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Diastereoselective Addition of Lower Order Vinylcuprates to (*R*)-2,3-*O*-Isopropylideneglyceraldehyde

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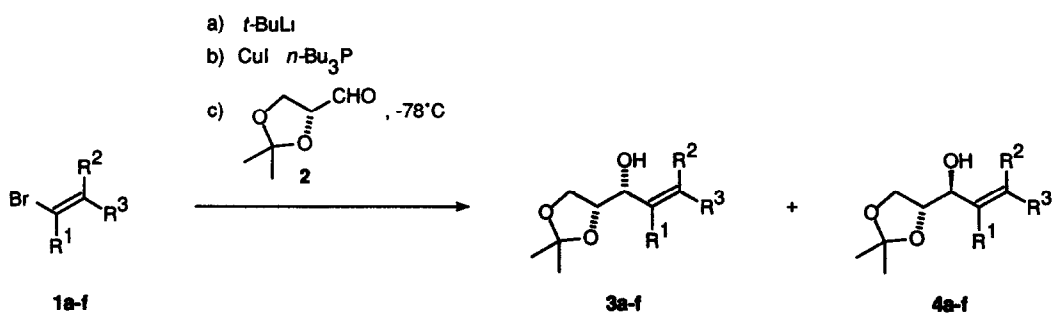
Abstract: Highly *syn* or *anti* selective addition of lower order lithium vinylcuprates generated from alkenyl bromides **1** to (*R*)-2,3-*O*-isopropylideneglyceraldehyde (**2**) can be achieved, respectively, depending on the substitution pattern of the vinyl moiety and the solvent α-Trimethylsilyl substituted vinylcuprates possessing an alkyl substituent *Z* to copper react with excellent *syn* selectivity in ether whereas a highly *anti* selective addition is observed for cuprates bearing a hydrogen atom *Z* or α to the metal in THF A model is proposed to rationalize these complementary selectivities

INTRODUCTION

The stereochemical course of nucleophilic addition to (*R*)-2,3-*O*-isopropylideneglyceraldehyde (**2**) has been widely investigated [1] Nevertheless, existing methodology[2] for highly diastereoselective addition of vinylic nucleophiles to **2** is so far limited to *syn* selective reactions of Grignard-derived organocopper reagents[3] and *anti* selective bond formation with higher order mixed metal cyanocuprates.[4] Since alkyl substituted vinylcopper species of both types are generated *via* titanium-catalyzed hydromagnesiation of 1-alkynylsilanes, they necessarily feature an (*E*)-configured alkene moiety As part of a program concerned with chirality transfer reactions of (*R*)-2,3-*O*-isopropylideneglyceraldehyde adducts,[5] we investigated the reaction of **2**[6] with lower order lithium vinylcuprates from alkenyl bromides **1**,[7] readily available with either olefin geometry (Scheme 1)



Scheme 1 Addition of lower order vinylcuprates to **2**

RESULTS AND DISCUSSION

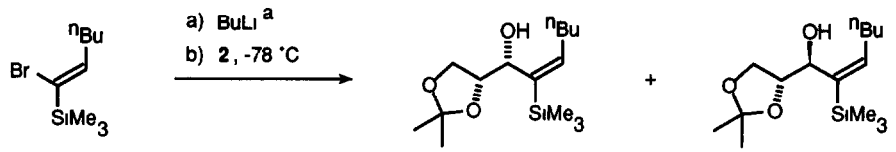
The results of the addition reactions are listed in Table 1 Extremely high *syn* selectivity is observed for cuprates with $R^1 = SiMe_3$ and R^2 = alkyl in ether (entry 3, 5, 8) The diastereoselectivity drops or changes to slightly *anti* if the reaction of these cuprates is run in THF (entry 4, 9) or if one of the substituents R^1, R^2 is equal to hydrogen and ether is used as the solvent (entry 1, 6, 10) Moreover, addition proceeds with good to excellent *anti* selectivity for cuprates with R^1 or R^2 = H in THF (entry 2, 7, 11)

Table 1 Diastereoselective Addition of Lower Order Vinylcuprates to **2** [a]

entry	bromide	R^1	R^2	R^3	solvent[b,c]	**3a-f**	**4a-f**[d]	Yield [%][e]
1	**1a**	$SiMe_3$	H	*n*-Bu	A	53	47	77
2	**1a**				B	3	97	89
3	**1b**	$SiMe_3$	*n*-Bu	H	A	97	3	87
4	**1b**				B	48	52	47
5	**1c**	$SiMe_3$	Me	H	A	98	2	86
6	**1d**	$SiMe_3$	H	H	A	75	25	91
7	**1d**				B	3	97	65
8	**1e**	$SiMe_3$	Me	Me	A	97	3	36 [f,g]
9	**1e**				B	37	63	[f,h]
10	**1f**	H	Me	Me	A	71	29	70
11	**1f**				B	12	88	92

[a] Following addition of aldehyde **2** to the vinylcuprate at -78 °C, the reaction mixture was allowed to warm to room temperature overnight [b] A = ether, B = THF [c] Solvent contained ca 30 vol % pentane [d] Ratios determined by capillary GC analysis of the crude products [e] Isolated yields of **3** + **4** [f] Competitive coupling of the vinylcuprate with **1e**, as well as addition of *t*-BuLi to **2** took place [g] Yield determined by ^1H NMR integration [h] Pure **4e** was isolated by HPLC in 6% yield

Since the vinyllithium reagent derived from bromide **1b** adds to **2** virtually stereorandomly in both ether and THF at -78 °C (Scheme 2), copper plays a decisive role in stereocontrol

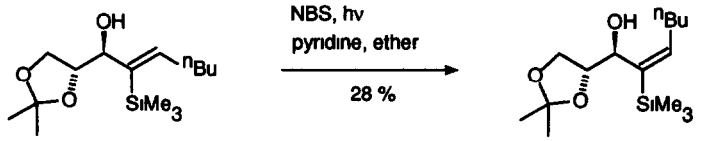


1b **3b** **4b**

ether,	60 %	56	44[b]
THF,	63 %	46	54[b]

Scheme 2 Addition of a vinyllithium compound to **2**
([a] Ether: *t*-BuLi, THF *s*-BuLi [b] Ratios determined by capillary GC analysis of the crude products)

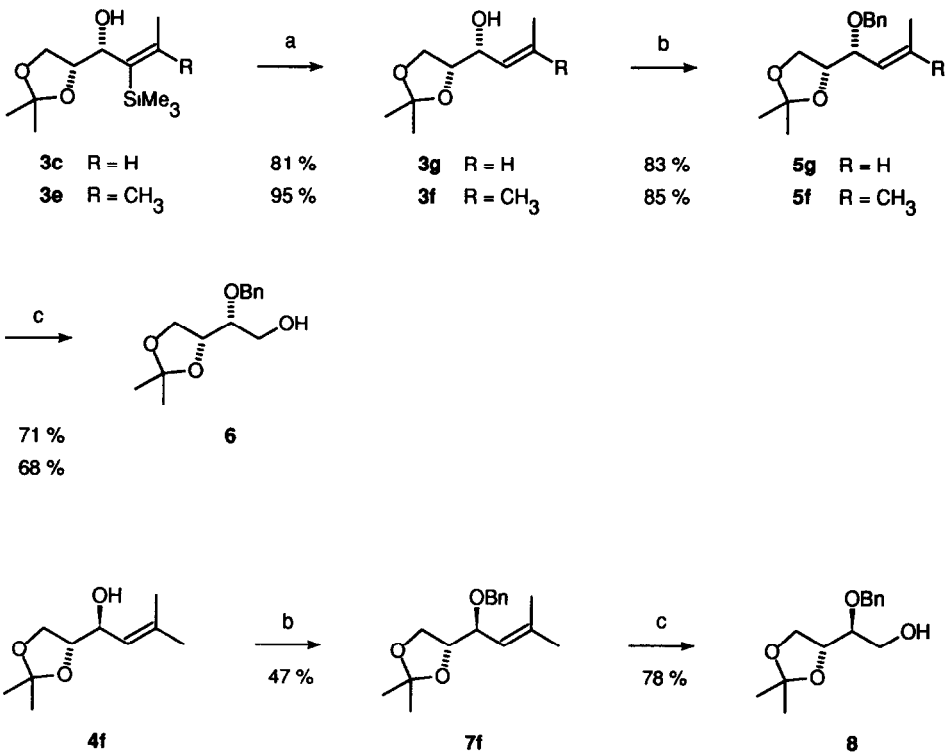
Allylic alcohols **3a**,[5,8] **4a**,[5] **3d**,[4] and **4d**[4] are known compounds As a stereochemical reference, **4b** was also prepared in low yield by isomerization[9] of **4a** through irradiation in the presence of NBS (Scheme 3)



4a **4b**

Scheme 3 Isomerization of adduct **4a**
(NBS = *N*-bromosuccinimide)

Configurational assignment for **3c**, **3e**, and **3f** which was also obtained after oxygen assisted desilylation[10] of **3e** rests on their conversion to threitol derivative **6**[11] (Scheme 4) The spectroscopic data of **6** were in accord with those reported for its enantiomer [12,13] Furthermore, alcohol **6** is easily distinguished from its diastereoisomer **8**[14] accessible from **4f** (Scheme 4) by ^{1}H NMR and ^{13}C NMR



3c R = H 81 % **3g** R = H 83 % **5g** R = H
3e R = CH_3 95 % **3f** R = CH_3 85 % **5f** R = CH_3

71 %
68 %

6

47 %

78 %

4f **7f** **8**

Scheme 4 Conversion of adducts to tetrol derivatives a KH, THF, then K_2CO_3, MeOH, H_2O, b NaH, DMF, then BnBr, c O_3, CH_2Cl_2, then $NaBH_4$, MeOH
(Bn = benzyl)

Whereas the lithium divinylcuprate from bromide **1d** has been shown to add to α-chiral β-alkoxyaldehydes in ether highly *anti* selectively *via* β-chelation-control,[15] the solvent effects noted in our study

with 2 suggest that *anti* isomers 4 are rather produced *via* a Felkin-Anh transition state, while attack on an α-chelate is responsible for the formation of *syn* isomers 3 [1]

As a rationale for the dependence of diastereoselectivity upon the substitution pattern of the lower order cuprates derived from bromides 1, we propose the following model (Figure 1) A linear[16] divinylcuprate unit[17] attacks aldehyde 2 in such a way that *the π-plane of the vinyl group to be transferred is coplanar to the carbonyl π-plane and coordination of the carbonyl oxygen to copper is possible* This geometric arrangement puts the carbonyl carbon close to the position that is occupied by the bridging lithium atom in dimeric lithium diarylcuprates [18,19] The second vinyl group (L) does not seem to influence the stereochemical course of addition, since the tri-*n*-butylphosphine complex of the lower order mixed lithium cuprate from bromide 1c with L = Me reacts extremely *syn* selectively in ether as well (Scheme 5), albeit less efficiently because of competing addition of the methyl group

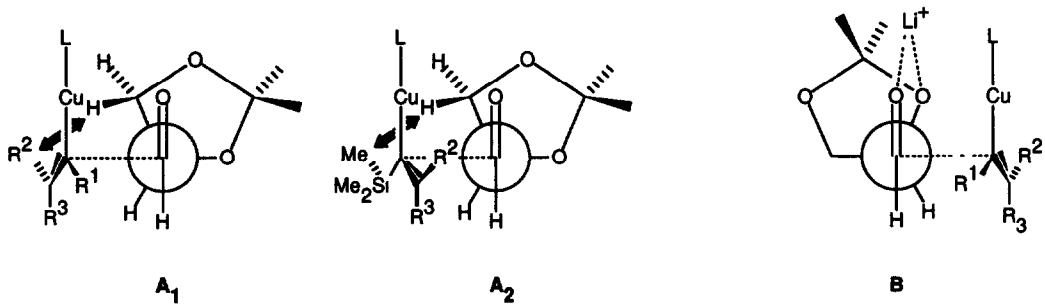
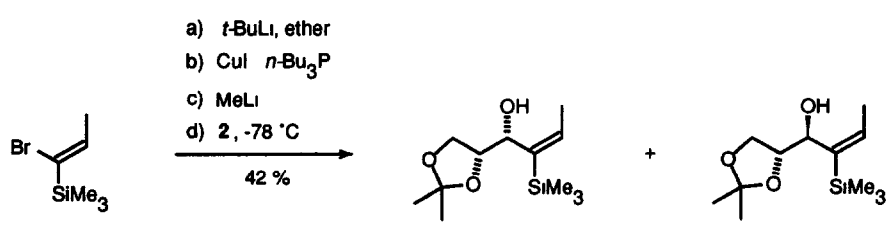


Figure 1 Proposed geometric arrangements for attack of lower order vinylcuprates on 2
A_1 and A_2 lead to *anti* alcohols 4, whereas *syn* alcohols 3 are formed *via* B

For vinylcuprates with both R^2 = alkyl and $R^1 = SiMe_3$, the Felkin-Anh approach or a topologically similar attack on a β-chelate involves a severe nonbonding interaction between the methylene group of 2 and either R^2 (A_1) or $SiMe_3$ (A_2) Attack of these copper species on an α-chelate (B) is sterically preferred and constitutes the nearly exclusive pathway in ether On the other hand, one of the Felkin-Anh ensembles provides a sterically and electronically favorable avenue for vinylcuprates with $R^2 = H$ (A_1) or $R^1 = H$ (A_2) that is followed to a high percentage in THF, where chelation is less important The same arguments can be put forth if the cuprate approaches 2 along the Burgi-Dunitz trajectory[20] rather than in the strictly perpendicular manner depicted in Figure 1



1c 3c 4c

99 6 0 4[a]

Scheme 5. Addition of a lower order mixed lithium cuprate to 2
([a] Ratio determined by capillary GC analysis of the crude product)

EXPERIMENTAL

General Remarks

All reactions were run under argon using flame-dried glassware THF and ether were freshly distilled from benzophenone ketyl Flash chromatography was performed on Merck silica gel 60 (40 - 63 μm). Capillary GC analyses were performed with a Shimadzu GC-14APFsc, a Shimadzu C-R6A integrator, a SE 54 CB column, 50 m length, 0.25 mm i d , 0 25 μm film (column 1), and a SE 54 CB column, 25 m length, 0.25 mm i d , 0 25 μm film (column 2) HPLC separations were performed with a Knauer 64 pump, a Knauer 51 78 differential refractometer, a Knauer 42.00 recorder, a Rheodyne 7125 injector, and a Nucleosil 100 (3 μm) column, 250 mm length, 8 mm i d Optical rotations were measured with a Perkin-Elmer 241 polarimeter ^{1}H NMR spectra (300 MHz, $CDCl_3$) and ^{13}C NMR spectra (75 47 MHz, $CDCl_3$) were obtained on a Bruker WM 300 - m_c = multiplet centered at, br = broad ^{13}C multiplicities were determined using INEPT or DEPT pulse sequences IR spectra (film) were obtained on a Shimadzu IR-408 and a Nicolet 5DXC FT-IR - s = strong, m = medium, w = weak Mass spectra (70 eV) were recorded with a Varian MAT CH-7A and a data system Finnigan MAT 200 (GC/MS) or else with a Varian MAT CH-7 and a data system Varian SS 200 Microanalyses were performed by the analytical laboratory of the Organisch-Chemisches Institut, Universität Münster, and by Mikroanalytisches Laboratorium M Beller, Gottingen

Vinylcuprate Addition to **2** *- General Procedure*

t-BuLi (20 mmol, 1 7 M in pentane) is added to a solution of the alkenyl bromide (10 mmol) in 10 ml solvent at -78 °C and the solution is stirred for 2 h at -50 °C The resulting vinyllithium compound is transferred to a solution of CuI (5 mmol) and *n*-Bu_3P (5 mmol) in 10 ml solvent at -78 °C The mixture is warmed to -40 °C and stirred for 2 h Aldehyde **2** (4 mmol) in 4 ml solvent is added over 20 min at -78 °C and the reaction mixture is allowed to warm to room temperature overnight, poured into ether (50 ml)/sat. aqueous NH_4Cl (50 ml), and extracted with ether (4 x 50 ml) The combined ethereal layers are dried over $MgSO_4$ and the solvent is removed *in vacuo* Flash chromatography using petroleum ether/ethyl acetate/triethylamine mixtures as eluent (95 4 1 for **3a/4a**, **3b/4b**, and **3c/4c**, 94 5 1 for **3d/4d** and **3e/4e**, 85 14 1 for **3f/4f**) affords the products as colorless oils (for combined yields of **3** + **4**, see Table 1) Whereas **3a-d** and **4a,b,d** were obtained as pure stereoisomers by this procedure, subsequent HPLC (eluents as above) was required to secure stereoisomerically homogeneous **3e,f** and **4e,f** For complete data of **3a** and **4a**, see ref 5

Diastereomeric ratios (Table 1) were determined by capillary GC analysis of the crude products using the following columns, initial temperatures, and heating rates - **3a/4a** column 1, 100 °C, 1 °C/min, **3b/4b** column 1, 100 °C, 1 °C/min, **3c/4c** column 2, 90 °C, 1 °C/min, **3d/4d** column 1, 50 °C, 5 °C/min, **3e/4e** after silylation with *N*-methyl-*N*-(trimethylsilyl)trifluoroacetamide (MSTFA), column 2, 100 °C, 5 °C/min, **3f/4f** column 2, 75 °C isothermal

(E)-(1S,4'R)-1-(2,2-Dimethyl-1,3-dioxolane-4-yl)-2-trimethylsilylhept-2-en-1-ol (**3b**) R_f = 0 59 (petroleum ether/ethyl acetate 6 1), $[\alpha]_D^{20}$ = -22 9 (c = 1 0, $CHCl_3$), $[\alpha]_{365}^{20}$ = -75 6 (c = 1 0, $CHCl_3$), ^{1}H NMR δ 0 13 [s, 9 H, $Si(CH_3)_3$], 0 90 (t, 3 H, *J* = 7 1 Hz, 7-H), 1 25 - 1 42 (m, 4 H, 5-H, 6-H), 1 37 [s, 3 H, $C(CH_3)_2$], 1 47 [s, 3 H, $C(CH_3)_2$], 1 99 - 2 11 (m, 1 H, 4-H_a), 2 19 - 2 29 (m, 1 H, 4-H_b), 2 34 (d, 1 H, *J* = 2 3 Hz, OH), 3 62 (dd, 1 H, *J* = 5 7, 8 6 Hz, 5'-H_a), 3 87 (dd, 1 H, *J* = 6 3, 8 6 Hz, 5'-H_b), 4 13 (m_c, apparent dt, 1 H, J_d = 8 2 Hz, J_t = 6 0 Hz, 4'-H), 4 60 (ddd, 1 H, *J* = 0 9, 2 3, 8 3 Hz, 1-H), 5 88 (dt, 1 H, J_d = 1 0 Hz, J_t = 7 1 Hz, 3-H), ^{13}C NMR δ 0 6 [q, $Si(CH_3)_3$], 13 9 (q, C-7), 22 4 (t, C-6), 25 5 [q, $C(CH_3)_2$], 27 2 [q, $C(CH_3)_2$], 29 4 (t), 31 7 (t), 66 0 (t, C-5'), 73 8 (d), 79 3 (d), 109 7 (s, C-2'), 140 1 (s, C-2), 144 5 (d, C-3), IR 3480 (s, OH), 2940 (s, CH), 2850 (s, CH), 1605 (w, C=C), 1450 (w, CH), 1365 [m, $C(CH_3)_2$], 1240 (s), 1210 (s), 1050 (s), 830 (s), 750 (m) cm^{-1}, MS (GC/MS) *m/e* (relative intensity) 271 (M^+ - CH_3, 2), 228 (M^+ - C_3H_6O, 4), 211 (4), 185 (M^+ - $C_5H_9O_2$, 18), 169 (39), 101 ($C_5H_9O_2^+$, 100), 75 (40), 73 ($SiMe_3^+$, 48), 59 ($C_3H_6OH^+$, 14), 43 ($C_3H_7^+$, 32) Anal Calcd for $C_{15}H_{30}O_3Si$ C, 62 89; H, 10 56 Found C, 62 72, H, 10 73

(E)-(1R,4'R)-1-(2,2-Dimethyl-1,3-dioxolane-4-yl)-2-trimethylsilylhept-2-en-1-ol (**4b**) R_f = 0 55 (petroleum ether/ethyl acetate 6 1), $[\alpha]_D^{28}$ = +13.6 (c = 0 85, $CHCl_3$), $[\alpha]_{365}^{28}$ = +28 7 (c = 0 85, $CHCl_3$), ^1H NMR δ 0 13 [s, 9 H, $Si(CH_3)_3$], 0 90 (t, 3 H, *J* = 7 1 Hz, 7-H), 1 26 - 1 39 (m, 4 H, 5-H, 6-H), 1.35 [s, 3 H, $C(CH_3)_2$], 1.42 [s, 3 H, $C(CH_3)_2$], 1 92 (d, 1 H, *J* = 2 2 Hz, OH), 2 03 - 2 27 (m, 2 H, 4-H), 3 93 - 3 96 (m, 2 H, 5'-H), 4 14 (m_c, apparent dt, 1 H, J_d = 5 9 Hz, J_t = 7 2 Hz, 4'-H), 4 80 (m, 1 H, 1-H), 5 82 (dt, 1 H, J_d = 1.7 Hz, J_t = 7 0 Hz, 3-H), ^{13}C NMR δ 0 6 [q, $Si(CH_3)_3$], 13 9 (q, C-7), 22 4 (t, C-6), 25 4 [q, $C(CH_3)_2$], 26 4 [q, $C(CH_3)_2$], 29 7 (t), 31 7 (t), 65 8 (t, C-5'), 72 7 (d), 78 0 (d), 108 9 (s, C-2'), 140 6 (s, C-2), 143 5 (d, C-3), IR 3480 (m, OH), 2950 (s, CH), 2900 (s, CH), 1600 (w, C=C), 1455 (w), 1365 [m, $C(CH_3)_2$], 1240 (m), 1220 (m), 1050 (s), 830 (s), 740 (m) cm^{-1}, MS (GC/MS) *m/e* (relative intensity) 271 (M^+ - CH_3, 2), 228 (M^+ - C_3H_6O, 3), 211 (15), 185 (M^+ - $C_5H_9O_2$, 16), 169 (35), 101 ($C_5H_9O_2^+$, 100), 75 (41), 73 ($SiMe_3^+$, 59), 59 ($C_3H_6OH^+$, 14), 43 ($C_3H_7^+$, 38) Anal Calcd for $C_{15}H_{30}O_3Si$ C, 62 89, H, 10 56 Found C, 62 79, H, 10 84

(E)-(1S,4'R)-1-(2,2-Dimethyl-1,3-dioxolane-4-yl)-2-trimethylsilylbut-2-en-1-ol (**3c**) R_f = 0 53 (petroleum ether/ethyl acetate 6 1), $[\alpha]_D^{20}$ = -15 0 (c = 1 0, $CHCl_3$), $[\alpha]_{365}^{20}$ = -45 8 (c = 1 0, $CHCl_3$), ^1H NMR δ 0 13 [s, 9 H, $Si(CH_3)_3$], 1 38 [s, 3 H, $C(CH_3)_2$], 1 48 [s, 3 H, $C(CH_3)_2$], 1 78 (d, 3 H, *J* = 6 9, 4-H), 2.37 (d, 1 H, *J* = 2 3 Hz, OH), 3 63 (dd, 1 H, *J* = 5 6, 8 6 Hz, 5'-H_a), 3 88 (dd, 1 H, *J* = 6 3, 8 6 Hz, 5'-H_b), 4.15 (ddd, 1 H, *J* = 5 7, 6 3, 8 3 Hz, 4'-H), 4 66 (ddd, 1 H, *J* = 1 2, 2 3, 8 3 Hz, 1-H), 6 03 (dq, 1 H, J_d = 1 2 Hz, J_q = 6 9 Hz, 3-H), ^{13}C NMR δ 0 5 [q, $Si(CH_3)_3$], 15 8 (q, C-4), 25 5 [q, $C(CH_3)_2$], 27 1 [q, $C(CH_3)_2$], 65 8 (t, C-5'), 73 3 (d), 79 3 (d), 109 6 (s, C-2'), 138 1 (s, C-2), 141 5 (d, C-3), IR 3484 (s, OH), 2987 (s, CH), 2974 (s, CH), 2954 (s, CH), 2896 (s, CH), 1614 (w, C=C),1454 (w, CH), 1381 [m, $C(CH_3)_2$], 1372 [m, $C(CH_3)_2$], 1279 (s), 1218 (s), 1067 (s), 841 (s) cm^{-1}, MS (GC/MS) *m/e* (relative intensity) 229 (M^+ - CH_3, 2), 186 (M^+ - C_3H_6O, 7), 169 (4), 143 (M^+ - $C_5H_9O_2$, 16), 127 (33), 101 ($C_5H_9O_2^+$, 100), 75 (30), 73 ($SiMe_3^+$, 30), 59 ($C_3H_6OH^+$, 8), 43 ($C_3H_7^+$, 41) Anal Calcd for $C_{12}H_{24}O_3Si$ C, 58 97, H, 9 90 Found C, 59 18, H, 10 16

(E)-(1R,4'R)-1-(2,2-Dimethyl-1,3-dioxolane-4-yl)-2-trimethylsilylbut-2-en-1-ol (**4c**) MS (GC/MS) *m/e* (relative intensity) 229 (M^+ - CH_3, 2), 186 (M^+ - C_3H_6O, 5), 169 (4), 143 (M^+ - $C_5H_9O_2$, 10), 127 (18), 101 ($C_5H_9O_2^+$, 100), 75 (38), 73 ($SiMe_3^+$, 40), 59 ($C_3H_6OH^+$, 11), 43 ($C_3H_7^+$, 45)

(1S,4'R)-1-(2,2-Dimethyl-1,3-dioxolane-4-yl)-2-trimethylsilylprop-2-en-1-ol (**3d**) [4] R_f = 0 50 (petroleum ether/ethyl acetate 6 1), $[\alpha]_D^{20}$ = -10.7 (c = 1 0, $CHCl_3$), $[\alpha]_{365}^{20}$ = -32 5 (c = 1 0, $CHCl_3$), ref 4 $[\alpha]_D^{25}$ = -10 4 (c = 1 07, $CHCl_3$), ^1H NMR δ 0 16 [s, 9 H, $Si(CH_3)_3$], 1 38 [s, 3 H, $C(CH_3)_2$], 1 46 [s, 3 H, $C(CH_3)_2$], 2.40 (m_c, 1 H, OH), 3 74 (dd, 1 H, *J* = 6 0, 8 5 Hz, 5'-H_a), 3.94 (dd, 1 H, *J* = 6 2, 8 5 Hz, 5'-H_b), 4 12 - 4 17 (m, 2 H, 1-H, 4'-H), 5 52 (dd, 1 H, *J* = 0 4, 2 3 Hz, 3-H_a), 5 81 (dd, 1 H, *J* = 1 0, 2 3 Hz, 3-H_b), ^{13}C NMR δ -0 5 [q, $Si(CH_3)_3$], 25 4 [q, $C(CH_3)_2$], 26 8 [q, $C(CH_3)_2$], 66 2 (t, C-5'), 78 3 (d), 78 5 (d), 109 8 (s, C-2'), 127 4 (t, C-3), 151 5 (s, C-2), IR 3483 (m, OH), 2987 (s, CH), 2955 (s, CH), 2920 (s, CH), 2898 (s, CH), 2878 (s, CH), 1456 (w), 1381 [m, $C(CH_3)_2$], 1372 [m, $C(CH_3)_2$], 1247 (s), 1215 (m), 1157 (m), 1067 (s), 1031 (s), 840 (s), 764 (m) cm^{-1}, MS (GC/MS) *m/e* (relative intensity) 215 (M^+ - CH_3, 3), 172 (M^+ - C_3H_6O, 3), 157 (3), 139 (4), 127 (4), 113 (10), 101 ($C_5H_9O_2^+$, 100), 75 (44), 73 ($SiMe_3^+$, 46), 59 ($C_3H_6OH^+$, 18), 43 ($C_3H_7^+$, 73). Anal Calcd for $C_{11}H_{22}O_3Si$ C, 57 35, H, 9 63 Found C, 57 16, H, 9 84

(1R,4'R)-1-(2,2-Dimethyl-1,3-dioxolane-4-yl)-2-trimethylsilylprop-2-en-1-ol (**4d**) [4] R_f = 0 47 (petroleum ether/ethyl acetate 6 1), $[\alpha]_D^{20}$ = +10 6 (c = 1 0, $CHCl_3$), $[\alpha]_{365}^{20}$ = +11 4 (c = 1 0, $CHCl_3$), ref 4. $[\alpha]_D^{25}$ = +11 5 (c = 1 08, $CHCl_3$), ^1H NMR δ 0 14 [s, 9 H, $Si(CH_3)_3$], 1 38 [s, 3 H, $C(CH_3)_2$], 1 46 [s, 3 H, $C(CH_3)_2$], 2 23 (d, 1 H, *J* = 2 0 Hz, OH), 3 82 (dd, 1 H, *J* = 6 8, 8 2 Hz, 5'-H_a), 3 89 (dd, 1 H, *J* = 7 2, 8 4 Hz, 5'-H_b), 4 22 (m_c, apparent dt, 1 H, J_d = 3 7 Hz, J_t = 6 9 Hz, 4'-H), 4 58 (dd, 1 H, *J* = 1 8, 3 6 Hz, 1-H), 5 53 (dd, 1 H, *J* = 1 6, 2 6 Hz, 3-H_a), 5 99 (dd, 1 H, *J* = 1 9, 2 6 Hz, 3-H_b), ^{13}C NMR δ -0 9 [q, $Si(CH_3)_3$], 25 2 [q, $C(CH_3)_2$], 26 4 [q, $C(CH_3)_2$], 64 0 (t, C-5'), 72 5 (d), 77 6 (d), 109 4 (s, C-2'), 125 5 (t, C-3), 149 8 (s, C-2); IR 3479 (m, OH), 2987 (s, CH), 2957 (s, CH), 2938 (s, CH), 2898 (s, CH), 1457 (w), 1409 (w), 1381 [m, $C(CH_3)_2$], 1372

[m, $C(CH_3)_2$], 1247 (s), 1214 (s), 1158 (s), 937 (s), 839 (s), 759 (m), 691 (m) cm^{-1}, MS (GC/MS) *m/e* (relative intensity). 215 (M^+ - CH_3, 3), 172 (M^+ - C_3H_6O, 3), 157 (2), 139 (4), 127 (3), 113 (10), 101 ($C_5H_9O_2^+$, 100), 75 (34), 73 ($SiMe_3^+$, 43), 59 ($C_3H_6OH^+$, 16), 43 ($C_3H_7^+$, 64) Anal Calcd for $C_{11}H_{22}O_3Si$ C, 57 35, H, 9 63 Found C, 57 26, H, 9 80

(1S,4'R)-1-(2,2-Dimethyl-1,3-dioxolane-4-yl)-3-methyl-2-trimethylsilylbut-2-en-1-ol (**3e**) R_f = 0 49 (petroleum ether/ethyl acetate 6 1), $[\alpha]_D^{20}$ = -13 2 (c = 1 0, $CHCl_3$), $[\alpha]_{365}^{20}$ = -46 4 (c = 1 0, $CHCl_3$), ^1H NMR δ 0 23 [s, 9 H, $Si(CH_3)_3$], 1 37 [s, 3 H, $C(CH_3)_2$], 1 47 [s, 3 H, $C(CH_3)_2$], 1 86 (s, 3 H, 4-H), 1 88 (s, 3 H, 3-CH_3), 2 23 (d, 1 H, *J* = 2 0 Hz, OH), 3 55 (dd, 1 H, *J* = 5 8, 8 5 Hz, 5'-H_a), 3 86 (dd, 1 H, *J* = 6 3, 8 5 Hz, 5'-H_b), 4 23 (m_c, apparent dt, 1 H, J_d = 8 9 Hz, J_t = 6 1 Hz, 4'-H), 4 58 (dd, 1 H, *J* = 2.0, 8 9 Hz, 1-H), ^{13}C NMR δ 2 3 [q, $Si(CH_3)_3$], 22 7 (q, 3-CH_3), 25.6 [q, $C(CH_3)_2$], 26 0 (q, C-4), 27 1 [q, $C(CH_3)_2$], 66 0 (t, C-5'), 75 5 (d), 79 0 (d), 109 6 (s, C-2'), 132 4 (s, C-2), 148 0 (s, C-3), IR 3483 (m, OH), 2986 (s, CH), 2956 (s, CH), 2935 (s, CH), 2899 (s, CH), 2876 (s, CH), 1603 (w, C=C), 1456 (w), 1380 [m, $C(CH_3)_2$], 1371 [m, $C(CH_3)_2$], 1249 (s), 1218 (s), 1158 (m), 1069 (s), 861 (s), 838 (s), 763 (m), 684 (m) cm^{-1}, MS (GC/MS) *m/e* (relative intensity) 258 (M^+, 0 2), 243 (M^+ - CH_3, 0 3), 200 (M^+ - C_3H_6O, 1), 185 (M^+ - $SiMe_3$, 3), 183 (4), 167 (8), 157 (M^+ - $C_5H_9O_2$, 31), 141 (100), 101 ($C_5H_9O_2^+$, 48), 75 (86), 73 ($SiMe_3^+$, 61), 43 ($C_3H_7^+$, 34) Anal Calcd for $C_{13}H_{26}O_3Si$ C, 60 42, H, 10 14 Found C, 60 33, H, 10 22

(1R,4'R)-1-(2,2-Dimethyl-1,3-dioxolane-4-yl)-3-methyl-2-trimethylsilylbut-2-en-1-ol (**4e**) R_f = 0 36 (petroleum ether/ethyl acetate 6 1), $[\alpha]_D^{20}$ = +19 7 (c = 1 0, $CHCl_3$), $[\alpha]_{365}^{20}$ = +66 9 (c = 1 0, $CHCl_3$); ^1H NMR δ 0 22 [s, 9 H, $Si(CH_3)_3$], 1 34 [s, 3 H, $C(CH_3)_2$], 1 40 [s, 3 H, $C(CH_3)_2$], 1 85 (s, 3 H, 4-H), 1 88 (s, 3 H, 3-CH_3), 2 16 (s, 1 H, OH), 3 92 (dd, 1 H, *J* = 6 3, 8 3 Hz, 5'-H_a), 4 06 (dd, 1 H, *J* = 6 0, 8 3 Hz, 5'-H_b), 4 11 - 4 19 (m, apparent q, 1 H, *J* = 7 6 Hz, 4'-H), 4 61 (d, 1 H, *J* = 7 2 Hz, 1-H), ^{13}C NMR δ 2 3 [q, $Si(CH_3)_3$], 22 8 (q, 3-CH_3), 25 4 [q, $C(CH_3)_2$], 26 2 (q, C-4), 26 5 [q, $C(CH_3)_2$], 67 2 (t, C-5'), 74 9 (d), 78 1 (d), 109 0 (s, C-2'), 133 5 (s, C-2), 147 2 (s, C-3), IR 3476 (m, OH), 2987 (s, CH), 2950 (s, CH), 2937 (s, CH), 2916 (s, CH), 2899 (s, CH), 1604 (m, C=C), 1456 (w), 1380 [m, $C(CH_3)_2$], 1371 [m, $C(CH_3)_2$], 1248 (s), 1214 (s), 1158 (m), 1063 (s), 1035 (s), 859 (s), 839 (s), 763 (m), 735 (m), 684 (m) cm^{-1}, MS (GC/MS) *m/e* (relative intensity) 258 (M^+, 0 7), 243 (M^+ - CH_3, 0 8), 200 (M^+ - C_3H_6O, 2), 185 (M^+ - $SiMe_3$, 4), 183 (5), 167 (6), 157 (M^+ - $C_5H_9O_2$, 28), 141 (100), 101 ($C_5H_9O_2^+$, 44), 75 (93), 73 ($SiMe_3^+$, 74), 43 ($C_3H_7^+$, 51) Anal Calcd for $C_{13}H_{26}O_3Si$ C, 60 42, H, 10 14 Found C, 60 56, H, 10 21

(1R,4'R)-1-(2,2-Dimethyl-1,3-dioxolane-4-yl)-3-methylbut-2-en-1-ol (**3f**) R_f = 0 49 (petroleum ether/ethyl acetate 1 1), $[\alpha]_D^{20}$ = -9 8 (c = 1 0, $CHCl_3$), $[\alpha]_{365}^{20}$ = -28 5 (c = 1 0, $CHCl_3$), ^1H NMR δ 1 37 [s, 3 H, $C(CH_3)_2$], 1 46 [s, 3 H, $C(CH_3)_2$], 1 74 (s, 6 H, 4-H, 3-CH_3), 2 25 (br s, 1 H, OH), 3 64 (dd, 1 H, *J* = 5 3, 7 9 Hz, 5'-H_a), 3 93 - 4 02 (m, 2 H, 5'-H_b, 4'-H), 4 26 (dd, 1 H, *J* = 7 1, 9 0 Hz, 1-H), 5 12 (dq, 1 H, J_d = 9 0 Hz, J_q = 1 3 Hz, 2-H), ^{13}C NMR δ 18 6 (q, 3-CH_3), 25 2 [q, $C(CH_3)_2$], 25 8 (q, C-4), 26 8 [q, $C(CH_3)_2$], 65 8 (t, C-5'), 69 9 (d), 79 5 (d), 109 6 (s, C-2'), 122 6 (d, C-2), 138 4 (s, C-3), IR 3454 (s, OH), 2986 (s, CH), 2934 (s, CH), 2916 (s, CH), 2890 (s, CH), 1677 (w, C=C), 1453 (m), 1379 [m, $C(CH_3)_2$], 1372 [m, $C(CH_3)_2$], 1256 (s), 1214 (s), 1158 (s), 1067 (s), 1025 (s), 983 (m), 856 (s), 819 (m) cm^{-1}, MS (GC/MS) *m/e* (relative intensity) 171 (M^+ - CH_3, 3), 143 (M^+ - C_3H_7, 2), 128 (M^+ - C_3H_6O, 4), 111 (9), 101 ($C_5H_9O_2^+$, 100), 85 (M^+ - $C_5H_9O_2$, 63), 73 (22), 59 ($C_3H_6OH^+$, 22), 55 (22), 43 ($C_3H_7^+$, 85) Anal Calcd for $C_{10}H_{18}O_3$ C, 64 49, H, 9 74 Found C, 64 52, H, 9 82

(1S,4'R)-1-(2,2-Dimethyl-1,3-dioxolane-4-yl)-3-methylbut-2-en-1-ol (**4f**) R_f = 0 49 (petroleum ether/ethyl acetate 1 1), $[\alpha]_D^{20}$ = +40 0 (c = 1 0, $CHCl_3$), $[\alpha]_{365}^{20}$ = +132 8 (c = 1 0, $CHCl_3$), ^1H NMR δ 1 37 [s, 3 H, $C(CH_3)_2$], 1 40 [s, 3 H, $C(CH_3)_2$], 1 72 (s, 3 H, 4-H), 1 75 (s, 3 H, 3-CH_3), 1 97 (br s, 1 H, OH), 3 91 - 4 02 (m, 2 H, 5'-H_a, 5'-H_b), 4 07 (m_c, apparent dt, 1 H, J_d = 4 2 Hz, J_t = 8 7 Hz, 4'-H), 4 52 (dd, 1 H, *J* = 4 2, 8 7 Hz, 1-H), 5 09 (dq, 1 H, J_d = 8 7 Hz, J_q = 1 3 Hz, 2-H), ^{13}C NMR δ 18 5 (q, 3-CH_3), 25 2 [q, $C(CH_3)_2$], 25 9 (q,

C-4), 26.4 [q, $C(CH_3)_2$], 64 8 (t, C-5'), 68 0 (d), 78 4 (d), 109.1 (s, C-2'), 122 6 (d, C-2), 138.1 (s, C-3), IR 3450 (s, OH), 2986 (s, CH), 2935 (s, CH), 2916 (s, CH), 2893 (s, CH), 2890 (s, CH), 1677 (w, C=C), 1452 (m), 1379 [s, $C(CH_3)_2$], 1372 [m, $C(CH_3)_2$], 1253 (s), 1214 (s), 1158 (s), 1110 (m), 1067 (s), 983 (m), 856 (s) cm^{-1}; MS (GC/MS) *m/e* (relative intensity)· 171 (M^+ - CH_3, 5), 143 (M^+ - C_3H_7, 5), 128 (M^+ - C_3H_6O, 8), 111 (12), 101 ($C_5H_9O_2^+$, 90), 85 (M^+ - $C_5H_9O_2$, 52), 73 (16), 59 ($C_3H_6OH^+$, 15), 55 (16), 43 ($C_3H_7^+$, 100) Anal Calcd for $C_{10}H_{18}O_3$· C, 64 49, H, 9 74 Found· C, 64.38, H, 9 57

Addition of a Lower Order Mixed Lithium Cuprate to **2**

The vinyllithium compound from **1c** (1.16 g, 6 mmol) prepared in ether as described above is transferred to CuI (1 31 g, 6.87 mmol) and *n*-Bu_3P (1 75 ml, 7 02 mmol) in ether (12 ml) at -78 °C. Subsequent addition of 1 6 M MeLi in hexane (3 75 ml, 6 mmol) at -78 °C and further stirring at -50 °C for 2 h generates the mixed cuprate to which is added **2** (3 64 ml of a 1.15 M ethereal solution, 4 2 mmol) at -78 °C Work-up following the general procedure leads to a crude product containing **3c** **4c** = 99.6·0.4 according to capillary GC Flash chromatography yields pure **3c** (434 mg, 42 %)

Addition of a Vinyllithium Compound to **2**

In ether 1 7 M *t*-BuLi in pentane (2 35 ml, 4 mmol) is added to a solution of **1b** (471 mg, 2 mmol) in ether (6 ml) at -78 °C and stirring is continued for further 15 min at -78 °C Aldehyde **2** (1 72 ml of a 0 7 M ethereal solution, 1 2 mmol) is added at -78 °C and the reaction mixture is allowed to warm to room temperature overnight After hydrolysis with sat. aqueous NH_4Cl, extraction with ether, drying over $MgSO_4$, and removal of the solvent *in vacuo*, capillary GC analysis of the crude product indicates a ratio **3b** **4b** = 56 44 Flash chromatography using petroleum ether/ethyl acetate/triethylamine 92 7 1 as eluent affords pure **3b** (114 mg) and **4b** (91 mg), 60 % combined yield

In THF. 1 41 M *s*-BuLi in cyclohexane (1 72 ml, 2.44 mmol) is added to a solution of **1b** (235 mg, 1 mmol) in THF (3 ml) at -78 °C and stirring is continued for further 15 min at -78 °C Aldehyde **2** (263 mg, 2 02 mmol) in THF (1.5 ml) is added at -78 °C and the reaction mixture is allowed to warm to room temperature overnight. Work-up as described above leads to a crude product containing **3b** **4b** = 46 54 according to capillary GC After flash chromatography, **3b** and **4b** are obtained in a combined yield of 63 % (181 mg)

Isomerization of Adduct **4a**

To a solution of **4a**[5] (287 mg, 1 mmol) in ether (10 ml) is added pyridine (81 µl, 1 mmol) and NBS (10 mg, 0 05 mmol) The resultant mixture is cooled in an ice-bath and irradiated for 45 min using a UV sunlamp (300 W) Additional NBS (10 mg, 0 05 mmol) is added and irradiation is continued for further 45 min This process is repeated until after ca 3 h a ratio **4b**:**4a** = 3 4 1 is reached The solution is decanted and the residue is extracted with ether (10 ml) The combined ethereal solutions are washed successively with 10 ml portions of 10 % aqueous Na_2SO_3, 20 % aqueous $CuSO_4$, sat aqueous NH_4Cl, sat aqueous $NaHCO_3$, and brine After drying over $MgSO_4$ and removal of the solvent *in vacuo*, flash chromatography using petroleum ether/ethyl acetate/triethylamine 92 7 1 as eluent affords pure **4b** (79 mg, 28 %) and a fraction (65 mg) containing a mixture of **4a** and **4b**

Oxygen Assisted Desilylation[10]

Of Vinylsilane **3c** A solution of **3c** (3 39 g, 13 9 mmol) in THF (30 ml) is added at room temperature to a suspension of hexane-washed potassium hydride (80 mg, 2 mmol) in THF (40 ml) After complete conversion (12 h) to the corresponding silyl ether as indicated by TLC, a solution of K_2CO_3 (6 g) in water (10 ml) and methanol (30 ml) are added The mixture is stirred for 1 h at room temperature, treated with sat aqueous

NH_4Cl, adjusted to pH 7, and the aqueous layer is extracted with ether (3 x) The combined ethereal layers are dried over $MgSO_4$, the solvent is removed *in vacuo*, and the residue is purified by flash chromatography using petroleum ether/ethyl acetate/triethylamine 84.15·1 as eluent to give **3g** (1.92 g, 81 %) as a colorless oil

(Z)-(1R,4'R)-1-(2,2-Dimethyl-1,3-dioxolane-4-yl)but-2-en-1-ol (**3g**) R_f = 0 43 (petroleum ether/ethyl acetate 1.1), $[\alpha]_D^{20}$ = -23 9 (c = 1.0, $CHCl_3$), $[\alpha]_{365}^{20}$ = -73 8 (c = 1 0, $CHCl_3$); ^1H NMR δ 1.36 [s, 3 H, $C(CH_3)_2$], 1.46 [s, 3 H, $C(CH_3)_2$], 1 73 (dd, 3 H, J = 1.8, 7 0 Hz, 4-H), 2 33 (d, 1 H, J = 2 8 Hz, OH), 3 66 (dd, 1 H, J = 5.5, 8 2 Hz, 5'-H_a), 3.96 (dd, 1 H, J = 6.5, 8 2 Hz, 5'-H_b), 4 01 - 4.06 (m, 1 H, 4'-H), 4 38 (m_c, apparent dt, 1 H, J_d = 2 4 Hz, J_t = 8.1 Hz, 1-H), 5.36 (ddq, 1 H, J_d = 9 1 Hz, J_d = 11 0 Hz, J_q = 1 8 Hz, 2-H), 5 73 (ddq, 1 H, J_d = 0.8 Hz, J_d = 11 0 Hz, J_q = 7.0 Hz, 3-H); ^{13}C NMR δ 13 7 (q, C-4), 25.2 [q, $C(CH_3)_2$], 26.8 [q, $C(CH_3)_2$], 65.7 (t, C-5'), 68 6 (d), 79 3 (d), 109 7 (s, C-2'), 128 1 (d), 129 4 (d); IR 3458 (s, OH), 2987 (s, CH), 2937 (s, CH), 2921 (s, CH), 2890 (s, CH), 1662 (w, C=C), 1455 (m), 1381 [s, $C(CH_3)_2$], 1371 [m, $C(CH_3)_2$], 1256 (s), 1214 (s), 1158 (s), 1065 (s), 1024 (m), 991 (w), 854 (s), 742 (w) cm^{-1}; MS (GC/MS) *m/e* (relative intensity)· 157 (M^+ - CH_3, 15), 129 (2), 115 (M^+ - C_3H_6O, 3), 102 (13), 101 ($C_5H_9O_2^+$, 100), 97 (16), 73 (20), 43 ($C_3H_7^+$, 38) Anal Calcd for $C_9H_{16}O_3$· C, 62.77; H, 9 36 Found C, 62 73, H, 9 52

Of Vinylsilane **3e** A solution of **3e** (128 mg, 0 495 mmol) in THF (2 ml) is added at room temperature to a suspension of hexane-washed potassium hydride (11 mg, 0 275 mmol) in THF (3 ml) After stirring for 12 h, a solution of K_2CO_3 (0 5 g) in water (1 ml) and methanol (3 ml) are added Following the procedure for desilylation of **3c** described above, **3f** (88 mg, 95 %) is obtained after flash chromatography.

Benzylation

Of Alcohol **3g**. A solution of **3g** (159 mg, 0 92 mmol) in DMF (7 ml) is added at room temperature to a suspension of 80 % sodium hydride (56 mg, 1 85 mmol) in DMF (5 ml) The mixture is stirred for 15 min, treated with benzylbromide (165 µl, 1 38 mmol), and stirring is continued for further 3 h After hydrolysis with sat aqueous NH_4Cl, extraction with ether, drying over $MgSO_4$, and removal of the solvent *in vacuo*, the residue is purified by flash chromatography using petroleum ether/ether 5 1 as eluent to give **5g** (202 mg, 83 %) as a colorless oil

(Z)-(1R,4'R)-1-Benzyloxy-1-(2,2-dimethyl-1,3-dioxolane-4-yl)but-2-ene (**5g**) R_f = 0 55 (petroleum ether/ethyl acetate 6 1), $[\alpha]_D^{20}$ = -21 0 (c = 1 0, $CHCl_3$), $[\alpha]_{365}^{20}$ = -51 4 (c = 1 0, $CHCl_3$), ^1H NMR δ 1.36 [s, 3 H, $C(CH_3)_2$], 1 41 [s, 3 H, $C(CH_3)_2$], 1 62 (dd, 3 H, J = 1 7, 7 1 Hz, 4-H), 3 65 (dd, 1 H, J = 6 0, 8.4 Hz, 5'-H_a), 3 94 (dd, 1 H, J = 6 5, 8 4 Hz, 5'-H_b), 4 17 - 4 23 (m, 2 H, 4'-H, 1-H), 4 45 (d, 1 H, J = 12 4 Hz, Ph-CH_a), 4 67 (d, 1 H, J = 12 4 Hz, Ph-CH_b), 5.25 - 5 37 (m, 1 H, 2-H), 5 73 (dq, 1 H, J_d = 11 3 Hz, J_q = 7.0 Hz, 3-H), 7 27 - 7 37 (m, 5 H, H_{arom}); ^{13}C NMR δ 13 7 (q, C-4), 25 3 [q, $C(CH_3)_2$], 26 4 [q, $C(CH_3)_2$], 65 6 (t, C-5'), 69 6 (t, Ph-CH_2), 74 3 (d), 78.0 (d), 109.5 (s, C-2'), 126 6 (d), 127 2 (d), 127 6 (d), 128 0 (d), 130.6 (d), 138 4 (s), IR 3064 (w), 3024 (w), 2986 (s, CH), 2935 (s, CH), 2919 (s, CH), 2885 (s, CH), 1497 (w, C=C_{arom}), 1455 (s), 1380 [s, $C(CH_3)_2$], 1370 [m, $C(CH_3)_2$], 1258 (s), 1214 (s), 1158 (s), 1087 (s), 1072 (s), 1029 (m), 969 (w), 944 (w), 919 (w), 853 (s), 735 (s, CH_{arom}), 698 (s, CH_{arom}) cm^{-1}, MS (GC/MS) *m/e* (relative intensity): 247 (M^+ - CH_3, 4), 162 (5), 161 (M^+ - $C_5H_9O_2$, 24), 102 (5), 101 ($C_5H_9O_2^+$, 68), 92 (9), 91 ($C_7H_7^+$, 100), 73 (12), 65 ($C_5H_5^+$, 9), 43 ($C_3H_7^+$, 18) HRMS Calcd for $C_{15}H_{19}O_3$ (M^+ - CH_3) 247 1334 Found 247 1339

Of Alcohol **3f** Following the procedure for benzylation of **3g** described above, from **3f** (96 mg, 0 52 mmol) in DMF (4 ml), 80 % sodium hydride (30 mg, 1 03 mmol) in DMF (5 ml), and benzylbromide (92 µl, 0 77 mmol) **5f** (121 mg, 85 %) is obtained as a colorless oil after flash chromatography using petroleum ether/ether 5·1 as eluent.

(1R,4'R)-1-Benzyloxy-1-(2,2-dimethyl-1,3-dioxolane-4-yl)-3-methylbut-2-ene (**5f**). R_f = 0 59 (petroleum ether/ethyl acetate 6:1); $[\alpha]_D^{20}$ = -32 3 (c = 1.0, $CHCl_3$), $[\alpha]_{365}^{20}$ = -92.3 (c = 1 0, $CHCl_3$); ^{1}H NMR δ 1.36 [s, 3 H, $C(CH_3)_2$], 1.40 [s, 3 H, $C(CH_3)_2$], 1.61 (d, 3 H, *J* = 1 3 Hz, 4-H), 1 77 (d, 3 H, *J* = 1.2 Hz, 3-CH_3), 3.61 (dd, 1 H, *J* = 6 5, 8.4 Hz, 5'-H_a), 3 92 (dd, 1 H, *J* = 6 6, 8 4 Hz, 5'-H_b), 4 09 (dd, 1 H, *J* = 7 1, 9 6 Hz, 1-H), 4.16 - 4 23 (m, 1 H, 4'-H), 4 44 (d, 1 H, *J* = 12 5 Hz, Ph-CH_a), 4.65 (d, 1 H, *J* = 12.5 Hz, Ph-CH_b), 5.06 (d, 1 H, *J* = 9 7 Hz, 2-H), 7.22 - 7 37 (m, 5 H, H_{arom}), ^{13}C NMR δ 18 7 (q, C-4), 25 4 [q, $C(CH_3)_2$], 25 9 (q, 3-CH_3), 26.5 [q, $C(CH_3)_2$], 65 8 (t, C-5'), 69 5 (t, Ph-CH_2), 76.0 (d), 78 3 (d), 109.6 (s, C-2'), 121 3 (d, C-2), 127.2 (d), 127.7 (d), 128.1 (d), 138.7 (s), 139.2 (s); IR 3064 (w), 3031 (w), 2985 (s, CH), 2934 (s, CH), 2914 (s, CH), 2885 (s, CH), 1674 (w, C=C), 1497 (w, C=C_{arom}), 1454 (s), 1379 [s, $C(CH_3)_2$], 1370 [m, $C(CH_3)_2$], 1258 (s), 1213 (s), 1158 (s), 1112 (s), 1087 (s), 1072 (s), 1029 (m), 983 (w), 943 (w), 853 (s), 821 (w), 737 (s, CH_{arom}), 698 (s, CH_{arom}) cm^{-1}; MS (GC/MS) *m/e* (relative intensity) 261 (M^+ - CH_3, 0 7), 176 (4), 175 (M^+ - $C_5H_9O_2$, 30), 101 ($C_5H_9O_2^+$, 12), 92 (8), 91 ($C_7H_7^+$, 100), 83 (9), 73 (6), 65 ($C_5H_5^+$, 8), 43 ($C_3H_7^+$, 18) HRMS Calcd for $C_{16}H_{21}O_3$ (M^+ - CH_3): 261.1491 Found· 261 1486

Of Alcohol **4f** Following the procedure for benzylation of **3g** described above, from **4f** (540 mg, 2 90 mmol) in DMF (20 ml), 80 % sodium hydride (155 mg, 6 46 mmol) in DMF (20 ml), and benzylbromide (574 µl, 4.83 mmol) **7f** (379 mg, 47 %, 65 % on conversion) as a colorless oil and reisolated educt **4f** (145 mg, 0 78 mmol) are obtained after flash chromatography using petroleum ether/ether/triethylamine 87 · 12 1 as eluent

(1S,4'R)-1-Benzyloxy-1-(2,2-dimethyl-1,3-dioxolane-4-yl)-3-methylbut-2-ene (**7f**). R_f = 0 57 (petroleum ether/ethyl acetate 6 1), $[\alpha]_D^{20}$ = +53 2 (c = 1 0, $CHCl_3$), $[\alpha]_{365}^{20}$ = +163 2 (c = 1 0, $CHCl_3$), ^{1}H NMR δ 1 35 [s, 3 H, $C(CH_3)_2$], 1 40 [s, 3 H, $C(CH_3)_2$], 1 66 (d, 3 H, *J* = 1 0 Hz, 4-H), 1 82 (d, 3 H, *J* = 1.0 Hz, 3-CH_3), 3 91 (m_c, 1 H), 4 02 - 4 10 (m, 3 H), 4 36 (d, 1 H, *J* = 12 0 Hz, Ph-CH_a), 4 59 (d, 1 H, *J* = 12 0 Hz, Ph-CH_b), 5 15 (dq, 1 H, J_d = 9.7 Hz, J_q = 1 3 Hz, 2-H), 7 27 - 7 33 (m, 5 H, H_{arom}), ^{13}C NMR δ 18.6 (q, C-4), 25 3 [q, $C(CH_3)_2$], 26.1 (q, 3-CH_3), 26 5 [q, $C(CH_3)_2$], 66 7 (t, C-5'), 69 8 (t, Ph-CH_2), 75 7 (d), 78.0 (d), 109 2 (s, C-2'), 122 4 (d, C-2), 127 4 (d), 127 7 (d), 128 2 (d), 138 6 (s), 138 9 (s), IR 3065 (w), 3031 (w), 2987 (s, CH), 2934 (s, CH), 2915 (s, CH), 2882 (s, CH), 1677 (w, C=C), 1479 (w, C=C_{arom}), 1454 (s), 1380 [s, $C(CH_3)_2$], 1370 [m, $C(CH_3)_2$], 1255 (s), 1212 (s), 1158 (s), 1121 (m), 1074 (s), 1048 (m), 1029 (s), 984 (w), 963 (w), 853 (s), 737 (s, CH_{arom}), 699 (s, CH_{arom}) cm^{-1}, MS (GC/MS) *m/e* (relative intensity) 261 (M^+ - CH_3, 0.3), 176 (6), 175 (M^+ - $C_5H_9O_2$, 42), 101 ($C_5H_9O_2^+$, 12), 92 (9), 91 ($C_7H_7^+$, 100), 83 (8), 73 (4), 65 ($C_5H_5^+$, 6), 43 ($C_3H_7^+$, 7) HRMS Calcd for $C_{12}H_{15}O$ (M^+ - $C_5H_9O_2$)· 175 1123 Found 175 1127

Ozonolysis

Of Alkene **5g**. A solution of **5g** (147 mg, 0.56 mmol) in CH_2Cl_2 (50 ml) is ozonized at -78 °C until the mixture turns blue. Excess ozone is removed by purging with argon. Methanol (20 ml) and sodium borohydride (50 mg, 1 32 mmol) are added and after stirring for 1 h at -78 °C, the mixture is allowed to warm to room temperature overnight After hydrolysis with sat. aqueous NH_4Cl, extraction with ethyl acetate (4 x), drying over $MgSO_4$, and removal of the solvent *in vacuo*, the residue is purified by flash chromatography using petroleum ether/ethyl acetate 1 1 as eluent to give **6** (100 mg, 71 %, 83 % on conversion) as a colorless oil and reisolated educt **5g** (21 mg, 0 08 mmol)

Of Alkene **5f** Following the procedure for ozonolysis of **5g** described above, from **5f** (79 mg, 0 286 mmol), methanol (50 ml), and sodium borohydride (25 mg, 0 66 mmol) **6** (49 mg, 68 %) is obtained as a colorless oil after flash chromatography

(1R,4'R)-1-Benzyloxy-1-(2,2-dimethyl-1,3-dioxolane-4-yl)ethan-2-ol (**6**) [11] R_f = 0 38 (petroleum ether/ethyl acetate 1 1), $[\alpha]_D^{20}$ = +15 6 (c = 1 0, $CHCl_3$), $[\alpha]_{365}^{20}$ = +50 0 (c = 1 0, $CHCl_3$) [optical rotation for the

enantiomer - ref 12 $[\alpha]_D$ = -16.4 (c = 0.18, $CHCl_3$), ref 13 $[\alpha]_D$ = -14.1 (c = 0 6, $CHCl_3$)]; ^{1}H NMR δ 1.37 [s, 3 H, $C(CH_3)_2$], 1 44 [s, 3 H, $C(CH_3)_2$], 2 11 (m_c, 1 H, OH), 3 56 - 3 62 (m, 2 H, 1-H, 2-H_a), 3.73 (m_c, 1 H, 2-H_b), 3.82 (m_c, apparent t, 1 H, J = 7 7 Hz, 5'-H_a), 4 01 (dd, 1 H, J = 6 7, 8 3 Hz, 5'-H_b), 4 31 (m_c, apparent q, 1 H, J = 6 5 Hz, 4'-H), 4 69 (d, 1 H, J = 11 9 Hz, Ph-CH_a), 4.77 (d, 1 H, J = 11 9 Hz, Ph-CH_b), 7.30 - 7.36 (m, 5 H, H_{arom}); ^{13}C NMR δ 25 3 [q, $C(CH_3)_2$], 26 4 [q, $C(CH_3)_2$], 61 7 (t, C-2), 65 5 (t, C-5'), 72.8 (t, Ph-CH_2), 76 6 (d, C-1), 79 2 (d, C-4'), 109 4 (s, C-2'), 127 81 (d), 127 84 (d), 128 4 (d), 138 2 (s); IR 3056 (s, OH), 2987 (s, CH), 2935 (s, CH), 2884 (s, CH), 1497 (m, C=C_{arom}), 1455 (s), 1381 [s, $C(CH_3)_2$], 1372 [m, $C(CH_3)_2$], 1257 (s), 1214 (s), 1158 (s), 1134 (s), 1073 (s), 1062 (s), 1029 (m), 854 (s), 739 (s, CH_{arom}), 699 (s, CH_{arom}) cm^{-1}, MS (GC/MS) *m/e* (relative intensity) 237 (M^+ - CH_3, 4), 194 (M^+ - C_3H_6O, 8), 163 (4), 145 (2), 134 (4), 120 (4), 101 ($C_5H_9O_2^+$, 37), 92 (12), 91 ($C_7H_7^+$, 100), 73 (10), 65 ($C_5H_5^+$, 9), 59 (10), 43 ($C_3H_7^+$, 18)

Of Alkene **7f** Following the procedure for ozonolysis of **5g** described above, from **7f** (240 mg, 0 87 mmol), CH_2Cl_2 (70 ml), methanol (30 ml), and sodium borohydride (90 mg, 2 4 mmol) **8** (170 mg, 78 %) is obtained as a colorless oil after HPLC using petroleum ether/ethyl acetate 1 1 as eluent.

(1S,4'R)-1-Benzyloxy-1-(2,2-dimethyl-1,3-dioxolane-4-yl)ethan-2-ol (**8**) [14] R_f = 0 45 (petroleum ether/ethyl acetate 1 1), ^{1}H NMR δ 1 36 [s, 3 H, $C(CH_3)_2$], 1 42 [s, 3 H, $C(CH_3)_2$], 2.17 (s, 1 H, OH), 3 53 (m_c, apparent dt, 1 H, J_d = 6 4 Hz, J_t = 4 2 Hz, 1-H), 3 71 (dd, 1 H, J = 4 2, 12 1 Hz, 2-H_a), 3 84 (dd, 1 H, J = 4 5, 12 1 Hz, 2-H_b), 3 88 (dd, 1 H, J = 5 7, 8 3 Hz, 5'-H_a), 4 09 (dd, 1 H, J = 6 4, 8 3 Hz, 5'-H_b), 4 19 (m_c, apparent q, 1 H, J = 6.3 Hz, 4'-H), 4 66 (m_c, 2 H, Ph-CH_2), 7 30 - 7 39 (m, 5 H, H_{arom}), ^{13}C NMR δ 25 1 [q, $C(CH_3)_2$], 26 5 [q, $C(CH_3)_2$], 61 8 (t, C-2), 66 8 (t, C-5'), 72 6 (t, Ph-CH_2), 75 8 (d, C-1), 79 7 (d, C-4'), 109 2 (s, C-2'), 127 8 (d), 127 9 (d), 128 5 (d), 137 9 (s), MS (GC/MS) *m/e* (relative intensity)· 252 (M^+, 0 5), 237 (M^+ - CH_3, 2), 194 (M^+ - C_3H_6O, 5), 163 (3), 145 (2), 134 (4), 120 (4), 101 ($C_5H_9O_2^+$, 35), 92 (12), 91 ($C_7H_7^+$, 100), 73 (10), 65 ($C_5H_5^+$, 13), 59 (10), 43 ($C_3H_7^+$, 38)

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REFERENCES AND NOTES

1 Jurczak, J , Pikul, S , Bauer, T *Tetrahedron* **1986**, *42*, 447-488

2 Lipshutz, B H In *Comprehensive Organic Synthesis, Vol 1, Additions to C-X π Bonds, Part 1*, Schreiber, S L , Ed , Pergamon Press Oxford, 1991, pp 107-138

3 Sato, F , Kobayashi, Y , Takahashi, O , Chiba, T , Takeda, Y , Kusakabe, M *J Chem Soc , Chem Commun* **1985**, 1636-1638

4 Kusakabe, M , Sato, F *J Chem Soc , Chem Commun* **1986**, 989-991

5 Metz, P , Mues, C , Schoop, A *Tetrahedron* **1992**, *48*, 1071-1080

6 For recent reports on the preparation and stability of **2**, see (a) Jackson, D Y *Synth Commun* **1988**, *18*, 337-341 (b) Schmid, C R., Bryant, J D , Dowlatzedah, M , Phillips, J. L , Prather, D E ; Schantz, R D ; Sear, N L , Vianco, C S *J Org Chem* **1991**, *56*, 4056-4058 (c) Hertel, L W , Grossman, C. S , Kroin, J S *Synth Commun* **1991**, *21*, 151-154

7 **1d** and **1f** are commercially available For the preparation of the other alkenyl bromides used, see (a) Zweifel, G , Lewis, W *J Org Chem* **1978**, 43, 2739-2744 (**1a**, **1b**) (b) Fukuzaki, K ; Nakamura, E , Kuwajima, I *Tetrahedron Lett* **1984**, *25*, 3591-3594 (**1c**) (c) Shimizu, N , Shibata, F., Tsuno, Y. *Bull Chem Soc Jpn* **1987**, *60*, 777-778 (**1e**)

8 Takeda, Y , Matsumoto, T.; Sato, F *J Org Chem.* **1986**, *51*, 4728-4731
9. Zweifel, G.; On, H. P. *Synthesis* **1980**, 803-805.
10 Sato, F.; Tanaka, Y.; Sato, M. *J Chem Soc , Chem Commun* **1983**, 165-166.
11 Fujita, K.; Nakai, H.; Kobayashi, S ; Inoue, K ; Nojima, S , Ohno, M. *Tetrahedron Lett* **1982**, *23*, 3507-3510.
12 Valverde, S., Herradon, B ; Martin-Lomas, M *Tetrahedron Lett* **1985**, *26*, 3731-3734
13 Al-Hakim, A. H., Haines, A H ; Morley, C. *Synthesis* **1985**, 207-208.
14 For the enantiomer of **8**, see Williams, D R ; Moore, J. L.; Yamada, M *J Org Chem* **1986**, *51*, 3916-3918.
15 Burke, S D ; Piscopio, A. D., Marron, B. E., Matulenko, M A ; Pan, G. *Tetrahedron Lett* **1991**, *32*, 857-858.
16. Hope, H ; Olmstead, M. M ; Power, P. P., Sandell, J., Xu, X *J. Am. Chem Soc* **1985**, *107*, 4337-4338.
17. The term "unit" refers to either a mononuclear entity or a CuR_2 moiety of a partially opened polynuclear aggregate
18. Lorenzen, N P.; Weiss, E *Angew Chem* **1990**, *102*, 322-324; *Angew Chem Int Ed Engl* **1990**, *29*, 300.
19. van Koten, G., Jastrzebski, J T. B H *J Am Chem Soc* **1985**, *107*, 697-698.
20 Bürgi, H. B ; Dunitz, J. D., Lehn, J M., Wipff, G *Tetrahedron* **1974**, *30*, 1563-1572