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ORIGINAL ARTICLE

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Absolute configuration of arylglycerol-β-aryl ethers obtained by asymmetric reduction of the corresponding α-ketonic compound with intact *Fusarium solani* cells

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Abstract When (±)-α-oxo-guaiacylglycerol-β-(vanillic acid) ether (**1**) is degraded by *Fusarium solani* M-13-1, the α-ketone is initially reduced to give *erythro* and *threo* guaiacylglycerol-β-(vanillic acid) ethers (**2**), arylglycerol-β-aryl ethers, both of which are enantiomerically pure. The absolute configuration in each **2** was determined by Mosher's method; the products were converted to α,γ-di-(*R*)-α-methoxy-α-trifluoromethylphenylacetates (MTPA esters) (**3′**) of *erythro* (−)- and *threo* (+)-veratrylglycerol-β-(methyl vanillate) ethers (**3**), whose ^{1}H nuclear magnetic resonance (NMR) spectra were examined and compared with those of four di-(*R*)-MTPA ester (**3′**) diastereomers from chemically synthesized *erythro* (±)-**3** and *threo* (±)-**3**. To assign the α- and γ-MTPA-OCH_3 peaks, the ^{1}H NMR scans of several compounds that have substructures of **3′** and their 3,4,5-trimethoxyphenyl analogues were examined. When a racemic alcohol reacts with (*R*)-MTPA to give a pair of (*R*)-MTPA ester diastereomers, the Δδ value was defined as the absolute value of the difference in the ^{1}H chemical shifts of the peak between the diastereomers. It was found that the Δδ values of α-MTPA-OCH_3 were larger than those of γ-MTPA-OCH_3 owing to a shielding effect of the veratryl ring located on the α-MTPA-OCH_3, and that the α-MTPA-OCH_3 peaks in the 3,4,5-trimethoxyphenyl compounds shifted downfield relative to those in the veratryl compounds. On the basis of the ^{1}H NMR data of (*R*)-MTPA esters, the absolute configuration of the four chemically prepared diastereomers (**3′**) were determined. The catabolic *erythro* **3′** [from *erythro* (−)-**3**] and *threo* **3′** [from *threo* (+)-**3**] were identical to (*R*, αS, βR)-*erythro* **3′** and (*R*, αS, βS)-*threo* **3′**, respectively. An hydrogen species in the fungal reduction would attack the α-ketone from *re*-face of both (βR)-**1** and (βS)-**1**, giving *erythro* (αS, βR)-**2** and *threo* (αS, βS)-**2**, respectively.

Key words Arylglycerol-β-aryl ether · MTPA · Absolute configuration · Asymmetric reduction · *Fusarium solani*

Introduction

Arylglycerol-β-aryl ethers are the major substructures in lignin, and α-carbonyl structures are considered to be characteristic in decayed wood lignin. We had studied the degradation of (±)-α-oxo-guaiacylglycerol-β-(vanillic acid) ether (**1**) (Fig. 1), which has both characteristics, by *Fusarium solani* M-13-1 and then found that the α-ketone is reduced to the secondary alcohols, giving *erythro* and *threo* guaiacylglycerol-β-(vanillic acid) ethers (**2**),[1] both of which are enantiomerically pure.[2] In the present paper, we report determination of their absolute configurations derived by Mosher's method[3–5] and the ^{1}H NMR spectroscopy of (*R*)-(+)-MTPA esters (**3′**) of veratrylglycerol-β-(methyl vanillate) ethers (**3**) derivatized from **2**; we preliminary reported this material for the first time previously.[2] There had been no reports on the absolute configuration of arylglycerol-β-aryl ethers, although these structures in lignins and as 8-*O*-4′ neolignans are considered to be most abundant ones on earth next to carbohydrates. On the basis of the absolute configuration, stereochemistry during the fungal reduction is discussed.

Results and discussion

Preparation of α,γ-di-(*R*)-MTPA esters (3′) of veratrylglycerol-β-(methyl vanillate) ethers (3)

The fungal reduction product **2** was methylated with diazomethane, giving **3**.[1] *Erythro* and *threo* isomers of both of the catabolic **3** and synthetic **3** were separated as de-

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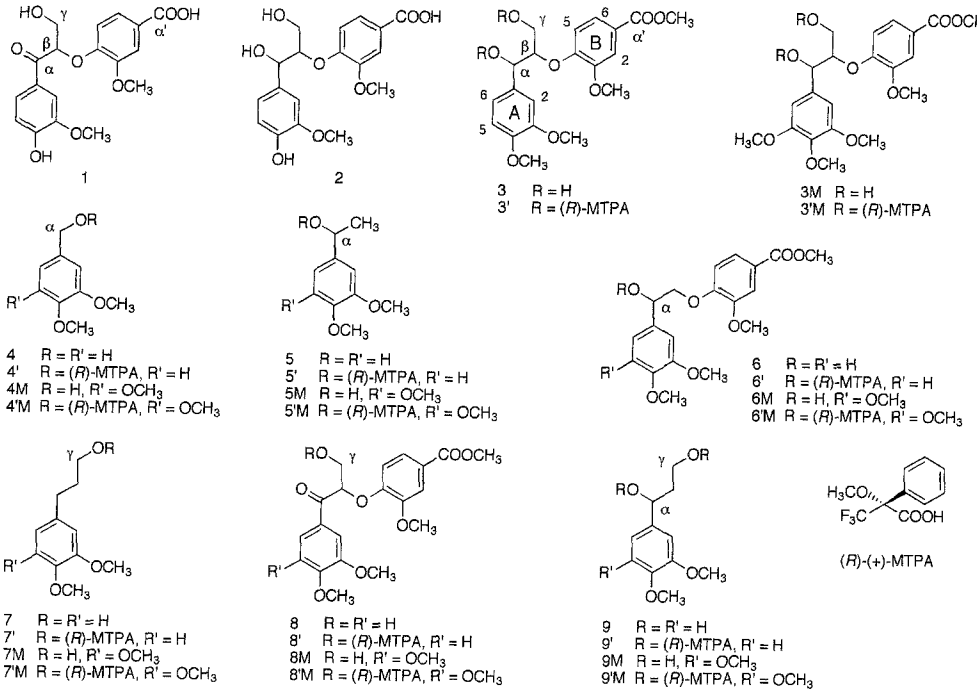

Fig. 1. Structures of compounds. Configurations of four stereoisomers of **2** or **3** are shown in Fig. 4

Table 1. Chemical shifts of MTPA-OCH_3 of synthetic (**3'**a and **3'**b) and catabolic (**3'**b) α,γ-di-(*R*)-MTPA esters of veratrylglycerol-β-(methyl vanillate) ethers and synthetic (**3'**Ma and **3'**Mb) α,γ-di-(*R*)-MTPA esters of 3,4,5-trimethoxyphenylglycerol-β-(methyl vanillate) ethers

Compound		^{1}H Chemical shifts (δ) of MTPA-OCH_3	
		α	γ
Synthetic *Erythro*	**3'**a	3.533	3.436
	3'b	3.384	3.502
Catabolic *Erythro*	**3'**b	3.385	3.503
Synthetic *Erythro*	**3'**Ma	3.565	3.437
	3'Mb	3.412	3.504
Synthetic *Threo*	**3'**a	3.585	3.401
	3'b	3.395	3.438
Catabolic *Threo*	**3'**b	3.396	3.439
Synthetic *Threo*	**3'**Ma	3.603	3.430
	3'Mb	3.456	3.442

scribed previously[2] and treated individually with (*R*)-MTPA chloride by a method described in the literature[3] to afford α,γ-di-(*R*)-MTPA esters (**3'**).

The α,γ-di-(*R*)-MTPA esters of the synthetic *erythro* (±)-**3** [(αR, βS)-**3** and (αS, βR)-**3**] are a pair of diastereomers that showed two spots [*erythro* **3'**a (upper spot) and *erythro* **3'**b (lower spot)] on thin-layer chromatography (TLC) (CH_2Cl_2/*n*-hexane 3:1, eight times). In contrast, di-(*R*)-MTPA esters **3'** of the catabolic *erythro* **3** gave one spot on TLC that was identical to the *erythro* **3'**b spot. Similarly, the α,γ-di-(*R*)-MTPA esters of the synthetic *threo* (±)-**3** [(αR, βR)-**3** and (αS, βS)-**3**] also gave a pair of diastereomers as two spots [*threo* **3'**a (upper spot) and *threo* **3'**b (lower spot)] on TLC (EtOAc/*n*-hexane 1:3, three times), whereas the di-(*R*)-MTPA esters **3'** of the catabolic *threo* **3** gave one spot on TLC that was identical to the spot of *threo* **3'**b.

The ^{1}H NMR spectra of both catabolic *erythro* **3'**b and *threo* **3'**b also were identical to those of the synthetic compounds. Table 1 shows the chemical shifts of the α,γ-MTPA-OCH_3 in *erythro* **3'**a and **3'**b and in *threo* **3'**a and **3'**b.

Mosher method

To determine the absolute configuration of chiral secondary benzyl alcohols, it is effective to measure the ^{1}H NMR spectra of the (*R*)- or (*S*)-MTPA ester derivatives of the sample alcohols: A preferred conformation of the MTPA ester has α-CF_3, the carbonyl (C=O) of the MTPA ester, and the benzyl C—H in an eclipsed arrangement.[4]

In case of a (*S*)-secondary veratryl (benzyl) ester of (*R*)-MTPA (Fig. 2),[4,5] the (*R*)-MTPA-OCH_3 is located on the veratryl ring and the X moiety is on the benzene ring of the MTPA moiety. In contrast, in the case of an (*R*)-secondary veratryl (benzyl) ester of (*R*)-MTPA,[4,5] the (*R*)-MTPA-OCH_3 is not on the veratryl ring nor is the X moiety on the benzene ring. Therefore, the ^{1}H chemical shift (δ_S) of the (*R*)-MTPA-OCH_3 in the (*S*)-veratryl ester is upfield relative to that (δ_R) in the (*R*)-veratryl ester, and the ^{1}H chemical shift (δ'_S) of the C—H in the X moiety of the (*S*)-veratryl ester is upfield relative to that (δ'_R) of the (*R*)-veratryl ester. Consequently, the absolute configuration of the secondary veratryl (benzyl) alcohol derivative is determined with the absolute values of the differences between the two chemical shifts, $|\delta_S - \delta_R| = \Delta\delta$ and $|\delta'_S - \delta'_R| = \Delta\delta'$.

In the case of *erythro* **3**, (αS)-*erythro*-**3'** would adopt a preferential conformation, as shown in Fig. 2. The MTPA-

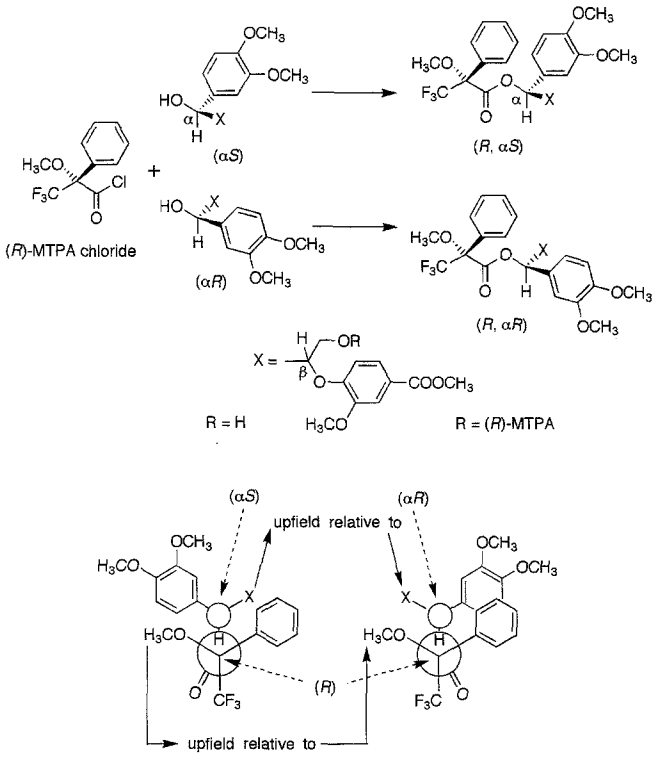

Fig. 2. Reaction of (αR)- and (αS)-secondary benzyl alcohols (veratryl alcohol derivatives) with (*R*)-(+)-MTPA chloride and preferred conformation of the resulting (*R*, αR) and (*R*, αS) MTPA esters. The Newman projection formulas show shielding effects of the veratryl ring on the MTPA-OCH_3 and of the benzene ring on the X moiety. (Ether oxygen atoms in the MTPA esters are omitted.) When the X is $-CH_3$ (**5′**) or $-CH_2CH_2$-OMTPA (**9′**), the symbols (αR) and (αS) should read (αS) and (αR), respectively

OCH_3 would be located on the veratryl ring, and the Cβ-H in the X moiety would be on the benzene ring of the MTPA. As a consequence, upfield shifts of both of the MTPA-OCH_3 peak and the Cβ-H peak are expected in the ^{1}H NMR spectra. In contrast, in (αR)-*erythro*-**3′**, neither the MTPA-OCH_3 nor the Cβ-H peaks have such effects because neither is located on the aromatic rings. Therefore, the α-(*R*)-MTPA-OCH_3 and the Cβ-H in (αS)-*erythro*-**3′** are expected to shift upfield rather than those in the (αR)-isomer. In this investigation, a pair of the diastereomers, *erythro* **3′**a and *erythro* **3′**b, were successfully separated by preparative TLC, their ^{1}H NMR scans were examined individually, and the $\Delta\delta$ values of the MTPA-OCH_3 were evaluated to distinguish between α- and γ-MTPA-OCH_3, as described in the following sections and to determine the absolute configuration. However, the $\Delta\delta'$ values for Cβ-H were not used because the Cβ-H peaks were broad multiplets and sometimes overlapped other peaks.

In the case of *threo* **3**, α-(*R*)-MTPA-OCH_3 and the Cβ-H in (*R*, αS, βS)-**3′** are expected to shift at a higher field than those in the (αR)-isomer. Thus, for *threo* **3′**a and *threo* **3′**b the $\Delta\delta$ values were examined by the same manner as the *erythro* isomers.

Distinction between α- and γ-(*R*)-MTPA-OCH_3 peaks of related compounds of 3′ by ^{1}H NMR

Because ^{1}H NMR peaks of the α-MTPA-OCH_3 of **3′** were close to or partially overlapped those of the γ-MTPA-OCH_3 of **3′**, it was necessary to assign the peaks as α or γ. To establish ^{1}H NMR assignments of the MTPA-OCH_3s of **3′**, the (*R*)-MTPA esters of veratryl compounds, **4′**, **5′**, **6′**, **7′**, **8′**, and **9′** with the substructure of **3′** and their 3,4,5-trimethoxyphenyl analogues (**3′**M to **9′**M) (Fig. 1) were synthesized, and chemical shifts (δ) of their MTPA-OCH_3 esters and the $\Delta\delta$ values were determined.

Figure 3 shows the chemical shifts of **3′** (white columns), **3′**M (black columns), and their related compounds **4′**, **5′**, **6′**, **7′**, **8′**, **9′** (white columns) and, **4′**M, **5′**M, **6′**M, **7′**M, **8′**M, and **9′**M (black columns). Because **5**, **6**, **8**, **9**, **5**M, **6**M, **8**M, and **9**M, which have an asymmetric carbon, were synthesized as racemates, their (*R*)-MTPA esters (**5′**, **6′**, **8′**, **9′**, **5′**M, **6′**M, **8′**M, **9′**M) are couples of diastereomers.

Compounds 4′, 4′M, 5′, 5′M, 6′, 6′M, 7′, 7′M, 8′, and 8′M

Figure 3 indicates that it is impossible to distinguish α- and γ-MTPA-OCH_3 by chemical shifts alone. The α-MTPA-OCH_3 peak of **4′** and **4′**M was at δ 3.508 and 3.537, respectively. The α-MTPA-OCH_3 peaks of **5′** appeared at δ 3.464 and 3.559, and those of **5′**M at δ 3.488 and 3.583. The upfield peaks would be under the shielding effect by the veratryl nuclei, but the downfield ones would not; hence the upfield peaks were assigned to α-MTPA-OCH_3 of (αR) form and the downfield ones to that of (αS) form. Two diastereomers, **6′**a (upper spot) and **6′**b (lower spot), showed their α-MTPA-OCH_3 peaks at δ 3.624 and 3.485, respectively. The configuration of **6′**b was determined to be αS, as the α-MTPA-OCH_3 peak of **6′**b was subject to the shielding effect by the veratryl ring, whereas that of **6′**a was determined to be αR. Similarly, the Cα configurations of **6′**M, whose MTPA-OCH_3 peaks appeared at δ 3.509 (αS) and at δ 3.641 (αR), were determined as in parentheses.

Compounds **7′**, **7′**M, **8′**, and **8′**M are mono-MTPA ester derivatives of the γ-primary alcohols. The MTPA-OCH_3 peaks of **7′** and **7′**M appeared at δ 3.558 and 3.557, respectively. The MTPA-OCH_3 peaks of the diastereomeric mixture **8′** were at δ 3.472 and 3.518, and those of **8′**M were at δ 3.464 and 3.513. There was little difference in the MTPA-OCH_3 chemical shifts between **7′** and **7′**M or between **8′** and **8′**M.

Rules 1 and 2

On the basis of the above results, it was confirmed (Fig. 3) that the $\Delta\delta$ of α-MTPA-OCH_3 attached to the asymmetric Cα (**5′**, **5′**M, **6′**, **6′**M) are larger than the $\Delta\delta$ of γ-MTPA-OCH_3 attached to Cγ adjacent to the asymmetric or achiral Cβ (**8′** and **8′**M) because of the shielding effect by the veratryl and 3,4,5-trimethoxyphenyl nuclei (rule 1).

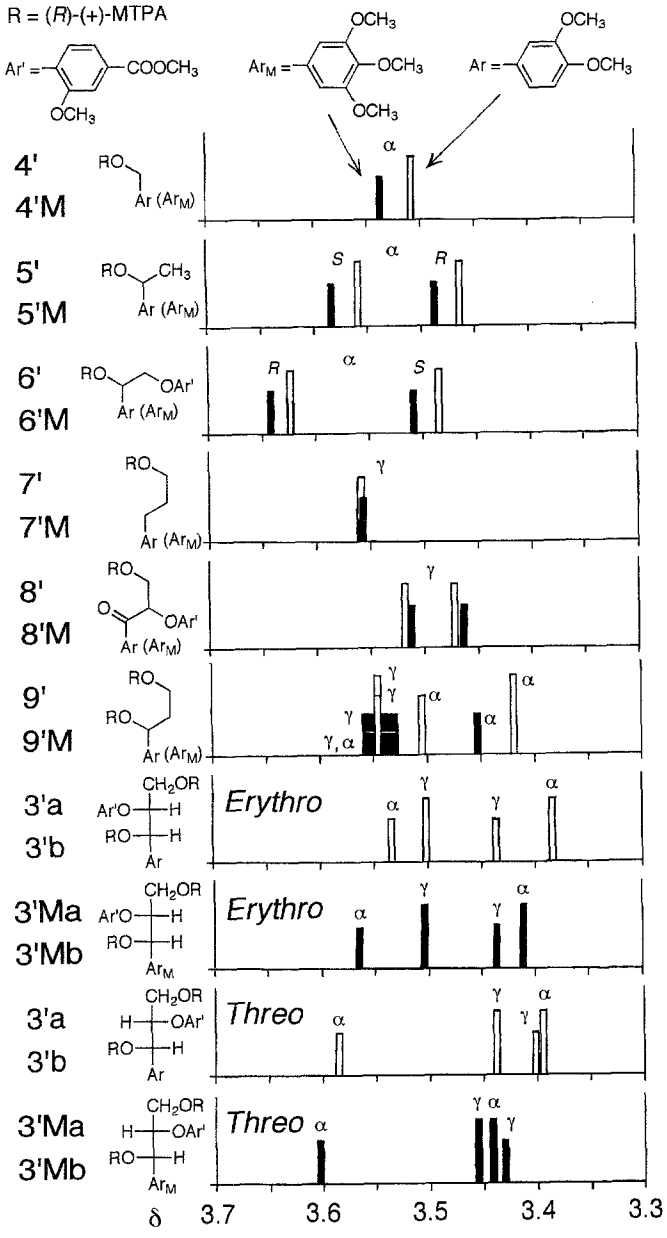

Fig. 3. ^{1}H NMR chemical shifts of MTPA-OCH_3 peaks. The white and black columns correspond to the chemical shifts of **3'**–**9'** with the Ar group and of **3'M**–**9'M** with the Ar_M group, respectively. Diastereomers **9'**a and **9'**Ma correspond to longer columns and **9'**b and **9'**Mb to the shorter columns. Diastereomers **3'**a and **3'**Ma correspond to shorter columns and **3'**b and **3'**Mb to longer columns

Furthermore, comparing the chemical shifts of (*R*)-MTPA-OCH_3 of **4'**–**6'** with those of **4'M**–**6'M**, it was found that the chemical shifts of α-(*R*)-MTPA-OCH_3 of **4'M**–**6'M** were shifted downfield (0.017–0.034ppm) relative to those of **4'**–**6'**, whereas there was little difference between the chemical shifts of γ-(*R*)-MTPA-OCH_3 of **7'M**–**8'M** and those of **7'**–**8'** (rule 2).

Compounds 9' and 9'M

Assignments of the peaks between α- and γ-(*R*)-MTPA-OCH_3 and determination of the absolute configuration of **9'**a, **9'**b, **9'**Ma, and **9'**Mb were attempted using the rules 1 and 2. Because two diastereomers (**9'**a and **9'**b) were partially separated by preparative TLC, giving two fractions, the MTPA-OCH_3 peaks of **9'**a (δ 3.418, 3.546) were able to distinguish from those of **9'**b (δ 3.504, 3.546) by the relative peak areas. Because the peak of **9'**a at δ 3.418 appeared to be upfield remarkably relative to the other peak of **9'**a and to the two peaks of **9'**b, rule 1 applies in this case; the $\Delta\delta$ values between δ 3.418 (**9'**a) and 3.504 (**9'**b) and between δ 3.418 (**9'**a) and δ 3.546 (**9'**b) were larger than the $\Delta\delta$ values between δ 3.546 (**9'**a) and 3.504 (**9'**b) and between 3.546 (**9'**a) and δ 3.546 (**9'**b). Therefore, the peak of **9'**a at δ 3.418 was assigned to α-MTPA-OCH_3 on the veratryl ring, and the absolute configuration of **9'**a was determined as (αR). Thus, the peak at δ 3.546 in **9'**a was assigned to γ-MTPA-OCH_3, and the absolute configuration of **9'**b was determined as (αS). Assignment of the peak of **9'**b is shown later.

In the case of **9'**Ma and **9'**Mb, similar to the above, the MTPA-OCH_3 peaks of **9'**Ma (δ 3.531–3.557) were distinguished from those of **9'**Mb (δ 3.453, 3.531–3.557) by their relative peak areas. Because the clearly resolved MTPA-OCH_3 peak of **9'**Mb at δ 3.453 appeared upfield relative to the other MTPA-OCH_3 peak of **9'**Mb and to the peaks of **9'**Ma (which also suggested that $\Delta\delta$ between the peak at δ 3.453 and the peak of **9'**Ma was larger than $\Delta\delta$ between the peak of **9'**Mb at δ 3.531–3.557 and the peak of **9'**Ma), the peak of **9'**Mb at δ 3.453 was assigned as the α-MTPA-OCH_3 located on the 3,4,5-trimethoxyphenyl ring, and absolute configuration of **9'**Mb was determined as (αR). Thus the peak of **9'**Mb at δ 3.531–3.557 was assigned to γ-MTPA-OCH_3, and the absolute configuration of **9'**Ma was determined as (αS). Thus, it was found that the α-peak at 3.453 of (αR)-**9'**Mb was shifted downfield relative to the α-peak at 3.418 of (αR)-**9'**a, which is consistent with rule 2. In the case of **9'**Ma, γ-MTPA-OCH_3 and α-MTPA-OCH_3, which was not shifted upfield, overlapped each other upon δ 3.531–3.557.

Finally, compared the peaks of (αS)-**9'**b (δ 3.504, 3.546) with those of (αS)-**9'**Ma [δ 3.531–3.557 (α and γ)], the peaks were assigned to 3.504 (α) and 3.546 (γ).

Distinction of α- and γ-(*R*)-MTPA-OCH_3 peaks of 3' and 3'M and the absolute configuration of *erythro* 3' and *threo* 3'

The assignment of α- and γ-(*R*)-MTPA-OCH_3 peaks of synthetic *erythro* and *threo* **3'**, and *erythro* and *threo* **3'**M, based on rules 1 and 2, are shown in Table 1 and Fig. 3. (*Erythro* **3'**Ma/**3'**Mb and *threo* **3'**Ma/**3'**Mb were defined in the same manner as *erythro* **3'**a/**3'**b and *threo* **3'**a/**3'**b.)

Erythro *isomer*

Because *erythro* **3'**b and **3'**Mb have ^{1}H peaks of MTPA-OCH_3 markedly upfield, it was suggested that both peaks were due to α-MTPA-OCH_3 with (αS)-configuration, and thus **3'**a and **3'**Ma have (αR)-configuration. The assignments in Table 1 were consistent with rules 1 and 2 as follows.

The $\Delta\delta$ values for α-MTPA-OCH_3 in **3′** ($|\delta_{3'b}-\delta_{3'a}|$) and **3′M** ($|\delta_{3'Mb}-\delta_{3'Ma}|$) are 0.149 and 0.153 ppm, respectively, which are apparently larger than those of γ-MTPA-OCH_3: 0.034 ppm in **3′** ($|\delta_{3'b}-\delta_{3'a}|$) and 0.068 ppm in **3′M** ($|\delta_{3'Mb}-\delta_{3'Ma}|$).

The differences of the chemical shifts of α-MTPA-OCH_3 between **3′** and **3′M** are obtained by subtracting $\delta_{3'a}$ from $\delta_{3'Ma}$ (0.032 ppm) and by subtracting $\delta_{3'b}$ from $\delta_{3'Mb}$ (0.028 ppm), whereas those of γ-MTPA-OCH_3 between **3′** and **3′M** are small ($\delta_{3'Ma}-\delta_{3'a}$ = 0.001 ppm; $\delta_{3'Mb}-\delta_{3'b}$ = 0.002 ppm).

Thus it was established that the α-MTPA-OCH_3 of **3′b** and **3′Mb** were affected by the shielding effect of veratryl and 3,4,5-trimethoxyphenyl rings, respectively, whereas those of neither **3′a** nor **3′Ma** were affected. Consequently, the Cα of **3′b** and **3′Mb** have an (*S*)-configuration, whereas the Cα of **3′a** and **3′Ma** have an (*R*)-configuration. The absolute configuration of catabolic product *erythro* **3′** (**3** and **2**) was determined to be (αS, βR).

The NOESY (two-dimensional nuclear Overhauser effect spectroscopy) spectrum of *erythro* **3′b** revealed the presence of a cross peak between the MTPA-OCH_3 peak at δ 3.384 and the peak of Ar-A2-H. Consequently, it was confirmed that (αS)-*erythro* **3′b** adopts the conformation that the α-MTPA-OCH_3 faces on the veratryl ring (Fig. 2).

Threo *isomer*

Because *threo* **3′a** and **3′Ma** have peaks that appeared markedly downfield relative to the other peaks, it was suggested that **3′a** and **3′Ma** do not have an (αS)-configuration but an (αR)-configuration; thus **3′b** and **3′Mb** have an (αS)-configuration. The assignments in Table 1 were consistent with the rules 1 and 2 as follows.

The $\Delta\delta$ values of α-MTPA-OCH_3 in **3′** ($|\delta_{3'b}-\delta_{3'a}|$) and **3′M** ($|\delta_{3'Mb}-\delta_{3'Ma}|$) are 0.190 and 0.147 ppm, respectively, which are obviously larger than those of γ-MTPA-OCH_3: 0.037 ppm in **3′** ($|\delta_{3'b}-\delta_{3'a}|$) and 0.012 ppm in **3′M** ($|\delta_{3'Mb}-\delta_{3'Ma}|$).

The differences in the chemical shifts of α-MTPA-OCH_3 between **3′** and **3′M** are 0.061 ppm ($\delta_{3'Mb}-\delta_{3'b}$) and 0.018 ppm ($\delta_{3'Ma}-\delta_{3'a}$), whereas those of γ-MTPA-OCH_3 between **3′** and **3′M** are 0.004 ppm ($\delta_{3'Mb}-\delta_{3'b}$) and 0.029 ppm ($\delta_{3'Ma}-\delta_{3'a}$). Although it could be an exception to rule 2 that the difference of the chemical shifts of the γ-MTPA-OCH_3, 0.029 ppm ($\delta_{3'Ma}-\delta_{3'a}$), is larger than that of α MTPA-OCH_3, 0.018 ppm ($\delta_{3'Ma}-\delta_{3'a}$), rule 1 takes precedence over rule 2. Upfield shifts of γ-MTPA-OCH_3 were found for *threo* **3′a** and **3′Ma**, probably because the OCH_3 is located on the aromatic B-ring, which might cause the above exception.

Thus it was established that the α-MTPA-OCH_3 of **3′b** and **3′Mb** were affected by the shielding effect of veratryl and 3,4,5-trimethoxyphenyl rings, respectively, whereas those of **3′a** and **3′Ma** were not. Consequently, the Cα of **3′b** and **3′Mb** were an (*S*)-configuration, whereas the Cα of **3′a** and **3′Ma** were an (*R*)-configuration. Therefore,

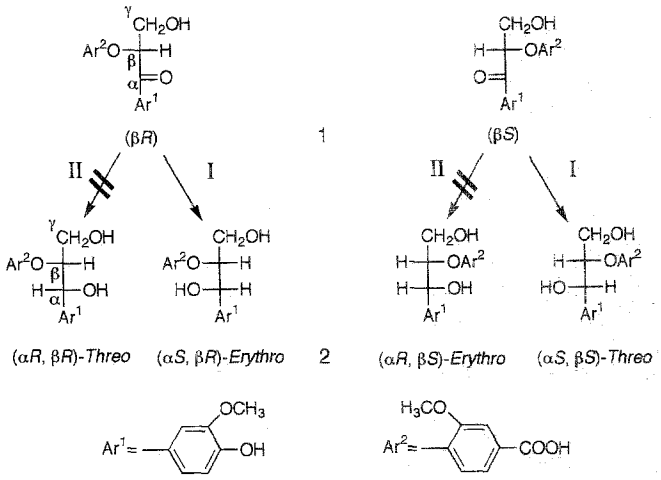

Fig. 4. Reduction of (±)-α-oxo-guaiacylglycerol-β-(vanillic acid) ether (**1**) to *erythro* and *threo* guaiacylglycerol-β-(vanillic acid) ethers (**2**) by *F. solani* M-13-1 would occur through pathway I

absolute configurations of catabolic *erythro* (−)-**3** and *threo* (+)-**3** were determined to be (αS, βR) and (αS, βS), respectively.

The NOESY spectrum of *threo* **3′b** showed the presence of cross peaks between the MTPA-OCH_3 peak at δ 3.395 and the peaks of Ar-A2-H and A6-H. Consequently, it was also confirmed that (αS)-*threo* **3′b** adopts the conformation that the α-MTPA-OCH_3 faces on the veratryl ring (Fig. 2).

Figure 4 shows that the fungal reduction of (±)-**1** would occur by pathway I in which an hydrogen species attacks the carbonyl groups of both *erythro* **1** and *threo* **1** from *re*-faces, giving *erythro* (αS, βR)-**2** and *threo* (αS, βS)-**2**, respectively. Determination of the absolute configuration with a modified Mosher's method for (*R*)- and (*S*)-MTPA esters of catabolic **3′** is under study. Recently, a study on the absolute configuration of 8-*O*-4′ neolignans from *Lonicera gracilipes* var. *glandulosa* by circular dichroism spectroscopy and NOESY was reported.[6]

Experimental

^{1}H NMR spectra were recorded on a Hitachi R-90H FT-NMR spectrometer (90 MHz), with tetramethylsilane as an internal standard. Chemical shifts and coupling constants (J) were expressed in δ and hertz, respectively. The concentration of the sample solution was 1% in $CDCl_3$. The good reproducibility of the chemical shifts was confirmed. NOESY spectra were measured on a JEOL JNM ALPHA-400 FT NMR spectrometer (400 MHz, data point 512, acquisition time 0.16–0.24 s, pulse delay 3.5 s, pulse width 10.8 μs, mixing time 1500 ms). Mass spectrometry (MS) and chromatography were the same as described previously.[1,2]

Synthesis of compounds and ^{1}H NMR of (*R*)-MTPA ester derivatives

Compounds with veratryl nuclei

Veratrylglycerol-β-(methyl vanillate) ether (**3**) was synthesized as a mixture of *erythro* and *threo* forms by way of compound (±)-**8** using a modified method of Adler and Eriksoo,[7] and Miksche:[8] (1) The methyl ketone of acetoveratrone was brominated with $CuBr_2$ in a mixture of ethyl acetate (EtOAc) and chloroform at 70°–80°C for 2.5 h giving α-bromoacetoveratrone.[9] (2) Stirring a mixture of α-bromoacetoveratrone, methyl vanillate, K_2CO_3, and KI in *N*,*N*-dimethylformamide (DMF) afforded α-oxo-veratrylglycol-β-(methyl vanillate) ether. (3) Condensation of the product with paraformaldehyde by use of K_2CO_3 in dimethylsulfoxide (DMSO) gave (±)-**8**.[8] (4) Reduction of the ketone of **8** with $NaBH_4$ in a mixture of MeOH and tetrahydrofuran (THF) at 0°C afforded **3**. Separation of (±)-*erythro* and (±)-*threo* isomers of **3** was achieved as reported previously.[2]

Veratryl alcohol (**4**) is available commercially. Compound (±)-**5** was obtained by the $NaBH_4$ reduction of acetoveratrone in MeOH at 0°C.

Compounds (±)-**6**, **7**, and (±)-**9** were prepared as follows. Acetoveratrone was treated as in steps (1) and (2) and then with reduction of the ketone of α-oxo-veratrylglycol-β-(methyl vanillate) ether with $NaBH_4$ in a mixture of MeOH and THF at 0°C, yielding (±)-**6**.

Compound **7**: Methylation of the phenolic hydroxyl group of coniferaldehyde with an ethereal solution of CH_2N_2 in MeOH at 0°C for 2 h, yielding coniferaldehyde methyl ether. Catalytic reduction of the allyl aldehyde moiety of the product with 10% palladium on activated carbon (Pd–C) in MeOH under hydrogen gas for 60 min then yielded **7**.

Compound (±)-**9**: Catalytic reduction of the allyl aldehyde moiety of coniferaldehyde with 10% Pd–C in MeOH under hydrogen gas for 65 min gave dihydroconiferyl alcohol. The α-methylene of dihydroconiferyl alcohol was oxidized with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (2 equivalent) in water saturated benzene, giving 1-guaiacyl-3-hydroxy-1-propanone. The phenolic hydroxyl group of the product was methylated with an ethereal solution of CH_2N_2 in MeOH at 0°C for 80 min to afford 3-hydroxy-1-veratryl-1-propanone. The ketone of the product was reduced with $NaBH_4$ (10 eq.) in MeOH at 0°C, yielding **9**. Structures of those compounds were confirmed by ^{1}H NMR and MS.

^{1}H NMR of (R)-MTPA esters of veratryl compounds

(*R*)-(+)-MTPA esters were prepared from alcohols with (*R*)-(+)-MTPA (Merck) by a method described in the literature.[3] Crude reaction products of *erythro* (±)-**3** with (*R*)-MTPA chloride were separated by TLC (CH_2Cl_2/*n*-hexane 3:1, eight times) giving two diastereomers: *erythro* **3′**a (upper spot, R_f 0.45–0.50) and *erythro* **3′**b (lower spot, R_f 0.37–0.45). Similarly, *threo* (±)-**3** gave *threo* **3′**a (upper spot, R_f 0.36–0.45) and *threo* **3′**b (lower spot, R_f 0.28–0.33) (EtOAC/*n*-hexane 1:3, three times).

Synthetic *erythro* **3′**a (upper spot): ^{1}H NMR: 3.436 [3H, doublet (d), J = 1.2, γ-MTPA-OCH_3], 3.533 (3H, d, J = 1.2, α-MTPA-OCH_3), 3.668, 3.746, 3.854, and 3.897 (3H × 4, four singlets (s), -$COOCH_3$ and three Ar-OCH_3), 4.430 [1H, double doublet (dd), J = 11.4, J = 3.5, γ-CH_a], 4.608 (1H, dd, J = 11.4, J = 6.4, γ-CH_b), 4.73–4.93 [1H, multiplet (m), β-CH], 6.141 (1H, d, J = 4.2, α-CH), 6.67–6.82 (4H, m, Ar-A-H and B5-H), 7.27–7.56 (12H, m, Ar-B2,6-H and two MTPA-C_6H_5). MS *m*/*z* (%): 824 (M^+, 5). Synthetic *erythro* **3′**b (lower spot): ^{1}H NMR: 3.384 (3H, d, J = 1.0, α-MTPA-OCH_3), 3.502 (3H, d, J = 1.1, γ-MTPA-OCH_3), 3.727, 3.791, 3.862, and 3.883 (3H × 4, four s, -$COOCH_3$ and three Ar-OCH_3), 4.33 (1H, dd, J = 11.9, J = 5.3, γ-CH_a), 4.48 (1H, dd, J = 11.9, J = 3.9, γ-CH_b), 4.73–4.95 (1H, m, β-CH), 6.114 (1H, d, J = 6.1, α-CH), 6.607 (1H, d, J = 9.0, Ar-B5-H), 6.802 (1H, d, J = 8.7, Ar-A5-H), 6.926 (1H, dd, J = 8.6, J = 1.8, Ar-A6-H), 6.947 (1H, d, J = 1.8, Ar-A2-H), 7.26–7.65 (12H, m, Ar-B2,6-H and two MTPA-C_6H_5). MS *m*/*z* (%): 824 (M^+, 5).

Synthetic *threo* **3′**a (upper spot): ^{1}H NMR: 3.401 (3H, d, J = 1.1, γ-MTPA-OCH_3), 3.585 (3H, d, J = 1.1, α-MTPA-OCH_3), 3.614, 3.783, 3.856, and 3.908 (3H × 4, four s, -$COOCH_3$ and three Ar-OCH_3), 3.6–3.9 (1H, dd, γ-CH_a), 4.56–4.78 (1H, dd, J = 11.4, J = 3.9, γ-CH_b), 4.76–4.90 (1H, m, β-CH), 6.192 (1H, d, J = 8.6, α-CH), 6.662 (3H, s, Ar-A-H), 6.886 (1H, d, J = 9.0, Ar-B5-H), 7.04–7.63 (12H, m, Ar-B2,6-H and two MTPA-C_6H_5). MS *m*/*z* (%): 824 (M^+, 4). Synthetic *threo* **3′**b (lower spot): ^{1}H NMR: 3.395 (3H, d, J = 1.1, α-MTPA-OCH_3), 3.438 (3H, d, J = 1.1, γ-MTPA-OCH_3), 3.768, 3.794, 3.883, and 3.902 (3H × 4, four s, -$COOCH_3$ and three Ar-OCH_3), 3.85–4.09 (1H, γ-CH_a), 4.524 (1H, dd, J = 11.9, J = 2.8, γ-CH_b), 4.826 [1H, double double doublet (ddd), J = 7.3, J = 4.7, J = 2.8, β-CH], 6.194 (1H, d, J = 7.3, α-CH), 6.746 (1H, d, J = 9.0, Ar-B5-H), 6.83–6.92 (3H, Ar-A-H), 7.06–7.60 (12H, m, Ar-B2,6-H and two MTPA-C_6H_5). MS *m*/*z* (%): 824 (M^+, 5).

Compound **4′**: ^{1}H NMR: 3.508 [3H, quartet (q), J = 1.2, MTPA-OCH_3], 3.801 (3H, s, Ar-OCH_3), 3.874 (3H, s, Ar-OCH_3), 5.283 (2H, s, -CH_2), 6.74–6.86 (1H, Ar-5-H), 6.81–6.86 (1H, d, Ar-2-H), 6.87–7.01(1H, dd, Ar-6-H), 7.371 (5H, m, MTPA-C_6H_5). MS *m*/*z* (%): 384 (M^+, 12).

Compound **5′** (a mixture of two diastereomers): ^{1}H NMR: 1.575 and 1.627 (3H × 2, d, J = 6.6, C-CH_3), 3.464 and 3.559 (3H × 2, d, J = 1.1, MTPA-OCH_3), 3.731, 3.836, 3.867, and 3.878 (3H × 4, s, Ar-OCH_3), 6.06 and 6.09 (1H × 2, q, J = 6.6, -CH), 6.70–7.01 (3H × 2, m, Ar-H), 7.366 (5H × 2, s, MTPA-C_6H_5). MS *m*/*z* (%): 398 (M^+, 7).

Compound **6′**: Two diastereomers (**6′**a and **6′**b) were separated by TLC (EtOAc/*n*-hexane = 1:4, six times). **6′**a (upper spot): ^{1}H NMR: 3.624 (3H, d, J = 1.2, MTPA-OCH_3), 3.719, 3.862, 3.882, and 3.891 (3H × 4, s, three Ar-OCH_3 and -$COOCH_3$), 4.11–4.30 (1H, β-CH_a), 4.26–4.57 (1H, β-CH_b), 6.370 (1H, dd, J = 8.2, J = 3.8, α-CH), 6.70–6.98 (4H, m, Ar-A-H and B5-H), 7.26–7.68 (7H, m, Ar-B2,6-H and MTPA-C_6H_5). MS *m*/*z* (%): 578 (M^+, 3). **6′**b (lower spot): ^{1}H NMR: 3.485 (3H, d, J = 1.1, MTPA-

OCH_3), 3.847 (3H, s), 3.860 (3H, s), 3.891 (6H, s) (three Ar-OCH_3 and -$COOCH_3$), 4.10–4.33 (1H, β-CH_a), 4.25–4.56 (1H, β-CH_b), 6.439 (1H, dd, J = 7.3, J = 4.6, α-CH), 6.70–7.07 (4H, m, Ar-A-H and Ar-B5-H), 7.26–7.56 (7H, m, Ar-B2,6-H and MTPA-C_6H_5).

Compound **7′**: ^{1}H NMR: 1.82–2.15 (2H, m, β-CH_2), 2.612 [2H, triplet (t), J = 7.6, α-CH_2], 3.558 (3H, d, J = 1.2, MTPA-OCH_3), 3.847 (6H, s, Ar-OCH_3), 4.326 (1H, t, J = 6.5, γ-CH_2), 6.56–6.84 (3H, m, Ar-H), 7.33–7.59 (5H, m, MTPA-C_6H_5). MS m/z (%): 412 (M^+, 70).

Compound **8′** (a mixture of two diastereomers): ^{1}H NMR: 3.472 and 3.518 (3H × 2, d, J = 1.2, MTPA-OCH_3), 3.746 (3H, s) and 3.782 (3H, s) (Ar-OCH_3), 3.871, 3.886, 3.897, 3.928, and 3.943 (9H × 2, five s) (Ar-OCH_3 and -$COOCH_3$), 4.72–4.89 (2H × 2, m, γ-CH_2), 5.64–5.87 (1H × 2, m, α-CH), 6.75 (1H, d, J = 9) and 6.85 (1H, d, J = 9) (Ar-A5 and B5-H), 7.26–7.85 (9H × 2, m, Ar-A2,6 and B2,6-H, and MTPA-C_6H_5).

Compound **9′**: Although separation of two diastereomers by TLC (EtOAC/*n*-hexane 1:5, five times) was unsuccessful, the band was divided into two fractions whose ^{1}H NMR spectra showed the presence of two diastereomers (***9′**a and ****9′**b) in a slightly different ratio. ^{1}H NMR: 2.06–2.44 (2H × 2, m, J = 8.2, β-CH_2), 3.418* (3H, d, J = 1.1, MTPA-OCH_3), 3.504** (3H, d, J = 1.2, MTPA-OCH_3), 3.546 (3H × 2, d, J = 1.1, MTPA-OCH_3), 3.701** (3H, s, Ar-OCH_3), 3.812* (3H, s, Ar-OCH_3), 3.868** (3H, s, Ar-OCH_3), 3.877* (3H, s, Ar-OCH_3), 4.11–4.40 (2H × 2, m, γ-CH_2), 5.84** (1H, dd, J = 8.2, J = 6.0, α-CH), 5.91* (1H, dd, J = 8.5, J = 6.0, α-CH), 6.61** and 6.76** (3H, Ar-H), 6.79* and 6.84* (3H, Ar-H), 7.26–7.55 (5H × 2, m, MTPA-C_6H_5).

Compounds with 3,4,5-trimethoxyphenyl nuclei

3,4,5-Trimethoxybenzyl alcohol (**4M**) was available commercially (Aldrich). Compound (±)-**5M** was prepared by $NaBH_4$ reduction of 3,4,5-trimethoxyacetophenone in MeOH at 0°C. Compound (±)-**6M** was synthesized from 3,4,5-trimethoxyacetophenone by the same method as (±)-**6**. For compound **7M**, Fischer esterification of 3,4,5-trimethoxycinnamic acid in MeOH in the presence of catalytic amounts of H_2SO_4 at refluxed temperature gave methyl 3,4,5-trimethoxycinnamate. The unsaturated ester moiety of the product was reduced with $LiAlH_4$ in anhydrous THF at 50°C to afford **7M**. Compound (±)-**8M** was synthesized from 3,4,5-trimethoxyacetophenone by the same method as (±)-**8**.[8] For compound (±)-**9M**, condensation of 3,4,5-trimethoxyacetophenone with diethyl carbonate by use of NaH in anhydrous benzene at refluxed temperature gave ethyl 3-oxo-3-(3,4,5-trimethoxyphenyl)propionate. Reduction of the ketone of the product with $NaBH_4$ in a mixture of THF and MeOH at 0°C afforded ethyl 3-hydroxy-3-(3,4,5-trimethoxyphenyl)propionate. The hydroxyl group of the product was then acetylated with Ac_2O – pyridine. The resulting 3-acetoxypropionate was reduced with $LiAlH_4$ in anhydrous THF at 50°C, giving (±)-**9M**. Structures of those compounds were confirmed by ^{1}H NMR and MS.

Erythro (±)- and *threo* (±)-3,4,5-trimethoxyphenylglycerol-β-(methyl vanillate) ethers (*erythro* **3M** and *threo* **3M**, respectively) were obtained by $NaBH_4$ reduction of **8M** followed by separation of the diastereomers as described previously.[2] *Erythro* **3M**: ^{1}H NMR: 3.78–3.98 (2H, γ-CH_2), 3.814, 3.894, and 3.911 (each 3H, three s, two Ar-OCH_3 and -$COOCH_3$), 3.833 (6H, s, Ar-OCH_3), 4.333 (1H, q, J = 5, β-CH), 4.960 (1H, d, J = 5.1, α-CH), 6.634 (2H, s, Ar-A-H), 6.933 (1H, d, J = 9.0, Ar-B5-H), 7.55–7.59 (1H, Ar-B2-H), 7.55–7.68 (1H, Ar-B6-H). MS m/z (%): 422 (M^+, 5.0). *Threo* **3M**: ^{1}H NMR: 3.59–3.70 (2H, m, γ-CH_2), 3.827, 3.902, and 3.952 (3H × 3, three s, two Ar-OCH_3 and -$COOCH_3$), 3.851 (6H, s, Ar-OCH_3), 4.21 (1H, m, β-CH), 4.977 (1H, d, J = 7.3, α-CH), 6.668 (2H, s, Ar-A-H), 7.108 (1H, d, J = 9.0, Ar-B5-H), 7.58–7.62 (1H, Ar-B2-H), 7.58–7.72 (1H, Ar-B6-H). MS m/z (%): 422 (M^+, 5.0).

^{1}H NMR of (R)-MTPA esters of 3,4,5-trimethoxyphenyl compounds

α,γ-Di-(+)-MTPA esters of *erythro* (±)-**3M** (*erythro* **3′M**): Crude *erythro* **3′M** after the esterification was separated repeatedly by TLC [EtOAC/*n*-hexane 1:2 (three times), and then 1:2 (four times)] giving two diastereomers, *erythro* **3′Ma** and **3′Mb**. *Erythro* **3′Ma** (upper): ^{1}H NMR: 3.437 (3H, d, J = 1.1, γ-MTPA-OCH_3), 3.565 (3H, d, J = 1.2, α-MTPA-OCH_3), 3.680 (6H, s, Ar-A3,5-OCH_3), 3.755 (3H, s), 3.807 (3H, s), 3.899 (3H, s) (Ar-A4 and B3-OCH_3, and -$COOCH_3$), 4.440 (1H, dd, J = 10.8, J = 2.7, γ-CH_a), 4.653 (1H, dd, J = 10.9, J = 6.6, γ-CH_b), 4.73–4.94 (1H, m, β-CH), 6.121 (1H, d, J = 4.1, α-CH), 6.397 (2H, s, Ar-A2,6-H), 6.755 (1H, d, J = 8.9, Ar-B5-H), 7.26–7.56 (12H, m, Ar-B2,6-H and two MTPA-C_6H_5). *Erythro* **3′Mb** (lower): ^{1}H NMR: 3.412 (3H, d, J = 1.1, α-MTPA-OCH_3), 3.504 (3H, d, J = 1.1, γ-MTPA-OCH_3), 3.767 (6H, s, Ar-A3,5-OCH_3), 3.731, 3.816, and 3.882 (3H × 3, three s, Ar-A4, B3-OCH_3, and -$COOCH_3$), 4.41 (1H, dd, J = 12, J = 5.4, γ-CH_a), 4.48 (1H, dd, J = 12, J = 3.7, γ-CH_b), 4.75–4.99 (1H, m, β-CH), 6.072 (1H, d, J = 5.9, α-CH), 6.597 (2H, s, Ar-A2,6-H), 6.616 (1H, d, J = 8.9, Ar-B5-H), 7.26–7.58 (12H, m, Ar-B2,6-H and two MTPA-C_6H_5).

α,γ-Di-(+)-MTPA esters of *threo* (±)-**3M** (*threo* **3′M**): Crude *threo* **3′M** obtained by the esterification was separated repeatedly by TLC [EtOAc/*n*-hexane 1:2 (twice); 1:5 (twice) and 1:4 (five times); 1:4 (once) and 1:2 (three times)], giving three fractions: pure *threo* **3′Ma** (upper), a mixture of *threo* **3′Ma** and **3′Mb**, and pure *threo* **3′Mb** (lower). *Threo* **3′Ma** (upper): ^{1}H NMR: 3.430 (3H, d, J = 1.0, γ-MTPA-OCH_3), 3.603 (9H, s, α-MTPA-OCH_3 and Ar-A3,5-OCH_3), 3.778, 3.819, and 3.910 (3H × 3, three s, two Ar-OCH_3 and -$COOCH_3$), 3.75–3.95 (1H, γ-CH_a), 4.68–4.78 (1H, γ-CH_b), 4.78–4.93 (1H, m, β-CH), 6.211 (1H, d, J = 8.0, α-CH), 6.410 (2H, s, Ar-A-H), 6.882 (1H, d, J = 8.9, Ar-B6-H), 7.10–7.63 (7H, m, Ar-H). MS m/z (%): 854 (M^+, 10). *Threo* **3′Mb** (lower): ^{1}H NMR: 3.442 and 3.456 (6H, two d, J = 1.4 and 1.0, γ- and α-MTPA-OCH_3, respectively), 3.774

(9H, s), 3.845 (3H, s), and 3.901 (3H, s) (Ar-OCH_3 and -$COOCH_3$), 3.9–4.07 (1H, dd, J = 12, J = 5, γ-CH_a), 4.585 (1H, dd, J = 12, J = 3, γ-CH_b), 4.70–4.90 (1H, m, β-CH), 6.156 (1H, d, J = 7.0, α-CH), 6.560 (2H, s, Ar-A-H), 6.770 (1H, d, J = 8.9, Ar-B6-H), 7.10–7.60 (7H, m, Ar-H). MS m/z (%): 854 (M^+, 8.6).

Compound **4′**M: ^{1}H NMR: 3.537 (3H, s, J = 1.2, MTPA-OCH_3), 3.790 (6H, s, Ar-3,5-OCH_3), 3.838 (3H, s, Ar-4-OCH_3), 5.279 (2H, s, -CH_2), 6.534 (2H, s, Ar-2,6-H), 7.26–7.50 (5H, m, MTPA-C_6H_5). MS m/z (%): 414 (M^+, 17).

Compound **5′**M: One diastereomer (*) was shown to be slightly predominant over the other (**) after purification by TLC. ^{1}H NMR: 1.577* (3H, d, J = 6.5, β-CH_3), 1.622** (3H, d, J = 6.6, β-CH_3), 3.488* (3H, d, J = 1.1, MTPA-OCH_3), 3.583** (3H, d, J = 1.2, MTPA-OCH_3), 3.741** (6H, s, Ar-3,5-OCH_3), 3.819* (6H, s, Ar-3,5-OCH_3), 3.827 (3H, s, Ar-4-OCH_3), 3.845 (3H, s, Ar-4-OCH_3), 6.024** (1H, q, J = 6.7, α-CH), 6.063* (1H, q, J = 6.7, α-CH), 6.441** (2H, s, Ar-2,6-H), 6.576* (2H, s, Ar-2,6-H), 7.26–7.48 (5H × 2, m, MTPA-C_6H_5). MS m/z (%): 428 (M^+, 15).

Compound **6′**M (a mixture of two diastereomers): ^{1}H NMR: 3.509 (3H, d, J = 1.0, MTPA-OCH_3), 3.641 (3H, d, J = 1.2, MTPA-OCH_3), 3.733 (3H × 2, s), 3.840–3.854 (6H × 2), 3.872 (3H × 2, s), and 3.894 (3H × 2, s) (Ar-OCH_3 and -$COOCH_3$), 4.11–4.47 (2H × 2, m, β-CH_2), 6.23–6.42 (1H × 2, m, α-CH), 6.473 (2H, s, Ar-A2,6-H), 6.658 (2H, s, Ar-A2,6-H), 6.70–6.88 (1H × 2, Ar-B5-H), 7.26–7.68 (7H × 2, m, Ar-B2,6-H and MTPA-C_6H_5). MS m/z (%): 608 (M^+, 12).

Compound **7′**M: ^{1}H NMR: 1.87–2.17 (2H, m, β-CH_2), 2.60 (2H, α-CH_2), 3.557 (3H, d, J = 1.1, MTPA-OCH_3), 3.822 (9H, s, Ar-OCH_3), 4.339 (2H, t, J = 6.3, γ-CH_2), 6.342 (2H, s, Ar-2,6-H), 7.30–7.57 (5H, m, MTPA-C_6H_5). MS m/z (%): 442 (M^+, 100).

Compound **8′**M: Two diastereomers (* and **) were obtained in a different ratio by TLC (EtOAc/*n*-hexane 1:4). ^{1}H NMR: 3.464* (3H, d, J = 0.9, MTPA-OCH_3), 3.513** (3H, d, J = 1.1, MTPA-OCH_3), 3.745–3.924 (15H × 2, Ar-OCH_3 and -$COOCH_3$), 4.60–5.00 (2H × 2, m, γ-CH_2), 5.60–5.83 (1H × 2, m, β-CH), 6.753* (1H, d, J = 9.0, Ar-B5-H), 6.771** (1H, d, J = 8.9, Ar-B5-H), 7.384 (2H × 2, s, Ar-A2,6-H), 7.20–7.60 (7H × 2, m, Ar-B2,6-H and MTPA-C_6H_5). MS m/z (%): 636 (M^+, 0.6).

Compound **9′**M: Although separation of two diastereomers by TLC (EtOAC/*n*-hexane 1:4, three times) was unsuccessful, the band was divided into two fractions. The ^{1}H NMR spectrum of the upper fraction showed that two diastereomers were present in almost the same ratio, whereas those of the lower fraction were in a slightly different ratio (***9′**Ma and ****9′**Mb). ^{1}H NMR: 2.06–2.42 (2H × 2, m, β-CH_2), 3.453* (3H, d, J = 1.2, MTPA-OCH_3), 3.531–3.557 (3H, MTPA-OCH_3)* and (6H, two MTPA-OCH_3)**, 3.711** and 3.790* (each 6H, s, Ar-3,5-OCH_3), 3.829** and 3.840* (each 3H, s, Ar-4-OCH_3), 4.01–4.43 (2H × 2, m, γ-CH_2), 5.70–5.96 (1H × 2, m, α-CH), 6.349** and 6.481* (each 2H, s, Ar-H), 7.26–7.58 (10H × 2, m, MTPA-C_6H_5). MS m/z (%): 674 (M^+, 13).

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References

1. Katayama T, Sogo M, Higuchi T (1986) Degradation and stereoselective reduction of an α-ketone derivative of guaiacylglycerol-β-vanillin ether, a lignin substructure model, by *Fusarium solani* M-13-1. Holzforschung 40:175–182
2. Katayama T, Sogo M (1989) An optically-active compound formed by the reduction of an α-ketonic lignin substructure model compound by *Fusarium solani* M-13-1. Mokuzai Gakkaishi 35:1116–1124
3. Dale JA, Dull DL, Mosher HS (1969) α-Methoxy-α-trifluoromethylphenylacetic acid, a versatile reagent for the determination of enantiomeric composition of alcohols and amines. J Org Chem 34:2543–2549
4. Dale JA, Mosher HS (1973) Nuclear magnetic resonance enantiomer reagents. Configuration correlations via nuclear magnetic resonance chemical shifts of diastereomeric mandelate, *O*-methylmandelate, and α-methoxy-α-trifluoromethylphenylacetate (MTPA) esters. J Am Chem Soc 95:512–519
5. Yamaguchi S (1985) The determination methods of chirality with NMR (in Japanese). Chem Today 168(3):14–21
6. Matsuda N, Kikuchi M (1996) Studies on the constitution of *Lonicera species*. X. Neolignan glycosides from the leaves of *Lonicera gracilipes* var. *glandulosa* Maxim. Chem Pharm Bull (Tokyo) 44:1676–1679
7. Adler E, Eriksoo E (1955) Guaiacylglycerol and its β-guaiacyl ether. Acta Chem Scand 9:341–342
8. Miksche GE (1973) Zum alkalischen Abbau von Arylglycerin-β-(2,6-dimethoxy-4-alkylaryl)-ätherstrukturen (in German). Acta Chem Scand 27:1355–1368
9. King LC, Ostrum GK (1964) Selective bromination with copper (II) bromide. J Org Chem 29:3459–3461