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Syntheses of the stereoisomers of neolignans morinol C and D

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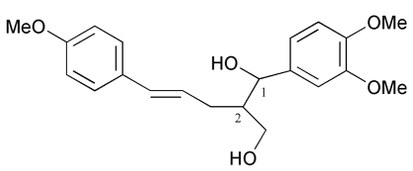
Morinol C and morinol D are neolignans isolated from the Chinese medicinal herb *Morina chinensis* as racemates. (1*R*,2*R*)-Morinol C and (1*S*,2*R*)-morinol D were synthesized from (+)-(3*R*,4*R*)-4-(3,4-dimethoxyphenyl)-3-pivaloyloxymethyl-4-butanolide **4**. On the other hand, (1*S*,2*S*)-morinol C and (1*R*,2*S*)-morinol D were synthesized from *anti*-aldol product **8**.

Introduction

Many kinds of lignans, with different degrees of oxidation and bonding patterns of the phenylpropanoide unit, are biosynthesized by many types of plant. Each lignan has many kinds of biological activity,[1] and the relationship between structure and activity is complex.[2] To understand how the structure of lignans effects biological activity, many kinds of lignans and their analogs must be synthesized. To achieve this aim, the establishment of synthetic pathways is important.[3]

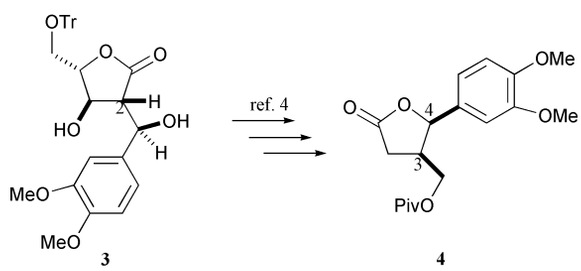
Morinol C (**1**) and morinol D (**2**) (Fig. 1), which were isolated from the Chinese medicinal herb *Morina chinensis* as racemates, are a new type of neolignans.[4] The biological activity of a racemic mixture of **1** and **2** is unknown. Since optically active compounds were not obtained by isolation, the synthetic study of optically active morinol C (**1**) and D (**2**) is valuable for further research on their own activity and the effect of **1** and **2** on the biological activity of Chinese medicinal herb. This is the first report on the synthesis of (1*R*,2*R*) and (1*S*,2*S*)-morinol C (**1**) and (1*S*,2*R*) and (1*R*,2*S*)-morinol D (**2**). The application of (+)-lactone **4**, which was previously constructed by using *threo* selective aldol condensation (Scheme 1),[5] to neolignan synthesis is also shown. The absolute configuration of *threo* aldol product **3** is confirmed for the first time by X-ray analysis in this paper.



1: morinol C (1*R*,2*R* and 1*S*,2*S*)

2: morinol D (1*S*,2*R* and 1*R*,2*S*)

Fig. 1 Morinol C and morinol D.



3 **4**

Scheme 1 Transformation of aldol product **3** to lactone **4**.

Scheme 2 shows the retrosynthetic analysis of (1*R*,2*R*) and (1*S*,2*S*)-morinol C and (1*S*,2*R*) and (1*R*,2*S*)-morinol D. (1*R*,2*R*)-Morinol C would be obtained from aldehyde **5** by using the Wittig–Horner reaction. (+)-Lactone **4** could be converted to aldehyde **5** by employing a ring opening reaction. In the case of the synthesis of (1*S*,2*R*)-morinol D, aldehyde **6** would be transformed to (1*S*,2*R*)-morinol D by the same method as described for (1*R*,2*R*)-morinol C. However, the isomerization of the benzylic position should be achieved during the conversion of (+)-lactone **4** to aldehyde **6**. It was assumed that the benzylic position would be isomerized under acidic conditions. If this isomerization is accomplished, both (1*R*,2*R*)-morinol C and (1*S*,2*R*)-morinol D are obtained from the same starting material (+)-**4**. On the other hand, the transformations of *anti*-aldol product **8**, which could be prepared by Evans' *anti*-aldol[6] condensation, to (1*S*,2*S*)-morinol C and (1*R*,2*S*)-morinol D were planned. The aldehyde **7**, which is an enantiomer of aldehyde **5**, would be obtained from **8**. This aldehyde could be converted to (1*S*,2*S*)-morinol C. *Anti*-aldol product **8** would also be converted to (−)-lactone **4**, which could be transformed to (1*R*,2*S*)-morinol D by the same process as described for (1*S*,2*R*)-morinol D.

Results and discussion

Firstly, the confirmation of the absolute configuration of **3** by X-ray analysis was achieved (Fig. 2). In a previous study,[5] the

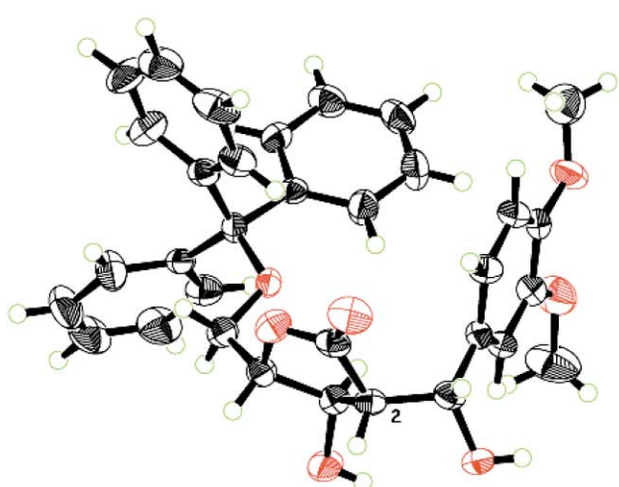


Fig. 2 Structure of aldol product **3** as determined by X-ray crystallography.

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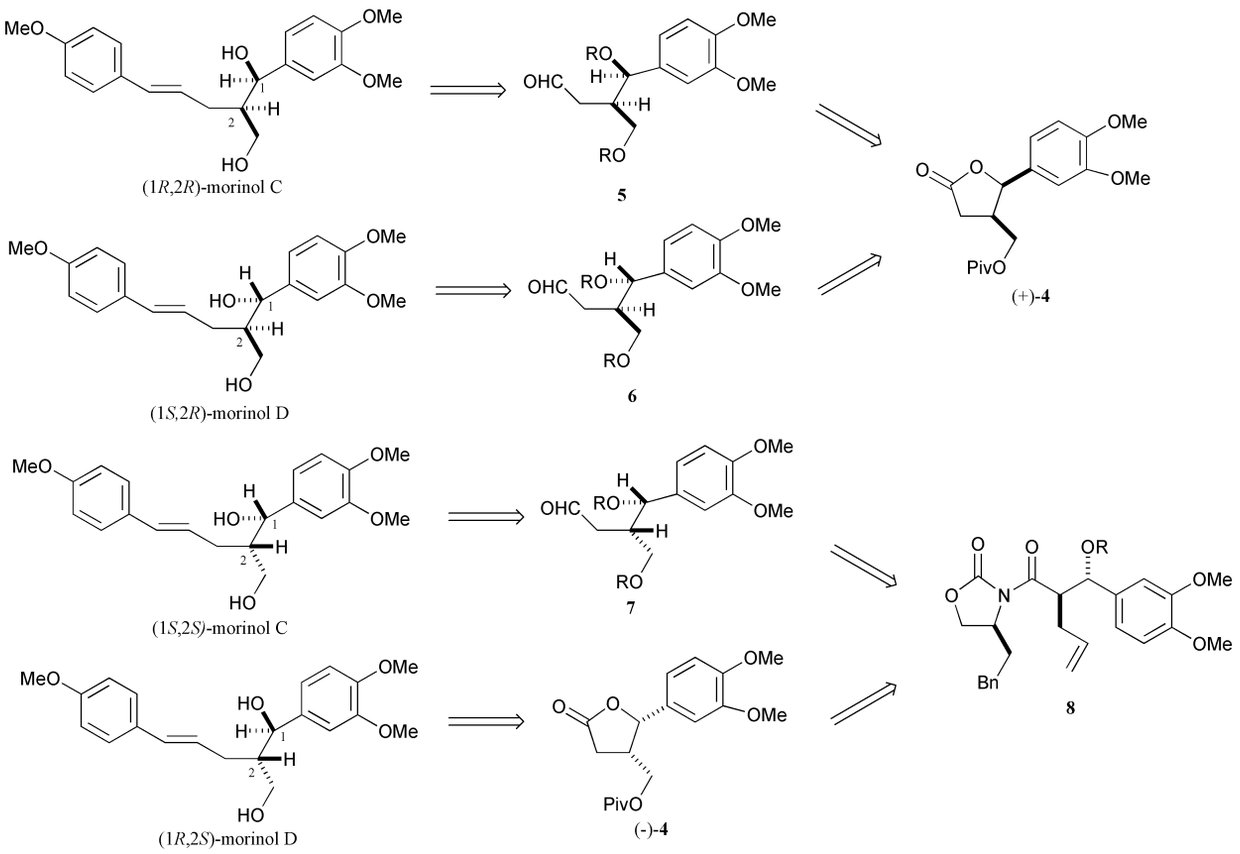


Scheme 2 Retrosynthetic analysis of optically active morinol C and morinol D.

absolute configuration of the benzylic position of **3** prepared by *threo* selective aldol condensation was assumed due to the coupling constant between a benzylic proton and 2-H (J = 8.3 Hz).[7] The X-ray analysis supported this result. The benzylic position and 2-position of *threo* aldol product **3** were converted to the 4 and 3 positions of (+)-lactone **4**, respectively (Scheme 1).

Scheme 3 shows the synthesis of (1*R*,2*R*)-morinol C (**1**). The lactone ring of (+)-**4** was opened to hydroxy amide **9**, by using Et_2NH and $AlMe_3$,[8] in 89% yield. After this, the pivaloyl ester was hydrolyzed to the corresponding diol, which was protected as diTIPS ether by treatment with TIPSOTf and 2,6-lutidine in 78% yield. The fully protected amide **10** was subjected to DIBAL-H reduction to give aldehyde **11** in 85% yield based on 47% recovery of **10**. Wittig–Horner reaction of aldehyde **11** gave the *trans* olefin **12** in 42% yield. Production of the *cis* isomer was not observed. At this stage, the construction of the skeleton of morinol C (**1**) was complete. Deprotection of **12** by *n*-Bu_4NF gave (1*R*,2*R*)-morinol C in 77% yield.

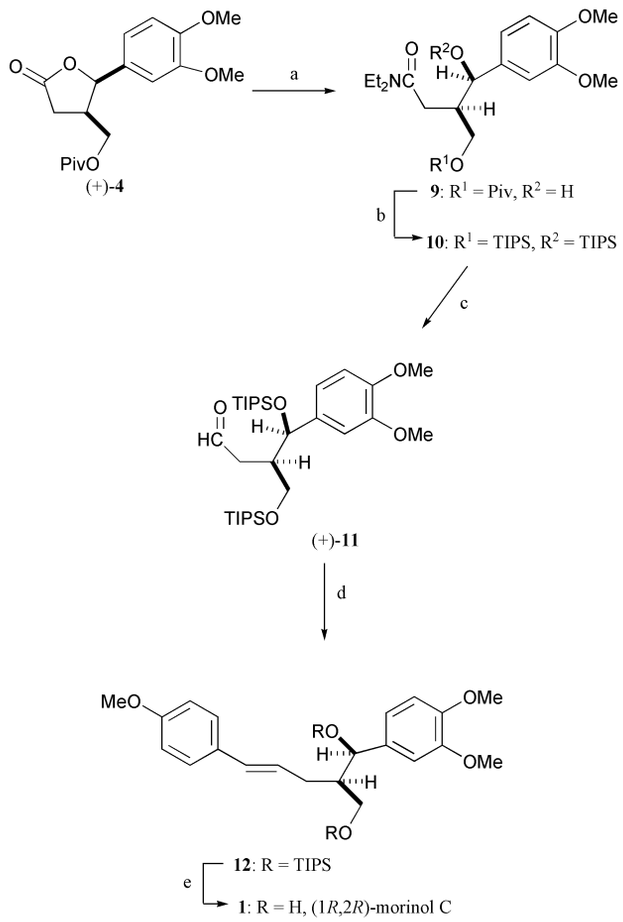
To synthesize (1*S*,2*R*)-morinol D, isomerization at the benzylic position of (+)-lactone **4** was examined. Acidic conditions were selected for this isomerization because of easy production of the benzyl cation. This isomerization was achieved by acidification with aqueous HCl after hydrolysis of pivaloyl ester **4** in EtOH and aqueous NaOH solution, giving hydroxy lactone **13** in 73% yield. This hydroxy lactone was converted to TIPS ether **14** by treatment with TIPSOTf and 2,6-lutidine in 95% yield. After lactone **14** was converted to hydroxy amide **15**, by reaction with Et_2NH and $AlMe_3$, in 85% yield, the hydroxy group was protected as TIPS ether by using TIPSOTf and 2,6-lutidine in 83% yield. By using the described method for the synthesis of (1*R*,2*R*)-morinol C, the amide **16** was converted to (1*S*,2*R*)-morinol D by reduction to aldehyde **17** (95% yield based on 39% recovery of **16**) and Wittig–Horner reaction (46% yield), followed by desilylation (86% yield) (Scheme 4). The ^1H and ^{13}C NMR data of synthesized (1*R*,2*R*)-morinol C and (1*S*,2*R*)-morinol D agreed with the data described in the literature.[4]

The syntheses of (1*S*,2*S*)-morinol C and (1*R*,2*S*)-morinol D are shown in Scheme 5. The aldol condensation of acyloxazolidinone **19**[9] with 3,4-dimethoxybenzaldehyde using Me_3SiCl, Et_3N, and $MgCl_2$ in EtOAc[6] gave *anti*-aldol product **20** in 93% yield. After protection of the hydroxy group as TIPS ether in 77% yield, the resulting product was subjected to $LiBH_4$ reduction to remove the oxazolidinone group in 57% yield. The resulting alcohol **22** was treated with TIPSCl and imidazole, giving diTIPS ether **23** in 75% yield. Osmium oxidation followed by $NaIO_4$ oxidation of **23** gave (−)-aldehyde **11** in 89% yield. This (−)-aldehyde **11** was converted to (1*S*,2*S*)-morinol C by the same process as described for the synthesis of (1*R*,2*R*)-morinol C. On the other hand, protection of the hydroxy group of **22** as a pivaloyl ester (86% yield), subsequent osmium and $NaIO_4$ oxidation gave aldehyde **25** in 92% yield. Treatment of this aldehyde **25** with *n*-Bu_4NF followed by pyridinium chlorochromate gave (−)-lactone **4** in 72% yield. (1*R*,2*S*)-Morinol D was obtained from (−)-lactone **4** by the same process described for the synthesis of (1*S*,2*R*)-morinol D. The ^1H and ^{13}C NMR data of synthesized (1*S*,2*S*)-morinol C and (1*R*,2*S*)-morinol D agreed with the data described in literature.[4]

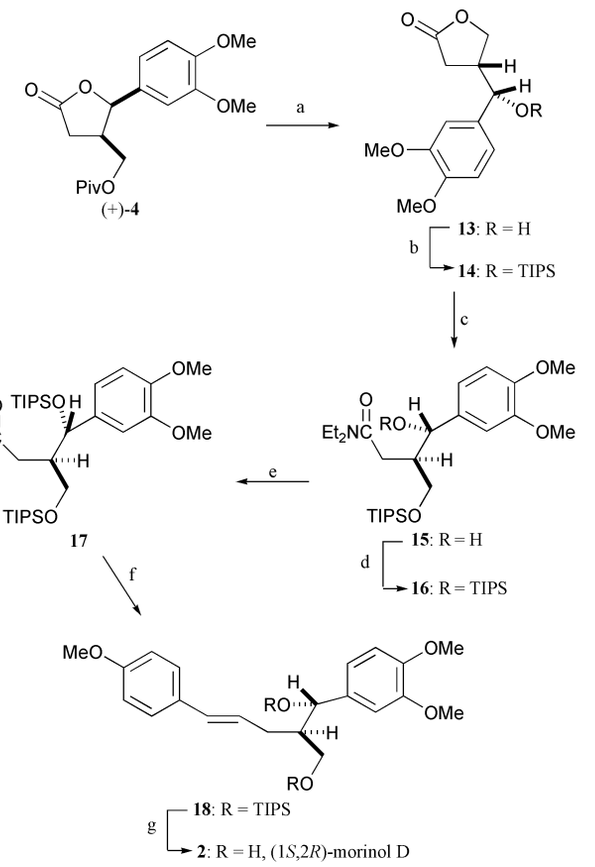
(1*R*,2*R*)-Morinol C and (1*S*,2*R*)-morinol D were first stereoselectively synthesized from (+)-lactone **4** in 19% overall yield involving 6 steps and in 18% overall yield involving 7 steps, respectively. This is a new example of utilization of (+)-lactone **4**. (1*S*,2*S*)-Morinol C and (1*R*,2*S*)-morinol D were also first stereoselectively synthesized from (−)-lactone **4** prepared by using Evans' *anti*-aldol condensation. This success will contribute to the biological study of morinol C and morinol D, because the natural products are a racemic mixture.

Experimental

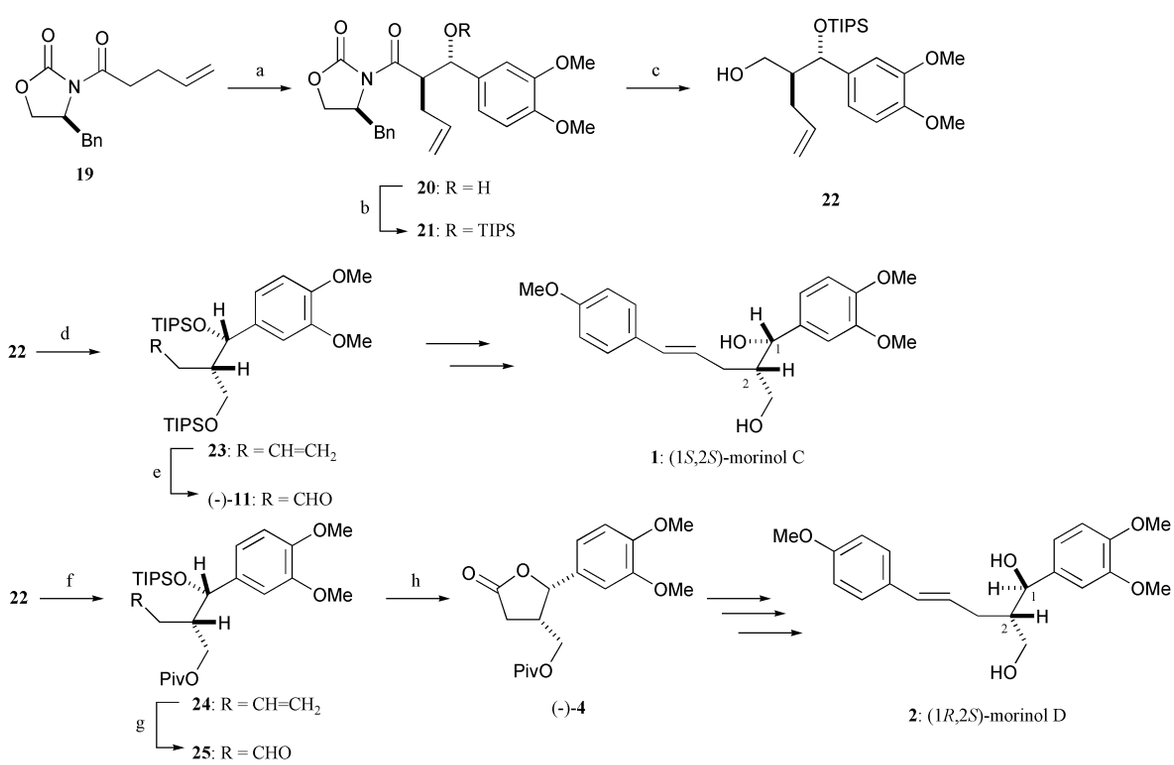
Melting point data (mp) are uncorrected. NMR data were measured with a JNM-EX 400 spectrometer. IR spectra were determined with a Shimadzu FTIR-8100 spectrophotometer. FABMS data were measured with JEOL HX-110 spectrometers



Scheme 3 *Reagents and conditions (yields)*: (a) $AlMe_3$, Et_2NH, CH_2Cl_2, rt, 34 h (89%); (b) i) 1 M aq NaOH, EtOH, rt, 1 h; ii) TIPSOTf, 2,6-lutidine, CH_2Cl_2, 0 °C, 3 h (78%); (c) DIBAL-H, ether, 0 °C, 2 h (85% based on 47% recovery of **10**); (d) $(EtO)_2P(O)CH_2$(4-MeOPh), NaOMe, DMF, rt, 1 h (42%); (e) *n*-Bu_4NF, THF, 0 °C, 2.5 h (77%).



Scheme 4 *Reagents and conditions (yields)*: (a) i) 1 M aq NaOH soln., EtOH, rt, 16 h; ii) 6 M aq HCl, rt, 2 h (73%); (b) TIPSOTf, 2,6-lutidine, 0 °C, 1 h (95%); (c) $AlMe_3$, Et_2NH, CH_2Cl_2, rt, 16 h (85%); (d) TIPSOTf, 2,6-lutidine, 0 °C, 1 h (83%); (e) DIBAL-H, ether, 0 °C, 2 h (95% based on 39% recovery of **16**); (f) $(EtO)_2P(O)CH_2$(4-MeOPh), NaOMe, DMF, rt, 1 h (46%); (g) *n*-Bu_4NF, THF, 0 °C, 2.5 h (86%).



Scheme 5 *Reagents and conditions (yields)*: (a) (i) $MgCl_2$, Et_3N, Me_3SiCl, 3,4-dimethoxybenzaldehyde, EtOAc, rt, 20 h; (ii) CF_3CO_2H, MeOH, rt, 1 h (93%); (b) TIPSOTf, 2,6-lutidine, CH_2Cl_2, 0 °C, 1 h (77%); (c) $LiBH_4$, MeOH, THF, rt, 16 h (57%); (d) TIPSCl, imidazole, DMF, 60 °C, 1.5 h (75%); (e) (i) NMO, OsO_4, acetone, *tert*-BuOH, H_2O, rt, 16 h; (ii) $NaIO_4$, MeOH, rt, 1 h (89%); (f) PivCl, Pyr, rt, 1 h (86%); (g) NMO, OsO_4, acetone, *tert*-BuOH, H_2O, rt, 16 h; (ii) $NaIO_4$, MeOH, rt, 1 h (92%); (h) (i) *n*-Bu_4NF, THF, 0 °C, 1 h; (ii) PCC, MS 4Å, CH_2Cl_2, rt, 16 h (72%).

and a JEOL Mstation (MS 700). Optical rotations were evaluated with a Horiba SEPA-200, $[\alpha]_D$-values are in units of 10^{-1} deg cm^2 g^{-1}. The silica gel used was Wakogel C-300 (Wako, 200–300 mesh). Preparative TLC was conducted with Merck silica gel $60F_{254}$ (0.5 mm thickness, 20 × 20 cm).

Crystal structure determination of compound 3

Crystallographic summary for **3**: $C_{33}H_{32}O_7$, colorless block crystal, *triclinic*, *P1*, $Z = 2$ in a cell of dimensions of $a = 8.962(2)$ Å, $b = 8.981(2)$ Å, $c = 19.587(4)$ Å, $\alpha = 82.32(2)°$, $\beta = 91.78(2)°$, $\gamma = 113.31(2)°$, $V = 1434.5(6)$ Å^3, $D_{calc} = 1.251$ g cm^{-3}, $F_{(000)} = 572$, $\mu = 0.873$ cm^{-1}, unique reflections, 7033 with $I_0 > -10\sigma(I_0)$. The final $R_1 = 0.070$ (4362 reflections with $I_0 > 2\sigma(I_0)$). $R = 0.103$ (all), $R_w = 0.149$ (all), goodness-of-fit = 1.21 for 732 parameters, Flack parameter = 0.0(9). Two independent molecules exist in the unit cell and the stereochemistry is the same. †

(3*R*,4*R*)-4-Hydroxy-4-(3,4-dimethoxyphenyl)-3-pivaloyloxymethyl-*N*,*N*-diethylbutanamide 9

To a solution of $AlMe_3$ (15.5 ml, 1 M in CH_2Cl_2, 15.5 mmol) in CH_2Cl_2 (30 ml) was added Et_2NH (1.73 ml, 16.7 mmol) and lactone **4** (2.60 g, 7.73 mmol) in CH_2Cl_2 (10 ml) at 0 °C under N_2 gas. The reaction solution was gradually warmed to room temperature, and then stirred at room temperature for 34 h before pouring into ice-cooled water. The resulting mixture was extracted with EtOAc. The organic solution was washed with sat. aq $NaHSO_4$ soln. and brine, and dried (Na_2SO_4). Concentration followed by silica gel column chromatography (EtOAc–hexane = 3 : 1) gave amide **9** (2.81 g, 6.86 mmol, 89%) as a colorless oil, $[\alpha]_{20}^{D} = +15$ (*c* 0.3, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 3250, 1725, 1617, 1516, 1464, 1264, 1157, 1142, 1028; δ_H ($CDCl_3$) 1.08–1.15 (6H, m, (CH_3CH_2)$_2$NC=O), 1.20 (9H, s, $C(CH_3)_3$), 2.30–2.32 (2H, m, 2-H_2), 2.78 (1H, m, 3-H), 3.23 (2H, m, CH_3CH_2NC=O), 3.39 (2H, m, CH_3CH_2NC=O), 3.86 (3H, s, OCH_3), 3.87 (3H, s, OCH_3), 4.07 (1H, dd, *J* 11.2, 5.9 Hz, C*H*HOPiv), 4.15 (1H, dd, *J* 11.2, 6.4, CH*H*OPiv), 4.50 (1H, d, *J* 4.9 Hz, OH), 4.82 (1H, dd, *J* 4.9, 4.4 Hz, ArC*H*OH), 6.83 (2H, s, ArH), 6.89 (1H, s, ArH); δ_C ($CDCl_3$) 13.0, 14.1, 27.2, 31.5, 38.8, 40.6, 41.7, 42.2, 55.9, 64.2, 73.5, 109.5, 111.0, 118.6, 134.7, 148.3, 149.0, 171.3, 178.4 (Found C, 64.34; H, 8.86; N, 3.47. $C_{22}H_{35}O_6N$ requires C, 64.52; H, 8.61; N, 3.42%).

(3*R*,4*R*)-4-(3,4-Dimethoxyphenyl)-4-(triisopropylsilyloxy)-3-(triisopropylsilyloxy)methyl-*N*,*N*-diethylbutanamide 10

A reaction solution of pivaloyl ester **9** (2.81 g, 6.86 mmol) in EtOH (25 ml) and 1 M aq NaOH soln. (25 ml) was stirred at room temperature for 1 h before the addition of H_2O and EtOAc. The organic solution was separated, washed with brine, and dried (Na_2SO_4). Concentration gave the crude diol. To a solution of the crude diol and 2,6-lutidine (3.32 ml, 28.5 mmol) in CH_2Cl_2 (20 ml) was added TIPSOTf (4.86 ml, 18.1 mmol) at 0 °C. The resulting reaction solution was stirred at 0 °C for 3 h before addition of sat. aq $NaHCO_3$ soln. The organic solution was separated, washed with brine, and dried (Na_2SO_4). After concentration, the residue was applied to a silica gel column (EtOAc–hexane = 1 : 9) to give disilyl ether **10** (3.41 g, 5.34 mmol, 78%) as a colorless oil, $[\alpha]_{20}^{D} = +5.6$ (*c* 3.7, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2946, 1630, 1512, 1464, 1258, 1088, 1065, 884; δ_H ($CDCl_3$) 0.98–1.69 (48H, m, (CH_3CH_2)$_2$NC=O, Si[CH(CH$_3$)$_2$]$_3$), 1.66 (1H, dd, *J* 15.1, 9.8 Hz, 2*H*H), 2.54 (1H, m, 3-H), 2.71 (1H, dd, *J* 15.1, 3.4 Hz, 2H*H*), 3.20 (2H, m, CH_3CH_2NC=O), 3.35–3.49 (4H, m, CH_3CH_2NC=O, CH_2-OTIPS), 3.85 (3H, s, OCH_3), 3.87 (3H, s, OCH_3), 5.37 (1H, d, *J* 4.4 Hz, ArCHOTIPS), 6.79 (1H, d, *J* 7.8 Hz, ArH), 6.91 (1H, dd, *J* 7.8, 1.5 Hz, ArH), 6.95 (1H, d, *J* 1.5 Hz, ArH); δ_C ($CDCl_3$) 12.0, 12.4, 13.0, 14.2, 18.0, 18.1, 29.3, 39.8, 41.9, 46.4, 55.7, 55.8, 63.0, 72.8, 110.3, 119.4, 134.5, 147.9, 148.2, 171.5 (Found C, 65.99; H, 10.62; N, 2.22. $C_{35}H_{67}O_5NSi_2$ requires C, 65.88; H, 10.58; N, 2.20%).

(3*R*,4*R*)-4-(3,4-Dimethoxyphenyl)-4-(triisopropylsilyloxy)-3-(triisopropylsilyloxy)methylbutanal 11

To a solution of amide **10** (1.49 g, 2.34 mmol) in ether (30 ml) was added DIBAL-H (2.57 ml, 1 M in toluene, 2.57 mmol) at 0 °C. After the resulting solution was stirred at 0 °C for 2 h, 6 M aq HCl soln. was added. The organic solution was separated, washed with sat. aq $NaHCO_3$ soln. and brine, and dried (Na_2SO_4). Concentration followed by silica gel column chromatography (5% EtOAc–hexane) gave aldehyde **11** (0.60 g, 1.06 mmol, 45%) as a colorless oil. Amide **8** (0.71 g, 1.11 mmol, 47%) was recovered. $[\alpha]_{20}^{D} = +23$ (*c* 1.9, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2946, 1721, 1514, 1464, 1262, 1086, 1065, 884; δ_H ($CDCl_3$) 0.96–1.10 (42H, m, Si[CH(CH$_3$)$_2$]$_3$), 1.94 (1H, ddd, *J* 16.5, 7.1, 2.0 Hz, 2-*H*H), 2.43 (1H, ddd, *J* 16.5, 6.6, 2.4 Hz, 2-H*H*), 2.78 (1H, m, 3-H), 3.48 (1H, dd, *J* 9.8, 8.3 Hz, C*H*HOTIPS), 3.53 (1H, dd, *J* 9.8, 6.8 Hz, CH*H*OTIPS), 3.88 (6H, s, OCH_3), 5.14 (1H, d, *J* 4.9 Hz, ArCHOTIPS), 6.79 (1H, d, *J* 8.3 Hz, ArH), 6.83 (1H, dd, *J* 8.3, 2.0 Hz, ArH), 6.92 (1H, d, *J* 2.0 Hz, ArH), 9.73 (1H, dd, *J* 2.4, 2.0 Hz, CHO); δ_C ($CDCl_3$) 11.9, 12.3, 17.9, 18.0, 41.2, 45.1, 55.8, 64.0, 73.6, 110.2, 110.4, 119.4, 133.6, 148.2, 148.5, 202.0 (Found C, 65.46; H, 10.39. $C_{31}H_{58}O_5Si_2$ requires C, 65.67; H, 10.31%). (**3***S*,4*S*)-**11**. A reaction solution of olefin **23** (0.66 g, 1.17 mmol), NMO (0.16 g, 1.37 mmol), and OsO_4 (2% in H_2O, 0.5 ml) in acetone (10 ml), *tert*-BuOH (2 ml) and H_2O (2 ml), was stirred at room temperature under N_2 gas for 16 h before addition of sodium thiosulfate. After the mixture was filtered, the filtrate was concentrated. The residue was dissolved in H_2O and EtOAc. The organic solution was separated, washed with brine, dried (Na_2SO_4) and concentrated. A reaction mixture of the residue and $NaIO_4$ (0.30 g, 1.40 mmol) in MeOH (10 ml) was stirred at room temperature for 1 h. After concentration, the residue was dissolved in EtOAc and H_2O. The organic solution was separated, washed with brine, dried (Na_2SO_4), and evaporated. The residue was applied to silica gel column chromatography (EtOAc–hexane 1 : 5) to give (3*S*,4*S*)-**11** (0.59 g, 1.04 mmol, 89%) as a colorless oil, $[\alpha]_{20}^{D} = -23$ (*c* 0.5, $CHCl_3$).

(1*R*,2*R*)-1-(3,4-Dimethoxyphenyl)-2-(4-methoxycinnamyl)-1,3-bis(triisopropylsilyloxy)propane 12

A solution of 4-methoxybenzyl chloride (4.92 ml, 36.3 mmol) and $(EtO)_3P$ (6.48 ml, 37.8 mmol) in DMF (24 ml) was heated under reflux for 1 h before addition to MeONa (2.0 g, 37.0 mmol). The resulting mixture was stirred at room temperature for 1 h. The resulting solution of ylide (1.26 ml, *ca.* 1.91 mmol) was added to a solution of aldehyde **11** (0.46 g, 0.81 mmol) in DMF (1 ml) at 0 °C. After the reaction solution was stirred at room temperature for 3 h, H_2O and EtOAc were added. The organic solution was separated, washed with brine, and dried (Na_2SO_4). After evaporation of the solvent, the residue was applied to a silica gel column (5% EtOAc–benzene) to give olefin **12** (0.23 g, 0.34 mmol, 42%) as a colorless oil, $[\alpha]_{20}^{D} = -24$ (*c* 0.9, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2944, 1510, 1466, 1248, 1090, 1067, 1030, 884; δ_H ($CDCl_3$) 0.98–1.09 (42H, m, Si[CH(CH$_3$)$_2$]$_3$), 1.51 (1H, ddd, *J* 14.7, 8.8, 5.9 Hz, 3-*H*H), 2.23 (1H, m, 4-H), 2.59 (1H, m, 3-H*H*), 3.33 (1H, dd, *J* 10.5, 9.8 Hz, C*H*HOTIPS), 3.71 (1H, dd, *J* 10.5, 5.1 Hz, CH*H*OTIPS), 3.79 (3H, s, OCH_3), 3.86 (3H, s, OCH_3), 3.88 (3H, s, OCH_3), 5.23 (1H, d, *J* 4.4 Hz, ArCHOTIPS), 5.99 (1H, ddd, *J* 15.6, 8.3, 6.3 Hz, 2-H), 6.20 (1H, d, *J* 15.6 Hz, 1-H), 6.79–6.83 (3H, m, ArH), 6.90 (1H, dd, *J* 8.3, 2.0 Hz, ArH), 6.99 (1H, d, *J* 2.0 Hz, ArH), 7.20 (2H, d, *J* 8.3 Hz, ArH); δ_C ($CDCl_3$) 12.0, 12.3, 18.0, 18.1,

† CCDC reference number 199073. See http://www.rsc.org/suppdata/ob/b2/b211801g/ for crystallographic data in .cif or other electronic format.

28.6, 49.5, 55.3, 55.7, 55.8, 64.3, 73.3, 110.1, 110.6, 113.9, 119.6, 126.9, 127.6, 130.3, 130.8, 134.6, 147.8, 148.2, 158.6 [Found (HRMS) M + Na^+, 693.4352. $C_{39}H_{66}O_5Si_2Na$ requires M + Na^+, 693.4347]. **(1*S*,2*S*)-12**, $[\alpha]_{20}^{D} = +24$ (*c* 1.4, $CHCl_3$).

(1*R*,2*R*)-1-(3,4-Dimethoxyphenyl)-2-(4-methoxycinnamyl)-1,3-propanediol 1 ((1*R*,2*R*)-morinol C)

To a solution of disilyl ether **12** (56 mg, 0.083 mmol) in THF (5 ml) was added *n*-Bu_4NF (0.18 ml, 1 M in THF, 0.18 mmol) at 0 °C. The reaction solution was stirred at 0 °C for 2.5 h before additions of sat. aq NH_4Cl soln. and EtOAc. The organic solution was separated, washed with brine, dried (Na_2SO_4) and concentrated. The residue was applied to silica gel TLC (EtOAc–hexane = 3 : 1) to give morinol C (**1**: 23 mg, 0.064 mmol, 77%) as a colorless oil, $[\alpha]_{20}^{D} = -48$ (*c* 0.3, $CHCl_3$). ^1H and ^{13}C NMR data agreed with that of the literature.[4] **(1*S*,2*S*)**-morinol C, $[\alpha]_{20}^{D} = +48$ (*c* 0.5, $CHCl_3$).

(3*R*)-3-[(*S*)-(Hydroxy)(3,4-dimethoxyphenyl)methyl]-4-butanolide 13

A reaction solution of lactone **4** (1.00 g, 2.97 mmol) in EtOH (17 ml) and 1 M aq NaOH soln. (17 ml) was stirred at room temperature for 16 h before acidification with 6 M aq HCl soln. The resulting mixture was stirred at room temperature for 2 h before neutralization with sat. aq $NaHCO_3$ soln. After concentration, the residue was dissolved in $CHCl_3$ and H_2O. The organic solution was separated, washed with brine, and dried (Na_2SO_4). After evaporation, the residue was applied to a silica gel column (50% EtOAc in benzene) to give hydroxy lactone **13** (0.55 g, 2.18 mmol, 73%) as colorless crystals, mp 126–127 °C (MeOH), $[\alpha]_{20}^{D} = +65$ (*c* 0.4, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 3607, 2936, 1775, 1518, 1260, 1238, 1179, 1156, 1140, 1026; δ_H ($CDCl_3$) 2.26 (1H, d, *J* 2.5 Hz, OH), 2.27 (1H, dd, *J* 17.8, 6.8 Hz, 2-*H*H), 2.39 (1H, dd, *J* 17.8, 9.0 Hz, 2-H*H*), 2.88 (1H, m, 3-H), 3.88 (3H, s, OCH_3), 3.89 (3H, s, OCH_3), 4.38–4.46 (2H, m, 4-H_2), 4.57 (1H, dd, *J* 7.8, 2.5 Hz, ArC*H*OH), 6.85–6.87 (3H, m, ArH); δ_C ($CDCl_3$) 31.4, 42.5, 55.9, 70.5, 75.3, 108.9, 111.2, 118.5, 134.4, 145.2, 149.4, 176.7 (Found C, 61.66; H, 6.36. $C_{13}H_{16}O_5$ requires C, 61.90; H, 6.39%). **(3*S*,4*R*)-13**, $[\alpha]_{20}^{D} = -65$ (*c* 0.5, $CHCl_3$).

(3*R*)-3-[(*S*)-(3,4-Dimethoxyphenyl)(triisopropylsilyloxy)-methyl]-4-butanolide 14

To a solution of alcohol **13** (0.87 g, 3.45 mmol) and 2,6-lutidine (0.83 ml, 7.13 mmol) in CH_2Cl_2 (10 ml) was added TIPSOTf (1.43 ml, 5.32 mmol). The resulting reaction solution was stirred at 0 °C for 1 h before addition of sat. aq $NaHCO_3$. The organic solution was separated, washed with brine, dried (Na_2SO_4) and concentrated. The residue was purified with silica gel column chromatography (EtOAc–hexane = 1 : 3) to give silyl ether **14** (1.34 g, 3.28 mmol, 95%) as a colorless oil, $[\alpha]_{20}^{D} = +23$ (*c* 2.6, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2946, 1775, 1518, 1466, 1266, 1163, 1142, 1115, 997; δ_H ($CDCl_3$) 1.00–1.18 (21H, m, Si[CH(CH_3)$_2$]$_3$), 2.60 (1H, m, 3-H), 2.69 (1H, dd, *J* 8.8, 8.3 Hz, 2-*H*H), 2.74 (1H, dd, *J* 8.8, 8.8 Hz, 2-H*H*), 3.78 (2H, d, *J* 4.4 Hz, 4-H), 3.88 (3H, s, OCH_3), 3.89 (3H, s, OCH_3), 5.40 (1H, d, *J* 6.3 Hz, ArCHOTIPS), 6.84–6.87 (3H, m, ArH); δ_C ($CDCl_3$) 11.9, 18.0, 31.0, 46.7, 55.9, 61.4, 82.7, 108.8, 111.1, 118.3, 131.2, 149.2, 149.3, 176.4 (Found C, 64.66; H, 8.90. $C_{22}H_{36}O_5Si$ requires C, 64.67; H, 8.88%). **(3*S*,4*R*)-14**, $[\alpha]_{20}^{D} = -23$ (*c* 1.2, $CHCl_3$).

(3*R*,4*S*)-4-Hydroxy-4-(3,4-dimethoxyphenyl)-3-(triisopropylsilyloxy)methyl-*N*,*N*-diethylbutanamide 15

To a solution of $AlMe_3$ (5.57 ml, 1 M in hexane, 5.57 mmol) in CH_2Cl_2 (14 ml) was added Et_2NH (0.58 ml, 5.61 mmol) at 0 °C. After the solution was stirred at 0 °C for 15 min, a solution of lactone **14** (1.14 g, 2.79 mmol) in CH_2Cl_2 (5 ml) was added at 0 °C. The resulting reaction solution was warmed to room temperature, stirred for 16 h, and poured into an ice-cooled sat. aq $NaHSO_4$ soln. The mixture was extracted with EtOAc. The organic solution was separated, washed with sat. aq $NaHCO_3$ soln. and brine, dried (Na_2SO_4) and concentrated. The residue was applied to silica gel column chromatography (EtOAc–hexane = 1 : 3) to give amide **15** (1.14 g, 2.37 mmol, 85%) as a colorless oil, $[\alpha]_{20}^{D} = -23$ (*c* 0.9, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 3455, 2869, 1611, 1516, 1464, 1260, 1235, 1140, 1063, 1028; δ_H ($CDCl_3$) 0.94–1.13 (27H, m, (CH_3CH_2)$_2$NC=O, Si[CH(CH_3)$_2$]$_3$), 2.38–2.46 (2H, m, 2-*H*H, 3-H), 2.67 (1H, dd, *J* 17.8, 8.1 Hz, 2-H*H*), 3.27 (2H, m, CH_3CH_2NC=O), 3.34 (2H, q, *J* 7.3 Hz, CH_3CH_2NC=O), 3.80–3.91 (2H, m, 4-H), 3.86 (3H, s, OCH_3), 3.89 (3H, s, OCH_3), 4.87 (1H, br t, *J* 3.9 Hz, ArC*H*OH), 4.95 (1H, d, *J* 3.9 Hz, OH), 6.81–6.89 (2H, m, ArH), 6.95 (1H, s, ArH); δ_C ($CDCl_3$) 11.8, 13.0, 14.1, 17.9, 29.1, 40.5, 42.2, 44.4, 55.8, 65.7, 75.9, 109.1, 110.9, 118.3, 136.3, 147.9, 148.8, 172.2 (Found C, 64.55; H, 9.82; N, 2.74. $C_{26}H_{47}O_5NSi$ requires C, 64.82; H, 9.83; N, 2.91%). **(3*S*,4*R*)-15**, $[\alpha]_{20}^{D} = +23$ (*c* 1.4, $CHCl_3$).

(3*R*,4*S*)-4-(3,4-Dimethoxyphenyl)-4-(triisopropylsilyloxy)-3-(triisopropylsilyloxy)methyl-*N*,*N*-diethylbutanamide 16

To a solution of alcohol **15** (0.32 g, 0.66 mmol) and 2,6-lutidine (0.15 ml, 1.29 mmol) in CH_2Cl_2 (10 ml) was added TIPSOTf (0.27 ml, 1.00 mmol) at 0 °C. After stirring at 0 °C for 1 h, sat. aq $NaHCO_3$ soln. was added. The organic solution was separated, washed with brine, dried (Na_2SO_4), and concentrated. The residue was applied to a silica gel column (EtOAc–hexane = 1 : 4) to give disilyl ether **16** (0.35 g, 0.55 mmol, 83%) as a colorless oil, $[\alpha]_{20}^{D} = -15$ (*c* 2.2, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2944, 1624, 1514, 1464, 1258, 1084, 1065, 884; δ_H ($CDCl_3$) 1.01–1.12 (48H, m, (CH_3CH_2)$_2$NC=O, Si[CH(CH_3)$_2$]$_3$), 2.31 (1H, m, 3-H), 2.40 (1H, dd, *J* = 15.1, 6.1 Hz, 2-*H*H), 2.62 (1H, dd, *J* 15.1, 7.8 Hz, 2-H*H*), 3.15 (1H, m, CH_3CHHNC=O), 3.25–3.36 (3H, m, (CH_3CH*H*)$_2$NC=O, C*H*HOTIPS), 3.41 (1H, m, CH_3CH*H*NC=O), 3.85 (3H, s, OCH_3), 3.87 (3H, s, OCH_3), 3.97 (1H, dd, *J* = 9.8, 4.4 Hz, CH*H*OTIPS), 5.12 (1H, d, *J* 5.9 Hz, 4-H), 6.77 (1H, d, *J* 8.6 Hz, ArH), 6.89 (1H, d, *J* 8.6 Hz, ArH), 6.98 (1H, s, ArH); δ_C ($CDCl_3$) 12.0, 12.5, 13.1, 14.1, 18.0, 30.2, 39.9, 41.8, 47.2, 55.6, 55.8, 62.1, 73.6, 110.2, 119.5, 136.1, 147.9, 148.4, 171.9 (Found C, 65.62; H, 10.49; N, 2.05. $C_{35}H_{67}O_5NSi_2$ requires C, 65.88; H, 10.60; N, 2.20%). **(3*S*,4*R*)-16**, $[\alpha]_{20}^{D} = +15$ (*c* 1.7, $CHCl_3$).

(3*R*,4*S*)-4-(3,4-Dimethoxyphenyl)-4-(triisopropylsilyloxy)-3-(triisopropylsilyloxy)methylbutanal 17

To a solution of amide **16** (0.46 g, 0.72 mmol) in ether (30 ml) was added DIBAL-H (0.86 ml, 1 M in toluene, 0.86 mmol) at 0 °C. After the resulting solution was stirred at 0 °C for 2 h, 6 M aq HCl soln. was added. The organic solution was separated, washed with sat. aq $NaHCO_3$ soln., and brine and dried (Na_2SO_4). Concentration followed by silica gel column chromatography (5% EtOAc–hexane) gave aldehyde **17** (0.24 g, 0.42 mmol, 58%). Amide **16** (0.18 g, 0.28 mmol, 39%) was recovered. $[\alpha]_{20}^{D} = -40$ (*c* 1.0, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2946, 1721, 1514, 1464, 1262, 1094, 1064, 884; δ_H ($CDCl_3$) 0.97–1.03 (42H, m, Si[CH(CH_3)$_2$]$_3$), 2.45 (1H, m, 3-H), 2.53 (1H, ddd, *J* 17.0, 7.6, 2.4 Hz, 2-*H*H), 2.66 (1H, ddd, *J* 17.0, 5.7, 1.5 Hz, 2-H*H*), 3.43 (1H, dd, *J* 9.8, 6.8 Hz, C*H*HOTIPS), 3.78 (1H, dd, *J* 9.8, 4.9 Hz, CH*H*OTIPS), 3.86 (3H, s, OCH_3), 3.87 (3H, s, OCH_3), 4.89 (1H, d, *J* 5.9 Hz, ArCHOTIPS), 6.78 (2H, s, ArH), 6.88 (1H, s, ArH), 9.74 (1H, dd, *J* 2.4, 1.5 Hz, CHO); δ_C ($CDCl_3$) 11.9, 12.6, 18.0, 18.1, 42.5, 46.2, 55.7, 55.9, 63.4, 74.5, 109.7, 110.5, 119.1, 135.9, 148.3, 148.7, 202.7 (Found C, 65.40; H, 10.38. $C_{31}H_{58}O_5Si_2$ requires C, 65.67; H, 10.31%). **(3*S*,4*R*)-17**, $[\alpha]_{20}^{D} = +40$ (*c* 0.7, $CHCl_3$).

(1*S*,2*R*)-1-(3,4-Dimethoxyphenyl)-2-(4-methoxycinnamyl)-1,3-bis(triisopropylsilyloxy)propane 18

A solution of 4-methoxybenzyl chloride (4.92 ml, 36.3 mmol) and $(EtO)_3P$ (6.48 ml, 37.8 mmol) in DMF (24 ml) was heated under reflux for 1 h before addition to MeONa (2.0 g, 37.0 mmol). The resulting mixture was stirred at room temperature for 1 h. The resulting ylide solution (0.41 ml, *ca.* 0.97 mmol) was added to a solution of aldehyde **17** (0.23 g, 0.41 mmol) in DMF (1 ml) at 0 °C. After the reaction solution was stirred at room temperature for 3 h, H_2O and EtOAc were added. The organic solution was separated, washed with brine and dried (Na_2SO_4). After evaporation of the solvent, the residue was applied to silica gel column chromatography (5% EtOAc–benzene) to give olefin **18** (0.13 g, 0.19 mmol, 46%) as a colorless oil, $[\alpha]_{20}^{D} = -30$ (*c* 0.5, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2959, 1510, 1464, 1248, 1102, 1064, 1030, 884; δ_H ($CDCl_3$) 0.97–1.26 (42H, m, Si[CH(CH_3)$_2$]$_3$), 1.89 (1H, m, 4-H), 2.39 (2H, dd, *J* 7.3, 6.6 Hz, 3-H_2), 3.37 (1H, dd, *J* 9.8, 5.9 Hz, C*H*HOTIPS), 3.80–3.86 (1H, m, CH*H*OTIPS), 3.80 (3H, s, OCH_3), 3.86 (3H, s, OCH_3), 3.87 (3H, s, OCH_3), 5.02 (1H, d, *J* = 4.9 Hz, 5-H), 6.05 (1H, dt, *J* = 16.1, 6.6 Hz, 2-H), 6.34 (1H, d, *J* = 16.1 Hz, 1-H), 6.77–6.84 (4H, m, ArH), 6.92 (1H, s, ArH), 7.23 (2H, d, *J* = 8.3 Hz, ArH); δ_C ($CDCl_3$) 12.1, 12.6, 18.0, 18.1, 29.9, 51.0, 55.2, 55.7, 55.8, 62.4, 74.1, 110.0, 110.3, 113.9, 119.1, 126.9, 128.0, 130.4, 130.8, 136.8, 147.9, 148.5, 158.6 [Found (HRMS) M + Na^+, 693.4352. $C_{39}H_{66}O_5Si_2Na$ requires M + Na^+, 693.4347]. **(1*R*,2*S*)-19**, $[\alpha]_{20}^{D} = +30$ (*c* 0.8, $CHCl_3$).

(1*S*,2*R*)-1-(3,4-Dimethoxyphenyl)-2-(4-methoxycinnamyl)-1,3-propanediol 2 ((1*S*,2*R*)-morinol D)

To a solution of disilyl ether **18** (44 mg, 0.065 mmol) in THF (8 ml) was added *n*-Bu_4NF (0.14 ml, 1 M in THF, 0.14 mmol) at 0 °C. The reaction solution was stirred at 0 °C for 2.5 h before additions of sat. aq NH_4Cl soln. and EtOAc. The organic solution was separated, washed with brine, dried (Na_2SO_4) and concentrated. The residue was applied to silica gel TLC (EtOAc–hexane = 3 : 1) to give morinol D (**2**: 20 mg, 0.056 mmol, 86%) as a colorless oil, $[\alpha]_{20}^{D} = +22$ (*c* 0.5, $CHCl_3$). ^1H and ^{13}C NMR data agreed with that of the literature.[4] **(1*R*,2*S*)**-morinol D, $[\alpha]_{20}^{D} = -22$ (*c* 0.4, $CHCl_3$).

(4*S*)-4-Benzyl-3-{(2*R*)-2-[(*S*)-(hydroxy)(3,4-dimethoxyphenyl)-methyl]-4-pentenoyl}-2-oxazolidinone 20

A reaction mixture of acyloxazolidinone **19** (21.7 g, 0.084 mol), $MgCl_2$ (0.79 g, 0.0083 mol), Et_3N (24.0 ml, 0.17 mol), 3,4-dimethoxybenzaldehyde (16.7 g, 0.10 mol), and Me_3SiCl (15.7 ml, 0.12 mol) in EtOAc (150 ml) was stirred at room temperature for 20 h. After the mixture was filtered through silica gel with ether, the filtrate was concentrated. The residue was dissolved in MeOH. To this solution was added a few drops of CF_3CO_2H, and then the resulting reaction mixture was stirred at room temperature for 1 h before addition of a few drops of Et_3N. Concentration followed by silica gel column chromatography (EtOAc–hexane 1 : 3 and 1 : 2) gave *anti*-aldol product **20** (33.1 g, 0.078 mol, 93%) as a colorless oil, $[\alpha]_{20}^{D} = -5.2$ (*c* 1.7, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 3494, 3025, 2919, 1779, 1698, 1518, 1387, 1254, 1198, 1028; δ_H ($CDCl_3$) 2.24 (1H, m, C*H*HCH=CH_2), 2.47 (1H, m, CH*H*CH=CH_2), 2.59 (1H, dd, *J* 13.7, 9.3 Hz, C*H*HPh), 3.14 (1H, dd, *J* 13.7, 3.4 Hz, CH*H*Ph), 3.19 (1H, d, *J* 7.8 Hz, OH), 3.86 (3H, s, OCH_3), 3.90 (3H, s, OCH_3), 4.10 (1H, dd, *J* 9.3, 2.9 Hz, 5-*H*H), 4.13 (1H, dd, *J* 9.3, 9.3 Hz, 5-H*H*), 4.58 (1H, m, 4-H), 4.65 (1H, ddd, *J* 12.7, 6.8, 3.4 Hz, O=CCH), 4.83 (1H, dd, *J* 7.3, 7.3 Hz, ArC*H*OH), 4.98–5.08 (2H, m, CH=CH_2), 5.75 (1H, m, C*H*=CH_2), 6.85 (1H, d, *J* 8.3 Hz, ArH), 6.96–7.00 (2H, m, ArH), 7.10–7.18 (2H, m, ArH), 7.23–7.31 (3H, m, ArH); δ_C ($CDCl_3$) 34.3, 37.5, 48.8, 55.3, 55.9, 65.8, 75.6, 109.3, 110.9, 117.4, 118.6, 127.3, 128.9, 129.4, 134.5, 134.7, 135.1, 148.7, 149.1, 153.5, 175.5 (Found C, 67.68; H, 6.56; N, 3.24. $C_{24}H_{27}O_6N$ requires C, 67.75; H, 6.40; N, 3.29%).

(4*S*)-4-Benzyl-3-{(2*R*)-2-[(*S*)-(3,4-dimethoxyphenyl)(triisopropylsilyloxy)methyl]-4-pentenoyl}-2-oxazolidinone 21

To an ice-cooled solution of *anti*-aldol product **20** (16.4 g, 0.039 mol) and 2,6-lutidine (9.02 ml, 0.077 mol) in CH_2Cl_2 (80 ml) was added TIPSOTf (12.5 ml, 0.047 mol). After stirring at 0 °C for 1 h, sat. aq $NaHCO_3$ solution was added. The organic solution was separated, washed with sat. aq $CuSO_4$ solution, $NaHCO_3$ solution, and brine and dried (Na_2SO_4). After concentration, the residue was applied to silica gel column chromatography (EtOAc–hexane 1 : 6) to give silyl ether **21** (17.0 g, 0.030 mol, 77%) as a colorless oil, $[\alpha]_{20}^{D} = -31$ (*c* 2.5, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2946, 2869, 1781, 1698, 1512, 1466, 1387, 1254, 1098, 909; δ_H ($CDCl_3$) 0.92–1.00 (21H, m, *iso*-Pr), 1.91 (1H, m, C*H*HCH=CH_2), 2.14 (1H, m, CH*H*CH=CH_2), 2.63 (1H, dd, *J* 13.2, 11.2 Hz, C*H*HPh), 3.54 (1H, dd, *J* 13.2, 2.9 Hz, CH*H*Ph), 3.88 (3H, s, OCH_3), 3.92 (3H, s, OCH_3), 4.07 (1H, dd, *J* 9.0, 7.8 Hz, 5-*H*H), 4.12 (1H, dd, *J* 9.0, 2.7 Hz, 5-H*H*), 4.54 (1H, m, 4-H), 4.61 (1H, m, O=CCH), 4.87–4.95 (2H, m, CH=CH_2), 5.06 (1H, d, *J* 8.8 Hz, ArCHOTIPS), 5.62 (1H, m, C*H*=CH_2), 6.79 (1H, d, *J* 8.3 Hz, ArH), 6.88 (1H, dd, *J* 8.3, 1.5 Hz, ArH), 7.07 (1H, d, *J* 1.5 Hz, ArH), 7.26–7.30 (3H, m, ArH), 7.34–7.37 (2H, m, ArH); δ_C ($CDCl_3$) 12.6, 17.9, 18.1, 34.3, 38.4, 51.4, 55.8, 56.0, 66.0, 77.0, 110.2, 110.4, 116.8, 120.2, 127.2, 129.0, 129.3, 134.9, 136.0, 148.9, 149.0, 153.4, 174.6 (Found C, 68.06; H, 8.07; N, 2.27. $C_{33}H_{47}O_6NSi$ requires C, 68.12; H, 8.14; N, 2.41%).

(2*S*)-2-[(*S*)-(3,4-Dimethoxyphenyl)(triisopropylsilyloxy)-methyl]-4-penten-1-ol 22

To an ice-cooled solution of acyloxazolidinone **21** (17.0 g, 0.030 mol) and MeOH (1.5 ml) in THF (80 ml) was added $LiBH_4$ (1.6 g, 0.073 mol). The resulting reaction mixture was stirred at room temperature for 16 h before addition of sat. aq NH_4Cl solution. The organic solution was separated, washed with brine, and dried (Na_2SO_4). After concentration, the residue was applied to silica gel column chromatography (EtOAc–hexane 1 : 8) to give alcohol **22** (6.95 g, 0.017 mol, 57%) as a colorless oil, $[\alpha]_{20}^{D} = -46$ (*c* 1.7, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 3500, 2946, 2869, 1514, 1466, 1262, 1140, 1084, 1065, 1028, 884; δ_H ($CDCl_3$) 0.97–1.03 (21H, m, *iso*-Pr), 1.85–1.95 (2H, m, 2-H, 3-*H*H), 2.20 (1H, m, 3-H*H*), 2.65 (1H, dd, *J* 5.4, 5.4 Hz, OH), 3.58 (1H, m, 1-*H*H), 3.79 (1H, m, 1-H*H*), 3.88 (6H, s, OCH_3), 4.88 (1H, d, *J* 5.4 Hz, ArCHOTIPS), 4.99–5.03 (2H, m, CH=CH_2), 5.75 (1H, m, C*H*=CH_2), 6.79–6.84 (2H, m, ArH), 6.93 (1H, s, ArH); δ_C ($CDCl_3$) 12.5, 18.0, 32.4, 48.5, 55.8, 63.2, 78.2, 109.9, 110.3, 116.4, 119.2, 135.8, 136.8, 148.3, 148.7 [Found (HRMS) ($M^+ - H$), 407.2619. $C_{23}H_{39}O_4Si$ requires $M^+ - H$, 407.2617].

(4*S*,5*S*)-5-(3,4-Dimethoxyphenyl)-5-(triisopropylsilyloxy)-4-(triisopropylsilyloxy)methyl-1-pentene 23

A reaction solution of alcohol **22** (0.74 g, 1.81 mmol), imidazole (0.25 g, 3.67 mmol), and TIPSCl (0.43 ml, 2.01 mmol) in DMF (3 ml) was heated at 60 °C for 1.5 h before additions of $NaHCO_3$ and EtOAc. The organic solution was separated, washed with brine and dried (Na_2SO_4). Concentration followed by silica gel column chromatography (2.5% EtOAc in hexane) gave diTIPS ether **23** (0.77 g, 1.36 mmol, 75%) as a colorless oil, $[\alpha]_{20}^{D} = -14$ (*c* 1.0, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2946, 2867, 1512, 1466, 1262, 1090, 1065, 884; δ_H ($CDCl_3$) 0.98–1.10 (42H, m, *iso*-Pr), 1.33 (1H, m, 4-H), 2.16 (1H, m, 3-*H*H), 2.50 (1H, m, 3-H*H*), 3.24 (1H, dd, *J* 10.3, 10.3 Hz, TIPSOC*H*H), 3.67 (1H, dd, *J* 10.3, 4.9 Hz, TIPSOCH*H*), 3.86 (3H, s, OCH_3), 3.88 (3H, s, OCH_3), 4.88–4.94 (2H, m, 1-H_2), 5.23 (1H, d, *J* 4.4 Hz, ArCHOTIPS), 5.75 (1H, m, 2-H), 6.79 (1H, d, *J* 8.3 Hz, ArH), 6.89 (1H, d, *J* 8.3 Hz, ArH), 6.96 (1H, s, ArH); δ_C ($CDCl_3$) 12.0, 12.3, 18.0, 18.1, 29.3, 48.9, 55.7, 63.2, 73.0, 110.0, 110.6, 115.5, 119.5, 134.5, 137.9, 147.7, 148.1

(Found C, 68.18; H, 11.07. $C_{32}H_{60}O_4Si_2$ requires C, 68.03; H, 10.70%).

(4*S*,5*S*)-5-(3,4-Dimethoxyphenyl)-4-pivaloyloxymethyl-5-(triisopropylsilyloxy)-1-pentene 24

To an ice-cooled solution of alcohol **22** (5.61 g, 0.014 mol) in pyridine (10 ml) was added PivCl (2.09 ml, 0.017 mol). The resulting reaction mixture was stirred at room temperature for 1 h before addition of EtOAc and H_2O. The organic solution was separated, washed with 1 M aq HCl solution and brine, and dried (Na_2SO_4). After concentration, the residue was applied to a silica gel column (EtOAc–hexane 1 : 9) to give pivaloyl ester **24** (5.82 g, 0.012 mol, 86%) as a colorless oil, $[a]_{20}^{D} = -13$ (*c* 4.1, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2946, 2869, 1721, 1514, 1466, 1262, 1159, 1092, 884; δ_H ($CDCl_3$) 0.97–1.02 (21H, m, *iso*-Pr), 1.24 (9H, s, *tert*-Bu), 1.57 (1H, m, 4-H), 2.22 (1H, m, 3-*H*H), 2.38 (1H, m, 3-H*H*), 3.81 (1H, dd, *J* 11.2, 8.8 Hz, PivOC*H*H), 3.86 (3H, s, OCH_3), 3.88 (3H, s, OCH_3), 4.16 (1H, dd, *J* 11.2, 4.4 Hz, PivOCH*H*), 4.93–4.98 (3H, m, 1-H_2, 5-H), 5.73 (1H, m, 2-H), 6.75 (1H, d, *J* 7.8 Hz, ArH), 6.79 (1H, d, *J* 7.8 Hz, ArH), 6.88 (1H, s, ArH); δ_C ($CDCl_3$) 12.3, 18.0, 27.3, 30.1, 38.8, 45.8, 55.7, 55.8, 63.9, 73.9, 110.1, 110.3, 116.4, 119.3, 134.3, 136.6, 148.2, 148.5, 178.2 (Found C, 68.07; H, 10.01. $C_{28}H_{48}O_5Si$ requires C, 68.25; H, 9.82%).

(3*S*,4*S*)-4-(3,4-Dimethoxyphenyl)-3-pivaloyloxymethyl-4-(triisopropylsilyloxy)butanal 25

A reaction solution of olefin **22** (5.78 g, 0.012 mol), NMO (1.64 g, 0.014 mol), and OsO_4 (2% in H_2O, 2 ml) in acetone (80 ml), *tert*-BuOH (28 ml), and H_2O (28 ml) was stirred at room temperature under N_2 gas for 16 h before addition of sodium thiosulfate. After the mixture was filtered, the filtrate was concentrated. The residue was dissolved in H_2O and EtOAc. The organic solution was separated, washed with brine, dried (Na_2SO_4), and concentrated. A reaction mixture of the residue and $NaIO_4$ (3.03 g, 0.014 mol) in MeOH (10 ml) was stirred at room temperature for 1 h. After concentration, the residue was dissolved in EtOAc and H_2O. The organic solution was separated, washed with brine, dried (Na_2SO_4), and evaporated. The residue was applied to a silica gel column (EtOAc–hexane 1 : 3) to give aldehyde **25** (5.50 g, 0.011 mol, 92%) as a colorless oil, $[a]_{20}^{D} = -12$ (*c* 4.8, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2961, 2869, 1725, 1514, 1466, 1264, 1159, 1090, 1065, 1028, 884; δ_H ($CDCl_3$) 0.96–1.06 (21H, m, *iso*-Pr), 1.23 (9H, s, *tert*-Bu), 2.06 (1H, ddd, *J* 16.6, 8.1, 0.9 Hz, 2-*H*H), 2.51 (1H, ddd, *J* 16.6, 6.7, 2.9 Hz, 2-H*H*), 2.91 (1H, m, 3-H), 3.87 (3H, s, OCH_3), 3.88 (3H, s, OCH_3), 3.89 (1H, dd, *J* 11.2, 7.8 Hz, PivO-C*H*H), 3.98 (1H, dd, *J* 11.2, 6.4 Hz, PivOCH*H*), 5.00 (1H, d, *J* 5.4 Hz, 4-H), 6.73 (1H, d, *J* 8.3 Hz, ArH), 6.80 (1H, d, *J* 8.3 Hz, ArH), 6.86 (1H, s, ArH), 9.72 (1H, br s, CHO); δ_C ($CDCl_3$) 12.3, 17.9, 18.0, 27.2, 38.8, 41.1, 41.3, 55.8, 64.4, 73.9, 110.1, 110.4, 119.2, 132.9, 148.5, 148.7, 178.0, 200.8 (Found C, 65.51; H, 9.45. $C_{27}H_{46}O_6Si$ requires C, 65.55; H, 9.37%).

(3*S*,4*S*)-3-Pivaloyloxymethyl-4-(3,4-dimethoxyphenyl)-4-butanolide (−)-4

To an ice-cooled solution of silyl ether **25** (5.46 g, 0.011 mol) in THF (50 ml) was added *n*-Bu_4NF (12 ml, 1 M in THF, 0.012 mol). The reaction solution was stirred in an ice-bath for 1 h before addition of sat. aq NH_4Cl solution. The organic solution was separated, washed with brine and dried (Na_2SO_4). After concentration, the residue was applied to a silica gel column (EtOAc–hexane 2 : 1) to give a hemiacetal (3.30 g, 9.75 mmol). A reaction mixture of the hemiacetal (3.30 g, 9.75 mmol), PCC (2.95 g, 0.014 mol), and MS 4A (0.5 g) in CH_2Cl_2 (50 ml) was stirred at room temperature for 16 h before addition of dry ether. After the mixture was filtered, the filtrate was concentrated. The residue was applied to silica gel column chromatography (EtOAc–hexane 1 : 3 and 1 : 1) to give (−)-lactone **4** (2.66 g, 7.91 mmol, 72%) as colorless crystals, mp 80–81 °C, $[a]_{20}^{D} = -48$ (*c* 0.5, $CHCl_3$). The NMR data of (−)-lactone **4** were in good accord with those of (+)-lactone **4**.[5]

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