Syntheses of All Four Stereoisomers of Pyriculol†

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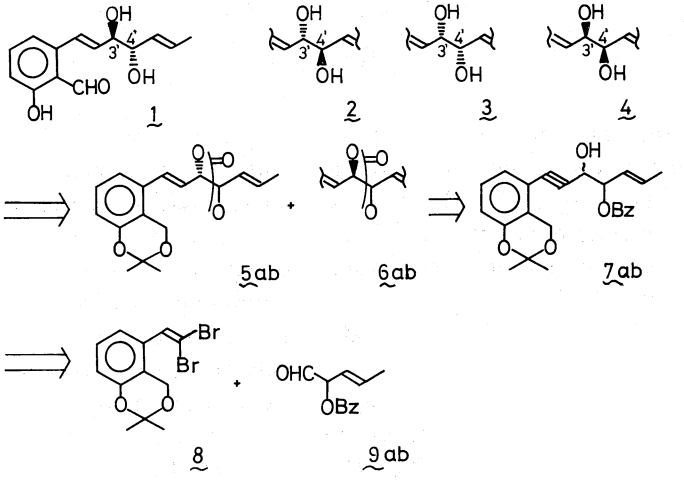
All four stereoisomers of pyriculol were synthesized to assist in forming a correlation between their chemical structure and biological activity. The (*R*,*E*)-2-hydroxy-3-pentenal derivative was coupled with a lithium acetylide derivative to give a diastereomeric mixture of the acetylenic alcohol, which led to the antipode of pyriculol and its 3′-epimer. Similarly obtained were the natural pyriculol and its 3′-epimer from the (*S*)-isomer of this aldehyde.

Pyriculol (**1**) is a phytotoxic metabolite that has been isolated from a culture broth of the rice blast fungus *Pyricularia oryzae* Cavara.[1] This substance causes dark necrotic spots on rice leaves, characteristic of the symptons of rice blast disease, and induces the growth-inhibitory activity in rice seedlings.

We have recently established the absolute configuration of **1** as (3′*R*,4′*S*) by total synthesis of optically active **1** from an aromatic part and an aldehyde with a protected glycol moiety, using a Wittig reaction between them.[2]

Alternatively, from synthetic studies on the optically active natural dihydropyranones, we could construct the target molecules using the nucleophilic addition of a lithium acetylide to chiral 2-benzoyloxy-aldehydes without affecting the ester group or the chiral center.[3] Although this latter reaction seemed to proceed less stereospecifically and resulted in a diastereomeric mixture of mono-benzoylated 1,2-glycols, it was thought to be applicable to the syntheses of stereoisomers of pyriculol. These isomers, including enantiomers and diastereomers, are needed to investigate the

SCHEME I



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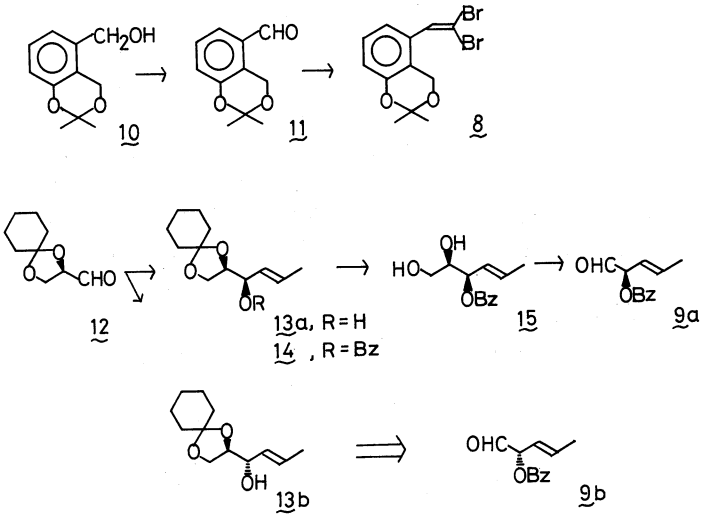
relationship between the streochemical structure and biological activity.

In this paper, we report the alternative synthesis of all four stereoisomers of pyriculol (**1**), the synthetic procedure being outlined in Scheme I. The addition reaction of a lithium phenylacetylide derived from **8** to (*E*)-1-formyl-2-butenyl benzoate (**9ab**) would provide a diastereomeric mixture of the acetylenic alcohols (**7ab**), which would then be transformed into the desired pyriculols (**1** and **2**) and their 3′-epimers (**3** and **4**). As both the (*R*)- and (*S*)-aldehydes (**9a** and **9b**) would be available from the same starting material,[2a,3b] all four stereoisomers of pyriculol could be synthesized.

The aromatic unit was prepared from a hydroxy-acetonide **10**[2,4] by the oxidation of **10** with active manganese dioxide in dichloromethane to give a quantitative yield of an aldehyde **11**. This was treated with carbon tetrabromide and triphenylphosphine[6] to afford a dibromide **8** as a prism in a good yield.

The (*S*,*E*)-1-formyl-2-butenyl benzoate **9b** was prepared from 2,3-*O*-cyclohexylidene-D-glyceraldehyde (**12**)[5] *via* **13b**[2a] as described in our previous paper.[3b] An enantiomer, (*R*)-aldehyde **9a**, was prepared in the same manner from (2*R*,3*R*,*E*)-1,2-*O*-cyclohexylidene-4-hexene-1,2,3-triol (**13a**)[2a] as in the case of the preparation of **9b** (Scheme II).

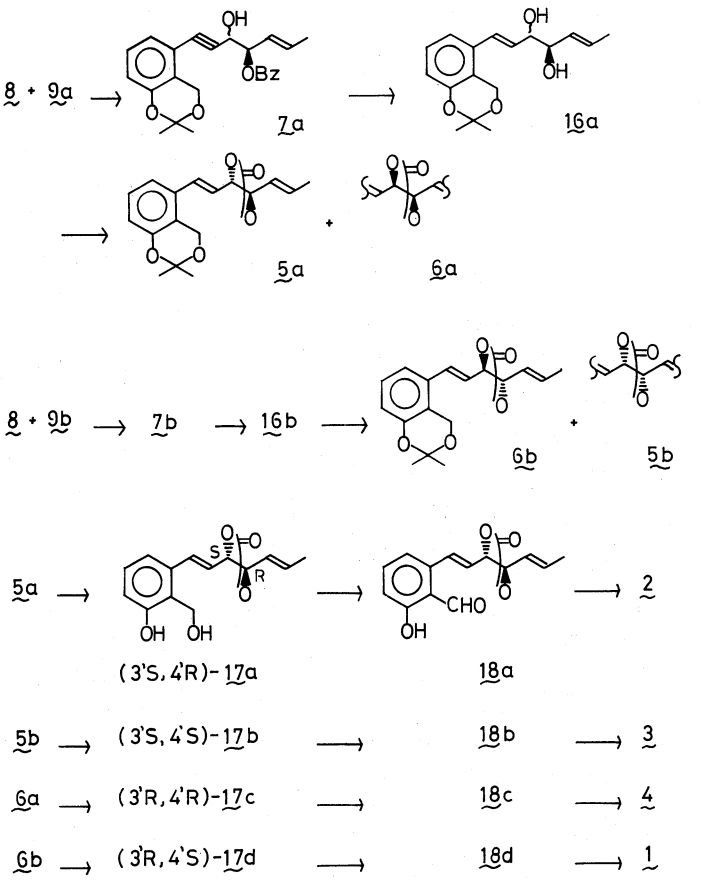
SCHEME II



With three kinds of synthons in hand, we carried out the convergent steps toward the four stereoisomers of pyriculol (**1**) (Scheme III). At first, the enantiomer of pyriculol **2** and its 3′-epimer **4** were synthesized as communicated previously.[2b]

The addition of a lithium phenylacetylide, prepared *in situ* from the dibromide **8** and butyllithium in dry ether, to the (*R*)-aldehyde **9a** yielded a diastereomeric mixture of an acetylenic alcohol (**7a**) in around a 67% yield. In the ^{1}H NMR spectrum of **7a**, the benzylic protons were observed at 4.82 and 4.84 ppm as two overlapping peaks, whereas **7a** showed a single spot on thin-layer chromatograms in spite of developments with various kinds of solvent systems. Therefore, **7a** was subjected to the next steps without separation of each component. Reduction of **7a** with lithium aluminum hydride in refluxing tetrahydrofuran afforded a dihydroxy-diene **16a**, which was then treated with dimethyl carbonate and a catalytic amount of sodium hydride at refluxing temperature to give an easily separable mixture of **5a** and **6a** in a 73% yield from **7a** (**5a** : **6a** = 1 : 1.5 by HPLC analysis). Each of them was isolated by thin-layer chromatography. The more polar isomer was proved to

SCHEME III



be **5a** ($Rf=0.32$, silica gel plate, hexane–ethyl acetate = 3 : 1) and the less polar isomer was **6a** ($Rf=0.50$).

Enantiomeric **5b** and **6b** were also synthesized under the same conditions as just mentioned from the dibromide **8** and (*S*)-aldehyde (**9b**). Thus, **5b** and **6b** were respectively identical with **5a** and **6a** in all respects except for the signs of optical rotation.

Conversion of each of the four intermediates **5a**, **5b**, **6a** and **6b** into the corresponding four isomers of pyriculol (**1**) was effected by following a similar procedure to that described in our previous report[2] with satisfactory yields.

(3′*S*,4′*R*)-Pyriculol (**2**), obtained in this way, showed mp 98 ~ 99°C and $[\alpha]_D^{22}-40°$ ($CHCl_3$), and was identical with natural **1**[7] except for the sign of the optical rotation. Diastereomeric **3** and **4** were obtained as viscous oils and showed $[\alpha]_D^{22}-33.2°$ and $[\alpha]_D^{22}+31.5°$ ($CHCl_3$), respectively.

The melting point of the admixture of synthetic **1** and natural **1** was not depressed at all, while that of **2** and natural **1** showed a significant depression of melting point (82 ~ 90°C). The acetonide derivative of the *vic*-glycol moiety of each isomer was prepared and subjected to an ^{1}H-NMR analysis. Two singlets assignable to the methyl groups on the acetonide ring from **1** and **2** appeared at 1.44 and 1.56 ppm; on the other hand, one singlet assigned to those from **3** and **4** was observed at 1.48 ppm.

These observations reaffirmed not only the *erythro* configuration of the *vic*-glycol part[8] of natural pyriculol (**1**), but also the absolute structure of natural **1** as (3′*R*,4′*S*,1′*E*,5′*E*)-2-(3′,4′-dihydroxy-1′,5′-heptadienyl)-6-hydroxybenzaldehyde.

EXPERIMENTAL

All melting points (mp) and boiling points (bp) were uncorrected. Optical rotations were measured on a JASCO DIP-4 polarimeter. IR spectra were taken on a JASCO IR-810 infrared spectrometer and NMR spectra were obtained on a JEOL JNM FX-100 spectrometer. Mass spectra were recorded on a Hitachi M-52 spectrometer, and HPLC was performed on a JASCO Tri Rotar equipped with a UVIDEC-100-II detector.

2,2-Dimethyl-4H-1,3-benzodioxin-5-carbaldehyde (**11**). A solution of hydroxy-acetonide (**10**,[2,4] 7.5 g) and active MnO_2 (60 g) in CH_2Cl_2 (80 ml) was shaken vigorously at room temperature. After 2 hr, the mixture was filtered through a short column of silica gel eluted with CH_2Cl_2. Evaporation of the solvent gave **11** (7.4 g, quant.), mp 54°C. *Anal.* Found: C, 68.77; H, 6.23. Calcd. for $C_{11}H_{12}O_3$ C, 68.73; H, 6.29%. IR ν_{max} (KBr) cm^{-1}: 3000, 2760, 1700, 1680, 1600, 1590, 1380, 1360, 960, 880. ^{1}H-NMR δ_{TMS} ($CDCl_3$): 1.54 (6H, s), 5.21 (2H, s), 7.09 (δ_8), 7.38 (δ_7) and 7.41 (δ_6). (Each 1H, higher order ABC splittings with $J_{6\text{-}7}=7.3$, $J_{6\text{-}8}=1.5$ and $J_{7\text{-}8}=7.8$ Hz).

5-(2′,2′-Dibromoethenyl)-2,2-dimethyl-4H-1,3-benzodioxin (**8**). To a solution of CBr_4 (24.8 g, 74.4 mmol) in dry CH_2Cl_2 (100 ml) was added dropwise a solution of triphenylphosphine (40 g, 153 mmol) in dry CH_2Cl_2 (100 ml) with stirring at 0°C under N_2 atmosphere. After 1 hr, a solution of **11** (6.4 g, 33.2 mmol) in dry CH_2Cl_2 (50 ml) was added over a period of 30 min at that temperature. The reaction mixture was stirred for 30 min at 0°C and then poured into hexane (400 ml). The precipitates were filtered off and the filtrate was concentrated *in vacuo* to afford 12 g of a crude crystal. Recrystallization from hexane gave **8** (8.6 g, 74%) as a prism, mp 55.0～55.5°C. *Anal.* Found: C, 41.64; H, 3.44; Br, 45.87. Calcd. for $C_{12}H_{12}O_2Br_2$: C, 41.41; H, 3.48; Br, 45.92%. IR ν_{max} (KBr) cm^{-1}: 3000, 1602, 1595, 1480, 1390, 1380, 950, 880, 780. ^{1}H-NMR δ_{TMS} ($CDCl_3$): 1.54 (6H, s), 4.74 (2H, s), 6.82 (1H, br. d, J= 7.8 Hz), 6.98 (1H, br. d, J=7.8 Hz), 7.19 (1H, t, J= 7.8 Hz), 7.29 (1H, s).

(1R,1′R,E)-1-(1′,2′-Cyclohexylidenedioxy)ethyl-2-butenyl benzoate (**14**). To a solution of the *threo*-alcohol (**13a**,[2a] 4.0 g, 18.8 mmol) in dry pyridine (60 ml) was added benzoyl chloride (2.6 ml, 22 mmol) at 0°C, and the reaction mixture was stirred for 30 min. Water (100 ml) was then added the mixture was extracted with ether. The extract was washed with dil. HCl, water, $NaHCO_3$ aq. and brine, and dried over anhyd. $MgSO_4$. Evaporation of the solvent and purification of the residue on an active alumina column with benzene afforded a colorless oil of **14** (6.0 g, quant.). *Anal.* Found: C, 72.37; H, 7.69. Calcd. for $C_{19}H_{24}O_4$: C, 72.12; H, 7.65%. $[\alpha]_D^{22}+26.2°$ (c=1.60, $CHCl_3$). IR ν_{max} (film) cm^{-1}: 1725, 1680, 1600, 1590, 1275, 970, 720. ^{1}H-NMR δ_{TMS} ($CDCl_3$): 1.45～1.66 (10H, m), 1.72 (3H, dd, J=6.4, 1 Hz), 3.82 (1H, dd, J=8.3, 6.1 Hz), 4.04 (1H, dd, J=8.3, 6.4 Hz), 4.32 (1H, q, J=6.1 Hz), 5.46～5.65 (2H, m), 5.94 (1H, dqd, J=15.1, 6.4, 1 Hz), 7.35～7.60 (3H, m), 8.02～8.12 (2H, m).

(1R,1′R,E)-1-(1′,2′-Dihydroxy)ethyl-2-butenyl benzoate (**15**). A solution of **14** (6.45 g, 20.4 mmol) and *p*-TsOH (775 mg) in aq. MeOH (60 ml) was heated at 60°C for 2 hr. The mixture was then poured into $NaHCO_3$ aq. and extracted with AcOEt. The extract was washed with water and brine, and dried over anhyd. $MgSO_4$. Evaporation of the solvent and purification of the residue by column chromatography on silica gel afforded **15** (4.6 g, 96%). *Anal.* Found: C, 65.86; H, 6.94. Calcd. for $C_{13}H_{16}O_4$: C, 66.08; H, 6.83%. $[\alpha]_D^{22}+35.2°$ (c=2.44, $CHCl_3$). IR ν_{max} (film) cm^{-1}: 3420, 1720, 1602, 1595, 1498, 1280, 1120, 970, 720. ^{1}H-NMR δ_{TMS} ($CDCl_3$): 1.72 (3H, dd, J=6.5, 1 Hz), 2.86 (2H, br. s), 3.60～4.00 (3H, m), 5.40～6.10 (3H, m), 7.35～7.65 (3H, m), 8.00～8.12 (2H, m).

(R,E)-1-Formyl-2-butenyl benzoate (**9a**). A mixture of **15** (2.4 g, 10.2 mmol), $NaIO_4$ (2.6 g, 12.3 mmol) and a catalytic amount of Bu_4NBr in ether (50 ml) and water (59 ml) was stirred at room temperature for 2 hr. The ether layer was separated, washed with water and brine, and dried over anhyd. Na_2SO_4. Evaporation of the solvent and distillation of the residue gave **9a** (1.55 g, 74%), bp 108～109°C (0.3 mmHg). *Anal.* Found: C, 70.74; H, 5.82. Calcd. for $C_{12}H_{12}O_3$: C, 70.57; H, 5.92%. $[\alpha]_D^{22}-95.8°$ (c= 1.44, benzene). The IR and NMR spectra were identical with those of **9b**.[3]

(3′RS,4′R,5′E)-5-(4′-Benzoyloxy-3-hydroxy-5′-hepten-1′-ynyl)-2,2-dimethyl-4H-1,3-benzodioxin (**7a**). To a stirred solution of **8** (1.71 g, 4.92 mmol) in dry ether (30 ml) was added *n*-butyllithium (6.5 ml, 1.56 M in hexane, 10 mmol) at −70°C. After 40 min, **9a** (956 mg, 4.68 mmol) in dry ether (20 ml) was added dropwise to the resulting solution of lithium phenylacetylide at −70°C. The mixture was stirred for 2 hr at that temperature. Then the reaction mixture was poured into dil. AcOH and extracted with ether. The extract was washed with $NaHCO_3$ aq. and brine, and dried over anhyd. $MgSO_4$. Evaporation of the solvent and purification of the residue by column chromatography on silica gel afforded **7a** (1.24 g, 67%). *Anal.* Found: C, 73.38; H, 6.35. Calcd. for $C_{24}H_{24}O_5$: C, 73.45; H, 6.16%. IR ν_{max} (film) cm^{-1}: 3470, 2240, 1730, 1635, 1595, 1390, 1380, 1280, 1120, 970, 860, 720. ^{1}H-NMR δ_{TMS} ($CDCl_3$): 1.51 (6H, s), 1.79 (3H, d, J=6 Hz), 2.20～2.60 (1H, OH), 4.82 and 4.84 (2H, two peaks), 5.70～6.20 (2H, m) 6.80～7.15 (2H, m), 7.40～7.50 (3H, m), 8.00～8.20 (2H, m).

(3′RS,4′S,5′E)-5-(4′-Benzoyloxy-3′-hydroxy-5′-hepten-1′-ynyl)-2,2-dimethyl-4H-1,3-benzodioxin (**7b**). The title compound was obtained from **9b**[3] in a 71% yield by

the same method as just described. *Anal.* Found: C, 73.10; H, 6.20. Calcd. for $C_{24}H_{24}O_5$: C, 73.45; H, 6.16%. The IR and NMR spectra were identical with those of **7a**.

(3′RS,4′R,1′E,5′E)-5-(3′,4′-Dihydroxy-1′,5′-heptadienyl-2,2-dimethyl-4H-1,3-benzodioxin (**16a**). To a suspension of $LiAlH_4$ (110 mg, 2.9 mmol) in dry THF (20 ml) was added dropwise a solution of **7a** (500 mg, 1.27 mmol) in dry THF (20 ml) with stirring at room temperature. The reaction mixture was then refluxed for 2 hr. After cooling, the reaction was quenched with water and filtered. The filtrate was diluted with water and extracted with AcOEt. The extract was washed with water, $NaHCO_3$ aq. and brine, and dried over anhyd. $MgSO_4$. Evaporation of the solvent gave a crude product, which was purified on a silica gel column to yield **16a** (300 mg, 84%). *Anal.* Found: C, 69.82; H, 7.71. Calcd. for $C_{17}H_{22}O_4$: C, 70.32; H, 7.64%. IR ν_{max} (film) cm^{-1}: 3400, 1670, 1590, 1385, 1375, 960, 870. ^{1}H-NMR δ_{TMS} ($CDCl_3$) 1.53 (6H, s), 1.74 (3H, dd, J=6.4, 1 Hz), 5.51 (1H, ddq, J=15, 5.9, 1 Hz), 6.56 (1H, d, J=15.6 Hz).

(3′RS,4′S)-Isomer (**16b**). This was also prepared from **7b** by a similar method in an 88% yield. *Anal.* Found: C, 69.98; H, 7.74. Calcd. for $C_{17}H_{22}O_4$: C, 70.32; H, 7.64%.

(3′S,4′R,1′E,5′E)-5-(3′,4′-Carbonyldioxy-1′,5′-heptadienyl)-2,2-dimethyl-4H-1,3-benzodioxin (**5a**) *and its (3′R,4′R)-isomer* (**6a**). The diol **16a** (550 mg, 1.89 mmol) was dissolved in dimethyl carbonate (10 ml), and a catalytic amount of NaH was added before the reaction mixture was stirred at 60～70°C for 2 hr. The mixture was then diluted with ether, washed with water and brine, and dried over anhyd. $MgSO_4$. Afte removing the solvent, a residual mixture of **5a** and **6a** was separated into each component to give **5a** (216 mg, 36%) as the more polar compound and **6a** (305 mg, 51%) as the less polar isomer.

5a. *Anal.* Found: C, 68.55; H, 6.53. Calcd. for $C_{18}H_{20}O_5$: C, 68.34; H, 6.37%. $[\alpha]_D^{22}-52.8°$ (c=1.78, $CHCl_3$). The IR and NMR spectra were identical with those of **5b** from our previous paper.[2a]

6a. *Anal.* Found: C, 67.87; H, 6.30. Calcd. for $C_{18}H_{20}O_5$: C, 68.34; H, 6.37%. $[\alpha]_D^{22}+68.8°$ (c=2.40, $CHCl_3$). IR ν_{max} (film) cm^{-1}: 1805, 1680, 1590, 1390, 1380, 1180, 1030, 970, 870. ^{1}H-NMR δ_{TMS} ($CDCl_3$): 1.54 (6H, s), 1.81 (3H, dd, J=6.3, 1 Hz), 4.65～4.94 (2H, m), 4.86 (2H, s), 5.55 (1H, ddq, J=15.1, 7.6, 1 Hz), 5.93 (1H, dq, J=15.1, 6.3 Hz), 6.06 (1H, dd, J=15.6, 6.8 Hz), 6.65 (1H, d, J=15.6 Hz), 6.80 (1H, dd, J=7.6, 1.7 Hz), 7.03 (1H, dd, J=7.6, 1.7 Hz), 7.19 (1H, t, J=7.6 Hz).

(3′S,4′S)- and (3′R,4′S)-isomers (**5b** *and* **6b**). **5b** and **6b** were obtained from **16b** in 51 and 35% yields respectively by a method similar to that already described. **6b** was identical with that of our previous report[2a] in all respects.

5b. *Anal.* Found: C, 68.39; H, 6.61. Calcd. for $C_{18}H_{20}O_5$: C, 68.34; H, 6.37%. $[\alpha]_D^{22}-74.4°$ (c=1.50, $CHCl_3$). The IR and NMR spectra agreed well with those of **6a** already described.

(3′S,4′R,1′E,5′E)-3-(3′,4′-carbonyldioxy-1′5′-heptadienyl)-2-hydroxymethylphenol (**17a**). A mixture of **5a** (216 mg, 0.683 mmol), and *p*-TsOH (20 mg) in THF (10 ml) and water (1 ml) was heated at refluxing temperature for 5 hr. The mixture was poured into $NaHCO_3$ aq. and extracted with AcOEt. The extract was dried over anhyd. $MgSO_4$ and concentrated to afford a crystalline residue. Recrystallization of the product from benzene–CH_2Cl_2 gave **17a** (120 mg, 64%). mp 119～120°C. $[\alpha]_D^{22}-64.7°$ (c=0.92, $CHCl_3$). *Anal.* Found: C, 65.27; H, 5.87. Calcd. for $C_{15}H_{16}O_5$: C, 65.21; H, 5.84%. The IR and NMR spectra were superimposable on those of **17b** from our previous paper.[2a]

(3′R,4′S)-Isomer (**17d**). **17d** was also prepared from **6b** by a similar method in an 82% yield.

(3′S,4′S)-Isomer (**17b**). In the same manner, **5b** was converted to **17b** in a 93% yield as a viscous oil. *Anal.* Found: C, 65.51; H, 5.86. Calcd for $C_{15}H_{16}O_5$: C, 65.21; H, 5.84%. $[\alpha]_D^{22}-88.4°$ (c=1.38, $CHCl_3$). IR ν_{max} (film) cm^{-1}: 3380, 1800, 1680, 1660, 1590, 1190, 1040, 970. ^{1}H-NMR δ_{TMS} ($CDCl_3$): 1.80 (3H, dd, J=6.3, 1 Hz), 2.73 (1H, br. s), 4.65～4.95 (2H, m), 4.93 (2H, broad), 5.54 (1H, ddq, J=15.1, 7.5, 1 Hz), 5.97 (1H, dd, J=15.6, 6.8 Hz), 5.98 (1H, dq, J=15.1, 6.3 Hz), 6.81～6.99 (3H, m), 7.11 (1H, t, J=7.6 Hz), 7.70 (1H, s).

(3′R,4′R)-Isomer (**17c**). This was obtained in the same manner from **6a** in a 71% yield. *Anal.* Found: C, 65.41; H, 5.99. Calcd. for $C_{15}H_{16}O_5$: C, 65.21; H, 5.84%. $[\alpha]_D^{22}+90.7°$ (c=0.81, $CHCl_3$). The IR and NMR spectra were identical with those of **17b**.

(3′S,4′R)-Pyriculol-3′,4′-carbonate (**18a**). A mixture of **17a** (88 mg, 0.32 mmol) and active MnO_2 (700 mg) in CH_2Cl_2 (5 ml) was shaken for 1 hr at room temperature. The mixture was filtered and the filtrate was concentrated *in vacuo*. The residual oil was purified by preparative TLC on silica gel to give **18a** (59 mg, 67%) as a yellow oil. MS (relative intensity): 274 (24.8, M+), 214/213/212 (4/3/3), 160/159 (9.3/7.8), 148/147 (21.8/100), 134/132 (14/5), 134/132 (14/5). Calcd for $C_{15}H_{14}O_5$=274.26. $[\alpha]_D^{22}-49.8°$ (c=1.85, $CHCl_3$). The IR and NMR spectra were identical with those of **18d** in ref. 2a.

(3′R,4′S)-Isomer (**18d**). This was also obtained according to a similar procedure from **17d** in an 88% yield, and agreed well with **18d** from our previous paper.[2a]

(3′S,4′S)-Isomer (**18b**). In a similar manner, **17b** was converted to **18b** in an 84% yield. MS (relative intensity): 275/274 (9/18, M+1/M), 161/160 (9/12), 149/148/147/146/145 (13/27/100/10/10), 134 (20), 131 (13), 82 (9). Calcd. for

$C_{15}H_{14}O_5$=274.26. $[\alpha]_D^{22}$ −80.1° (c=1.34, $CHCl_3$). IR ν_{max} (film) cm^{-1}: 1805, 1650, 1610, 1580, 1180, 1040, 970. ^{1}H-NMR δ_{TMS} ($CDCl_3$): 1.82 (3H, dd, J=6.4, 1 Hz), 4.77 (1H, dd, J=8.3, 7.3 Hz), 4.92 (1H, dd, J=15.1, 6.4 Hz), 6.10 (1H, dd, J=15.6, 6.3 Hz), 6.95 (1H, d, J=7.3 Hz), 6.96 (1H, d, J=8.8 Hz), 7.31 (1H, d, J=15.6 Hz), 7.50 (1H, dd, J=8.8, 7.3 Hz), 10.29 (1H, s), 11.85 (1H, s).

(3′R,4′R)-Isomer (**18c**). **18c** was obtained from **17c** under conditions similar to those already described in a 67% yield. MS (relative intensity): 275/274 (1/5, M+1/M), 161/160 (1/3), 149/148/147/146/ (4/19/100/2), 134 (14), 131 (3), 82 (1.5). Calcd for $C_{15}H_{14}O_5$=274.26. $[\alpha]_D^{22}$ +78.5° (c=1.08, $CHCl_3$). The IR and NMR spectra were identical with those of **18b**.

(3′S,4′R)-Pyriculol (**2**). A solution of **18a** (50 mg) in 5% K_2CO_3 in MeOH–water (2:1, 2 ml) was stirred at room temperature for 4 hr. The reaction mixture was neutralized with AcOH aq. and extracted with AcOEt. The extract was washed with $NaHCO_3$ aq. and dried over anhyd. $MgSO_4$. Removal of the solvent gave a crude product, which was purified by preparative TLC to yield **2** (38 mg, 84%) as a pale yellow fine needle. mp 98~99°C (natural **1**: 97.5~98.5°C,[1] 98~98.5°C;[7] synthetic **1**: 97.4~98.2°C[2]). *Anal.* Found: C, 67.59; H, 6.53. Calcd. for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50%). $[\alpha]_D^{22}$ −40.0° (c=0.53, $CHCl_3$); (natural **1**: +41.0° ($CHCl_3$)[2]). The IR and NMR spectra were superimposable on those of **1** from our previous report.[2]

(3′R,4′S)-Pyriculol (**1**). **1** was also obtained in a 78% yield from **18d** under conditions similar to those just described. Thus, **1** obtained was identical in all respects with the natural and previously synthesized **1**.[2]

(3′S,4′S)-Isomer (**3**). In the same manner, **18b** was converted to **3** in a 76% yield as a yellow viscous oil. MS (relative intensity): 179/178/177 (12/57.8/9.9, C3′-C4′ ion cleavage), 161/160 (5.87/100), 149/147 (3.3/1.4), 134/133/132/131 (3/7/27.6/3), 71 (99). Calcd. for $C_{14}H_{16}O_4$= 248.27. $[\alpha]_D^{22}$ −33.2° (c=1.10, $CHCl_3$). ^{1}H-NMR δ_{TMS} ($CDCl_3$): 1.75 (3H, dd, J=6.0, 1 Hz), 2.50 (1H, br. s), 2.92 (1H, br. s), 4.01 (1H, dd, J=6.8, 6.3 Hz), 4.21 (1H, dd, J= 6.8, 5.4 Hz), 5.53 (1H, ddq, J=15.2, 6.3, 1 Hz), 5.70~6.00 (1H, m), 6.08 (1H, dd, J=15.6, 5.4 Hz), 6.89 (1H, d, J= 8.3 Hz), 6.90 (1H, d, J=7.9 Hz), 7.20 (1H, d, J=15.6 Hz), 7.45 (1H, dd, J=8.3, 7.9 Hz), 10.30 (1H, s), 11.86 (1H, s). IR ν_{max} ($CHCl_3$) cm^{-1}: 1640, 1605, 1572, 1450, 970.

(3′R,4′R)-Isomer (**4**). This was obtained in the same manner as that already mentioned from **18c** in a 75% yield. $[\alpha]_D^{22}$ +31.5° (c=1.30, $CHCl_3$). The IR, NMR and mass spectra were identical with those of **3**.

(3′R,4′R)-3′,4′-O-Isopropylidenepyriculol (*typical procedure*). Two milligrams of **4** and a catalytic amount of *p*-TsOH in 2,2-dimethoxypropane (1 ml) were stirred for 30 min at room temperature. The mixture was then purified by preparative TLC on silica gel to give *ca.* 2 mg of acetonide. IR ν_{max} (film) cm^{-1}: 1650, 1618, 1580, 1382, 1375, 970, 880. ^{1}H-NMR δ_{TMS} ($CDCl_3$): 1.48 (6H, s), 1.75 (3H, dd, J=6.3, 1 Hz), 4.14 (1H, dd, J=8.3, 6.8 Hz), 4.28 (1H, dd, J=8.3, 6.4 Hz), 5.49 (1H, ddq, J=15.1, 6.8, 1 Hz), 5.87 (1H, dq, J=15.1, 6.3 Hz), 6.05 (1H, dd, J= 15.6, 6.4 Hz), 6.90 (1H, d, J=8.3 Hz), 6.93 (1H, d, J= 7.3 Hz), 7.18 (1H, d, J=15.6 Hz), 7.46 (1H, dd, J=8.3, 7.3 Hz), 10.28 (1H, s), 11.85 (1H, s).

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