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Chiral γ-(tetrahydropyranyloxy)allylstannane: a new chiral reagent for the asymmetric synthesis of *syn* 1,2-diols

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Summary – (2*R*,3*S*)-3-Allyloxy-3,4,5,6-tetrahydro-2*H*-pyran-2-methanol was prepared in high yield from tri-*O*-acetyl-D-glucal, an easily available and cheap chiral source. The hydroxyl group was protected as the *t*-butyldiphenylsilyl ether, and the allyl group was converted to the corresponding allyl stannane via formation of allyl carbanion and subsequent trapping with tributylstannyl chloride. The γ-alkoxy allyl stannane **1** bearing the (2*R*,3*S*)-2-[(*t*-butyldiphenylsilyloxy)methyl]-3,4,5,6-tetrahydro-2*H*-pyran-3-yloxy auxiliary at the allyl terminus was prepared by this procedure. The reaction of **1** with aldehydes in the presence of $AlCl_3 \cdot OEt_2$ or $AlCl_3$ gave the corresponding *syn* adducts **2** with high diastereoselectivities; the ratio of *syn/anti* > 97:3. The diastereomeric excess of the *syn* adducts **2**, that is, the ratio **2**/(**2** + the (*S*,*S*) isomer of **2**), varied from 85 to 94%. Removal of the protecting group of **2** gave the (*R*,*R*) diols **3**. The high diastereo- and enantioselectivity in the formation of the (*R*,*R*) isomer is accounted for by an *anti* S_E' transition state **18**.

allylstannane / γ-alkoxyallylstannane / asymmetric synthesis / *syn*-1,2-diol / Lewis acid / allylstannane-aldehyde condensation / γ-(tetrahydropyranyloxy)allylstannane / *anti* S_E'

Asymmetric synthesis of *syn* and/or *anti* 1,2-diols via the "α-alkoxyallylation" [1p] of aldehydes with γ-alkoxyallylmetal reagents has received considerable attention in recent years [1]. Enantioselective synthesis of *syn* and *anti* 1,2-diols [1q] has been accomplished by using allyl boranes with chiral auxiliaries directly bonded to the boron atom (BL_n^*). Allyl boranes with a chiral auxiliary at the allyl terminus have been used for the asymmetric synthesis of *syn* 1,2-diols [1j]. Although allyl boranes are useful reagents for allylation of electrophiles, they are less air- and moisture-stable than allyl stannanes. This characteristic of the borane reagents becomes a significant drawback when they are used for intramolecular reactions, since the starting materials including the borane group are often exposed to air and/or moisture before the cyclization. We needed a stable γ-alkoxy-substituted allyl stannane with a chiral alkoxy auxiliary. *Syn* 1,2-diols have been prepared with high enantiomeric excess (ee) via the intermolecular reaction of allyl stannanes with an asymmetric center at the α-position [1i].

We report herein an alternative strategy for the stereoselective and enantioselective synthesis of *syn* 1,2-diols via the reactions of aldehydes and the new chiral allylstannane reagent **1** (eq 1).

Synthesis of chiral γ-alkoxyallylstannanes

Tri-*O*-acetyl-D-glucal **4**, an easily available and cheap chiral starting material, was converted to diol **5** according to the literature procedure [2]. As shown in scheme 1, selective protection of the primary OH of **5** with trityl chloride, conversion of the secondary OH to allyl ether, and removal of the trityl group produced **6**, which was converted to **1** through protection of the primary OH as the *tert*-butyldiphenylsilyl (TBDPS) ether and subsequent lithiation and trapping with Bu_3SnCl [3]. The γ-(tetrahydropyranyloxy)allylstannane **1** was obtained in 54% overall yield from **4**. Treatment of **6** with MeI/NaH gave the methyl ether derivative of **6**, which was transformed to **7** by the usual stannylation procedure. Compound **7** was obtained in 47% yield from **6**. The γ-alkoxyallylstannane **9** was prepared from **5** in 5.5% overall yield : the selective protection of the primary OH of **5** with TrCl, protection of the secondary OH with TBDPSCl, the selective removal of the trityl group followed by allylation afforded **8**, which was converted to **9** by the usual stannylation procedure. (2*R*,4*R*)-(−)-Pentanediol was converted to the corresponding mono-allylated alcohol in 78% upon treating it with KH/allyl bromide. Treatment with KH/MeI gave the corresponding mono-methyl-mono-allylated derivative, which was transformed to **10** by the usual stannylation procedure.

Reaction of aldehydes

The reaction of **1** with aldehydes proceeded smoothly in the presence of $BF_3 \cdot OEt_2$, $AlCl_3$, or $AlCl_3 \cdot OEt_2$ in CH_2Cl_2. The results are summarized in table I.

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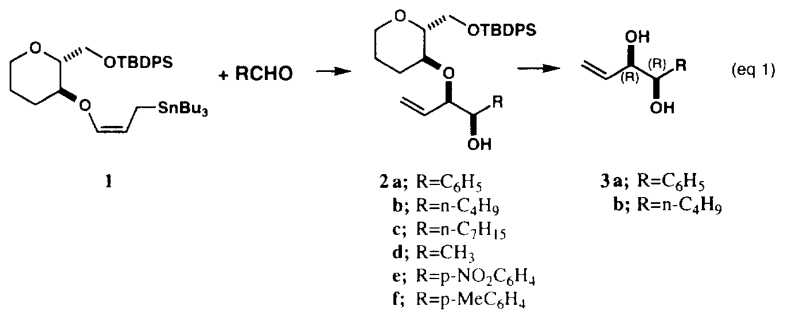
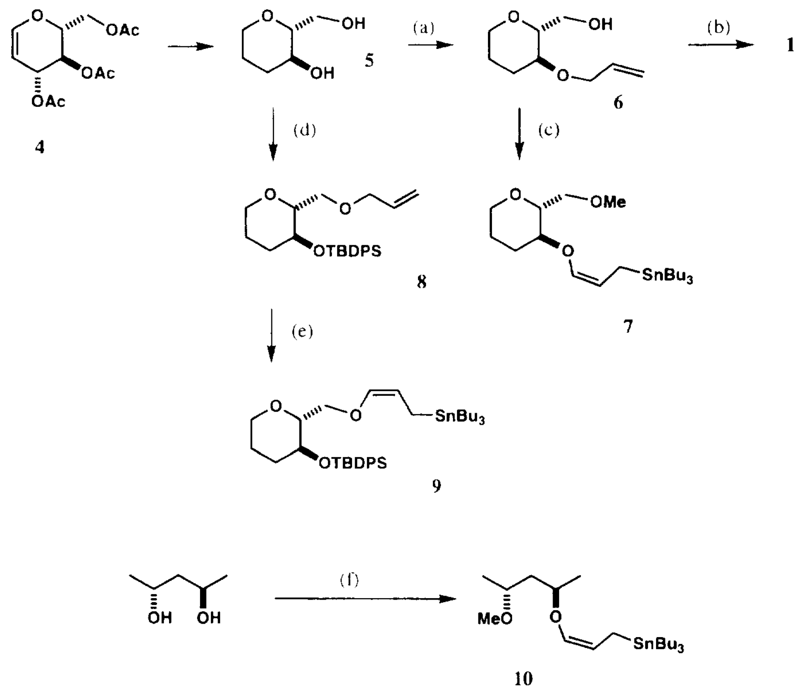
[*] Correspondence and reprints





Key; (a) (1) TrCl, DMAP, DMF; (2) allyl bromide, KH; (3) HCl, MeOH. (b) (1) TBDPSCl, imidazole, DMF; (2) sec-BuLi, TMEDA, Bu_3SnCl. (c) (1) MeI, NaH; (2) sec-BuLi, MeOH; (4) allyl bromide, KH. (e) sec-BuLi, TMEDA, Bu_3SnCl. (f) (1) KH, allyl bromide; (2) KH, MeI; (3) sec-BuLi, TMEDA; (4) Bu_3SnCl.

Scheme 1. Synthesis of γ-alkoxyallylstannanes.

Both aromatic and aliphatic aldehydes afforded the *syn* adducts **2** with very high diastereoselectivities upon treatment with $BF_3 \cdot OEt_2$, or $AlCl_3$, or $AlCl_3 \cdot OEt_2$. The ratio of **2** to its *anti* isomer was greater than 97:3; the use of $TiCl_4$ and SnC_4 gave unsatisfactory results (entries 4 and 5). Reactive aldehydes such as benzaldehyde and 4-nitrobenzaldehyde gave **2** in high to good chemical yields (entries 1-3, 6), but the reaction of *p*-tolualdehyde and some aliphatic aldehydes resulted in moderate to low yields (entries 7-13). The diastereomeric excess of **2** (the ratio of **2**/(**2** + its (*S*,*S*) isomer)) was high when $AlCl_3 \cdot OEt_2$ or $AlCl_3$ was used as Lewis acid (entries 2, 3, 7, 10, 12, and 13); while $BF_3 \cdot OEt_2$ led to decreased diastereomeric excess (de) ratios. For aliphatic aldehydes the use of $AlCl_3$ gave higher stereoselectivity than $AlCl_3 \cdot OEt_2$, whereas both Lewis acids produced high de ratios with aromatic aldehydes. The aluminum chloride-etherate complex is soluble in CH_2Cl_2, but $AlCl_3$ itself is insoluble. The aldehydes and $AlCl_3$ (solid) were first combined in a 2:1.2 ratio, and the resulting mixture, upon stirring, became homogeneous, and finally soluble in CH_2Cl_2.

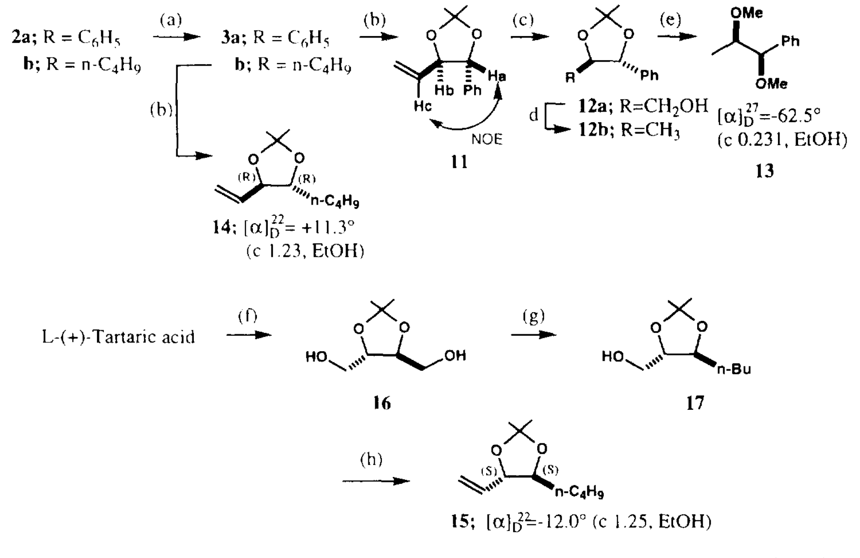
Stereochemistry of the adducts

The absolute configurations of **2a** and **2b** were determined in the following manner (scheme 2). The hydroxyl groups of **2a** (obtained in entry 1, 67% de) and **2b** (obtained in entry 12, 89% de) were protected as MOM ethers, and the TBDPS group was removed by treatment with Bu_4NF. The resulting primary OH was oxidized to give the corresponding aldehyde. A retro-Michael reaction in the presence of base, followed by removal of the MOM protecting group afforded **3a** in 64% overall yield. Diol **3a** was converted to acetonide **11** in 80% yield. NOE enhancement was observed between the Ha and Hc protons of **11**, but not between

Table I. Asymmetric synthesis of 1,2-diol derivatives[a].

Entry	Aldehyde (RCHO)R	Lewis acid	Reaction time at −78°C	Product **2** yield, %	Isomer ratio *syn*(**2**):*anti*	de of **2**, % (absolute confign at C-1, C-2)
1	C_6H_5	$BF_3 \cdot OEt_2$	1	82	97:3	67(*R*,*R*)
2	C_6H_5	$AlCl_3 \cdot OEt_2$	1	68	97:3	88(*R*,*R*)
3	C_6H_5	$AlCl_3$	0.17	52	97:3	92(*R*,*R*)
4	C_6H_5	$TiCl_4$	1	48	73:27	73(*R*,*R*)
5	C_6H_5	$SnCl_4$	1	no reaction		
6	p-$NO_2C_6H_4$	$AlCl_3 \cdot OEt_2$	3	80	100:0	76
7	p-MeC_6H_4	$AlCl_3 \cdot OEt_2$	3	47	98:2	90
8	n-C_7H_{15}	$BF_3 \cdot OEt_2$	3	17	100:0	63
9	n-C_7H_{15}	$AlCl_3 \cdot OEt_2$	2	26	93:7	63
10	n-C_7H_{15}	$AlCl_3$	0.25	47	98:2	85
11	n-C_4H_9	$AlCl_3 \cdot OEt_2$	2	21	96:4	65(*R*,*R*)
12	n-C_4H_9	$AlCl_3$	0.67	53	98:2	89(*R*,*R*)
13	CH_3	$AlCl_3$	0.17	47	100:0	94

[a] The reaction was carried out, in general, with the following molar ratios; Lewis acid/aldehyde : **1** = 1.2:1.1. However, in entries 3, 10, 12 and 13, two equivalents of the aldehydes were used. The isomer ratios and de in entries 1-7 were determined by ^1H NMR; the coupling constants of the *syn*-isomers were 7.5 Hz whereas those of the *anti*-isomers were 4.0 Hz. The aldehydes were recovered when the addition resulted in low yields. The ratios and de in entries 8-13 were determined by HPLC. (Shimadzu LC-6A); **2b** (R = *n*-Bu), column Merck Hibar Rt 250-4, hexane/EtOAc = 5:1, flow rate 1.5 mL/min, R_t/min 6.80 (*RR*) 9.50 (*SS*) 9.75 (*anti*), 10.47 (*anti*); **2c** (R = n-C_7H_{15}, column YMC R-SIL S-5 60A, hexane/EtOAc = 10:1, flow rate 1.5 mL/min, R_t/min 8.03 (*RR*) 11.13 (*SS* + *anti*) 12.11 (*anti*); **2d** (R = Me), column YMC R-SIL-5-06 S-5 60A, hexane/EtOAc = 5:1, flow rate 1.5 mL/min, R_t/min 9.62 (*RR*) 12.57 (*SS*).

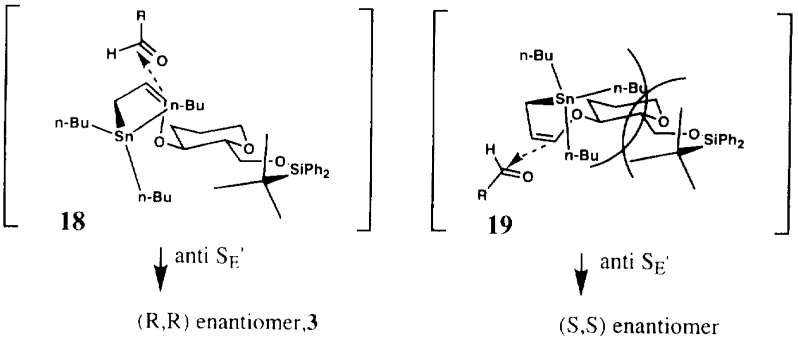


Key : (a) (1) MOMCl, iPr$_2$NEt; (2) Bu_4NF; (3) $(COCl)_2$, DMSO, Et_3N; (4) K_2CO_3; (5) HCl. (b) $Me_2C(OMe)_2$, PPTS, CH_2Cl_2. (c) (1) O_3/MeOH, Me_2S; (2) $LiAlH_4$. (d) (1) MsCl, pyridine; (2) $LiAlH_4$. (e) (1) TsOH/MeOH; (2) MeI/NaH. (f) (1) MeOH, HCl; (2) $Me_2C(OMe)_2$, TsOH; (3) $LiAlH_4$. (g) (1) KH, TsCl; (2) n-Pr_2CuLi. (h) (1) $(COCl)_2$, DMSO, Et_3N; (2) Ph_3PCH_3Br, n-BuLi.

Scheme 2. Determination of absolute configuration.

the Ha and Hb protons, indicating the *syn* stereochemistry of **3a**. Ozonolysis of **11** (O_3/MeOH/Me_2S) followed by $LiAlH_4$ reduction gave alcohol **12a** in 87% yield. The conversion of the alcohol to methanesulfonate followed by reduction gave **12b** in 83% yield. Hydrolysis of the acetonide followed by methylation afforded **13** in 56% yield; $[\alpha]_D^{27} = -62.5$ (c 0.23, EtOH). This rotation was compared with that of authentic *R*,*R* enantiomer; $[\alpha]_D^{24} = -83.8$ (c 0.370, EtOH) [4]. Similarly, **2b** was converted to **3b**, which was transformed to **14** by standard procedures; $[\alpha]_D^{22} = +11.3$ (c 1.23, EtOH).

Authentic **15** was prepared in the following manner. L-(+)-Tartaric acid was treated with MeOH/HCl to give the corresponding methyl ester, and the two hydroxyl groups were protected with acetonide. $LiAlH_4$ reduction of the ester groups afforded the corresponding diol **16**, which was converted to mono-tosylate upon treatment with KH/TsCl. Substitution of the tosylate with n-Pr_2CuLi gave the carbon-chain elongated product **17**. The remaining primary OH was oxidized to the corresponding aldehyde, which was converted to **15** by a Wittig reaction. By this reaction, **15** was obtained in



Scheme 3. Transition state structures.

6% overall yield; $[\alpha]_D^{22} = -12.0$ (c 1.25, EtOH). Accordingly, it is clear that the absolute configurations of **2a** and **2b** are (1R,2R) and (3R,4R), respectively.

Other γ-alkoxyallylstannanes

Reaction of **9** with benzaldehyde in the presence of $BF_3 \cdot OEt_2$ gave the corresponding *syn* adducts exclusively in high yield, but the de was only 24%. This lower de is presumably attributable to the fact that the asymmetric center of **9** is three bond lengths away from the γ-carbon at which the carbon-carbon bond formation takes place, whereas alkylation of **1** occurs at only two bond lengths from the nearest chiral center. The $BF_3 \cdot OEt_2$ mediated reaction of benzaldehyde with **10**, in which the asymmetric center is separated by two bond lengths from the γ-carbon, produced the corresponding *syn* adducts with 28% de. Although the chiral center of **10** is close to the reactive carbon, efficient blocking of one face of the double bond is not accomplished with this chiral auxiliary. Perhaps, the high diastereoselectivity obtained in the reaction of **1** may be due primarily to a sterically demanding TBDPS group which would effectively block one face of the double bond of allylstannane.

It seemed likely that the steric size of the 2-hydroxymethyl substituent on the tetrahydropyran ring would play an important role in the asymmetric induction of these allylstannane-aldehyde condensations. To test this hypothesis, we prepared the corresponding OCH_3 (**7**, 2-methoxymethyl THP) derivative of the γ-alkoxy allyl stannane (scheme 1). The Lewis acid-mediated reaction of **7** with benzaldehyde gave the *syn* adducts in good yield, but the diastereomer ratio of *RR*/*RS* was 2.5:1. Therefore, it is now clear that steric bulk of the alkoxy group is important to obtain high enantio- and diastereoselection.

Transition state structures

The enantioselective formation of the (R,R) isomer via **1** may be accounted for by transition state **18** shown in scheme 3. The front side of the plane consisting of the γ-oxygen and the three carbon atoms at the α,β, and γ-positions is blocked by the sterically bulky TBDPS group, forcing the aldehyde to approach the carbon from the back side of the plane. Although antiperiplanar approach of the aldehyde is shown in both **18** and **19**, a synclinal orientation of the aldehyde is also conceivable; both approaches lead to the same result. An important question is why **18** is favored over **19**. It is well accepted that the Lewis-acid-mediated allylstannane-aldehyde condensation proceeds in an *anti* $S_{E'}$ manner [5]; the tributylstannyl group has to be located on the front side of the allyl plane. A molecular model of **19** clearly indicates severe steric repulsion between Bu_3Sn and TBDPS groups, whereas such steric hindrance is significantly diminished in **18**.

Conclusion

Asymmetric synthesis of *syn* 1,2-diols **3** has been accomplished via the reaction of the γ-alkoxy-substituted allylstannane **1** with aldehydes in the presence of $AlCl_3$ or $AlCl_3 \cdot OEt_2$, followed by a five-step operation to remove the chiral auxiliary.

Experimental section

General

All reactions were conducted in oven-dried glassware under dry nitrogen or argon. All solvents were purified before use. Ether and THF were distilled from sodium benzophenone ketyl. Methylene chloride, DMF, and pyridine were distilled from CaH_2. Methanol was distilled from magnesium methoxide. $AlCl_3$ was purified through sublimation. $BF_3 \cdot OEt_2$ and $TiCl_4$ were distilled under argon. Other commercially available chemicals were used as such. ^1H NMR spectra were measured at 270 MHz on a Jeol JNM-GSX instrument. Infrared spectra were recorded on Hitachi model 260-10 spectrophotometer. Low- and high-resolution mass spectra were measured on a Jeol JMS-HX-110 mass spectrometer. Optical rotations were measured on a Jusco DIP-370 polarimeter using a 1 mL capacity quartz cell with a 10 cm path length. Elemental analyses were performed by the Analytical Center of Department of Chemistry.

(2R,3S)-3-Allyloxy-3,4,5,6-tetrahydro-2H-pyran-2-methanol **6**

In a 300 mL three-necked flask were placed DMF (100 mL) and (2R,3S)-3-hydroxy-3,4,5,6-tetrahydro-2H-pyran-2-methanol **5** (9.30 g, 70 mmol), prepared by the reported procedure [2]. To the mixture at room temperature with stirring was added trityl chloride (21.47 g, 77 mmol) and then DMAP (9.41 mg, 77 mmol), and the resulting mixture was stirred overnight at 70°C. The mixture was diluted with ether, and then water was added. The organic layer was separated, washed with brine, dried with anhydrous $\mathrm{MgSO_4}$, and concentrated *in vacuo*. Purification of the crude product by silica-gel column chromatography ($\mathrm{SiO_2}$ 150 g, using hexane/AcOEt = 5:1 → 3:1 as an eluent) gave (2*R*,3*S*)-2-(trityloxymethyl)-3,4,5,6-tetrahydro-2*H*-pyran-3-ol (24.2 g) in 92% yield.

In a 300 mL three-necked flask kept under Ar was placed KH (35 wt %, 6.88 g; 60 mmol), which was then washed with dry hexane two times. Dry THF (50 mL) was added at 0°C, and (2*R*,3*S*)-2-(trityloxymethyl)-3,4,5,6-tetrahydro-2*H*-pyran-3-ol (18.9 g, 50 mmol) dissolved in dry THF (50 mL) was added. The mixture was stirred at 0°C for 20 min. Allyl bromide (5.19 mL, 60 mmol) was added, and the mixture was stirred at room temperature for 30 min. The resulting mixture was cooled to 0°C, and the reaction was quenched by adding MeOH. Extraction with ether, washing with brine, drying with anhydrous $\mathrm{MgSO_4}$, and concentration *in vacuo* gave the corresponding allyl ether. Removal of trityl group was carried out by adding MeOH (100 mL) and conc HCl (5 drops) and subsequent stirring for 3 h at room temperature. Purification with silica-gel column chromatography ($\mathrm{SiO_2}$ 100 g, hexane/AcOEt = 3:1 → 1:1 as an eluent) gave (2*R*,3*S*)-3-allyloxy-2-hydroxymethyl-3,4,5,6-tetrahydro-2*H*-pyran **6** (7.41 g, 43.0 mmol) in 86% yield; a colorless oil :

^{1}H NMR (270 MHz, $\mathrm{CDCl_3}$) δ 5.89 (dddd, J = 17.0, 10.0, 6.0, 6.0 Hz, 1H, olefinic), 5.26 (dd, J = 17.0, 1.0 Hz, 1H, olefinic), 5.17 (d, J = 10.0, 1.0 Hz, 1H, olefinic), 4.11 (ddd, J = 14.5, 6.0, 1.0 Hz, 1H, one of allylic protons), 3.98-3.89 (m, 3H), 3.48 (dd, J = 13.0, 5.0 Hz, 1H), 3.43-3.18 (m, 3H), 2.30-2.20 (m, 1H), 2.30-1.90 (br, 1H, OH), 1.75-1.50 (m, 2H), 1.44-1.23 (m, 1H).

(2R,3S)-2-[(tert-Butyldiphenylsilyl)oxy]methyl-3-[((Z)-3-tributylstannyl-1-propenyl)oxy]-3,4,5,6-tetrahydro-2H-pyran **1**

To a DMF (30 mL) solution of **6** (1.72 g, 10 mmol) in 100 mL flask were added TBDPSCl (3.12 mL, 12 mmol) and imidazole (0.82 g, 12 mmol), and the mixture was stirred for 2 h at room temperature. Extraction with ether, washing with brine, drying over anhydrous $\mathrm{MgSO_4}$, concentration *in vacuo*, and purification with silica-gel column chromatography ($\mathrm{SiO_2}$ 120 g, hexane/AcOEt = 15:1 as an eluent) gave (2*R*,3*S*)-3-allyloxy-2-(*tert*-butyldiphenylsilyloxymethyl)-3,4,5,6-tetrahydro-2*H*-pyran (3.99 g, 9.74 mmol) in 97% yield; a colorless oil :

^{1}H NMR (270 MHz, $\mathrm{CDCl_3}$) δ 7.78-7.65 (m, 4H, aromatic), 7.47-7.31 (m, 6H, aromatic), 5.82 (dddd, J = 17.0, 10.0, 6.0, 6.0 Hz, 1H, olefinic), 5.20 (dd, J = 17.0, 1.0 Hz, 1H, olefinic), 5.09 (dd, J = 10.0, 1.0 Hz, 1H, olefinic), 4.15 (ddd, J = 14.5, 6.0, 1.0 Hz, 1H, one of allylic protons), 3.95-3.86 (m, 4H), 3.48-3.25 (m, 2H), 3.23-3.16 (m, 1H), 2.30-2.17 (m, 1H), 1.70-1.60 (m, 2H), 1.45-1.27 (m, 1H), 1.04 (s, 9H, *t*-Bu).

To a dry THF (30 mL) solution of (2*R*,3*S*)-3-allyloxy-2-[(*tert*-butyldiphenylsilyl)oxymethyl]-3,4,5,6-tetrahydro-2H-pyran (2.62 g, 6.34 mmol) cooled at −78°C under Ar were added *sec*-BuLi (1.07 M in hexane, 7.2 mL, 7.7 mmol) and TMEDA (1.15 mL, 7.62 mmol), and the resulting mixture was stirred for 15 min at −78°C. Tributylstannyl chloride (95% purity, 2.17 mL, 7.6 mmol) was added and stirring was continued for 30 min at −78°C. Water was added and the reaction mixture was allowed to warm to room temperature. Extraction with ether, washing with brine, drying over anhydrous $\mathrm{MgSO_4}$, concentration *in vacuo*, and flash column chromatography ($\mathrm{siO_2}$ 150 g, hexane/AcOH = 50:1 as an eluent) gave **1** (16 g, 4.51 mmol) in 71% yield; a colorless oil : R_f (silica, hexane/AcOEt =5:1) = 0.59.

IR (neat) 3 055, 2 975, 2 945, 2 870, 2 710, 1 460, 1 420, 1 155, 1 100, 1 080, 1 000, 740, 700 cm^{-1}.

^{1}H NMR (270 MHz, $\mathrm{CDCl_3}$) δ 7.73 (m, 4H, aromatic), 7.35 (m, 6H, aromatic), 5.89 (ddd, J = 6.0, 1.1, 1.1 Hz, 1H, olefinic), 4.49 (ddd, J = 9.5, 8.5, 6.0 Hz, 1H, olefinic), 4.0-3.85 (m, 3H), 3.72 (ddd, J = 11.0, 9.0, 5.0 Hz, 1H), 3.32 (m, 1H), 3.23 (m, 1H), 1.69 (m, 1H), 1.58-1.40 (m, 9H, $\mathrm{CH_2}$), 1.37-1.20 (m, 9H, $\mathrm{CH_2}$), 1.04 (s, 9H, *t*-Bu), 0.93-0.78 (m, 9H, Me of $\mathrm{SnBu_3}$).

HRMS calc for $\mathrm{C_{33}H_{51}O_3SiSn}$ ($\mathrm{M^+}$ − *t*-Bu) 643.2629, found 643.2657.

(2R,3S)-2-Methoxymethyl-3-[((Z)-3-tributylstannyl-1-propenyl)oxy]-3,4,5,6-tetrahydro-2H-pyran **7**

Sodium hydride (60 wt%, 300 mg, 7.5 mmol) was washed with hexane under Ar, and then THF (10 mL) was added. The mixture was cooled at 0°C, and **6** (0.86 g, 5.0 mmol) dissolved in THF (3 mL) was added slowly with stirring. The mixture was stirred at 0°C for 30 min. Methyl iodide (1.0 mL, 16 mmol) was added, and the mixture was warmed to room temperature and stirred for 1 h. Addition of water, extraction with ether, washing with brine, drying with anhydrous $\mathrm{MgSO_4}$, removal of solvents *in vacuo*, and purification using column chromatography ($\mathrm{SiO_2}$ 50 g, hexane/ethyl acetate = 3:1) gave (2*R*,3*S*)-3-allyloxy-2-methoxymethyl-3,4,5,6-tetrahydro-2*H*-pyran (812 mg, 4.36 mmol) in 87% yield. To a THF (5 mL) solution of this product (812 mg, 4.36 mmol) cooled at −78°C were added, with stirring, *sec*-BuLi (1.13 M hexane solution, 4.63 mL, 5.23 mmol) and TMEDA (0.79 mL, 5.23 mmol). The mixture was stirred for 10 min, and then $\mathrm{Bu_3SnCl}$ (1.42 mL, 5.23 mmol) was added. The mixture was stirred for 30 min at −78°C and then warmed slowly to room temperature. Addition of water, extraction with ether (twice), washing with brine, drying with anhydrous $\mathrm{MgSO_4}$, removal of solvents *in vacuo*, and purification with column chromatography ($\mathrm{Al_2O_3}$ 150 g, hexane/ethyl acetate = 50:1) gave **7** (1.108 g, 2.3 mmol) in 54% yield; a colorless oil :

^{1}H NMR (270 MHz, $\mathrm{CDCl_3}$) δ 5.82 (ddd, J = 6.0, 1.1, 1.1 Hz, 1H, olefinic), 4.53 (ddd, J = 9.5, 8.5, 6.0 Hz, 1H, olefinic), 4.02-3.92 (m, 1H), 3.76 (dd, J = 9.5, 2.0 Hz, 1H, one of $\mathrm{CH_2OMe}$), 3.67-3.46 (m, 2H), 3.41-3.29 (m, 1H), 3.37 (s, 3H, MeO), 2.28-2.13 (m, 1H), 1.71-1.60 (m, 6H), 1.60-1.40 (m, 12H), 1.40-1.12 (m, 6H), 1.00-0.70 (m, 9H, Me of $\mathrm{SnBu_3}$).

(2R,3S)-3-[(tert-Butyldiphenylsilyl)oxy]-2-[(Z)-3-tributylstannyl-1-propenyl)oxymethyl]-3,4,5,6-tetrahydro-2H-pyran **9**

To a DMF (100 mL) solution of **5** (9.30 g, 70 mmol) were added trityl chloride (21.47 g, 77 mmol) and 4-(dimethylamino)pyridine (9.41 g, 77 mmol), and the mixture was stirred for 12 h at 70°C. Dilution with ether, washing with water and brine, drying with anhydrous $\mathrm{MgSO_4}$, removal of the solvents *in vacuo*, and purification with column chromatography ($\mathrm{SiO_2}$ 150 g, hexane/ethyl acetate = 5:1 ~ 3:1) gave (2*R*,3*S*)-3-hydroxy-2-trityloxymethyl-3,4,5,6-tetrahydro-2*H*-pyran (24.188 g, 64 mmol) in 92% yield. To a DMF (20 mL) solution of this trityl ether (3.74 g, 10 mmol) were added *t*-butyldiphenylsilyl chloride (2.60 mL, 12 mmol) and imidazole (1.36 g, 20 mmol), and the mixture was stirred for 2 h at room temperature. Addition of ether, washing with water and brine, drying with anhydrous $\mathrm{MgSO_4}$, and removal of the solvents *in vacuo* gave the corresponding TBDPS-protected pyran. A mixture of this product, methanol (30 mL), and catalytic amounts of *p*-toluenesulfonic acid was stirred for 20 h at room temperature. Removal of the trityl group was confirmed by TLC. The usual work-up and purification with column chromatography (SiO_2 100 g, hexane/ethyl acetate = 5:1 ~ 3:1) gave the corresponding 2-hydroxymethyl derivative (2.046 g, 5.5 mmol) in 55% yield. Potassium hydride (35 wt%, 754 mg, 6.6 mmol) was washed twice with hexane under Ar, and THF (10 mL) was added. A THF (5 mL) solution of the above product (2.0 g, 5.5 mmol) was added slowly at 0°C, and the mixture was stirred for 1 h at 0°C. 3-Bromo-1-propene (0.57 mL, 6.6 mmol) was added, and the mixture was warmed to room temperature. After stirring for 1 h, the usual work-up and purification with column chromatography (SiO_2 60 g, hexane/ethyl acetate = 20:1) gave **8** (1.87 g, 4.6 mmol) in 84% yield. To a THF (5 mL) solution of **8** (1.87 g, 4.6 mmol) were added, with stirring at −78°C, *sec*-BuLi (1.05 M hexane solution, 5.26 mL, 5.52 mmol) and TMEDA (0.83 mL, 5.52 mmol). The mixture was stirred for 10 min at this temperature, and Bu_3SnCl (1.50 mL, 5.52 mmol) was added. The mixture was stirred for 30 min at −78°C, and warmed to room temperature. The usual work-up and purification with column chromatography (SiO_2 500 g, hexane/ethyl acetate = 50:1) gave **9** (440 mg, 0.62 mmol) in 13% yield.

- *(2R,3S)-2-(Allyloxymethyl)-3-[(tert-butyldiphenylsilyl)oxy]-3,4,5,6-tetrahydro-2H-pyran* **8**

A colorless oil :

^{1}H NMR (270 MHz, $CDCl_3$) δ 7.70-7.65 (m, 4H, aromatic), 7.48-7.35 (m, 6H, aromatic), 5.90 (dddd, J = 17.0, 10.0, 6.0, 6.0 Hz, 1H, olefinic), 5.27-5.13 (m, 2H, olefinic), 3.95 (dddd, J = 5.5, 5.5, 1.0, 1.0 Hz, 1H, allylic), 3.90-3.83 (m, 1H), 3.77 (dd, J = 10.0, 1.5 Hz, 1H, one of CH_2 at 2nd position of tetrahydropyran ring), 3.65-3.56 (m, 1H), 3.49-3.26 (m, 2H), 1.83-1.75 (m, 1H), 1.50-1.40 (m, 3H), 0.28 (m, 1H), 1.04 (s, 9H, *t*-Bu).

- *(2R,3S)-3-[(tert-Butyldiphenylsilyl)oxy]-2-[((Z)-3-tributylstannyl-1-propenyl)oxymethyl]-3,4,5,6-tetrahydro-2H-pyran* **9**

A colorless oil :

^{1}H NMR (270 MHz, $CDCl_3$) δ 7.77-7.65 (m, 4H, aromatic), 7.50-7.33 (m, 6H, aromatic), 5.80 (ddd, J = 6.0, 1.1, 1.1 Hz, 1H, olefinic), 4.45 (ddd, J = 9.5, 8.5, 6.0 Hz, 1H, olefinic), 4.06 (dd, J = 10.0, 1.0 Hz, 1H, one of CH_2 at 2nd position of tetrahydropyran ring), 3.90-3.77 (m, 1H), 3.78 (dd, J = 10.0, 6.0 Hz, 1H, one of CH_2 at 2nd position of tetrahydropyran ring), 3.56-3.47 (m, 1H), 3.42-3.32 (m, 1H), 3.32-3.20 (m, 1H), 1.83-1.72 (m, 1H), 1.72-1.02 (m, 2H), 1.37-1.23 (m, 6H), 1.04 (s, 9H, *t*-Bu), 0.95-0.75 (m, 9H, Me of Bu).

(2R,4R)-2-Methoxy-4-[((Z)-3-tributylstannyl-1-propenyl)oxy]pentane **10**

Potassium hydride (35 wt%, 4.58 g, 40 mmol) was washed twice with hexane under Ar, and THF (40 mL) was added. A THF (10 mL) solution of (2*R*,4*R*)-(−)-pentane-2,4-diol (4.16 g, 40 mmol) was added, with stirring, slowly at 0°C and the mixture was stirred for 1 h at 0°C. 3-Bromo-1-propene (3.46 mL,40 mmol) was added and the mixture was warmed to room temperature. After stirring for 1 h, water was added. The usual work-up followed by purification with column chromatography (SiO_2 150 g, hexane/ethyl acetate = 4:1) gave the mono-allylated alcohol (4.49 g, 31 mmol) in 78°C yield. Potassium hydride 35 wt%, 600 mg, 5.25 mmol) was washed twice with hexane under Ar and THF (5 mL) was added. A THF (2 mL) solution of the mono-allylated alcohol (721 mg, 5.0 mmol) was added slowly at 0°C, and the mixture was stirred for 1 h at this temperature. Methyl iodide (0.37 mL, 6.0 mmol) was added and the mixture was warmed slowly to room temperature, and stirring was continued for 1 h. The usual work-up gave the corresponding mono-methylated-mono-allylated product (671 mg). To a THF (5 mL) solution of this product cooled at −78°C were added, with stirring, *sec*-BuLi (1.0 M hexane solution, 5.0 mL, 5.0 mmol) and TMEDA (0.75 mL, 5.0 mmol) and the mixture was stirred for 10 min. Bu_3SnCl (1.36 mL, 5.0 mmol) was added at −78°C and the mixture was stirred for 30 min. The usual work-up and purification with column chromatography (SiO_2 75 g, hexane/ethyl acetate = 5:1) gave **10** (844 mg, 1.9 mmol) in 38% yield; a colorless oil :

^{1}H NMR (270 MHz, $CDCl_3$) δ 5.84 (ddd, J = 6.0, 1.1, 1.1 Hz, 1H, olefinic), 4.58 (ddd, J = 9.5, 8.5, 6.0 Hz, 1H, olefinic), 3.96-3.87 (m, 1H, one of C*H*OR), 3.55-3.43 (m, 1H, one of C*H*OR), 3.32 (s, 3H, MeO), 1.69-1.55 (m, 4H), 1.55-1.43 (m, 6H), 1.38-1.22 (m, 6H), 1.20-1.10 (m, 6H), 0.95-0.81 (m, 15H, Me).

Reaction of **1** *with aldehydes*

Synthesis of **2a** is representative (entry 3 of table I). In a 50 mL two-necked flask under Ar were placed dry CH_2Cl_2 (1 mL) and anhydrous $AlCl_3$ (35 mg, 0.26 mmol), purified by sublimation of commercially available material. Benzaldehyde (45 μL, 0.44 mmol) was slowly added at −78°C, and the resulting mixture was stirred for 30 min. To the resulting homogeneous solution was added slowly a dry CH_2Cl_2 (1 mL) solution of **1** (158 mg, 0.22 mmol), cooled to −78°C. The reaction was continued for 10 min and quenched with MeOH. The mixture was allowed to warm to rt. Extraction with ether, concentration *in vacuo*, treatment with aqueous KF solution at rt for 1 h, extraction with ether, washing with brine, drying ($MgSO_4$), concentration *in vacuo*, and purification by flash column chromatography (15 cm x 17 mm ; hexane, 50 mL then hexane/AcOEt = 10:1) gave **2a** (58.9 mg, 0.114 mmol) in 52% yield.

2a : colorless oil; R_f 0.39 (major), 0.36 (minor), silica, hexane/ethyl acetate = 4:1.

IR (neat) ν max 3 510 (brOH) 3 080, 2 950, 2 870, 1 750, 1 600, 1 590, 1 430, 1 390, 1 220, 1 108, 1 000, 940, 840, 820, 765, 742, 705 cm^{-1}.

^{1}H NMR (270 MHz, $CDCl_3$) δ 7.75 (m, 4H, aromatic), 7.38 (m, 6H, aromatic), 7.23 (m, 5H, aromatic), 5.63 (ddd, J = 11.5, 7.0, 4.5 Hz, 1H, olefinic, major), 5.39 (ddd, J = 11.5, 7.0, 4.5 Hz, olefinic, *syn*-minor), 5.10-4.95 (m, 2H, olefinic), 4.68 (d, J = 4.5 Hz, PhC*H*OH, *anti*), 4.45 (d, J = 7.5 Hz, 1H, PhC*H*OH, major), 4.35 (d, J = 7.5 Hz, PhC*H*OH, *syn*-minor), 4.00-3.80 (m, 4H), 3.61 (ddd, J = 11.0, 9.0, 5.0 Hz, 1H), 3.35-3.16 (m, 3H), 2.08 (m, 1H), 1.60-1.35 (m, 2H, CH_2), 1.05 (s, 9H, *t*-Bu).

Exact mass calc for $C_{32}H_{40}O_4Si$ M, 516.2696, found m/z 516.2696.

2b (R = *n*-Bu) : colorless oil; R_f 0.38 (major isomer) 0.35 (minor isomer), silica, hexane:ethylacetate = 4:1.

IR (neat) ν max 3 500 (br, s, OH), 3 100, 2 955, 2 880, 1 600, 1 470, 1 440, 1 400, 1 270, 1 105, 1 000, 940, 880, 835, 745, 705 cm^{-1}.

^{1}H NMR (270 MHz, $CDCl_3$) δ 7.70 (m, 4H, aromatic), 7.40 (m, 4H, aromatic), 5.72 (ddd, J = 18.0, 10.0, 8.0 Hz, 1H, olefinic), 5.23 (m, 2H, olefinic), 3.95 (dd, J = 11.0, 4.0 Hz, 1H), 3.95-3.80 (m, 2H), 3.71 (dd, J = 7.5, 7.5 Hz, 1H, allylic), 3.56 (ddd, J = 10.5, 8.5, 4.0 Hz, 1H), 3.38 (m, 1H), 3.25 (m, 1H), 3.18 (m, 1H), 2.63-2.55 (br, 1H, OH), 2.05 (m, 1H), 1.61 (m, 2H, CH(OH)C*H*$_2$), 1.45-1.20 (m, 7H, CH_2), 1.05 (s, 9H, *t*-Bu), 1.04 (s, *t*-Bu, minor), 0.87 (dd, J = 7.5, 7.5 Hz, 3H, Me).

Exact mass calc for $C_{30}H_{44}O_4Si$ M, 496.3009, found m/z 496.3008.

2c (R = n-C_7H_{15}) : colorless oil; R_f 0.45 (major isomer), (minor isomer), silica, hexane/ethyl acetate = 4:1.

IR (neat) ν max 3 500 (br, OH), 3 195, 3 155, 2 950, 2 875, 1 730, 1 590, 1 460, 1 430, 1 395, 1 290, 1 100, 1 000, 935, 870, 830, 740, 705 cm^{-1}.

^1H NMR (270 MHz, $CDCl_3$) δ 7.72 (m, 4H, aromatic), 7.40 (m, 6H, aromatic), 5.72 (ddd, J = 18.0, 10.0, 8.0 Hz, 1H, olefinic), 5.24 (m, 2H, olefinic), 3.97 (dd, J = 11.0, 4.0 Hz, 1H), 3.95-3.80 (m, 2H), 3.71 (dd, J = 7.5, 7.5 Hz, 1H, allylic), 3.56 (ddd, J = 10.5, 8.5, 4.0 Hz, 1H), 3.38 (m, 1H), 3.25 (m, 1H), 3.18 (m, 1H), 2.65-2.40 (br, 1H, OH), 2.05 (m, 1H), 1.60 (m, 2H), 1.50-1.20 (m, 13H), 1.05 (s, 9H, t-Bu), 1.04 (s, t-Bu, minor), 0.87 (dd, J = 1.5, 1.5 Hz, 3H, Me).

Exact mass calc for $C_{33}H_{50}O_4Si$ M,538.3479, found m/z 538.3480.

2d (R = Me) : colorless oil; R_f = 0.28 (major), 0.26 (minor), silica, hexane/ethyl acetate = 4:1.

IR (neat) ν max 3 500 (br, s, OH), 3 080, 3 060, 2 950, 2 860, 1 590, 1 460, 1 430, 1 395, 1 363, 1 260, 1 100 (br, s), 1 040, 1 000, 940, 870, 820, 770, 740, 705 cm^{-1}.

^1H NMR (270 MHz, $CDCl_3$) δ 7.72 (m, 4H, aromatic), 7.38 (m, 6H, aromatic), 5.70 (ddd, J = 18.0, 10.0, 8.0 Hz, 1H, olefinic), 5.25 (m, 2H, olefinic), 3.99 (dd, J = 11.0, 4.0 Hz, 1H), 3.90-3.80 (m, 2H), 3.70-3.50 (m, 3H), 3.25 (m, 1H), 3.16 (m, 1H), 2.73-2.60 (br, 1H, OH), 2.05 (m, 1H), 1.60 (m, 1H), 1.05 (d, J = 7.2 Hz, 12H, t-Bu and $CH_2(OH)Me$).

Exact mass calc for $C_{27}H_{38}O_4Si$ M, 454.2540, found m/z 454.2538.

2e (R = p-NO_2-C_6H_4) : ^1H NMR (270 MHz, $CDCl_3$) δ 8.10 (d, J = 6.5 Hz, 2H, aromatic), 7.73 (m, 4H, aromatic), 7.40 (m, 8H, aromatic), 5.63 (ddd, J = 11.5, 7.0, 4.5 Hz, 1H, olefinic), 5.14 (d, J = 7.0 Hz, 1H, olefinic), 5.02 (d, J = 11.5 Hz, 1H, olefinic), 4.55 (dd, J = 7.5, 1.5 Hz, 1H, CH(OH)Ar, major), 4.48 (dd, J = 7.5, 1.5 Hz, CH(OH)Ar, minor), 3.97-3.78 (m, 4H), 3.62 (ddd, J = 11.0, 9.05, 5.0 Hz, 1H), 3.46 (dd, J = 7.5, 4.5 Hz, 1H, allylic), 3.33-3.15 (m, 2H), 2.05 (m, 1H), 1.70-1.25 (m, 2H), 1.05 (s, 9H, t-Bu, major), 1.04 (s, t-Bu, minor).

Exact mass calc for $C_{32}H_{39}O_6NSi$ M, 561.2547, found m/z 561.2545.

2f (R = p-CH_3-C_6H_4) : ^1H NMR (270 MHz, $CDCl_3$) δ 7.74 (m, 4H, aromatic), 7.38 (m, 6H, aromatic), 7.10 (d, J = 6.5 Hz, 2H, aromatic), 7.04 (d, J = 6.5 Hz, 2H, aromatic), 5.62 (ddd, J = 11.5, 7.0, 4.5 Hz, 1H, olefinic), 5.07 (d, J = 7.0 Hz, 1H, olefinic), 5.02 (d, J = 11.5 Hz, 1H, olefinic), 4.40 (d, J = 7.5 Hz, 1H, CH(OH)Ar), 4.00-3.80 (m, 4H), 3.60 (ddd, J = 11.0, 9.0, 5.0 Hz, 1H), 3.33-3.16 (m, 3H), 2.29 (s, 3H, Ar-Me), 2.05 (m, 1H), 1.62 (m, 2H), 1.05 (s, 9H, t-Bu).

Exact mass calc for $C_{33}H_{42}O_4Si$ M, 530.2853, found m/z 530.2850.

Determination of absolute configuration. Conversion of **2a** *to* **3a**

In a 50 mL two-necked flask under Ar were placed **2a** (97:3 diastereomer mixture) (518 mg, 1.00 mmol), CH_2Cl_2 (5 mL), chloromethylmethylether (0.1 mL, 1.30 mmol), and diisopropylethylamine (0.22 mL, 1.30 mmol), and the resulting mixture was refluxed for several hours. The mixture was cooled to room temperature and diluted with ether and water. The organic layer was separated, washed with brine, dried over anhydrous $MgSO_4$, and concentrated. THF (3 mL) and Bu_4NF (excess) were added, and the mixture was stirred at room temperature for 5 h. Extraction with ether, washing with brine, drying with anhydrous $MgSO_4$, concentration, and purification by silica-gel column chromatography (SiO_2 10 g, hexane/AcOEt = 2:1 → 1:2) gave (2R,3S)-3[-2-((1-phenyl-1-methoxymethoxy)but-3-en)yloxy]-3,4,5,6-tetrahydro-2H-pyran-2-methanol (282 mg, 0.87 mmol) in 87% yield. To a CH_2Cl_2 (2.0 mL) solution of dimethyl sulfoxide (0.2 mL, 2.78 mmol), cooled to −78°C, in 50 mL two-necked flask under Ar was added oxalyl chloride (0.16 mL, 1.83 mmol), and then the mixture was stirred for 20 min at −78°C. (2R,3S)-2-methanol-3 [-2-((1-phenyl-1-methoxymethoxy)but-3-en)yloxy]-3,4,5,6-tetrahydro-2H-pyran (282 mg, 0.87 mmol) was added, and the mixture was stirred for 1 h at −78°C. Et_3N (excess) was added, and the mixture was allowed to warm to room temperature. Addition of a 1:1 mixture of sat aqueous NH_4Cl and aqueous NH_3, extraction with ether, drying over anhydrous Na_2SO_4, and concentration *in vacuo* gave the corresponding crude aldehyde (60 mg). To this aldehyde were added MeOH and K_2CO_3, and the mixture was stirred for 15 h at room temperature. Extraction with ether, drying over anhydrous Na_2SO_4, concentration *in vacuo*, addition of MeOH and a few drops of conc HCl, stirring overnight at room temperature, extraction with ether, and purification by silica gel column chromatography (SiO_2 5 g, hexane/AcOEt = 3:1) gave **3a** (106 mg, 0.64 mmol) in 74% yield.

3a : ^1H NMR (270 MHz, $CDCl_3$) δ 7.35 (m, 5H, aromatic), 5.74 (ddd, J = 17.0, 10.5, 5.5 Hz, 1H, olefinic), 5.27 (ddd, J = 17.0, 1.5, 1.5 Hz, 1H, olefinic), 5.15 (ddd, J = 10.5, 1.5, 1.5 Hz, 1H, olefinic), 4.52 (d, J = 6.5 Hz, 1H, benzylic), 4.24 (dddd, J = 6.5, 5.5, 1.5, 1.5 Hz, 1H, allylic), 2.35-2.10 (br,2H, OH).

*(4*R*,5*R*)-2,2-Dimethyl-4-phenyl-5-vinyl-1,3-dioxolane* **11**

To a CH_2Cl_2 (2 mL) solution of **3a** (106 mg, 0.64 mmol) were added 2,2-dimethoxypropane (0.16 mL, 1.28 mmol) and p-toluenesulfonic acid pyridinium salt (80 mg, 0.32 mmol), and the mixture was stirred for 1 h at room temperature. Water was added. The usual work-up and purification with column chromatography (SiO_2 5 g, hexane/ethyl acetate = 4:1) gave **11** (112 mg, 0.55 mmol) in 86% yield; a colorless oil :

^1H NMR (270 MHz, $CDCl_3$) δ 7.4-7.31 (m, 5H, aromatic), 5.88 (ddd, J = 17.0, 10.0, 7.0 Hz, 1H, olefinic), 5.28-5.20 (m, 2H, olefinic), 4.63 (d, J = 10.0 Hz, 1H, PhCH), 4.28 (dd, J = 10.0, 9.5 Hz, 1H, allylic), 1.60 (s, 3H, Me of isopropylidene), 1.52 (s, 3H, Me of isopropylidene).

*(1*R*,2*R*)-(−)-1,2-Dimethoxy-1-phenylpropane* **13**

A MeOH (10 mL) solution of **11** (112 mg, 0.55 mmol), cooled at −78°C, was bubbled with a mixture of ozone and oxygen. After the ozonolysis was over, argon was passed to remove excess amounts of ozone. Dimethyl sulfide was added and the mixture was warmed to room temperature. Addition of water, extraction with ether, washing with brine, drying with anhydrous $MgSO_4$, and removal of the solvent *in vacuo* gave the corresponding aldehyde. Reduction with $LiAlH_4$ (15 mg) in ether afforded **12a** (108 mg). To a pyridine (3 mL) solution of **12a** was added mesyl chloride (0.06 mL, 0.78 mmol), and the mixture was stirred overnight at room temperature. The usual work-up and purification with column chromatography (SiO_2 7.5 g, hexane/ethyl acetate = 10:1) gave the corresponding mesylate (124 mg, 0.43 mmol) in 78% yield. The reduction of this mesylate was carried out with $LiAlH_4$ (17 mg, 0.43 mmol) in ether

(2 mL) at 0°C. The mixture was stirred for several hours at room temperaturre. Ether and small amounts of water were added, and the mixture was dried with anhydrous $MgSO_4$. Filtration through celite and removal of the solvent gave **12b** (74 mg, 0.38 mmol). To a MeOH (3 mL) solution of **12b** (58 mg, 0.30 mmol) was added 1 N aqueous HCl solution (3 mL), and the mixture was stirred for 1 h at room temperature. The usual work-up gave the corresponding diol. Sodium hydride (60 wt%, 50 mg, 1.15 mmol) was washed with hexane, and THF (2 mL) was added. To this suspension, cooled at 0°C, was added a THF (1 mL) solution of the diol (35 mg, 0.23 mmol), and the mixture was stirred for 30 min at 0°C. Methyl iodide (0.15 mL, 2.3 mmol) was added. The mixture was stirred for 1 h at room temperature. The usual work-up followed by distillation gave **13** (23.1 mg, 0.13 mmol) in 24% overall yield from **11**; a colorless oil.

^{1}H NMR (270 MHz, $CDCl_3$) δ 7.40-7.27 (m, 5H, aromatic), 4.54 (d, J = 6.0 Hz, 1H, PhCHOMe), 4.22 (m, 1H, MeCHOMe), 3.39 (s, 3H, MeO), 3.27 (s, 3H, MeO), 1.43 (d, J = 6.0 Hz, 3H, MeCH).

*(4*R*, 5*R*)-(+)-4-Butyl-2,2-dimethyl-5-vinyl-1,3-dioxolane* **14**

This compound was synthesized from **3b** in the similar procedure as described for **3a**; colorless oil; R_f = 0.66 (silica, hexane/ethyl acetate = 4:1); $[\alpha]_D^{22}$ = +11.3 (c 1.23, EtOH).

IR (neat) ν max 3 070, 2 990, 2 960, 2 940, 2 860, 1 720, 1 670, 1 460, 1 430, 1 380, 1 370, 1 260, 1 240, 1 170, 1 100, 1 050, 985, 923, 865, 795, 740, 720, 695 cm^{-1}.

^{1}H NMR (270 MHz, $CDCl_3$) δ 5.81 (ddd, J = 17.0, 10.0, 7.0 Hz, 1H, olefinic), 5.36 (ddd, J = 17.0, 1.5, 1.0 Hz, 1H, olefinic), 5.25 (ddd, J = 10.0, 1.5, 1.0 Hz, 1H, olefinic), 3.91 (ddd, J = 8.0, 7.0, 1.0 Hz, 1H, allylic), 3.60 (ddd, J = 8.0, 4.5, 4.5 Hz, 1H, CH-nBu), 1.55-1.17 (m, 6H, CH_2), 1.36 (s, 3H, Me of isopropylidene), 1.34 (s, 3H, Me of isopropylidene), 0.85 (dd, J = 7.0, 7.0 Hz, 3H, Me).

Exact mass calc for $C_{11}H_{20}O_2$ M, 184.1463, found m/z 184.1462.

*(4*S*,5*S*)-(−)-4-Butyl-2,2-dimethyl-5-vinyl-1,3-dioxolane* **15**

To MeOH (500 mL), cooled at 0°C, was slowly added acetyl chloride (42.5 mL, 3 mol%/methanol). L-(+) Tartaric acid (50 g, 333 mmol) was added, and the mixture was stirred for 16 h at room temperature. Removal of methanol and distillation (5 mmHg, 132°C) gave the corresponding dimethyl ester of tartaric acid (39.3 g, 221 mmol) in 66% yield. To a benzene (900 mL) solution of this ester (39.3 g) were added 2,2-dimethoxypropane (41 mL, 332 mmol) and p-toluenesulfonic acid monohydrate (2.0 g, 5 mol%/diol). The mixture was heated, with stirring, to remove methanol produced. Potassium carbonate was added at room temperature to neutralize the mixture. Filtration through celite and distillation (0.4 mmHg, 80°C) gave the corresponding acetonide (40.6 g, 190 mmol) in 86% yield. To an ether (500 mL) suspension of $LiAlH_4$ (9.7 g, 247 mmol) was added slowly at 0°C an ether (100 mL) solution of the acetonide (40.6 g, 190 mmol). The mixture was stirred at room temperature for several hours and then cooled to 0°C. Brine (19 mL) was added. The mixture was stirred for 1 h and anhydrous $MgSO_4$ was added. Filtration through celite and distillation (0.4 mmHg, 80°C) gave (+)-2,3-O-isopropylidene-L-threitol **16**. Purification of the residue with column chromatography (SiO_2 200 g, hexane/ethyl acetate = 1:1 and then ethyl acetate) also gave **16**. The combined yield of **16** was 45% (13.86 g, 85.5 mmol). Potassium hydride (35 wt%, 0.85 g, 6.82 mmol) was washed twice with hexane under Ar and THF (30 mL) was added. A THF (5 mL) solution of **16** (1.0 g, 6.2 mmol) was added slowly with stirring at 0°C. The mixture was stirred at room temperature for 20 min, and then cooled to 0°C again. A THF (5 mL) solution of tosyl chloride (1.18 mL, 6.2 mmol) was added, and the mixture was stirred for 1 h at room temperature. Methanol was added. The usual work-up and purification with column chromatography (SiO_2 25 g, hexane/ethyl acetate = 3:1 ~ 1:1) gave the corresponding tosylate (1.189 g, 3.75 mmol) in 60% yield.

In a 100 mL two-necked flask under Ar were placed CuI (1.02 g, 5.34 mmol) and dry ether (5 mL), and the mixture was cooled to −15°C. An ether solution of n-propyllithium (0.76 M in Et_2O, 14 mL, 10.68 mmol) was added, and the mixture was stirred for 10 min at −15°C. An ether (3 mL) solution of the tosylate (283 mg, 0.89 mmol) was added, and the mixture was stirred for 15 min at −15°C. The reaction was quenched with a 1:1 mixture of sat aqueous NH_4Cl and aqueous ammonia solution. The usual work-up and purification by silica gel column chromatography (SiO_2 25 g, hexane/AcOEt = 6:1) gave the corresponding chain elongated product **17** (115.9 mg, 0.365 mmol) in 41% yield.

To a mixture of CH_2Cl_2 (5 mL) and dimethyl sulfoxide (0.36 mL, 5.10 mmol), kept under Ar, was added oxalyl chloride (0.30 mL, 3.40 mmol) at −78°C, and the mixture was stirred for 20 min at −78°C. A CH_2Cl_2 (5 mL) solution of **17** (319.6 mg, 1.70 mmol) was added slowly, and the mixture was stirred for 1 h at −78°C. Triethylamine (1.18 mL, 8.5 mmol) was added, and the mixture was allowed to warm to room temperature. The reaction was quenched with sat aqueous NH_4Cl solution. The usual work-up gave the corresponding crude aldehyde. In a separate 100 mL two-necked flask under Ar were placed methyltriphenylphosphonium bromide (0.911 g, 2.55 mmol) and dry THF (10 mL), and the mixture was cooled to 0°C. A hexane solution of n-BuLi (1.65 M in hexane, 1.55 mL, 2.55 mmol) was added slowly, and the mixture was stirred for 20 min at room temperature. To this solution cooled at −78°C was added a THF (5 mL) solution of the aldehyde prepared above. The mixture was stirred for 1.5 h at −78°C, for 1.5 h at 0°C, and then the reaction was quenched by adding water. The usual work-up and purification by flash column chromatography (depth 20 cm, ∅ 27 mm, hexane/AcOEt = 30:1 → 20:1) gave the corresponding vinyl derivative **15** (92.8 mg, 0.50 mmol) in 30% yield : $[\alpha]_D^{22}$ = −12.0 (c 1.25, EtOH); a colorless oil : R_f (silica, hexane/AcOEt = 4:1) = 0.66.

IR (neat) 3 070, 2 990, 2 960, 2 940, 2 860, 1 720, 1 670, 1 460, 1 430, 1 380, 1 370, 1 260, 1 240, 1 170, 1 100, 1 050, 985, 923, 865, 795, 740, 720, 695 cm^{-1}.

^{1}H NMR (270 MHz, $CDCl_3$) δ 5.81 (ddd, J = 17.0, 10.0, 7.0 Hz, 1H, olefinic), 5.36 (ddd, J = 17.0, 1.5, 1.0 Hz, 1H, olefinic), 5.25 (ddd, J = 10.0, 1.5, 1.0 Hz, 1H, olefinic), 3.91 (ddd, J = 8.0, 7.0, 1.0 Hz, 1H, allylic), 3.60 (ddd, J = 8.0, 4.5, 4.5 Hz, 1H, CHO), 1.55-1.17 (m, 6H, CH_2 of Bu), 1.36 (s, 3H, Me of isopropylidene), 1.34 (s, 3H, Me of isopropylidene), 0.85 (t, J = 7.0 Hz, 3H, Me of Bu).

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