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Synthesis and plant growth inhibitory activity of both enantiomers of pyricuol, a phytotoxin isolated from rice blast disease fungus *Magnaporthe grisea*

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ABSTRACT

Both enantiomers and racemate of pyricuol, a phytotoxin isolated from the rice blast disease fungus, *Magnaporthe grisea*, have been synthesized by using Stille coupling and [2,3]-Wittig rearrangement reactions as the key steps. Both enantiomers induced dark necrotic lesions on rice leaves almost equally, but did not affect the growth of rice second leaf sheath and the germination of lettuce. Only natural enantiomer promoted the root growth of rice and lettuce.

1. Introduction

Rice blast disease, caused by infection of rice blast fungus, *M. grisea* (Hebert) Barr, is one of the most harmful disease for rice.[1] Many efforts have been paid to clarify phytotoxic substances, and several compounds with 6-substituted salicylaldehyde structure were isolated from the culture filtrate of the fungus. These compounds, such as pyricuol (**1**),[2] pyriculol (**2a**),[3] pyricurariol (**3a**),[4] and pyriculone (**4**),[5] induced dark necrotic spot, when being applied to wounded rice leaves. Synthetic studies have been made for these phytotoxins, and the absolute configuration of pyriculol (**2a**) was elucidated by our synthesis of four possible stereoisomers.[6] Ley et al. reported the synthesis of 10-*epi*-pyricuol,[7] also isolated from *M. grisea*.[8] Recently, we determined the absolute configuration of pyricurariol (**3a**) by the total synthesis.[9] In this relation, we communicated the synthesis of racemic[10a] and unnatural form[10b] of **1** to determine the absolute configuration. Here, we describe in detail the synthesis of both enantiomers and their plant growth inhibitory activities (Fig. 1).

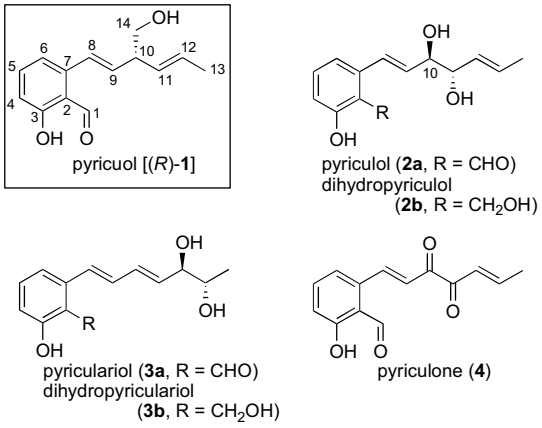

Figure 1. Structures of salicylaldehyde-type phytotoxins from *M. grisea*.

2. Results and discussion

2.1. Synthesis of the compounds

Our synthetic plan of **1** is shown in Scheme 1. The key step is [2,3]-Wittig rearrangement reaction[11] to construct the branched carbon framework, from dienol **A**. **A** can be prepared in two ways: (a) chain elongation in a racemic form via enyne **B**, which is accessible from the known aldehyde **E**,[6c] and (b) metal-catalyzed coupling reaction of **C** with optically active iodide **D**, preparable from alkyne **F** and ethyl (*S*)-lactate, respectively. **F** is also to be synthesized from **E**.

Scheme 2 shows the racemic synthesis of the key alcohol **A** (route a). Horner–Emmons reaction of the aldehyde **5** (**E**),[6c] prepared from 2,3-dimethylphenol in six steps, afforded exclusively (*E*)-ester **6** in 92% yield. The ethoxycarbonyl group was reduced (**7**) and oxidized to aldehyde **8**. Michel's modified Corey–Fuchs reaction[12] of **8** afforded terminal alkyne **9** (**B**), which was coupled

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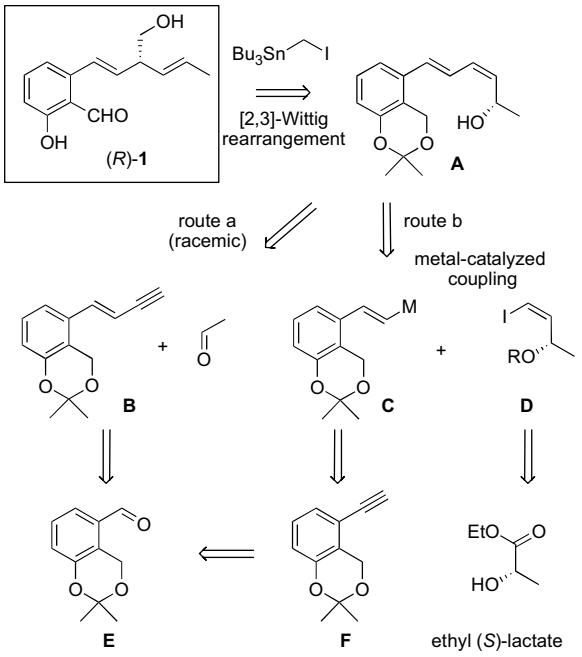
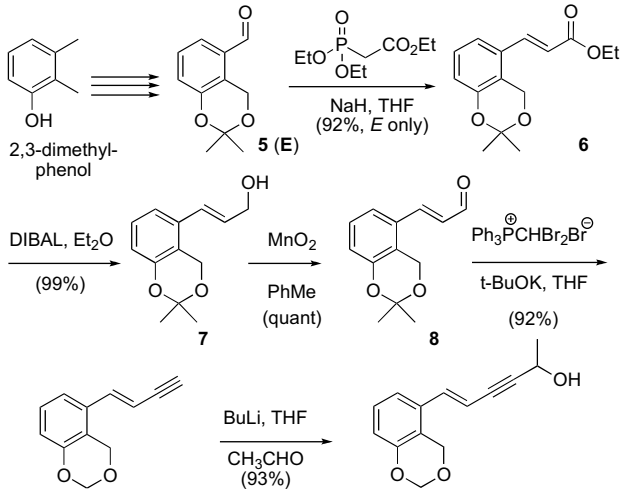


Scheme 1. Retrosynthetic analysis of pyricuol (**1**).

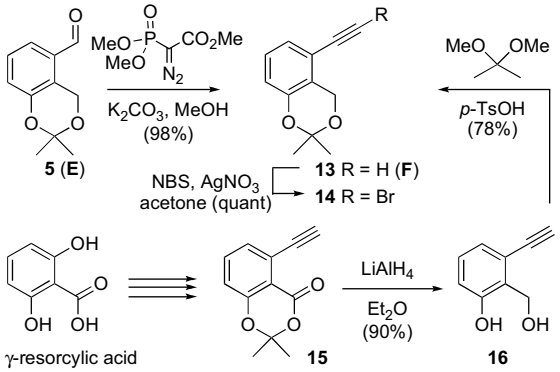


Scheme 2. Racemic synthesis of the key dienol **11**.

with acetaldehyde to give alcohol (±)-**10**. Partial hydrogenation of the triple bond on Pd/$BaSO_4$ in the presence of hex-1-ene afforded (*Z*,*E*)-dienol (±)-**11** (**A**), the key precursor of [2,3]-Wittig rearrangement. However, this step was troublesome because of poor reproducibility: over-reduction to (±)-**12** sometimes inevitable. Although this compound had led to the total synthesis of (±)-**1** as described previously,[10a] the scheme for enantioselective synthesis was changed.

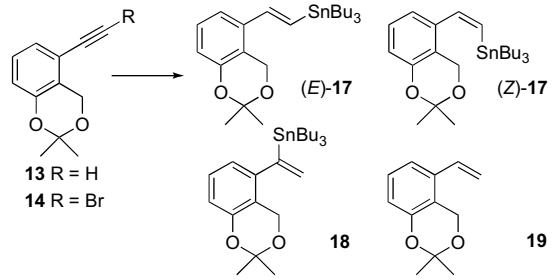
We chose metal-catalyzed coupling reactions to access the key alcohol **11** for enantioselective synthesis of **1** (route b). Scheme 3 shows the preparation of the precursor alkyne **13** (**F**). Treatment of **5** with Ohira–Bestmann reagent[13] gave **13** in 98%, which was converted to acetylenic bromide **14** in quantitative yield. We also tried to prepare **13** from the known compound **15**,[14] which was easily prepared from γ-resorcylic acid. Compound **15** was converted to **13** in two steps via diol **16**.

Table 1 shows the trial of hydrostannylation. High yield of (*E*)-**17** was formed under usual conditions (Bu_3SnH/AIBN in toluene, entry 1).[15] Concomitant *Z*-isomer was separated after the following coupling reaction. Undesired regioisomer **18** and styrene derivative **19** were obtained under palladium-catalyzed conditions (entry 2).[16] Stannylcupuration was accompanied by a styrene derivative **19** (entry 3).[17] Bromo acetylene **14** gave poorer result (entry 4).



Scheme 3. Preparation of acetylene derivatives.

Table 1
Hydrostannylation of the ethynylbenzene derivatives

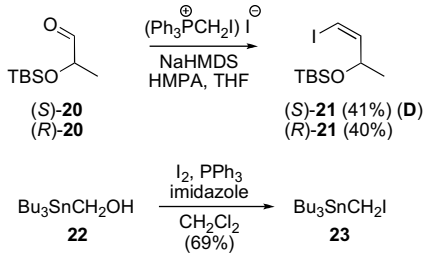


Entry	Starting material	Conditions	Yields (%)			
			(*E*)-**17**	(*Z*)-**17**	**18**	**19**
1	**13**	Bu_3SnH, AIBN, PhMe, reflux	84[a]	10	—	—
2	**13**	Bu_3SnH, $Pd_2(PPh_3)_2Cl_2$, THF, 20 °C	~3[a]	—	44	—
3	**13**	$(Bu_3Sn)BuCuCNLi_2$, THF, −78 to −30 °C	46	—	—	41
4	**14**	Bu_3SnH, Pd_2dba_3, PPh_3, THF, 20 °C	21[a]	21	42	—

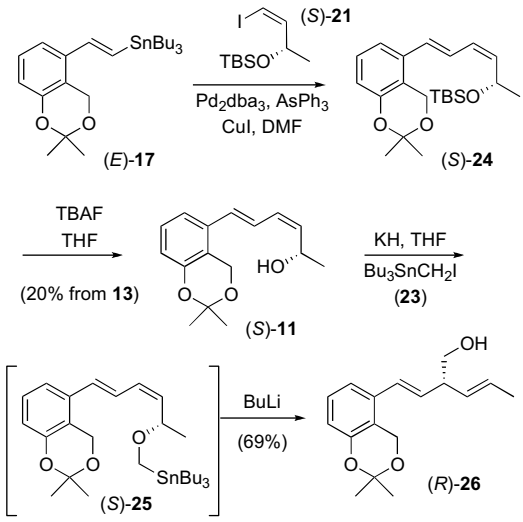
[a] The yields were calculated on the basis of ^1H NMR spectra.

Preparation of the chiral building partners is shown in Scheme 4. The source of chirality was ethyl (*S*)-lactate (>96% ee, Kanto) and isopropyl (*R*)-lactate (>98% ee, Aldrich). *Z*-vinyl iodides (*S*)-**21** (*Z*/*E*=33:1)[18] and (*R*)-**21** (*Z*/*E*=25:1) were prepared from the corresponding aldehydes (*S*)-**20**[19] and (*R*)-**20**,[20] respectively. Undesired *E*-isomers were separated by column chromatography. The C_1 fragment, (tributylstannyl)methyl iodide (**23**)[21] was prepared from the corresponding alcohol **22**.[22]

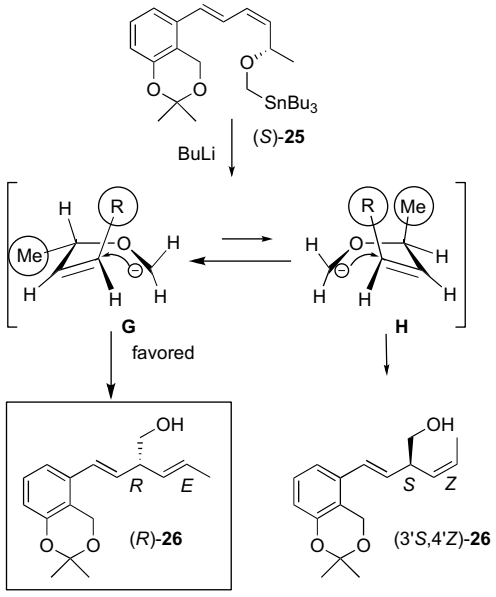
With both of the fragments in hand, Stille coupling reactions were examined. Compound (*E*)-**17** was coupled with (*S*)-**21** to afford (*S*)-**24**, followed by removal of the TBS group gave the key intermediate dienol (*S*)-**11** (Scheme 5). The hydroxy group was etherified with Bu_3SnCH_2I (**23**). The resulting stannylmethyl ether (*S*)-**25** was treated with BuLi, giving a [2,3]-Wittig rearranged product (*R*)-**26**. The chirality of (*S*)-**25** is believed to be completely transferred to 3′-position of (*R*)-**26** through a favored transition state **G** (Scheme 6). This was supported by the fact that no epimerization occurred during the synthesis of (*S*)-**1** (>98% ee) from isopropyl (*R*)-lactate (vide infra). In addition, a disfavored transition state **H**, in which the R and Me groups were repulsive, should have lead to (3′*S*,4′*Z*)-**26**, however, none of the signal due to the *Z*-isomer was detected in the ^1H NMR spectrum.



Scheme 4. Preparation of the chiral building blocks.

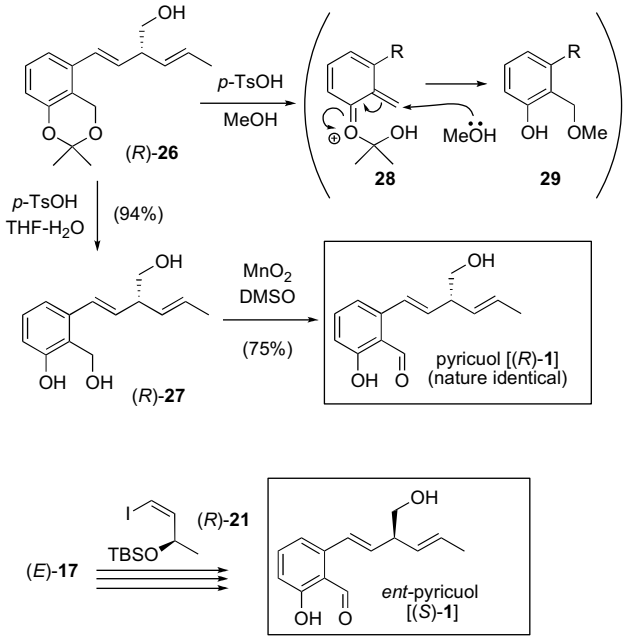


Scheme 5. The Stille coupling and [2,3]-Wittig rearrangement reactions.



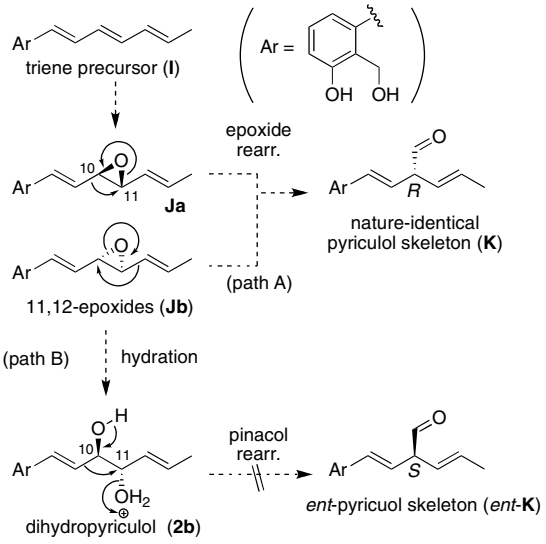
Scheme 6. Stereochemical course of the [2,3]-Wittig rearrangement reaction.

Removal of the acetonide group of (*R*)-**26** (*p*-TsOH, THF/H_2O) afforded triol (*R*)-**27** (Scheme 7). Unwanted side product **29** was formed, when methanol was used as solvent, probably due to Michael addition of methanol to an intermediate **28**. Finally, selective oxidation of the benzylic hydroxy group with MnO_2 gave (*R*)-pyricuol [(*R*)-**1**] of the nature identical form {$[\alpha]_D^{24}$ −22.2 (*c* 0.105, $CHCl_3$), lit.[2] $[\alpha]_D^{25}$ −17.4° (*c* 0.03, $CHCl_3$)}. The overall yield of (*R*)-**1** was 8.0% in seven steps from **5**. The enantiomeric purity of (*R*)-**1** was determined to be >94% ee by the ^1H NMR spectral data of its 14-*O*-MTPA esters. Similarly, unnatural *ent*-pyricuol {(*S*)-**1**, $[\alpha]_D^{20}$ +19 (*c* 0.070, $CHCl_3$), >98% ee} was synthesized from vinyl iodide (*R*)-**21**.



Scheme 7. Total synthesis of (*R*)-**1** and (*S*)-**1**.

The *R*-absolute configuration of natural pyricuol leads us to hypothesize its biosynthetic pathway (Scheme 8). Nukina et al. proposed triene **I** and epoxides **Ja** and/or **Jb** as the common synthetic intermediates for salicylaldehyde phytotoxins.[23] Our results show that natural pyricuol should be biosynthesized by epoxide rearrangement reaction[24] from either epoxides **Ja** or **Jb** (path A), while pinacol rearrangement reaction via dihydropyriculol (**2b**) will afford the enantiomer (*ent*-**K**).



Scheme 8. Plausible biosynthetic route of **1**.

2.2. Plant growth inhibition

Phytotoxic activities of synthetic compounds were assessed on the growth of rice and lettuce. In foliar application test, both (*R*)-**1** and (*S*)-**1** induced dark necrotic lesions on rice leaves almost

Table 2
Foliar application test on rice leaves[a]

Compounds	Concentration (μg/μL)		
	10	5	2.5
(*R*)-**1**	++++	++	+
(*S*)-**1**	+++	++	+

[a] Acetone solution of the sample with 0.01% of Tween-80 was pasted onto the rice leaf, and the whole plant was incubated at 25 °C under fluorescent light (6500 lux) for 7 d. The area of decolorized lesion was measured for two replicates.

equally when 2.5, 5.0, and 10 μg/μL solutions in acetone were pasted (Table 2). Both enantiomers did not inhibit the growth of second leaf sheath of rice and the seed germination of lettuce. The activity of (*R*)-**1** in foliar application agrees with that of natural product, but the results of growth of rice second sheaths differ.[2] The natural product inhibited 42% of growth at 200 ppm.[2] The natural enantiomer slightly promoted the root lengths of rice and lettuce, while (*S*)-**1** little affected (Fig. 2).

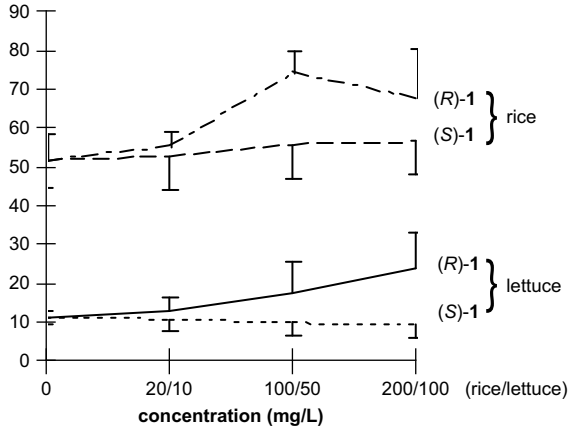


Figure 2. Effects of both enantiomers of pyricuol (**1**) on the root lengths of lettuce and rice. A group of twenty lettuce seeds (*L. sativa* cv. Colorado) on a 0.7% agar medium was incubated at 25 °C under fluorescent light (6500 lux) for 4 d. A group of 10 rice seedlings (*O. sativa* L. cv. Notohikari) that had been germinated in water at 30 °C for 2 d was transplanted to a test tube (36Φ×100 mm) with 6 mL of a 0.7% agar medium, and this was incubated at 25 °C under fluorescent light (6500 lux) for 4 d.

3. Conclusions

Synthesis of both enantiomers of pyricuol, a phytotoxin isolated from the rice blast fungus, *M. grisea*, was achieved using the Stille coupling and [2,3]-Wittig rearrangement reactions as the key steps. Both enantiomers induced dark necrotic lesions on rice leaves almost equally, but did not affect the growth of rice second leaf sheath and the germination of lettuce. Only natural enantiomer promoted the root growth of rice and lettuce.

4. Experimental

4.1. General

Melting points were uncorrected. Optical rotation values were measured by a Horiba Sepa-300 polarimeter. FTIR spectra were recorded as films by a Jasco 4100 spectrometer (ATR, Zn/Se). IR spectra were recorded as films by a Jasco Report-100 spectrometer. UV spectrum was recorded with a Shimadzu UV-1600 spectrometer. ^{1}H NMR spectra were recorded with a Varian Inova 600 (600 MHz), Inova 500 (500 MHz), and Gemini 2000 (300 MHz) spectrometers in $CDCl_3$ with tetramethylsilane as an internal standard. Mass spectra were recorded with a Jeol JMS-700 spectrometer. Merck silica gel 60 and Kanto silica gel 60N (neutral) were used for column chromatography.

4.2. (*E*)-5-(2′-Ethoxycarbonyl)ethenyl-2,2-dimethyl-4*H*-benzo[*e*][1,3]dioxin (6)

To an ice-cold suspension of NaH (60% mineral oil dispersion, FW: 24.00, 108 mg, 2.7 mmol) and diethyl phosphonoacetate (FW: 224.19, *d*=1.12, 1.10 mL, 1.23 g, 5.50 mmol) in dry THF (20 mL) was added a solution of **5**[6c] (FW: 192.21, 0.490 g, 2.54 mmol) in THF (3 mL), and the resulting mixture was stirred at room temperature for 12 h. The mixture was poured into satd aq NH_4Cl soln and extracted with ether. The organic layer was washed with brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on silica gel. Elution with hexane/EtOAc (10:1) gave **6** (FW: 262.30, 0.610 g, 2.33 mmol, 91.7%) as a colorless oil. IR (film): ν=1710 (s, C=O), 1640 (s, C=C), 1580 (s, C=C), 1255 (s, C–O), 1180 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=1.34 (t, *J*=7.2 Hz, 3H, CH_3CH_2), 1.55 (s, 6H, 2-Me_2), 4.27 (q, *J*=7.2 Hz, 2H, CH_3CH_2), 4.98 (s, 2H, H-4), 6.35 (d, *J*=15.9 Hz, 1H, H-1′), 6.85 (dd, *J*=7.2, 2.1 Hz, 1H), 7.15–7.19 (m, 2H), 7.61 (d, *J*=15.9 Hz, 1H, H-2′). EIMS: *m*/*z*=262 ($M^{+\bullet}$), 224, 204 [M−Me_2C=O]$^+$, 197, 179, 132. HREIMS: calcd for $C_{12}H_{22}O_2$ ($M^{+\bullet}$) 262.1205; found 262.1205.

4.3. (*E*)-5-(3′-Hydroxy-1′-propenyl)-2,2-dimethyl-4*H*-benzo[*e*][1,3]dioxin (7)

To a solution of **6** (FW: 262.30, 269 mg, 1.03 mmol) in dry toluene (5 mL) was added dropwise DIBAL in hexane (0.94 M, 3.25 mL, 3.06 mmol) at −78 °C under nitrogen and stirred for 2 h at this temperature. After the temperature of the mixture was gradually raised to 20 °C, to this was added satd aq Rochelle's salt and extracted with ether. The organic layer was washed with brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on silica gel. Elution with hexane/EtOAc (4:1) gave **7** (FW: 220.26, 224 mg, 1.02 mmol, 99.0%) as a colorless oil. FTIR: ν=3400 (vs, O–H), 3076 (s, H–C=), 1584 (s, C=C), 1286 (s, C–O), 1145 (s, C–O), 870 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=1.54 (s, 6H, 2-Me_2), 4.34 (br t, *J*=4.9 Hz, 2H, OH), 4.89 (s, 2H, H-4), 6.29 (dt, *J*=15.6, 5.4 Hz, 1H, H-2′), 6.51 (d, *J*=15.6 Hz, 1H, H-1′), 6.74 (d, *J*=8.1 Hz, 1H), 7.04 (d, *J*=7.8 Hz, 1H), 7.14 (t, *J*=7.8 Hz, 1H, H-7). EIMS: *m*/*z*=220 ($M^{+\bullet}$), 162 [M−Me_2C=O]$^+$, 147, 132, 86, 84. HREIMS: calcd for $C_{13}H_{16}O_3$ ($M^{+\bullet}$) 220.1099; found 220.1100.

4.4. (*E*)-5-(2′-Formylethenyl)-2,2-dimethyl-4*H*-benzo[*e*][1,3]dioxin (8)

A suspension of **7** (FW: 220.26, 330 mg, 1.5 mmol) and active MnO_2 (3.37 g, 47.5 mmol) in toluene (20 mL) was shaken for 12 h. The mixture was filtered through a Celite pad and concentrated in vacuo. The residue was chromatographed on silica gel. Elution with hexane/EtOAc (3:2) gave **8** (FW: 218.25, 330 mg, 1.5 mmol, quant.) as a white crystal. Analytical sample was recrystallized from hexane/toluene, mp 106–107 °C. FTIR: ν=2870 (w, C–H), 1666 (s, C=O), 1624 (m), 1580 (s, C=C), 1280 (s, C–O), 1132 (s, C–O), 871 (s), 783 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=1.57 (s, 6H, 2-Me_2), 5.01 (s, 2H, H-4), 6.44 (dd, *J*=15.9, 7.5 Hz, 1H, H-2′), 6.92 (dd, *J*=7.5, 2.1 Hz, 1H), 7.21–7.25 (m, 2H), 7.41 (d, *J*=15.9 Hz, 1H, H-1′), 9.71 (d, *J*=7.8 Hz, 1H, CHO). EIMS: *m*/*z*=218 ($M^{+\bullet}$), 192, 132, 106, 85, 83, 47. HREIMS: calcd for $C_{13}H_{14}O_3$ ($M^{+\bullet}$) 218.0943; found 218.0944.

4.5. (*E*)-5-(But-1′-en-3′-ynyl)-2,2-dimethyl-4*H*-benzo[*e*][1,3]dioxin (9)

To a suspension of dibromomethyl(triphenyl)phosphonium bromide (FW: 515.01, 4.95 g, 9.61 mmol) in dry THF (46 mL) was

added KO*t*-Bu (FW: 112.21, 974 mg, 8.68 mmol) at room temperature under nitrogen and stirred for 5 min, and then added **8** (FW: 219, 1.00 g, 4.58 mmol). After being stirred for 40 min, the mixture was cooled to −78 °C and to this was added KO*t*-Bu (2.59 g, 23.1 mmol), and the mixture was stirred for 3 h. The mixture was poured into water and extracted with ether. The organic layer was washed with brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on silica gel. Elution with hexane/EtOAc (10:1) gave **9** (FW: 214.26, 898 mg, 4.20 mmol, 91.7%) as a pale yellow oil. IR (film): ν=3300 (s, ≡C–H), 1590 (s, C═C), 1480 (s), 1460 (s), 1395 (s), 1380 (s), 1300 (s), 1260 (s), 1220 (s), 1155 (s), 880 (s), 790 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ=1.54 (s, 6H, 2-Me_2), 3.08 (d, J=2.1 Hz, 1H, H-4′), 4.89 (s, 2H, H-4), 6.06 (dd, J=16.2, 2.4 Hz, 1H, H-2′), 6.79 (dd, J=7.8, 0.9 Hz, 1H), 6.93 (d, J=16.2 Hz, 1H, H-1′), 7.05 (d, J=7.5 Hz, 1H), 7.15 (t, J=7.8 Hz, 1H, H-7). EIMS: m/z=214 ($M^{+\bullet}$), 190, 188, 173, 150, 128, 93, 63, 47. HREIMS: calcd for $C_{14}H_{14}O_2$ ($M^{+\bullet}$) 214.0994; found 214.0997.

4.6. (±)-(*E*)-5-(5′-Hydroxyhex-1′-en-3′-ynyl)-2,2-dimethyl-4*H*-benzo[*e*][1,3]dioxin (10)

To a solution of **9** (FW: 214.26, 684 mg, 3.20 mmol) in dry THF (50 mL) was added dropwise BuLi in hexane (1.50 M, 2.2 mL, 3.3 mmol) at −78 °C under nitrogen. To this was added dropwise acetaldehyde (FW: 44.05, d=0.795, 0.36 mL, 0.29 g, 6.5 mmol) for 12 h while the temperature of the solution gradually raised to 20 °C. The mixture was poured into satd aq NH_4Cl soln and extracted with ether. The organic layer was washed with satd aq NH_4Cl soln and brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on silica gel. Elution with hexane/EtOAc (4:1) gave **10** (FW: 258.31, 765 mg, 2.97 mmol, 92.8%) as pale yellow crystal. Analytical sample was recrystallized from hexane/*i*-Pr_2O, mp 72–73 °C. IR (KBr): ν=3400 (s, O–H), 1590 (s, C═C), 1480 (s), 1460 (s), 1390 (s), 1380 (s), 1300 (s), 1260 (s), 1150 (s), 960 (s), 880 (s), 760 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ=1.53 (t, J=6.8 Hz, 3H, H-6′), 1.54 (s, 6H, 2-Me_2), 1.83 (d, J=5.4 Hz, OH), 4.72 (dq, J=2.1, 6.8 Hz, 1H, H-5′), 4.89 (s, 2H, H-4), 6.10 (dd, J=16.2, 2.1 Hz, 1H, H-2′), 6.78 (d, J=8.7 Hz, 1H), 6.82 (d, J=16.2 Hz, 1H, H-1′), 7.04 (d, J=7.8 Hz, 1H), 7.14 (t, J=8.1 Hz, 1H, H-7). EIMS: m/z=258 ($M^{+\bullet}$), 200 [M−Me_2C═O]$^+$, 157, 128, 86, 84. HREIMS: calcd for $C_{16}H_{18}O_3$ ($M^{+\bullet}$) 258.1256; found 258.1259.

4.7. (1′*E*,3′*Z*,5′*RS*)-5-(5′-Hydroxyhexa-1′,3′-dienyl)-2,2-dimethyl-4*H*-benzo[*e*][1,3]dioxin [(±)-11]

A suspension of **10** (FW: 258.31, 18.1 mg, 0.0701 mmol), Pd/$BaSO_4$ (10.6 mg), quinoline (0.01 mL), and hex-1-ene (0.10 mL, 68 mg, 0.805 mmol) in MeOH (1 mL) was stirred for 1 min under hydrogen atmosphere. The mixture was filtered through a Celite pad and concentrated in vacuo. The residue was purified by preparative TLC (toluene/Et_2O=2:1) to give (±)-**11** [FW: 260.33, 16.4 mg, 0.630 mmol, 89.9%, quant. taking into account the recovered **10** (1.8 mg)] as a colorless oil. The spectral data of (±)-**11**: see compound (*R*)-**11**.

HRFABMS: calcd for $C_{16}H_{20}O_3Na$ [M+Na]$^+$ 283.1310; found 283.1314.

4.8. 3-Ethynyl-2-hydroxymethylphenol (16)

To a suspension of $LiAlH_4$ (FW: 37.95, 150 mg, 3.95 mmol) in THF (4 mL) was added **15**[14] (FW: 202.21, 200 mg, 0.99 mmol) in THF (0.6 mL) at −78 °C, and the mixture was stirred at −60 °C for 1 h. Then to this was added 0.5 M HCl in MeOH/H_2O and EtOAc. The whole mixture was filtered through a Celite pad, washed with H_2O and brine, dried with $MgSO_4$ and concentrated in vacuo to give **16** (FW: 146.14, 130 mg, 0.89 mmol, 90%) as a colorless oil. R_f=0.10 (hexane/EtOAc=3:1). FTIR (ATR, Zn/Se) ν_{max}: 3290 (vs, O–H), 1580 (s), 1463 (s), 993 (m), 792 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ: 2.47 (1H, br s, OH), 3.26 (1H, s, ≡CH), 5.17 (2H, s, CH_2), 6.90 (1H, d, J=7.8 Hz), 7.05 (1H, dd, J=7.3 Hz), 7.15 (1H, t, J=7.8 Hz, H-5), 7.99 (1H, s, OH). EIMS: m/z: 148 (M^+), 130 [M−H_2O]$^+$, 102, 63, 62. FABMS: m/z: 149 [M+H]$^+$, 131 [M−H_2O]$^+$. HRFABMS: calcd for $C_9H_8O_2$ [M+H]$^+$ 149.0603; found 149.0611.

4.9. 5-Ethynyl-2,2-dimethyl-4*H*-benzo[*e*][1,3]dioxin (13)

(a) A solution of **16** (FW: 146.14, 100 mg, 0.68 mmol) and *p*-TsOH·H_2O (FW: 190.22, 6.5 mg, 0.03 mmol) in 2,2-dimethoxypropane (3 mL) was stirred at 20 °C for 1 h, poured into satd aq $NaHCO_3$ soln, and extracted with Et_2O. The extract was washed with H_2O and brine, dried with $MgSO_4$ and concentrated in vacuo. The residue was chromatographed on SiO_2 (hexane/EtOAc=20:1) to give **13** (FW: 188.22, 100 mg, 0.53 mmol, 78%).

(b) To a solution of the aldehyde **5**[6c] (FW: 192.21, 486 mg, 2.53 mmol) in dry MeOH (15 mL) was added a solution of dimethyl (1-diazo-2-oxopropyl)phosphonate (FW: 193.12, 1.11 g, 5.74 mmol) in MeOH (5 mL) and then potassium carbonate (FW: 138.21, 0.87 g, 6.29 mmol) at 0 °C. After being stirred at room temperature for 1.5 h, the mixture was poured into a satd aq $NaHCO_3$ soln and extracted with ether. The organic layer was washed with brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on silica gel (hexane/EtOAc=20:1) to give **13** (FW: 188.22, 469 mg, 2.49 mmol, 98.4%) as a colorless oil. R_f=0.67 (hexane/EtOAc=10:1). FTIR (Zn/Se): ν=3849 (s, ≡C–H), 2104 (vw, C≡C), 1582 (s), 1465 (s), 1276 (s, C–O), 864 (m), 785 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ=1.54 (s, 6H, Me_2C), 3.29 (s, 1H, ≡CH), 4.91 (s, 2H, H-4), 6.83 (dd, J=8.1, 1.2 Hz, 1H), 7.07 (dd, J=7.5, 1.2 Hz, 1H), 7.13 (t, J=7.8 Hz, 1H, H-7). EIMS: m/z=188 (M^+), 130 [M−Me_2C═O]$^+$, 102, 76, 61, 43, 32. HREIMS: calcd for $C_{12}H_{22}O_2$ (M^+) 188.0837; found 188.0838.

4.10. 5-Bromoethynyl-2,2-dimethyl-4*H*-benzo[*e*][1,3]-dioxin (14)

To a solution of **13** (FW: 188.22, 58 mg, 0.31 mmol) in dry acetone (2 mL) were added *N*-bromosuccimide (FW: 177.98, 63 mg, 0.35 mmol) and silver nitrate (FW: 169.87, 11 mg, 0.065 mmol), and the mixture was stirred at room temperature for 1 h. Then the mixture was poured in H_2O and extracted with ether. The organic layer was washed with H_2O, dried with $MgSO_4$, and concentrated in vacuo to give **14** (FW: 267.12, 83 mg, 0.31 mmol, quant) as a brown oil. R_f 0.5 (hexane/EtOAc=10:1). This compound was used as crude. ^1H NMR ($CDCl_3$, 300 MHz): δ=1.53 (s, 6H, Me_2C), 4.89 (s, 2H, H-4), 6.82 (dd, 1H, J=8.4, 1.2 Hz), 7.03 (dd, 1H, J=8.4, 1.2 Hz), 7.12 (pseudo t, 1H, J=8.4 Hz, H-7).

4.11. (*E*)-5-(1′-Tributylstannyl)ethenyl-2,2-dimethyl-4*H*-benzo[*e*][1,3]dioxin (17)

(a) *Stannylcupuration*. To a suspension of CuCN (FW: 89.56, 164.6 mg, 1.838 mmol, 1.16 equiv) in THF (10 mL) was added a solution of BuLi in hexane (1.6 M, 2.3 mL, 3.6 mmol, 2.3 equiv) at −76 °C and the mixture was gradually raised to −35 °C with stirring and then cooled to −76 °C. To this was added dropwise Bu_3SnH (FW: 291.06, d =1.08, 0.964 mL, 1.04 g, 3.57 mmol, 2.26 equiv) over 10 min and the temperature of this was raised to −37 °C. Then to this was added a solution of **13** (FW: 188.08, 298 mg, 1.58 mmol) in THF (5 mL) and the mixture was stirred for 3 h at −37 °C. The mixture was poured into a mixture of a satd aq NH_4Cl soln (3 mL) and aq NH_3 (0.6 mL) and extracted with ether. The organic layer was washed with brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on neutral silica gel

(hexane/EtOAc=100:1) to give **17** (FW: 479.29, 454 mg, 0.724 mmol, 46%) as a colorless oil. This compound was very unstable. R_f=0.71 (hexane/EtOAc=10:1). ^{1}H NMR ($CDCl_3$, 300 MHz): δ=0.91 (t, J=7.2 Hz, 9H, CH_2CH_3), 0.92–1.00 (m, 6H), 1.34 (sext, 6H, CH_2CH_3), 1.48–1.61 (m, 6H), 1.54 (s, 3H, Me_2C), 1.56 (s, 3H, Me_2C), 4.93 (s, 2H, H-4), 6.72 (dd, J=8.1, 1.2 Hz, 1H), 6.76 (s, 2H, H-1′, 2′), 7.07 (pseudo d, J=8.1 Hz, 1H), 7.15 (t, J=8.1 Hz, 1H, H-7). FABMS: m/z=479 $[M+H]^+$, 423, 365, 291, 251, 235, 179, 177, 115. HRFABMS: calcd for $C_{24}H_{41}O_2Sn$ $[M+H]^+$ 479.2123; found 479.2123.

(b) *Radical-mediated hydrostannylation*. To a solution of **13** (52.8 mg, 0.293 mmol) in dry toluene (5 mL) were added AIBN (FW: 164.22, 9.3 mg, 0.057 mmol) and Bu_3SnH (124 mg, 0.426 mmol), and the mixture was stirred at reflux for 3 h. Then, the mixture was diluted with EtOAc and washed with water and brine, dried with $MgSO_4$, and concentrated in vacuo to give **17** (ca. 94%, E/Z=89:11) as a crude yellow oil. Compound (*Z*)-**17** was assigned by ^{1}H NMR ($CDCl_3$, 300 MHz): δ=4.76 (s, 2H, H-4), 6.27 (d, 1H, J=13.5 Hz), 6.32 (d, 1H, J=13.5 Hz).

(c) *Palladium-catalyzed hydrostannylation*. To a solution of **14** (FW: 267.11, 147 mg, 0.550 mmol), PPh_3 (FW: 262.29, 6.0 mg, 0.023 mmol), and Pd_2dba_3 (FW: 915.7, 3.1 mg, 0.0034 mmol) in dry THF (4 mL) was added dropwise Bu_3SnH (FW: 291.06, 0.33 mL, 360 mg, 1.2 mmol) over 0.5 h. After being stirred at 20 °C for 2 h, the mixture was filtrated through a Celite pad and the pad was washed with EtOAc. The combined filtrate was concentrated in vacuo to give a crude brown oil containing [(*E*)-**17**/**18**/**19**=21:21:42]. Compound **18**: ^{1}H NMR ($CDCl_3$, 300 MHz): δ=4.67 (s, 2H, H-4), 5.52 (d, 1H, J=3.0 Hz, vinyl), 5.77 (d, 1H, J=3.0 Hz, vinyl), 6.47 (d, J=7.7 Hz), 6.64 (d, J=8.2 Hz), 7.07 (dd, J=8.2, 7.7 Hz).Compound **19**: ^{1}H NMR ($CDCl_3$, 300 MHz): δ=1.55 (s, 6H, Me_2C), 4.90 (s, 2H, 4–H), 5.3 5(dd, 1H, J=10.8, 1.2 Hz, *Z*-vinyl), 5.69 (dd, 1H, J=17.4, 1.2 Hz, *E*-vinyl), 6.66 (dd, 1H, J=17.4, 10.8 Hz), 6.77 (dd, 1H, J=7.8, 2.0 Hz), 7.09 (dd, 1H, J=7.8, 1.5 Hz), 7.16 (t, 1H, J=7.8 Hz).

4.12. (1*Z*,3*R*)-3-*tert*-Butyldimethylsilyloxy-1-iodobut-1-ene (*R*)-21

After a mixture of iodomethyltriphenylphoshonium iodide (FW: 530.12, 5.70 g, 10.8 mmol) and NaN(TMS)$_2$ (1.0 M in THF, 10.8 mL, 10.8 mmol) in THF (15 mL) being stirred at 20 °C for 5 min under nitrogen, HMPA (FW: 179.20, 0.48 g, 2.7 mmol), was added and the resulting mixture was cooled to −78 °C. Then to this was added aldehyde (*R*)-**20**[20] (FW: 188.34, 50.6 mg, 2.69 mmol) in THF (15 mL), and the resulting mixture being stirred at −78 °C for 20 min before poured into satd aq NH_4Cl soln, and extracted with Et_2O. The organic layer was washed with H_2O and brine, dried with $MgSO_4$, and concentrated in vacuo to give crude product (Z/E=25:1). This was chromatographed on silica gel (hexane/Et_2O=75:1) to give (*R*)-**21** (FW: 312.05, 337 mg, 1.08 mmol, 40.1%) as a colorless oil, $[\alpha]_D^{24}$ −62 (*c* 0.86, $CHCl_3$). R_f=0.75 (hexane/Et_2O=10:1). The ^{1}H NMR datum was identical with the that reported for (*S*)-**21**.[18]HREIMS: calcd for $C_{10}H_{21}OISi$ ($M^{+\bullet}$) 312.0406; found 312.0410.

Compound (*S*)-**21:** Compound (*S*)-**20** (0.54 g, 2.3 mmol) afforded (*S*)-**21** (0.30 g, 0.97 mmol, 41% in two steps), $[\alpha]_D^{24}$ +60 (*c* 0.62, $CHCl_3$) {lit.[18] $[\alpha]_D^{23}$ +68.1 (*c* 0.79, $CHCl_3$)}.

4.13. Tributylstannylmethyl iodide (23)

To an ice-cooled suspension of imidazole (FW: 68.08, 1.70 g, 24.9 mmol) in CH_2Cl_2 (20 mL) was added PPh_3 (FW: 262.3, 3.28 g, 12.5 mmol), and then dropwise a solution of Bu_3SnCH_2OH (**22**, FW: 321.09, 2.04 g, 6.23 mmol) in THF (10 mL). The mixture was stirred at room temperature for 12 h. Then the mixture was poured into a satd aq $Na_2S_2O_3$ soln and extracted with hexane. The organic layer was dried with $MgSO_4$ and concentrated in vacuo. The residue was chromatographed on silica gel. Elusion with hexane/EtOAc (100:1) gave **23** (FW: 430.98, 1.85 g, 4.29 mmol, 69%) as a colorless oil. This oil was pure enough for the further reaction.

4.14. (1′*E*,3′*Z*,5′*R*)-5-(5′-*tert*-Butyldimethylsilyloxyhexa-1′,3′-dienyl)-2,2-dimethyl-4*H*-benzo[*e*][1,3]dioxin [(*R*)-24]

To a solution of (*R*)-**21** (FW: 312.05, 55.6 mg, 0.178 mmol), Pd_2dba_3 (FW: 915.72, 5.3 mg, 0.0058 mmol), $AsPh_3$ (FW: 306.24, 3.6 mg, 0.012 mmol) and CuI (FW: 190.45, 2.2 mg, 0.012 mmol) in DMF (0.5 mL) was added dropwise **17** (FW: 479.29, 55.6 mg, 0.116 mmol) in DMF (1.5 mL) at 22 °C, and the mixture was stirred for 2 days, before poured into satd aq NH_4Cl soln and extracted with Et_2O. The organic layer was washed with satd aq $NaHCO_3$ soln and brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on SiO_2. Elution with hexane/EtOAc (100:1) gave (*R*)-**24** (FW: 374.59, 34 mg, 0.091 mmol, 78.4%) as a colorless oil, $[\alpha]_D^{24}$ −100 (*c* 0.20, Et_2O). R_f=0.59 (hexane/EtOAc=10:1), 0.58 (hexane/Et_2O=5:1). UV (Et_2O, 1.7×10^{-5} mol/l): λ (log ε)=288 (4.32), 237 (4.18), 219 (4.23) nm. FTIR (Zn/Se): ν=1579 (m), 1283 (m), 1253 (m, Si–C), 1079 (m), 834 (m) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=0.063 (s, 3H, MeSi), 0.082 (s, 3H, MeSi), 0.89 (s, 9H, *t*-Bu), 1.27 (d, J=6.3 Hz, 3H, H-6′), 1.54 (s, 6H, Me_2C), 4.84 (m, 1H, H-5′), 4.90 (s, 2H, H-4), 5.55 (dd, J=11.2, 8.5 Hz, 1H, H-4′), 6.05 (t, J=11.2 Hz, 1H, H-3′), 6.39 (d, J=15.3 Hz, 1H, H-1′), 6.74 (dd, J=8.0, 1.2 Hz, 1H, Ar), 6.95 (ddd, J=15.3, 11.2, 1.2 Hz, 1H, H-2′), 7.09 (dd, J=7.4, 1.1 Hz, 1H, Ar), 7.16 (dd, J=8.0, 7.4 Hz, 1H, H-7). EIMS: m/z=374 (M^+), 316 [M+H−*t*-Bu]$^+$, 259 [M−HOTBS]$^+$. HREIMS: calcd for $C_{22}H_{34}O_3Si$ ($M^{+\bullet}$) 374.2277; found 374.2279.

Compound (***S***)-**24**: A colorless oil, $[\alpha]_D^{25}$ +119 (*c* 1.53, Et_2O). HREIMS: calcd for $C_{22}H_{34}O_3Si$ (M^+) 374.2277; found 374.2284.

4.15. (1′*E*,3′*Z*,5′*R*)-5-(5′-Hydroxyhexa-1′,3′-dienyl)-2,2-dimethyl-4*H*-benzo[*e*][1,3]dioxin [(*R*)-11]

A solution of (*R*)-**24** (FW: 374.59, 12.9 mg, 0.0344 mmol) in a 0.25 M solution of TBAF in THF (0.8 mL, 0.2 mmol) was stirred at 20 °C for 3 h. The mixture was diluted with EtOAc and washed with water, a satd aq $NaHCO_3$ soln and brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on silica gel (hexane/EtOAc=10:1 to 5:1) to give unreacted (*R*)-**24** (2.1 mg, 0.0056 mmol, 16%) and (*R*)-**11** [FW: 260.33, 7.1 mg, 0.027 mmol, 79%; 94% taking into account the recovered (*R*)-**24**] as a colorless oil, $[\alpha]_D^{25}$ −15 (*c* 0.36, Et_2O). R_f=0.17 (hexane/EtOAc=4:1). FTIR (Zn/Se): ν=3380 (s, O–H), 1578 (s), 1283 (s), 1144 (s), 1117 (s), 872 (m), 785 (m) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=1.33 (d, J=6.3 Hz, 3H, H-6′), 1.54 (s, 6H, Me_2C), 1.71 (br s, 1H, OH), 4.89 (m, 1H, H-5′), 4.89 (s, 2H, H-4), 5.57 (ddd, J=9.9, 8.7, 0.9 Hz, 1H, H-4′), 6.16 (t, J=11.1 Hz, 1H, H-3′), 6.43 (d, J=15.3 Hz, 1H, H-1′), 6.74 (dd, J=7.5, 1.8 Hz, 1H, Ar), 7.00 (ddd, J=15.3, 11.1, 1.2 Hz, 1H, H-2′), 7.11 (dd, J=8.1, 1.8 Hz, 1H, Ar), 7.15 (t, J=7.4 Hz, 1H, H-7). EIMS: m/z=260 ($M^{+\bullet}$), 242, 218, 202, 192, 184, 144. HREIMS: calcd for $C_{16}H_{20}O_3$ (M^+) 260.1412; found 260.1418.

Compound (***S***)-**11:** Compound **13** (692 mg, 3.68 mmol) was converted to (*S*)-**11** (192 mg, 0.738 mmol, 20.1% from **13** in three steps) as a colorless oil, $[\alpha]_D^{24}$ +9.6 (c 0.05, Et_2O). HREIMS: calcd for $C_{16}H_{20}O_3$ ($M^{+\bullet}$) 260.1412; found 260.1412.

4.16. (1′*E*,3′*S*,4′*E*)-5-(3′-Hydroxymethylhexa-1′,4′-dienyl)-2,2-dimethyl-4*H*-benzo[*e*][1,3]dioxin [(*S*)-26]

To a suspension of KH (FW: 40.11, 30% oil dispersion, 30 mg, 0.22 mmol) in THF (0.3 mL) was added (*R*)-**11** (FW: 260.33, 23 mg, 0.088 mmol) in THF (0.7 mL) at 0 °C and the mixture was stirred for 10 min. Then Bu_3SnCH_2I (FW: 430.98, 57 mg, 0.13 mmol) was added

and the resulting mixture was stirred for 1 h at 0 °C. After the mixture being cooled to −78 °C, BuLi (1 6 M in hexane, 0.088 mL, 0.13 mmol) was added and stirred for 1 h. The mixture was poured into satd aq NH_4Cl soln and extracted with Et_2O. The organic layer was washed with satd aq $NaHCO_3$ soln and brine, dried with $MgSO_4$, and concentrated. in vacuo. The residue was chromatographed on SiO_2. Elution with hexane/EtOAc (10:1) gave (*R*)-**26** (FW: 274.16, 14 mg, 0.051 mmol, 58%) as a colorless oil, $[\alpha]_D^{24}$ +9.4 (*c* 0.16, Et_2O). R_f=0.60 (hexane/EtOAc=2:1). FTIR (Zn/Se): ν=3408 (m, O–H), 1583 (m), 1282 (m), 1145 (m), 968 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ: 1.54 (s, 6H, Me_2C), 1.74 (pseudo d, *J*=6.4 Hz, 3H, H-6′), 3.09 (pseudo quint, *J*=7.4 Hz, 1H, H-3′), 3.60 (br. s, 2H, CH_2OH), 4.87 (s, 2H, H-4), 5.42 (ddq, *J*=15.7, 1.7, 7.4 Hz, 1H, H-4′), 5.65 (ddq, *J*=15.7, 0.8, 6.5 Hz, 1H, H-5′), 6.04 (dd, *J*=15.7, 6.7 Hz, 1H, H-2′), 6.35 (d, *J*=15.7 Hz, 1H, H-1′), 6.73 (dd, *J*=7.8, 1.1 Hz, 1H), 7.04 (d, *J*=7.8 Hz, 1H), 7.13 (t, *J*=7.8 Hz, 1H, H-7). EIMS: *m*/*z*=274 (M^+), 260, 256 $[M-H_2O]^+$, 144, 83, 74. HREIMS: calcd for $C_{17}H_{22}O_3$ ($M^{+\bullet}$) 274.1569; found 274.1575.

Compound (*R*)-**26**: Compound (*S*)-**11** (110 mg, 0.43 mmol) was converted to (*R*)-**26** (81.8 mg, 0.60 mmol, 69%) as a colorless oil, $[\alpha]_D^{24}$ −13.3 (*c* 1.35, Et_2O). HREIMS: calcd for $C_{17}H_{22}O_3$ ($M^{+\bullet}$) 274.1569; found 274.1565.

4.17. (1′*E*,3′*S*,4′*E*)-2-Hydroxymethyl-3-(3′-hydroxymethylhexa-1′,4′-dienyl)phenol [(*S*)-27]

A solution of the acetonide (*S*)-**26** (FW: 274.35, 9.0 mg, 0.033 mmol) and *p*-TsOH (cat.) in MeOH/H_2O (1:1, 2 mL) was stirred at room temperature for about 12 h. To the mixture was added a satd aq $NaHCO_3$ soln and concentrated in vacuo to remove most of MeOH. The residue was extracted with EtOAc and the organic layer was washed with brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on silica gel (hexane/EtOAc=3:1) to give (*S*)-**27** (FW: 234.29, 7.1 mg, 0.030 mmol, 92%) as a colorless oil, $[\alpha]_D^{25}$ +9.0 (*c* 0.10, $CHCl_3$). R_f=0.11 (hexane/EtOAc=2:1). FTIR (Zn/Se) ν=3350 (s, O–H), 2919 (m), 1582 (s), 1468 (s), 1267 (m, C–O), 970 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz) δ: 1.74 (dd, *J*=6.5, 1.2 Hz, 3H, H-6′), 2.32 (br, 1H, OH), 3.08 (m, 1H, H-3′), 3.57–3.64 (m, 2H, CHCH_2OH), 4.99 (s, 2H, ArCH_2OH), 5.42 (ddq, *J*=15.0, 1.4, 7.3 Hz, 1H, H-4′), 5.65 (ddq, *J*=15.5, 6.4, 0.5 Hz, 1H, H-5′), 5.92 (dd, *J*=15.6, 7.6 Hz, 1H, H-2′), 6.63 (d, *J*=15.6 Hz, 1H, H-1′), 6.80 (d, *J*=7.9 Hz, 1H), 6.95 (d, *J*=7.6 Hz, 1H), 7.14 (t, *J*=7.9 Hz, 1H, H-5). FABMS: *m*/*z*=235 $[M+H]^+$, 219, 155, 154. HRFABMS: calcd for $C_{14}H_{19}O_3$ $[M+H]^+$ 235.1334; found 235.1333.

Compound (*R*)-**27**: A solution of (*R*)-**26** (61.8 mg, 0.225 mmol) and *p*-TsOH (cat.) in THF/H_2O (1:1, 6 mL) was stirred at 20 °C for 48 h. The mixture was poured into satd aq $NaHCO_3$ soln and extracted with EtOAc. The organic layer was washed with brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on silica gel (hexane/EtOAc=2:1 to 1:1) to give (*R*)-**27** (53.3 mg, 0.227 mmol, quant) as a colorless oil, $[\alpha]_D^{24}$ −18 (*c* 0.47, $CHCl_3$). HREIMS: calcd for $C_{14}H_{18}O_3Na$ $[M+Na]^+$ 257.1154; found 257.1160.

4.18. (1′*E*,3′*S*,4′*E*)-2-Hydroxy-5-(3′-hydroxymethyl-1′,4′-hexadienyl)benzenecarbaldehyde [*ent*-pyricuol, (*S*)-1]

A suspension of the triol (*S*)-**27** (FW: 234.29, 1.6 mg, 6.8 μmol) and MnO_2 (chemicals treated, FW: 86.94, 36 mg, 0.41 mmol, 60 equiv) in DMSO/$CHCl_3$ (7:3, 1 mL) was stirred at 60 °C for 1 h. The mixture was filtered through a Celite pad and the pad was washed with EtOAc. The combined filtrate was concentrated in vacuo. The residue was chromatographed on silica gel (hexane/EtOAc=5:1) to give (*S*)-**1** (FW: 233.28, 1.6 mg, 6.8 mmol, quant) as a colorless oil, $[\alpha]_D^{20}$ +19 (*c* 0.070, $CHCl_3$). R_f=0.70 (hexane/EtOAc=2:1). FTIR (Zn/Se): ν=3390 (s, O–H), 3025 (w), 2923 (s), 2854 (s), 1642 (s, C=O), 1609 (s), 1569 (m, Ar), 1450 (s), 1327 (m), 1311 (m), 1195 (m), 1165 (m), 970 (m), 722 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ=1.76 (dd, *J*=6.4, 1.0 Hz, 3H, H-13), 3.15 (pseudo quint, *J*=7.3 Hz, 1H, H-10), 3.63 (m, 1H, H-14), 3.68 (m, 1H, H-14), 5.43 (ddq, *J*=15.1, 7.8, 1.5 Hz, 1H, H-11), 5.68 (dq, *J*=15.1, 6.3 Hz, 1H, H-12), 6.04 (dd, *J*=15.6, 7.3 Hz, 1H, H-9), 6.87 (d, *J*=8.3 Hz, 1H, H-6), 6.93 (d, *J*=7.3 Hz, 1H, H-4), 6.96 (d, *J*=15.6 Hz, 1H, H-8), 7.44 (t, *J*=8.0 Hz, 1H, H-5), 10.31 (s, 1H, CHO), 11.87 (s, 1H, OH). FABMS: *m*/*z*=233 $[M+H]^+$, 215 $[M+H-H_2O]^+$, 185, 147, 115, 93, 75, 55, 41. HRFABMS: calcd for $C_{14}H_{17}O_3$ $[M+H]^+$ 233.1178; found 233.1179.

Compound (*R*)-**1**: Compound (*R*)-**27** (9.7 mg, 0.040 mmol) was converted to (*R*)-**1** (7.5 mg, 0.032 mmol, 75%) as a colorless oil, $[\alpha]_D^{24}$ −22.2 (*c* 0.105, $CHCl_3$) {lit.[2] $[\alpha]_D^{25}$ −17.4 (*c* 0.03, $CHCl_3$)}. HREIMS: calcd for $C_{14}H_{17}O_3$ $[M+H]^+$ 233.1178; found 233.1178.

4.19. (*R*)-1 14-*O*-MTPA esters

Compound (*R*)-**1** was converted to the corresponding (*S*)- and (*R*)-14-*O*-MTPA esters using (*R*)- and (*S*)-MTPA chlorides (>99% ee, Aldrich), respectively, in pyridine and $CHCl_3$. ^1H NMR ($CDCl_3$, 600 MHz) of H-14: δ=4.31 [dd, 1H, *J*=10.7, 7.5 Hz,(*S*)-MTPA], 4.36 [dd, 1H, *J*=10.6, 5.3 Hz,(*R*)-MTPA], 4.38 [dd, 1H, *J*=10.6, 10.6 Hz, (*R*)-MTPA], 4.44 [dd, 1H, *J*=1.07, 5.9 Hz, (*S*)-MTPA].

4.20. Foliar application test for rice leaves[1]

Acetone solution of the sample with 0.01% Tween-80 was pasted onto the rice leaves, and the whole plant was incubated at 25 °C under fluorescent light (6500 lux) for 7 days. The area of decolorized lesion was measured for two replicates.

4.21. Lettuce germination assay

The inhibitory effect on lettuce germination was assayed in the same manner as that described.[25] A group of 20 lettuce seeds (*Lactuca sativa* cv. Colorado) was placed in a 5-cm Petri dish with a test solution of a 0.7% agar medium. After being incubated at 25 °C under fluorescent light (6500 lux) for 4 days, the germination ratio and the root length were measured for two replicates.

4.22. Rice seedling assay

The inhibitory effect on rice seedling growth was assayed in the same manner as that described previously[25] under non-sterile conditions. A group of 10 rice seedlings (*Oryza sativa* L. cv. Notohikari) that had been germinated in water at 30 °C for 2 days was transplanted to a test tube (36Φ×100 mm) with 6 mL of a 0.7% agar medium, and this was incubated at 25 °C under fluorescent light (6500 lux) for 4 days. The length of the second leaf sheath and root was measured for two replicates.

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