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Systematic Asymmetric Synthesis of All Diastereomers of (–)-Talaumidin and Their Neurotrophic Activity

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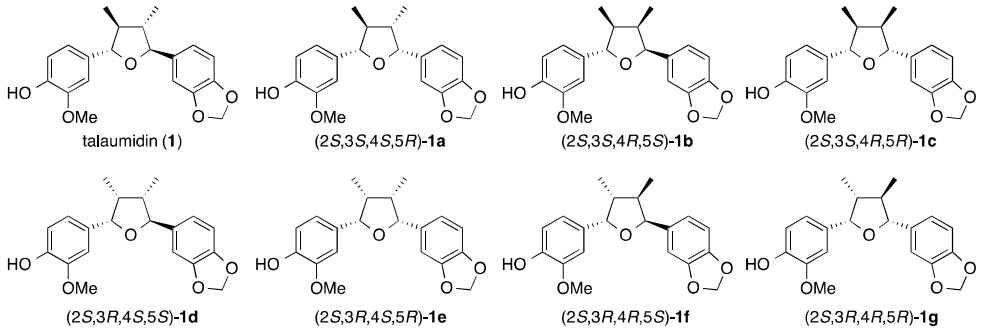


ABSTRACT

(–)-Talaumidin (**1**), a 2,5-biaryl-3,4-dimethyltetrahydrofuran lignan isolated from *Aristolochia arcuata* Masters, shows significant neurite-outgrowth promotion and neuroprotection in primary cultured rat cortical neurons and in NGF-differentiated PC12 cells. The four stereogenic centers on the tetrahydrofuran moiety in **1** result in the presence of seven diastereomers except for their enantiomers. In order to investigate the stereochemistry–activity relationships of the stereoisomers, the systematic synthesis of all stereoisomers of **1** was accomplished by employing Evans aldol, diastereoselective hydroboration, reductive deoxygenation, and Mitsunobu reactions as key steps. The ability of all of synthesized stereoisomers to promote neurite-outgrowth in PC12 and neuronal cells was evaluated. All stereoisomers exhibited moderate to potent neurotrophic activities in

NGF-differentiated PC12 cells at 30 μM and in primary cultured rat cortical neuronal cells at 0.01 μM. In particular, **1e** bearing all *cis* substituents resulted in the most potent neurite-outgrowth promotion.

INTRODUCTION

Neurotrophic factors have been recognized to play important roles in the life of neuron, namely in regard to differentiation of nerve stem cells, neurite-outgrowth, and survival of neurons.[1–4] Their activities are postulated to beneficial in the treatment of neurodegenerative diseases, such as Alzheimer's and Parkinson's diseases. However, their high molecular weight and peptidyl properties restrict their clinical applications owing to their decreased bioavailability and unfavorable pharmacokinetics.[5] Therefore, research on small neurotrophic molecules has garnered significant scientific attention. As part of our ongoing research in this area, we have continued to search for neurotrophic molecules from plants.[6–10] In the course of our studies on neurotrophic compounds, we isolated a tetrahydrofuran-type lignan, (–)-(2*S*,3*S*,4*S*,5*S*)-talaumidin (**1**) from *Aristolochia arcuata* Masters. (Figure 1) Remarkably, **1** exhibits not only significant neurite-outgrowth promotion in primary cultured rat cortical neurons and in NGF-differentiated PC12 cells, but also exhibits protective effects against cell death induced by several insults.[11] In addition to its neurotrophic activity, talaumidin possesses an interesting structure consisting of a 2,5-biaryl-3,4-dimethyltetrahydrofuran skeleton with four continuous stereogenic centers. Thus, its intriguing structure and biological activity have stimulated considerable efforts in regard to its synthesis. In 2006, we accomplished the first synthesis of (–)-talaumidin (**1**)[12,13] by employing Evans asymmetric *anti*-selective aldol reaction, diastereoselective hydroboration, and Friedel-Crafts arylation as key steps. Subsequently, several groups reported the synthesis of talaumidin and its analogues. Specifically, Hanessian *et al.* synthesized **1** together with four related compounds using stereoselective cyclizations.[14] Hong *et al.* reported a $BF_3{\cdot}OEt_2$ promoted reductive deoxygenation reaction in the synthesis of talaumidin analogues.[15] Moreover, Ghosh and Matcha[16] used a diastereoselective aldol reaction, and Liang *et al.*[17] and Barker *et al.*[18] also achieved the synthesis of talaumidin. After our inaugural report on the synthesis of **1**, we focused on the stereochemistry–activity relationships imparted by the four continuous stereogenic centers. From a synthetic point of view, it is attractive not only to synthesize all seven diastereomers, but also to prepare a library of stereoisomers, which would provide useful information on the structure–activity relationships of **1**. Herein, we report the synthesis of all stereoisomers of talaumidin and their neurotropic activities.

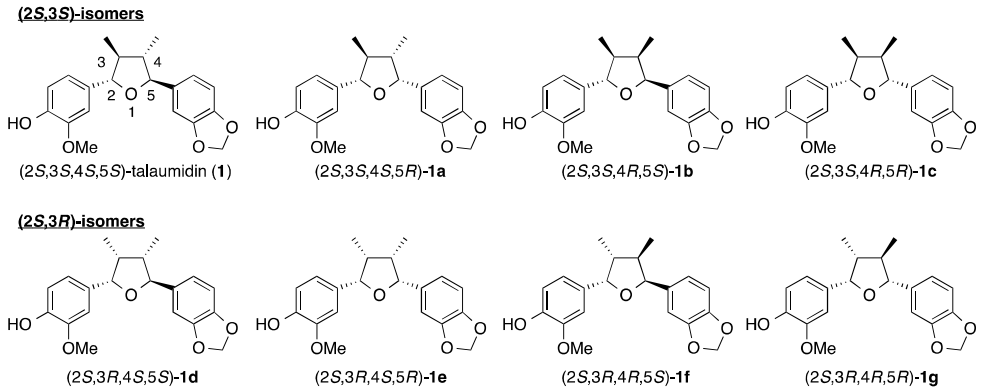
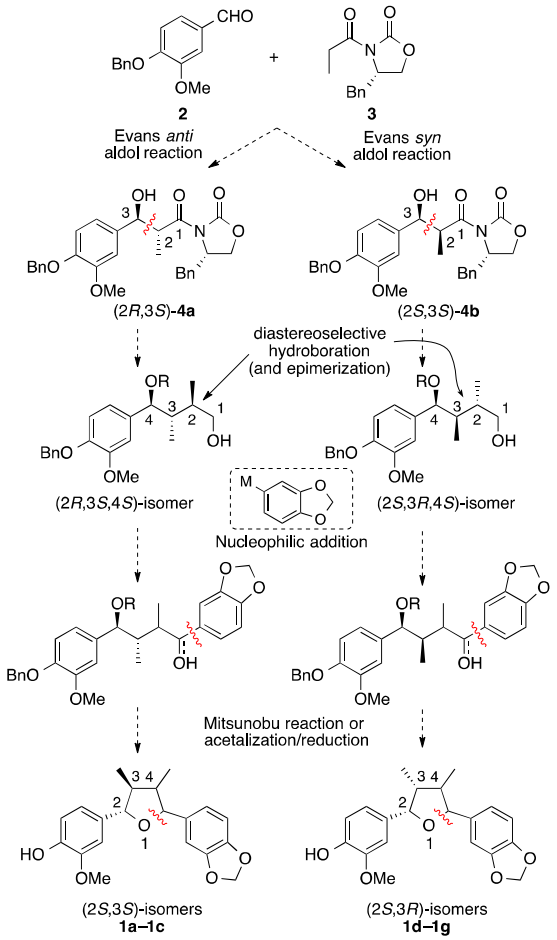


Figure 1. The structures of talaumidin (**1**) and stereoisomers **1a**–**1g**.

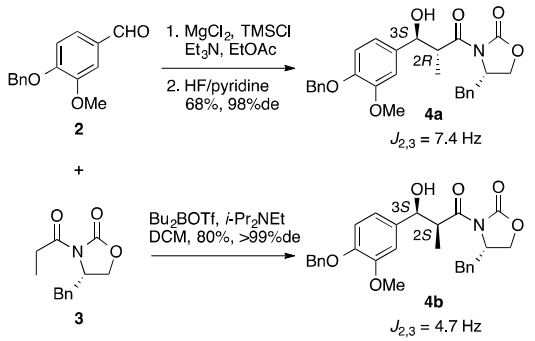
RESULTS AND DISCUSSION

We envisioned that the systematic synthesis of all stereoisomers could be accomplished using the same starting materials, 4-benzyloxy-3-methoxybenzaldehyde (**2**) and (+)-4-benzyl-3-propionyloxazolidinone (**3**). (Scheme 1) The Evans aldol reaction between **2** and **3** would be a key step for the construction of the desired absolute configurations at C2 and C3 in all isomers. The *anti*-selective Evans aldol reaction could form (2*R*,3*S*)-**4a**, which would be converted to (2*S*,3*S*)-isomers **1a**–**1c**, whereas the *syn*-selective Evans aldol reaction would be employed for the synthesis of (2*S*,3*S*)-**4b**, which would generate the (2*S*,3*R*)-configuration of **1d**–**1g**. The neighboring C4 stereochemistry could be controlled by the diastereoselective hydroboration/epimerization procedure, which was utilized for the previously reported synthesis of talaumidin.[12,13] The methylenedioxybenzene moiety would be introduced via nucleophilic addition of a Grignard reagent or aryl lithium reagent. In the final stage, the stereoselective cyclization of the core THF ring would be attained by an intramolecular cyclization under Mitsunobu conditions or an acetalization/reduction procedure.



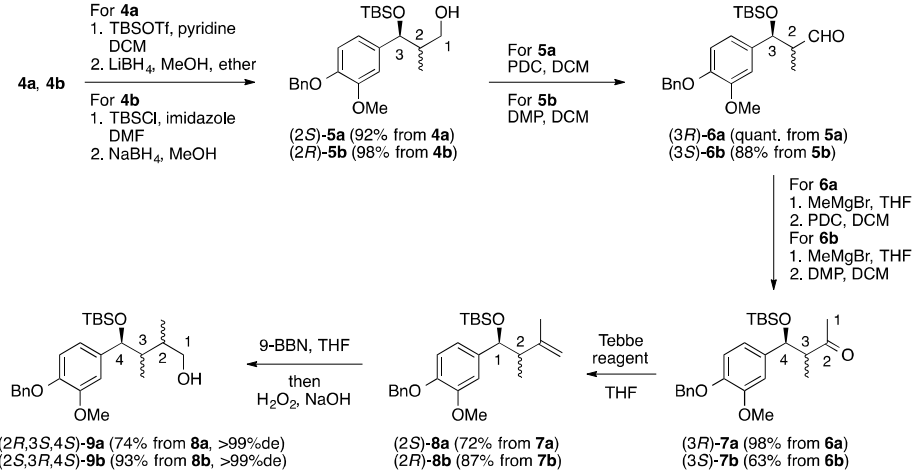
Scheme 1. Systematic strategy used to synthesize all stereoisomers of 1

Our synthetic study commenced with the Evans aldol reaction between **2** and **3**. (Scheme 2) In accordance with Evans procedure, the *anti*-selective aldol reaction was carried out with $MgCl_2$, TMSCl, and Et_3N in EtOAc.[19] The obtained TMS ether was treated with HF/pyridine to afford (2*R*,3*S*)-aldol **4a** in 68% yield with 98%de. On the other hand, the *syn*-selective aldol reaction was performed using Bu_2BOTf and *i*-Pr_2NEt in DCM, giving rise to (2*S*,3*S*)-aldol **4b** in 80% yield with >99%de.[20,21] The relative configurations of the compounds were confirmed by comparison of the coupling constants between H_{C2} and H_{C3}. Referring to Cha's report,[22] the *anti*- and *syn*-configurations were determined by the $J_{2,3}$ values of **4a** (7.4 Hz) and **4b** (4.7 Hz).



Scheme 2. Evans *syn*- and *anti*-selective aldol reactions of 2 and 3

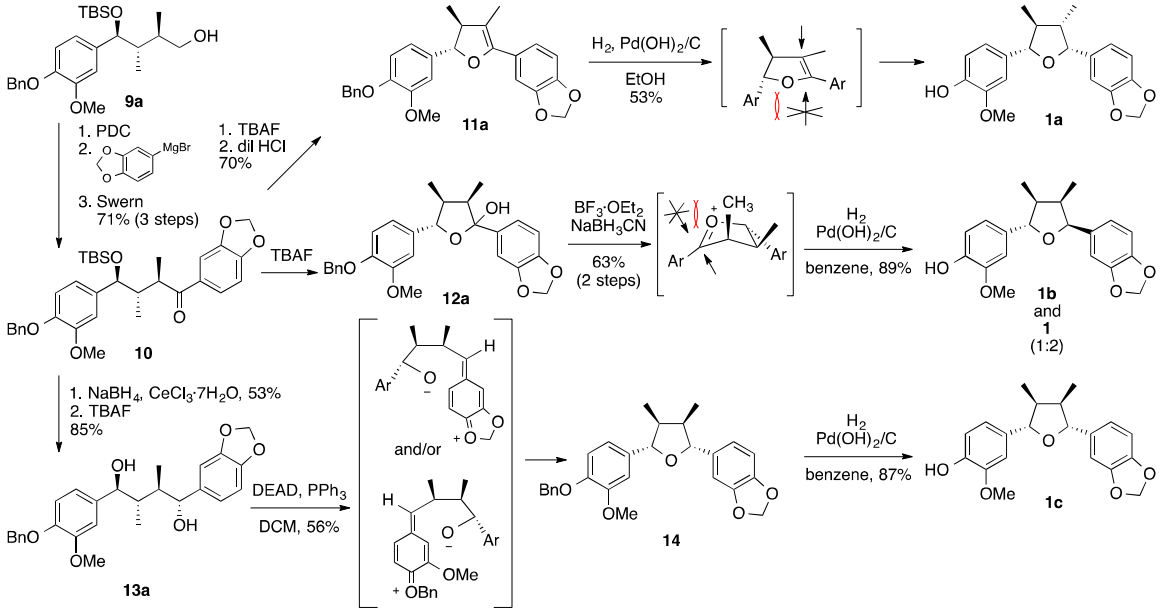
Next, key intermediates (2*R*,3*S*,4*S*)-**9a** and (2*S*,3*R*,4*S*)-**9b** were prepared from **4a** and **4b** by the same procedures.[23] (Scheme 3) Protection of the secondary alcohols in **4a** and **4b** as TBS ethers, followed by reductive removal of the oxazolidinone auxiliaries with a metal hydride afforded **5a** and **5b**. Alcohols **5a** and **5b** were oxidized to aldehydes **6a** and **6b**, respectively. The Grignard reaction of **6a** and **6b** with methyl magnesium bromide, followed by subsequent oxidation of the generated secondary alcohols, gave ketones **7a** and **7b** in 98% and 83% yields. Treatment of the ketones with Tebbe reagent afforded **8a** and **8b**. The absolute configurations of C1 in **8a** and **8b** were confirmed by Kusumi's method[24] after removal of the TBS group and esterification with MTPA.[13,25] Diastereoselective hydroboration of **8a** and **8b** proceeded smoothly, giving **9a** and **9b** with >99%de.[26,27]



Scheme 3. Preparation of 9a and 9b

With (2*R*,3*S*,4*S*)-**9a** in hand, the synthesis of (2*S*,3*S*)-isomers **1a**–**1c** was investigated.[13,28] (Scheme 4) A series of oxidation/Grignard reaction/re-oxidation reactions of **9a** gave a ketone **10** in 71%

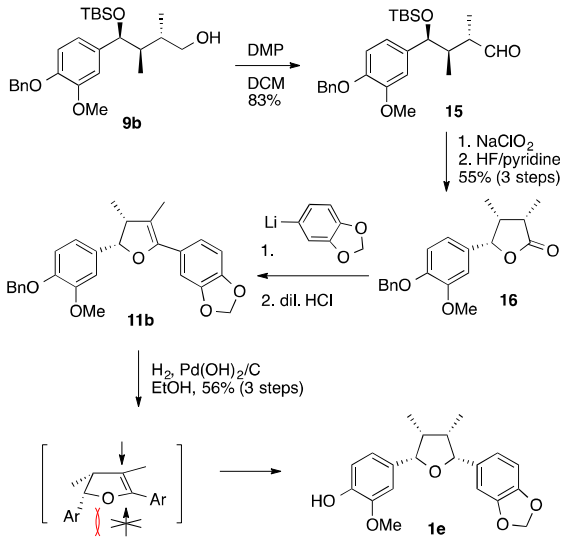
yield over 3 steps. Compound **10** was treated with TBAF, and then a diluted HCl solution, giving rise to a dihydrofuran **11a** in 70% yield. The reduction of dihydrofuran **11a** and removal of the benzyl group was carried out with $Pd(OH)_2/C$ in EtOH under a hydrogen atmosphere, giving (2*S*,3*S*,4*S*,5*R*)-**1a** in 53% yield. Notably, $NaBH_3CN$ reduction of cyclic hemi-acetal **12a**, which was derived from **10** via treatment with TBAF followed by removal of the benzyl group, produced a 1:2 diastereomeric mixture of (2*S*,3*S*,4*R*,5*S*)-**1b** and talaumidin (**1**). Furthermore, the synthesis of **1c** was achieved by the intramolecular cyclization under Mitsunobu conditions. Hydride reduction of **10** proceeded stereoselectively according to the Felkin–Anh model;[29–31] subsequent deprotection of the TBS group yielded diol **13a**. Intramolecular cyclization under Mitsunobu conditions[28] of **13a** surprisingly gave rise to **14** as a single product, and then hydrogenolysis of the benzyl group furnished (2*S*,3*S*,4*R*,5*R*)-**1c** in 87% yield. It should be noted that the intramolecular addition of hydroxy anion to the quinone methide species can account for the formation of **14**.



Scheme 4. Synthesis of 1a, 1b, and 1c

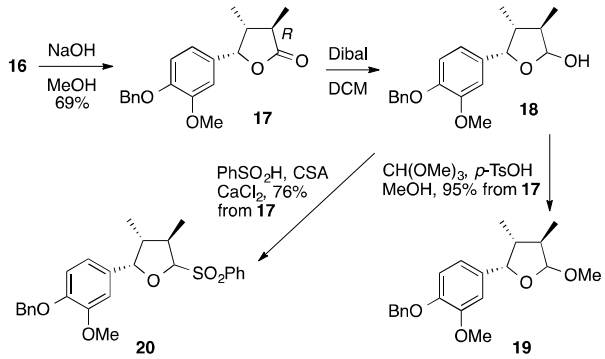
After the completion of synthesis of (2*S*,3*S*)-isomers, we focused on the synthesis of (2*S*,3*R*)-isomers **1d**–**1g**. First, the synthesis of **1e** was examined. (Scheme 5) The primary alcohol moiety in (2*S*,3*R*,4*S*)-**9b** was oxidized by Dess–Martin periodinane to give aldehyde **15** in 87% yield. After the Pinnick oxidation of **15**, removal of the TBS group by HF/pyridine brought about concomitant cyclization, which afforded lactone **16** in a good yield. Nucleophilic addition of **16** with methylenedioxyphenyl lithium and subsequent dehydration of the generated alcohol under

acidic conditions produced dihydrofuran **11b**. The hydrogenation of the dihydrofuran under Pd-catalytic conditions gave rise to *cis*-substituted (2*S*,3*R*,4*S*,5*R*)-**1e**, following the removal of the benzyl group.



Scheme 5. Synthesis of 1e

Subsequently, we prepared acetal **19** and sulfone **20**, which are intermediates in the synthesis of **1f**. (Scheme 6) The 3*R*-configuration of **1f** was formed by the epimerization of **16** under basic conditions. After Dibal reduction of **17**, **18** was converted to acetal **19** and sulfone **20** by Hong's procedure.[32]

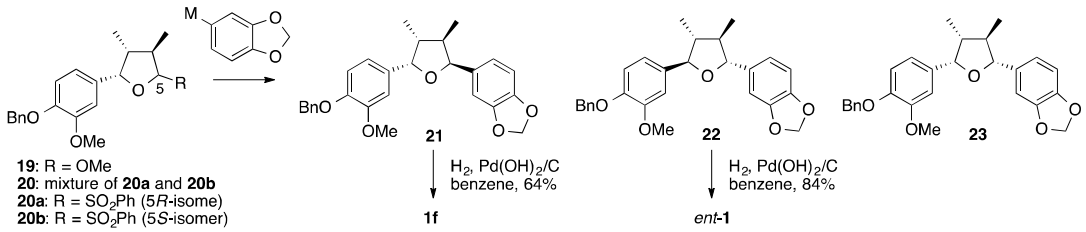


Scheme 6. Preparation of acetal 19 and sulfone 20

With **19** and **20** in hand, we investigated the stereoselective introduction of methylenedioxybenzene. (Table 1) At first, Friedel–Crafts reaction was attempted under $SnCl_4$-catalyzed conditions, which were used previously.[12,13] (Table 1, entry 1) Disappointingly, undesired epimerization occurred to

give (2*R*,3*R*,4*R*,5*R*)-isomer **22** in 49% yield, which was converted to (+)-talaumidin (*ent*-**1**) by removal of the benzyl group.[14,15] This epimerization would be attributed to the low reactivity of the methylenedioxybenzene. In order to improve the nucleophilicity and prevent the epimerization, we applied Ley's procedure[33] by treating the sulfone acetal with a Grignard reagent in the presence of $ZnBr_2$. (Table 1, entries 2–4) Although the Grignard reaction of methyl acetal **19** did not give the desired product, the reaction of sulfone **20** at room temperature afforded **21** in 37% yield, in addition to small amounts of stereoisomers **22** and **23**. Finally, removal of the benzyl group afforded (2*S*,3*R*,4*R*,5*S*)-**1f** in 64% yield. In order to understand the outcome of the Grignard reaction, **20a** and **20b**, which were easily separated by silica gel column chromatography, were subjected to the same reaction conditions. The Grignard reaction of **20a** smoothly proceeded to give **21** in 50% yield, whereas the reaction of **20b** yielded only 16% of **21** along with unreacted starting material. (Table 1, entries 5 and 6)

Table 1. Stereoselective arylation of 19 and 20



entry	substrate	M	additive	solvent	temp (°C)	**21** (%)	**22** (%)	**23** (%)
1	**19**	H	$SnCl_4$	DCM	−78	-	49	-
2	**19**	MgBr	$ZnBr_2$	THF	rt	-	-	-
3	**20**	MgBr	$ZnBr_2$	THF	−78	-	-	-
4	**20**	MgBr	$ZnBr_2$	THF	rt	37	6	15
5	**20a**	MgBr	$ZnBr_2$	THF	rt	50	3	21
6	**20b**	MgBr	$ZnBr_2$	THF	rt	16	0	trace

The difference in the reactivity between **20a** and **20b** is caused by the rate of sulfone elimination, which is the rate-determining step in this reaction. (Figure 2) In each isomer, the phenyl sulfone is oriented in two kinds of conformations: pseudo-axial or pseudo-equatorial. Considering the anomeric effect,[34] the elimination of pseudo-axial oriented sulfones **B** and **C** is faster than that of pseudo-equatorial **A** and **D**. In the case of **20a**, the less hindered conformer **B** is favored over **A**,

whereas conformer **D** is superior to **C** due to steric repulsion between the aryl and sulfone groups. It should be noted that less reactive **20b** can be readily converted to **20a** in $CHCl_3$ in 1 day.

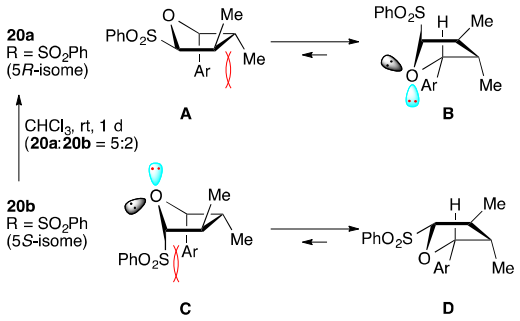
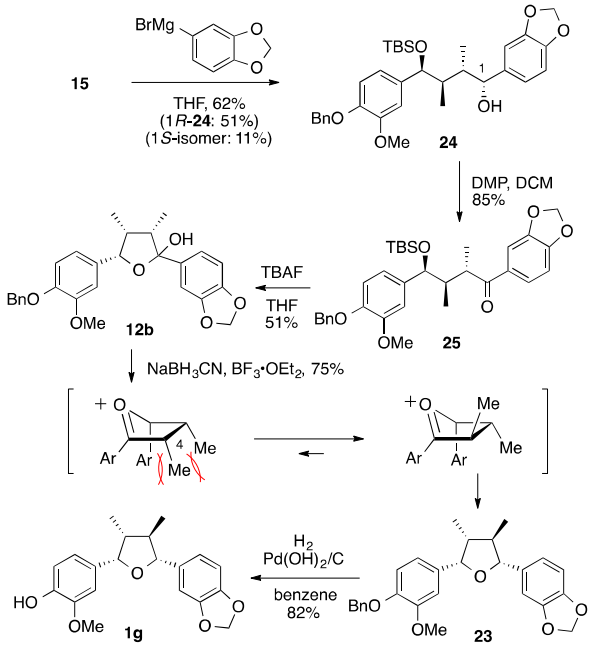


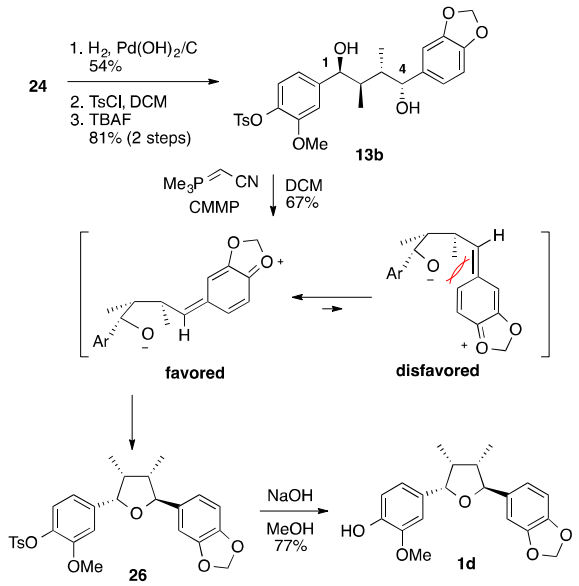
Figure 2. Difference in reactivity between **20a** and **20b**.

Next, the synthesis of (2*S*,3*R*,4*R*,5*R*)-**1g** was carried out. (Scheme 7) Aldehyde **15** was reacted with methylenedioxyphenyl magnesium bromide, and afforded **24** stereoselectively, in accordance with the Felkin–Anh model (1*R*-**24**:1*S*-isomer = 5:1). The obtained alcohol **24** was oxidized by Dess–Martin periodinane to give ketone **25** in 98% yield. After removal of the TBS group, treatment of cyclic hemi-acetal **12b** with $BF_3 \cdot OEt_2$ led to the oxonium ion, which induced epimerization at C4; subsequent reduction with $NaBH_3CN$ gave rise to **23**.[15] Epimerization is caused by the steric repulsion between the adjacent methyl and aryl groups. The synthesis of (2*S*,3*R*,4*R*,5*R*)-**1g** was attained by the hydrogenolysis of the benzyl ether moiety in **23**.



Scheme 7. Synthesis of 1g

Finally, (2*S*,3*R*,4*S*,5*S*)-**1d** was synthesized by the intramolecular cyclization under Mitsunobu conditions of diol **13b**.[25] (Scheme 8) In order to facilitate the selective elimination of the C4-hydroxy group, the benzyl group in **24** was converted to a tosyl group in 2 steps. After removal of the TBS group, diol **13b** was subjected to the intramolecular cyclization under Mitsunobu conditions using Tsunoda reagent, CMMP,[35] which resulted in the formation of **26** with high stereoselectivity. The synthesis of **1d** was completed by the hydrolysis of the tosyl group under basic conditions.



Scheme 8. Synthesis of 1d

The systematic synthesis of talaumidin isomers **1a**–**1g** was successfully accomplished and facilitated the evaluation of the neurotrophic activities of the synthesized stereoisomers. According to a previously reported experimental procedure,[36] compounds **1** and **1a**–**1g** were evaluated for their ability to induce neurite-outgrowth in NGF-differentiated PC12 cells at 10 μM and 30 μM, together with *ent*-talaumidin (*ent*-**1**). (Figure 3) *Ent*-talaumidin showed similar neurotrophic activity as (−)-**1**, and all stereoisomers resulted in moderate to potent neurite-outgrowth promotion. In particular, **1e**, bearing all *cis* substituents, was found to exhibit higher activity than natural product (−)-**1**. In addition, we also evaluated the ability of the compounds to promote neurite-outgrowth in primary cultured rat cortical neurons at 0.01 μM.[37] (Figure 4) Notably, all of the compounds exhibited potent neurite-outgrowth activity. Further, **1e** also resulted in significant promotion of neurite-outgrowth.

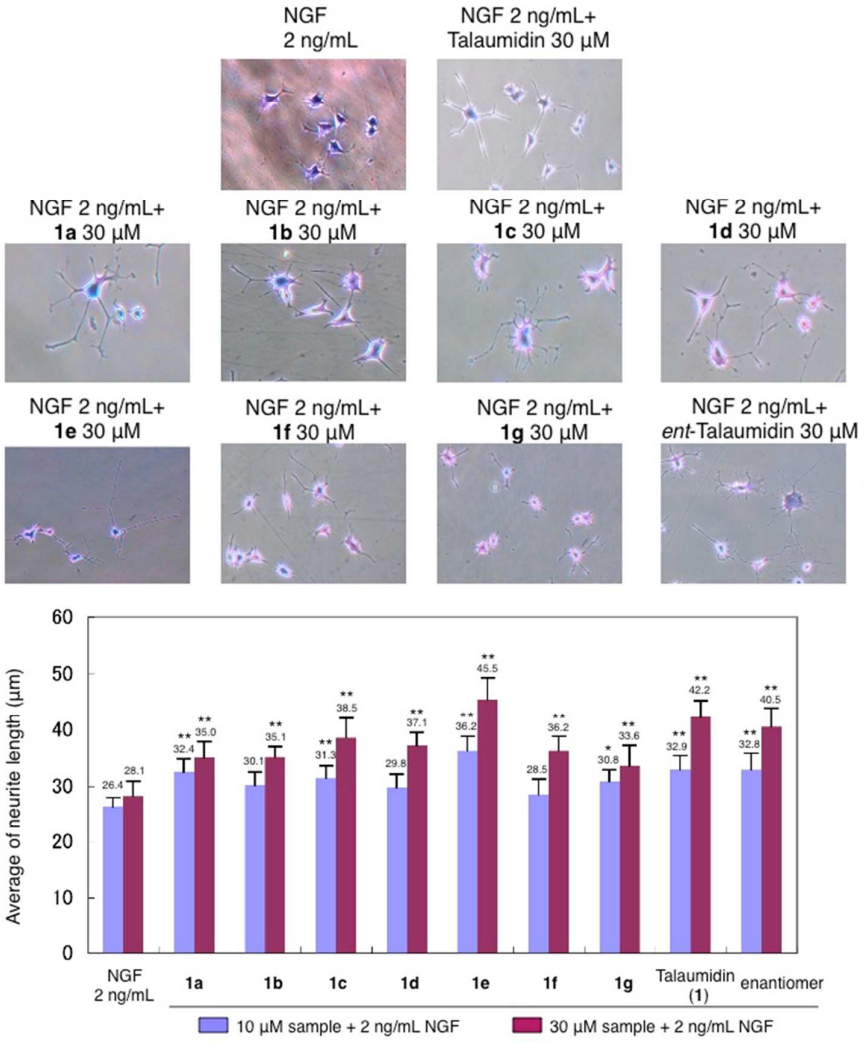


Figure 3. Comparison of neurite length of NGF-differentiated PC12 cells promoted by **1** and **1a**–**1g** at 10 and 30 μM. PC12 cells were cultured in a 24-well plate in DMEM/10% HS + 5%FBS for 1day at a cell density of 2000 cells cm^{-2}; the medium was changed to DMEM/2% HS + 1% FBS with control (0.5% EtOH), NGF 2 ng mL^{-1}, NGF 2 ng mL^{-1} + samples (10 μM and 30 μM). After 96 h, PC12 cells were fixed and stained with methylene blue, and the neurite length was quantified. At least 100 cells were used to calculate the neurite length. Data were expressed as mean as ± SE. *, $P<0.05$; **, $P<0.01$ compared with NGF by Dunnett's t-test.

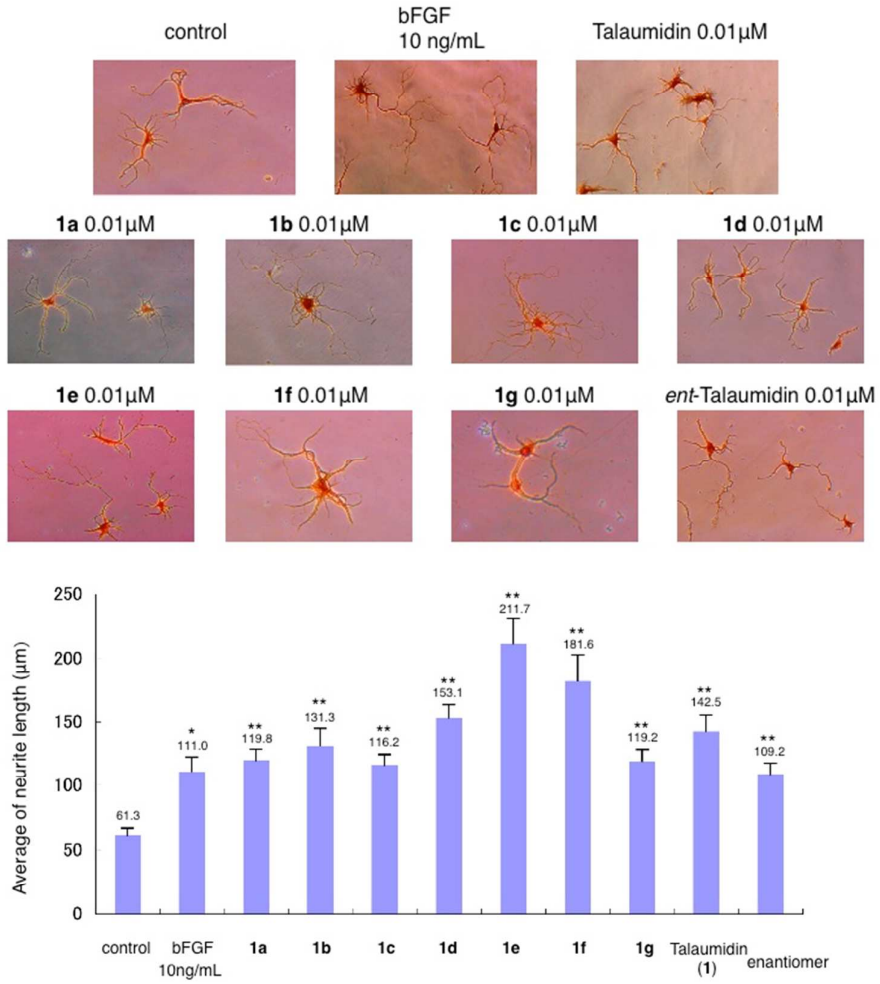


Figure 4. Comparison of neurite length of neuronal cells promoted by **1** and **1a**–**1g** at 0.01 μM. The neuronal cells (5000 cell cm^{-2}) were cultured for 7 days in the presence of 0.5% EtOH, bFGF, **1a**, **1b**, **1c**, **1d**, **1e**, **1f**, **1g**, talaumidin, and *ent*-talaumidin and were fixed with 4% paraformaldehyde. Morphometric analysis was carried out on these neurons according to the described criteria. The data are expressed ± S.E. (n = 60); Dunnett's *t*-test vs. control, *, $P<0.05$, **, $P<0.01$.

CONCLUSION

We accomplished the systematic synthesis of all stereoisomers of (−)-talaumidin. The (2*S*,3*S*)- and (2*S*,3*R*)-configurations were constructed by Evans *syn*- and *anti*-selective aldol reactions with **2** and **3**, and the configuration at C4 was controlled by diastereoselective hydroboration and epimerization. (2*S*,3*S*,4*S*,5*R*)-**1a** was synthesized from dehydrofuran **11** by stereoselective hydrogenation. Reduction of hemi-acetal **12** with $NaBH_3CN$ in the presence of $BF_3{\cdot}OEt_2$ gave rise to (2*S*,3*S*,4*R*,5*S*)-**1b**. Furthermore, diol **13** was subjected to the intramolecular cyclization under

Mitsunobu conditions, resulting in the formation of (2*S*,3*S*,4*R*,5*R*)-**1c**. (2*S*,3*R*,4*S*,5*S*)-**1d** was synthesized by the intramolecular cyclization of tosylate **25** using Tsunoda reagent, CMMP; (2*S*,3*R*,4*S*,5*R*)-**1e** was prepared by the catalytic reduction of dihydrofuran **21**. The synthesis of (2*S*,3*R*,4*R*,5*S*)-**1f** was achieved according to Ley's and Hong's procedures, which is the Grignard reaction of sulfone **22** in the presence of $ZnBr_2$. In addition, treatment of **26** with $BF_3{\cdot}OEt_2$ and $NaBH_3CN$ furnished (2*S*,3*R*,4*R*,5*R*)-**1g** via the epimerization at C4. The ability of all synthesized stereoisomers to promote neurite-outgrowth promotion was evaluated. Among the talaumidin isomers, *cis*-substituted **1e** exhibited the most significant neurotrophic activity in PC12 cells as well as in neuronal cells.

EXPERIMENTAL SECTION

General Method.

The melting points were measured with a melting point apparatus and were uncorrected. IR spectra were recorded on an infrared. High-resolution mass spectra were obtained using a magnetic sector analyzer with electron ionization (EI), chemical ionization (CI), and fast atom bombardment (FAB) mass spectrometry. ^{1}H and ^{13}C NMR spectra were referenced relative to peaks of TMS (0 ppm for ^{1}H NMR) and $CDCl_3$ (77.03 ppm for ^{13}C NMR). Column chromatography was carried out with silica gel (70–230 and 230–400 mesh). Specific rotations were measured with 3.5×10 mm, 3.5×100 mm, and 10×100 mm cells.

(2*S*,3*S*,4*S*,5*R*)-1a: To a solution of **11a** (4.0 mg, 9.30 μmol) in benzene (1.00 mL) was added $Pd(OH)_2/C$ (1.5 mg). This mixture was stirred vigorously under hydrogen atmosphere at rt for 16 h. After being filtered, removal of solvent afforded the residue, which was purified by prep. TLC (hexane:EtOAc = 2:1) to yield **1a** (1.7 mg, 53%) as a colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.67 (3H, d, *J* = 7.0 Hz), 1.04 (3H, d, *J* = 6.6 Hz), 1.75 (1H, ddq, *J* = 9.6, 9.3, 6.6 Hz), 2.23 (1H, ddq, *J* = 9.6, 8.8, 7.0 Hz), 3.93 (3H, s), 4.36 (1H, d, *J* = 9.3 Hz), 5.09 (1H, d, *J* = 8.8 Hz), 5.59 (1H, s), 5.96 (2H, s), 6.78 (2H, br-s), 6.88 (1H, br-s), 6.92 (1H, d, *J* = 8.1 Hz), 6.97 (1H, dd, *J* = 8.1, 1.5 Hz), 7.04 (1H, d, *J* = 1.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.9, 15.1, 46.0, 48.1, 55.9, 83.0, 87.5, 100.9, 107.6, 107.8, 109.2, 114.2, 119.5, 120.3, 132.6, 135.2, 145.2, 146.5, 146.5, 147.4; IR (ATR) 3463 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{20}H_{22}O_5$ 342.1467; Found 342.1465; $[\alpha]^{26}_D$ +29.0 (*c* 0.43, $CHCl_3$).

(2*S*,3*S*,4*R*,5*S*)-1b: To a solution of **10** (9.30 mg, 16.6 μmol) in THF (500 μL) was added TBAF (20.0 μL, 1.0 M solution in THF). This mixture was stirred for 11 h, and quenched with H_2O. The aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The residue was dissolved in DCM (1.00 mL) and the resulting solution was cooled to −78 °C. To this solution was added $NaBH_3CN$ (1.8 mg, 28.6 μmol) and $BF_3{\cdot}OEt_2$ (2.0 μL, 34.4 μmol). The reaction mixture was stirred at the same temperature for 20 min. After saturated aqueous $NaHCO_3$ was added, the aqueous layer was extracted with EtOAc. The combined organic layers were dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The residue was purified by prep. TLC (hexane:EtOAc = 3:1) to yield a diastereomeric mixture (6.2 mg, 63% in two steps). To a solution of this mixture (6.20 mg, 14.4 μmol) in benzene (1.0 mL) was added 20% $Pd(OH)_2/C$ (3.10 mg). The reaction mixture was stirred vigorously under hydrogen atmosphere at rt for 10 h. After being filtered, removal of solvent afforded the residue, which was purified by prep. TLC (benzene:ether = 5:1) to yield **1b** (1.5 mg, 30%) and **1** (2.9 mg, 59%). **1b** as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.62 (3H, d, *J* = 7.3 Hz), 0.99 (3H, d, *J* = 6.2 Hz), 2.37–2.48 (2H, m), 3.91 (3H, s), 4.63 (1H, d, *J* = 9.5 Hz), 5.43 (1H, d, *J* = 4.0 Hz), 5.56 (1H, s), 5.95 (2H, s), 6.78 (1H, d, *J* = 8.1 Hz), 6.81 (1H, dd, *J* = 8.1, 1.1 Hz), 6.84 (1H, dd, *J* = 8.1, 1.5 Hz), 6.86 (1H, d, *J* = 1.1 Hz), 6.89 (1H, d, *J* = 8.1 Hz), 6.93 (1H, d, *J* = 1.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 9.6, 11.9, 43.5, 47.5, 56.0, 84.8, 85.8, 100.9, 106.9, 108.0, 108.5, 114.1, 119.1, 119.3, 134.7, 134.9, 145.1, 146.3, 146.7, 147.5; IR (ATR) 3493, 1513 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{20}H_{22}O_5$ 342.1467; Found 342.1476; $[\alpha]^{22}_D$ −46.5 (*c* 0.32, $CHCl_3$).

(2*S*,3*S*,4*R*,5*R*)-1c: To a solution of **14** (12.8 mg, 29.6 μmol) in benzene (1.50 mL) was added $Pd(OH)_2/C$ (2.90 mg). The mixture was stirred vigorously under hydrogen atmosphere at rt for 75 h. After being filtrated, the solution was concentrated in *vacuo*. The residue was purified by column chromatography (hexane:EtOAc = 3:1) to yield **1c** (8.8 mg, 87%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.02 (6H, d, *J* = 6.6 Hz), 2.22–2.34 (2H, m), 3.91 (3H, s), 4.45 (1H, d, *J* = 6.4 Hz), 4.46 (1H, d, *J* = 6.7 Hz), 5.57 (1H, s), 5.96 (2H, s), 6.79 (1H, d, *J* = 7.8 Hz), 6.88 (1H, dd, *J* = 7.8, 1.6 Hz), 6.90 (1H, s), 6.94 (1H, d, *J* = 1.6 Hz), 6.97 (1H, s), 6.97 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.9, 44.5, 44.5, 55.9, 77.3, 87.4, 87.5, 101.0, 106.8, 108.0, 109.0, 114.1, 119.4, 119.9, 134.0, 136.2, 145.0, 146.5, 147.0, 147.8; IR (ATR) 3482 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{20}H_{22}O_5$ 342.1467, Found 342.1470; $[\alpha]^{20}_D$ +8.4 (*c* 0.65, $CHCl_3$).

(2*S*,3*R*,4*S*,5*S*)-1d: To a solution of **27** (6.30 mg, 12.7 μmol) in ethanol (100 μL) was added aq NaOH (0.5 g/mL, 200 μL). After being stirred rt for 15 h, the reaction mixture was added brine (1.00 mL) and extracted with EtOAc. The combined organic layers were dried over Na_2SO_4, concentrated in *vacuo*. The residue was purified by prep. TLC (benzene:EtOAc = 20:1) to afford **1d** (3.31 mg, 77%) as colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.61 (3H, d, *J* = 7.1 Hz), 1.00 (3H, d, *J* = 6.6 Hz), 2.37–2.46 (2H, m), 3.89 (3H, s), 4.62 (1H, d, *J* = 9.3 Hz), 5.43 (1H, d, *J* = 4.4 Hz), 5.52 (1H, s), 5.94 (1H, d, *J* = 1.5 Hz), 5.95 (1H, d, *J* = 1.5 Hz), 6.77 (1H, dd, *J* = 8.1, 1.7 Hz), 6.78 (1H, d, *J* = 7.9 Hz), 6.83 (1H, dd, *J* = 8.1, 1.7 Hz), 6.88 (1H, d, *J* = 7.9 Hz), 6.92 (1H, d, *J* = 1.7 Hz), 6.93 (1H, d, *J* = 1.7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 9.4, 11.8, 43.5, 47.7, 56.0, 84.8, 85.7, 100.9, 106.5, 108.0, 108.7, 113.9, 118.8, 119.6, 132.5, 137.2, 144.3, 146.2, 146.9, 147.8; IR (ATR) 3464 cm^{-1}; HRMS (CI) *m/z*: $[M + H]^+$ Calcd for $C_{20}H_{23}O_5$ 343.1546, Found 343.1540; $[\alpha]^{20}_D$ −134.3 (*c* 1.01, $CHCl_3$).

(2*S*,3*R*,4*S*,5*R*)-1e: To a solution of **16** (58.9 mg, 181 μmol) in THF was added a solution of 3,4-methylenedioxyphenyl lithium (in THF, 1.80 mL, 397 μmol). After being stirred for 23 h, the reaction was worked up with saturated aqueous NH_4Cl and extracted with ether. The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated in *vacuo*. The residue was purified by column chromatography (hexane:EtOAc = 5:1) to afford a dihydrofuran (56.4 mg) as colorless oil. The solution of the dihydrofuran (12.6 mg, 30.3 μmol) in benzene (1.00 mL) was added $Pd(OH)_2$/C (1.30 mg). The mixture was stirred vigorously under hydrogen atmosphere at rt for 17 h. After being filtrated, the solution was concentrated in *vacuo*. The residue was purified by column chromatography (hexane:$CHCl_3$ = 1:5) to yield **1e** (7.70 mg, 56%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.59 (3H, d, *J* = 6.1 Hz), 0.61 (3H, d, *J* = 6.1 Hz), 2.61–2.68 (2H, m), 3.91 (3H, s), 5.09 (2H, d, *J* = 6.4 Hz), 5.97 (2H, s), 6.81 (1H, d, *J* = 8.1 Hz), 6.86 (1H, dd, *J* = 8.1, 1.5 Hz), 6.88 (1H, dd, *J* = 8.0, 1.4 Hz), 6.92 (1H, d, *J* = 8.0 Hz), 6.94 (1H, d, *J* = 1.4 Hz), 6.96 (1H, d, *J* = 1.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.8, 11.8, 41.5, 41.5, 56.0, 82.7, 82.8, 100.9, 107.1, 107.9, 109.0, 114.0, 118.0, 119.3, 119.5, 132.4, 134.5, 144.3, 146.2, 147.4; IR (ATR) 3472, 2969, 1516, 1236, 1038, 455 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{20}H_{22}O_5$ 342.1467, Found 342.1476; $[\alpha]^{20}_D$ −121.2 (*c* 0.10, $CHCl_3$).

(2*S*,3*R*,4*R*,5*S*)-1f: To a solution of **21** (35.5 mg, 82.0 μmol) in benzene (3.00 mL) was added $Pd(OH)_2$/C (6.00 mg). The mixture was stirred vigorously under hydrogen atmosphere at rt for 75 h. After being filtrated, the solution was concentrated in *vacuo*. The residue was purified by column

chromatography (hexane:EtOAc = 6:1) to yield **1f** (17.9 mg, 64%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.68 (3H, d, *J* = 6.5 Hz), 0.69 (3H, d, *J* = 6.5 Hz), 2.20–2.29 (2H, m), 3.91 (3H, s), 5.40 (2H, d, *J* = 6.0 Hz), 5.53 (1H, s), 5.96 (2H, s), 6.81 (1H, d, *J* = 8.1 Hz), 6.86 (1H, dd, *J* = 8.1, 1.5 Hz), 6.88 (1H, dd, *J* = 8.0, 1.5 Hz), 6.91 (1H, d, *J* = 8.0 Hz), 6.94 (1H, d, *J* = 1.5 Hz), 6.96 (1H, d, *J* = 1.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.6, 14.7, 43.8, 43.9, 56.0, 83.7, 100.9, 107.0, 107.8, 108.9, 113.9, 119.2, 119.4, 133.4, 135.5, 144.5, 146.2, 146.4, 147.5; IR (ATR) 3490 cm^{-1}; HRMS (CI) *m/z*: $[M + H]^+$ Calcd for $C_{20}H_{23}O_5$ 343.1546, Found 343.1540; $[\alpha]^{20}_D$ −13.3 (*c* 1.04, $CHCl_3$).

(2*S*,3*R*,4*R*,5*R*)-1g: To a solution of **23** (2.0 mg, 4.63 μmol) in benzene (1.00 mL) was added $Pd(OH)_2$/C (0.5 mg). The mixture was stirred vigorously under hydrogen atmosphere at rt for 75 h. After being filtrated, the solution was concentrated in *vacuo*. The residue was purified by column chromatography (hexane:EtOAc = 6:1) to yield **1g** (1.3 mg, 82%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.65 (3H, d, *J* = 6.8 Hz), 1.04 (3H, d, *J* = 6.6 Hz), 1.71–1.77 (1H, m), 2.18–2.24 (1H, m), 3.89 (3H, s), 4.36 (1H, d, *J* = 9.3 Hz), 5.10 (1H, d, *J* = 8.5 Hz), 5.54 (1H, s), 5.98 (2H, s), 6.82 (1H, d, *J* = 8.1 Hz), 6.82 (1H, dd, *J* = 8.1, 1.9 Hz), 6.87 (1H, d, *J* = 1.9 Hz), 6.90 (1H, d, *J* = 8.1 Hz), 6.94 (1H, d, *J* = 8.1, 1.7 Hz), 7.04 (1H, d, *J* = 1.7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.0, 15.1, 45.9, 48.3, 55.9, 83.1, 87.4, 101.0, 106.9, 108.1, 109.5, 113.9, 119.9, 120.1, 133.1, 134.8, 144.6, 146.2, 147.1, 147.8; IR (ATR) 3470 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{20}H_{22}O_5$ 342.1467, Found 342.1476; $[\alpha]^{20}_D$ −8.65 (*c* 0.17, $CHCl_3$).

(2*R*,3*R*,4*R*,5*R*)-talaumidin (*ent*-1): To a solution of **22** (6.55 mg, 14.7 μmol) in benzene (2.00 mL) was added $Pd(OH)_2$/C (5.60 mg). The mixture was stirred vigorously under hydrogen atmosphere at rt for 75 h. After being filtrated, the solution was concentrated in *vacuo*. The residue was purified by column chromatography (hexane:EtOAc = 6:1) to yield *ent*-**1** (4.21 mg, 84%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.02 (3H, d, *J* = 5.8 Hz), 1.04 (3H, d, *J* = 5.8 Hz), 1.73–1.78 (2H, m), 3.92 (3H, s), 4.61 (2H, d, *J* = 9.1 Hz), 5.57 (1H, s), 5.95 (2H, s), 6.77 (1H, d, *J* = 8.0 Hz), 6.84 (1H, dd, *J* = 8.0, 1.6 Hz), 6.84 (1H, dd, *J* = 8.0, 1.6 Hz), 6.89 (1H, d, *J* = 8.0 Hz), 6.93 (1H, d, *J* = 1.6 Hz), 6.94 (1H, d, *J* = 1.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.8 ,50.9, 51.2, 56.0, 88.2, 88.4, 101.0, 106.6, 107.9, 108.5, 114.0, 119.4, 119.7, 134.1, 136.6, 147.0, 147.8; IR (ATR) 3459 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{20}H_{22}O_5$ 342.1467, Found 342.1471; $[\alpha]^{20}_D$ +88.3 (*c* 2.10, $CHCl_3$).

(*S*)-4-benzyl-3-((2*R*,3*S*)-3-(4-(benzyloxy)-3-methoxyphenyl)-3-hydroxy-2-methylpropanoyl)oxazolidin-2-one (4a): To a solution of (*S*)-(+)-4-benzyl-3-propionyl-2-oxazolidinone (1.01 g, 4.33

mmol) in EtOAc (8.60 mL) was successively added 4-benzyloxy-3-methoxybenzaldehyde (1.23 g, 5.45 mmol), magnesium chloride (84.2 mg, 866 μmol), triethylamine (800 μL, 8.66 mmol), and trimethylsilyl chloride (830 μL, 6.50 mmol). The resulting mixture was stirred at rt for 14 h. The reaction was quenched by the addition of saturated aqueous $NaHCO_3$. The mixture was stirred for 10 min. The aqueous layer was extracted with Et_2O and the combined organic layers were washed with brine, dried over anhydrous $MgSO_4$ and concentrated in *vacuo*. To the residue was added HF/pyridine/MeCN (1:3:5; 70.0 mL) at 0 °C and the mixture was stirred overnight. To a saturated aqueous $NaHCO_3$ was added the reaction mixture. The aqueous layer was extracted with EtOAc and the combined organic layers were dried over anhydrous $MgSO_4$ and concentrated in *vacuo*. The residue was purified by column chromatography (hexane:ether = 3:2 to 2:1) to afford **4a** (1.39 g, 68%) as colorless solids: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.10 (3H, d, *J* = 6.9 Hz), 2.68 (1H, dd, *J* = 13.7, 9.3 Hz), 3.00 (1H, d, *J* = 7.1 Hz), 3.21 (1H, dd, *J* = 13.7, 3.3 Hz), 3.93 (3H, s), 4.14 (1H, dd, *J* = 9.1, 3.2 Hz), 4.21 (1H, d, *J* = 9.1 Hz), 4.34 (1H, dq, *J* = 6.9, 7.4 Hz), 4.71 (1H, ddd, *J* = 9.3, 3.3, 3.2 Hz), 4.76 (1H, dd, *J* = 7.4, 7.1 Hz), 5.14 (2H, s), 6.87 (1H, dd, *J* = 8.1, 1.6 Hz), 7.02 (1H, d, *J* = 1.6 Hz), 7.16 (1H, d, *J* = 8.1 Hz), 7.28–7.43 (10H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.9, 37.6, 44.2, 55.5, 56.0, 66.0, 71.1, 76.6, 110.0, 113.7, 118.9, 127.3, 127.4, 127.8, 128.6, 129.0, 129.5, 135.2, 135.3, 137.1, 147.9, 149.9, 153.6, 176.7; IR (ATR) 3482, 1771, 1695 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{28}H_{29}O_6N$ 475.1994; Found 475.2000; $[\alpha]^{20}_D$ −118.9 (*c* 1.09, $CHCl_3$); m.p. 91–92 °C.

(*S*)-4-benzyl-3-((2*S*,3*S*)-3-(4-(benzyloxy)-3-methoxyphenyl)-3-hydroxy-2-methylpropanoyl)oxazolidin-2-one (4b): To a solution of (+)-(*S*)-4-benzyl-3-propyl-2-oxazolidinone (3.00 g, 12.9 mmol) in DCM (70.0 mL) was added 1.0 M dibutylboron triflate in DCM (14.2 mL, 14.2 mmol) and Et_3N (2.69 mL, 19.3 mmol) at −78 °C, and then stirring was continued for 30 min at −40 °C. To the reaction mixture cooled to −78 °C was added a solution of 4-benzyloxy-3-methoxybenzaldehyde (3.40 g, 14.2 mmol) in DCM (60.0 mL). After being stirred for 11 h, the reaction was quenched by addition of phosphoric buffer (15.4 mL), methanol (51.5 mL), and 30% H_2O_2 (15.4 mL) at 0 °C. The mixture was stirred for 1 h. The aqueous layer was extracted with DCM and the combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by column chromatography (hexane:EtOAc = 2:1) to afford **4b** (4.88 g, 80%, 99%de) as colorless solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.25 (3H, d, *J* = 6.8 Hz), 2.74 (1H, dd, *J* = 13.3, 9.6 Hz), 3.22 (1H, dd, *J* = 13.3, 3.4 Hz), 3.86 (3H, s), 3.94 (1H, dd, *J* = 9.0, 8.4 Hz), 4.08 (1H, dd, *J* = 9.0, 2.4 Hz), 4.11 (1H, qd, *J* = 6.8, 4.7 Hz), 4.49 (1H, dddd, *J* = 9.6, 8.4, 3.4, 2.4 Hz), 4.97 (1H, d,

J = 4.7 Hz), 5.14 (2H, s), 6.80 (1H, dd, *J* = 8.0, 1.7 Hz), 6.83 (1H, d, *J* = 8.0 Hz), 6.92 (1H, d, *J* = 1.7 Hz), 7.17–7.19 (2H, m), 7.24–7.35 (6H, m), 7.40–7.43 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.4, 37.8, 44.6, 55.3, 56.0, 66.1, 70.9, 74.0, 109.7, 113.5, 118.3, 127.3, 127.4, 127.8, 128.5, 129.0, 129.4, 134.5, 135.0, 137.1, 147.4, 149.5, 152.9, 176.5; IR (ATR) 3509, 1775, 1695 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{28}H_{29}O_6N$ 475.1995, Found 475.1979; $[\alpha]^{20}_D$ +58.9 (*c* 1.00, $CHCl_3$); m.p. 116–117 °C.

(2*S*,3*S*)-3-(4-(benzyloxy)-3-methoxyphenyl)-3-((*tert*-butyldimethylsilyl)oxy)-2-methylpropan-1-ol (5a): To a solution of **4** (1.13 g, 2.39 mmol) and 2,6-lutidine (560 μL, 4.78 mmol) in DCM (2.40 mL) was added *t*-butyldimethylsilyl trifluorometanesulfonate (830 μL, 3.59 mmol). After being stirred for 5 min, the reaction mixture was cooled to 0 °C followed by quenched with water. The aqueous layer was extracted with EtOAc and the combined organic layers were washed with water and brine, dried over anhydrous $MgSO_4$ and concentrated in *vacuo*. The residue was purified by column chromatography (hexane:EtOAc = 5:1 to 3:1) to yield TBS-protected compound (1.40 g, 99%) as a yellow oil. To a solution of this compound (101 mg, 4.64 mmol) in MeOH (7.60 μL, 188 μmol) and Et_2O (3.20 mL) was added lithium borohydride (4.31 mg, 188 μmol) and THF (86.0 μL) at 0 °C. The reaction mixture was warmed to rt and stirred for 1 h. The reaction mixture was added to 3 mol/L aqueous NaOH (150 μL) and the aqueous layer was extracted with EtOAc and the combined organic layers were dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (hexane:EtOAc = 8:1 to 4:1) to yield **5a** (65.4 mg, 92%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ −0.24 (3H, s), 0.04 (3H, s), 0.81 (3H, d, *J* = 6.9 Hz), 0.88 (9H, s), 1.91 (1H, dddq, *J* = 6.9, 6.0, 3.6, 6.9 Hz), 3.59 (1H, dd, *J* = 11.0, 6.0 Hz), 3.61 (1H, dd, *J* = 11.0, 3.6 Hz), 3.88 (3H, s), 4.48 (1H, d, *J* = 6.9 Hz), 5.13 (2H, s), 6.70 (1H, dd, *J* = 8.2, 1.6 Hz), 6.80 (1H, d, *J* = 8.2 Hz), 6.90 (1H, d, *J* = 1.6 Hz), 7.28–7.45 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ −5.2, −4.5, 14.3, 18.0, 25.8, 43.1, 55.9, 66.5, 71.1, 80.9, 110.1, 113.4, 119.0, 127.4, 127.8, 128.5, 136.9, 137.2, 147.4, 149.5; IR (neat) 3437 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{24}H_{36}O_4Si$ 416.2383 for; found 416.2393; Anal. Cacld for $C_{24}H_{36}O_4Si$: C, 68.19; H, 8.71. Found: C, 68.74; H, 8.58; $[\alpha]^{26}_D$ −83.8 (*c* 1.00, $CHCl_3$).

(2*R*,3*S*)-3-(4-(benzyloxy)-3-methoxyphenyl)-3-((*tert*-butyldimethylsilyl)oxy)-2-methylpropan-1-ol (5b): To a solution of **4b** (7.80 g, 16.3 mmol) in DMF (163 mL) was added imidazole (3.30 g, 49.0 mmol) and TBSCl (4.90 g, 32.6 mmol). After being stirred for 13 h, the reaction mixture was cooled to 0 °C, the reaction was quenched with saturated aqueous $NaHCO_3$ (163 mL). The aqueous

layer was extracted with ether and the combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by column chromatography (hexane:EtOAc = 3:1) to afford a TBS ether (9.60 g, 99%) as colorless oil: To a solution of the TBS ether (7.60 g, 12.8 mmol) in THF:methanol = 30:1 (205 mL) was added $NaBH_4$ (4.60 g, 123 mmol) and water (66.0 mL). After the reaction mixture was stirred for 3 h, the solution was extracted with EtOAc and the combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by column chromatography (hexane:EtOAc = 4:1) to afford **5b** (5.27 g, 99%) as colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ −0.17 (3H, s), 0.05 (3H, s), 0.78 (3H, d, *J* = 6.6 Hz), 0.90 (9H, s), 1.99–2.00 (1H, qddd, *J* = 6.6, 8.1, 4.7, 4.4 Hz), 3.44 (1H, dd, *J* = 10.5, 4.7 Hz), 3.57 (1H, dd, *J* = 10.5, 8.1 Hz), 3.88 (3H, s), 4.74 (1H, d, *J* = 4.4 Hz), 5.13 (2H, s), 6.72 (1H, dd, *J* = 8.3, 1.2 Hz), 6.83 (1H, d, *J* = 8.3 Hz), 6.91 (1H, d, *J* = 1.2 Hz), 7.31 (1H, br-t, *J* = 7.1 Hz), 7.37 (2H, br-dd, *J* = 7.3, 7.1 Hz), 7.45 (2H, br-d, *J* = 7.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ −5.3, −4.6, 12.1, 18.1, 25.8, 43.0, 55.9, 65.6, 71.1, 110.3, 113.2, 118.8, 127.4, 127.8, 128.5, 135.7, 137.2, 147.2, 149.2; IR (ATR) 3437 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{24}H_{36}O_4Si$ 416.2382, Found 416.2387; $[\alpha]^{20}_D$ −47.7 (*c* 1.00, $CHCl_3$).

(2*R*,3*S*)-3-(4-(benzyloxy)-3-methoxyphenyl)-3-((*tert*-butyldimethylsilyl)oxy)-2-methylpropanal (6a): To a solution of **5a** (347 mg, 834 μmol) in DCM (8.34 mL) was added PDC (471 mg, 1.25 mmol) and 4Å MS (471 mg) at rt. After being stirred for 12 h, the mixture was added to excess ether, filtered through celite and the filtrate was concentrated in *vacuo*. The residue was purified by column chromatography (hexane:EtOAc = 10:1) to afford **6a** (345 mg, quant.) as colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ −0.23 (3H, s), 0.01 (3H, s), 0.85 (9H, s), 0.85 (3H, d, *J* = 7.4 Hz), 2.66 (1H, ddq, *J* = 7.7, 2.7, 7.4 Hz), 3.88 (3H, s), 4.69 (1H, d, *J* = 7.7 Hz), 5.13 (2H, s), 6.72 (1H, dd, *J* = 8.2, 1.6 Hz), 6.82 (1H, d, *J* = 8.2 Hz), 6.90 (1H, d, *J* = 1.6 Hz), 7.27–7.45 (5H, m), 9.78 (1H, d, *J* = 2.7 Hz): ^{13}C NMR (125 MHz, $CDCl_3$) δ −5.2, −4.5, 11.2, 18.1, 25.7, 54.7, 55.9, 71.1, 76.6, 109.9, 113.3, 119.0, 127.4, 127.9, 128.5, 135.5, 137.1, 147.7, 149.7, 204.7; IR (ATR) 1729 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{24}H_{34}O_4Si$ 414.2226, Found 414.2241; $[\alpha]^{20}_D$ +83.9 (*c* 0.26, $CHCl_3$).

(2*S*,3*S*)-3-(4-(benzyloxy)-3-methoxyphenyl)-3-((*tert*-butyldimethylsilyl)oxy)-2-methylpropanal (6b): To a solution of **5b** (6.20 g, 15.0 mmol) in DCM (100 mL) was added Dess–Martin periodinane (9.50 g, 22.4 mmol). After being stirred at rt for 26 h. the mixture was added to excess diethyl ether (40.0 mL), filtered through celite and the filtrate was concentrated in *vacuo*. The residue was purified by column chromatography (hexane:EtOAc = 5:1) to afford **6b** (5.40 g, 88%)

as colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ −0.16 (3H, s), 0.03 (3H, s), 0.88 (9H, s), 1.04 (3H, d, *J* = 6.6 Hz), 2.57 (1H, qdd, *J* = 6.6, 4.2, 1.5 Hz), 3.87 (3H, s), 5.06 (1H, d, *J* = 4.2 Hz), 5.13 (2H, s), 6.73 (1H, dd, *J* = 8.2, 1.8 Hz), 6.83 (1H, d, *J* = 8.2 Hz), 6.88 (1H, d, *J* = 1.8 Hz), 7.30 (1H, br-t, *J* = 6.5 Hz), 7.35 (2H, br-dd, *J* = 6.5, 7.4 Hz), 7.44 (2H, br-d, *J* = 7.4 Hz), 9.73 (1H, d, *J* = 1.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ −5.2, −4.5, 8.3, 18.1, 25.7, 54.9, 55.9, 71.1, 74.0, 109.9, 113.5, 118.3, 127.4, 127.8, 128.5, 135.6, 137.1, 147.4, 149.4, 204.5; IR (ATR) 1724 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{24}H_{34}O_4Si$ 414.2226, Found 414.2240; $[\alpha]^{20}_D$ −15.2 (*c* 1.00, $CHCl_3$).

(3*R*,4*S*)-4-(4-(benzyloxy)-3-methoxyphenyl)-4-((*tert*-butyldimethylsilyl)oxy)-3-methylbutan-2-one (7a): To a solution of **6a** (83.2 mg, 201 μmol) in THF (1.00 mL) at rt was added 3.0 M MeMgBr in THF solution (80.3 μL, 241 μmol). After being stirred 30 min, the reaction was quenched with sat. NH_4Cl (5.00 mL) and extracted with ether. The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by column chromatography (hexane:EtOAc = 3:1) to afford an alcohol (86.0 mg, 100%) as colorless oil. To a solution of the alcohol (86.0 mg, 200 μmol) in DCM (2.00 mL) was added PDC (376 mg, 1.00 mmol) and powdered 4Å MS (376 mg). After being stirred at rt for 1.5 h. the mixture was added to excess ether (10.0 mL), filtered through celite and the filtrate was concentrated in *vacuo*. The residue was purified by column chromatography (hexane:EtOAc = 4:1) to afford **7a** (83.6 mg, 98%) as colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ −0.30 (3H, s), −0.05 (3H, s), 0.73 (3H, d, *J* = 7.1 Hz), 0.80 (9H, s), 2.25 (3H, s), 2.86 (1H, dq, *J* = 9.3, 7.1 Hz), 3.88 (3H, s), 4.59 (1H, d, *J* = 9.3 Hz), 5.13 (2H, s), 6.71 (1H, dd, *J* = 8.2, 1.6 Hz), 6.81 (1H, d, *J* = 8.2 Hz), 6.88 (1H, d, *J* = 1.6 Hz), 7.28–7.46 (5H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ −5.4, −4.6, 13.7, 18.0, 25.7, 31.3, 55.0, 55.9, 71.1, 78.2, 110.0, 113.2, 119.5, 127.4, 127.8, 128.5, 135.9, 137.1, 147.6, 149.6, 212.6; IR (ATR) 836, 1258, 1513, 1715 cm^{-1}; HRMS (CI) *m/z*: $[M]^+$ Calcd for $C_{25}H_{36}O_4Si$ 428.2383, Found 428.2387; $[\alpha]^{20}_D$ +84.2 (*c* 1.47, $CHCl_3$).

(3*S*,4*S*)-4-(4-(benzyloxy)-3-methoxyphenyl)-4-((*tert*-butyldimethylsilyl)oxy)-3-methylbutan-2-one (7b): To a solution of **6b** (5.44 g, 13.1 mmol) in THF (66.0 mL) at 0 °C was added 3.0 M MeMgBr in THF solution (6.60 mL, 19.7 mmol). After being stirred 3 h, the reaction was quenched with sat. NH_4Cl (66.0 mL) and extracted with ether. The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by column chromatography (hexane:EtOAc = 5:1) to afford an alcohol (4.28 g, 76%) as colorless oil. To a solution of the alcohol (5.28 g, 12.3 mmol) in DCM (80.0 mL) was added Dess–Martin periodinane

(DMP, 7.80 g, 18.4 mmol). After being stirred at rt for 15 h. the mixture was added to excess ether (40.0 mL), filtered through celite and the filtrate was concentrated in *vacuo*. The residue was purified by column chromatography (hexane:EtOAc = 6:1) to afford **7b** (4.40 g, 83%) as colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ −0.22 (3H, s), 0.01 (3H, s), 0.87 (9H, s), 1.14 (3H, d, *J* = 6.8 Hz), 1.87 (3H, s), 2.78 (1H, qd, *J* = 6.8, 6.8 Hz), 3.87 (3H, s), 4.72 (1H, d, *J* = 6.8 Hz), 5.11 (2H, s), 6.69 (1H, dd, *J* = 8.0, 1.8 Hz), 6.79 (1H, d, *J* = 8.0 Hz), 6.87 (1H, d, *J* = 1.8 Hz), 7.30 (1H, br-t, *J* = 7.1 Hz), 7.36 (2H, br-dd, *J* = 7.3, 7.1 Hz), 7.43 (2H, br-d, *J* = 7.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ −5.1, −4.6, 12.9, 18.2, 25.8, 56.0, 56.1, 71.1, 76.1, 110.0, 113.5, 118.7, 127.4, 127.8, 128.5, 136.7, 137.1, 147.3, 149.4, 211.9; IR (ATR) 1714 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{25}H_{36}O_4Si$ 428.2383, Found 428.2391; $[\alpha]^{20}_D$ −22.8 (*c* 1.00, $CHCl_3$).

(((1*S*,2*S*)-1-(4-(benzyloxy)-3-methoxyphenyl)-2,3-dimethylbut-3-en-1-yl)oxy)(*tert*-butyl)dimethylsilane (8a): To a solution of **7a** (249 mg) in THF (3.70 mL) was added 0.5 M Tebbe reagent (1.28 mL, 640 μmol) at −40 °C. The mixture was stirred at −40 °C for 30 min and then at rt for 15 min. Saturated aqueous $NaHCO_3$ was added dropwise, and the aqueous layer was extracted with Et_2O. The combined organic layers were dried over anhydrous $MgSO_4$, and concentrated in *vacuo*. The residue was purified by column chromatography (hexane:EtOAc = 60:1) to yield **8a** (208 mg, 72% in four steps) as a pale green solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ −0.28 (3H, s), −0.01 (3H, s), 0.78 (3H, d, *J* = 6.9 Hz), 0.84 (9H, s), 1.72 (3H, br-s), 2.39 (1H, dq, *J* = 7.4, 6.9 Hz), 3.87 (3H, s), 4.41 (1H, d, *J* = 7.4 Hz), 4.68 (1H, d, *J* = 1.6 Hz), 4.76 (1H, d, *J* = 1.6 Hz), 5.12 (2H, s), 6.68 (1H, dd, *J* = 8.2, 1.6 Hz), 6.79 (1H, d, *J* = 8.2 Hz), 6.87 (1H, d, *J* = 1.6 Hz), 7.30–7.46 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ −5.3, −4.6, 16.1, 18.2, 20.7, 25.7, 49.7, 55.9, 71.2, 78.1, 110.5, 111.6, 113.2, 119.3, 127.4, 127.8, 128.5, 137.4, 137.5, 147.2, 147.6, 149.3; IR (ATR) 1515 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{26}H_{38}O_3Si$ 426.2590; Found 426.2545; $[\alpha]^{22}_D$ −46.5 (*c* 0.54, $CHCl_3$); m.p. 135–136 °C.

(((1*S*,2*R*)-1-(4-(benzyloxy)-3-methoxyphenyl)-2,3-dimethylbut-3-en-1-yl)oxy)(*tert*-butyl)dimethylsilane (8b): To a solution of **7b** (1.50 g, 3.50 mmol) in THF (30.0 mL) was added a Tebbe reagent solution (14.4 mL in toluene, 7.0 mmol) dropwise at −40 °C. After being stirred for 5 h, the reaction mixture was poured into aq $NaHCO_3$ and exracted with ether. The organic layers were washed with brine, dried over $MgSO_4$ and concentrated in *vacuo*. The residue was purified by column chromatography (hexane:EtOAc = 9:1) to afford **8b** (1.30 g, 87%) as yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ −0.24 (3H, s), 0.00 (3H, s), 0.87 (9H, s), 1.07 (3H, d, *J* = 7.1 Hz), 1.58 (3H, s), 2.31 (1H, qd, *J* = 7.1, 6.3 Hz), 3.86 (3H, s), 4.46 (1H, d, *J* = 6.3 Hz), 4.59 (1H, s), 4.67 (1H, s), 5.11

(2H, s), 6.67 (1H, dd, *J* = 8.1, 1.7 Hz), 6.77 (1H, d, *J* = 8.1 Hz), 6.88 (1H, d, *J* = 1.7 Hz), 7.30 (1H, br-t, *J* = 7.3 Hz), 7.36 (2H, br-dd, *J* = 7.3, 7.3 Hz), 7.44 (2H, br-d, *J* = 7.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ −5.1, −4.6, 15.1, 18.3, 21.7, 25.9, 49.8, 55.9, 71.1, 77.8, 110.4, 111.6, 113.1, 118.9, 127.4, 127.8, 128.5, 137.3, 138.1, 146.9, 147.5, 149.1; IR (ATR) 2954, 1512, 1255 cm^{-1}; HRMS (CI) *m/z*: $[M + H]^+$ Calcd for $C_{26}H_{39}O_3Si$ 427.2668, Found 427.2662; $[\alpha]^{20}_D$ −24.9 (*c* 1.00, $CHCl_3$).

(2*R*,3*S*,4*S*)-4-(4-(benzyloxy)-3-methoxyphenyl)-4-((*tert*-butyldimethylsilyl)oxy)-2,3-dimethylbutan-1-ol (9a): To a solution of **8a** (456 mg, 1.07 mmol) in THF (7.1 mL) was added 0.5 mol/L 9-BBN (8.60 mL, 4.28 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 1 h, and then at rt for 20 h. The reaction mixture was treated with 3 mol/L aqueous NaOH (1.95 mL) and 30% H_2O_2 (1.95 mL, 4.28 mmol) for 1 h. The aqueous layer was extracted with EtOAc. The combined organic layers were dried over anhydrous $MgSO_4$, and concentrated in *vacuo*. The residue was purified by column chromatography (hexane:EtOAc = 20:1 to 6:1) to yield **9a** (356 mg, 74%, >99% de) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ −0.17 (3H, s), 0.07 (3H, s), 0.78 (3H, d, *J* = 7.0 Hz), 0.91 (9H, s), 0.91 (3H, d, *J* = 6.9 Hz), 1.77–1.84 (1H, m), 1.91–1.99 (1H, m), 3.30 (1H, dd, *J* = 11.0, 4.8 Hz), 3.52 (1H, dd, *J* = 11.0, 8.9 Hz), 3.88 (3H, s), 4.65 (1H, d, *J* = 4.8 Hz), 5.13 (2H, s), 6.72 (1H, dd, *J* = 8.2, 1.9 Hz), 6.83 (1H, d, *J* = 8.2 Hz), 6.91 (1H, d, *J* = 1.9 Hz), 7.29–7.46 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ −5.1, −4.6, 12.2, 17.2, 18.2, 25.8, 33.9, 45.7, 55.9, 63.9, 71.1, 78.8, 110.5, 113.5, 118.8, 127.4, 127.8, 128.5, 136.7, 137.2, 147.0, 149.2; IR (neat) 3416 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{26}H_{40}O_4Si$ 444.2696; Found 444.2698; $[\alpha]^{19}_D$ –39.4 (*c* 1.00, $CHCl_3$).

(2*S*,3*R*,4*S*)-4-(4-(benzyloxy)-3-methoxyphenyl)-4-((*tert*-butyldimethylsilyl)oxy)-2,3-dimethylbutan-1-ol (9b): To a solution of **8b** (1.30 g, 3.05 mmol) in THF (30.0 mL) was added 0.5 M 9-BBN in THF solution (24.4 mL, 12.2 mmol) at 0 °C. After being stirred at rt for 5 h, a mixture of 3.0 M aq NaOH (5.10 mL, 15.3 mmol) and 30% H_2O_2 (5.10 mL) was added to the reaction mixture. After further 2 h, the reaction mixture was exracted with EtOAc. The organic layers were washed with brine, dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by column chromatography (hexane:EtOAc = 4:1) to afford **9b** (1.26 g, 93%, >99%de) as colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ −0.25 (3H, s), 0.02 (3H, s), 0.89 (12H, m), 0.98 (3H, d, *J* = 6.3 Hz), 1.56–1.66 (2H, m), 3.41 (1H, dd, *J* = 10.4, 6.3 Hz), 3.61 (1H, dd, *J* = 10.4, 4.5 Hz), 3.87 (3H, s), 4.66 (1H, d, *J* = 4.7 Hz), 5.12 (2H, s), 6.70 (1H, dd, *J* = 8.1, 1.8 Hz), 6.80 (1H, d, *J* = 8.1 Hz), 6.89 (1H, s), 7.30 (1H, br-t, *J* = 6.6 Hz), 7.36 (2H, br-dd, *J* = 7.5, 6.6 Hz), 7.44 (2H, br-d, *J* = 7.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.0, −4.3, 10.5, 16.4, 18.2, 25.9, 36.9, 45.4, 56.0, 65.6, 71.2, 76.8,

110.4, 113.3, 118.9, 127.4, 127.8, 128.5, 137.3, 138.2, 147.0, 149.2; IR (ATR) 3402 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{26}H_{40}O_4Si$ 444.2696, Found 444.2690; $[\alpha]^{20}_D$ −35.0 (*c* 1.00, $CHCl_3$).

(2*R*,3*S*,4*S*)-1-(benzo[*d*][1,3]dioxol-5-yl)-4-(4-(benzyloxy)-3-methoxyphenyl)-4-((*tert*-butyldimethylsilyl)oxy)-2,3-dimethylbutan-1-one (10): To a solution of **9a** (209 mg, 471 μmol) in DMF (4.70 mL) was added pyridinium dichromate (509 mg, 1.54 mmol). The mixture was stirred at rt for 2 h. The reaction was taken up with water and 2 mol/L HCl. The aqueous layer was extracted with EtOAc. The combined organic layers were washed with water, and brine, dried over anhydrous $MgSO_4$, and concentrated in *vacuo* to give an aldehyde. To a solution of this aldehyde (198 mg, 448 μmol) in THF (4.50 mL) was added anhydrous $CeCl_3$ (276 mg, 1.12 mmol) at 0 °C. After the mixture was cooled to −78 °C, 3,4-methylenedioxyphenylmagnesium bromide (1.12 mL, 1.0 mol/L solution in THF) was added dropwise and the reaction mixture was further stirred at rt for 2 h and the reaction was quenched with saturated aqueous NH_4Cl. The aqueous layer was extracted with EtOAc. The combined organic layers were washed with H_2O and brine, dried over anhydrous $MgSO_4$, and concentrated in *vacuo*. The residue (340 mg) was dissolved in DCM and to the resulting solution was added pyridine (57.2 μL, 672 μmol) and Dess–Martin periodinane (228 mg, 538 μmol). The reaction mixture was stirred at rt for 1 h. After being taken up with saturated aqueous $NaHCO_3$, the aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and concentrated in *vacuo*. The residue was purified by column chromatography (hexane:EOAc = 6:1) to yield **10** (188 mg, 71% in three steps) as a colorless oil: ^1H NMR (400 MHz, $CDCl_3$) δ −0.29 (3H, s), −0.10 (3H, s), 0.82 (9H, s), 0.83 (3H, d, *J* = 7.2 Hz), 1.23 (3H, d, *J* = 7.0 Hz), 2.09 (1H, ddq, *J* = 6.6, 6.0, 7.2 Hz), 3.52 (1H, dq, *J* = 6.6, 7.0 Hz), 3.86 (3H, s), 4.69 (1H, d, *J* = 6.0 Hz), 5.15 (2H, s), 6.02 (2H, s), 6.73 (1H, dd, *J* = 8.3, 2.0 Hz), 6.79 (1H, d, *J* = 8.0 Hz), 6.83 (1H, d, *J* = 8.3 Hz), 6.90 (1H, d, *J* = 2.0 Hz), 7.28–7.47 (7H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.1, −4.6, 13.0, 17.2, 18.1, 25.8, 40.1, 45.8, 55.9, 71.1, 76.2, 101.7, 107.7, 108.2, 110.7, 113.2, 119.1, 124.4, 127.4, 127.8, 128.5, 132.4, 136.8, 137.2, 147.1, 148.1, 149.2, 151.4, 202.3; IR (ATR) 1673 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{33}H_{42}O_6Si$ 562.2751; Found 562.2746; $[\alpha]^{21}_D$ −100.0 (*c* 3.90, $CHCl_3$).

5-((4*S*,5*S*)-5-(4-(benzyloxy)-3-methoxyphenyl)-3,4-dimethyl-4,5-dihydrofuran-2-yl)benzo[*d*][1,3]dioxole (11a): To a solution of **10** (50.2 mg, 893 μmol) in THF (2.00 mL) was added 1.0 mol/L TBAF solution (1.34 mL, 1.34 mmol) at rt. After being stirred for 1 h, water was added to the reaction mixture and extracted with ether. The combined organic layers were washed with brine,

dried over anhydrous $MgSO_4$, and concentrated in *vacuo*. The residue was dissolved in THF (2.00 mL). 2.0 mol/L HCl (0.5 mL) was added to the solution. After being stirred for 3 h, water was added to the reaction mixture and extracted with ether. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and concentrated in *vacuo*. The residue was purified by column chromatography (hexane:EOAc = 10:1) to yield **11a** (26.9 mg, 70%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.22 (3H, d, *J* = 6.0 Hz), 1.85 (3H, d, *J* = 1.4 Hz), 2.93 (1H, dqq, *J* = 8.5, 6.0, 1.4 Hz), 3.90 (3H, s), 4.85 (1H, d, *J* = 8.5 Hz), 5.16 (2H, s), 5.97 (2H, s), 6.82 (1H, dd, *J* = 8.6, 1.7 Hz), 6.86 (2H, brs), 6.98 (1H, brs), 7.08 (1H, d, *J* = 1.7 Hz), 7.09 (1H, d, *J* = 8.6 Hz), 7.28–7.46 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.0, 18.0, 51.7, 56.1, 71.1, 88.0, 101.1, 107.6, 108.1, 108.7, 109.5, 113.8, 118.2, 121.1, 126.2, 127.2, 127.8, 128.5, 135.7, 137.2, 147.0, 147.4, 147.7, 149.7; IR (ATR) 1505 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{27}H_{26}O_5$ 430.1780; Found 430.1788.

(1*R*,2*R*,3*S*,4*S*)-1-(benzo[*d*][1,3]dioxol-5-yl)-4-(4-(benzyloxy)-3-methoxyphenyl)-2,3-dimethylbutane-1,4-diol (13a): To a solution of **10a** (45.0 mg, 80.0 μmol) in methanol (800 μL) was added $NaBH_4$ (6.00 mg, 160 μmol) and $CeCl_3 \cdot 7H_2O$ (28.8 mg, 80.0 μmol) at rt. After being stirred for 1 h, H_2O (2.00 mL) was added to the reaction mixture and extracted with EtOAc. The organic layers were dried over $MgSO_4$ and concentrated in *vacuo*. The residue was purified by column chromatography (hexane:ether = 3:1) to afford a mono-alcohol (23.8 mg, 53%). The mono-alcohol (35.5 mg, 62.9 μmol) was dissolved in THF (600 μL). TBAF (THF solution, 75.5 μL, 75.5 μmol) was added to the mixture at 0 °C. After being stirred for 1 h, H_2O was added to the reaction flask and extracted with EtOAc. The organic layers were washed with brine and dried over $MgSO_4$ and concentrated in *vacuo*. The residue was purified by column chromatography (hexane:EtOAc = 1:1) to afford **13a** (24.2 mg, 85%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.78 (3H, d, *J* = 6.0 Hz), 0.80 (3H, d, *J* = 6.6 Hz), 2.04–2.11 (2H, m), 3.90 (3H, s), 4.51 (2H, d, *J* = 7.4 Hz), 5.14 (2H, s), 5.94 (2H, s), 6.76 (2H, s), 6.76 (1H, dd, *J* = 7.1, 1.6 Hz), 6.83 (1H, d, *J* = 7.1 Hz), 6.85 (1H, s), 6.91 (1H, d, *J* = 1.6 Hz), 7.29–7.44 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.9, 15.1, 41.9, 42.2, 56.0, 71.1, 100.9, 102.1, 107.0, 107.9, 110.1, 113.7, 118.9, 120.0, 127.3, 127.8, 128.5, 137.7, 138.0, 138.7, 146.7, 147.7, 149.6; IR (ATR) 3221 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{27}H_{30}O_6$ 450.2043, Found 450.2068; $[\alpha]^{22}_D$ +14.6 (*c* 1.80, $CHCl_3$).

4-((1*S*,2*R*,3*S*,4*R*)-4-(benzo[*d*][1,3]dioxol-5-yl)-1,4-dihydroxy-2,3-dimethylbutyl)-2-methoxyphenyl 4-methylbenzenesulfonate (13b): To a solution of **24** (16.2 mg, 30.0 μmol) in

benzene:methanol = 4:1 (500 μL) was $Pd(OH)_2/C$ (1.60 mg). The reaction mixture was stirred under H_2 for 8 h, and the mixture was filtered through celite and the filtrate was concentrated in *vacuo*. The residue was purified by column chromatography (hexane:EtOAc = 3:1) to afford a phenol (7.40 mg, 54%) as colorless oil. To a solution of the phenol (15.3 mg, 320 μmol) in DCM (500 μL) was added Et_3N (12.0 μL, 840 μmol) and *p*-toluenesulfonyl chloride (14.8 mg, 780 μmol). The reaction mixture was stirred at 45 °C for 2 d, and quenched with sat. NH_4Cl, and extracted with EtOAc. The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated in *vacuo*. The residue was purified by column chromatography (hexane:EtOAc = 15:1 then 3:1) to afford a tosylate (16.4 mg, 82%) as colorless oil. To a solution of the tosylate (83.9 mg, 133 μmol) in THF (1.50 mL) was added 1.0 M TBAF in THF (200 μL, 200 μmol). After being stirred for 10 h, the reaction mixture was added water (2.00 mL), and extracted ether. The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by column chromatography (hexane:EtOAc = 2:1 then 1:1) to afford **13b** (67.5 mg, 99%) as colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (3H, d, J = 6.6 Hz), 0.99 (3H, d, J = 6.6 Hz), 1.82–1.89 (4H, m), 2.44 (3H, br-s), 3.55 (3H, s), 4.89 (1H, br-s), 4.97 (1H, br-s), 5.95 (1H, d, J = 1.4 Hz), 5.96 (1H, d, J = 1.4 Hz), 6.77–6.83 (5H, m), 7.09 (1H, d, J = 8.2 Hz), 7.28 (2H, d, J = 8.0 Hz), 7.74 (2H, br-d, J = 8.0 Hz),; ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.7, 10.7, 21.7, 42.5, 43.0, 55.6, 73.7, 74.6, 101.0, 106.5, 108.0, 110.3, 117.6, 119.0, 123.5, 128.6, 129.3, 133.2, 137.0, 138.3, 144.8, 144.9, 146.5, 147.7, 151.5; IR (ATR) 3545, 3422 cm^{-1}; HRMS (FAB) *m/z*: $[M + Na]^+$ Calcd for $C_{27}H_{30}O_8SNa$ 537.1559, Found 537.1578; $[\alpha]^{20}_D$ −3.6 (*c* 1.10, $CHCl_3$).

5-((2*R*,3*R*,4*S*,5*S*)-5-(4-(benzyloxy)-3-methoxyphenyl)-3,4-dimethyltetrahydrofuran-2-yl)benzo[*d*][1,3]dioxole (14): To a solution of **13a** (16.3 mg, 36.2 μmol) in DCM (1.00 mL) was added PPh_3 (49.4 mg, 188 μmol) and DIAD (30.8 μL, 159 μmol). After being stirred for 12 h, the solution was concentrated in *vacuo*. The residue was purified by column chromatography (hexane:ether = 1:1) to afford **14** (8.80 mg, 56%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.01 (3H, d, J = 4.4 Hz), 1.01 (3H, d, J = 4.4 Hz), 2.22–2.35 (2H, m), 3.90 (3H, s), 4.45 (1H, d, J = 6.6 Hz), 4.46 (1H, d, J = 6.6 Hz), 5.13 (2H, s), 5.94 (2H, s), 6.79–6.98 (5H, m), 7.27–7.58 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.9, 15.1, 41.9, 42.2, 56.0, 71.1, 76.7, 77.3, 101.0, 107.0, 107.9, 110.1, 113.8, 119.0, 120.1, 127.3, 127.8, 128.5, 137.2, 137.7, 138.7, 146.7, 147.4, 147.7, 149.7; IR (ATR) 2961, 1506 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{27}H_{28}O_5$ 432.1936, Found 432.1929.

(2*S*,3*R*,4*S*)-4-(4-(benzyloxy)-3-methoxyphenyl)-4-((*tert*-butyldimethylsilyl)oxy)-2,3-dimethylbu

tanal (15): To a solution of **9b** (5.28 g, 12.3 mmol) in DCM (80.0 mL) was added Dess–Martin periodinane (7.80 g, 18.4 mmol). After being stirred at rt for 15 h. the mixture was added to excess ether (40.0 mL), filtered through celite and the filtrate was concentrated in *vacuo*. The residue was purified by column chromatography (hexane:EtOAc = 6:1) to afford **15** (4.40 g, 83%) as colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ −0.24 (3H, s), 0.03 (3H, s), 0.89 (9H, s), 1.00 (3H, d, *J* = 7.0 Hz), 1.11 (3H, d, *J* = 7.0 Hz), 1.91 (1H, qdd, *J* = 7.0, 5.9, 5.9 Hz), 2.32 (1H, qdd, *J* = 7.0, 5.9, 2.4 Hz), 3.87 (3H, s), 4.66 (1H, d, *J* = 5.9 Hz), 5.12 (2H, s), 6.72 (1H, dd, *J* = 8.2, 2.0 Hz), 6.81 (1H, d, *J* = 8.2 Hz), 6.88 (1H, d, *J* = 2.0 Hz), 7.30 (1H, dd, *J* = 6.2, 1.3 Hz), 7.34–7.45 (4H, m), 9.54 (1H, d, *J* = 2.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.1, −4.4, 12.0, 12.5, 18.2, 25.9, 44.8, 48.2, 55.9, 71.1, 76.2, 110.3, 113.3, 119.0, 127.4, 127.8, 128.5, 136.8, 137.2, 147.4, 149.4, 205.1; IR (ATR) 1722 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{26}H_{38}O_4Si$ 442.2539, Found 442.2545; $[\alpha]^{20}_D$ –25.9 (c 1.22, $CHCl_3$).

(3*S*,4*R*,5*S*)-5-(4-(benzyloxy)-3-methoxyphenyl)-3,4-dimethyldihydrofuran-2(3*H*)-one (16): To a solution of **9b** (3.00 g, 6.75 mmol) in DCM (60.0 mL) was added Dess–Martin periodinane (5.70 g, 13.5 mmol). After being stirred at rt for 1 h. the mixture was added to excess ether (120 mL), filtered through celite and the filtrate was concentrated in *vacuo*. To a solution of the residue (3.04 g) in *t*-BuOH (14.0 mL) was added a solution of 2-methyl-2-butene (3.20 mL, 30.4 mmol), anhydrous NaH_2PO_4 (891 mg, 7.43 mmol), and $NaClO_2$ (2.44 g, 27.0 mmol) in *t*-BuOH/H_2O (3.6:1, 86.0 mL) at rt. After being stirred for 40 min, 5% HCl was added to the reaction mixture, then extracted with EtOAc. The organic layers were dried over Na_2SO_4 and concentrated in *vacuo*. The residue (2.90 g) was added to a solution of HF/pyridine/MeCN (1:3:5, 92.0 mL) at 0 °C. After being stirred for 23 h, saturated NaH_2PO_4 (100 mL) was added to the reaction mixture, and then extracted with EtOAc. The organic layers were dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by column chromatography (hexane:EtOAc = 3:1) to afford **16** (1.20 g, 55%, over 3 steps) as yellow oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.56 (3H, d, *J* = 7.4 Hz), 1.22 (3H, d, *J* = 7.4 Hz), 2.73 (1H, qdd, *J* = 7.4, 7.1, 4.9 Hz), 2.98 (1H, qd, *J* = 7.4, 7.1 Hz), 3.88 (3H, s), 5.15 (2H, s), 5.46 (1H, d, *J* = 4.9 Hz), 6.72 (1H, dd, *J* = 8.2, 2.1 Hz), 6.83 (1H, d, *J* = 2.1 Hz), 6.88 (1H, d, *J* = 8.2 Hz), 7.25–7.45 (5H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 9.4, 10.1, 40.1, 41.0, 56.1, 71.0, 82.2, 109.1, 114.0, 117.5, 127.8, 128.5, 129.3, 130.2, 137.0, 147.7, 149.7, 180.0; IR (ATR) 1771 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{20}H_{22}O_4$ 326.1518, Found 326.1506; $[\alpha]^{20}_D$ –53.7 (c 1.00, $CHCl_3$).

(3*R*,4*R*,5*S*)-5-(4-(benzyloxy)-3-methoxyphenyl)-3,4-dimethyldihydrofuran-2(3*H*)-one (17): To a

solution of **16** (15.9 mg, 48.7 μmol) in MeOH (200 μL) was added 1.0 mol/L NaOMe solution (in MeOH, 122 μL, 122 μmol) at rt. After being stirred for 16 h, saturated NaCl solution (2.00 mL) was added to the reaction mixture and extracted with ether. The organic layers were dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by column chromatography (hexane:EtOAc = 2:1) to afford **17** (11.0 mg, 69%) as yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.76 (3H, d, *J* = 7.0 Hz), 1.29 (3H, d, *J* = 7.0 Hz), 2.31–2.39 (1H, m), 2.42–2.51 (1H, m), 3.88 (3H, s), 5.15 (2H, s), 5.49 (1H, d, *J* = 7.6 Hz), 6.66 (1H, dd, *J* = 8.3, 2.0 Hz), 6.67 (1H, d, *J* = 2.0 Hz), 6.87 (1H, d, *J* = 8.3 Hz), 7.28–7.44 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.7, 14.6, 40.0, 42.4, 56.1, 71.1, 82.4, 109.5, 113.8, 118.1, 127.3, 127.9, 128.6, 129.2, 136.9, 148.0, 149.6, 179.8; IR (ATR) 1771 cm^{-1}; HRMS (CI) *m/z*: $[M + H]^+$ Calcd for $C_{20}H_{23}O_4$ 327.1597, Found 327.1601; $[\alpha]^{20}_D$ +27.1 (*c* 1.00, $CHCl_3$).

(2*S*,3*R*,4*R*)-2-(4-(benzyloxy)-3-methoxyphenyl)-5-methoxy-3,4-dimethyltetrahydrofuran (19): To a solution of **17** (330 mg, 1.01 mmol) in DCM (10.0 mL) was added 1 mol/L Dibal solution (in toluene, 1.20 mL, 1.20 mmol) at −78 °C. After being stirred for 30 min, the reaction was worked up with methanol (600 μL), H_2O (2.20 mL), and 2 mol/L aqueous NaOH (2.20 mL) and extracted with DCM. The organic layers were dried over Na_2SO_4 and concentrated in *vacuo*. The residue (345 mg) was dissolved in methanol (10.0 mL). $HC(OCH_3)_3$ (409 μL, 3.74 mmol) and *p*-TsOH·H_2O (652 mg, 3.43 mmol) was added to the solution. After being stirred for 7 h, the reaction was cooled to 0 °C and worked up with saturated aqueous $NaHCO_3$ (10.0 mL), then extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by column chromatography (hexane:EtOAc = 8:1) to afford acetal **19** (328 mg, 95% yield over 2 steps) as colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.91 (3H, d, *J* = 6.9 Hz), 1.00 (3H, d, J = 7.4 Hz), 2.24–2.46 (2H, m), 3.48 (3H, s), 3.90 (3H, s), 4.51 (1H, d, *J* = 9.6 Hz), 4.70 (1H, s), 5.15 (2H, s), 6.76 (1H, dd, *J* = 8.2, 2.0 Hz), 6.82 (1H, d, *J* = 8.2 Hz), 6.99 (1H, d, *J* = 2.0 Hz), 7.27–7.45 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.9, 11.4, 42.9, 44.1, 54.9, 55.8, 71.1, 87.7, 110.4, 110.9, 113.4, 119.4, 127.2, 127.8, 128.5, 135.4, 137.3, 147.7, 149.8; IR (ATR) 2960, 1511, 1261 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{21}H_{26}O_4$ 342.1831, Found 342.1840.

(2*S*,3*R*,4*R*)-2-(4-(benzyloxy)-3-methoxyphenyl)-3,4-dimethyl-5-(phenylsulfonyl)tetrahydrofuran (20): To a solution of hemi-acetal **18** (15.7 mg, 0.05 mmol) in DCM (500 μL) was added $PhSO_2H$ (13.6 mg, 0.10 mmol), CSA (1.20 mg, 0.01 mmol), and $CaCl_2$ (15.4 mg, 0.14 mmol). After

being stirred for 1 h, the reaction was worked up with saturated aquepus $NaHCO_3$ (2.00 mL) and extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by column chromatography (hexane: EtOAc = 3:1) to afford **20a** (10.9 mg, 51%) and **20b** (5.5 mg, 25%) as colorless oils: **20a** (major isomer): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.60 (3H, d, *J* = 6.6 Hz), 1.56 (3H, d, *J* = 7.1 Hz), 2.38–2.48 (1H, m), 2.84–2.95 (1H, m), 3.83 (3H, s), 5.05 (1H, d, *J* = 7.2 Hz), 5.10 (2H, s), 5.50 (1H, d, *J* = 9.0 Hz), 6.56 (1H, d, *J* = 8.2 Hz), 6.60 (1H, s), 6.79 (1H, d, *J* = 8.2 Hz), 7.15–7.60 (8H, m), 7.92 (2H, d, *J* = 7.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.2, 14.4, 42.4, 43.7, 56.1, 71.0, 86.2, 96.3, 110.4, 113.7, 118.8, 127.3, 127.8, 128.5, 128.9, 129.2, 132.7, 133.6, 137.1, 138.5, 147.6, 149.4; IR (ATR) 2965, 1514, 1146 cm^{-1}; HRMS (CI) *m/z*: $[M]^+$ Calcd for $C_{26}H_{28}O_5S$ 452.1657, Found 452.1658; $[\alpha]^{20}_D$ +71.6 (*c* 0.99, $CHCl_3$). **20b** (minor isomer): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.65 (3H, d, *J* = 6.9 Hz), 1.36 (3H, d, *J* = 6.6 Hz), 2.19–2.27 (1H, m), 2.61–2.69 (1H, m), 4.00 (3H, s), 4.53 (1H, d, *J* = 8.8 Hz), 5.10 (1H, d, *J* = 8.6 Hz), 5.17 (2H, s), 6.71 (1H, dd, *J* = 8.3, 1.9 Hz), 6.84 (1H, d, *J* = 8.3 Hz), 7.27–7.67 (9H, m), 7.98 (2H, dd, *J* = 8.1, 1.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8, 16.1, 39.7, 45.7, 56.3, 71.0, 86.4, 98.1, 110.6, 113.2, 119.0, 127.3, 127.8, 128.6, 129.0, 129.2, 132.5, 133.9, 137.2, 137.8, 147.5, 149.7; IR (ATR) 2865, 1591, 1512, 1149 cm^{-1}; HRMS (CI) *m/z*: $[M]^+$ Calcd for $C_{26}H_{28}O_5S$ 452.1657, Found 452.1659; $[\alpha]^{20}_D$ −187.3 (*c* 1.07, $CHCl_3$).

5-((2*S*,3*R*,4*R*,5*S*)-5-(4-(benzyloxy)-3-methoxyphenyl)-3,4-dimethyltetrahydrofuran-2-yl)benzo[*d*][1,3]dioxole (21): To a mixture of $ZnBr_2$ (14.6 mg, 64.9 μmol) in THF (250 μL) was added 1.0 mol/L 3,4-methylenedioxyphenyl magnesium bromide (in toluene/THF, 124 μL, 124 μmol). After being stirred for 30 min, a solution of **20a** (8.00 mg, 17.7 μmol) in THF (180 μL) was added to the reaction mixture. After being stirred for 1 h at rt, the reaction was cooled to 0 °C and worked up with saturated aqueous NH_4Cl, extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by column chromatography (toluene:EtOAc = 20:1) to afford **21** (3.80 mg, 50%), **22** (0.20 mg, 3%), and **23** (1.60 mg, 21%) as colorless oils: Data of **21** ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.67 (3H, d, *J* = 6.4 Hz), 0.69 (3H, d, *J* = 6.5 Hz) 2.23–2.26 (2H, m), 3.91 (3H, s), 5.15 (2H, s), 5.40 (2H, d, *J* = 6.0 Hz), 5.95 (2H, s), 6.74 (1H, dd, *J* = 8.2, 1.2 Hz), 6.75 (1H, dd, *J* = 7.8, 1.5 Hz), 6.79 (1H, d, *J* = 7.8 Hz), 6.81 (1H, d, *J* = 1.5 Hz), 6.85 (1H, d, *J* = 1.2 Hz), 6.86 (1H, d, *J* = 8.2 Hz), 7.31–7.46 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.6, 14.7, 43.8, 43.8, 56.1, 71.2, 83.6, 83.7, 100.9, 107.0, 107.8, 110.2, 113.8, 118.4, 119.4, 127.3, 127.8, 128.5, 134.6, 135.5, 137.3, 146.4, 147.1, 147.5, 149.4; IR (ATR) 2950, 1500, 1037 cm^{-1}; HRMS (CI) *m/z*: $[M]^+$ Calcd for $C_{27}H_{28}O_5$ 432.1937, Found 432.1942; $[\alpha]^{20}_D$ –

58.4 (*c* 0.14, $CHCl_3$). Data of **22** ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.02 (3H, d, *J* = 5.8 Hz), 1.03 (3H, d, *J* = 5.8 Hz), 1.71–1.83 (2H, m), 3.92 (3H, s), 4.61 (2H, d, *J* = 8.0 Hz), 5.15 (2H, s), 5.94 (2H, s), 6.77 (1H, d, *J* = 8.0 Hz), 6.83 (1H, dd, *J* = 8.0, 1.1 Hz), 6.84 (2H, br-s), 6.92 (1H, d, *J* = 1.1 Hz), 6.97 (1H, br-s), 7.28–7.45 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.8, 13.8, 50.8, 51.2, 56.0, 71.0, 88.3, 88.3, 100.9, 106.5, 107.9, 113.7, 118.6, 119.6, 127.2, 127.7, 128.5, 135.3, 136.5, 137.2, 146.9, 147.6, 147.7, 149.7; IR (ATR) 2961, 1506 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{27}H_{28}O_5$ 432.1937; Found 432.1942; $[\alpha]^{20}_D$ +57.1 (*c* 3.30, $CHCl_3$)

5-((2*R*,3*R*,4*R*,5*S*)-5-(4-(benzyloxy)-3-methoxyphenyl)-3,4-dimethyltetrahydrofuran-2-yl)benzo[*d*][1,3]dioxole (23): To a solution of **25** (85.0 mg, 151 μmol) in THF (2.00 mL) was added 1.0 mol/L TBAF solution (300 μL, 300 μmol). After being stirred overnight, H_2O was added to the reaction mixture and extracted with EtOAc. The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated in *vacuo*. The residue was purified by column chromatography (hexane:EtOAc = 3:1) to afford a diastereomeric mixture of hemi-acetal (10.9 mg, 51%). To a solution of the hemi-acetal (185 mg, 413 μmol) in DCM (4.00 mL) was added $NaBH_3CN$ (51.9 mg, 826 μmol) and $BF_3{\cdot}OEt_2$ (109 μL, 413 μmol) at −78 °C. After being stirred for 1.5 h, the reaction was worked up with saturated aqueous $NaHCO_3$ (4.00 mL) and extracted with EtOAc. The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated in *vacuo*. The residue was purified by column chromatography (benzene:ehter = 20:1) to afford **23** (134 mg, 75%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.65 (3H, d, *J* = 7.1 Hz), 1.05 (3H, d, *J* = 6.6 Hz), 1.71–1.76 (1H, m), 2.20–2.25 (1H, m), 3.90 (3H, s), 4.37 (1H, d, *J* = 9.3 Hz), 5.11 (1H, d, *J* = 8.8 Hz), 5.16 (2H, s), 5.98 (2H, s), 6.81 (1H, dd, *J* = 8.2, 1.8 Hz), 6.82 (1H, d, *J* = 8.1 Hz), 6.87 (1H, d, *J* = 8.1 Hz), 6.91 (1H, d, *J* = 1.6 Hz), 6.94 (1H, dd, *J* = 8.2, 1.8 Hz), 7.04 (1H, d, *J* = 1.6 Hz), 7.29–7.46 (5H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.9, 15.1, 45.9, 48.3, 56.0, 71.1, 83.0, 87.4, 101.0, 106.9, 108.1, 110.8, 113.6, 119.2, 120.1, 127.3, 127.8, 128.5, 134.3, 134.8, 137.3, 147.1, 147.2, 147.8, 149.3; IR (ATR) 2925, 1507, 1037 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{27}H_{28}O_5$ 432.1937; Found 432.1920 for; $[\alpha]^{20}_D$ −92.5 (*c* 0.19, $CHCl_3$).

(1*R*,2*S*,3*R*,4*S*)-1-(benzo[*d*][1,3]dioxol-5-yl)-4-(4-(benzyloxy)-3-methoxyphenyl)-4-((*tert*-butyldimethylsilyl)oxy)-2,3-dimethylbutan-1-ol (24): To a solution of **15** (366 mg, 826 μmol) in THF (8.30 mL) was added 1.0 mol/L 3,4-methylenedioxyphenyl magnesium bromide in ether (1.00 mL, 1.00 mmol) at 0 °C. After being stirred for 1 h, the reaction was quenched with sat. NH_4Cl, and

extracted with EtOAc. The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated in *vacuo*. The residue was purified by column chromatography (hexane:EtOAc = 4:1) to afford 1*R*-isomer **24** (237 mg, 51%) as a colorless oil and 1*S*-isomer (50.0 mg, 11%) as colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ −0.23 (3H, s), −0.01 (3H, s), 0.91 (3H, d, *J* = 6.8 Hz), 0.92 (9H, s), 0.99 (3H, d, *J* = 7.4 Hz), 1.62–1.68 (1H, m), 1.69–1.82 (1H, m), 3.87 (3H, s), 4.77 (1H, d, *J* = 3.6 Hz), 4.82 (1H, br-s), 5.13 (2H, s), 5.95 (2H, s), 6.69–6.71 (2H, m), 6.76 (1H, d, *J* = 7.8 Hz), 6.77 (1H, d, *J* = 1.4 Hz), 6.82 (1H, d, *J* = 8.2 Hz), 6.85 (1H, d, *J* = 2.0 Hz), 7.26–7.29 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.0, −4.2, 11.1, 11.4, 18.3, 25.9, 41.7, 45.1, 55.9, 71.2, 74.0, 75.0, 100.9, 106.4, 107.9, 110.3, 113.3, 118.5, 118.8, 127.4, 127.8, 128.5, 137.3, 138.2, 138.8, 146.3, 146.8, 147.6, 149.1; IR (ATR) 3525 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{33}H_{44}O_6Si$ 564.2907, Found 564.2907; $[\alpha]^{20}_D$ −23.1 (*c* 1.01, $CHCl_3$).

(2*S*,3*R*,4*S*)-1-(benzo[*d*][1,3]dioxol-5-yl)-4-(4-(benzyloxy)-3-methoxyphenyl)-4-((*tert*-butyldimethylsilyl)oxy)-2,3-dimethylbutan-1-one (25): To a solution of **24** (100 mg, 179 μmol) in DCM (2.00 mL) was added Dess–Martin periodinane (153 mg, 361 μmol). After being stirred for 10 min, the reaction mixture was filtrated through celite and concentrated in *vacuo*. The residue (111 mg) was purified by column chromatography (hexane:EtOAc = 12:1) to afford **25** (85.0 mg, 85%) as colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ −0.17 (3H, s), 0.11 (3H, s), 0.77 (3H, d, *J* = 6.6 Hz), 0.99 (9H, s), 1.27 (3H, d, *J* = 6.9 Hz), 1.80 (1H, ddq, 3.0, 3.3, 6.6 Hz), 3.46 (1H, dq, *J* = 3.0, 6.9 Hz), 3.82 (3H, s), 4.87 (1H, d, *J* = 3.3 Hz), 5.11 (2H, s), 6.02 (2H, s), 6.67 (2H, dd, *J* = 8.2, 1.6 Hz), 6.79 (1H, d, *J* = 8.2 Hz), 6.81 (1H, d, *J* = 8.2 Hz), 6.81 (1H, d, *J* = 1.6 Hz), 6.82 (1H, d, *J* = 1.6 Hz), 7.25–7.47 (5H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ −4.9, −4.1, 11.6, 16.6, 18.3, 26.0, 41.8, 45.5, 55.8, 71.2, 74.2, 76.4, 101.8, 107.8, 108.1, 110.4, 113.5, 118.6, 124.3, 127.4, 127.8, 128.5, 132.5, 137.3, 146.9, 148.2, 149.1, 151.6, 203.2; IR (ATR) 2931, 1506, 1440, 1254, 1038, 580 cm^{-1}; HRMS (EI) *m/z*: $[M]^+$ Calcd for $C_{33}H_{42}O_6Si$ 562.2751, Found 562.2730; $[\alpha]^{20}_D$ −57.5 (*c* 0.39, $CHCl_3$).

4-((2*S*,3*R*,4*S*,5*S*)-5-(benzo[*d*][1,3]dioxol-5-yl)-3,4-dimethyltetrahydrofuran-2-yl)-2-methoxyphenyl 4-methylbenzenesulfonate (26): To a solution of **13b** (8.10 mg, 15.7 μmol) in DCM (1.60 mL) was added CMMP (14.5 mg, 126 μmol). After being stirred at 40 °C for 24 h, the reaction mixture was concentrated in *vacuo*. The residue was purified by column chromatography (hexane:EtOAc = 3:1 then 1:1) to afford **26** (5.20 mg, 67%, b.o.r.s.m. = 99%) as colorless oil and recover the starting material **13b** (2.43 mg): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.56 (3H, d, *J* = 7.1 Hz), 1.00 (3H, d, *J* = 6.6 Hz), 2.41–2.51 (2H, m), 2.43 (3H, s), 3.52 (3H, s), 4.61 (1H, d, *J* = 9.8 Hz),

5.44 (1H, d, J = 4.7 Hz), 5.95 (1H, d, J = 1.4 Hz), 5.96 (1H, d, J = 1.4 Hz), 6.78–6.81 (3H, m), 6.86 (1H, d, J = 1.8 Hz), 6.91 (1H, d, J = 1.4 Hz), 7.16 (1H. d, J = 8.2 Hz), 7.26 (2H, d, J = 8.3 Hz), 7.72 (2H, d, J = 8.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 9.3, 11.7, 21.7, 43.2, 47.6, 55.5, 84.4, 85.9, 101.0, 106.4, 108.0, 110.2, 117.9, 119.6, 123.6, 128.8, 129.2, 133.0, 136.7, 136.9, 140.9, 144.9, 147.1, 147.9, 151.5; IR (ATR) 2964, 1598 cm^{-1}; HRMS (CI) *m/z*: $[M + H]^+$ Calcd for $C_{27}H_{29}O_7S$ 497.1634, Found 497.1631; $[\alpha]^{20}_D$ −2.3 (*c* 1.03, $CHCl_3$).

ASSOCIATED CONTENT

Supporting Information

The copies of ^{1}H NMR and ^{13}C NMR. This material is available free of charge via the Internet at http://pubs.acs.org.

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