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Stereoselective [2,3]-Sigmatropic Wittig Rearrangement of Benzyl Ethers Derived from Vinylcuprate Adducts of (*R*)-2,3-*O*-Isopropylideneglyceraldehyde

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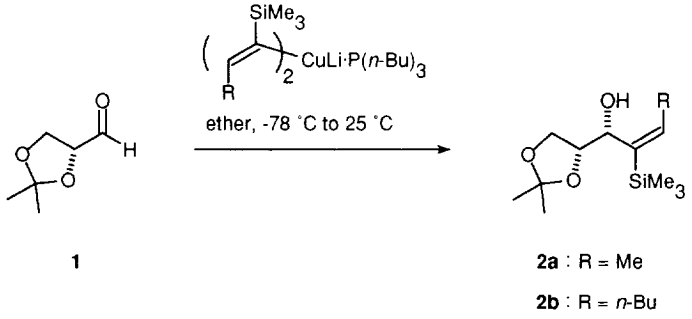
Abstract: Allyl alcohols **2** prepared by addition of lithium vinylcuprates to (*R*)-2,3-*O*-isopropylideneglyceraldehyde (**1**) are converted to 3,4,5-trimethoxybenzyl ethers **3** by a one-pot desilylation/alkylation. After deprotonation using potassium *t*-butoxide/*t*-butyllithium/*N,N,N',N'*-tetramethylethylenediamine in *t*-butyl methyl ether at -78 °C, substrates **3** undergo a [2,3]-sigmatropic Wittig rearrangement with complete 1,3-chirality transfer and good simple diastereoselectivity to give homoallyl alcohols **5** as the major products.

INTRODUCTION

Recently, we reported an efficient and highly diastereoselective access to *syn* allyl alcohols **2** by addition of lithium vinylcuprates to (*R*)-2,3-*O*-isopropylideneglyceraldehyde (**1**) in ether (Scheme 1).[1]



1

2a : R = Me

2b : R = *n*-Bu

Scheme 1. Diastereoselective addition of lithium vinylcuprates to **1**

1,3-Chirality transfer processes with allyl alcohols such as **2** lead to enantiomerically pure, polyfunctional products featuring two stereogenic centers in a defined 1,4-relationship.[2] While a subsequent oxidative alkene cleavage completes an overall protocol for enantioselective synthesis using **1** as a chiral

auxiliary,[2] elaboration of the entire structures formed upon chirality transfer is an alternative option. In connection with studies toward an enantioselective synthesis of the cytotoxic neolignan (-)-megaphone[3] (Figure 1) from **1**, we investigated the [2,3]-sigmatropic Wittig rearrangement[4] of 3,4,5-trimethoxybenzyl ethers derived from **2**.

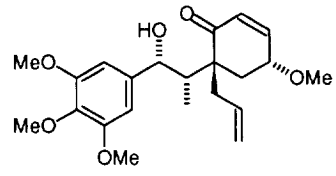
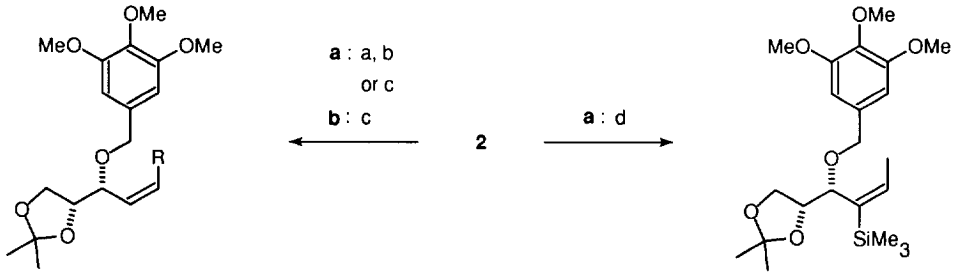


Fig. 1. (-)-Megaphone

RESULTS AND DISCUSSION

Ether **3a** was readily available from **2a** *via* oxygen assisted desilylation and subsequent benzylation[5] of the resultant alcohol[1] with 3,4,5-trimethoxybenzyl bromide[6] (Scheme 2). Gratifyingly, desilylation and alkylation of **2** to **3** could be performed in a single operation when the benzylic bromide (1.2 - 2 equiv.) and 10 mol % of tetraethylammonium iodide were added to a mixture of **2** and sodium hydride in *N,N*-dimethylformamide. Homo-Brook rearrangement[7] of the sodium alkoxide of **2** to an intermediate silyl ether which in turn is cleaved by a halide ion prior to benzylation probably account for this finding. On the other hand, treatment of **2a** with 3,4,5-trimethoxybenzyl bromide (5 equiv.) under phase transfer catalysis conditions[8] effected a clean conversion to trimethylsilyl substituted ether **4**.



3a : R = Me

3b : R = *n*-Bu

4

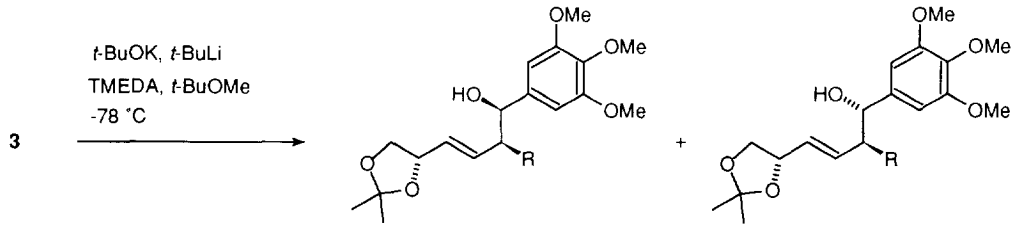
Scheme 2. Preparation of benzyl ethers **3** and **4**. a: (i) KH, THF, 20 °C, (ii) K_2CO_3, MeOH, H_2O, 20 °C, 81 %; b: (i) KH, DMF, 20 °C, (ii) 3,4,5-trimethoxybenzyl bromide, cat. Et_4NI, 20 °C, 83 %; c: (i) NaH, DMF, 20 °C, (ii) 3,4,5-trimethoxybenzyl bromide, cat. Et_4NI, 20 °C, 74 % **3a**, 80 % **3b**; d: 3,4,5-trimethoxybenzyl bromide, cat. $(n\text{-Bu})_4NHSO_4$, 50 % aqueous NaOH, 60 °C, 76 %

Attempts to induce a [2,3]-sigmatropic Wittig rearrangement of benzyl ether **3b** with the standard base *n*-butyllithium[4] (5 equiv., THF, -78 °C to room temperature) only led to recovery of starting material. The

same observation was made when the reaction was performed in the presence of *N,N,N',N'*-tetramethylethylenediamine (TMEDA)[9] using either *n*-butyllithium in THF or *t*-butyllithium in ether (5 equiv. base, -78 °C to room temperature). However, the mixed metal superbase[10] potassium *t*-butoxide (3 equiv.)/*t*-butyllithium (3 equiv.) which had previously been applied successfully to the deprotonation of bis-allyl ethers[11] effected a smooth rearrangement (5 h at -78 °C) of benzyl ethers **3** to homoallylic alcohols **5** and **6** in *t*-butyl methyl ether containing 6 - 9 equiv. TMEDA (Scheme 3). No rearrangement of **3** occurred if only 2 equiv. of this mixed metal base were employed, possibly due to directed ortho metalation[12] of the arene moiety under these conditions,[13] whereas further addition of *t*-butyllithium in excess of 3 equiv. during the reaction course led to a competitive decomposition of **3** to give 3,4,5-trimethoxybenzyl alcohol.[11a,14]

Subjecting trimethylsilyl substituted benzyl ether **4** to the optimum conditions found for **3** or to lithium dicyclohexylamide (THF, -30 °C)[8] did not induce [2,3]-sigmatropic Wittig rearrangement but produced the parent benzylic alcohol instead.[8,15] Presumably, enhanced steric hindrance in the transition state of the [2,3]-rearrangement is responsible for this outcome.[16]

The stereoselectivity of the [2,3]-sigmatropic Wittig rearrangement of benzyl ethers **3** was determined by capillary gas chromatography using samples of the crude products (Scheme 3). Since only isomers **5** and **6** were detected, the reaction proceeds with complete 1,3-chirality transfer.[17] Additionally, the major products **5** are obtained with good simple diastereoselectivity.[18]



		5		6
a : R = Me	(63 %)	85	:	15
b : R = *n*-Bu	(57 %)	89	:	11

Scheme 3. [2,3]-sigmatropic Wittig rearrangement of benzyl ethers **3**
(TMEDA = *N,N,N',N'*-tetramethylethylenediamine)

Configurational assignment for **5** and **6** rests on diagnostic ^{1}H NMR chemical shifts observed for the vinylic protons (3-H and 4-H) and the group R (Figure 2, Table 1).

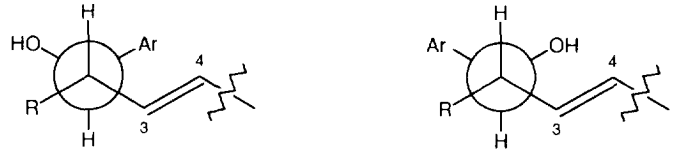


Fig. 2. Newman projections for **5** and **6**
(Ar = 3,4,5-trimethoxyphenyl)

Table 1. Selected Chemical Shifts (ppm) of **5a,b** and **6a,b**.[a]

	3-H and 4-H	R
5a	5.42 , 5.70	1.08
6a	5.57 , 5.82	0.92
5b	5.32 , 5.47	1.23-1.42
6b	5.52 , 5.64	1.16-1.34

[a] **a**: R = Me, **b**: R = *n*-Bu.

Newman projections of the preferred conformations of isomers **5** and **6** down the C-2 C-1 bond are depicted in Figure 2. The anisotropy introduced by the aryl ring causes a significant upfield shift for the gauche substituent, vinyl protons 3-H and 4-H in the *syn* isomers **5** and R group protons in the *anti* isomers **6**, respectively.[19]

Benzylic alcohol **5a** prepared from (*R*)-2,3-*O*-isopropylideneglyceraldehyde (**1**) in only 3 steps contains the arylpropane side chain of (-)-megaphone[3] with the correct relative and absolute configuration at the stereogenic centers. Moreover, the allylic 1,2-diol unit offers a handle for subsequent construction of the cyclohexenone moiety of this neolignan. Work along this line will be reported in due course.

EXPERIMENTAL

For general experimental information, see ref 1.

Preparation of Benzyl Ethers **3**

The one-step conversion of **2**[1] to **3** is performed as follows. A solution of the alcohol **2** (**a**: 150 mg, 0.614 mmol; **b**: 150 mg, 0.524 mmol) in DMF (15 ml) is added at room temperature to a suspension of 80 % sodium hydride (**a**: 50 mg, 1.7 mmol; **b**: 60 mg, 2.0 mmol) in DMF (2 ml). The resultant mixture is stirred for 15 min, a solution of 3,4,5-trimethoxybenzyl bromide[6] (**a**: 192 mg, 0.737 mmol; **b**: 273 mg, 1.05 mmol) in DMF (2 ml) and tetraethylammonium iodide (15 mg, 0.058 mmol) are added, and stirring is continued for 5 h. After hydrolysis with sat. aqueous NH_4Cl (40 ml), extraction with ether (4 x 40 ml), drying over $MgSO_4$, and removal of the solvent *in vacuo*, the residue is purified by flash chromatography using petroleum ether/ethyl acetate/triethylamine 92 : 7 : 1 to give **3a** (160 mg, 74 %) or **3b** (165 mg, 80 %), respectively.

For the two-step conversion of **2a** to **3a**, **2a** is desilylated to (*Z*)-(1*R*,4'*R*)-1-(2,2-dimethyl-1,3-dioxolan-4-yl)but-2-en-1-ol as described in ref 1 (81 %). A solution of the resultant alcohol (800 mg, 4.65 mmol) in DMF (10 ml) is added at room temperature to a suspension of hexane-washed potassium hydride (551 mg, 13.8 mmol) in DMF (30 ml). The mixture is stirred for 30 min, a solution of 3,4,5-trimethoxybenzyl bromide (2.43 g, 9.29 mmol) and tetraethylammonium iodide (124 mg, 0.482 mmol) in DMF (20 ml) is slowly added, and stirring is continued overnight. After hydrolysis with sat. aqueous NH_4Cl (500 ml), adjustment to pH 7 with 1 N HCl, extraction with ethyl acetate (4 x 120 ml), drying over $MgSO_4$, and removal of the solvent *in vacuo*, purification of the residue by flash chromatography using petroleum ether/dichloromethane/ethyl acetate/triethylamine 61 : 25 : 12 : 2 affords **3a** (1.37 g, 83 %).

(Z)-(1R,4'R)-1-(2,2-Dimethyl-1,3-dioxolan-4-yl)-1-[(3,4,5-trimethoxybenzyl)oxy]but-2-ene (**3a**). R_f = 0.52 (petroleum ether/ethyl acetate 1 : 1); $[\alpha]_D^{20}$ = -10.2 (c = 1.0 in $CHCl_3$), $[\alpha]_{365}^{20}$ = -17.3 (c = 1.0 in $CHCl_3$); ^1H NMR δ 1.37 [s, 3 H, $C(CH_3)_2$], 1.40 [s, 3 H, $C(CH_3)_2$], 1.64 (dd, 3 H, $^4J_{4,2}$ = 1.6, $J_{4,3}$ = 7.0 Hz,

4-H), 3.62 (dd, 1 H, $J_{5a',4'}$ = 6.4, $J_{5a',5b'}$ = 8.3 Hz, 5'-H_a), 3.83 (s, 3 H, 4"-OCH_3), 3.86 (s, 6 H, 3"-OCH_3, 5"-OCH_3), 3.94 (dd, 1 H, $J_{5b',4'}$ = 6.4, $J_{5b',5a'}$ = 8.4 Hz, 5'-H_b), 4.16 - 4.25 (m, 2 H, 1-H, 4'-H), 4.38 (d, 1 H, ^2J = 12.4 Hz, benzylic H_a), 4.62 (d, 1 H, ^2J = 12.4 Hz, benzylic H_b), 5.27 - 5.36 (m, 1 H, 2-H), 5.85 (dq, 1 H, $J_{3,4}$ = 7.0, $J_{3,2}$ = 11.0 Hz, 3-H), 6.59 (s, 2 H, 2"-H, 6"-H); ^{13}C NMR δ 13.87 (q, C-4), 25.31 [q, $C(CH_3)_2$], 26.53 [q, $C(CH_3)_2$], 56.00 (q, 3"-OCH_3, 5"-OCH_3), 60.74 (q, 4"-OCH_3), 65.77 (t, C-5'), 69.70 (t, benzylic C) 74.32 (d, C-1 or C-4'), 78.06 (d, C-4' or C-1), 104.60 (d, C-2", C-6"), 109.66 (s, C-2'), 126.52 (d, C-2 or C-3), 130.90 (d, C-3 or C-2), 134.08 (s, C-1"), 137.11 (s, C-4"), 153.07 (s, C-3", C-5"); IR (film) 2986 (s), 2939 (s), 2886 (s), 2840 (m), 1592 (s, C=C), 1507 (s, C=C), 1460 (s), 1422 (s), 1380 [s, $C(CH_3)_2$], 1370 [s, $C(CH_3)_2$], 1330 (s), 1236 (s), 1129 (s), 1068 (s), 1010 (s), 852 (m) cm^{-1}; MS (GC/MS) *m/e* (relative intensity): 352 (M^+, 9), 337 (M^+ - CH_3, 2), 282 (4), 196 (5), 182 (16), 181 [$CH_2C_6H_2(OCH_3)_3^+$, 100], 148 (5), 101 ($C_5H_9O_2^+$, 29), 43 (7). Anal. Calcd for $C_{19}H_{28}O_6$: C, 64.75; H, 8.01. Found: C, 64.69; H, 8.22.

(Z)-(1R,4'R)-1-(2,2-Dimethyl-1,3-dioxolan-4-yl)-1-[(3,4,5-trimethoxybenzyl)oxy]hept-2-ene (**3b**). R_f = 0.23 (petroleum ether/ethyl acetate 6 : 1); $[\alpha]_D^{20}$ = -13.5 (c = 1.0 in $CHCl_3$), $[\alpha]_{365}^{20}$ = -26.0 (c = 1.0 in $CHCl_3$); ^{1}H NMR δ 0.88 (t, 3 H, $J_{7,6}$ = 7.1 Hz, 7-H), 1.25 - 1.35 (m, 4 H, 5-H, 6-H), 1.37 [s, 3 H, $C(CH_3)_2$], 1.41 [s, 3 H, $C(CH_3)_2$], 1.95 - 2.06 (m, 2 H, 4-H), 3.62 (dd, 1 H, $J_{5a',4'}$ = 6.5, $J_{5a',5b'}$ = 8.3 Hz, 5'-H_a), 3.83 (s, 3 H, 4"-OCH_3), 3.86 (s, 6 H, 3"-OCH_3, 5"-OCH_3), 3.94 (dd, 1 H, $J_{5b',4'}$ = 6.4, $J_{5b',5a'}$ = 8.3 Hz, 5'-H_b), 4.15 - 4.22 (m, 2 H, 1-H, 4'-H), 4.37 (d, 1 H, ^2J = 12.5 Hz, benzylic H_a), 4.62 (d, 1 H, ^2J = 12.5 Hz, benzylic H_b) 5.27 (dd, 1 H, $J_{2,1}$ = 9.5, $J_{2,3}$ = 11.2 Hz, 2-H), 5.75 (dt, 1 H, $J_{3,4}$ = 7.4, $J_{3,2}$ = 11.2 Hz, 3-H), 6.59 (s, 2 H, 2"-H, 6"-H); ^{13}C NMR δ 13.85 (q, C-7), 22.34 (t, C-6), 25.39 [q, $C(CH_3)_2$], 26.60 [q, $C(CH_3)_2$], 27.91 (t, C-5 or C-4), 31.73 (t, C-4 or C-5), 56.00 (q, 3"-OCH_3, 5"-OCH_3), 60.77 (q, 4"-OCH_3), 65.89 (t, C-5'), 69.72 (t, benzylic C), 74.90 (d, C-1 or C-4'), 78.15 (d, C-4' or C-1), 104.56 (d, C-2", C-6"), 109.71 (s, C-2'), 125.32 (d, C-2 or C-3), 134.18 (s, C-1"), 136.98 (d, C-3 or C-2), 137.23 (s, C-4"), 153.07 (s, C-3", C-5"); IR (film) 2985 (s), 2957 (s), 2935 (s), 2874 (s), 1592 (s, C=C), 1507 (s, C=C), 1458 (s), 1422 (s), 1380 [m, $C(CH_3)_2$], 1370 [m, $C(CH_3)_2$], 1331 (s), 1236 (s), 1130 (s), 1071 (s), 1012 (m), 852 (w) cm^{-1}; MS (GC/MS) *m/e* (relative intensity): 394 (M^+, 4), 379 (M^+ - CH_3, 0.5), 282 (2), 196 (3), 182 (14), 181 [$CH_2C_6H_2(OCH_3)_3^+$, 100], 148 (5), 101 ($C_5H_9O_2^+$, 36), 73 (5), 43 ($C_3H_7^+$, 14). Anal. Calcd for $C_{22}H_{34}O_6$: C, 66.98; H, 8.69. Found: C, 66.84; H, 8.92.

Preparation of Benzyl Ether **4**

To a solution of **2a** (100 mg, 0.409 mmol) and tetra-*n*-butylammonium hydrogensulfate (120 mg, 0.353 mmol) in dichloromethane (5 ml) is slowly added 3,4,5-trimethoxybenzyl bromide (536 mg, 2.05 mmol) and 50 % NaOH (5 ml). The mixture is cautiously concentrated using a rotary evaporator and subsequently heated at 60 °C overnight. Dichloromethane (10 ml) is added to the residue and the resultant mixture is poured into sat. aqueous NH_4Cl (15 ml). After extraction of the aqueous layer with dichloromethane (4 x 10 ml), drying over $MgSO_4$, and evaporation of the solvent *in vacuo*, the residue is purified by flash chromatography using petroleum ether/dichloromethane/ethyl acetate 20 : 10 : 1 and then petroleum ether/ethyl acetate/triethylamine 84 : 15 : 1 to give **4** (131 mg, 76 %).

(E)-(1S,4'R)-1-(2,2-Dimethyl-1,3-dioxolan-4-yl)-1-[(3,4,5-trimethoxy-benzyl)oxy]-2-trimethylsilylbut-2-ene (**4**). R_f = 0.70 (petroleum ether/ethyl acetate 1 : 1); $[\alpha]_D^{20}$ = -33.6 (c = 1.0 in $CHCl_3$), $[\alpha]_{365}^{20}$ = -90.2 (c = 1.0 in $CHCl_3$); ^{1}H NMR δ 0.15 [s, 9 H, $Si(CH_3)_3$], 1.34 [s, 3 H, $C(CH_3)_2$], 1.37 [s, 3 H, $C(CH_3)_2$], 1.68 (d, 3 H, $J_{4,3}$ = 6.7 Hz, 4-H), 3.39 - 3.45 (m, 1 H, 5'-H_a), 3.76 - 3.82 (m, 1 H, 5'-H_b), 3.83 (s, 3 H, 4"-OCH_3), 3.86 (s, 6 H, 3"-OCH_3, 5"-OCH_3), 4.26 (d, 1 H, ^2J = 12.9 Hz, benzylic H_a), 4.37 - 4.40 (m, 2 H, 1-H, 4'-H), 4.61 (d, 1 H, ^2J = 12.9 Hz, benzylic H_b), 6.19 (q, 1 H, $J_{3,4}$ = 6.7 Hz, 3-H), 6.61 (s, 2 H, 2"-H, 6"-H); ^{13}C NMR δ 0.51 [q, $Si(CH_3)_3$], 15.74 (q, C-4), 25.66 [q, $C(CH_3)_2$], 26.84 [q, $C(CH_3)_2$], 56.01 (q, 3"-OCH_3, 5"-OCH_3), 60.78 (q, 4"-OCH_3), 65.89 (t, C-5'), 69.85 (t, benzylic C) 76.43 (d, C-1 or C-4'), 79.22 (d, C-4' or C-1), 104.54 (d, C-2", C-6"), 109.59 (s, C-2'), 134.39 (s, C-1"), 137.07 (s, C-4"), 139.49 (s, C-2), 140.78 (d, C-3), 153.07 (s, C-3", C-5"); IR (film) 2986 (s), 2952 (s), 2941 (s), 2899 (s), 2839 (m), 1593 (s, C=C), 1507 (s, C=C), 1458 (s),

1422 (s), 1380 [m, $C(CH_3)_2$], 1370 [m, $C(CH_3)_2$], 1331 (s), 1243 (s), 1150 (s), 1130 (s), 1067 (s), 1013 (m), 841 (s), 758 (w), 690 (w) cm^{-1}; MS *m/e* (relative intensity): 424 (M^+, 2), 282 (3), 249 (1), 196 (2), 182 (14), 181 [$CH_2C_6H_2(OCH_3)_3^+$, 100], 148 (6), 101 ($C_5H_9O_2^+$, 13), 75 ($SiMe_2OH^+$, 2), 73 ($SiMe_3^+$, 5). Anal. Calcd for $C_{22}H_{36}O_6Si$: C, 62.23; H, 8.55. Found: C, 62.21; H, 8.59.

[2,3]-Sigmatropic Wittig Rearrangement of Benzyl Ethers **3**

5a/6a: To a solution of potassium *t*-butoxide (1.94 g, 11.6 mmol) in *t*-butyl methyl ether (80 ml) cooled to -40 °C is added dropwise 1.7 M *t*-butyllithium in pentane (6.81 ml, 11.6 mmol), and stirring is continued for 1.5 h at -20 °C. At -78 °C, *N,N,N',N'*-tetramethylethylenediamine (3.5 ml, 23.2 mmol) and a solution of **3a** (1.36 g, 3.86 mmol) in *t*-butyl methyl ether (22 ml) are added, and the resultant mixture is stirred for 5 h at the same temperature. After hydrolysis with sat. aqueous NH_4Cl, extraction with ether (5 x), drying over $MgSO_4$, and removal of the solvent *in vacuo*, purification of the crude product (**5a** : **6a** = 85 : 15 by GC; 25 m SE 54 CB column, heating rate 2 °C/min starting at 150 °C) by flash chromatography (silica gel deactivated with 3 % H_2O) using petroleum ether/ethyl acetate/toluene 55 : 40 : 5 affords a mixture of **5a** and **6a** (853 mg, 63 %). Separation of **5a** and **6a** is achieved by HPLC [Eurosphere 100 (5 µm) column, 250 mm length, 8 mm i.d.] using petroleum ether/ethyl acetate/triethylamine 75 : 24 : 1 (5 ml/min).

5b/6b: The procedure described above for **5a/6a** is followed using potassium *t*-butoxide (191 mg, 1.14 mmol) in *t*-butyl methyl ether (6 ml), 1.7 M *t*-butyllithium in pentane (0.67 ml, 1.14 mmol), *N,N,N',N'*-tetramethylethylenediamine (0.5 ml, 3.32 mmol), and **3b** (150 mg, 0.38 mmol) in *t*-butyl methyl ether (1 ml). The crude product [**5b** : **6b** = 89 : 11 by GC after silylation of the hydroxyl function with *N*-methyl-*N*-(trimethylsilyl)trifluoroacetamide (MSTFA); 25 m SE 54 CB column, heating rate 5 °C/min starting at 100 °C] is purified by flash chromatography using petroleum ether/ethyl acetate/triethylamine 66 : 33 : 1 to give **5b** (78 mg, 52 %) and **6b** (7 mg, 5 %).

(E)-(1R,2S,4'S)-4-(2,2-Dimethyl-1,3-dioxolan-4-yl)-2-methyl-1-(3,4,5-trimethoxyphenyl)but-3-en-1-ol (**5a**). mp 64 °C; R_f = 0.41 (petroleum ether/ethyl acetate 1 : 1); $[\alpha]_D^{20}$ = +5.15 (c = 2.0 in $CHCl_3$), $[\alpha]_{365}^{20}$ = -3.55 (c = 2.0 in $CHCl_3$); ^1H NMR δ 1.08 (d, 3 H, $J_{2\text{-Me},2}$ = 7.2 Hz, 2-CH_3), 1.36 [s, 3 H, $C(CH_3)_2$], 1.39 [s, 3 H, $C(CH_3)_2$], 1.69 (d, 1 H, $J_{1\text{-OH},1}$ = 2.7 Hz, 1-OH), 2.53 (m_c, 1 H, 2-H), 3.45 (m_c, 1 H, apparent t with *J* = 8.0 Hz, 5'-H_a), 3.84 (s, 3 H, 4"-OCH_3), 3.86 (s, 6 H, 3"-OCH_3, 5"-OCH_3), 3.98 (dd, 1 H, $J_{5b',4'}$ = 6.2, $J_{5b',5a'}$ = 8.2 Hz, 5'-H_b), 4.43 (m_c, 1 H, 4'-H), 4.49 (dd, 1 H, $J_{1,1\text{-OH}}$ = 2.8, $J_{1,2}$ = 6.1 Hz, 1-H), 5.42 (dd, 1 H, *J* = 7.8, $J_{3,4}$ = 15.6 Hz, 3-H or 4-H), 5.70 (dd, 1 H, *J* = 7.0, $J_{4,3}$ = 15.6 Hz, 4-H or 3-H), 6.51 (s, 2 H, 2"-H, 6"-H); ^{13}C NMR δ 14.48 (q, 2-CH_3), 25.84 [q, $C(CH_3)_2$], 26.65 [q, $C(CH_3)_2$], 43.59 (d, C-2), 56.07 (q, 3"-OCH_3, 5"-OCH_3), 60.82 (q, 4"-OCH_3), 69.38 (t, C-5'), 77.09 (d, C-1 or C-4'), 77.70 (d, C-4' or C-1), 103.41 (d, C-2", C-6"), 109.16 (s, C-2'), 128.30 (d, C-3 or C-4), 136.81 (d, C-4 or C-3), 137.04 (s, C-4"), 138.46 (s, C-1"), 152.96 (s, C-3", C-5"); IR (film) 3438 (m, OH), 2987 (m), 2937 (m), 2902 (m), 2877 (m), 2834 (m), 1592 (s, C=C), 1511 (s, C=C), 1459 (s), 1423 (s), 1379 [m, $C(CH_3)_2$], 1371 [m, $C(CH_3)_2$], 1332 (m), 1239 (s), 1227 (m), 1132 (m), 1058 (m), 1037 (m), 1013 (m), 988 (w), 831 (w) cm^{-1}; MS (GC/MS) *m/e* (relative intensity): 352 (M^+, 0.6), 337 (M^+ - CH_3, 0.9), 277 (2), 259 (3), 197 [$CHOHC_6H_2(OCH_3)_3^+$, 100], 196 (96), 181 (18), 169 (88), 154 (28), 138 (32), 98 (23), 59 (18), 43 (18). Anal. Calcd for $C_{19}H_{28}O_6$: C, 64.75; H, 8.01. Found: C, 64.64; H, 8.04.

(E)-(1S,2S,4'S)-4-(2,2-Dimethyl-1,3-dioxolan-4-yl)-2-methyl-1-(3,4,5-trimethoxyphenyl)but-3-en-1-ol (**6a**). ^1H NMR δ 0.92 (d, 3 H, $J_{2\text{-Me},2}$ = 6.9 Hz, 2-CH_3), 1.39 [s, 3 H, $C(CH_3)_2$], 1.42 [s, 3 H, $C(CH_3)_2$], 2.17 (s, 1 H, 1-OH), 2.48 (m_c, 1 H, 2-H), 3.56 (m_c, 1 H, apparent t with *J* = 7.9 Hz, 5'-H_a), 3.83 (s, 3 H, 4"-OCH_3), 3.86 (s, 6 H, 3"-OCH_3, 5"-OCH_3), 4.08 (dd, 1 H, $J_{5b',4'}$ = 6.1, $J_{5b',5a'}$ = 8.1 Hz, 5'-H_b), 4.31 (d, 1 H, $J_{1,2}$ = 7.7 Hz, 1-H), 4.51 (m_c, 1 H, 4'-H), 5.57 (ddd, 1 H, *J* = 0.7, *J* = 7.3, $J_{3,4}$ = 15.9 Hz, 3-H or 4-H), 5.82 (dd, 1 H, *J* = 8.1, $J_{4,3}$ = 15.5 Hz, 4-H or 3-H), 6.53 (s, 2 H, 2"-H, 6"-H).

(E)-(1R,2S,4"S)-2-Butyl-4-(2,2-dimethyl-1,3-dioxolan-4-yl)-1-(3,4,5-trimethoxyphenyl)but-3-en-1-ol (**5b**). mp 54 °C - 56 °C; R_f = 0.46 (petroleum ether/ethyl acetate 1 : 1); $[\alpha]_D^{20}$ = +20.0 (c = 1.0 in $CHCl_3$), $[\alpha]_{365}^{20}$ = +59.9 (c = 1.0 in $CHCl_3$); ^{1}H NMR δ 0.86 (t, 3 H, $J_{4',3'}$ = 7.0 Hz, 4'-H), 1.23 - 1.42 (m, 6 H, 3'-H, 2'-H, 1'-H), 1.35 [s, 3 H, $C(CH_3)_2$], 1.37 [s, 3 H, $C(CH_3)_2$], 1.59 - 1.68 (m, 1 H, 1-OH), 2.34 (m_c, 1 H, 2-H), 3.33 (m_c, 1 H, apparent t with J = 8.0 Hz, 5"-H_a), 3.82 (s, 3 H, 4'''-OCH_3), 3.85 (s, 6 H, 3'''-OCH_3, 5'''-OCH_3), 3.91 (dd, 1 H, $J_{5b",4"}$ = 6.2, $J_{5b",5a"}$ = 8.0 Hz, 5"-H_b), 4.39 (m_c, 1 H, 4"-H), 4.48 (d, 1 H, $J_{1,2}$ = 6.4 Hz, 1-H), 5.32 (dd, 1 H, J = 7.3, $J_{3,4}$ = 15.3 Hz, 3-H or 4-H), 5.47 (dd, 1 H, J = 8.8, $J_{4,3}$ = 15.3 Hz, 4-H or 3-H), 6.46 (s, 2 H, 2'''-H, 6'''-H); ^{13}C NMR δ 13.95 (q, C-4'), 22.75 (t, C-3'), 25.86 [q, $C(CH_3)_2$], 26.62 [q, $C(CH_3)_2$], 29.45 (t, C-2' or C-1'), 29.57 (t, C-1' or C-2'), 50.08 (d, C-2), 56.13 (q, 3'''-OCH_3, 5'''-OCH_3), 60.83 (q, 4'''-OCH_3), 69.44 (t, C-5"), 76.92 (d, C-1 or C-4"), 77.39 (d, C-4" or C-1), 103.73 (d, C-2''', C-6'''), 109.19 (s, C-2"), 130.07 (d, C-3 or C-4), 134.67 (d, C-4 or C-3), 137.28 (s, C-4'''), 138.53 (s, C-1'''), 152.94 (s, C-3''', C-5'''); IR (film) 3448 (m, OH), 2959 (s), 2935 (s), 2877 (s), 2838 (m), 1590 (s, C=C), 1512 (s, C=C), 1465 (s), 1421 (s), 1340 [m, $C(CH_3)_2$], 1326 [m, $C(CH_3)_2$], 1236 (s), 1137 (s), 1063 (s), 1038 (s), 1000 (m), 965 (w), 857 (w) cm^{-1}; MS (GC/MS) *m/e* (relative intensity): 394 (M^+, 7), 337 (M^+ - C_4H_9, 8), 318 (9), 303 (10), 198 (13), 197 [$CHOHC_6H_2(OCH_3)_3^+$, 62], 196 (100), 181 (43), 169 (60), 154 (36), 138 (45), 93 (39), 81 (57), 67 (51), 55 (57). Anal. Calcd for $C_{22}H_{34}O_6$: C, 66.98; H, 8.69. Found: C, 66.73; H, 8.68.

(E)-(1S,2S,4"S)-2-Butyl-4-(2,2-dimethyl-1,3-dioxolan-4-yl)-1-(3,4,5-trimethoxyphenyl)but-3-en-1-ol (**6b**). ^{1}H NMR δ 0.82 (t, 3 H, $J_{4',3'}$ = 6.7 Hz, 4'-H), 1.16 - 1.34 (m, 6 H, 3'-H, 2'-H, 1'-H), 1.39 [s, 3 H, $C(CH_3)_2$], 1.42 [s, 3 H, $C(CH_3)_2$], 1.98 (d, 1 H, $J_{1\text{-OH},1}$ = 2.7 Hz, 1-OH), 2.23 - 2.33 (m, 1 H, 2-H), 3.52 (m_c, 1 H, apparent t with J = 8.0 Hz, 5"-H_a), 3.84 (s, 3 H, 4'''-OCH_3), 3.86 (s, 6 H, 3'''-OCH_3, 5'''-OCH_3), 4.07 (dd, 1 H, $J_{5b",4"}$ = 6.1, $J_{5b",5a"}$ = 8.0 Hz, 5"-H_b), 4.40 (dd, 1 H, $J_{1,1\text{-OH}}$ = 2.4, $J_{1,2}$ = 8.0 Hz, 1-H), 4.53 (m_c, 1 H, 4"-H), 5.52 (dd, 1 H, J = 6.9, $J_{3,4}$ = 15.6 Hz, 3-H or 4-H), 5.64 (dd, 1 H, J = 8.8, $J_{4,3}$ = 15.4 Hz, 4-H or 3-H), 6.51 (s, 2 H, 2'''-H, 6'''-H).

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