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ASYMMETRIC REACTIONS BASED ON 1,3-OXATHIANES—3

SECONDARY α-HYDROXYACIDS, $RCHOHCO_2H$ AND GLYCOLS $RCHOHCH_2OH$[1]

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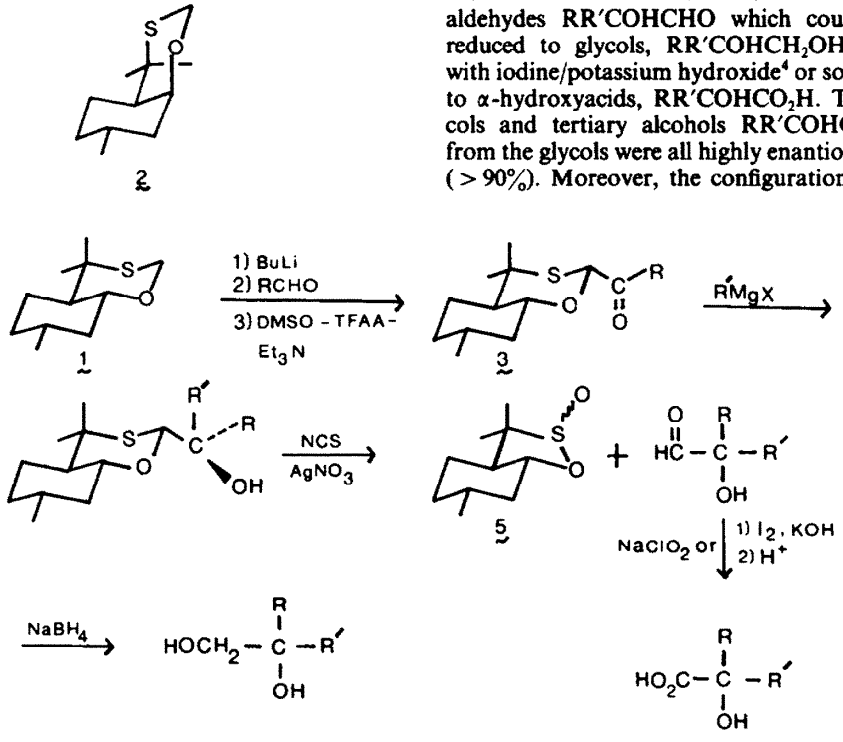
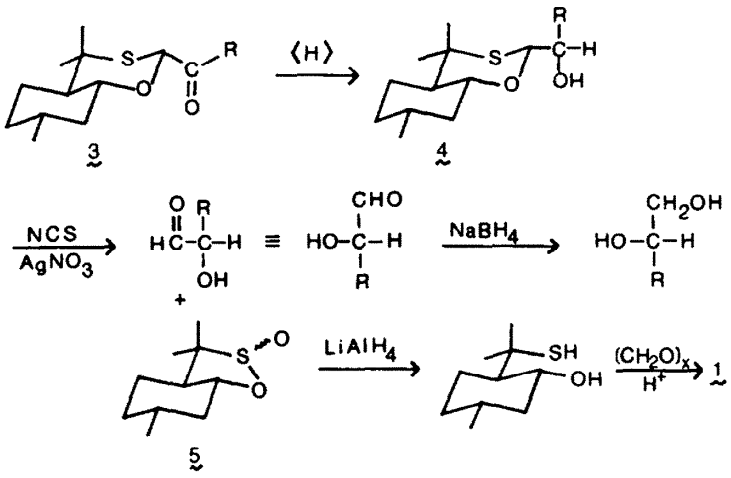
Abstract—Reduction of the previously prepared[1] chiral 2-acyl-1,3-oxathianes derived from (+)-pulegone with various metal hydride combinations proceeds stereoselectively, with diastereomer excess (d.e.) of as much as 97% in the case of reduction of phenyl ketones with lithium tri-sec.butylborohydride. Lesser selectivity (maximum 82% d.e.) is achieved with primary or tertiary alkyl ketones: the predominant diastereomer is readily purified by chromatography. The major product in these cases is that predicted by Cram's chelate rule. The product ratio is reversed with diisobutylaluminum hydride and also in the reduction of secondary alkyl ketones with lithium sec.butylborohydride, where stereoselectivity is low. The 2-hydroxyalkyl-1,3-oxathianes are cleaved to α-hydroxyaldehydes with N-chlorosuccinimide—silver nitrate and the aldehydes reduced to glycols, $RCHOHCH_2OH$ with sodium borohydride with little or no racemization. Esters, $RCHOHCO_2CH_3$, are obtained in high enantiomeric purity by O-benzylating the 2-hydroxyalkyl-1,3-oxathianes prior to cleavage, oxidizing with sodium chlorite following cleavage, esterifying and debenzylating. A method for measuring the enantiomeric purity of glycols $RCHOHCH_2OH$ by conversion to 2-phenyl-1,3-dioxolanes with benzaldehyde, followed by proton NMR analysis of the resulting 2-phenyl-4-alkyl-1,3-dioxolane diastereomer pair in the presence of a chiral europium shift reagent is described.

In the previous paper[1] we have described the synthesis of enantiomerically pure oxathianes **1** and **2** from (+)-pulegone, the conversion (Scheme 1) of these oxathianes into their diastereomerically pure equatorial 2-acyl derivatives (**3**) by lithiation with butyllithium, treatment with an aldehyde and oxidation of the resulting carbinol with Swern's reagent (dimethyl sulfoxide–trifluoroacetic anhydride–triethylamine[2]), and the highly stereoselective reaction of the resulting 2-acyl-1,3-oxathianes (**3**) with Grignard reagents at −78° to give nearly (>90%) diastereomerically pure tertiary alcohols. The latter were then cleaved with N-chlorosuccinimide–silver nitrate[3] to tertiary α-hydroxyaldehydes $RR'COHCHO$ which could be further reduced to glycols, $RR'COHCH_2OH$ or oxidized, with iodine/potassium hydroxide[4] or sodium chlorite[5] to α-hydroxyacids, $RR'COHCO_2H$. The acids, glycols and tertiary alcohols $RR'COHCH_3$ prepared from the glycols were all highly enantiomerically pure (>90%). Moreover, the configuration of the prod-



Scheme 1.



Scheme 2.

ucts could be predicted on the basis of the assumption that the Grignard addition proceeded according to Cram's chelate rule.[6,7]

The present paper is concerned with an extension of this reaction to secondary alcohols, e.g. **4** and the synthesis of secondary α-hydroxyacids, $RCHOHCO_2H$ and glycols, $RCHOHCH_2OH$. It is clear that, if reduction of the 2-acyl-1,3-oxathianes **3** to alcohols **4** (Scheme 2) can be effected highly stereoselectively, if the resulting alcohols of high diastereomeric purity can be cleaved to α-hydroxyaldehydes, RCHOHCHO without racemization (which is more likely to occur with these compounds than with the tertiary analogs RR'COHCHO because of the presence of a H alpha to the CO group) and if these aldehydes can be oxidized to acids and reduced to glycols without racemization, the desired objective will be at hand. We shall deal with these various problems in turn.

RESULTS

In Table 1 the results of reduction of a model system,[8] *cis*-2-benzoyl-4,6,6-trimethyl-1,3-oxathiane, with a variety of chemical reducing agents are sum-

Table 1. Reduction of *cis*-2-benzoyl-4,6,6-trimethyl-1,3-oxathiane[a]

Entry No.	Reducing Agent	Solvent(s)(ratio,v/v)[d]	Temp. °C	Product Ratio
1	$LiAlH_4$	Et_2O	0	92:8
2	$LiAlH_4$	Et_2O	-78	95:5
3	$LiAlH_4$	Et_2O-THF (11:5)	-78	90:10
4	$LiAlH_4$	Et_2O-THF (11:5)	25	88:12
5	$LiAlH_4$-t-BuMgCl	Et_2O	-78	94:6
6	$LiAlH_4$-$MgBr_2$	Benzene-Et_2O (1:9)	0	90:10[b]
7	L-Selectride[c]	Toluene	-78→25	98.5:1.5
8	L-Selectride-LiI	Et_2O	-78	95:5
9	L-Selectride[c]	Benzene-hexane (2:5)	-78→25	88:12
10	L-Selectride[c]	Et_2O-THF (10:1)	-78	73:27
11	K-Selectride[c]	THF	0→25	70:30
12	K-Selectride[c]	THF	-78	78:22
13	$NaBH_4$	i-PrOH	25	73:27
14	$NaBH_4$	Et_2O-THF-H_2O (6:2:1)	25	80:20
15	$NaBH_4$-LiBr	Et_2O	25	84:16
16	$NaBH_4$-LiI	Et_2O	0	97:3
17	$NaBH_4$ - $LiClO_4$	Et_2O	25	94:6
18	$NaBH_4$ - $LiClO_4$	THF	30	67:33
19	$LiBH_4$	Et_2O	-15	86:14
20	$LiAlH(Ot\text{-}Bu)_3$	Et_2O	25	82:18
21	$LiAlH(OMe)_3$	Et_2O-THF	0	75:25
22	$NaBH_3CN$-HOAc	MeOH	25	56:44
23	BH_3	THF	0→25	53:47[d]
24	$Al(Oi\text{-}Pr)_3$	i-PrOH-THF (1:1)	ca.70	40:60
25	$i\text{-}Bu_2AlH$	Benzene-hexane (2:1)	0	35:65

[a]Yields range from 80 to 100% unless otherwise indicated. [b]Yield 75%.
[c]Selectride is tri-sec.butylborohydride. [d]Yield 62%.

marized. Substantial stereoselectivity is found with a number of reagents; the diastereomer excess (d.e. = %A − %B) as measured by proton or ^{13}C NMR is 97% with L-Selectride® (lithium tri-sec.butylborohydride) in toluene (entry 7), 94% with sodium borohydride–lithium iodide in ether at 0° (entry 16) and 90% with lithium aluminum hydride in ether at −78° (entry 2). As in addition of Grignard reagents,[8] stereoselectivity increases with decreasing temperature (compare entries 1 and 2) and decreases with increasing solvating power of the solvent (compare entries 3 with 2, 10 with 7 and 13 with 14; the comparison of 14 and 13 might be inappropriate because of the heterogeneous nature of the medium in 14). The more ion-pairing lithium borohydride (entry 19) seems to be better than the less ion-pairing sodium borohydride (entry 14) but here again the difference in solvent (as well as temp.) blurs the comparison. The addition of lithium salts to sodium borohydride (entries 15–17), making it soluble (presumably as lithium borohydride) in ether, greatly increases stereoselectivity, but the same trick seems to fail in tetrahydrofuran (entry 18).

The above results, as the corresponding ones in Grignard and organolithium additions,[8] are best interpreted in terms of a mechanism involving Cram's chelate rule.[6,7] While the alternative open-chain rule[7,9] leads to the same prediction[10] of the configuration of the products (which, *vide infra*, is in accord with the facts), stereoselectivity in the operation of the open-chain rule tends to be lower than in the operation of the chelate one.[7,8] Therefore, conditions which favor chelation with the cation of the reducing agent (low temp., low-dielectric solvent, Li over Na cation) enhance stereoselectivity.[26]

An entirely different picture is presented by the acidic reducing agents BH_3.THF, diisobutylaluminum hydride (Dibal) and aluminum isopropoxide (entries 23-25). The borane complex (entry 23) is

Table 2. Hydride reductions of *cis* - 2 - acetyl - 4,6,6 - trimethyl - 1,3 - oxathiane

	%A[a]	%B[a]	Yield %
$LiAlH_4$, Et_2O, -78°C	69	31	100
L-Selectride®, toluene, -78°C	80	20	85
$NaBH_4$-LiI, Et_2O, 0°C	79	21	80
$NaBH_4$-$LiClO_4$, Et_2O, 25°C	80	20	91
$NaBH_4$-$LiClO_4$, benzene, 25°C	62	38	74
$NaBH_4$-LiI, benzene, 25°C	74	26	85

[a] A is the stereoisomer predicted by Cram's rule, B the opposite diastereoisomer.

Table 3. Hydride reductions of 3, R = n-C_6H_{13}[d]

Entry	Reducing Agent[a]	Solvent	Temp. °C	%A	%B[c]
1	$LiAlH_4$	Ether	RT[b]	30	70
2	$LiAlH_4$	Ether	-78°	22	78
3	$LiAlH_4$	THF	RT	30	70
4	$LiAlH_4$	THF	-78°	50	50
5	$LiAlH_4$-$TiCl_4$ (1:1)	THF	RT	35	65
6	$LiAlH_4$-$TiCl_4$ (1:1)	THF	-78°	36	64
7	L-Selectride®	THF	RT	25	75
8	L-Selectride®	THF	-78°	60	40
9	L-Selctride®	Toluene	RT	15	85
10	L-Selectride®	Toluene	-78°	11	89
11	L-Selectride®-$MgCl_2$ (2 eq.)	Toluene	-78°	15	85
12	L-Selectride®-LiI (2 eq.)	Toluene	-78°	9	91
13	L-Selectride®-LiI (10 eq.)	Toluene	-78°	10	90
14	L-Selectride®, 15-Crown-5 (2 eq.)	Toluene	-78°	26	74
15	K-Selectride®	Toluene	-78°	17	83
16	K-Selectride®, 18-Crown-6	Toluene	-78°	22	78
17	$LiEt_3BH$	Toluene	-78°	16	84
18	$NaBH_4$	i-PrOH	RT	30	70
19	$NaBH_4$	i-PrOH	-78°	29	71
20	$NaBH_4$, LiI	THF	RT	37	63
21	$NaBH_4$, LiI	THF	-78°	28	72
22	BH_3.SMe_2	THF	-78°	53	47
23	Dibal	Ether	-78°	80	20
24	Dibal	THF	-78°	68	32
25	Dibal	Hexane	-78°	90	10
26	Dibal	Toluene	-78°	89	11
27	Dibal-$AlCl_3$	Toluene	-78°	88	12

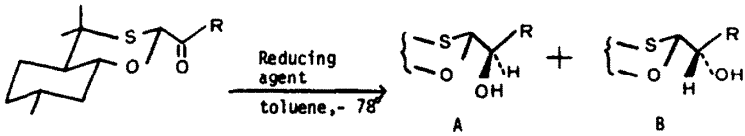
[a] L-Selectride® is lithium tri-sec.butylborohydride; K-Selectride® is the corresponding potassium salt. [b] Room temperature. [c] Product predicted by Cram's chelate rule.[4] See also "note added" at end of paper.

quite unstereoselective and the selectivity of the other two reagents (entries 24, 25), while modest, is in the opposite direction from that of the complex metal hydride reagents. Here the central atom of the reagent (B or Al) presumably complexes with the carbonyl oxygen but (because of the difficulty Al, or impossibility B, of forming a pentacoordinate intermediate) not with the oxathiane. Under these circumstances the dipolar rule[7,11] may operate;[10] this rule leads to a prediction of predominance of the stereoisomer epimeric with that formed when the chelate or open-chain rules are in effect.[7,26]

In Table 2 are shown the results of hydride reduction of methyl ketones in the model system and in Table 3 the results of reduction of the n-hexyl ketone in the actual chiral system derived from **1**. It is clear from Table 2 that selectivity in the methyl ketone system is less than in the phenyl ketone analog; this difference is a common one and has previously been observed in addition of Grignard reagents.[8] One possible explanation[8] is in terms of a reactivity-selectivity relationship; the phenyl ketone, being less selective, is more reactive. An alternative interpretation [12] is in terms of the angle of approach of the nucleophile to the ketone which will be closer to the side of the alkyl group (and therefore further away from the asymmetric influence of the oxathiane moiety) in the acyloxathiane with an aliphatic acyl group than with an aromatic one. The results with the n-hexyl ketone (Table 3) nevertheless show that appreciable stereoselectivity (over 80% d.e. meaning a stereoisomer ratio greater than 9 : 1) can be attained by using lithium Selectride^R under appropriate conditions (entries 12, 13). The reverse ratio (1 : 9) is achieved in this instance with Dibal (entry 25). Since the two alcohol diastereomers differ considerably in polarity, it is easy to separate mixtures by even low-efficiency column chromatography and both isomers can thus be obtained pure. Detailed perusal of Table 3 shows some interesting anomalies: for example, lowering the temperature, in the $LiAlH_4$ reduction in THF, from room temperature to $-78°$ leads to complete loss of stereoselectivity (entries 3, 4) and a similar lowering in the case of L-Selectride^R (entries 7 and 8) actually leads to a reversal of the predominant product. Yet for reductions with $LiAlH_4$ in ether (entries 1, 2) and with L-Selectride^R in toluene (entries 9, 10) the temperature effects are normal. Addition of crown ethers to the Selectrides diminishes stereoselectivity (entries 10 vs 14, 15, vs 16) as one might expect; the effect—presumably due to interference with chelation of the cation by the oxathiane ketone **3**–is greater with the otherwise more complexing lithium than with the less complexing potassium reagent.

Results for L-Selectride^R and Dibal reduction for a wider range of ketones are shown in Table 4. Dibal always reduces with high selectivity and in the sense contrary to Cram's chelate rule. The high selectivity of L-Selectride^R, on the other hand, is confined to primary and (to a slighly lesser extent) tertiary ketones. With secondary alkyl groups in the ketone, the selectivity with L-Selectride^R is greatly reduced and may even disappear altogether; moreover, the major product (if any) is now the one formed counter to Cram's chelate rule. We note that a diminution (though not reversal) of stereoselectivity had also been noted in addition of Grignard reagents to 2-isobutyroyl-1,3-oxathianes (i.e. with an isopropyl ketone);[8] the explanation given, which may also hold

Table 4. Reduction of 2-acyl-1,3-oxathianes derived from pulegone with L-Selectride^R and with Dibal



		A	B
Methyl	L-Selectride®	21	79
	Dibal	78	22
n-Hexyl	L-Selectride®	11	89
	Dibal	87	13
Isopropyl	L-Selectride®	67	33
	Dibal	88	12
Cyclohexyl	L-Selectride®	52	48
	Dibal	89	11
tert-Butyl	L-Selectride®	22	78
	Dibal	81	19

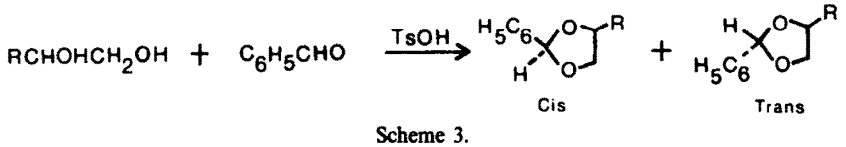
[a] L-Selectride® = lithium tri-sec.butylborohydride. Dibal = diisobutylaluminum hydride. [b] Product predicted by Cram's chelate rule. This is the more polar (less easily chromatographically eluted) isomer.

here, is that the extra α-alkyl substituents will tend to block the approach of the nucleophile from the top face (i.e. the side of H-2 of the oxathiane) of the ketone, which is otherwise the preferred side of approach. With the t-butyl ketones high selectivity is regained[8] because now approach to *both* faces of the CO group is equally impeded by the α-Me substituents and the oxathianyl group (on the other side of the carbonyl function) can again exert its natural tendency to direct apprach toward the less hindered top face (the side of H-2 as opposed to the S moiety of the ring).

Cleavage of the oxathianecarbinols **4** with N-chlorosuccinimide–silver nitrate[3] proceeds much as in the tertiary carbinol series[1] and leads to α-hydroxy-aldehydes and sultines (Scheme 2). The aldehydes may be reduced to glycols, $RCHOHCH_2OH$ with borohydride and separated by chromatography; the sultines are reduced to the corresponding hydroxy-thiols by means of $LiAlH_4$ and then reconverted to the starting oxathiane **1** as previously described.[1] There is little or no racemization in this sequence. The optically active glycols obtained in this way are shown in Table 5. Fortunately the configurations of all these glycols are known in the literature: (*S*)-(−)-1,2-octanediol,[13] (*R*)-(−)-methyl-1,2-butanediol, $(CH_3)_2CHCHOHCH_2OH$,[14] (*R*)-(+)-cyclohexylethylene glycol, $c\text{-}C_6H_{11}CHOHCH_2OH$,[15] (*R*)-(−)-3,3-dimethyl-1,2-butanediol, $(CH_3)_3CCHOHCH_2OH$,[16] and (*S*)-(+)-styrene glycol, $C_6H_5CHOHCH_2OH$.[17] Thus the configurations of the glycol precursors, given in Table 4 (Cram or anti-Cram products) were deduced except for that of the methyl ketone (**3**, R = CH_3) reduction product, which is based on analogy with the *n*-hexyl compound as to order of chromatographic elution, i.e. polarity, and the relative chemical shifts and coupling constants of the C-2 protons in the oxathiane moiety.

Determination of the enantiomeric purity of the glycols by known methodology proved difficult. We did not feel we could rely on optical rotation values because of the sensitivity of the rotation to the presence of chemical impurities, including solvent residues, and even concentration.[18] Esterification of the glycols with chiral acids, such as Mosher's acid [19] is equivocal because either the primary or the secondary hydroxyl function may be esterified.[20] Direct treatment with a chiral shift reagent was not fruitful because the proton NMR spectrum of the ABC system of the gylcol remained too complex for analysis. Therefore we converted the glycols to pairs of diastereomeric 2-phenyl-1,3-dioxolanes, as shown in Scheme 3.

The two dioxolanes are formed in somewhat un-



Scheme 3.

Table 5. Optically active glycols $RCHOHCH_2OH$ synthesized

	Precursor Purity, d.e.%[a]	Yield %	$[\alpha]_D^{20}$	e.e.%[b]
n-C_6H_{11}	85	42	c	84±2
$(CH_3)_2CH$	93	66	10.0[d]	90±3
c-C_6H_{11}	94	53	4.8[e]	94±2
$(CH_3)_3C$	91	76	22.7[f]	93±2
C_6H_5	100	22	30.3[g]	94±3

[a]Diastereomeric purity of compound 4 as determined by proton nmr. These compounds all have the S configuration at the secondary carbinol center. [b]Enantiomeric purity of glycol as determined by chiral shift reagent. [c]This value was not determined, but the rotation of a sample of 81% e.e. (from cyanoborohydride reduction of the precursor) was -15.2° (Abs. EtOH). From this, a maximum specific rotation of -18.8° is calculated. There is no rotation for the pure material in the literature. [d]Maximum rotation calculated 11.1°. Reported[14] maximum rotation for R-isomer $[\alpha]_D^{25}$ -10.95 (c=1, $CHCl_3$). [e]Maximum rotation calculated 5.1°. Reported[15] value for S-isomer $[\alpha]_D^{26}$ +4.20° (C=1.5, $CHCl_3$). [f]Maximum rotation calculated 24.4°; lit.[16] -28.1° for isomer. The discrepancy is rather large; with this glycol we have observed sizeable fluctuations of specific rotation which seems to depend on concentration; cf. footnote 18. [g]The calculated rotation is 37.3°; the sample was contaminated by about 20 wt.% of succinimide (determined by proton nmr) explaining its low rotation.

Table 6. Benzaldehyde derivatives of glycols, $RCHOHCH_2OH$ in absence and presence of $Eu(hfc)_3$

R in Glycol (Scheme 1)	d.e. %[a]	δ[b] A	δ[b] B	mole %[c]	Δδ[d] A	Δδ[d] B	e.e. %[e]
n-C_6H_{13}	35,85,99[f]	5.91	5.78	8	0.11	0.16	36,84,98[f]
$(CH_3)_2CH$	78	5.89	5.78	28	0.06	0.08	78[g]
cyclo-C_6H_{11}	96,94[f]	5.87	5.76	14	0.04	0.08	95,94[f]
$(CH_3)_3C$	91	5.88	5.61	18	0.08	0.15	93
C_6H_5	100	6.16	5.96	10	0.02	0.06	94

[a]Diastereomer excess in glycol precursor. [b]Shift (ppm) of H(2) in 2-phenyldioxolanes in absence of shift reagent A, trans isomer; B cis isomer. [c]Ratio of $Eu(hfc)_3$ to glycol. The optimal ratio should be determined by trial and error, since it seems to depend not only on the nature of the glycol, but also on the presence, if any, and nature of impurities (which may also complex). [d]Differential shift for the two enantiomers of diastereomers A and B, respectively, in the presence of the amount of $Eu(hfc)_3$ indicated. [e]Enantiomeric excess of glycol; average of two determinations (for the cis- and trans-2-phenyl-4-alkyl-1,3-dioxolanes). Generally these determinations were within 1% of each other. Absolute accuracy is estimated as ±2%. [f]Samples of different diastereomeric) purity. [g]Since the "inner" peaks originated from the two diastereomers (A,B) were not well resolved, the e.e. was calculated from the ratio of the sum of the outer peaks to the sum of the inner peak.

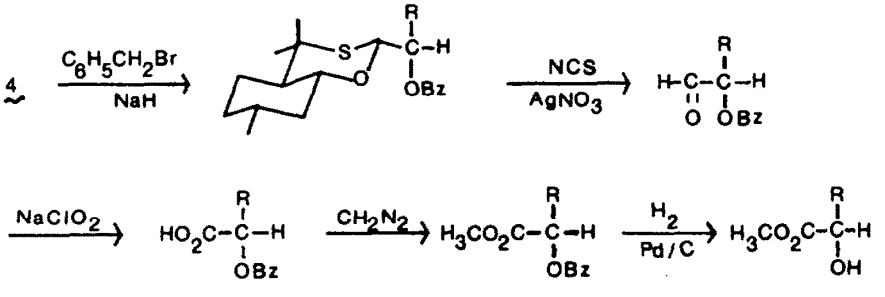
equal amounts (*ca* 55:45) as expected. Treatment of the mixture with a chiral shift reagent [$Eu(hfc)_3$] leads to doubling of the H-2 (benzylic) peak in both diastereomers. Integration of either pair of peaks allows one to determine the enantiomeric purity; since there are two diastereomers, two sets of (concordant) ratios are thus obtained, permitting a check of internal consistency.

The data on enantiomeric purity of glycols in Table 6 were obtained in this way. In the case of R = n-hexyl we have ascertained that no racemization has occurred in the dioxolane formation by hydrogenolyzing (Pd–C) the dioxolane back to the starting gylcol and comparing the rotation before and after dioxolane formation.

To obtain esters, $RCHOHCO_2CH_3$, it was necessary to protect the oxathianecarbinol **4** by O-benzylation prior to cleavage. Cleavage, followed by oxidation with sodium chlorite[5] (Scheme 4) and esterification produced the O-benzylated ester which was separated from the sultine congener by chromatography and debenzylated in the usual way. To check the enantiomeric purity of the resulting ester, it was reduced ($LiAlH_4$) to the glycol and the enantiomeric purity of the latter determined as indicated above. The results with chiral α-benzyloxyesters are summarized in Table 7.

CONCLUSIONS

Representative aliphatic glycols, $RCHOHCH_2OH$ and α-hydroxyesters, $RCHOHCO_2CH_3$ have been prepared by the oxathiane method here described; extension to additional cases is undoubtedly possible. Dibal reduction leads to one of the intermediate diastereomeric oxathianecarbinols (**4**) in 60–80% d.e. in all five cases studied. High selectivity in the opposite sense with L-Selectride® can be achieved only with primary, and, to a lesser extent, tertiary alkyl groups (R in **4**). Purification of the diastereomers by chromatography is facile because of their very different polarity. Cleavage and borohydride reduction of **4** to glycols $RCHOHCH_2OH$ and cleavage, after benzylation, and sodium chlorite oxidation to α-benzyloxyacids, $RCHOBzCO_2H$ proceeds without racemization in the aliphatic series. Chiral α-hydroxyesters, $RCHOHCO_2CH_3$ are acces-



Scheme 4.

Table 7. Optically active α-benzyloxyesters, $RCHOBzCO_2CH_3$ synthesized

R	Precursor[a] Purity d.e.%	Yield%	$[\alpha]_D^{20}$[b]	e.e.[c]
n-C_6H_{11}	99	81	+62.5°	98[d]
$(CH_3)_2CH$	78	82	+77.3°	78
c-C_6H_{11}	96	74	+66.9°	95[e]
$(CH_3)_3C$	99	86	+76.1°	≥100[f]

[a]Diastereomeric purity of compound 4 as determined by proton nmr. These compounds all have the R configuration at the secondary carbinol center. [b]All rotations in $CHCl_3$. [c]Determined by reduction ($LiAlH_4$) to glycol benzyl ether followed by hydrogenolysis and determination of e.e. of $RCHOHCH_2OH$ as earlier described. [d]Material hydrogenolyzed to n-$C_6H_{13}CHOHCO_2CH_3$, $[\alpha]_D^{20}$ -9.91°. Lit.[20] $[\alpha]_D^{16}$ +11° (c = 10, $CHCl_3$) for S isomer. [e]Material hydrogenolyzed to c-$C_6H_{11}CHOHCO_2CH_3$, $[\alpha]_D^{20}$ -31.3°. Lit.[21] $[\alpha]_D$ (neat) - 21.4° for R isomer, temp. not specified. [f]Material hydrogenolyzed to $(CH_3)_3CCHOHCO_2CH_3$, $[\alpha]_D^{20}$ -35.8°. Lit.[16] $[\alpha]_D^{22}$ -31.2° (neat) calculated for R isomer of 100% e.e.

sible in this way by esterification and debenzylation of the precursor. In the aromatic series (4, R = C_6H_5) reduction of the aroyloxathianes (3, R = Phenyl) to the corresponding carbinols (4, R = phenyl) can be carried out with very high stereoselectivity (> 95% d.e.) and there is again little loss of enantiomeric purity in the subsequent cleavage and reduction to styrene glycol.

EXPERIMENTAL

Mps were measured on an Electrothermal mp apparatus and are uncorrected. Bps are air bath temps in Kugelrohr distillations. Optical rotations were measured on a Perkin–Elmer Model 141 polarimeter equipped with Na and Hg light sources using a 10-cm thermostated cell at 20°. IR spectra were recorded on a Beckman model 4250 spectrophotometer. Proton NMR spectra were recorded on Perkin–Elmer R24B (60-MHz), Varian XL-100 (100-MHz), or Bruker WM-250 (250-MHz) spectrometers using TMS as an internal standard. The following abbreviations are used to designate the multiplicity of individual signals: s = singlet, brs = broad singlet, d = doublet, t = triplet, dd = double doublet, dt = double triplet, m = multiplet. ^{13}C NMR spectra were recorded on Varian XL-100 (25.16) MHz) or Bruker WM-250 (62.89 MHz) spectrometers using TMS as internal standard. TLC was performed by using E.Merck 0.2 mm silica gel 60 F-254 aluminum backed sheets. Developed plates were visualized by staining with a 10% soln of phosphomolybdic acid in EtOH. Flash column chromatography was performed with EM Reagent Kieselgel 60 (230-400 mesh ASTM) as described.[23] Preparative High-Pressure liquid chromatography was performed on a Waters LS 500A instrument using one or two columns [2.0 in (i.d.) × 11.25 in, packed with silica (Waters Prepak-500 (silica)].

Syntheses of 2-(1-*hydroxyalkyl*)-1,3-*oxathianes*

2-(1R-*Hydroxyheptyl*)-1 and 2-(1S-*hydroxyheptyl*)-1 (4, R = n-C_6H_{13}). A stirred soln of 5.00 g (25.0 mmol) of 1, prepared as described,[1] and 3.20 g (27.5 mmol) of N, N, N′, N′-tetramethylenediamine in 100 mL of dry THF, cooled to −78° was treated with 16.3 mL of 1.69 M n-BuLi (27.5 mmol) over 30 min. The mixture was stirred for an additional 4 hr at −78°, then a soln of 3.00 g (26.3 mmol) of n-heptanal in 50 mL of dry THF was added dropwise over 30 min. After stirring for 30 min at −78°, the mixture was warmed to room temp and treated with 50 mL of sat NH_4Claq, then 30 mL of water. The THF phase was separated and concentrated under reduced pressure. To the residue was added 20 mL of water and the product was extracted with three 50-mL portions of ether. The ether extract was dried ($MgSO_4$) and concentrated to give 7.70 g (98%) pale yellow oil. TLC showed a presence of small amount of starting material 1. A ^1H NMR spectrum showed that the product consists of 55% 2-(1*R*-hydroxyheptyl)-1 and 45% 2-(1*S*-hydroxyheptyl)-1. *R* isomer, ^1H NMR ($CDCl_3$) δ 2.55 (brs, 1H), 3.43 (dt, 1H, J = 10.0, 4.0 Hz), 3.62 (dt, 1H, J = 6.8, 4 Hz), 4.75 (d, 1H, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$) δ 82.3, 77.1, 73.2, 50.8, 42.9, 41.7, 34.8, 32.6, 31.8, 31.4, 29.6, 29.2, 25.2, 24.4, 23.0, 22.6, 21.1, 14.0, *S* isomer, ^1H NMR ($CDCl_3$) δ 2.46 (brs 1H), 3.43 (dt, 1H, J = 10.0, 4.0 Hz), 3.76 (dt, J = 7, 4 Hz), 4.93 (d, 1H, J = 3.4 Hz); ^{13}C NMR ($CDCl_3$) δ 82.9, 77.3, 73.3, 51.0, 42.5, 41.8, 34.7, 32.5, 31.9, 31.4, 29.7, 29.2, 25.7, 24.4, 22.8, 22.6, 22.0, 14.0. (Found: C, 68.53; H, 11.26. Calc for $C_{18}H_{34}O_2S$: C, 68.74; H, 10.90%).

2-(1R-*Hydroxy*-2-*methylpropyl*)-1 and 2-(1S-*hydroxy*-2-*methylpropyl*)-1 (4, R = isopropyl) were similarly obtained in 97% yield, *R*:*S*, 63:37. *R* isomer, m.p. 47–48°; ^1H NMR ($CDCl_3$) δ0.93 (d, 6H, J = 5Hz), 0.99 (d, 3H, J = 6 Hz), 1.28 (s, 3H), 1.43 (s, 3H), 2.50 (brs, 1H), 3.51–3.37 (m, 2H), 4.90 (d, 1H, J = 6.3 Hz); ^{13}C NMR ($CDCl_3$) δ80.7, 77.2, 77.1, 50.8, 42.9, 41.7, 34.7, 31.4, 29.6, 24.4, 22.9, 22.1, 19.8, 15.7. *S* isomer ^1H NMR ($CDCl_3$) δ 0.95, (d, 6H, J = 4.8 Hz), 0.99 (d, 3H, J = 4.2 Hz). 1.28 (s, 3H), 1.43 (s, 3H), 2.62 (brs, 1H), 3.50-3.36 (m, 3H), 4.99 (d, 1H, J = 4.3 Hz); ^{13}C NMR ($CDCl_3$) δ 81.5, 77.4, 76.1, 51.0, 42.3, 41.8, 34.7, 31.4, 29.8, 24.4, 22.7, 22.1, 19.0, 18.2. (Found: C, 66.09, H, 10.24. Calc for $C_{15}H_{28}O_2S$: C, 66.13, H, 10.36%).

2-(1R-*Hydroxycyclohexylmethyl*)-1 and 2-(1S-*hydroxy-cyclohexylmethyl*)-1 (4, R = cyclohexyl) were similarly obtained by reaction the 2-lithio salt of 1 with cyclohexanecarboxaldehyde in 92% crude yield and in a 51:49 isomer ratio. *R* isomer, ^1H NMR ($CDCl_3$) δ 0.94 (d, 3H, J = 6 Hz), 1.28 (s, 3H), 1.42 (s, 3H), 2.48 (brs, 1H), 3.48-3.36 (m, 2H), 4.90 (d, 1H, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$) δ 80.1, 77.1,

77.0, 50.8, 42.9, 41.7, 39.6, 34.7, 31.4, 29.9, 29.6, 26.5, 26.4, 26.3, 26.1, 24.4, 22.9, 22.1, *S* isomer ^{1}H NMR ($CDCl_3$) δ 0.92 (d, 3H, J = 6 Hz), 1.27 (s, 3H), 1.43 (s 3H), 2.48 (brs, 1H), 3.48-3.36 (m, 1H), 3.54 (dd, 1H, J = 8, 4 Hz), 4.99 (s, 1H, J = 4.4 Hz); ^{13}C NMR ($CDCl_3$) δ 81.2, 77.4, 77.3, 51.0, 42.4, 41.8, 39.4, 34.8, 31.5, 29.1, 28.9, 28.6, 26.5, 26.0, 25.8, 24.4, 22.7, 22.1.

2-(1R-*Hydroxy*-2,2-*dimethylpropyl*)-**1** and 2-(1S-*hydroxy*-2,2-*dimethylpropyl*)-**1** (**4**, R = t-Bu). The reaction of the 2-lithio salt of **1** with trimethylacetaldehyde gave the diastereomer mixture in 92% crude yield. Evaporative distillation: b.p. 110-130° (0.05 mmHg). *R* isomer, ^{1}H NMR ($CDCl_3$) δ 0.92 (d, 3H, J = 6 Hz), 0.97 (s, 9H), 1.99 (s, 3H), 1.40 (s, 3H), 2.52 (brs, 1H), 3.10 (d, 1H, J = 2 Hz), 3.47 (dt, 1H, J = 8.4 Hz), 5.12 (d, 1H, J = 2.0 Hz); ^{13}C NMR ($CDCl_3$) δ 79.5, 78.0, 77.1, 50.3, 43.2, 41.7, 35.3, 34.6, 31.3, 29.5, 26.4, 24.2, 22.8, 22.0. *S* isomer, ^{1}H NMR ($CDCl_3$) δ 0.91 (d, 3H, J = 6 Hz), 1.01 (s, 9H), 1.26 (s, 3H), 1.42 (s, 3H), 3.41 (dt, 1H, J = 8, 4 Hz), 3.52 (d, 1H, J = 4 Hz), 5.04 (d, 1H, J = 4.3 Hz); ^{13}C NMR ($CDCl_3$) δ 81.8, 80.9, 77.3, 50.7, 42.6, 41.8, 34.7, 34.4, 31.5, 29.7, 26.5, 24.4, 22.8, 22.1. (Found: C, 66.80, H, 10.95. Calc for $C_{16}H_{30}O_2S$: C, 67.08, H 10.56%).

2-(1R-*Hydroxyphenylmethyl*)-**1** and 2-(1S-*hydroxyphenylmethyl*)-**1** (**4**, R = C_6H_5). The reaction of the 2-lithio salt of **1** with benzaldehyde gave the *R* and *S* isomers in 95% crude yield in a 2 : 1 ratio. *S* isomer, m.p. 92-92.5 (methanol). ^{1}H NMR ($CDCl_3$) δ 0.93 (d, 3H, J = 5 Hz), 1.25 (s, 3H), 1.35 (s, 3H), 2.81 (brs, 1H), 3.47 (dt, 1H, J = 4, 10 Hz), 4.97 (d, 1H, J = 4 Hz), 5.15 (d, 1H J = 4 Hz), 7.24 (s, 5H); ^{13}C NMR ($CDCl_3$) δ 139.6, 127.9, 127.6, 126.5, 83.6, 77.3, 75.3, 50.8, 42.6, 41.6, 34.6, 31.3, 29.6, 24.3, 22.7, 22.0. *R* isomer, ^{1}H NMR ($CDCl_3$) δ 4.56 (d, 1H, J = 8 Hz), 4.89 (d, 1H, J = 8 Hz). (Found: C, 70.98, H, 8.70. Calc for $C_{18}H_{26}O_2S$: C, 70.55 H, 8.55%).

Syntheses of 2-(1-*acyl*)-1,3-*oxathianes* (**3**)

2-*Heptanoyl*-**1** (**3**, R = n-C_6H_{13}). A soln of 3.95 g (37.5 mmol) of trifluoroacetic anhydride in 20 mL of dry CH_2Cl_2 was added to a stirred soln of 1.96 g (50 mmol) of dimethyl sulfoxide in 50 mL of dry CH_2Cl_2 over 30 min at −78°. A white ppt was formed. After 30 min, a soln of 7.88 g (25.1 mmol) of a mixture of **4**, R = n-C_6H_{13} in 50 mL of dry CH_2Cl_2 was added dropwise over 1 hr. After 1 hr stirring, 3.80 g (75 mmol) of Et_3N was added at −78° over 10 min and the mixture was allowed to warm. The resulting yellow soln was carefully concentrated under reduced pressure, using a Clorox trap to oxidize bad-smelling sulfide. To the residue was added 50 mL of ether and the ethereal soln was successively washed with three 50-mL portions of 1M HCl, two 50-ml portions of 10% Na_2CO_3aq and two 50-mL of water. Drying ($MgSO_4$) and concentration gave 7.06 g (90%) of yellow oil. IR (CCl_4) 2970, 2940, 1735, 1465, 1380, 1155, 1090, 1079 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.37 (s, 1H, H(C-2)); ^{13}C NMR ($CDCl_3$) δ 205.6, 82.8, 77.1, 50.5, 43.9, 41.6, 38.0, 34.7, 31.6, 31.5, 29.4, 28.8, 24.4, 23.2, 22.5, 22.1, 14.0. (Found: C, 69.09; H, 10.13. Calc for $C_{18}H_{32}O_2S$: C, 69.18; H, 10.32%).

2-(2-*Methylpropanoyl*)-**1** (**3**, R = isopropyl) was similarly prepared, m.p. 51.5-52.5°; IR (CCl_4) 2980, 2940, 2880, 1730, 1465, 1390, 1375, 1305, 1155, 1120, 1090, 1070, cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.96 (d, 3H, J = 4.8 Hz), 1.14 (d, 6H, J = 6.6 Hz), 1.31 (s, 3H), 1.56 (s, 3H), 3.22 (octet, 1H, J = 6.6 Hz), 5.56 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 208.7, 81.9, 77.1, 50.4, 43.8, 41.6, 36.0, 34.6, 31.3, 29.3, 24.3, 22.5, 22.1, 18.6, 18.3. (Found: C, 66.66, H, 9.72. Calc for $C_{15}H_{26}O_2S$: C, 66.62, H, 9.69%).

2-*Cyclohexylcarbonyl*-**1** (**3**, R = cyclohexyl) was similarly prepared. IR (CCl_4) 2940, 2860, 1725, 1460, 1375, 1150, 1090, 1070 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.52 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 207.5, 81.9, 77.1, 76.0, 50.4, 45.9, 43.8, 41.6, 34.7, 31.4, 29.3, 28.7, 28.4, 25.8, 25.5, 24.3, 22.5, 22.1.

2-(2,2-*Dimethylpropanoyl*-**1** (**3**, R = t-Bu) and 2-*benzoyl*-1(**3**, R = phenyl) had been previously reported.[1]

Hydride reduction of 2-*heptanoyl*-**1** (**3**, R = n-C_6H_{13}) *with L-Selectride*^{R}

A soln of 0.24 g (0.76 mmol) of the ketone in 20 mL of dry toluene was treated with 1.5 mL of 1M soln of L-Selectride^R in THF at −78°. After 4 hr stirring the excess reducing agent was quenched with 1 mL of sat NH_4Claq at −78°. The mixture was allowed to warm. Separation of the toluene layer and concentration gave an oil, whose ^{1}H NMR spectrum showed unresolved peaks around 5.2 ppm. Basic hydrolysis of the oil by refluxing with 50 mL of 1M NaOH in MeOH for several hr gave 0.22 g (92%) of product whose ^{1}H NMR spectrum showed two clean sets of peaks for the diastereomers of **4**, R = n-C_6H_{13} in a 89 : 11 ratio. Other ketones were reduced similarly.

Dibal reduction of 2-(1-*acyl*)-1,3-*oxathianes* **3**

The following is a typical example. A soln of 0.086 g (0.275 mmol) of 2-(-heptanoyl)-**1** (**3**, R = n-C_6H_{13}) in 10 mL of dry toluene was treated with 0.55 mL of 1M Dibal soln in hexane at −78°. After 2 hr stirring, the soln was quenched with 1 mL sat NH_4Claq at −78°. The mixture was allowed to warm to room temp and the product extracted with two 10-mL portions of ether. Drying ($MgSO_4$) and concentration under reduced pressure gave 0.086 g (99% crude yield) of product. The analyses of pertinent products are summarized in Table 4.

Separation of the diastereomers of **4** *by column chromatography and measurement of diastereomer excess* (*d.e.*). Small amounts (1 g) were separated by flash chromatography.[23] (Solvent: 5% EtOAc in hexanes). Larger amounts (6–7 g) were conveniently separated using a Waters LS 500A instrument using the same solvent mixture. The *R*-isomer is the less polar one. Diastereomer excess (d.e.) was determined by integration of the two sets of doublets due to H(2) corresponding to the two diastereomers, in the ^{1}H NMR spectrum. Shifts (δ ppm in $CDCl_3$, more polar diastereomer first, coupling constant in parentheses): **4**, R = n-C_6H_{13}, 4.93 (3.4), 4.75 (6.8); R = $(CH_3)_2CH$, 4.99 (4.3), 4.90 (6.3); R = cyclohexyl, 4.99 (4.4), 4.9 (7.0); R = $(CH_3)_3C$, 5.04 (4.3), 5.12 (2.0).

Syntheses of 2-(1-*benzyloxyalkyl*)-1,3-*oxathianes*

2-(1-R-*Benzyloxyheptyl*)-**1**. A soln of 1.21 g (3.85 mmol, d.e. 99%) of 2-(1R-hydroxyheptyl)-1,3-oxathiane-**1**, obtained by hplc separation of an enriched sample, in 50 mL of dry THF was treated with 0.46 g (19 mmol) of NaH. The mixture was refluxed for $\frac{1}{2}$ hr; then a soln of 0.79 g (4.62 mmol) of benzyl bromide in 5 mL of dry THF was added over 5 min. After 10 hr refluxing under N_2, the mixture was cooled to room temp and the excess NaH was quenched with several drops followed by 10 mL of water. The THF layer was separated and washed with two 20 mL portions of sat NH_4Claq. Drying ($MgSO_4$) and concentration gave 1.51 g (97%) of oil. ^{1}H NMR ($CDCl_3$) δ 4.93, 4.69 (AB(q), 2H, J = 12 Hz), 5.11 (d, 1H, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 139.1, 128.2, 128.0, 127.4, 82.8, 81.1, 77.3, 73.9, 50.8, 43.1, 41.9, 34.8, 31.7, 31.5, 31.2, 29.8, 29.2, 25.4, 24.4, 22.9, 22.6, 22.2, 14.1. (For *S* diastereomer, similarly prepared, ^{1}H NMR ($CDCl_3$) δ 4.67, 4.49 (AB(q), 2H, J = 12 Hz), 4.91 (d, 1H, J = 4 Hz); ^{13}C NMR ($CDCl_3$) δ 139.0, 128.22, 128.18, 127.5, 82.3, 80.9, 77.5, 72.7, 51.1, 42.7, 41.9, 34.9, 31.8, 31.5, 31.4, 29.8, 29.3, 25.5, 24.5, 22.8, 22.6, 21.1, 14.1).

2-(1R-*Benzyloxy*-2-*methylpropyl*)-**1**. Similar reaction of the appropriate alcohol (**4**, R = isopropyl, d.e. 78%) with NaH and $PhCH_2Br$ gave the benzyl ether in 97% crude yield. IR (CCl_4) 3080, 3050, 2940, 1465, 1380, 1375, 1190, 1160, 1125, 1080 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.7–3.2 (m, 2H), 4.66, 5.02 (AB(q), 2H, J = 12 Hz), 5.13 (d, 1H, J = 8 Hz), 7.43 (s, 5H); ^{13}C NMR ($CDCl_3$) δ 139.4, 128.1, 127.8, 127.2, 85.4, 82.6, 77.1, 75.3, 50.7, 43.0, 41.8, 34.8, 31.4, 29.7, 29.4, 24.3, 22.8, 22.1, 20.3, 15.6.

2-(1R-*Benzyloxy*-1-*cyclohexylmethyl*)-**1**. Reaction of al-

cohol 4, R = cyclohexyl, (d.e. 96%) with NaH and $PhCH_2Br$ gave the benzyl ether in 95% crude yield. IR (CCl_4) 3100, 3080, 3040, 2940, 1460, 1395, 1160, 1120, 1095, 1080, 1070 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.86, 4.52 (AB(q), 2H, J = 12 Hz), 5.02 (d, 1H, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 139.4, 128.1, 127.9, 127.3, 85.5, 82.1, 77.2, 75.3, 50.8, 43.2, 41.9, 39.6, 34.8, 31.5, 30.4, 29.7, 26.5, 26.53, 26.47, 26.2, 26.1, 24.4, 22.9, 22.2.

2-(1R-*Benzyloxy*-2,2-*dimethylpropyl*)-1. Reaction of alcohol 4, R = $(CH_3)_3C$, (d.e. 100%) with NaH and $PhCH_2Br$ gave the benzyl ether in 100% crude yield. m.p. 103–104° (plates, from methanol); IR (CCl_4) 1500, 1480, 1460, 1390, 1375, 1370, 1155, 1095, 1070 cm^{-1}; ^1H NMR($CDCl_3$) δ 3.02 (d, 1H, J = 4 Hz), 3.36 (dt, 1H, J = 5, 9 Hz), 4.49, 4.97 (AB(q), 2H, J = 12 Hz), 5.13 (d, 1H, J = 4 Hz), 7.26 (s, 5H);^{13}C NMR ($CDCl_3$) δ 139.2, 128.0, 127.2, 87.9, 80.3, 77.7, 75.6, 50.5, 43.6, 41.8, 36.1, 34.8, 31.5, 29.7, 27.1, 24.4, 22.6, 22.1.

Syntheses of methyl (R)-2-*benzyloxyalkanoates from* 2-(1R-*benzyloxyalkyl*)-1,3-*oxathianes*

Methyl (R)-2-*Benzyloxyoctanoate*. A soln of 1.66 g (4.10 mmol d.e. 99%) of 2-(1*R*-benzyloxyheptyl)-1 in 5 mL of acetone was added all at once to a mixture of 1.65 g (12.4 mmol, 50% excess) of N-chlorosuccinimide, 1.74 g (10.2 mmol, 25% excess) of $AgNO_3$ and 1.38 g (1.64 mmol, 100% excess) of $NaHCO_3$ in 50 mL of 80% acetone in water at 50°. A white ppt was formed immediately. The mixture was stirred at 45–50° for 10 min, then treated with 1 ml of sat Na_2SO_3aq, followed by 10 mL of sat NaClaq. AgCl was filtered off and the filtrate transferred to a separatory funnel. The upper organic layer was separated and the aqueous layer extracted with two 20-mL portions of ether. The combined organic phases were concentrated under reduced pressure below 40°. To the resulting residue were added 50 mL of t-BuOH and 10 ml of 2-methyl-2-butene. A soln of 3.32 g (purity 80%, 30 mmol) of $NaClO_2$ and 3.74 g of KH_2PO_4 in 15 mL of water was added to the above mixture over 10 min at room temp. After 1hr, the organic layer was separated and the aqueous layer (yellow) was extracted with 20 mL of ether. The combined organic soln was dried ($MgSO_4$) and concentrated under reduced pressure. The resulting residue was dissolved in 20 mL of ether and treated with excess ethereal CH_2N_2. After removal of solvent, flash chromatography of the residue on 160 g of silica gel with 9% EtOAc in hexanes provided 0.88 g (81%) of the ester (R_f = 0.38) and 0.70 g (85%) of sultines 5 (R_f = 0.12). The ester was further purified by evaporative distillation at 110–120° (0.01 mmHg); $[\alpha]_D^{20}$ + 62.5° (c = 2.42, $CHCl_3$), $[\alpha]_{578}^{20}$ + 65.7°, $[\alpha]_{546}^{20}$ + 74.5°, $[\alpha]_{436}^{20}$ + 126.0°, $[\alpha]_{365}^{20}$ + 197.6°, IR (CCl_4) 1765, 1745, 1470, 1460, 1440, 1400, 1385, 1280, 1200, 1180, 1110, 1030 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.71 (s, 3H), 3.93 (t, 1H, J = 6 Hz), 4.68, 4.38 (AB(q), 2H, J = 12 Hz), 7.31 (s, 5H); ^{13}C NMR ($CDCl_3$) δ 173.5, 137.8, 128.4, 128.1, 127.8, 78.2, 51.7, 33.1, 31.7, 29.0, 25.2, 22.6, 14.0. (Found: C, 72.61, H, 9.15. Calc for $C_{16}H_{24}O_3$: C, 72.69, H, 9.15%).

Methyl (R)-2-*benzyloxy*-3-*methylbutanoate* was similarly prepared from 2-(1*R*-benzyloxy-2-methylpropyl)-1 (d.e. 78%). Yield 82%; $[\alpha]_D^{20}$ + 77.3 (c = 2.44, $CHCl_3$), also $[\alpha]_{578}^{20}$ + 80.7°, $[\alpha]_{546}^{20}$ + 91.7°, $[\alpha]_{436}^{20}$ + 155.7°, $[\alpha]_{365}^{20}$ + 245.7°; IR (CCl_4) 1765, 1750, 1465, 1445, 1395, 1375, 1270, 1205, 1150, 1100 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.95 (dd, 6H, J = 1.4, 7 Hz), 2.10 (m, 1H, J = 7 Hz), 3.69 (s, 4H), 4.66, 4.34 (AB(q), 2H, J = 11.4 Hz), 7.28 (s, 5H); ^{13}C NMR ($CDCl_3$) δ 172.7, 137.8, 128.3, 127.9, 127.7, 83.4, 72.5, 51.4, 31.6, 18.8, 17.8.

Methyl (R)-2-*Benzyloxy*-2-*cyclohexylacetate*. This compound was prepared similarly by the NCS-$AgNO_3$, $NaClO_2$, CH_2N_2 sequence from 2-(1*R*-benzyloxycyclohexylmethyl)-1 (d.e. 96%) in 74% yield; $[\alpha]_D^{20}$ + 66.9° (c = 2.20, $CHCl_3$), $[\alpha]_{578}^{20}$ + 69.8°, $[\alpha]_{546}^{20}$ + 79.1°, $[\alpha]_{436}^{20}$ + 133.4°, $[\alpha]_{365}^{20}$ + 212.4°; IR (CCl_4) 1765, 1745, 1460, 1440, 1400, 1320, 1270, 1200, 1140, 1125 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.73 (d, 1H, J = 5 Hz), 3.76 (s, 3H), 4.69, 4.37 (AB(q), 2H, J = 12 Hz), 7.34 (s, 5H); ^{13}C NMR ($CDCl_3$) δ 172.9, 137.8, 128.3, 128.0, 127.8, 83.1, 72.6, 51.5, 41.2, 29.1, 28.3, 26.2, 26.1, 26.0. (Found: C, 73.60, H, 8.56. Calc for $C_{16}H_{22}O_3$: C, 73.25, H, 8.45%).

Methyl (R)-2-*benzyloxy*-3,3-*dimethylbutanoate* was similarly prepared from 2-(1*R*-benzyloxy-2,2-dimethylpropyl)-1 (d.e. 100%). Yield 86%. $[\alpha]_D^{20}$ + 76.1° (c = 2.78, $CHCl_3$), $[\alpha]_{578}^{20}$ + 79.6°, $[\alpha]_{546}^{20}$ + 90.2°, $[\alpha]_{436}^{20}$ + 153.7°, $[\alpha]_{365}^{20}$ + 243.2°; IR (CCl_4) 1760, 1745, 1490, 1440, 1400, 1380, 1370, 1275, 1210, 1170, 1105, 1060, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.97 (s, 9H), 3.57 (s, 1H), 7.27 (s, 5H); ^{13}C NMR ($CDCl_3$) δ 172.3, 137.8, 128.3, 127.9, 127.7, 86.4, 72.5, 51.1, 34.8, 26.3. (Found: C, 70.89, H, 8.73. Calc for $C_{14}H_{20}O_3$: C, 70.16, H, 8.73%).

$LiAlH_4$ *Reduction of* 2-*benzyloxymethyl esters to* 2-*benzyloxy alcohols*

(R)-2-*Benzyloxy*-1-*octanol*. To a mixture of 40 mg (1.06 mmol) of LAH and 30 mL of dry ether was added a soln of 280 mg (1.06 mmol) of ester (precursor d.e. 99%) in 20 mL of ether over 20 min. After 30 min stirring, the excess LAH was decomposed by adding several drops of ethyl acetate and 10 ml of water. The mixture was made acidic (pH 4) by adding 2M HCl. The ethereal soln was separated and the aqueous phase was washed with 20mL of ether. The combined organic soln was dried ($MgSO_4$) and concentrated under reduced pressure. Kugelrohr distillation (110-120°, 0.01 mmHg) provided 240 mg (96%) of alcohol. $[\alpha]_D^{20}$ − 18.2° (c = 1.97, $CHCl_4$), $[\alpha]_{578}^{20}$ − 18.9°, $[\alpha]_{546}^{20}$ − 21.4°, $[\alpha]_{436}^{20}$ − 36.4°, $[\alpha]_{365}^{20}$ − 57.2°; IR (CCl_4) 3650, 1460, 1355, 1210, 1095, 1070, 1030 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.13 (s, 1H), 3.8–3.2 (m, 3H); 4.56 (s, 2H); 7.33 (s, 5H); ^{13}C NMR ($CDCl_3$) δ 138.8, 128.4, 127.9, 127.7, 80.0, 71.6, 64.3, 31.8, 31.0, 29.5, 25.4, 22.6, 14.1.

(R)-2-*Benzyloxy*-3-*methyl*-1-*butanol*. LAH reduction of methyl (*R*)-2-benzyloxy-3-methylbutanoate (precursor d.e. 78%) gave the alcohol in 98% yield, evaporatively distilled at 90–100° (0.5 mmHg); $[\alpha]_D^{20}$ − 8.77° (c = 2.41, $CHCl_3$) [lit.[24] $[\alpha]_D^{20}$ − 10.63° (c = 5.04, benzene)]. Also $[\alpha]_{578}^{20}$ − 9.14°, $[\alpha]_{546}^{20}$ − 10.3°, $[\alpha]_{436}^{20}$ − 17.5°, $[\alpha]_{365}^{20}$ − 27.0°. IR (CCl_4) 3660, 3610, 1550, 1475, 1460, 1390, 1370, 1090, 1060, 1030 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89 (d, 3H, J = 3 Hz), 1.00 (d, 3H, J = 3 Hz), 2.13 (s, 1H), 3.25 (dt, 1H, J = 2.4 Hz), 3.62 (d, 2H, J = 4 Hz), 4.55 (s, 1H), 7.28 (s, 5H); ^{13}C NMR ($CDCl_3$) δ 138.8, 128.5, 127.8, 127.7, 85.2, 72.6, 62.0, 29.3, 18.6, 18.4. (Found: C, 74.14 H, 9.20. Calc for $C_{12}H_{18}O_2$: C, 74.19, H, 9.34%).

(R)-2-*Benzyloxy*-2-*cyclohexyl*-1-*ethanol*. LAH reduction of methyl (*R*)-2-benzyloxy-2-cyclohexylacetate (d.e. 96%) gave the alcohol in 93% yield. Evaporative distillation: 110–120° (0.02 mmHg); $[\alpha]_D^{20}$ − 12.5° (c = 1.82, $CHCl_3$), $[\alpha]_{578}^{20}$ − 13.1°, $[\alpha]_{546}^{20}$ − 14.7°, $[\alpha]_{436}^{20}$ − 24.2°, $[\alpha]_{365}^{20}$ − 36.5°; IR (CCl_4) 3600, 2930, 2860, 1460, 1100, 1080, 1060, 1050, 1030 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.03 (s, 1H), 3.3–3.1 (m, 1H), 3.8–3.5 (m, 2H), 4.58 (s, 2H), 7.34 (s, 5H); ^{13}C NMR ($CDCl_3$) δ 138.7, 128.5, 127.8, 127.7, 84.6, 72.6, 61.9, 39.3, 29.3, 28.9, 26.6, 26.4. (Found: c, 77.27, H, 9.27. Calc for $C_{15}H_{22}O_2$: C, 76.88, H, 9.46%).

(R)-2-*Benzyloxy*-3,3-*dimethyl*-1-*butanol*. LAH reduction of methyl (*R*)-2-benzyloxy-3,3-dimethylbutanoate (100% d.e.) gave the alcohol in 95% yield after evaporative distillation at 100–110° (0.1 mmHg); $[\alpha]_D^{20}$ − 8.91° (c = 2.28, $CHCl_3$), $[\alpha]_{578}^{20}$ − 9.25°, $[\alpha]_{546}^{20}$ − 10.5°, $[\alpha]_{436}^{20}$ − 17.9°, $[\alpha]_{365}^{20}$ − 29.0°; IR (CCl_4) 3660, 3600, 1480, 1400, 1365, 1345, 1205, 1110, 1100, 1065, 1040, 1025 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.97 (s, 9H), 2.01 (s, 1H, OH), 3.9–3.0 (m, 3H), 4.68 (s, 2H), 7.33 (s, 5H); ^{13}C NMR ($CDCl_3$) δ 138.9, 128.5, 127.7, 127.6, 88.4, 75.0, 62.3, 35.0, 26.7. (Found: C, 74.81, H, 9.72. Calc for $C_{13}H_{20}O_2$: C, 74.96, H, 9.68%).

Direct syntheses of glycols from 2-*hydroxyalkyl*-1,3-*oxathianes* (4).

(*S*)-1,2-*Octanediol*. A soln of 390 mg (1.24 mmol) of 2-(1 *S*-hydroxyheptyl)-1,3-oxathiane-1 (4, R = n-C_6H_{13}, d.e. 85%) in 10 mL of MeCN was added all at once to a mixture

of 500 mg (3.72 mmol) of N-chlorosuccinimide, 530 mg (3.10 mmol) of $AgNO_3$ and 420 mg (4.96 mmol) of $NaHCO_3$ in 80 mL of 80% CH_3CN in water at 45°. The mixture was stirred at 40–45° for 15 min. Then 1 mL of sat Na_2SO_3aq and 1 mL of sat NaClaq was added. AgCl was filtered off and the filtrate was added dropwise to a soln of 1.0 g (26 mmol) of $NaBH_4$ in 30 mL of water over 15 min. Solvent was removed under reduced pressure and the resulting aqueous soln continuously extracted with $CHCl_3$. Concentration of the $CHCl_3$ extract yielded an oil, which was subjected to column chromatography (solvent: 33% hexanes in EtOAc). However, the diol was not obtained free of succinimide. For determination of enantiomeric purity the mixture of diol and succinimide in 50 mL of benzene was treated with 200 mg (1.89 mmol) of benzaldehyde and 3–4 mg of *p*-TsOH, refluxed for 10 min in a flask equipped with a Dean and Stark trap, cooled and washed, successively, with 10 mL of 2% Na_2CO_3aq, 10 mL of water, 20 ml of 35% $NaHSO_3$aq and 10 mL of water. Drying (Na_2SO_4) and concentration gave an oil, which was Kugelrohr distilled (0.05 mmHg 120–125°) to give 122 mg (42%, based on 1,3-oxathiane) of 4-hexyl-2-phenyl-1,3-dioxolanes. The ^{1}H NMR spectrum of the 1,3-dioxolanes doped with Eu(hfc)$_3$ showed that enantiomeric excess of diol was 84%. Pertinent data are shown in Table 6.

(S)-3-*Methyl*-1,2-*butanediol* was similarly prepared in 66% yield from 2-(1*S*-hydroxy-2-methylpropyl)-1 (4, R = $(CH_3)_2CH$, d.e. 93%) by the NCS-$AgNO_3$ and $NaBH_4$ sequence. $[\alpha]_D^{20}$ + 10.0° (*c* = 2.1, $CHCl_3$) [lit.[14] for *R* isomer $[\alpha]_D^{25}$ −10.95° (*c* = 0.9, $CHCl_3$) lit.[16] $[\alpha]_D^{25}$ −10.4° (c = 1, $CHCl_3$)]. Also $[\alpha]_{578}^{20}$ +10.4°, $[\alpha]_{546}^{20}$ +11.6°, $[\alpha]_{436}^{20}$ +18.0° $[\alpha]_{365}^{20}$ +24.6°. E.e. (as above, see Table 6): 90%.

(S)-2-*Cyclohexyl*-1,2-*ethanediol* was similarly prepared from 2-(1*S*-hydroxy-1-cyclohexylmethyl)-1, (4, R = cyclohexyl, d.e. 94%) in 53% yield. $[\alpha]_D^{20}$ +4.80° (*c* = 1.33, $CHCl_3$) [lit.[15] $[\alpha]_D^{26}$ +4.20° (*c* = 1.5, $CHCl_3$)]. Also $[\alpha]_{578}^{20}$ +4.95°, $[\alpha]_{546}^{20}$ +5.41°, $[\alpha]_{436}^{20}$ +7.66°, $[\alpha]_{365}^{20}$ +9.08°. E.e. (as above, see Table 6): 94%.

(S)-3,3-*Dimethyl*-1,2-*butanediol*. NCS-$AgNO_3$ cleavage of 2-(1S-hydroxy - 2,2 - dimethylpropyl)-1 (4, R = $(CH_3)_3C$, d.e. 91%) followed by $NaBH_4$ reduction gave the diol in 76% yield. $[\alpha]_D^{20}$ +22.7° (*c* = 1.38, $CHCl_3$) [lit.[16] for (*R*-isomer) $[\alpha]_D^{25}$ −28.1° (*c* = 0.69, $CHCl_3$)]. Also $[\alpha]_{578}^{20}$ −23.6°, $[\alpha]_{546}^{20}$ +26.5°, $[\alpha]_{436}^{20}$ +42.3, $[\alpha]_{365}^{20}$ +61.0° E.e. (as above, see Table 6): 93%.

(S)-1-*Phenyl*-1,2-*ethanediol*. NCS-$AgNO_3$ cleavage of 2-(1S-hydroxyphenylmethyl)-1 (4, R = C_6H_5, d.e. 100%) followed by $NaBH_4$ reduction gave the diol in 22% yield. ^{1}H NMR spectrum showed that the diol was contaminated by 20 wt% of succinimide. $[\alpha]_D^{20}$ +30.3° (*c* = 2.60, abs. EtOH) [lit.[17] for *R*-isomer $[\alpha]_D^{25}$ −39.7° (*c* = 4.33, 95% EtOH)]. Also $[\alpha]_{578}^{20}$ +31.6°, $[\alpha]_{546}^{20}$ +35.8°, $[\alpha]_{436}^{20}$ +59.7°, $[\alpha]_{365}^{20}$ +90.9° E.e. (as above, see Table 6): 94 ± 3%.

Catalytic hydrogenolysis of (R)-2-*benzyloxy*-1-*alkanols to* (R)-1,2-*Diols*.(R)-1,2-*Octanediol*

A soln of 220 mg (0.93 mmol) of (*R*)-2-benzyloxy-1-octanol (1,3-oxathiane precursor d.e. 99%) in 20 mL of EtOH was treated with 50 mg of 10% Pd-C and hydrogenolysed at 50 psi and R.T. for 3 hr. Filtration, concentration of the filtrate and Kugelrohr distillation (100–110°, 0.4 mmHg) provided 133 mg (98%) of white solid. $[\alpha]_D^{20}$ + 17.5°(*c* = 1.164, abs EtOH) [lit.[10] for *S*-isomer of unknown optical purity $[\alpha]_D^{17}$ −4.7°]. Also $[\alpha]_{578}^{20}$ +18.1°, $[\alpha]_{546}^{20}$ +20.5°, $[\alpha]_{436}^{20}$ +34.0°, $[\alpha]_{365}^{20}$ +51.7°. IR (CCl_4) 3400 (broad), 2960, 2930, 2860, 1475, 1385, 1185, 1080 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.00 (s, 2H), 3.20–3.84 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 72.5, 66.8, 33.3, 31.9, 29.5, 25.7, 22.7, 14.0. The ^{1}H NMR study of the derived 2-phenyl-1,3-dioxolanes (*vide supra*) doped with Eu(hfc)$_3$ showed 98% e.e.

(R)-3-*Methyl*-1,2-*butanediol*. Hydrogenolysis of the benzyl ether (precursor d.e. 78%) and Kugelrohr distillation (100-110°, 20 mmHg) provided the diol in 90% yield. $[\alpha]_D^{20}$ −8.76° (*c* = 1.22, $CHCl_3$). Proton NMR study of its 2-phenyl-1,3-dioxolane doped with Eu(hfc)$_3$ showed 78% e.e.

(R)-2-*Cyclohexyl*-1,2-*ethanediol*. Catalytic hydrogenolysis of the benzyl ether (from 1,3-oxathiane precursor d.e. 96%) and Kugelrohr distillation (100–110°, 0.5 mmHg) gave the diol in 81% yield. $[\alpha]_D^{20}$ −4.17° (*c* = 1.73, $CHCl_3$) [lit.[15] for *S*-isomer $[\alpha]_D^{26}$ +4.20° (*c* = 1.5, $CHCl_3$)]. In abs. EtOH the sign is reversed: $[\alpha]_D^{20}$ +3.58° (*c* = 1.17 abs. EtOH), $[\alpha]_{578}^{20}$ +3.67°, $[\alpha]_{546}^{20}$ +4.09°,$[\alpha]_{436}^{20}$ +7.16°, $[\alpha]_{365}^{20}$ +11.9°; IR (CCl_4) 3660, 3610, 2940, 2860, 1460, 1090, 1070, 1055 cm^{-1}. Proton NMR study of its 2-phenyl-1,3-dioxolane in the present of Eu(hfc)$_3$ showed 95% e.e.

(R)-3,3-*Dimethyl*-1,2-*butanediol*. Catalytic hydrogenolysis of benzyl ether (precursor d.e. 100%) and Kugelrohr distillation (100–105°, 10 mmHg) provided the diol in 98% yield. $[\alpha]_D^{20}$ −19.7° (*c* = 1.58, $CHCl_3$) [lit.[16] $[\alpha]_D^{25}$ −28.1° (*c* = 0.69, $CHCl_3$)]. IR (CCl_4) 3620, 3430 (broad), 2970, 2920, 2880, 1490, 1410, 1370, 1190, 1095, 1045, 940, 925 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.91 (s, 9H) 4.0-3.2 (m, 5H). Proton NMR-Eu(hfc)$_3$ study of its 2-phenyl-1,3-dioxolanes showed 100% e.e.

Catalytic hydrogenolysis of (R)-2-*benzyloxy esters to* (R)-2-*hydroxy esters*

Methyl (R)-2-*hydroxyoctanoate*. A soln of 300 mg (1.14 mmol) of the 2-benzyloxy ester (precursor d.e. 99%) in 40 mL of ethanol was treated with 100 mg of 10% Pd-C and hydrogenolyzed at 50 psi and R.T. for 12 hr. Filtration, concentration of the filtrate and Kugelrohr distillation (110.120°, 10 mmHg) gave 190 mg (97%) of product. $[\alpha]_D^{20}$ −9.91° (*c* = 1.95, $CHCl_3$) [lit.[21] for *S*-isomer, $[\alpha]_D^{16}$ +11° (*c* = 10, $CHCl_3$)]. Also $[\alpha]_{578}^{20}$ −10.6°, $[\alpha]_{546}^{20}$ −12.4°, $[\alpha]_{436}^{20}$ −25.9° $[\alpha]_{365}^{20}$ −51.6°; IR (CCl_4) 3560, 2960, 2030, 2860, 1745, 1470, 1445, 1380, 1270, 1225, 1135, 1090 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.90 (brs, 1H), 3.85 (s, 3H), 4.27 (t, 1H, J = 6 Hz); ^{13}C NMR ($CDCl_3$) δ 175.9, 70.8, 52.2, 34.7, 31.8, 29.1, 25.0, 22.7, 14.0; (Found: C, 61.94, H, 10.23. Calc for $C_9H_{18}O_3$: C, 62.04, H, 10.41%).

Methyl (R)-2-*Hydroxycyclohexylacetate*. Catalytic hydrogenolysis of the 2-benzyloxy ester (precursor d.e. 96%) gave the 2-hydroxy ester in 95% yield; $[\alpha]_D^{20}$ −31.3° (*c* = 2.36, $CHCl_3$) [lit.[25] *S*-isomer, $[\alpha]_D$ +23.11° (neat)] also $[\alpha]_{578}^{20}$ −32.8°, $[\alpha]_{546}^{20}$ −38.0°, $[\alpha]_{436}^{20}$ −71.3°, $[\alpha]_{365}^{20}$ −127.4°, IR (CCl_4) 3640, 3560, 2940, 2870, 1750, 1460, 1450, 1270, 1225, 1150, 1120 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.9–0.8 (m, 11H), 3.18 (s, 1H), 3.79 (s, 3H), 4.00 (d, 1H, J = 4 Hz); ^{13}C NMR ($CDCl_3$) δ 175.3, 75.1, 52.2, 42.2, 29.2, 26.4, 26.3, 26.2, 26.15.

Methyl (R)-2-*hydroxy*-3,3-*dimethylbutanoate*. Catalytic hydrogenolysis of the 2-benzyloxy ester (precursor d.e. 100%) yielded the 2-hydroxy ester in 82% yield. $[\alpha]_D^{20}$ −35.8° (*c* = 3.16, $CHCl_3$) [lit.[16] $[\alpha]_D^{22}$ −31.2° (neat)] Also $[\alpha]_{578}^{20}$ −37.5°, $[\alpha]_{546}^{20}$ −43.2°, $[\alpha]_{436}^{20}$ −80.2° $[\alpha]_{356}^{20}$ −141.8°; IR (CCl_4) 3560, 2960, 1740, 1485, 1445, 1400, 1370, 1280, 1220, 1180, 1090 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.97 (s, 9H), 2.73 (s, 1H), 3.74 (s, 3H), 3.77 (s, 1H).

$LiAlH_4$ *Reduction of* 2-*hydroxyesters to* 1,2-*Diols*

(R)-1,2-*Octanediol*. To a mixture of 80 mg (2.1 mmol) of LAH and 30 mL of ether was added a soln of 164 mg (0.95 mmol) of methyl (*R*)-2-hydroxyoctanoate (precursor d.e. 99%) in 10 mL of ether over 5 min. After 30 min stirring, the excess LAH was quenched with 2 mL of 1M NaOH soln. The ether layer was separated, dried ($MgSO_4$) and concentrated to give an oil, which was Kugelrohr-distilled (105-110°, 0.03 mmHg) to yield 130 mg (94%) of white solid. $[\alpha]_D^{20}$ +17.1° (*c* = 1.57, abs EtOH) [lit[13] for *S*-isomer of unknown optical purity $[\alpha]_D^{17}$ −4.7°]. Proton NMR study of its 2-phenyl-1,3-dioxolanes in the presence of Eu(hfc)$_3$ showed the e.e. of the diol to be 98%.

(R)-2-*Cyclohexyl*-1,2-*ethanediol*. LAH reduction of methyl (*R*)-2-hydroxy-2-cyclohexylacetate (precursor d.e. 96%) provided the diol in 80% yield. $[\alpha]_D^{20}$ −4.28° (*c* = 1.68°, $CHCl_3$) [lit.[15] for *S*-isomer $[\alpha]_D^{26}$ +4.20° (*c* = 1.5, $CHCl_3$)].

The e.e. of the glycol, determined by ^{1}H NMR-Eu(hfc) method of its 2-phenyl-1,3-dioxolanes, was 95%.

Note added in proof: Reduction of **3** with n-Bu_4NBH_4 at room temp gave **A** (Table 3) as the major product (87:13 in THF, 72:28 in CH_2Cl_2) thus resembling Dibal rather than $NaBH_4$. This finding supports the hypothesis that chelation (impossible with n-Bu_4NBH_4) is responsible for the predominance of **B** in other hydride reductions.

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