Stereoselective Reactions of Ester Enolates with Epoxides[1]

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The development of stereoselective aldol reactions has been a critical advance in organic synthesis.[2] The development of analogous chemistry involving the reactions of enolates with epoxides is less documented. Indeed, to the best of our knowledge, only one preliminary study has been published on the reactions of ketone enolates with epoxides,[3] and the same is true for ester enolate/epoxide reactions.[1] This is unfortunate since if this area were exploited, it would open up numerous chiral synthesis opportunities because an unlimited number of optically active epoxides are available through Sharpless[4] and other epoxidation techniques.[5]

Nitrogen-containing enolates (e.g., of nitriles,[6] amides,[7] enamines,[8] and ketimines[9]) do react with epoxides. However, these methods have drawbacks. For example, enamines require formation from a ketone and then a second extra step to regenerate the carbonyl precursors. In other work, diastereoselective amide enolate/epoxide reactions were demonstrated.[7] However, hydrolysis to desired compounds could only be done under harsh conditions.[7] Clearly, methods are needed to promote the reactions of epoxides with the enolates of esters and ketones. In one study, $LiClO_4$ was added to ketone enolates to get them to react with epoxides.[3] In the present report, we show how aluminum enolates of esters do react diastereoselectively with epoxides[1] and detail attempts to do enantioselective reactions. Optically active epoxides were used to generate hydroxy esters with ee's of 98%. These compounds can then be cyclized to important optically active lactones.

Results and Discussion

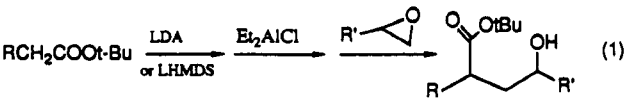
We prepared the lithium enolate of *tert*-butyl acetate by treatment with LDA in THF by established methods.[10]

Table I. Ester Enolate/Epoxide Reaction Products

entry	R	base	R′	product no.	yield,[a] %	syn:anti
1	H	LDA	Me	1	46[b]	
2	H	LDA	Et	2	52[b]	
3	H	LDA	*t*-Bu	3	49	
4	Me	LDA	Me	4	56[b] (70)	84:16
5	Me	LDA	Et	5	43[b]	84:16
6	Me	LDA	*i*-Pr	6	56[b]	88:12
7	Me	LDA	*t*-Bu	7	38[b]	95:5
8	H	LHMDS	Me	1	66 (58[b])	
9	H	LHMDS	Et	2	71	
10	H	LHMDS	*t*-Bu	3	54	
11	Me	LHMDS	Me	4	12	56:44
12	Me	LHMDS	Et	5	28	62:38
13	Me	LHMDS	*t*-Bu	7	12	89:11

[a] GC yield. [b] Distilled yield.

After propylene oxide was added to the enolate, stirring at −45 °C (to prevent Claisen reaction) for over 24 h produced <1% of the desired product. However, when the enolate was prepared as usual and then Et_2AlCl in hexanes was added, addition of an epoxide produced the desired reaction in reasonable yields (eq 1 and Table I).



(1)

Presumably, the enolate containing the Lewis-acidic aluminum assists in the ring-opening of the epoxide. Recently, we found that LHMDS-generated enolates give higher yields (Table I; up to 71% GC yield) than the LDA-generated enolates. Presumably, the bis(trimethylsilyl)-amine generated during the reaction does not coordinate to the aluminum promoter as strongly as does the diisopropylamine generated during the LDA reaction.[3] However, the use of either base in our method led to crude products that showed only small amounts of volatile side product (e.g., only small amounts of Claisen product), and therefore GC yields are comparable to distilled yields.

Diastereoselectivity. To test the diastereoselectivity of the reaction, we prepared the enolate of *tert*-butyl propionate by an established LDA method[10] (*E*:*Z* enolate ratio of 95:5) and then combined it with Et_2AlCl followed by an epoxide (eq 1, R = Me; R′ = Me, Et, *i*-Pr, *t*-Bu). The resulting *syn*/*anti* product ratios (Table I) varied from 84:16 for propylene oxide to 95:5 for 3,3-dimethyl-1,2-epoxybutane (*tert*-butyloxirane). The stereochemistry of the major product was established by cyclizing it (see below) to a lactone of known stereochemistry, e.g., *trans*-2,4-dimethyl-γ-butyrolactone,[11] and comparing the known lactone's spectral and physical properties to those of our product. The transition state that leads to predominantly *syn* product has been described.[1]

We also tried the same reaction only using the LHMDS-generated aluminum enolate of *tert*-butyl propionate. In this case, low yields and low selectivity were obtained (Table I). The low yield has been observed in other work involving the formation of propionate enolates using LHMDS.[12] To overcome this problem, HMPA was used

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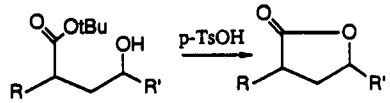
0022-3263/93/1958-7304$04.00/0

as a cosolvent with THF.[12] However, when HMPA was used in our reactions with epoxides, no hydroxy ester was obtained. We attribute this to the fact that HMPA would strongly coordinate with the Lewis-acidic aluminum and prevent its assistance in the reaction. We also wanted to prepare the *Z* enolate of *tert*-butyl propionate so that *anti* hydroxy esters could be made from it. However, that method involved the use of HMPA[13] too, and we were unable to obtain enolate/epoxide reaction products when that solvent was used.

Since a major value of this chemistry would lie in its potential use with optically active epoxides, we wanted to explore this area. When the LHMDS-generated aluminum enolate of *tert*-butyl acetate was combined with (*R*)- and (*S*)-propylene oxide, the enantiomeric hydroxy ester products, $[\alpha]^{21}_D = -8.1$ (*c* 0.0108, $CHCl_3$) and +8.3 (*c* 0.0496, $CHCl_3$), respectively, were formed in ee's of 98% as determined by Pirkle HPLC methods. The use of this chemistry was shown by cycling the (*S*)-*tert*-butyl 4-hydroxypentanoate product to a lactone by treatment with *p*-toluenesulfonic acid[14] in refluxing $CHCl_3$ (eq 2). The



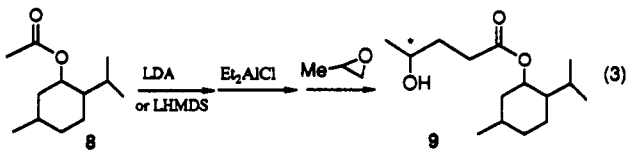
(2)

resulting (*S*)-4-methyl-γ-butyrolactone ($[\alpha]^{21}_D = -32.9$ (*c* 0.0203, $CHCl_3$) was formed in 98% ee, as shown by β-cyclodextrin column GC. This compound is an important precursor in the synthesis of (*S*)-(+)-sulcatol, an aggregation pheromone,[15] Geodiamolide A, a potent insecticidal,[16] and (−)-botryococcene.[17] It is noteworthy that our method gives a more optically pure product than the same compound produced by an enzymatic method.[18] Considering the importance of lactones in organic natural and medicinal products,[15-17,19] this approach to their synthesis may be the most significant aspect of our research. To further illustrate this, we used this chemistry to make a pheromone of the *Trogoderma sp.* of beetle.[20] The LDA-generated aluminum enolate of *tert*-butyl acetate was treated with (*R*)-1,2-epoxybutane[21] to give the (*R*)-hydroxy ester of **2** (eq 1, R = H, R′ = Et). The hydroxy ester was then carefully treated with *p*-toluenesulfonic acid to give (*R*)-4-ethyl-γ-butyrolactone[20,22] (eq 2, R = H, R′ = Et), the beetle pheromone, in 94% ee (by chiral GC). The enantiomeric purity of the product compares favorably with that of other reported syntheses.[20,22]

When the aluminum enolate of *tert*-butyl propionate was treated with (*S*)-propylene oxide, the stereoisomeric product ratio was 83:16:1:<1 (2*S*,4*S*:2*R*,4*S*:2*S*,4*R*:2*R*,4*R*, assuming an inversion reaction). The diastereomeric products can be separated by column chromatography, leaving an almost optically pure product. The use of this chemistry in the synthesis of chiral compounds shows high promise.

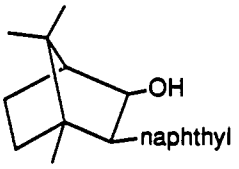
Further proof of the value of this enolate chemistry was demonstrated earlier in the use of it in the first syntehsis of (±)-rubrynolide.[23] In this case, a key step was the combination of the aluminum enolate of *tert*-butyl 4-pentenoate with 1,2-epoxy-11-dodecyne.

Enantioselectivity. In attempts to achieve kinetic enantioselection, we prepared the aluminum enolates of (+)- and (−)-menthol acetate and treated them with racemic propylene oxide (eq 3). The reactions were



(3)

stopped at 20% GC yield, and the ratio of stereoisomers was determined by Pirkle HPLC methods. Also, the (−)-menthol acetate enolate was treated with (*R*)-propylene oxide to get a pure stereoisomer for comparison and to be sure which chiral center predominated in each reaction. The ratio of *R*:*S* centers formed at the new chiral center for the (−)-menthol acetate reaction product was 57:43, and for the (+)-menthol acetate reaction it was 43:57. Although this stereoselection is modest, it is the first reported for an ester enolate/epoxide reaction. We also tried Taber[24] methods of enantioselection, namely using 4,7,7-trimethyl-3-*exo*-(1-naphthyl)bicyclo[2.2.1]heptan-2-*exo*-ol (**10**) as a chiral auxiliary. When we tried to make



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the enolate of the acetate of this compound by our methods, and then treated it with propylene oxide, only starting material and the alcohol **10** were recovered after 5.5 h reaction time. This chemistry was not pursued further since no yield of the desired product was obtained.

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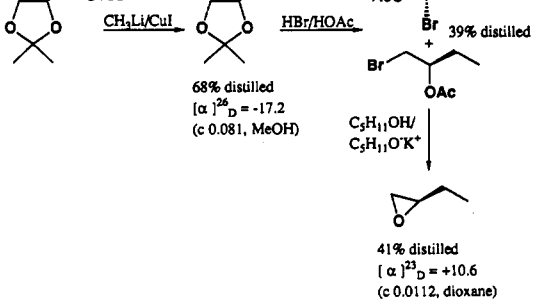
(21) The epoxide was made exactly as described in: Schmidt, U.; Talbiersky, J.; Bartkowiak, F.; Wild, J. *Chem. Int. Ed. Eng.* **1980**, *19*, 198. The only difference was that commercial L-α,β-isopropylideneglycerol-γ-tosylate was used as the starting material as shown below.



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(23) Taylor, S. K.; Hopkins, J. A.; Spangenberg, K. A.; McMillen, D. W.; Grutzner, J. B. *J. Org. Chem.* **1991**, *56*, 5951.
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In summary, the aluminum enolate of *tert*-butyl acetate reacts with epoxides in the highest yields when it is prepared from LHMDS. Propionate ester enolates (and probably other complex enolates[23]) give highest yields when prepared with LDA. The aluminum enolates described herein react with optically active epoxides to produce compounds that are nearly optically pure. Modest enantioselection can be achieved by using an ester chiral auxiliary. Important lactones can be made by cyclizing the hydroxy ester enolate/epoxide reaction products without loss of enantiomeric purity.

Experimental Section[25]

THF used in our reactions was distilled from sodium/benzophenone immediately before use. Diisopropylamine was distilled from CaH_2 and stored under N_2 before use. GC was done on 25 M 5% phenylmethylsilicone or 15 M SP-2330 capillary columns using biphenyl as an internal standard. The hydroxy ester products were purified for C, H analysis by semipreparative HPLC using a mobile phase of 85:14:1 hexane/CH_2Cl_2/EtOH. Distilled yields were determined by weighing product after distillation on a 2.5- or 5-cm Vigreux column. The resulting distillates were at least 95% pure by GC. A D-naphthylamine (95:5 hexane/*i*-PrOH mobile phase) HPLC column was used to determine the ee's of hydroxy ester products after they were derivatized with ICDNA reagent (a 3,5-dinitrobenzoate derivatization reagent purchased from Regis Chemical Co.). All reactions were done under a dry nitrogen atmosphere. (*R*)- and (*S*)-propylene oxide and (+)- and (−)-menthol acetate were purchased from Fluka.

LDA-Generated Enolate. In a typical reaction, 34.4 mmol of dry diisopropylamine was added dropwise to a mixture of 60 mL of dry THF and 34.4 mmol of *n*-BuLi (13.8 mL, 2.5 M in hexane) that was cooled to −78 °C under N_2. After the solution was stirred for 30 min, 34 mmol of *tert*-butyl propionate was added dropwise, and then after 30 min of stirring and warming the solution to −35 to −45 °C, 34.4 mmol of Et_2AlCl (1 M solution in hexane) was added over 5 min. After 15 min, 17.2 mmol of the epoxide was added dropwise. After 5 h at −45 to −35 °C, 20 mL of saturated NH_4Cl was added dropwise, and the mixture was added to 50 g of ice in 50 mL of 6 M HCl. The mixture was extracted twice with ether, and the organic layers were washed twice with 5% $NaHCO_3$ and once with saturated aqueous NaCl. The dried ($MgSO_4$) organic extract was concentrated by rotary evaporation and distilled using a 2.5-cm Vigreux column. Physical and spectral data on compounds 1–7 prepared in this manner are included below. The enolate prepared as above was combined with (*S*)-propylene oxide to give a stereoisomer product ratio of 86:14:1:<1 (see text for details). (*R*)-2 was prepared from the enolate of *tert*-butyl acetate and (*R*)-1,2-epoxybutane and is described below.

LHMDS-Generated Enolates. To a solution of 8.5 mmol of LHMDS (8.5 mL, 1 M in THF) and 15 mL of dry THF cooled to −78 °C was added 8.5 mmol of *tert*-butyl acetate over 15–20 min. After the solution was stirred at −78 °C for 30 min, 8.5 mmol of Et_2AlCl (8.5 mL, 1 M in hexanes) was added over 7 min, and then the mixture was stirred 15 min. The epoxide (4.3 mmol) was added over several min, and then the solution was stirred at −45 to −35 °C for at least 6 h. After 7 mL of saturated NH_4Cl was added to the mixture, it was added to a mixture of 12 mL of 6 M HCl and 12 g of ice. The mixture was extracted twice with ethyl ether, and the combined ether layers were washed twice with 5% $NaHCO_3$ and once with 15% NaCl and dried ($MgSO_4$). Distilled yields were obtained as described above or GC yields were obtained using biphenyl as an internal standard. (*R*)- and (*S*)-propylene oxide was reacted with the enolate of *tert*-butyl acetate in this way to get optically active hydroxy ester products (optical rotations and ee's are reported in the text).

***tert*-Butyl 4-hydroxypentanoate (1):** bp 75–77 °C (1.3 mm); NMR (CCl_4) δ 1.13 (d, 3 H, J = 7 Hz), 1.4 (s, $-C(CH_3)_3$), 1.65 (m, 2 H), 2.25 (t, 2 H, J = 7 H), 2.95 (s, –OH), 3.7 (m, 1 H, C*H*OH); IR (NaCl disks) 3600–3200 (br, s, OH), 1720 (s, C=O), 1160 (s) cm^{-1}; mass spectrum *m/e* (relative intensity) 118 (3), 101 (18), 85 (22), 59 (73), 57 (68), 56 (74), 55 (25), 43 (45), 41 (100), 39 (46), 31 (31), 29 (52), 28 (48). Anal. Calcd for $C_9H_{18}O_3$: C, 62.04; H, 10.41. Found: C, 62.13; H, 10.39.

***tert*-Butyl 4-hydroxyhexanoate (2):** bp 86–88 °C (1.6 mm); NMR ($CDCl_3$) δ 0.94 (t, CH_3, J = 8 Hz), 1.44 (s, $-C(CH_3)_3$), 1.3–1.8 (m, 4 H), 2.16 (s, –OH), 2.37 (t, 2 H, J = 7 Hz), 3.53 (m, –C*H*OH); IR (NaCl disks) 3600–3200 (OH), 1700 (s, C=O), 1160 (s) cm^{-1}; mass spectrum *m/e* (relative intensity) 114 (3), 85 (80), 59 (84), 57 (82), 41 (66), 29 (100). Anal. Calcd for $C_{10}H_{20}O_3$: C, 63.85; H, 10.64. Found: C, 63.43, H, 10.82. The (*R*)-2 enantiomer was made similarly by treating 63 mg of (*R*)-1,2-epoxybutane[21] with 2 equiv of enolate (44% yield). The spectral data of the product were the same as that of the racemic product, $[\alpha]^{22}_D$ = +5.2 (*c* 0.0042, $CDCl_3$).

***tert*-Butyl 5,5-dimethyl-4-hydroxyhexanoate (3):** bp 51–54 °C (0.05 mm); NMR (CCl_4) δ 0.9 (s, $-C(CH_3)_3$), 1.45 (s, $-OC(CH_3)_3$), 1.5–2.0 (m, 2 H), 2.30 (t, 2 H, J = 7 Hz), 3.0 (s, OH), 3.2 (d of d, C*H*OH, J = 10 and 3 Hz); IR (NaCl disks) 3600–3200 (s, OH), 1720 (s, C=O), 1180 (s) cm^{-1}; mass spectrum *m/e* (relative intensity) 142 (1, $M^+ - t$-Bu), 85 (49), 59 (97), 57 (60), 41 (100). Anal. Calcd for $C_{12}H_{24}O_3$: C, 66.29; H, 11.18. Found: C, 66.55; H, 11.27.

***tert*-Butyl 4-hydroxy-2-methylpentanoate (4):** bp 72–73 °C (1.2 mm); NMR ($CDCl_3$) δ 1.0–1.4 (overlapping doublets, 6 H, J = 8 Hz), 1.45 (s, $-C(CH_3)_3$), 1.6–2.0 (m, 2 H), 2.4–3.0 (m, 1 H), 2.6 (s, OH), 3.7–4.2 (m, 1 C*H*OH); IR (NaCl disks) 3600–3200 (s, OH), 1730 (s, C=O), 1160 (s) cm^{-1}; mass spectrum *m/e* (relative intensity) 144 (1), 132 (5), 115 (24), 70 (48), 59 (100), 55 (77), 43 (70), 42 (70), 41 (99), 39 (57), 31 (35), 29 (36). Anal. Calcd for $C_{10}H_{20}O_3$: C, 63.85; H, 10.64. Found: C, 63.57; H, 10.55.

***tert*-Butyl 4-hydroxy-2-methylhexanoate (5):** bp 78–82 °C (1.4 mm); NMR ($CDCl_3$) δ 0.9 (t, 3 H, J = 7 Hz), 1.1–1.15 (d, 3 H, J = 7 Hz), 1.5 (s, $C(CH_3)_3$), 1.3–2.0 (m, 4 H), 2.4–2.8 (m, 2 H including OH), 3.4–3.7 (m, C*H*OH); IR (NaCl disks) 3600–3200 (s, OH), 1720 (s, C=O), 1153 (s) cm^{-1}; mass spectrum *m/e* (relative intensity) 173 (0.5), 146 (2), 99 (49), 59 (76), 57 (100), 43 (57), 42 (36), 41 (89), 39 (39), 31 (37), 29 (43). Anal. Calcd for $C_{11}H_{22}O_3$: C, 65.31; H, 10.96. Found: C, 65.11; H, 10.96.

***tert*-Butyl 2,5-dimethyl-4-hydroxyhexanoate (6):** bp 84–89 °C (1.2 mm); NMR ($CDCl_3$) δ 0.95 (d, 6 H, J = 7 Hz), 1.2 (d, 3 H, J = 7 Hz), 1.5 (s, $-OC(CH_3)_3$), 1.55–2.0 (m, 3 H), 2.4–2.8 (m, 2 H), 3.1–3.6 (m, C*H*OH); IR (NaCl disks) 3600–3200 (s, OH), 1720 (s, C=O), 1160 (s) cm^{-1}; mass spectrum *m/e* (relative intensity) 173 (2), 117 (35), 99 (100), 71 (44), 59 (53), 57 (84), 56 (40), 43 (69), 41 (77), 39 (33). Anal. Calcd for $C_{12}H_{24}O_3$: C, 66.29; H, 11.18. Found: C, 66.53; H, 11.34.

***tert*-Butyl 2,5,5-trimethylheptanoate (7):** bp 79–82 °C (1.0 mm); NMR ($CDCl_3$) δ 0.9 (s, $-C(CH_3)_3$), 1.15–1.2 (d, 3 H, J = 7 Hz), 1.3–1.5 (m, 2 H), 1.45 (s, $-OC(CH_3)_3$), 2.2 (s, OH), 2.6–2.8 (m, 1 H), 3.25 (d of d, 1 H, J = 10 and 3 Hz); IR (NaCl disks) 3600–3200 (s, OH), 1720 (s, C=O), 1160 (s) cm^{-1}; mass spectrum *m/e* (relative intensity) 173 (2), 157 (4), 117 (41), 99 (77), 71 (32), 59 (37), 57 (100), 43 (43), 41 (71). Anal. Calcd for $C_{13}H_{26}O_3$: C, 67.84; H, 11.31. Found: C, 67.74; H, 11.39.

Lactonization.[14] A solution of 66 mg of *p*-toluenesulfonic acid, 1.2 g of *tert*-butyl 2-methyl-4-hydroxyhexanoate (4), and 65 mL of $CDCl_3$ (the reaction was followed by NMR) was refluxed for 30 min, cooled, washed with 5% $NaHCO_3$ and 16% NaCl, and dried ($MgSO_4$). The distilled lactone, bp 99–100 °C (25 mm), 0.47 g (60%; other yields were as high as 84%), was identical in all respects to the known *trans*-2,4-dimethyl-γ-butyrolactone.[11] Compound (*S*)-1, made from (*S*)-propylene oxide and the enolate of *tert*-butyl acetate, was treated similarly except that the solution was stirred at room temperature for 30 min and 3 h at 35 °C and then several mg of solid Na_2SO_4 and Na_2CO_3 were added and the mixture was stirred 5 min. It was then run through a plug of silica gel to give (*S*)-4-methyl-γ-butyrolactone (optical rotation and ee, determined by GC on a β-cyclodextrin column, are given in the text). (*R*)-2 (62.9 mg; 0.61 mmol), prepared as described above, was treated similarly in 4 mL of $CDCl_3$. Some 2 was still present, so the product was purified by silica gel column

(25) Instruments used were described earlier: Taylor, S. K.; Bischoff, D. S.; Blankespoor, C. L.; Deck, P. A.; Harvey, S. M.; Johnson, P. L.; Marolewski, A. E.; Mork, S. W.; Motry, D. H.; Van Eenenaam, R. *J. Org. Chem.* **1990**, *55*, 4202.

chromatography (50:50:trace hexane/CH_2Cl_2/EtOH). A pure (>98% by GC) fraction (11 mg, 29%; the total yield of product in all fractions was >70%) gave the same spectral data as racemic (*R*)-4-ethyl-γ-butyrolactone: ^{13}C NMR ($CDCl_3$) δ 9.9, 28.0, 29.0, 29.3, 82.7, 177.8;[22,25] $[\alpha]^{21}_D$ = +49.7 (*c* 0.0029, $CDCl_3$) (lit.[26] $[\alpha]^{20}_D$ = +50 ($CHCl_3$)).

Menthol Acetate Enolates. At −78 °C, 1.4 mL of diisopropylamine (10.08 mmol) was added dropwise to a solution of 20 mL of dry THF and 5.25 mL of 1.92 M *n*-BuLi in hexane. After 0.5 h, 2.16 mL (10.08 mmol) of (+)-menthol acetate was added dropwise. After 15 min, 10.08 mmol of Et_2AlCl (1 M in hexane) was added to the mixture over 10 min. After 10 min, 2.68 mL (40.32 mmol) of propylene oxide was added, and the mixture was stirred at −40 to −50 °C for 5.5 h. Saturated NH_4Cl (10 mL) and a mixture of 10 mL of 6 M HCl and 10 g of ice were added, and the mixture was stirred for 5 min. The organic layer was separated and washed with 5% $NaHCO_3$ and 15% NaCl and dried ($MgSO_4$). The concentrated organic layer was purified by HPLC using a 10-μm silica gel semipreparative column (57:42:1 hexane/CH_2Cl_2/EtOH) to give 0.52 g of **(+)-2-isopropyl-5-methylcyclohexyl 4-hydroxypentanoate** (20% yield, >97% GC pure): $[\alpha]^{20}_D$ = +61.4 ($CHCl_3$); ratio of 4*R*:4*S* isomers 43:57; ^1H NMR ($CDCl_3$) δ 0.74 (d of d, 3 H, *J* = 3.4 and 1.0 Hz), 0.89 (d of d, 6 H, *J* = 3.4 and 2.4 Hz), 1.2 (d, 3 H, *J* = 6.3 Hz), 0.9–2.0 (m, 12 H), 2.4 (t, 2 H, *J* = 7.3 Hz), 3.8 (sextet, 1 H, *J* = 5.7 Hz), 4.6 (t of d, 1 H, *J* = 11 and 4 Hz); ^{13}C NMR ($CDCl_3$) δ 16.9, 21.3, 22.6, 24.0, 24.1, 26.9, 31.8, 32.0, 34.9, 41.5, 47.6, 68.1, 74.9, 174.4; IR (NaCl disks) 3600–3200 (br, s, –OH), 1721, 1710, 1175 (s) cm^{-1}. Anal. Calcd for $C_{15}H_{28}O_3$: C, 70.27; H, 11.01. Found: C, 70.15; H, 11.08.

(−)-2-Isopropyl-5-methylcyclohexyl 4-hydroxypentanoate was prepared as described above from (−)-menthol acetate: $[\alpha]^{20}_D$ = −60.1 ($CHCl_3$), ratio of 4*R*:4*S* isomers from Pirkle column HPLC 57:43; ^1H NMR ($CDCl_3$) δ 0.74 (d of d, 3 H, *J* = 3.4 and 1.0 Hz), 0.89 (d of d, 6 H, *J* = 3.4 and 2.9 Hz), 1.2 (d, 3 H, *J* = 5.9 Hz), 0.9–2.0 (m, 12 H), 2.4 (t, 2 H, *J* = 7.3 Hz), 3.8 (sextet, 1 H, *J* = 5.9 Hz), 4.6 (t of d, 1 H, *J* = 10.7 and 4.4 Hz); ^{13}C NMR ($CDCl_3$) δ 17.0, 21.3, 22.6, 24.1, 24.2, 27.0, 31.8, 32.0, 34.7, 35.0, 41.6, 47.7, 68.0, 75.0, 174.3; IR (NaCl disks) 3600–3200 (br, s, –OH), 1732 (s), 1714 (s), 1175 (s) cm^{-1}. Anal. Calcd for $C_{15}H_{28}O_3$: C, 70.27; H, 11.01. Found: C, 70.19; H, 11.12. The reaction was repeated only using (*R*)-propylene oxide, giving a compound that was >90% 4*R* isomer by Pirkle column HPLC, $[\alpha]^{20}_D$ = −71.2 ($CHCl_3$).

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(26) Yadav, J. S.; Rao, S. E.; Rao, S. V. *Synth. Commun.* **1989**, *19*, 705.