$(PMe_3)_4Ru_4(OAc)Cl$, 88968-54-1; $Ru(PMe_3)_4Cl_2$, 96615-09-7; $HOCHMe_2$, 67-63-0; $H_2C{=}CH_2$, 74-85-1; $PhC{\equiv}N$, 100-47-0; PMe_3-d_9, 22529-57-3; acetophenone, 98-86-2; *p*-cresol, 106-44-5; aniline, 62-53-3; di-*p*-tolylacetylene, 2789-88-0; benzaldehyde, 100-52-7; ethylene-*1,1*-d_2, 6755-54-0; styrene-β,β-d_2, 934-85-0; styrene-α,α-d_2, 93185-51-4.

Supplementary Material Available: Tables of general temperature factor expressions (*B*'s), positional parameters and their estimated standard deviations, and root mean square amplitudes of anisotropic displacements for **9** and **15** (4 pages). Ordering information is given on any current masthead page. Analogous data for the structure of **1** have been submitted as supplementary material with the previously published communication.[8]

Enantioselective Aldol Chemistry via Alkyl Enol Ethers. Scope of the Lewis Acid Catalyzed Condensation of Optically Active Trimethylsilyl and Methyl 2-[(*E*)-1-Alkenyloxy]ethanoates with Acetals

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Abstract: Optically active, mono- and disubstituted trimethylsilyl 2-[(*E*)-1-alkenyloxy]ethanoates of the type $RR^1CH{=}CHOCHR^2CO_2SiMe_3$ (R = Me, $PhCH_2$, *n*-Bu, $MeO_2CCMe_2CH_2$, $PhSCH_2$; R^1 = H, Me; R^2 = Me, c-C_6H_{11}) undergo highly diastereoselective, Lewis acid catalyzed reactions with aliphatic and aromatic acetals $R^3CH(OR^4)_2$ (R^3 = H, Me, *t*-Bu, Ph; R^4 = Me, CH_2Ph) to afford *cis*-2-[$RR^1CH(R^3CHOR^4)$]-5-R^2-1,3-dioxolanones corresponding to erythro-diastereoselective aldol reactions involving net syn-periplanar addition of the acetal-derived electrophile and trimethylsilyl ester oxygen across the enol ether double bond. Analysis of the alcohols $RR^1C(R^3CHOR^4)CH_2OH$ obtained by reductive removal of the ethanoate auxiliary reveals the following points. (1) Enantiomeric excesses in the range 90–98% ee are possible with dimethyl and dibenzyl acetals derived from formaldehyde, acetaldehyde, pivalaldehyde, and benzaldehyde. (2) The aldol reactions are moderately to highly erythro diastereoselective (e/t = 4:1–99:1), even when quaternary and tertiary centers are juxtaposed (R^1 = Me; e/t = 13:1–32:1). (3) The highest diastereoselectivities are observed with a bulky cyclohexyl substituent at the primary chiral center (R^2 = Cy); however, diastereoselectivities as high as 88% ee are possible even with lactic acid derivatives (R^2 = Me). (4) The enantiomeric excesses are catalyst dependent, with Me_3SiOTf giving slightly better results than Ph_3CSbCl_6 in reactions with benzaldehyde dimethyl acetal but Ph_3CSbCl_6 giving much better results than Me_3SiOTf in reactions with acetaldehyde dimethyl acetal. (5) Perhaps most notably, *the diastereoselectivities are remarkably insensitive to changes in substitution at the nucleophilic enol ether carbon*, so that essentially identical results are observed regardless of whether R = $PhCH_2$, $MeO_2CCMe_2CH_2$, or $PhSCH_2$ and regardless of whether R^1 = H or Me. Reaction of the symmetrically disubstituted enol ether $Me_2C{=}CHOCH(c\text{-}C_6H_{11})CO_2SiMe_3$ with $PhCH(OMe)_2$ affords, after reduction with $LiAlH_4$, $Me_2C(PhCHOMe)CH_2OH$ of 94% ee. PhCHO and $PhCH_2CH{=}CHOCH(c\text{-}C_6H_{11})CO_2SiMe_3$ undergo a similar reaction to afford, after aqueous workup and reduction, *threo*-$PhCH_2CH(PhCHOH)CH_2OH$ (e/t = 1:13; 98% ee). The corresponding methyl ester, $PhCH_2CH{=}CHOCH(c\text{-}C_6H_{11})CO_2Me$, undergoes related aldol condensation/transacetalization chemistry upon reaction with the same acetals and Me_3SiOTf to afford *erythro*-$PhCH_2CH(R^3CHOR^4)CH(OR^4)_2$ products in 61–86% nonoptimized yield, with erythro/threo ratios and enantiomeric excesses identical with those observed for the corresponding trimethylsilyl ester reaction products.

Introduction

Enantioselective aldol reactions[1-6] are among the most powerful and versatile means of introducing stereochemistry and functionality in organic synthesis. A variety of metal enolate,[2] metalloid enolate,[3] allylborane,[4] allylboronic ester,[5] and other methods[6] have been developed for this purpose; we report herein the first *alkyl* enol ether based approach,[7] involving the Lewis acid catalyzed condensation of acetals with optically active trimethylsilyl and methyl 2-[(*E*)-1-alkenyloxy]ethanoates.[8] Our interest in these reactions was stimulated, initially, by the ready availability of optically active 2-[(*E*)-1-alkenyloxy]ethanoic acid esters[9,10] and, subsequently, by the potential of these enol ethers to undergo reactions analogous to the Lewis acid catalyzed reactions of silyl enol ethers with acetals[11] (eq 1).

In particular, we speculated that trimethylsilyl 2-[(*E*)-1-alkenyloxy]ethanoates would undergo oxocarbenium ion induced cyclization to give a charged intermediate, which would lose a trimethylsilyl cation from oxygen to afford a neutral, protected aldol product (eq 2).

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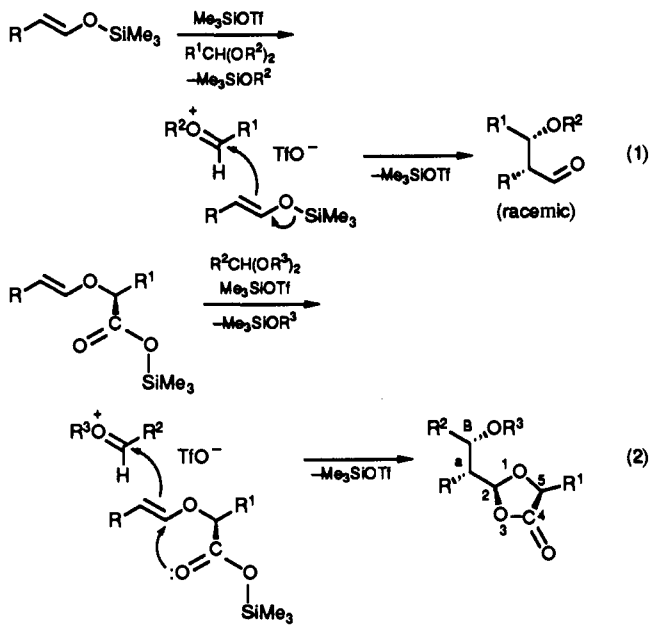
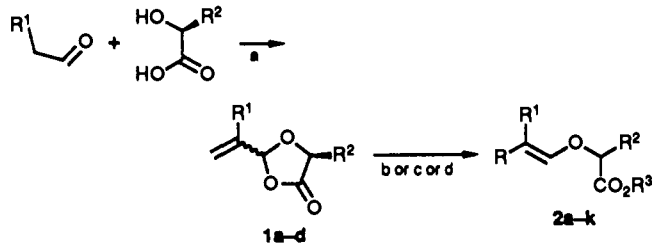


By loose analogy with iodolactonization chemistry,[12] we reasoned that oxocarbenium ion attack and cyclization might be *concerted*[13] and involve *antiperiplanar* addition across the enol ether double bond, so that ring conformational preferences associated with the nascent dioxolanone ring would correlate the stereochemistry at C(5) with that at C(2), which would, in turn, be correlated with that at C(α) (cf. eq 2). Given control of stereochemistry at C(α), we anticipated that Coulombic and steric effects analogous to those responsible for the erythro diastereoselectivity of the corresponding silyl enol ether reaction would correlate the stereochemistry at C(β) with that at C(α). In the event, successful reactions are observed but give rise to erythro aldol products corresponding to (net) syn-periplanar addition across the enol ether double bond. We describe herein the scope and limitations of these reactions; studies of the reaction mechanism are in progress and will be the subject of a future report.[14]

Starting Materials

As will be discussed in more detail elsewhere,[9,10] the enol ether starting materials were prepared via (a) initial condensation of acrolein or methacrolein with commercially available (*S*)-lactic acid or (*R*)- or (*S*)-hexahydromandelic acid to afford the corresponding 2-ethenyl-1,3-dioxolanones **1a–d** in 21–86% yield (Scheme I), followed by (b) nickel- or palladium-catalyzed conjugate addition of organotin or organoborate nucleophiles,[10] by (c) (stoichiometric) nickel-mediated coupling reactions with halocarbon electrophiles[9] and organometallic nucleophiles,[10] or by (d) Lewis acid catalyzed conjugate addition of trimethylsilylketene acetals or $PhSSiMe_3$[15] to afford optically active, mono- and disubstituted trimethylsilyl and methyl 2-[(*E*)-1-alkenyloxy]ethanoates **2a–k** (*E*/*Z* = 96:4–100:0) in 31–86% yield (Scheme I, Table I).

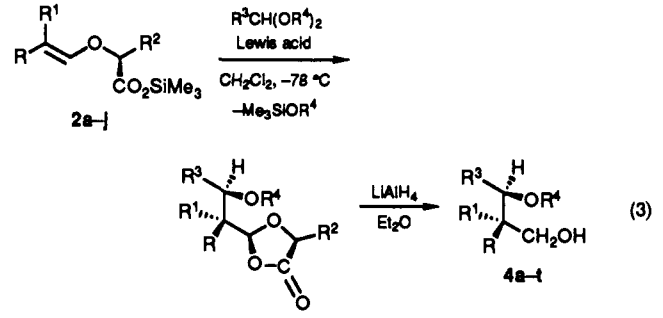
Scheme I[a]



[a] Cy = cyclohexyl. (a) 1 mol % TsOH. **1a**: R^1 = H, R^2 = Cy, 86%. **1b**: R^1 = H, R^2 = Me, 34%. **1c**: R^1 = Me, R^2 = Cy, 80%. **1d**: R^1 = Me, R^2 = Me, 21%. (b) (R^1 = H, Me; R = CH_2Ph) (i) $NaBPh_4$, 0.1 mol % $(CH_3CN)_2PdCl_2$; (ii) (R^3 = $SiMe_3$) Me_3SiCl; (ii) (R^3 = Me) MeI. (R^1 = H, Me; R = $CH_2CH{=}CH_2$) (i) $H_2C{=}CHSnBu_3$, LiCl, 2.5 mol % $(PhCH{=}CHC(O)CH{=}CHPh)_3Pd_2$; (ii) ($R^3$ = $SiMe_3$) Me_3SiCl. (c) (one-pot) (R^1 = H, Me; R = CH_2R^0; R^3 = Me_3Si) (i) $Ni(1,5\text{-}COD)_2$; (ii) TMSCl; (iii) $R^0X/h\nu$; R^0 = Ph, $H_2CH{=}CH$, Bu; (iv) $NaHB(OMe)_3$; R^0 = H. (d) (R^1 = H, Me; R = $CH_2CMe_2CO_2Me$; R^3 = Me_3Si) $(Me_3SiO)(MeO)CCMe_2$, 10 mol % Me_3SiOTf. (R^1 = Me; R = CH_2SPh) $PhSSiMe_3$, 10 mol % Me_3SiOTf.

Aldol Reactions

In the presence of Lewis acid catalysts such as Me_3SiOTf or Ph_3CSbCl_6, trimethylsilyl 2-[(*E*)-1-alkenyloxy]ethanoates **2a–j** were found to react with dimethyl and dibenzyl acetals to afford protected aldol products **3a–t** in 44–89% yield; subsequent reduction with $LiAlH_4$ afforded the corresponding alcohols **4a–t** (eq 3, Lewis acid = Me_3SiOTf or Ph_3CSbCl_6, Table II).



X-ray crystallography[16] showed both **3g** and **3r** to be *cis*-2,5-disubstituted-1,3-dioxolanones corresponding to erythro-diastereoselective reactions involving (net) syn-periplanar addition of the acetal-derived electrophile and ester oxygen nucleophile across the enol ether double bond. Similar stereochemical relationships were established for **3e**, **3j**, and **3a**. In the case of **3e**, the results of NOE experiments (see under Experimental Section) on **3e** and its C(2) epimer clearly support a *cis*-2,5-disubstituted-1,3-dioxolanone geometry. Optical rotation results showed the reduction product **4e** to correspond to the *enantiomer* of the known compound (2*S*)-2-[(benzyloxy)methyl]-3-phenyl-1-propanol.[17] Reduction of **3j** to alcohol **4j**, followed by reductive demethoxylation and Jones oxidation, similarly afforded the *enantiomer* of the known compound (2*S*)-2-benzyl-1-hexanoic acid,[18] in agreement with the above results. Compound **3a** was shown to be the erythro product by establishing that the dimethyl ether obtained by O-methylation of alcohol **4a** was *not* the threo diastereomer (the preparation of which is described below).

Quantitative stereochemical analysis of the erythro alcohols derived from reduction of the *unenriched* aldol products reveals

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(13) Factors that should tend to favor a concerted (albeit presumably highly nonsynchronous) mechanism include (1) the electron-withdrawing nature of the $CHR^2CO_2SiMe_3$ group, which should destabilize a $RCH(R^3CHOR^4)CH{=}O^+CHR^2CO_2SiMe_3$ oxocarbenium ion intermediate in a stepwise mechanism, (2) dipole–dipole interactions between the incipient oxocarbenium ion and the pendant trimethylsilyl ester, which should tend to hold the ester carbonyl oxygen near the oxocarbenium ion carbon in the transition state, and (3) the relatively limited conformational mobility of the pendant trimethylsilyl ester side chain, the flexibility of which should be diminished by virtue of restricted rotation about the $RCHCH{-}OCHR^2CO_2SiMe_3$ bond, arising from oxygen to carbon electron donation in the transition state (i.e., partial oxocarbenium ion character), and by the tendency of 2-alkoxyethanoates to adopt a conformation in which the alkoxy oxygen to C(2) bond lies in the plane of the ester: Trost, B. M.; Belletire, J. L.; Godleski, S.; McDougal, P. G.; Balkovec, J. M.; Baldwin, J. J.; Christy, M. E.; Ponticello, G. S.; Varga, S. L.; Springer, J. P. *J. Org. Chem.* **1986**, *51*, 2370.

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Table I. Optically Active 2-[(*E*)-1-Alkenyloxy]ethanoate Starting Materials (cf. Scheme I)

entry	compd	R	R^1	R^2	config	R^3	method[a]	*E*/*Z*	yield[b]
1	**2a**	$PhCH_2$	H	Cy[c]	2*S*	$SiMe_3$	I	100:0	49%
2	**2b**	$PhCH_2$	H	Me	2*S*	$SiMe_3$	I	100:0	36%
3	**2c**	$PhCH_2$	Me	Cy[c]	2*R*[d]	$SiMe_3$	I	100:0	47%
4	**2d**	*n*-Bu	H	Cy[c]	2*R*[d]	$SiMe_3$	II	21:1	82%[e]
5	**2e**	$MeO_2CCMe_2CH_2$	H	Cy[c]	2*R*[d]	$SiMe_3$	III	>95:5	86%[f]
6	**2f**	$MeO_2CCMe_2CH_2$	H	Me	2*S*	$SiMe_3$	III	>95:5	66%
7	**2g**	$MeO_2CCMe_2CH_2$	Me	Cy[c]	2*R*[d]	$SiMe_3$	III	>95:5	44%[f]
8	**2h**	$MeO_2CCMe_2CH_2$	Me	Me	2*S*	$SiMe_3$	III	>95:5	69%
9	**2i**	$PhSCH_2$	Me	Cy[c]	2*R*[d]	$SiMe_3$	III	96:4	79%[f]
10	**2j**	Me	Me	Cy[c]	2*R*[d]	$SiMe_3$	II	na	75%
11	**2k**	$PhCH_2$	H	Cy[c]	2*S*	Me	I	100:0	45%

[a] Method of preparation (cf. Scheme I). Method I: nickel- or palladium-catalyzed organotin or organoborate conjugate addition.[10] Method II: Stoichiometric nickel-mediated coupling with halocarbon electrophiles[9] or organometallic nucleophiles.[10] Method III: Lewis acid catalyzed conjugate addition.[15] [b] Overall yield of trimethylsilyl or methyl 2-[(*E*)-1-alkenyloxy]ethanoate from 2-ethenyl-1,3-dioxolanone, unless otherwise noted. [c] Cy = cyclohexyl. [d] Product enantiomeric to that depicted. [e] Yield based on intermediate nickel complex. [f] Enol ether not isolated. Yield is for the recrystallized aldol product, starting from 2-ethenyl-1,3-dioxolanone.

Table II. Aldol Reaction Products[a]

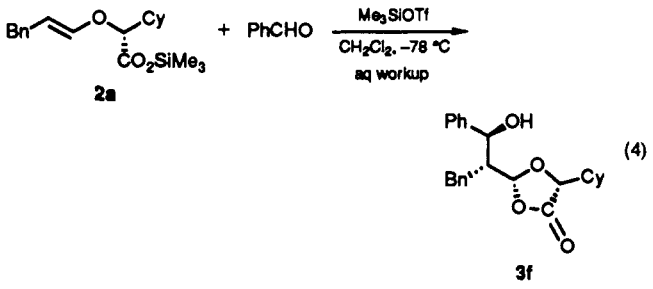
entry	ester	product	R	R^1	R^2 config	R^3	R^4	% yield[b] 3	% yield[b] 4	% ee 4[c]	*e*/*t*-4[d]
1	**2a**	**3a**	Bn[e]	H	Cy[f] 2*R*[g]	Ph	Me	72	70	92 (92)[h]	99:1
2	**2a**	**3b**	Bn[e]	H	Cy[f] 2*R*[g]	*t*-Bu	Me	86	84	92 (92)[h]	99:1
3	**2a**	**3c**	Bn[e]	H	Cy[f] 2*R*[g]	Me	Me	80	75	60 (60)[h] (74)[i]	9:1
4	**2a**	**3c**	Bn[e]	H	Cy[f] 2*R*[g]	Me	Me	95[j]	70	98[i]	4:1
5	**2a**	**3d**	Bn[e]	H	Cy[f] 2*S*	H	Me	89	63	98[i]	
6	**2a**	**3e**	Bn[e]	H	Cy[f] 2*R*[g]	H	Bn[e]	88	52	94[i]	
7	**2a**	**3f**	Bn[e]	H	Cy[f] 2*R*[g]	Ph	H	84	68	98	1:13
8	**2b**	**3g**	Bn[e]	H	Me 2*S*	Ph	Me	81[j]	72	85 (68)[i]	32:1
9	**2b**	**3h**	Bn[e]	H	Me 2*S*	H	Bn[e]	81[j]	64[h]	88[i]	
10	**2c**	**3i**	Bn[e]	Me	Cy[f] 2*R*[g]	Ph	Me	*k*	67	90 (84)[i]	16:1
11	**2d**	**3j**	*n*-Bu	H	Cy[f] 2*R*[g]	Ph	Me	76	92	87[m,n]	*l*
12	**2e**	**3k**	$MeO_2CCMe_2CH_2$	H	Cy[f] 2*R*[g]	Ph	Me	86[o]	71	92	>19:1
13	**2e**	**3l**	$MeO_2CCMe_2CH_2$	H	Cy[f] 2*R*[g]	*t*-Bu	Me	78	71	90	>46:1
14	**2e**	**3m**	$MeO_2CCMe_2CH_2$	H	Cy[f] 2*R*[g]	Me	Me	53[j,o]	68	76[j]	7:1
15	**2f**	**3n**	$MeO_2CCMe_2CH_2$	H	Me 2*S*	Ph	Me	84[j]	*k*	76	>19:1
16	**2f**	**3o**	$MeO_2CCMe_2CH_2$	H	Me 2*S*	*t*-Bu	Me	61[j]	*k*	50	99:1
17	**2f**	**3p**	$MeO_2CCMe_2CH_2$	H	Me 2*S*	Me	Me	52[j]	*k*	40[j]	6.5:1
18	**2g**	**3q**	$MeO_2CCMe_2CH_2$	Me	Cy[f] 2*R*[g]	Ph	Me	44[p]	*k*	96	32:1
19	**2h**	**3r**	$MeO_2CCMe_2CH_2$	Me	Me 2*S*	Ph	Me	55	62	68[i]	13:1
20	**2i**	**3s**	$PhSCH_2$	Me	Cy[f] 2*R*[g]	Ph	Me	75[j]	42	96 (90)[i]	19:1
21	**2j**	**3t**	Me	Me	Cy[f] 2*R*[g]	Ph	Me	72	78	94	
22	**2k**	**6d**	Bn[e]	H	Cy[f] 2S	*t*-Bu	Bn[e]	73	*k*	92[h]	>99:1

[a] All aldol reactions were carried out in CH_2Cl_2 at −78 °C with 10–20 mol % Me_3SiOTf unless otherwise noted. [b] Isolated, purified yield. [c] Enantiomeric excess of *erythro*-**4**, determined by LISR analysis. [d] Erythro/threo ratio of **4**. [e] Bn = benzyl. [f] Cy = cyclohexyl. [g] Starting materials and products enantiomeric to those depicted. [h] Enantiomeric excess of **6a** (entry 1), **6b** (entry 2), and **6c** (entry 3), cf. eq 6. [i] Et_2O reaction. [j] Crude yield. [k] Not determined. [l] Reaction catalyzed by 2–5 mol % Ph_3CSbCl_6. [m] Starting enol ether E/Z ratio 21:1. [n] Enantiomeric excess determined by optical rotation (see Experimental). [o] Overall yield starting from dioxolanone **1** for a one-pot conjugate addition/aldol reaction sequence.[15] [p] Overall yield starting from methacrolein for a one-pot acetalization/conjugate addition/aldol reaction sequence.[15]

the following points. (1) Enantiomeric excesses ≥90% are possible with dimethyl and dibenzyl acetals derived from formaldehyde, acetaldehyde, pivalaldehyde, and benzaldehyde. (2) The aldol reactions are moderately to highly erythro diastereoselective (Table II, e/t = 4:1–99:1), even when quaternary and tertiary centers are juxtaposed (entries 10, 18–20, e/t = 13:1–32:1). (3) The highest diastereoselectivities are observed with a bulky cyclohexyl substituent at the primary chiral center (R^2 = Cy); however, synthetically useful diastereoselectivities are possible even with lactic acid derivatives (e.g., entry 8, 85% ee). (4) The enantiomeric excesses are significantly catalyst dependent, Me_3SiOTf giving better results than Ph_3CSbCl_6 in reactions with benzaldehyde dimethyl acetal (entry 20, 96% ee versus 90% ee) and Ph_3CSbCl_6 giving better results than Me_3SiOTf in reactions with acetaldehyde dimethyl acetal (cf. entry 3, 60% ee versus entry 4, 98% ee). (5) Perhaps most notably, *the diastereoselectivities are remarkably insensitive to changes in substitution at the nucleophilic enol ether carbon*, so that essentially identical results are observed regardless of whether R = $PhCH_2$ or $MeO_2CCMe_2CH_2$ or $PhSCH_2$ (cf. entries 1 versus 12 versus 20) and regardless of whether R^1 = H or Me (cf. entries 1 versus 10 and 12 versus 18). Indeed, high diastereoselectivities are observed even when both enol ether substituents are the same (entry 21, R = R^1 = Me, 94% ee)! Inasmuch as several of the protected aldol products have been found to crystallize to diastereomeric purity (**3g,q,r,t**) and the remainder have been found to be at least partially enriched by chromatography, it is expected that enantiomerically pure compounds will be accessible via this approach.

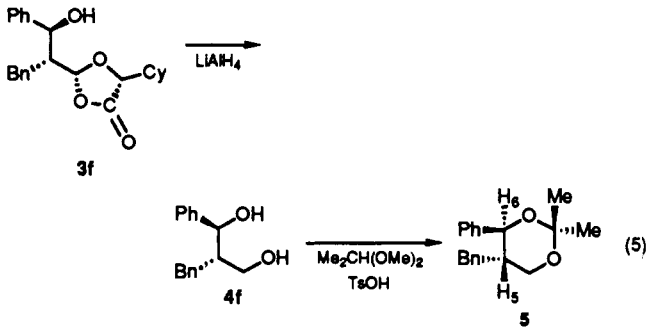
Although the reaction *diastereoselectivities* are remarkably insensitive to changes in substitution at the reacting centers, the reaction *rates* are sensitive to both steric and electronic effects. Whereas acetaldehyde dimethyl acetal, pivaladehyde dimethyl acetal, and benzaldehyde dimethyl acetal all give complete reaction in 4–14 h at 78 °C with 10–20 mol % Me_3SiOTf in dichloromethane, formaldehyde dimethyl acetal is completely unreactive under these conditions, requiring instead the more potent catalyst Ph_3CSbCl_6 and 4–5 days at −78 °C in dichloromethane. 3-Bromopropanal dimethyl acetal is also relatively unreactive, giving only a trace of product (ca. 2%) under standard conditions with Me_3SiOTf and again requiring Ph_3CSbCl_6 catalysis for complete reaction. 2-Chloroacetaldehyde dimethyl acetal, trimethyl orthobenzoate, tris(methylthio)methane, and acetonitrile are unreactive under standard Me_3SiOTf-catalyzed conditions (but have not been reacted under Ph_3CSbCl_6-catalyzed conditions). Methyl trifluoromethanesulfonate does not react with enol ether **2a**. The more sterically hindered *di*substituted enol ethers are unreactive

with both formaldehyde dibenzyl acetal and with pivalaldehyde dimethyl acetal at −78 °C in dichloromethane, even in the presence of Ph_3CSbCl_6. Simple aliphatic aldehydes such as 1-hexanal react with **2a** to give complex mixtures, possibly because of competing aldehyde cyclotrimerization and/or acetalization chemistry. On the other hand, benzaldehyde does react cleanly with **2a** to afford, after aqueous workup, threo aldol product **3f** (eq 4, Table II, entry 7).



(4)

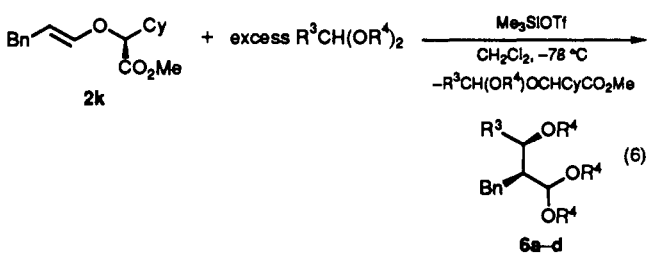
The absolute configuration at the secondary alcohol stereocenter was determined by ^1H NMR analysis of the corresponding (2*R*)- and (2*S*)-*O*-methylmandelate derivatives, following the method of Trost et al.[13] The relative configuration between this center and the adjacent stereocenter was determined by reduction of **3f** to diol **4f** and conversion of the latter to cyclic acetonide **5** (eq 5), for which ^1H NMR spectroscopy showed $^3J_{H(5)-H(6)}$ = 10.4 Hz. By way of comparison, $^3J_{H(5)-H(6)}$ = 10.0 Hz for *trans*-2,2-dimethyl-4-formyl-5-phenyl-1,3-dioxirane, while $^3J_{H(5)-H(6)}$ = 2.0 Hz for *cis*-2,2-dimethyl-4-formyl-5-phenyl-1,3-dioxirane.[19] Compound **5** was therefore assigned as the trans cyclic acetonide, corresponding to threo relative stereochemistry for **3f**. Additional evidence of this stereochemistry was obtained by methylation of diol **4f** to afford the corresponding di-*O*-methyl ether, which was shown to be the diastereomer of the dimethyl ether obtained from reduction and methylation of the corresponding benzaldehyde dimethyl acetal reaction product. LISR analysis of the threo di-*O*-methyl ether product of the benzaldehyde reaction showed it to be nearly enantiomerically pure (Table II, entry 7, 98% ee).



(5)

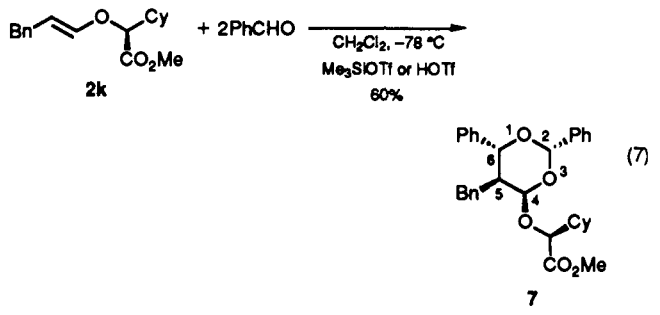
Remarkably, whereas the benzaldehyde dimethyl acetal reaction is highly erythro diastereoselective (Table II, entry 1, e/t = 99:1), the benzaldehyde reaction is highly threo diastereoselective[20] (Table II, entry 7, e/t = 1:13), the two compounds differing in stereochemistry at the β-hydroxy/alkoxy position but being the same at the α-position, a result we tentatively attribute to a change from an open transition state for the acetal reactions to a closed transition state for the benzaldehyde reaction (vide infra).

In another variant, the reactions of methyl ester **2k** with acetals and with benzaldehyde have also been examined. Dimethyl and dibenzyl acetals derived from benzaldehyde, acetaldehyde, and pivalaldehyde react with **2k** to afford β-alkoxy dialkyl acetals **6a–d**, the auxiliary being recovered either as the mixed acetal of the type $R^3CH(OR^4)(OCHCyCO_2Me)$ and/or as methyl hexahydromandelate (eq 6, Table II entries 1–3, 22). (An excess of the starting acetal is required, in its absence the aldol product is recovered as a complex mixture of **6**, the aldol product mixed acetal $RCH(R^3CHOR^4)CH(OR^4)(OCHCyCO_2Me)$ (both epimers), the corresponding aldehyde $RCH(R^3CHOR^4)CHO$, $R^3CH(OR^4)(OCHCyCO_2Me)$, and free hexahydromandelate. Since control experiments show that **6** is an especially unreactive type of acetal,[21] it is clear that the role of excess acetal is to ensure complete transacetalization and not to prevent polymerization.)



(6)

Stereochemical analysis of aldol products **6a–d**, or suitable derivatives thereof, shows the methyl ester reactions to be characterized by erythro/threo ratios and enantiomeric excesses essentially identical with those observed for the corresponding silyl ester reactions (Table II, entries 1–3, 22). In a similar vein, methyl ester **2k** reacts with 2 equiv of benzaldehyde to afford 4-alkoxy-5-benzyl-6-phenyl-1,3-dioxane **7** (eq 7). The diastereoselectivity estimated by ^1H NMR analysis of the crude product was >90% ds; chromatography and crystallization gave a nonoptimized 42% yield of a single diastereomer.



(7)

Both Me_3SiOTf and trifluoromethanesulfonic acid (TfOH) were found to be effective catalyst precursors and to give identical results, clearly suggesting that the TfOH is the actual catalyst in both cases, notwithstanding efforts to exclude moisture (see under Experimental Section). The depicted stereochemistry is based, first, on the assumption that the absolute configuration at C(5) corresponds to that observed for the other reactions and, second, on analysis of the ^1H NMR coupling constants for the 1,3-dioxane ring protons. In particular, the observation that $^3J_{H(5)-H(6)}$ = 10.8 Hz clearly indicates a trans-diaxial arrangement for H(5) and H(6), corresponding to threo stereochemistry, in accord with the corresponding silyl ester chemistry (cf. eq 4), while the observation that $^3J_{H(4)-H(5)}$ = 3.2 Hz indicates that the methyl hexahydromandelate auxiliary is in an axial position. Extending the analogy with silyl ester chemistry, it is anticipated that LISR analysis of the deprotected aldol product will show it to have an excellent enantiomeric excess. Further explorations of the scope, selectivity and mechanism of this variant are in progress.

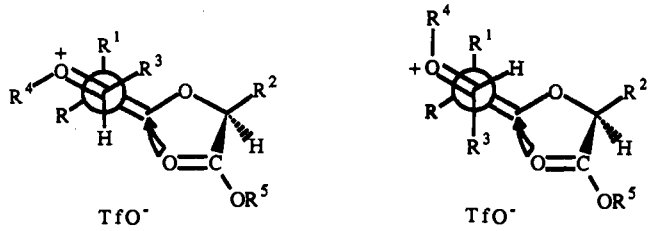
Discussion

The above results demonstrate that net enantioselective aldol chemistry can indeed be achieved with optically active 2-[(*E*)-1-alkenyloxy]ethanoates. Although the quoted chemical yields are moderate, both for the enol ether starting materials and the aldol products, it is to be emphasized that these are nonoptimized isolated yields and correspond to crude yields that are in excess of 90% in most cases. Unenriched enantiomeric excesses ≥90% ee are possible with acetals derived from formaldehyde, acet-

(19) Brewster, A. G.; Caulkett, P. W. R. (Imperial Chemical Industries PLC) U.S. Patent 4,567,197, 1986.

(20) A similar reversal of erythro/threo selectivity has been observed for the corresponding reactions of (achiral) silyl enol ethers with acetals[11] and aldehydes: Kobayashi, S.; Murakami, M.; Mukaiyama, T. *Chem. Lett.* **1985**, 1535.

(21) Reaction of **6b** with silyl ester **2a** in the presence of 50 mol % Me_3SiOTf in CH_2Cl_2 at −78 °C gave only ca. 50% reaction after 24 h. Faunce, J. A.; Mackenzie, P. B., unpublished results.



(a) (b)

Figure 1. Newman projections of the proposed concerted, syn-periplanar transition state showing (a) the favored approach of R^3 gauche to R^1 and (b) the disfavored approach of R^3 anti to R^1, interfering with dioxolanone ring closure (R^5 = Me_3Si or Me).

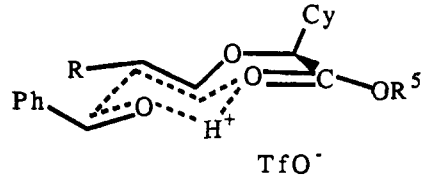


Figure 2. Proposed bicyclic transition state for the trifluoromethanesulfonic acid catalyzed reaction of **2a** with benzaldehyde (R^5 = Me_3Si or Me).

aldehyde, pivalaldehyde, and benzaldehyde in reactions with both mono- and disubstituted enol ethers, yielding acyclic tertiary and quaternary carbon compounds. High erythro/threo ratios (e/t = 9:1–99:1) are observed in all cases except the Ph_3CSbCl_6-catalyzed reaction of acetaldehyde dimethyl acetal with **2a**, for which e/t = 4:1. Enantiomerically pure erythro compounds are expected to be accessible via crystallization or chromatography of the initial products.

Our working hypothesis for the mechanism of these reactions is similar to that originally envisaged (vide supra), with the added assumption that the addition of the acetal-derived oxocarbenium ion and the trimethylsilyl or methyl ester oxygen across the enol ether double bond is a concerted, syn-periplanar reaction, wherein the need to minimize ion separation in the dichloromethane reaction solvent acts to disfavor the competing antiperiplanar pathway. In agreement with the model proposed by Noyori et al.[11] to account for the erythro diastereoselectivity of the corresponding silyl enol ether reactions (cf. eq 1), we suppose that the acetal-derived oxocarbenium ion oxygen is anti to the nascent enol ether derived oxocarbenium ion (Figure 1) so as to minimize charge–charge repulsion. However, in order to account for the high diastereoselectivity observed with **2j** (for which R = R^1 = Me and a 94% ee was observed for alcohol **5t**), we further speculate that R^3 prefers to be gauche to R^1 so as to avoid interfering with dioxolanone ring closure.

We account for the threo diastereoselectivity of the benzaldehyde reactions by invoking a change in mechanism, from an open transition state to a closed, bicyclic transition state, tied together by the proton of the trifluoromethanesulfonic acid catalyst (Figure 2). (If it is assumed that the triflic acid is always hydrogen bonded to ester and/or aldehyde oxygens, then this becomes, in effect, a bimolecular, rather than termolecular, transition state.)

Obviously, many other possibilities exist for these reactions; we defer further analysis and speculation pending the outcome of experiments in progress.[14]

Experimental Section

A. General Procedures. All manipulations were conducted in a nitrogen atmosphere drybox or on a dual-manifold Schlenk line using purified, deoxygenated solvents and standard inert atmosphere techniques unless otherwise noted. ^1H and ^{13}C NMR spectra were recorded on a Varian XLA-400 spectrometer (400 MHz for ^1H and 101 MHz for ^{13}C). Mass spectra were obtained on a VG high-resolution mass spectrometer Model 70-250SE. Optical rotations were measured on an optical activity AA-100 polarimeter. Melting points were obtained on a Fisher-Jones melting point apparatus and are uncorrected. Elemental analysis were performed by G.D. Searle Research and Development, Skokie, IL, Oneida Research Services, Inc., Whitesboro, NY, or Galbraith Laboratories, Inc., Knoxville, TN. Enantiomeric excesses were determined via lanthanide-induced shift reagent (LISR) experiments using tris[3-[(heptafluoropropyl)hydroxymethylene]-(+)-camphorato]europium(III) (Aldrich), with the ratios of major to minor enantiomer being determined by ^1H NMR peak integration and/or by cutting and weighing the peaks. Erythro/threo ratios were estimated by ^1H NMR analysis of the alcohols **4**, or related derivatives, specified below. All chromatographic separations were accomplished by gravity column chromatography employing silica gel (Aldrich, 70–270 mesh). All solvents were purified and deoxygenated as follows: Chloroform, chloroform-*d*, acetonitrile, and dimethylformamide (DMF) were refluxed over and distilled from calcium hydride. Diethyl ether, tetrahydrofuran (THF), and pentane were dried with and vacuum transferred from sodium benzophenone ketyl. Benzaldehyde, benzaldehyde dimethyl acetal, acetaldehyde dimethyl acetal, and formaldehyde dimethyl acetal were purchased from Aldrich, degassed, and stored under nitrogen over 4-Å molecular sieves. The following reagents were used as received or as otherwise noted: lithium aluminum hydride (Alfa Products), methyl trimethylsilyl dimethylketene acetal (Aldrich, degassed), chlorotrimethylsilane (Aldrich, distilled from quinoline), trimethylsilyl trifluoromethanesulfonate (Me_3SiOTf) (Aldrich, vacuum transferred), triphenylcarbenium hexachloroantimonate (Aldrich). Pivalaldehyde dimethyl acetal,[22] pivalaldehyde dibenzyl acetal,[23] formaldehyde dibenzyl acetal,[23] bis(1,5-cyclooctadiene)nickel(0) ($Ni(COD)_2$),[24] and optically active 2-ethenyl-1,3-dioxolanones **1a–d**[10] were prepared according to literature procedures.

B. Enol Ether Preparations. Optically active trimethylsilyl 2-[(*E*)-1-alkenyloxy]ethanoates **2a–c**[10] and methyl 2-[(*E*)-1-alkenyloxy]-ethanoate **2k**[10] were prepared via the palladium-catalyzed reaction of $NaBPh_4$ with 2-ethenyl-1,3-dioxolanones **1a–c**,[10] followed by silylation or methylation of the resultant sodium 2-[(*E*)-1-alkenyloxy]ethanoates with Me_3SiCl or MeI, respectively, following procedures that will be described elsewhere.[10] Optically active trimethylsilyl 2-[(*E*)-1-alkenyloxy]ethanoates **2e–i**[15] were prepared via the Me_3SiOTf-catalyzed conjugate addition of $(MeO)(Me_3SiO)CCMe_2$ and $PhSSiMe_3$ to 2-ethenyl-1,3-dioxolanones **1a–c**,[10] also following procedures that will be described elsewhere.[15]

Preparation of Trimethylsilyl (2*R*)-2-Cyclohexyl-2-[(*E*)-1-hexenyloxy]ethanoate (2d). Bis[(μ-chloro)(1,2,3-η^3-1-[(*R*)-1-(carbotrimethylsilyloxy)-1-cyclohexylmethoxy]-2-propenyl)nickel(II)][11] was prepared from (2*RS*,5*R*)-5-cyclohexyl-2-ethenyl-1,3-dioxolan-4-one (**1a**),[10] $Ni(COD)_2$,[24] and Me_3SiCl and coupled with ^nPrI according to previously published procedures[9] to afford the crude trimethylsilyl ester, which was purified by short-path distillation to afford **2d** (82% based on $Ni(COD)_2$, bp 76–77 °C at 0.001 mmHg, E/Z = 21:1) as a clear, colorless oil. 400-MHz ^1H NMR ($CDCl_3$): δ 6.13 (1 H, d, J = 12.4 Hz), 4.75 (1 H, dt, J = 12.4, 7.2 Hz), 3.86 (1 H, d, J = 5.2 Hz), 1.87–0.82 (20 H, m), 0.275 (9 H, s). 101 MHz ^{13}C NMR ($CDCl_3$): δ 171.6, 145.0, 105.8, 82.7, 40.4, 32.6, 28.9, 28.0, 27.3, 26.1, 26.0, 25.9, 21.9, 13.8, 0.3. Anal. Calcd for $C_{17}H_{32}O_3Si$: C, 65.33; H, 10.32. Found: C, 65.60; H, 10.47.

Preparation of Trimethylsilyl (2*R*)-2-Cyclohexyl-2-[(2-methyl-1-propenyl)oxy]ethanoate (2j). (2*RS*,5*R*)-5-Cyclohexyl-2-(1-methyl-1-ethenyl)-1,3-dioxolan-4-one (**1c**) (4.67 g, 22.0 mmol, 1.21 equiv),[10] $Ni(COD)_2$[24] (5.01 g, 18.2 mmol, 1.00 equiv), and Me_3SiCl (4.75 mL, 37.5 mmol, 2.05 equiv) were reacted according to published procedures[9] and modified to include $(MeO)(Me_3SiO)CCMe_2$ (0.750 mL, 3.69 mmol, 0.20 equiv) added as a proton-scavenging reagent, to afford a burgandy/red solid, presumed to be bis[(μ-chloro)(1,2,3-η^3-1-[(*R*)-1-(carbotrimethylsilyloxy)-1-cyclohexylmethoxy]-2-methyl-2-propenyl)nickel(II)] (5.23 g, 76%). Reaction of a portion of this product (5.01 g, 0.0133 monomer/mol, 1.00 monomer/equiv) with $NaB(OMe)_3H$ (1.89 g, 14.8 mmol, 1.11 equiv) in THF (60 mL) for 30 min gave a black mixture, which was concentrated at 15 mmHg to obtain a gummy black oil. This was treated with NaOMe (911 mg, 16.9 mmol, 1.27 equiv) in $MeOH/CH_3CN$ (50 mL of a 1:1 mixture), stirred for 30 min, filtered through Celite, and concentrated at 15 mmHg to afford the crude sodium salt corresponding to **2j**. Recrystallization from methanol/acetonitrile gave pure sodium (2*R*)-2-cyclohexyl-2-[(2-methyl-1-propenyl)oxy]ethanoate (2.339 g, 75%) as a white, crystalline solid. 400-MHz ^1H NMR (D_2O): δ 5.67 (1 H, s), 3.55 (1 H, d, J = 4.0 Hz), 1.57–1.37 (6 H, m), 1.46 (3 H, s), 1.37 (3 H, s), 1.07–0.93 (5 H, m). 101-MHz ^{13}C NMR (D_2O): δ 182.1, 141.7, 115.3, 89.9, 43.2, 31.7, 30.8, 28.5, 28.4, 21.2, 17.2. HRMS calcd for $C_{12}H_{19}O_3Na_2$ (M + Na): 257.1130. Found: 257.1161. A portion of this material (2.20 g, 94.2 mmol, 1.00 equiv) was suspended in CH_2Cl_2

(22) Kreevoy, M. M.; Taft, R. W. *J. Am. Chem. Soc.* **1955**, *77*, 5590.
(23) Rosen, I.; Nelson, V. U.S. Patent 3,068,294, Dec 11, 1962.
(24) Krysan, D. J.; Mackenzie, P. B. *J. Org. Chem.* **1990**, *55*, 4229.

(40 mL) in a 250-mL round-bottom flask that had been rinsed with $(Me_3Si)_2NH$ and subsequently heated under vacuum to remove protic impurities. $(MeO)(Me_3SiO)CCMe_2$ (1.91 mL, 94.0 mmol, 1.00 equiv) and Me_3SiCl (3.60 mL, 186 mmol, 2.00 equiv) were added and the mixture was stirred for 3 h to give a milky white suspension. Removal of the volatiles under reduced pressure (15 mmHg) afforded a white slurry, which was extracted with pentane (3 × 40 mL) via filter paper/tipped cannulation. The combined pentane extracts were concentrated at 15 mmHg to afford the crude silyl ester. Distillation through a 10-cm Vigreux column afforded **2j** (1.71 g, 66%) as a clear, colorless oil (bp 98–99 °C at 2 mmHg). 400-MHz ^{1}H NMR ($CDCl_3$): δ 5.74 (1 H, s), 3.76 (1 H, d, J = 5.2 Hz), 1.81–1.60 (6 H, m), 1.64 (3 H, s), 1.52 (3 H, s), 1.29–1.11 (5 H, m), 0.29 (9 H, s). 101-MHz ^{13}C NMR ($CDCl_3$): δ 172.0, 139.0, 112.4, 84.8, 40.6, 29.1, 27.8, 26.2, 26.1, 26.0, 19.4, 15.1, −0.2. HRMS calcd for $C_{15}H_{28}O_3Si$: 284.1808. Found: 284.1808.

C. Aldol Reactions. The preparation and characterization of aldol products **3k–n** and **3q–s** and the corresponding alcohols **4k–n** and **4q–s** will be described elsewhere[15] (and involve procedures essentially identical with those given below).

Typical Procedure for the Reaction of Trimethylsilyl Esters 2a–d,f,j–k with Aromatic and Aliphatic Acetals. Preparation of (2*R*,5*R*)-2-[(1*R*,2*R*)-1-Benzyl-2-methoxy-3,3-dimethylbutyl]-5-cyclohexyl-1,3-dioxolan-4-one (3b). A 25-mL Schlenk tube was charged with **2a** (0.490 g, 1.41 mmol, 1.00 equiv), *t*-BuCH(OMe)$_2$ (243 mg, 1.84 mmol, 1.30 equiv), and CH_2Cl_2 (6 mL), then cooled to −78 °C, and treated with Me_3SiOTf (54.1 μL, 0.281 mmol, 0.200 equiv) (in the cases where Ph_3CSbCl_6 was used as catalyst, it was added to the −78 °C mixture in 1 mL of CH_2Cl_2). After 6 h, the mixture was cannulated into a stirring mixture of CH_2Cl_2 (5 mL) and saturated aqueous $NaHCO_3$ (5 mL). The aqueous layer was washed with CH_2Cl_2 (3 × 5 mL) and the combined extracts were dried ($MgSO_4$), filtered, and concentrated under vacuum to remove the solvent. Chromatography (65 g of SiO_2, 95:5 hexane/EtOAc) afforded **3b** as a clear, colorless oil (0.451 g, 86%). 400-MHz ^{1}H NMR ($CDCl_3$): δ 7.31–7.18 (5 H, m), 5.28 (1 H, s), 3.97 (1 H, d, J = 3.6 Hz), 3.43 (3 H, s), 3.07–3.03 (2 H, m), 2.61 (1 H, dd, J = 14.4, 12.0 Hz), 2.38 (1 H, d, J = 12.0 Hz), 1.86–1.14 (11 H, m), 0.98 (9 H, s). 101-MHz ^{13}C NMR ($CDCl_3$): δ 172.6, 140.3, 129.1, 128.5, 126.2, 103.4, 83.8, 79.1, 60.5, 44.0, 38.8, 37.0, 32.0, 29.2, 27.4, 26.3, 26.1, 26.0, 25.9. Anal. Calcd for $C_{23}H_{34}O_4$: C, 73.76; H, 9.15. Found: C, 73.59; H, 8.82.

Typical Procedure for the Reduction of Aldol Products 3a–j,o,p,t To Afford the Corresponding Alcohols 4a–j,o,p,t. Preparation of (2*S*,3*R*)-2-Benzyl-3-methoxy-4,4-dimethylpentanol (4b). A solution of *crude, unenriched* **3b** (0.419 g, 1.12 mmol, 1.00 equiv) in Et_2O (6 mL) was added dropwise via cannula to a stirring mixture of $LiAlH_4$ (506 mg, 13.3 mmol, 10.0 equiv) and Et_2O (6 mL) at 0 °C. After stirring for 1.5 h at 25 °C, the reaction was carefully quenched by sequential addition of water (2.5 mL), aqueous NaOH (2.5 mL, 10% NaOH by weight), water (5 mL), and more aqueous NaOH (5 mL, 10% w/w). The layers were separated and the aqueous layer was extracted with Et_2O (3 × 15 mL). The combined organic extracts were dried ($MgSO_4$), filtered, concentrated at 10 mmHg, and chromatographed (45 g of SiO_2, 70:30 hexane/EtOAc) to afford **4b** as a clear, colorless oil (0.237 g, 84% yield, erythro/threo = 99:1, 92% ee by LISR analysis). 400-MHz ^{1}H NMR ($CDCl_3$): δ 7.30–7.19 (5 H, m), 3.53–3.50 (5 H, m), 3.09 (1 H, d, J = 2.0 Hz), 2.99 (1 H, dd, J = 22.4, 3.2 Hz), 2.42 (1 H, dd, J = 14.4, 11.6 Hz), 2.11–2.04 (1 H, m), 1.32 (1 H, s), 1.01 (9 H, s). 101-MHz ^{13}C NMR ($CDCl_3$): δ 141.7, 129.0, 128.4, 125.9, 88.8, 64.9, 61.5, 44.0, 36.9, 32.6, 26.8. Anal. Calcd for $C_{15}H_{24}O_2$: C, 76.23; H, 10.23. Found: C, 76.08; H, 10.20.

(2*R*,5*R*)-5-Cyclohexyl-2-[(1*R*,2*R*)-1-benzyl-2-methoxy-2-phenylethyl]-1,3-dioxolan-4-one (3a). **2a** (1.00 g, 2.89 mmol, 1.00 equiv), $PhCH(OMe)_2$ (574 μL, 3.82 mmol, 1.30 equiv), and Me_3SiOTf (66.1 μL, 0.382 mmol, 0.120 equiv) were reacted as per **3b** to afford, after chromatography (60 g of SiO_2, 95:5 hexane/EtOAc), **3a** as a clear, colorless oil (817 mg, 72%). 400-MHz ^{1}H NMR ($CDCl_3$): δ 7.40–6.94 (10 H, m), 5.47 (1 H, dd, J = 5.4, 1.2 Hz), 4.55 (1 H, d, J = 4.0 Hz), 3.96 (1 H, d, J = 3.2 Hz), 3.29 (3 H, s), 2.92 (1 H, dd, J = 14.8, 4.4 Hz), 2.76 (1 H, dd, J = 14.8, 8.0 Hz), 2.34–2.29 (1 H, m), 1.73–0.87 (11 H, m). 101-MHz ^{13}C NMR ($CDCl_3$): δ 172.6, 140.9, 139.4, 134.4, 129.7, 129.0, 128.5, 128.1, 128.0, 127.6, 126.8, 125.7, 104.3, 81.7, 78.7, 57.2, 51.8, 38.8, 29.8, 28.9, 26.7, 25.9, 25.7, 25.7. MS (70 eV) (rel intensity) 362 (M^+, 2.3), 222 (2.3), 194 (4.4), 193 (16.4), 169 (2.6), 141 (2.1), 133 (2.2), 131 (5.4), 122 (9.8), 121 (B), 95 (16.5), 91 (20.4), 77 (12.3). Anal. Calcd for $C_{25}H_{30}O_4$: C, 76.11; H, 7.66. Found: C, 75.86; H, 7.71.

(2*S*,3*R*)-2-Benzyl-3-methoxy-3-phenylpropanol (4a). Crude, unenriched **3a** (545 mg, 1.38 mmol, 1.00 equiv) and $LiAlH_4$ (450 mg, 11.9 mmol, 8.6 equiv) were reacted as per **4b** and chromatographed (160 g of SiO_2, 93:7 hexane/EtOAc) to afford **4a** as a clear, colorless oil (249 mg, 70%). 400-MHz ^{1}H NMR ($CDCl_3$): δ 7.39–7.10 (10 H, m), 4.44 (1 H, d, J = 4.8 Hz), 3.52–3.43 (2 H, m), 3.28 (3 H, s), 2.73 (1 H, dd, J = 13.8, 4.8 Hz), 2.57 (1 H, dd, J = 13.8, 10.0 Hz), 2.29 (1 H, m), 2.22–2.15 (1 H, m). 101-MHz ^{13}C NMR ($CDCl_3$): δ 140.3, 139.4, 131.1, 129.1, 128.4, 128.3, 127.7, 127.2, 125.9, 86.1, 62.5, 57.2, 48.5, 32.0. Anal. Calcd for $C_{17}H_{20}O_2$: C, 79.65; H, 7.86. Found: C, 79.55; H, 7.86.

(1*R*,2*S*)-2-Benzyl-1,3-dimethoxy-1-phenylpropane (8a). In the drybox, a 50-mL round-bottom flask containing a stir bar was charged with **4a** (150 mg, 0.585 mmol, 1.00 equiv) and THF (7 mL). NaH (0.035 g of a 60% dispersion, 0.878 mmol, 1.50 equiv) was added with stirring resulting in rapid gas evolution and affording a milky grey mixture. After equipping the flask with a reflux condensor fitted with a nitrogen inlet, the mixture was transferred to the Schlenk line where MeI (166 mg, 1.17 mmol, 2.00 equiv) was added and the mixture was heated to reflux. After a 3-h reflux, water (5 mL) was added and the mixture was transferred to a separatory funnel where the aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic extracts were dried ($MgSO_4$), filtered, concentrated at 15 mmHg, and chromatographed (17 g of SiO_2, 95:5 hexane/EtOAc) to afford **8a** as a clear, colorless oil (0.113 g, 72% yield, erythro/threo = 99:1, 92% ee by LISR analysis). 400-MHz ^{1}H NMR ($CDCl_3$): δ 7.38–7.14 (10 H, m), 4.25 (1 H, d, J = 7.2 Hz), 3.26 (3 H, s), 3.18 (3 H, s), 3.10 (1 H, dd, J = 9.2, 5.2 Hz), 3.03 (1 H, dd, J = 13.6, 4.0 Hz), 2.80 (1 H, dd, J = 9.6, 4.4 Hz), 2.68 (1 H, dd, J = 13.6, 10.4 Hz), 2.11–2.03 (1 H, m). 101-MHz ^{13}C NMR ($CDCl_3$): δ 140.9, 140.8, 129.3, 128.2, 128.1, 127.4, 127.2, 125.7, 83.5, 70.4, 58.6, 57.2, 47.9, 32.7. HRMS calcd for $C_{17}H_{18}O$ (M^+ − MeOH): 238.1357. Found: 238.1356.

(2*R*,5*R*)-5-Cyclohexyl-2-[(1*R*,2*S*)-1-benzyl-2-methoxypropyl]-1,3-dioxolan-4-one (3c). **2a** (227 mg, 0.655 mmol, 1.00 equiv), $MeCH(OMe)_2$ (150 mg, 1.66 mmol, 1.30 equiv), CH_2Cl_2 (3 mL), and Me_3SiOTf (14.4 mg, 0.0655 mmol, 0.100 equiv) were reacted as per **3b** to afford, after chromatography (40 g of SiO_2, 95:5 hexane/EtOAc), **3c** as a clear, colorless oil (0.173 g, 80%). 400-MHz ^{1}H NMR ($CDCl_3$): δ 7.32–7.18 (5 H, m), 5.65 (1 H, d, J = 4.0 Hz), 4.07 (1 H, d, J = 3.2 Hz), 3.49–3.43 (1 H, m), 3.25 (3 H, s), 2.85 (1 H, dd, J = 14.4, 5.6 Hz), 2.73 (1 H, dd, J = 14.4, 8.0 Hz), 2.35–2.30 (1 H, m), 1.86–1.09 (14 H, m). 101-MHz ^{13}C NMR ($CDCl_3$): δ 172.7, 140.2, 129.0, 128.9, 128.5, 128.4, 126.1, 103.8, 79.1, 74.8, 56.4, 48.4, 38.9, 29.8, 29.1, 26.8, 26.0, 25.9, 25.8, 16.0. Anal. Calcd for $C_{20}H_{28}O_4$: C, 72.26; H, 8.49. Found: C, 71.99; H, 8.19.

(2*S*,3*S*)-2-Benzyl-3-methoxybutanol (4c). Crude, unenriched **3c** (89.0 mg, 0.267 mmol, 1.00 equiv) and $LiAlH_4$ (102 mg, 2.67 mmol, 10.0 equiv) were reacted as per **4b** to afford, after chromatography (15 g of SiO_2, 75:25 hexane/EtOAc), **4c** as a clear, yellow oil (39.0 mg, 75% yield, erythro/threo = 9:1, 60% ee by LISR analysis). 400-MHz ^{1}H NMR ($CDCl_3$): δ 7.31–7.18 (5 H, m), 3.73–3.67 (1 H, m), 3.61–3.54 (2 H, m), 3.34 (3 H, s), 2.85 (1 H, dd, J = 6.4, 4.4 Hz), 2.58 (2 H, d, J = 7.6 Hz), 2.19–2.12 (1 H, m), 1.25 (3 H, d, J = 6.4 Hz). 101-MHz ^{13}C NMR ($CDCl_3$): δ 128.9, 128.4, 126.0, 99.3, 96.1, 79.7, 63.4, 56.4, 45.8, 33.0, 14.4. HRMS calcd for $C_{12}H_{16}O$ ($M^{\cdot+}$ − OH_2): 176.1201. Found: 176.1237.

Diethyl Ether Reaction To Afford 3c and Subsequent Conversion to Alcohol 4c. **2a** (1.41 mmol), $MeCH(OMe)_2$ (5.52 mmol), and Me_3SiOTf (0.282 mmol) were reacted as per **3b**, but with Et_2O in place of CH_2Cl_2 and a reaction time of 21 h, to afford **3c** (85% crude yield). Reduction as per **4b** gave **4c** (erythro/threo = 9:1, 74% ee by LISR analysis).

Ph_3CSbCl_6-Catalyzed Reaction To Afford 3c and Subsequent Conversion to Alcohol 4c. **2a** (115 mg, 0.332 mmol, 1.00 equiv), $MeCH(OMe)_2$ (45.6 μL, 0.431 mmol, 1.30 equiv), and CH_2Cl_2 (1.00 mL) were reacted as per **3b**, but with Ph_3CSbCl_6 (8.00 mg, 0.0120 mmol, 0.0400 equiv) as the catalyst and a reaction time of 21 h, to afford **3c** (0.105 g, 95% crude yield). Reduction as per **4b** afforded, after chromatography (75 g of SiO_2, 80:20 hexane/EtOAc), **4c** (0.0430 g, 70% yield, erythro/threo = 4:1, 98% ee by LISR analysis).

(2*S*,5*S*)-5-Cyclohexyl-2-[(1*S*)-1-benzyl-2-methoxyethyl]-1,3-dioxolan-4-one (3d). **2a** (496 mg, 1.43 mmol, 1.00 equiv), $H_2C(OMe)_2$ (165 μL, 1.86 mmol, 1.30 equiv), CH_2Cl_2 (1.00 mL), and Ph_3CSbCl_6 (165 mg, 0.0286 mmol, 0.0200 equiv, in 1 mL of CH_2Cl_2) were reacted as per **3b**, but with a reaction time of 120 h, to afford, after chromatography (300 g of SiO_2, 95:5 hexane/EtOAc), **3d** as a clear, colorless oil (0.403 g, 89%). 400-MHz ^{1}H NMR ($CDCl_3$): δ 7.32–7.19 (5 H, m), 5.54 (1 H, d, J = 4.0 Hz), 4.10 (1 H, d, J = 3.2 Hz), 3.39 (1 H, d, J = 2.4 Hz), 3.38 (1 H, d, J = 1.6 Hz), 3.30 (3 H, m), 2.87 (1 H, dd, J = 13.6, 5.6 Hz), 2.72 (1 H, dd, J = 13.6, 9.2 Hz), 2.30–2.22 (1 H, m), 1.89–1.19 (11 H, m). 101-MHz ^{13}C NMR ($CDCl_3$): δ 172.5, 139.1, 129.3, 128.5, 126.3, 103.5, 78.9, 69.6, 58.9, 44.8, 39.1, 31.4, 29.0, 27.0, 26.1, 26.0, 25.9. HRMS calcd for $C_{19}H_{26}O_4$: 318.1831. Found: 318.1830. Anal. Calcd for $C_{19}H_{26}O_4$: C, 71.67; H, 8.23. Found: C, 72.07; H, 8.21.

(2*R*)-2-Benzyl-3-methoxypropanol (4d). Crude, unenriched **3d** (158 mg, 0.496 mmol, 1.00 equiv) and $LiAlH_4$ (188 mg, 4.96 mmol, 10.0 equiv) were reacted as per **4b** to afford, after chromatography (75 g of SiO_2, 70:30 hexane/EtOAc), **4d** as a clear, yellow oil (56.0 mg, 63% yield, 98% ee by LISR analysis). 400-MHz ^1H NMR ($CDCl_3$): δ 7.31–7.17 (5 H, m), 3.74–3.70 (1 H, br dd), 3.65–3.60 (1 H, br dd), 3.49 (1 H, dd, J = 9.2, 4.0 Hz), 3.39 (1 H, dd, J = 8.8, 3.2 Hz), 3.34 (3 H, s), 2.69–2.58 (2 H, m), 2.51 (1 H, t, J = 4.8 Hz), 2.15–2.08 (1 H, m). 101-MHz ^{13}C NMR ($CDCl_3$): δ 139.9, 129.0, 128.4, 126.1, 75.7, 65.6, 59.1, 42.4, 34.5. HRMS calcd for $C_{11}H_{16}O_2$: 180.1150. Found: 180.1146.

(2*R*,5*R*)-5-Cyclohexyl-2-[(1*R*)-1-benzyl-2-(benzyloxy)ethyl]-1,3-dioxolan-4-one (3e). **2a** (1.00 g, 2.89 mmol, 1.00 equiv), CH_2Cl_2 (1.00 mL), $H_2C(OCH_2Ph)_2$ (856 mg, 3.75 mmol, 1.30 equiv), and Ph_3CSbCl_6 (33.0 mg, 0.0577 mmol, 0.0200 equiv in 1.5 mL of CH_2Cl_2) were reacted as per **3b**, but with a reaction time of 120 h, to afford, after chromatography (200 g of SiO_2, 95:5 hexane/EtOAc), **3e** as a clear, colorless oil (1.00 g, 88%). 400-MHz ^1H NMR ($CDCl_3$): δ 7.36–7.17 (10 H, m), 5.59 (1 H, d, J = 4.8 Hz), 4.46 (2 H, dd, J = 22.0, 11.6 Hz), 4.08 (1 H, d, J = 3.2 Hz), 3.50 (2 H, dd, J = 4.8, 3.6 Hz), 2.89 (1 H, dd, J = 13.2, 5.6 Hz), 2.77 (1 H, dd, J = 13.6, 9.2 Hz), 2.34–2.27 (1 H, m), 1.85–1.15 (11 H, m). 101-MHz ^{13}C NMR ($CDCl_3$): δ 172.7, 139.0, 138.1, 129.2, 128.5, 128.4, 127.6, 127.5, 126.3, 103.5, 78.9, 73.2, 67.1, 44.8, 39.0, 31.4, 29.0, 26.8, 26.0, 25.9, 25.8. Anal. Calcd for $C_{25}H_{30}O_4$: C, 76.11; H, 7.66. Found: C, 76.01; H, 7.77. Chromatography also yielded a small amount of a minor diastereomer, assigned as the corresponding *trans*-2,5-disubstituted-1,3-dioxolan-4-one, (2*S*,5*R*)-5-cyclohexyl-2-[(1*R*)-1-benzyl-2-(benzyloxy)ethyl]-1,3-dioxolan-4-one. (This assignment is based upon the close similarity of the C(2)H region of this compound with that of the corresponding (2*R*,5*R*)-5-cyclohexyl-2-[(1*R*)-1-benzyl-2-*methoxy*ethyl]-1,3-dioxolan-4-one (**3d**), for which the minor diastereomer resonances have been assigned.)[14] Whereas irradiation of the C(5)H resonance of the putative cis isomer **3e** resulted in an 8% enhancement of the C(2)H resonance, irradiation of the C(5)H resonance of the putative trans isomer had no effect on its C(2)H resonance.

(2*S*)-2-Benzyl-3-(benzyloxy)propanol (4e). Crude, unenriched **3e** (710 mg, 1.80 mmol, 1.00 equiv) and $LiAlH_4$ (683 mg, 18.0 mmol, 10.0 equiv) were reacted as per **4b** to afford, after chromatography (55 g of SiO_2, 75:25 hexane/EtOAc), **4e** as a clear, colorless oil (0.238 g, 52% yield, 94% ee by LISR analysis). 400-MHz ^1H NMR ($CDCl_3$): δ 7.37–7.16 (10 H, m), 4.50 (2 H, dd, J = 18.4, 12.0 Hz), 3.76–3.73 (2 H, m), 3.68–3.58 (2 H, m), 3.49 (1 H, dd, J = 8.8, 6.8 Hz), 2.66 (2 H, dd, J = 7.6, 1.6 Hz), 2.41 (1 H, t, J = 6.0 Hz), 2.19–2.10 (1 H, m). 101-MHz ^{13}C NMR ($CDCl_3$): δ 140.0, 138.0, 129.0, 128.5, 128.4, 127.8, 127.7, 126.1, 73.5, 72.9, 65.5, 42.6, 34.5. $[\alpha]^{24}_D$ = −24.3° (*c* 0.74, EtOH) [cf. Holladay, M.W., et al., $[\alpha]_D^{24}$ = +23.6° (*c* 0.72, EtOH) for (2*R*)-2-benzyl-3-(benzyloxy)propanol].[17] Anal. Calcd for $C_{17}H_{20}O_2$: C, 79.65; H, 7.86. Found: C, 79.27; H, 7.88.

(2*R*,5*R*)-5-Cyclohexyl-2-[(1*R*,2*S*)-1-benzyl-2-hydroxy-2-phenylethyl]-1,3-dioxolan-4-one (3f). **2a** (347 mg, 1.00 mmol, 1.00 equiv), PhCHO (318 mg, 3.00 mmol, 3.00 equiv), and Me_3SiOTf (23.2 μL, 0.120 mmol, 0.120 equiv) were reacted as per **3b** for 3 h to afford, after chromatography (50 g of SiO_2, 75:25 hexane/EtOAc), **3f** as a clear, colorless oil (0.325 g, 84%). 400-MHz ^1H NMR ($CDCl_3$): δ 7.35–7.11 (10 H, m), 5.45 (1 H, d, J = 1.2 Hz), 4.82 (1 H, t, J = 6.0 Hz), 4.04 (1 H, d, J = 2.8 Hz), 2.85 (2 H, d, J = 5.6 Hz), 2.74 (1 H, dd, J = 13.6, 6.4 Hz), 2.67 (1 H, dd, J = 13.6, 8.0 Hz), 2.61–2.54 (1 H, m), 1.96–1.63 (6 H, m), 1.37–1.14 (5 H, m). 101-MHz ^{13}C NMR ($CDCl_3$): δ 171.8, 150.9, 141.6, 139.1, 133.7, 129.0, 128.6, 128.5, 128.3, 127.8, 126.3, 126.1, 103.2, 79.2, 72.1, 49.5, 38.8, 30.6, 29.0, 27.0, 25.9, 25.8, 25.7. MS (15 eV) (rel intensity) 380 (M^+, 4.7), 289 (10.6), 274 (16.9), 240 (4.7), 194 (9.0), 193 (12.7), 149 (16.7), 134 (46.2), 133 (B), 116 (26.2), 107 (25.8), 95 (22.9), 92 (19.1), 91 (4.1). Anal. Calcd for $C_{24}H_{28}O_4$: C, 75.76; H, 7.42. Found: C, 75.70; H, 7.42.

(1*S*,2*S*)-2-Benzyl-3-hydroxy-1-phenylpropanol (4f). Crude, unenriched **3f** (3.03 g, 7.96 mmol, 1.00 equiv) and $LiAlH_4$ (1.80 g, 47.8 mmol, 6.00 equiv) were reacted as per **4b** to afford, after flash chromatography (SiO_2, 3:1 hexane/EtOAc), **4f** as a clear, colorless oil (1.31 g, 68% yield). 400-MHz ^1H NMR ($CDCl_3$): δ 7.36–7.12 (10 H, m), 4.77 (1 H, dd, J = 6.4, 4.0 Hz), 3.77–3.73 (1 H, m), 3.60–3.54 (1 H, m), 2.94 (1 H, d, J = 4.4 Hz), 2.71 (1 H, dd, J = 13.6, 5.6 Hz), 2.60 (1 H, dd, J = 13.6, 9.6 Hz), 2.47 (1 H, d, J = 4.4 Hz), 2.14–2.09 (1 H, m). 101-MHz ^{13}C NMR ($CDCl_3$): δ 143.4, 140.1, 129.0, 128.5, 128.4, 127.7, 126.3, 126.1, 78.0, 63.2, 48.5, 34.7. MS (15 eV) (rel intensity) 242 (M^+, 1.8), 193 (1.2), 133 (4.0), 118 (B), 117 (30.5), 107 (19.7), 105 (2.4), 92 (3.9), 91 (2.6), 79 (5.7). HRMS calcd for $C_{16}H_{18}O_2$: 242.1306. Found: 242.1321.

(1*S*,2*S*)-2-Benzyl-1,3-dimethoxy-1-phenylpropane (8b). **4f** (166 mg, 0.479 mmol, 1.00 equiv), NaH (58.0 mg of a 60% dispersion, 1.43 mmol, 3.00 equiv), and MeI (201 mg, 1.43 mmol, 3.00 equiv) were reacted in THF (3 mL) as per **8a** to afford, after chromatography (17 g of SiO_2, 90:10 hexane/EtOAc), **8b** as a clear, colorless oil (0.107 g, 83% yield, erythro/threo = 1:13, 98% ee by LISR analysis). 400-MHz ^1H NMR ($CDCl_3$): δ 7.38–7.09 (10 H, m), 4.23 (1 H, d, J = 6.4 Hz), 3.45 (1 H, dd, J = 9.2, 5.2 Hz), 3.27 (3 H, s), 3.23 (3 H, s), 3.11 (1 H, dd, J = 9.2, 4.8 Hz), 2.58 (1 H, dd, J = 13.2, 6.0 Hz), 2.49 (1 H, dd, J = 13.6, 9.2 Hz), 2.23–2.15 (1 H, m). 101-MHz ^{13}C NMR ($CDCl_3$): δ 140.8, 140.3, 129.2, 128.2, 127.5, 127.4, 125.8, 82.7, 70.3, 58.7, 57.1, 47.5, 33.5 Anal. Calcd for $C_{18}H_{22}O_2$: C, 79.96; H, 8.20. Found: C, 79.77; H, 8.29.

(4*S*,5*S*)-5-Benzyl-2,2-dimethyl-4-phenyl-1,3-dioxane (5). **4f** (458 mg, 1.89 mmol, 1.00 equiv), $Me_2C(OMe)_2$ (30.0 mL), and *p*-toluenesulfonic acid (4.10 mg, 0.022 mmol, 0.011 equiv) were combined and stirred vigorously for 5 min and then allowed to stand for 14 h at 25 °C. After NEt_3 was added (8 drops, distilled from CaH_2), the solvent was removed at 15 mmHg to afford, after flash chromatography (85:15 hexane/ethyl acetate), **5** as a clear, colorless oil (445 mg, 83% yield), ca. 95% pure by ^1H NMR. Further purification of a 400-mg portion of this material was achieved by gravity column chromatography (100 g of SiO_2, 94:6 hexane/ethyl acetate), yielding analytically pure **5** (301 mg, 62%) as a white solid. 400-MHz ^1H NMR ($CDCl_3$): δ 7.43–7.10 (8 H, m), 6.94 (2 H, d, J = 7.2 Hz), 4.58 (1 H, d, J = 10.4 Hz), 3.75–3.64 (2 H, m), 2.47 (1 H, dd, J = 13.2, 3.2 Hz), 2.23–2.18 (1 H, m), 2.12 (1 H, dd, J = 13.2, 11.2 Hz), 1.55 (3 H, s), 1.44 (3 H, s). 101-MHz ^{13}C NMR ($CDCl_3$): δ 140.0, 138.5, 128.6, 128.5, 128.3, 127.7, 126.1, 98.8, 77.7, 64.5, 42.4, 34.4, 29.8, 19.1. MS (15 eV) (rel intensity) 282 (M^+, 1.2), 207 (5.3), 166 (2.7), 165 (24.6), 119 (9.7), 118 (B), 117 (29.6), 107 (16.1), 91 (11.4). Anal. Calcd for $C_{19}H_{22}O_2$: C, 80.82; H, 7.85. Found: C, 80.67; H, 7.83.

Preparation of the (*R*)-*O*-Methylmandelate Derivative of 3f, (2*R*,5*R*)-5-Cyclohexyl-2-[(1*R*,2*S*)-1-benzyl-2-[(*R*)-carbomethoxyphenylmethoxy]-2-phenylethyl]-1,3-dioxolan-4-one (9a). Following the procedure of Trost et al.,[13] a solution of dry DMF (164 mg, 2.24 mmol, 1.5 equiv) in dry CH_3CN (4 mL) was cooled to 0 °C and treated with oxalyl chloride (208 mg, 1.64 mmol, 1.1 equiv), added over 5 min, to give a white suspension. Solid (*R*)-*O*-methylmandelic acid was added through a funnel and the resultant mixture was stirred at 0 °C for 10 min to yield a slightly yellow solution. A mixture of **3f** (625 mg, 1.64 mmol, 1.10 equiv) and pyridine (260 mg, 3.28 mmol, 2.20 equiv) was added via cannula over 10 min and the mixture was maintained at 0 °C for 40 min. The solution was diluted with Et_2O (10 mL), washed with H_2O (15 mL), saturated aqueous $CuSO_4$ (2 × 20 mL), and again with H_2O (15 mL), then dried ($MgSO_4$), filtered, and concentrated at 0.01 mmHg to afford, after chromatography (80 g of SiO_2, 97:3 hexane/EtOAc), **9a** (0.173 g, 22%). 400-MHz ^1H NMR ($CDCl_3$): δ 7.55–7.08 (13 H, m), 6.62–6.60 (2 H, m), 5.75 (1 H, d, J = 6.5 Hz), 5.07 (1 H, d, J = 1.6 Hz), 4.82 (1 H, s), 3.73 (1 H, d, J = 2.4 Hz), 3.37 (3 H, s), 2.68 (1 H, dd, J = 13.6, 4.8 Hz), 2.65–2.60 (1 H, m), 2.30 (1 H, dd, J = 13.6, 7.2 Hz), 1.83–1.21 (11 H, m). HRMS calcd for $C_{33}H_{37}O_6$ (M + H): 529.2590. Found: 529.2586.

Preparation of the (*S*)-*O*-Methylmandelate Derivative of 4f, (2*R*,5*R*)-5-Cyclohexyl-2-[(1*R*,2*S*)-1-benzyl-2-[(*S*)-carbomethoxyphenylmethoxy]-2-phenylethyl]-1,3-dioxolan-4-one (9b). Repeating the above procedure with (*S*)-*O*-methylmandelate gave **9b** (35% after chromatography). 400-MHz ^1H NMR ($CDCl_3$): δ 7.42–6.88 (15 H, m), 5.86 (1 H, d, J = 6.0 Hz), 5.38 (1 H, d, J = 2.4 Hz), 4.81 (1 H, s), 3.94 (1 H, d, J = 3.6 Hz), 3.41 (3 H, s), 2.77 (1 H, dd, J = 14.0, 4.8 Hz), 2.70–2.64 (1 H, m), 2.55 (1 H, dd, J = 14.0, 7.6 Hz), 1.87–1.16 (11 H, m). HRMS calcd for $C_{33}H_{37}O_6$ (M + H): 529.2590. Found: 529.2683.

(2*S*,5*S*)-2-[(1*S*,2*S*)-1-Benzyl-2-methoxy-2-phenylethyl]-5-methyl-1,3-dioxolan-4-one (3g). **2b** (425 mg, 1.53 mmol, 1.00 equiv), $PhCH(OMe)_2$ (302 mg, 1.98 mmol, 1.30 equiv), and Me_3SiOTf (29.2 μL, 0.153 mmol, 0.100 equiv) were reacted as per **3b** for 3 h to afford crude **3g** (404 mg, 81%) as a clear, colorless oil, ca. 95% pure by ^1H NMR. Crystallization from pentane afforded **3g** as a white crystalline solid (269 mg, 54%), mp 87–88 °C. 400-MHz ^1H NMR ($CDCl_3$): δ 7.38–7.05 (10 H, m), 5.35 (1 H, dd, J = 3.6, 1.2 Hz), 4.42 (1 H, d, J = 6.0 Hz), 4.18 (1 H, dq, J = 6.4, 1.2 Hz), 3.24 (3 H, s), 3.02 (1 H, dd, J = 14.4, 4.4 Hz), 2.82 (1 H, dd, J = 14.8, 4.4 Hz), 2.48–2.43 (1 H, m), 1.29 (3 H, d, J = 6.8 Hz). 101-MHz ^{13}C NMR ($CDCl_3$): δ 173.4, 140.3, 139.6, 129.0, 128.4, 128.2, 127.8, 127.2, 125.9, 103.8, 81.9, 71.1, 56.9, 50.5, 30.7, 15.6. Anal. Calcd for $C_{20}H_{22}O_4$: C, 73.60; H, 6.79. Found: C, 73.53; H, 6.91. (The structure of **3g** has been determined by X-ray crystallographic analysis. Crystallographic details, including ORTEP diagrams, tables of atomic coordinates, thermal parameters, bond angles, and bond lengths are available as supplementary material from an earlier communication.[8]

(2*R*,3*S*)-2-Benzyl-3-methoxy-3-phenylpropanol (4g). Crude, unenriched **3g** (224 mg, 0.686 mmol, 1.00 equiv) and $LiAlH_4$ (260 mg, 6.86 mmol, 10.0 equiv) were reacted as per **4b** to afford crude **4g** as a clear, colorless oil (126 mg, 72% yield, erythro/threo = 32:1, 85% ee by LISR

analysis), ca. 95% pure by ^{1}H NMR analysis but otherwise evincing an ^{1}H NMR spectrum identical with that observed for the enantiomeric alcohol **4a**.

Ph_3CSbCl_6-Catalyzed Reaction To Afford 3g and Subsequent Reduction to 4g. 2b (325 mg, 1.17 mmol, 1.00 equiv), $PhCH(OMe)_2$ (231 mg, 1.52 mmol, 1.30 equiv), CH_2Cl_2 (1 mL), and Ph_3CSbCl_6 (14.0 mg, 0.0233 mmol, 0.0200 equiv, in 0.5 mL of CH_2Cl_2) were reacted as per **3b** for 3 h to afford crude **3g** as a clear, colorless oil (0.298 g, 78%), ca. 95% pure by ^{1}H NMR. Reduction with $LiAlH_4$ (273 mg, 7.20 mmol, 10.0 equiv) as per **4b** gave crude **4g** (0.157 g, 66% overall, erythro/threo = 19:1, 68% ee by LISR analysis), ca. 95% pure by ^{1}H NMR analysis, the ^{1}H NMR spectrum being otherwise identical with that observed for the enantiomeric alcohol **4a**.

(2*S*,5*S*)-2-[(1*S*)-1-Benzyl-2-(benzyloxy)ethyl]-5-methyl-1,3-dioxolan-4-one (3h). 2b (620 mg, 2.23 mol, 1.00 equiv), $H_2C(OCH_2Ph)_2$ (661 mg, 2.89 mmol, 1.30 equiv), CH_2Cl_2 (1 mL), and Ph_3CSbCl_6 (25.7 mg, 0.0454 mmol, 0.0200 equiv in 1 mL of CH_2Cl_2) were reacted as per **3b** for 120 h to afford crude **3h** as a colorless oil (0.589 g, 81%), ca. 95% pure by ^{1}H NMR. Chromatography (90:10 hexane/EtOAc) of a small portion yielded analytically pure material. 400-MHz ^{1}H NMR ($CDCl_3$): δ 7.36–7.16 (10 H, m), 5.64 (1 H, d, J = 4.4 Hz), 4.45 (2 H, d, J = 4.0 Hz), 4.35 (1 H, q, J = 5.6 Hz), 3.53–3.47 (2 H, m), 2.88 (1 H, dd, J = 13.6, 5.2 Hz), 2.75 (1 H, dd, J = 14.0, 9.2 Hz), 2.35–2.28 (1 H, m), 1.51 (3 H, d, J = 6.8 Hz). 101-MHz ^{13}C NMR ($CDCl_3$): δ 173.7, 138.8, 138.0, 129.3, 129.2, 128.5, 128.4, 127.7, 127.6, 126.3, 103.7, 73.3, 71.5, 67.1, 44.6, 31.1, 16.2. Anal. Calcd for $C_{20}H_{22}O_4$: C, 73.60; H, 6.79. Found: C, 73.40; H, 6.61.

(2*R*)-2-Benzyl-3-(benzyloxy)propanol (4h). Crude, unenriched **3h** was reduced with $LiAlH_4$ as per **4b** to afford **4h** (64% crude yield, 88% ee by LISR analysis) ca. 95% pure by ^{1}H NMR analysis, the ^{1}H NMR spectrum being otherwise identical with that observed for the enantiomeric alcohol **4e**.

Ph_3CSbCl_6-Catalyzed Preparation of (2*R*,5*R*)-5-Cyclohexyl-2-[(1*R*,2*S*)-1-benzyl-2-methoxy-1-methyl-2-phenylethyl]-1,3-dioxolan-4-one (3i). 2c (486 mg, 1.35 mmol, 1.00 equiv), $PhCH(OMe)_2$ (265 μL, 1.77 mmol, 1.31 equiv), CH_2Cl_2 (2 mL), and Ph_3CSbCl_6 (40.0 mg, 0.0690 mmol, 0.0500 equiv) were reacted as per **3b** for 15 h to afford, after chromatography (24 g of SiO_2, 95:5 hexane/EtOAc), **3i** as a clear, colorless oil (0.164 g, 81%). 400-MHz ^{1}H NMR ($CDCl_3$): δ 7.38–7.10 (10 H, m), 5.39 (1 H, d, J = 1.2 Hz), 4.39 (1 H, s), 3.89 (1 H, dd, J = 4.8, 1.2 Hz), 3.18 (3 H, s), 3.12 (1 H, d, J = 14.0 Hz), 2.75 (1 H, d, J = 13.6 Hz), 1.85–1.46 (6 H, m), 1.27–1.02 (5 H, m), 0.82 (3 H, s). 101-MHz ^{13}C NMR ($CDCl_3$): δ 172.6, 137.9, 137.5, 131.1, 128.8, 127.9, 127.8, 127.5, 125.9, 106.4, 85.8, 78.6, 56.7, 55.4, 45.6, 38.6, 36.9, 29.0, 27.3, 25.9, 25.7, 15.5. Anal. Calcd for $C_{26}H_{32}O_4$: C, 76.44; H, 7.90. Found: C, 76.35; H, 8.03.

(2*S*,3*S*)-2-Benzyl-3-methoxy-2-methyl-3-phenylpropanol (4i). Crude, unenriched **3i** (383 mg, 0.937 mmol, 1.00 equiv) and $LiAlH_4$ (370 mg, 9.75 mmol, 10.4 equiv) were reacted as per **4b** to afford, after chromatography (24 g of SiO_2, 75:25 hexane/EtOAc), **4i** as a clear, colorless oil (150 mg, 65% yield, erythro/threo = 19:1, 84% ee by LISR analysis). 400-MHz ^{1}H NMR ($CDCl_3$): δ 7.40–7.16 (10 H, m), 4.28 (1 H, s), 3.35 (1 H, d, J = 7.2 Hz), 3.30 (1 H, d, J = 7.4 Hz), 3.26 (4 H, br s), 3.13 (1 H, d, J = 12.8 Hz), 2.39 (1 H, d, J = 13.2 Hz), 0.65 (3 H, s). 101-MHz ^{13}C NMR ($CDCl_3$): δ 138.1, 137.9, 131.0, 128.6, 128.0, 127.8, 127.2, 125.9, 91.7, 68.4, 57.1, 43.3, 37.2, 18.6. Anal. Calcd for $C_{18}H_{22}O_2$: C, 79.96; H, 8.20. Found: C, 79.92; H, 8.00.

Me_3SiOTf-Catalyzed Preparation of 3i and Subsequent Reduction to 4i. 2c (218 mg, 0.605 mmol, 1.00 equiv), $PhCH(OMe)_2$ (125 μL, 0.833 mmol, 1.38 equiv), CH_2Cl_2 (1.3 mL), and Me_3SiOTf (11.7 μL, 0.0605 mmol, 0.100 equiv) were reacted as per **3b** for 18 h to afford crude **3i**, which was isolated but not analyzed before being reduced with $LiAlH_4$ as per **4b** to obtain **4i** (0.110 g, 67% yield, erythro/threo = 16:1, 90% ee by LISR analysis).

(2*R*,5*R*)-5-Cyclohexyl-2-[(1*R*)-1-[(*R*)-methoxyphenylmethyl]-pentyl]-1,3-dioxolan-4-one (3j) and Subsequent Conversion to (2*R*)-2-Benzylhexanoic Acid.[18] **2d** (500 mg, 1.60 mmol, 1.00 equiv), $PhCH(OMe)_2$ (320 μL, 2.13 mmol, 1.33 equiv), CH_2Cl_2 (12.5 mL), and Me_3SiOTf (37.1 μL, 0.192 mmol, 0.120 equiv) were reacted as per **3b** for 3 h to afford, after chromatography (35 g of SiO_2, 5:1 hexane/EtOAc), **3j** as a clear, colorless oil (0.438 g, 76%). 400-MHz ^{1}H NMR ($CDCl_3$): δ 7.38–7.26 (5 H, m), 5.39 (1 H, dd, J = 5.6, 1.2 Hz), 4.44 (1 H, d, J = 4.8 Hz), 4.02 (1 H, d, J = 3.2 Hz), 3.25 (3 H, s), 1.94–1.09 (18 H, m), 0.077 (3 H, t, J = 7.2 Hz). 101-MHz ^{13}C NMR ($CDCl_3$): δ 172.8, 139.6, 128.3, 127.5, 126.7, 104.8, 82.4, 78.8, 57.1, 49.0, 39.0, 30.5, 29.0, 26.9, 26.0, 25.9, 25.8, 23.4, 22.7, 13.7. Anal. Calcd for $C_{22}H_{32}O_4$: C, 73.30; H, 8.95. Found: C, 73.04; H. 8.98. **Reduction to (2*S*)-2-[(*R*)Methoxyphenylmethyl]-1-hexanol (4j).** Crude, unenriched **3j** (2.21 g, 6.14 mmol, 1.00 equiv) and $LiAlH_4$ (1.40 g, 36.8 mmol, 6.00 equiv) were reacted as per **4b** to afford, after flash chromatography (3:1 hexane/ethyl acetate), **4j** (1.26 g, 92%) as a clear, colorless oil. 400-MHz ^{1}H NMR ($CDCl_3$): δ 7.37–7.24 (5 H, m), 4.39 (1 H, d, J = 4.8 Hz), 3.64–3.51 (2 H, m), 3.24 (3 H, s), 2.62 (1 H, t, J = 5.2 Hz), 1.93–1.88 (1 H, m), 1.34–1.13 (6 H, m), 0.820 (3 H, t, J = 7.2 Hz). 101-MHz ^{13}C NMR ($CDCl_3$): δ 139.1, 128.2, 127.5, 127.2, 87.1, 63.5, 57.2, 46.1, 29.7, 25.6, 22.9, 14.0. MS (15 eV) (rel intensity) 222 (M^+, 0.7), 190 (0.4), 160 (0.9), 123 (1.0), 122 (15.7), 121 (B), 91 (2.7), 77 (1.2). Anal. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97. Found: C, 75.26; H, 9.99. Demethoxylation to (2*R*)-2-benzyl-1-hexanol: Dry ammonia (ca. 12 mL) was condensed under nitrogen into a flask immersed in a −78 °C dry ice/acetone bath. THF (6.0 mL) and lithium metal (61.0 mg, 8.78 mmol) were added to afford a dark blue solution, and then **4j** (650 mg, 2.93 mmol, dissolved in 5 mL of THF under N_2) was added dropwise over 7 min, followed by THF wash (1 mL). The mixture was stirred for 10 min, after which time solid ammonium chloride (1.5 g) was added, causing the mixture to turn greyish white. The cold bath was removed, allowing the ammonia to evaporate, and then the residue was taken up in a mixture of saturated aqueous NaCl (50 mL) and Et_2O (25 mL) and transferred to a separatory funnel. The aqueous layer was separated and washed with Et_2O (3 × 15 mL) and then the combined Et_2O extracts were dried ($MgSO_4$), filtered, and concentrated at 15 mmHg to afford a 1:1 mixture of the desired (2*R*)-2-benzyl-1-hexanol and (2*R*)-2-cyclohexadienyl-1-hexanol. The latter was reoxidized to the desired 2-benzyl derivative by refluxing the mixture with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (427 mg, 1.88 mmol, 0.640 equiv based on starting **4j**) in C_6H_6 (25 mL) for 1.5 h, during which time a white precipitate formed. After it cooled to room temperature, the mixture was diluted with diethyl Et_2O (50 mL) and the supernatent was transferred via filter paper tipped cannula into a separatory funnel, washed with 1% aqueous NaOH (2 × 30 mL) and then with H_2O (50 mL), dried ($MgSO_4$), filtered, and concentrated at 15 mmHg to afford crude (2*R*)-2-benzyl-1-hexanol (340 mg, 61% yield) as a yellow oil (converted without purification to the corresponding acid). 400-MHz ^{1}H NMR ($CDCl_3$): δ 7.29–7.16 (5 H, m), 3.51 (2 H, t, J = 3.6 Hz), 2.62 (2 H, d, J = 7.2 Hz), 1.79–1.76 (1 H, m), 1.38–1.22 (7 H, m), 0.87 (3 H, t, J = 7.2 Hz). Oxidation to afford (2*R*)-2-benzylhexanoic acid: A portion of the crude (2*R*)-2-benzyl-1-hexanol (180 mg, 0.936 mmol, 1.00 equiv) was dissolved in acetone (10 mL), cooled to 0 °C, and treated with Jones reagent ($K_2Cr_2O_7/H_2SO_4$/acetone), added dropwise until the orange color of the latter persisted, ca. 0.60 mL of Jones reagent solution being required. The mixture was allowed to warm to 25 °C, stirred for 20 min, and then treated with a few drops of 2-propanol to give a mixture of a green supernatent and a green precipitate. The supernatent was then decanted and the solid washed with acetone (2 × 5 mL). The supernatent and acetone washes were combined and diluted with an equal volume of Et_2O and then washed with saturated aqueous NaCl (3 × 100 mL). The organic layer was then separated, dried ($MgSO_4$), filtered, and concentrated at 15 mmHg to afford, after chromatography (42 g of SiO_2, 95:5 hexane/EtOAc increasing to 85:15 hexane/EtOAc), pure (2*R*)-2-benzyl-1-hexanoic acid (91.2 mg, 47%). 400-MHz ^{1}H NMR ($CDCl_3$): δ 7.28–7.15 (5 H, m), 2.96 (1 H, dd, J = 13.6, 8.0 Hz), 2.74 (1 H, dd, J = 13.6, 6.8 Hz), 2.69–2.64 (1 H, m), 1.66–1.59 (1 H, m), 1.54–1.47 (1 H, m), 1.36–1.24 (4 H, m), 0.860 (3 H, t, J = 7.2 Hz). 101-MHz ^{13}C NMR ($CDCl_3$): δ 139.2, 128.9, 128.8, 126.4, 38.1, 31.5, 29.4, 22.5, 13.9. MS (70 eV) (rel intensity) 206 (M^+, 7.7), 150 (7.6), 149 (5.9), 131 (7.6), 117 (3.6), 115 (4.3), 104 (3.8), 103 (2.9), 92 (12.3), 91 (B), 79 (2.2), 78 (6.5), 77 (4.0), 65 (7.4). Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.36; H, 8.81. Optical rotation showed that $[\alpha]^{24}_D$ = −19.86° (*c* 2.024, C_6H_6), corresponding to 87% ee based on the reported rotation of the enantiomeric acid $[[\alpha]^{24}_D$ = 22.8° (*c* 2.063, C_6H_6) for (2*S*)-2-benzyl-1-hexanoic acid].[18] (We note that while all efforts were made to avoid enrichment or depletion of diastereomers during chromatography of the foregoing aldol product and alcohol derivatives, we cannot rule out the possibility that some *minor* enrichment or depletion may have occurred, thereby altering the final enantiomeric excess.)

Preparation of (2*S*,5*S*)-2-[(1*S*)-3-Carbomethoxy-3-methyl-1-[(1*S*)-1-methoxy-2,2-dimethylpropyl]butyl]-5-methyl-1,3-dioxolan-4-one (3o) and Subsequent Reduction to (2*R*)-4,4-Dimethyl-2-[(1*S*)-1-methoxy-2,2-dimethylpropyl]pentane-1,5-diol (4o). 2f (173 mg, 0.572 mmol, 1.00 equiv), CH_2Cl_2 (2 mL), *t*-$BuCH(OMe)_2$ (98.4 mg, 0.744 mmol, 1.30 equiv), and Me_3SiOTf (11.0 μL, 0.0572 mmol, 0.100 equiv) were reacted as per **3b** to afford crude **3o** as a clear, yellow oil (115 mg, 61%). This compound was not characterized as such and was instead reduced with $LiAlH_4$ as per **4b** to afford crude **4o** (erythro/threo = 99:1, 50% ee by LISR analysis) ca. 95% pure by ^{1}H NMR analysis, the ^{1}H NMR spectrum being otherwise identical with that observed for the enantiomeric alcohol **4l**.[15]

Preparation of (2*S*,5*S*)-2-[(1*S*)-3-Carbomethoxy-1-[(1*R*)-1-methoxyethyl]-3-methylbutyl]-5-methyl-1,3-dioxolan-4-one (3p) and Conversion

to (2*R*)-2-[(1*R*)-1-Methoxyethyl]-4,4-dimethylpentane-1,5-diol (4p). 2f (212 mg, 0.701 mmol, 1.00 equiv), $MeCH(OMe)_2$ (96.4 μL, 0.911 mmol, 1.30 equiv), and Me_3SiOTf (13.4 μL, 0.0701 mmol, 0.100 equiv) were reacted as per **3b**, but with Et_2O as the reaction solvent, to afford crude **3p** as a clear, yellow oil (133 mg, 52%). This compound was not characterized as such but was instead reduced as per **4b** to afford alcohol **4p** (erythro/threo = 6.5:1, 40% ee by LISR analysis) ca. 95% pure by ^1H NMR analysis, the ^1H NMR spectrum being otherwise identical with that observed for the enantiomeric alcohol **4m**.[15]

(2*R*,5*R*)-5-Cyclohexyl-2-[(2*S*)-2-methoxy-1,1-dimethyl-2-phenylethyl]-1,3-dioxolan-4-one (3t). 2j (520 mg, 1.83 mmol, 1.00 equiv), $PhCH(OMe)_2$ (360 μL, 2.40 mmol, 1.31 equiv), and Me_3SiOTf (35.5 μL, 0.184 mmol, 0.100 equiv) were reacted as per **3b** for 17 h. Recrystallization of half of this product from pentane afforded **3t** as a white crystalline solid (218 mg, 72%). 400-MHz ^1H NMR ($CDCl_3$): δ 7.37–7.26 (5 H, m), 5.51 (1 H, s), 4.21 (1 H, s), 4.07 (1 H, d, J = 2.8 Hz), 3.18 (3 H, s), 1.90–1.63 (6 H, m), 1.36–1.16 (5 H, m), 0.97 (3 H, s), 0.75 (3 H, s). 101-MHz ^{13}C NMR ($CDCl_3$): δ 173.0, 137.5, 128.6, 127.8, 127.7, 106.2, 86.2, 79.0, 57.0, 42.3, 39.0, 29.1, 27.2, 26.1, 25.9, 16.7, 15.9. HRMS calcd for $C_{20}H_{28}O_4$: 332.1988. Found: 332.1980. Anal. Calcd for $C_{20}H_{28}O_4$: C, 72.26; H, 8.49. Found: C, 72.19; H, 8.51.

(3*S*)-3-Methoxy-2,2-dimethyl-3-phenylpropanol (4t). Crude, unenriched **3t** (265 mg, 0.798 mmol, 1.00 equiv) and $LiAlH_4$ (308 mg, 8.12 mmol, 10.2 equiv) were reached as per **4b** to afford, after chromatography (35 g of SiO_2, 70:30 hexane/Et_2O), **4t** as a clear, colorless oil (139 mg, 78%; 94% ee by LISR analysis). 400-MHz ^1H NMR ($CDCl_3$): δ 7.37–7.26 (5 H, m), 4.11 (1 H, s), 3.53 (1 H, dd, J = 10.8, 6.4 Hz), 3.44 (1 H, dd, J = 11.2, 5.2 Hz), 3.21 (4 H, br s), 0.88 (3 H, s), 0.81 (3 H, s). 101-MHz ^{13}C NMR ($CDCl_3$): δ 138.1, 128.2, 127.6, 92.1, 71.7, 57.3, 39.4, 22.9, 19.6. Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.44; H, 9.38.

Preparation of (2*S*,3*S*)-2-Benzyl-1,1,3-trimethoxy-3-phenylpropane (6a) and Subsequent Reductive Demethoxylation To Afford (1*S*,2*R*)-2-Benzyl-1,3-dimethoxy-1-phenylpropane (10). 2k (205 mg, 0.711 mmol, 1.00 equiv), CH_2Cl_2 (4 mL), $PhCH(OMe)_2$ (1.17 mL, 7.82 mmol, 11.0 equiv), and Me_3SiOTf (13.7 μL, 0.0711 mmol, 0.100 equiv) were reacted as per **3b** for 3 h to afford, after chromatography (90 g of SiO_2, 95:5 hexane/EtOAc), **6a** as a clear, colorless oil (155 mg, 73%) [along with a separate fraction containing the free auxiliary, methyl hexahydromandelate (76.0 mg, 63%)]. 400-MHz ^1H NMR ($CDCl_3$): δ 7.36–6.96 (10 H, m), 4.44 (1 H, d, J = 4.8 Hz), 4.16 (1 H, d, J = 6.0 Hz), 3.29 (3 H, s), 3.27 (3 H, s), 3.11 (3 H, s), 2.83 (1 H, dd, J = 14.4, 4.0 Hz), 2.73 (1 H, dd, J = 14.4, 6.8 Hz), 2.26–2.21 (1 H, m). 101-MHz ^{13}C NMR ($CDCl_3$): δ 142.4, 140.9, 129.0, 128.3, 127.8, 127.2, 126.9, 125.2, 106.3, 83.1, 57.2, 54.5, 53.8, 50.3, 31.1. Anal. Calcd for $C_{19}H_{24}O_3$: C, 75.97; H, 8.05. Found: C, 75.99; H, 7.80. **Reductive Demethoxylation to afford 10**: Crude, unenriched **6a** (180 mg, 0.600 mmol, 1.00 equiv) Et_3SiH (105 μL, 0.659 mmol, 1.10 equiv), CH_2Cl_2 (0.5 mL), and Me_3SiOTf (1.1 μL, 0.0060 mmol, 0.010 equiv) were reacted according to the procedure of Noyori et al.[25] to afford, after aqueous workup and chromatography (40 g of SiO_2, 95:5 hexane/EtOAc), **10** (112 mg, 65% yield, erythro/threo = 46:1, 92% ee by LISR analysis) as a clear, colorless oil, identical by ^1H NMR analysis with the enantiomeric di-O-ether **8a**.

Preparation of (2*S*,3*S*)-2-Benzyl-1,1,3-trimethoxy-4,4-dimethylpentane (6b), Hydrolysis to (2*S*,3*S*)-2-Benzyl-3-methoxy-4,4-dimethylpentanal (11), and Reduction of the Latter To (2*R*,3*S*)-2-Benzyl-3-methoxy-4,4-dimethylpentanol (4u). 2k (286 mg, 0.992 mmol, 1.00 equiv), CH_2Cl_2 (5 mL), t-$BuCH(OMe)_2$ (1.44 g, 10.9 mmol, 11.0 equiv), and Me_3SiOTf (38.3 μL, 0.198 mmol, 0.200 equiv) were reacted as per **3b** to give a mixture of **6b**, the (tentatively characterized) mixed acetal t-BuCH(OMe)(OCHCyCO$_2$Me), and methyl hexahydromandelate. The mixture was refluxed with base (0.8 g of NaOH in 2 mL of H_2O/5 mL of THF/3 mL of MeOH) for 1 h and then extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated at 15 mmHg to afford **6b** as a clear, colorless oil (220 mg, 79%), pure by ^1H NMR. 400-MHz ^1H NMR ($CDCl_3$): δ 7.30–7.19 (5 H, m), 3.89 (1 H, d, J = 2.8 Hz), 3.46 (3 H, s), 3.42 (3 H, s), 3.16 (3 H, s), 3.12 (1 H, d, J = 1.6 Hz), 2.89 (1 H, dd, J = 14.8, 3.6 Hz), 2.55 (1 H, dd, J = 14.8, 11.2 Hz), 2.18–2.14 (1 H, m), 0.95 (9 H, s). 101-MHz ^{13}C NMR ($CDCl_3$): δ 142.0, 129.0, 128.3, 125.6, 107.1, 84.8, 60.1, 56.0, 55.7, 44.1, 36.9, 32.4, 26.3. HRMS calcd for $C_{16}H_{24}O_2$ (M^+ – MeOH): 248.1776. Found: 248.1779. Hydrolysis to the corresponding aldehyde: Crude **6b** (82.0 mg, 0.270 mmol, 1.00 equiv), $LiBF_4$ (256 mg, 2.73 mmol, 10.0 equiv), CH_3CN (5.5 mL), and H_2O (110 μL) were reacted according to the method of Lipshultz et al.[26] to afford **11** as a clear, colorless oil (60.0 mg, 87%), ca. 95% pure by ^1H NMR (converted without purification to the corresponding alcohol, as described below). 400-MHz ^1H NMR ($CDCl_3$): δ 9.76 (1 H, d, J = 1.6 Hz), 7.31–7.18 (5 H, m), 3.37 (3 H, s), 3.27 (1 H, d, J = 3.6), 3.11 (1 H, dd, J = 13.6, 2.4 Hz), 2.99–2.86 (2 H, m), 0.98 (9 H, s). 101-MHz ^{13}C NMR ($CDCl_3$): δ 204.3, 139.9, 128.9, 128.6, 126.3, 86.6, 60.6, 55.0, 36.7, 31.0, 26.6. Reduction to the corresponding alcohol: Crude **11** (28 mg, 0.12 mmol), 1.0 equiv) and $LiAlH_4$ (45 mg, 1.2 mmol, 10 equiv) were reacted as per **4b** to afford **4u** (26 mg, 93%, erythro/threo > 99:1, 96% ee by LISR analysis), ca. 95% pure by ^1H NMR analysis and evincing an otherwise identical ^1H NMR spectrum with that observed for the enantiomeric alcohol **4b**.

(2*S*,3*R*)-2-Benzyl-1,1,3-trimethoxybutane (6c). 2k (228 mg, 0.791 mmol, 1.00 equiv), CH_2Cl_2 (4 mL), $MeCH(OMe)_2$ (784 mg, 8.79 mmol, 11.0 equiv), and Me_3SiOTf (30.6 μL, 0.158 mmol, 0.200 equiv) were reacted as per **3b** for 18 h to afford, after workup as per **6b**, **6c** as a clear yellow oil (110 mg, 61% yield, erythro/threo = 9:1, 60% ee by LISR analysis), pure by ^1H NMR. 400-MHz ^1H NMR ($CDCl_3$): δ 7.28–7.16 (5 H, m), 4.37 (1 H, d, J = 5.6 Hz), 3.48–3.42 (1 H, m), 3.38 (3 H, s), 3.29 (3 H, s), 3.27 (3 H, s), 2.79 (1 H, dd, J = 14.4, 5.6 Hz), 2.72 (1 H, dd, J = 14.4, 7.2 Hz), 2.12–2.06 (1 H, m), 1.13 (3 H, d, J = 6.4 Hz). 101-MHz ^{13}C NMR ($CDCl_3$): δ 142.0, 129.0, 128.1, 125.5, 106.0, 76.0, 56.4, 54.7, 54.4, 48.0, 31.3, 16.4. HRMS calcd for $C_{13}H_{19}O_2$ (M^+ – CH_3OH): 206.13068. Found: 206.13063.

Preparation of (2*S*,3*S*)-2-Benzyl-1,1,3-tris(benzyloxy)-4,4-dimethylpentane (6d) and Subsequent Hydrogenolysis To Afford (2*R*,3*S*)-2-Benzyl-4,4-dimethylpentane-1,3-diol (12). 2k (314 mg, 1.09 mmol, 1.00 equiv), t-$BuCH(OCH_2Ph)_2$ (1.55 g, 5.44 mmol, 5.00 equiv), CH_2Cl_2 (6 mL), and Me_3SiOTf (42.1 μL, 0.218 mmol, 0.200 equiv) were reacted as per **3b** for 15 h to afford, after workup as per **6b**, a 2:1 mixture of **6d** and pivalaldehyde dibenzyl acetal, which was subjected to hydrogenolysis (Parr apparatus, 45 psi, 20 h, 50 mL of EtOAc, 0.5 equiv of 10% Pd/C) to afford a clear, colorless oil. Crystallization from ether at –40 °C gave **12** (120 mg, 50% yield based on **2k**) as a white crystalline solid, mp 137–138 °C. 400-MHz ^1H NMR ($CDCl_3$): 7.31–7.18 (5 H, m), 3.68 (1 H, s), 3.58 (2 H, d, J = 2.4 Hz), 2.98 (1 H, dd, J = 14.0, 3.2 Hz), 2.72 (1 H, dd, J = 14.4, 11.6 Hz), 2.30 (1 H, br s), 2.07–2.01 (1 H, m), 1.90 (1 H, br s), 1.06 (9 H, s). 101-MHz ^{13}C NMR ($CDCl_3$): δ 141.2, 129.1, 128.4, 125.9, 81.5, 65.7, 42.6, 35.8, 30.7, 27.0. HRMS calcd for $C_{14}H_{20}O$ (M^+ – H_2O): 204.1514. Found: 204.1502. Anal. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97. Found: C, 75.67; H, 10.05. Analysis of the *crude*, *unenriched* diol showed the erythro/threo ratio to be >99:1 and the optical purity to be 96% ee, as established by LISR analysis.

Preparation of (2*S*,4*R*,5*S*,6*R*)-5-Benzyl-4-[(*S*)-cyclohexylcarbomethoxymethoxy]-2,6-phenyl-1,3-dioxane (7). 2k (132 mg, 0.457 mmol, 1.00 equiv), PhCHO (102 μL, 1.01 mmol, 2.20 equiv), and CH_2Cl_2 (1 mL) were reacted as per **3b**, but with trifluoromethanesulfonic acid (4.10 μL, 0.0457 mmol, 0.100 equiv) in CH_2Cl_2 (0.5 mL) as the catalyst and a reaction time of 4 h, to afford, after chromatography (30 g of SiO_2, 95:5 hexane/EtOAc), **7** (137 mg, 60%), >95% pure by ^1H NMR. Crystallization from pentane at 0 °C afforded analytically pure material (96.0 mg, 42%), mp 125 °C, diastereomerically pure ^1H and ^{13}C NMR analysis. 400-MHz ^1H NMR ($CDCl_3$): δ 7.52–7.01 (15 H, m), 6.16 (1 H, S), 5.05 (1 H, d, J = 10.8 Hz), 5.02 (1 H, d, J = 3.2 Hz), 4.24 (1 H, d, J = 6.0 Hz), 3.55 (3 H, s), 2.79 (1 H, dd, J = 14.0, 10.4 Hz), 2.63 (1 H, tt, J = 10.8, 3.2 Hz), 2.32 (1 H, dd, J = 14.0, 3.2 Hz), 1.97–1.23 (11 H, m). 101-MHz ^{13}C NMR ($CDCl_3$): δ 171.7, 139.3, 138.1, 128.9, 128.8, 128.5, 128.4, 128.3, 128.0, 127.8, 126.3, 125.7, 96.0, 93.8, 79.9, 78.1, 51.4, 47.0, 41.1, 31.8, 29.7, 28.7, 26.2, 26.1, 26.0. Anal. Calcd for $C_{32}H_{36}O_5$: C, 76.77; H, 7.25. Found: C, 76.58; H, 7.35. A 400-MHz COSY ^1H NMR spectrum (provided as supplementary material) was used to assign resonances and establish that $J_{C(5)H-C(6)H}$ = 10.8 Hz and $J_{C(4)H-C(5)H}$ = 3.2 Hz.

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Supplementary Material Available: Four figures containing 400-MHz ^1H NMR COSY spectra for **7** and the (*R*)- and (*S*)-*O*-methylmandelate derivatives of **3f** (4 pages). Ordering information is given on any current masthead page.

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