 4H, H-10,17), 2.46 (t, 7 Hz, 2H, H-9), 2.54 (m, ³2H, H-16), 2.71 (m, 1H, H-14), 2.73 (1H, H-5), 3.09 (m, 1H, H-14), 3.31 (s, 2H, H-7), 5.29 (br s, 1H, H-1); NOE (CDCl₃) δ : [1.10] (H-22): 3.31 (H-7) (3%), 2.73 (H-5) (3%); [1.35] (H-23): 5.29 (H-1) (2.5%), 2.73 (H-5) (1%); [1.53] (H-21): 5.29 (H-1) (2.5%), 3.31 (H-7) (2%); [3.31] (H-7): 1.53 (H-21) (7%), 2.46 (H-9) (4%), 1.10 (H-22) (1%); ¹³C NMR spectrum: see Table 1; HREIMS: 448.2831 (calcd. for C₂₆H₄₀O₆: 448.2826, 0.1%), 404 (M – CO₂, 0.2), 246 (41), 147 (47), 135 (6), 133 (42), 121 (16), 99 (100), 71 (72). Acetylation of β -decahydrotrichodermolide (**6b**) in a similar way gave *O*-acetyl- β -decahydrotrichodermolide (**7b**) (1.5 mg): FTIR ν_{\max} (cm⁻¹): 2956, 2927, 2873, 2858, 1772, 1742, 1716, 1374, 1231, 1093, 1056, 1028; UV (MeOH): no absorption detected; ¹H NMR (CDCl₃) δ : 0.89 (t, 7 Hz, 6H, H-13, 20), 1.04 (s, 3H, H-22), 1.30 (m, 8H, H-11,12,18,19), 1.32 (s, 3H, H-23), 1.49 (s, 3H, H-21), 1.58 (m, 4H, H-10, 17), 2.43 (dd, 18, 3 Hz, 1H, H-14), 2.44 (t, 7 Hz, 2H, H-9), 2.55 (m, 2H, H-16), 2.92 (dd, 8.5, 3 Hz, 1H, H-5), 3.28 (dd, 18, 8.5 Hz, 1H, H-14), 3.29 (AB, 18 Hz, 2H, H-7), 5.40 (br s, 1H, H-1); HREIMS: 448.2817 (calcd. for C₂₆H₄₀O₆: 448.2826, 0.1%), 403 (M – CO₂, 8%), 248 (30), 245 (42), 133 (44), 121 (22), 99 (100), 71 (71); CIMS: 466 (M + 18, 100%), 449 (M + 1, 3%).

Aromatization of anhydrodecahydrotrichodermolide (**9**)

Anhydrodecahydrotrichodermolide (**9**) (8 mg) was refluxed overnight in 1% methanolic *p*-toluenesulphonic acid (2 mL). The reaction mixture was evaporated and purified by column chromatography (3% Et₂O – C₆H₆) to give the aromatic compound **10** (4 mg) and unreacted starting material.

Hydrogenation of sorbiquinol (**3**)

A mixture (58 mg) containing sorbiquinol and trichodimerol, obtained from the mycelial extract of *T. longibrachiatum* (UAMH 5068), was hydrogenated with excess 5% palladium on carbon in ethyl acetate (4 mL) at room temperature and pressure for 1 h. The reaction mixture was filtered through celite, evaporated, and purified by column chromatography (silica gel, 3% EtOH – CHCl₃) to give tetrahydrosorbiquinol (**14**) (15 mg, 95% pure): [α]_D +86 (*c* 0.23, MeOH); FTIR ν_{\max} (cm⁻¹): 3450, 2960, 2870, 2850, 1730, 1625, 1490, 1380, 1292, 1165, 1145; UV (MeOH) ν_{\max} nm (ϵ): 217 (13 800), 232 sh, 290 (19 000); NaOH: 258 (12 400), 309 sh, 344 (29 000);

⁴ The chemical shift and multiplicity was obtained from NOE difference spectra since these signals overlap in the regular ¹H NMR spectrum.

HCl regenerated the original spectrum; ^1H NMR (CDCl_3) δ : 0.78 (t, 7.5 Hz, 3H, H-14), 1.00 (m, 4H, H-12, 13), 1.16 (s, 3H, $\text{CH}_3\text{-C-1}$), 1.23 (s, 3H, $\text{CH}_3\text{-C-5}$), 1.45 (m, 2H, H-11), 1.60 (dd, 7, 1.5 Hz, 3H, H-17), 1.96 (t, 8 Hz, 2H, H-10), 2.13 (s, 3H, $\text{CH}_3\text{-C-21}$), 2.26 (s, 3H, $\text{CH}_3\text{-C-23}$), 2.87 (s, 1H, OH-5), 3.245 (dd, 4 10, 6.5 Hz, 1H, H-7), 3.247 (d, 4 1.5 Hz, 1H, H-4), 4.27 (dd, 7, 1.5 Hz, 1H, H-8), 4.99 (ddq, 15, 10, 1.5 Hz, 1H, H-15), 5.44 (dq, 15, 7 Hz, 1H, H-16), 7.60 (s, 1H, H-24), 12.79 (s, 1H, OH-20), 14.37 (s, 1H, OH-2); NOE (CDCl_3) δ : [1.16] ($\text{CH}_3\text{-C-1}$): 3.245 (H-7) (2.3%), 4.99 (H-15) (1.1%), 5.44 (H-16) (0.4%); [1.23] ($\text{CH}_3\text{-C-5}$): 3.247 (H-4) (2%); [1.96] (H-10): 3.247 (H-4) (7%); [2.26] ($\text{CH}_3\text{-C-23}$): 7.60 (H-24) (2%); [4.27] (H-8): 3.245 (H-4, H-7) (7%), 4.99 (H-15) (13%), 7.60 (H-24) (23%); [5.44] (H-16): 3.245 (H-7) (10%), 4.99 (H-15) (2%); [7.60] (H-24): 2.26 ($\text{CH}_3\text{-C-23}$) (7%), 3.247 (H-4) (6%), 4.27 (H-8) (22%), 4.99 (H-15) (-2.4%); ^{13}C NMR spectrum: see Table 2; CD (MeOH) $\lambda_{\text{extremum}}$ nm ($\Delta\epsilon$): 318 (+37), 284 (-41); A = +78; HREIMS: 484.2460 (calcd. for $\text{C}_{28}\text{H}_{36}\text{O}_7$: 484.2462, 3.3%), 252 (2), 232 (25), 165 (100), 99 (10), 95 (3); CIMS: 502 (M + 18, 3%), 485 (M + 1, 41%), 253 (32), 233 (100), 106 (82); tlc: R_f 0.26 (2% EtOH - CHCl_3), 0.52 (6%); and octahydrotrichodimerol (20 mg).

When the hydrogenation is allowed to proceed for 2 days, work-up of the reaction mixture in a similar way gave hexahydrosorbiquinol (**15**) (6 mg). $[\alpha]_D^{+117}$ (c 0.23, MeOH); FTIR ν_{max} (cm^{-1}): 3480, 2955, 2865, 1732, 1627, 1482, 1450, 1382, 1188, 757; UV (MeOH) λ_{max} nm (ϵ): 215 (15 900), 230 sh, 290 (19 000); NaOH: 257 (6900), 315 sh, 344 (23 000); HCl regenerated the original spectrum; ^1H NMR (CDCl_3) δ : 0.79 (m, 6H, H-14,17), 1.1 (m, 8H, H-12, 13, 15, 16), 1.21 (s, 3H, $\text{CH}_3\text{-C-5}$), 1.29 (s, 3H, $\text{CH}_3\text{-C-1}$), 1.47 (m, 2H, H-11), 1.94 (t, 7 Hz, 2H, H-10), 2.14 (s, 3H, $\text{CH}_3\text{-C-21}$), 2.27 (s, 3H, $\text{CH}_3\text{-C-23}$), 2.72 (m, 1H, H-7), 2.81 (s, 1H, OH-5), 3.22 (d, 1.5 Hz, 1H, H-4), 4.18 (dd, 7, 1.5 Hz, 1H, H-8), 5.36 (s, 1H, OH-22), 7.64 (s, 1H, H-24), 12.84 (s, 1H, OH-20), 14.38 (s, 1H, OH-2); NOE (CDCl_3) δ : [1.21] ($\text{CH}_3\text{-C-5}$): 1.47 (H-11) (3%), 2.81 (OH-5) (1%), 3.22 (H-4) (15%); [1.29] ($\text{CH}_3\text{-C-1}$): 2.72 (H-7) (2%); [1.94] (H-10): 1.47 (H-11) (10%), 3.22 (H-4) (7%); [3.22] (H-4): 1.21 ($\text{CH}_3\text{-C-5}$) (3%), 4.18 (H-8) (4%), 7.64 (H-24) (5%); [7.64] (H-24): 3.22 (H-4) (6%), 4.18 (H-8) (19%); ^{13}C NMR spectrum: see Table 2; CD (MeOH) $\lambda_{\text{extremum}}$ nm ($\Delta\epsilon$): 316 (+29), 285 (-34); A = +63; HREIMS: 486.2616 (calcd. for $\text{C}_{28}\text{H}_{38}\text{O}_7$: 486.2618, 17%), 253 (1.4), 235 (28), 191 (28), 165

(100), 99 (5); CIMS: 504 (M + 18, 34), 487 (M + 1, 100), 253 (78), 233 (79), 165 (54); TLC: R_f 0.25 (2% EtOH - CHCl_3), 0.56 (6%).

Acknowledgements

We acknowledge with thanks the financial support provided by the Natural Sciences and Engineering Research Council of Canada, the International Development Research Centre, and the Alberta Heritage Foundation for Medical Research. We also thank Lynne Sigler, University of Alberta Microfungus Herbarium, for cultures and valuable discussion.

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