THE PREPARATION OF SECONDARY ALLYLIC ALCOHOLS BY THE REACTION OF TRIBUTYLTIN DIETHYLALUMINUM WITH α-HALOEPOXIDES

by

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The Preparation of Secondary Allylic Alcohols by the Reaction of Tributyltin Diethylaluminum with α-Haloepoxides

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(name)

Sept 24, 1986
(date)

ABSTRACT

This study reports the discovery that tributyltin diethylaluminum efficiently converts α-bromoepoxides to allylic alcohols via reductive elimination. Other reagents may be utilized for this reaction, so the stereochemistry of the reductive elimination of an α-bromoepoxide using zinc powder and tributyltin diethylaluminum was determined. The reaction of *cis-erythro*-2-bromo-3,4-epoxyoctane mediated with zinc powder or tributyltin diethylaluminum produced *anti* elimination. The synthesis of *cis-threo*-2-bromo-3,4-epoxyoctane proved to be difficult so the corresponding *threo*-chloroepoxide was synthesized; it did not react with either zinc powder or tributyltin diethylaluminum. The reaction of *cis-threo*-2-bromo-3,4-epoxyoctane mediated with zinc powder or tributyltin diethylaluminum produced a 9:1 mixture of *E*:*Z* 2-octen-4-ol. It is suspected that the latter reaction proceeds initially to give the *Z* olefin via *anti* elimination but that isomerization occurs in the reaction.

ACKNOWLEDGEMENTS

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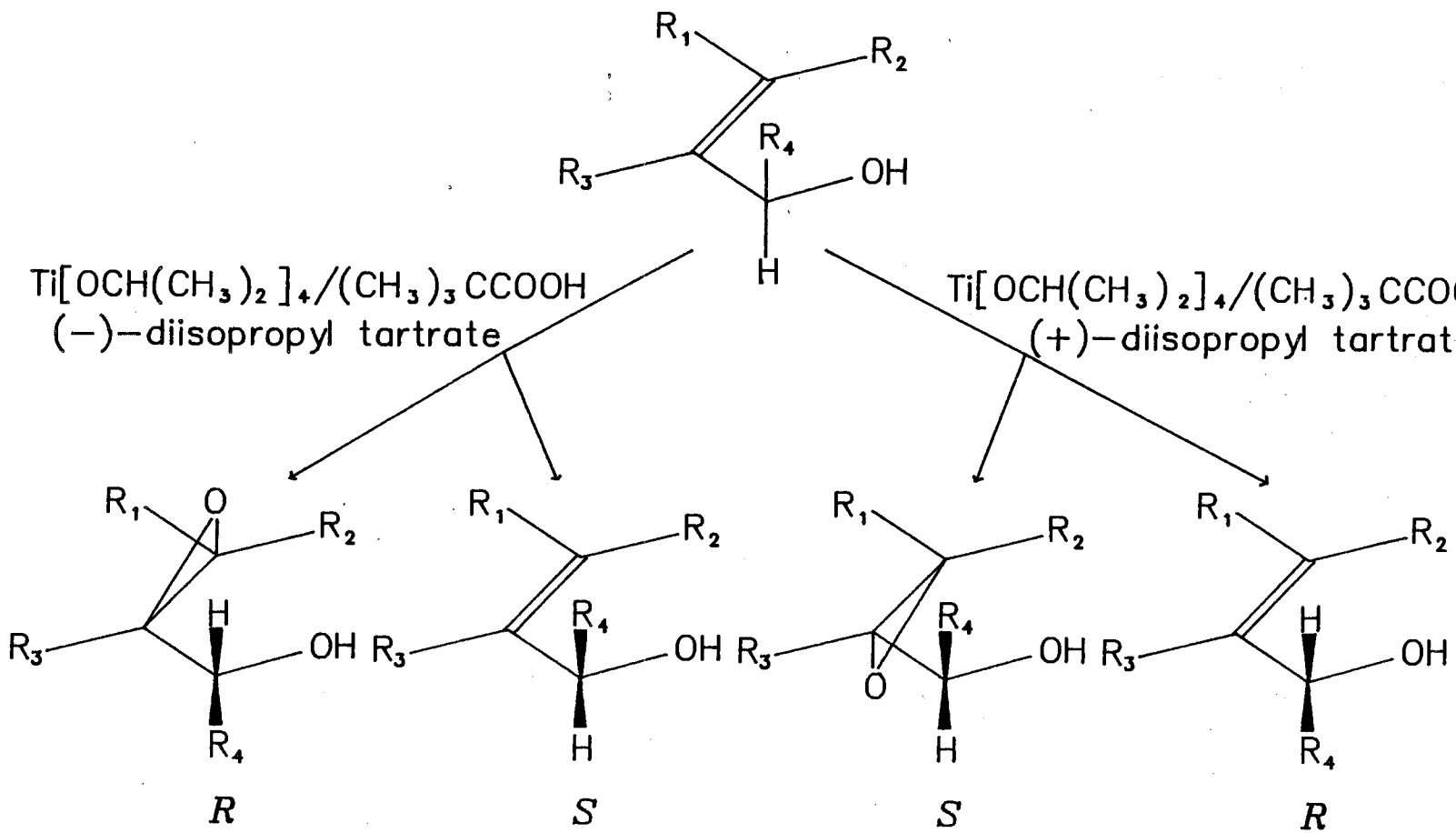
INTRODUCTION

Chiral secondary alcohols are valuable synthetic intermediates since many synthetic transformations allow the maintenance of chirality at the hydroxyl bearing carbon. The development of the Sharpless asymmetric epoxidation has facilitated access to chiral secondary allylic alcohols via kinetic resolution.[1] In this process, one enantiomer of the secondary allylic alcohol is epoxidized rapidly leaving the less reactive enantiomer chirally enriched (Scheme 1). One may selectively obtain either enantiomer of the secondary allylic alcohol by using either (+) or (-) diisopropyl tartrate as the chiral auxillary ligand.[1] The maximum theoretical yield of the least reactive enantiomer using kinetic resolution is 50% from a racemic mixture, but practical yields are much less. The chemical yield of the desired enantiomer from a kinetic resolution depends significantly upon the rate at which each enantiomer reacts as well as the chiral purity desired. Both Sharpless[1] and Sih[2] have analyzed the chemical yields and chiral purity of the expected enantiomer from a kinetic resolution in terms of the enantiomer rate ratio for a racemic mixture (Figure 1).

Sharpless has determined the enantiomeric rate differences in asymmetric epoxidation giving rise to kinetic resolution for several compounds (Table 1).[1] Enantiomeric rate differences of less then ten are not practical for the preparation of secondary allylic alcohols of high chiral purity, ie. >95% enantiomeric excess (ee.), since most of the desired enantiomer is consumed prior to achievement of high chiral purity (Figure 1). Fortunately, several secondary allylic alcohol substitution patterns exhibit rate differences of this magnitude (Table 1).


R1
R2
R3
R4
OH
H
Ti[OCH(CH3)2]4/(CH3)3CCOOH
(−)−diisopropyl tartrate
Ti[OCH(CH3)2]4/(CH3)3CCOOH
(+)−diisopropyl tartrate
O
R
S
S
R

Scheme 1

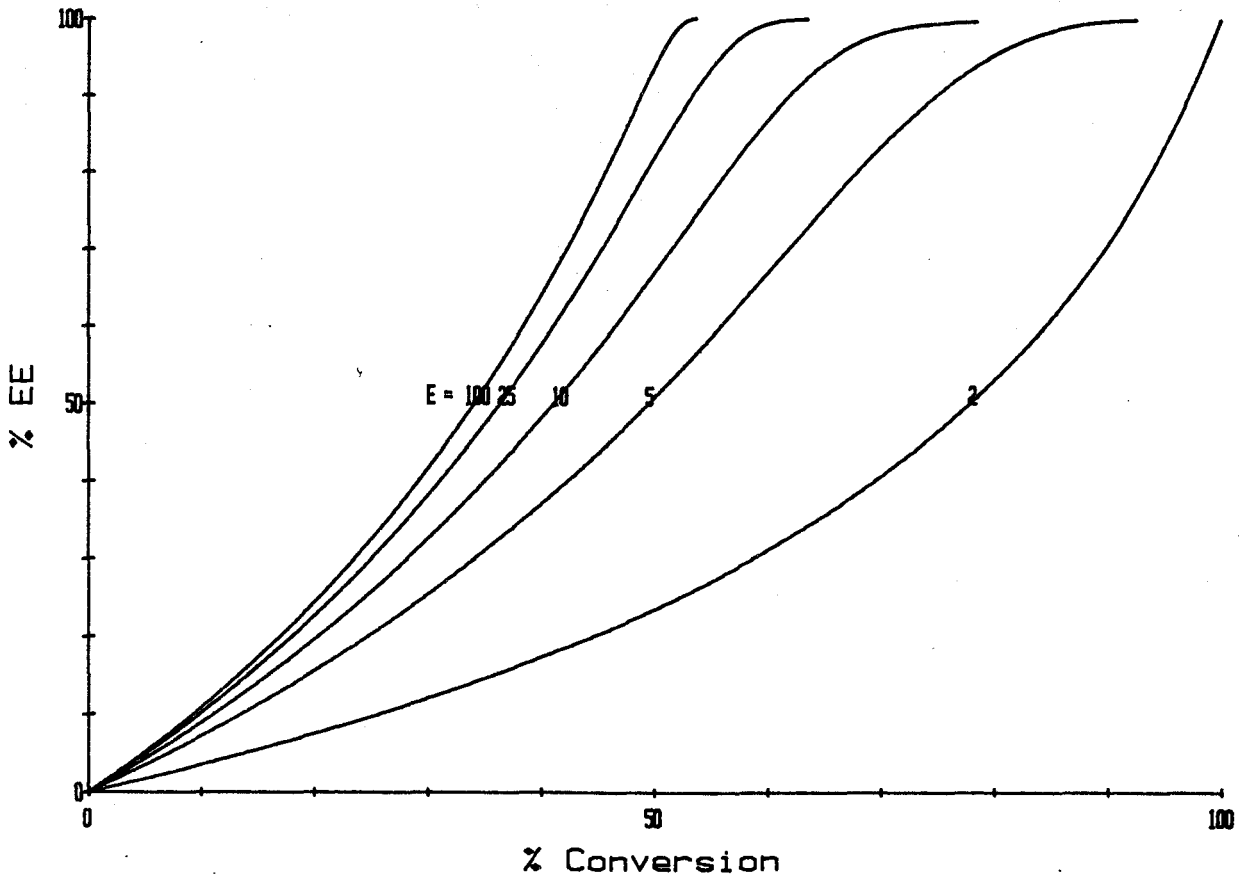


Figure 1: Enantiomeric Excess of Least Reactive Compound on Enantiomeric Rate Difference (E) and Percent Conversion

Allylic alcohol	Config	E	%ee
1-nonen-3-ol	*R*	83	>96
E-1-cyclohexyl-2-buten-1-ol	*R*	104	>96
E-1,4-dicyclohexyl-2-buten-1-ol	*R*	-	>96
Z-1,4-dicyclohexyl-2-buten-1-ol	*S*	-	10
Z-4-undecen-3-ol	*R*	16	82
Z-3-penten-2-ol	*R*	20	91
2-methyl-1-hepten-3-ol	*R*	138	>96
1-(1-cyclohexene)-ethanol	*R*	83	>96
2-cyclohexen-1-ol	*R*	-	30
2-cyclohepten-1-ol	*R*	-	80

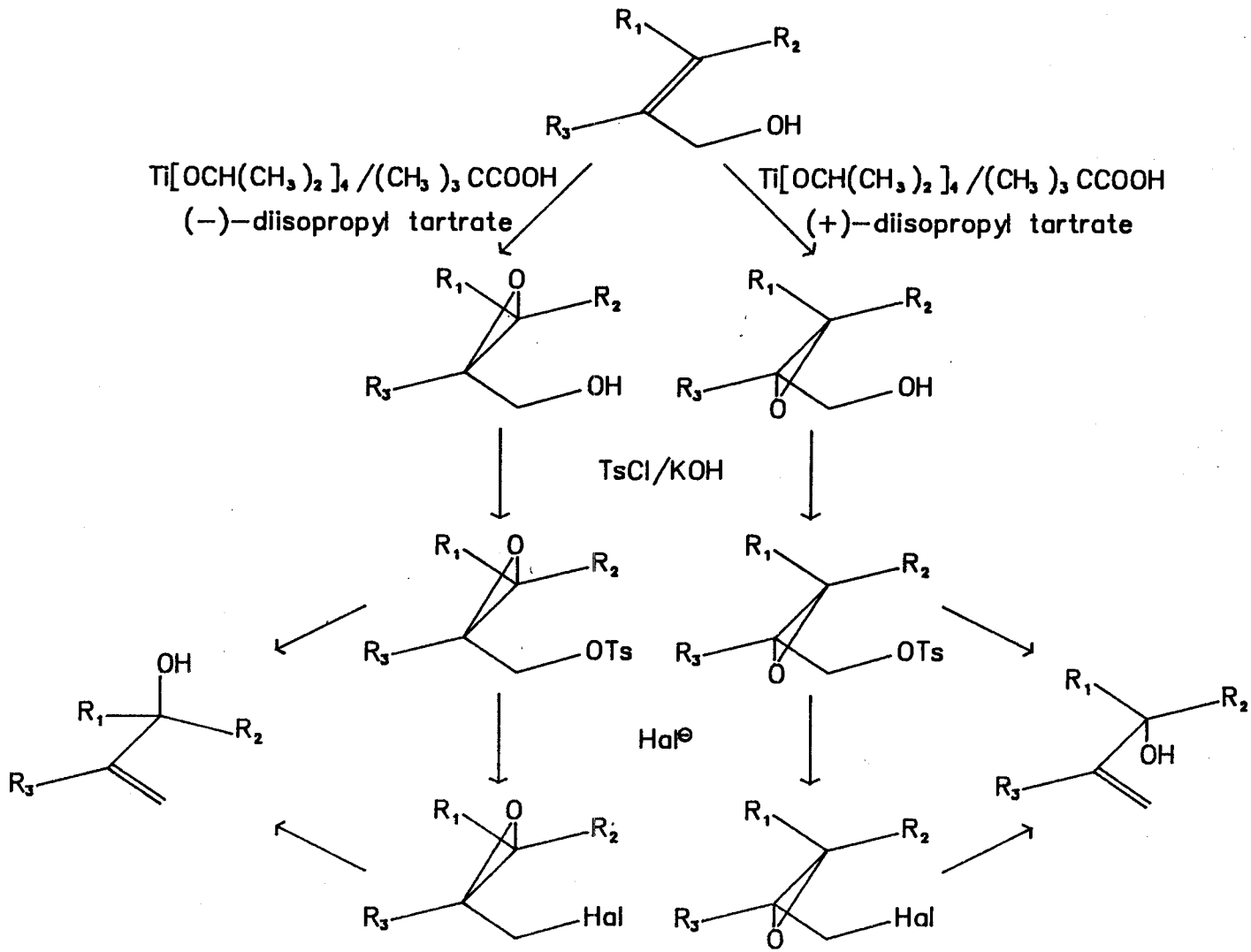
E - Enantiomeric Rate Ratio (k_{fast}/k_{slow})

Table 1: Enantiomeric Excess of Least Reactive Enantiomer of Allylic Alcohols After Asymmetric Epoxidation at 55±5% Conversion

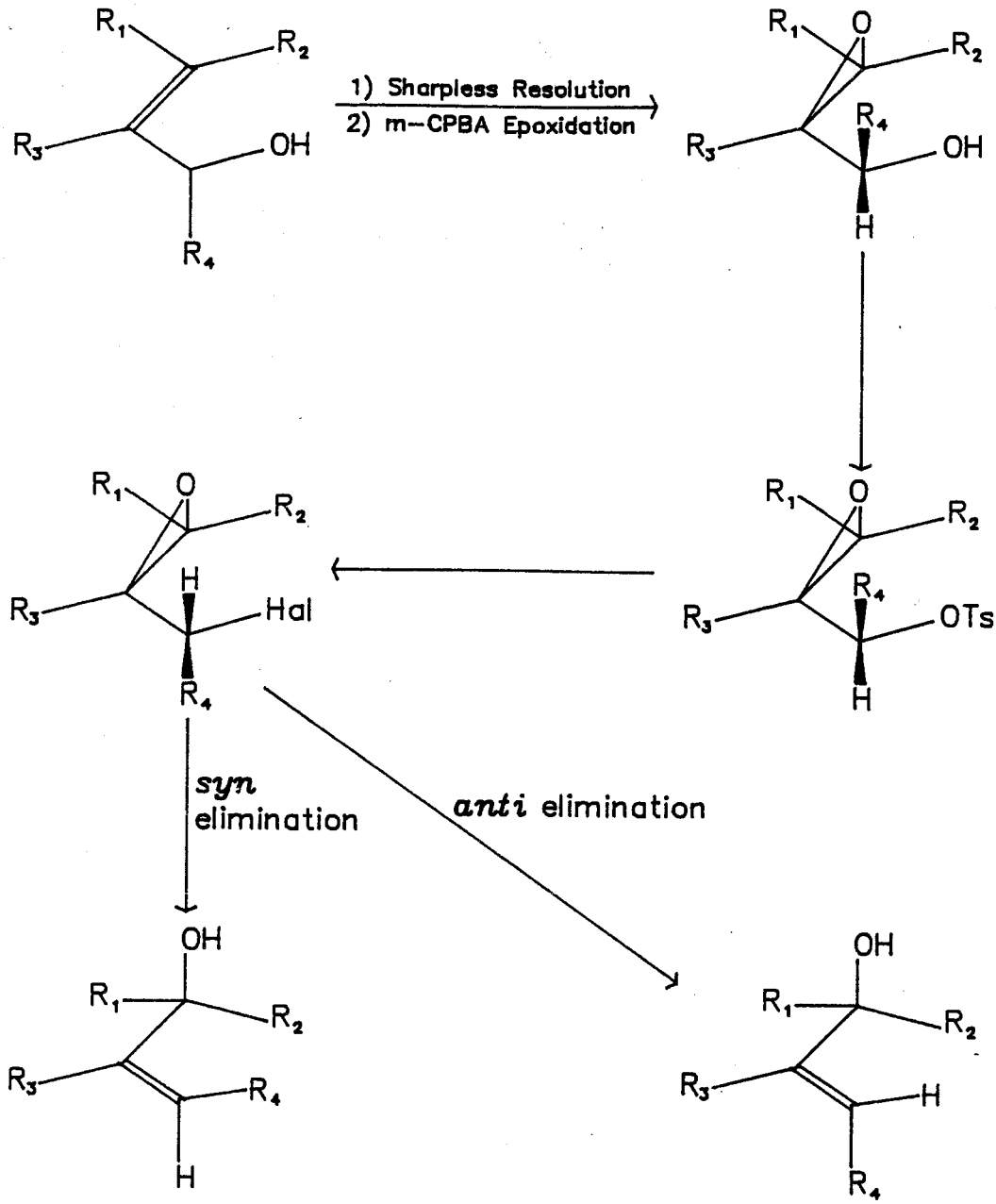
Primary allylic alcohols undergo asymmetric epoxidation with high chiral induction and high chemical yields (Scheme 2).[3] In this case, essentially all of the allylic alcohol is converted to one chiral epoxy alcohol. It is easy to project that the conversion of the chiral epoxy alcoholic product of a Sharpless epoxidation to a chiral secondary allylic alcohol could result in higher conversion of a valuable starting material to a chiral alcohol product than is achieved by kinetic resolution. A strategy for this transformation could involve conversion of the primary hydroxyl of the epoxy alcohol to the corresponding tosylate and then to halogen. This functional group relationship is capable of reductive elimination of the halogen substituent with concomitant cleavage of the C_2-O bond (Scheme 2) which is the subject of the present investigation.

The route chosen for investigation could also provide chiral secondary allylic alcohols from chiral isomeric secondary allylic alcohols using Sharpless kinetic resolution. In this case, epoxidation of the resolved *Z* secondary allylic alcohol with m-chloroperoxybenzoic acid, (m-CPBA), would yield an *threo* epoxy alcohol with high *threo*:*erythro* selectively (95:5).[4] Conversion of the secondary hydroxyl to a tosylate and thence to a halogen provides for the reductive elimination to give a chiral secondary allylic alcohol. For the route to be widely applicable, methods for both *anti* and *syn* elimination of the halogen should be available (Scheme 3).

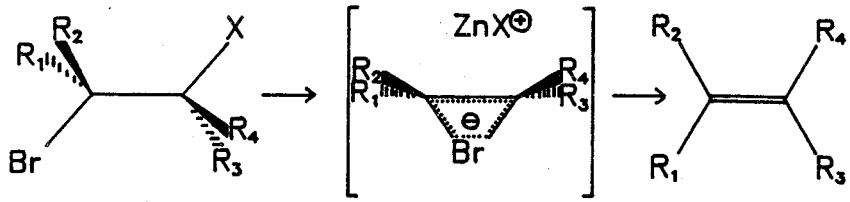
The conversion of alcohols, esters and halogens possessing an α-halogen to olefin is known to be mediated by several reagents (Scheme 4).[5] Although the stereochemistry of the elimination is inconsequential for compounds having a primary group, for those compounds which have two leaving groups on secondary carbons produce olefins resulting from an *anti*


R1
R2
R3
OH
Ti[OCH(CH3)2]4 /(CH3)3CCOOH
(−)−diisopropyl tartrate
Ti[OCH(CH3)2]4 /(CH3)3CCOOH
(+)−diisopropyl tartrate
O
TsCl/KOH
OTs
Hal⊖
Hal

Scheme 2


1) Sharpless Resolution
2) m-CPBA Epoxidation
syn elimination
anti elimination

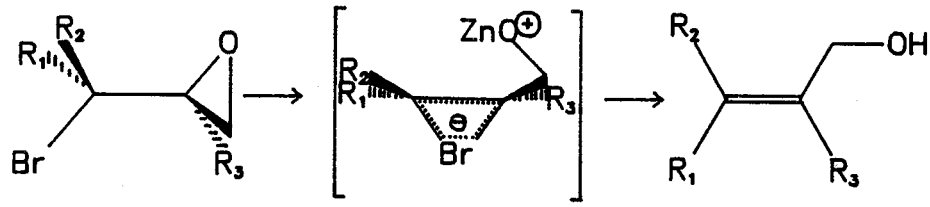
Scheme 3



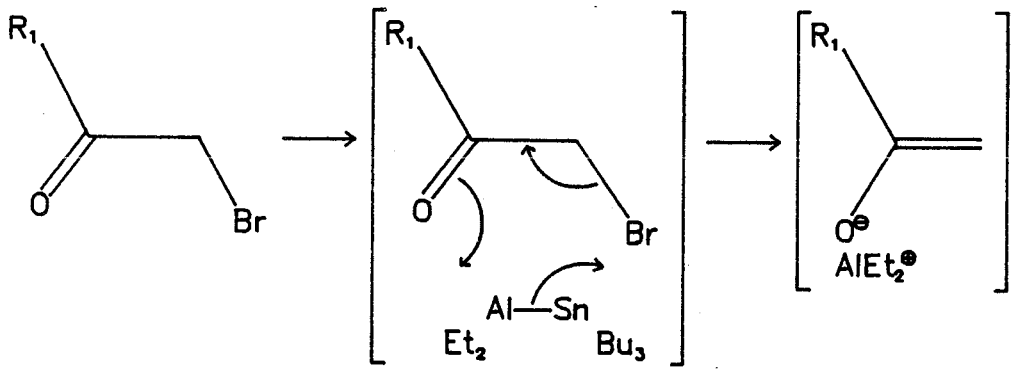
X = hal, OAc, OTs, ...

Reagents: Zn; NaI; Cr(II); Bu_3SnH; KSCN; Na_2S; Sn/Cu; $LiAlH_4$; NaH/DMSO; NaSEt; Fe/graphite; ...

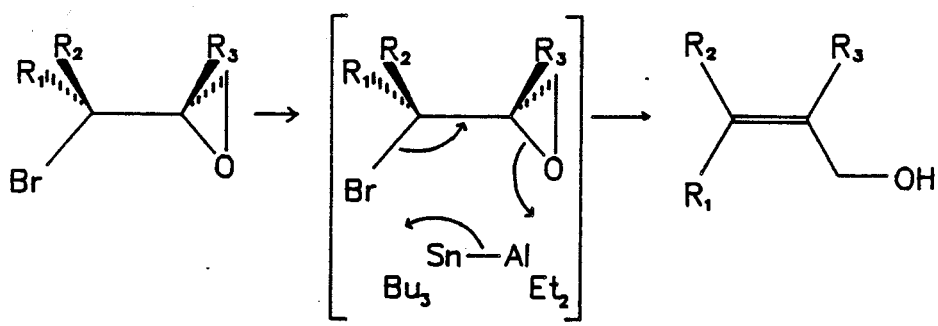
Scheme 4



Scheme 5



Scheme 6



Scheme 7

elimination.[6] There are a few known eliminations from steroids which proceed via *syn* elimination.[6]

One widely used reducing agent is metallic zinc. The zinc powder mediated *anti* elimination of vicinal dibromides is envisioned to react as follows. Two single electron transfers or transfer of two electrons from zinc could force one of the bromide atoms to leave as the anion while the adjacent bromide initiates a backside attack to the carbon that connected to the bromide atom. This would result in an ion pair of $ZnBr^+$ and a bridged organobromide anion. Elimination of the bromide from the anion results in the formation of the olefin. It is realistic to consider that the zinc mediated elimination of halogen and hydroxyl moieties will proceed in a similar manner to produce olefin via an *anti* elimination product (Scheme 4). Recently Nicolaou *et al*,[7] has shown that zinc powder induces elimination of bromide from α-bromoepoxides. Mori[8] has employed this reaction on 2,3-epoxy-1-iodo-2,6-dimethyl-5-heptene to produce, via C_2-O bond cleavage, 2,6-dimethyl-1,5-heptadiene-3-ol. Although the stereochemistry of the reaction was not reported, it is easy to envision that an antiparallel arrangement could be involved (Scheme 5). Therefore, an *erythro*-α-bromoepoxide would be expected to yield an *E*-allylic alcohol and a *threo*-α-bromoepoxide would yield a *Z*-allylic alcohol.

One of the goals of this work was to investigate the stereochemistry of this reaction by subjecting *erythro*- and *threo*-α-bromoepoxides to the zinc powder in methanol reduction. Although this would be useful for the conversion given in Scheme 2 and would accomplish part of the chemistry desired in Scheme 3, we clearly need a complementary *syn* elimination process to complete the chemistry outlined in Scheme 3 and to provide an

alternative to the zinc powder reduction illustrated in Scheme 2; we envisioned that the reaction of tributyltin diethylaluminum, ($Bu_3SnAlEt_2$),[9] with α-haloepoxides would yield allylic alcohols via reductive elimination of halogen and cleavage of the adjacent C-O epoxide bond. We considered it highly probable that this reaction would proceed by the desired *syn* elimination and thus exhibit a stereochemical course complimentary to the expected *anti* elimination of the zinc powder reductive elimination. The basis for this hypothesis lies in the reported formation of aluminum enolates from α-bromoketones using this reagent (Scheme 6).[9] This reaction was envisioned by its discoverers to involve a cyclic process. Conversion of an α-haloepoxide to a secondary allylic alcohol by a similar cyclic process would yield a *syn* elimination product (Scheme 7).

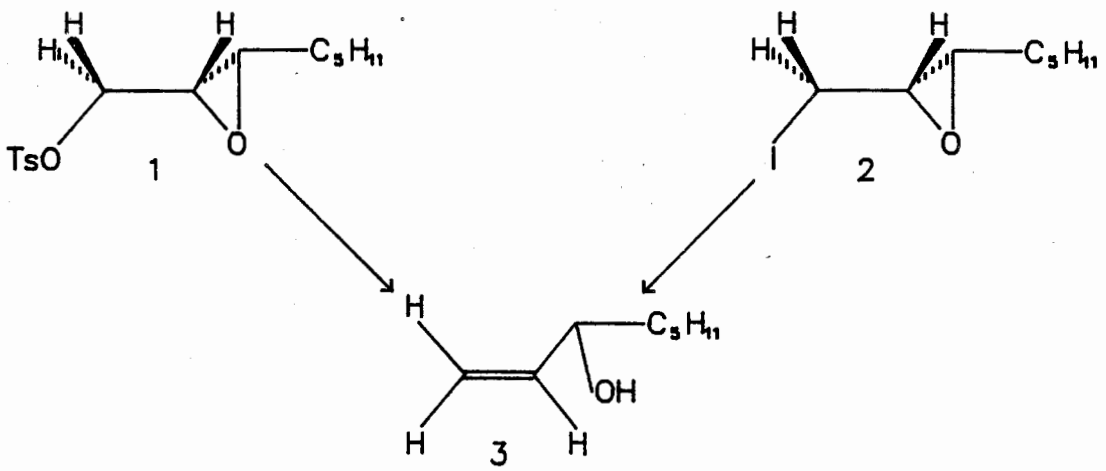
The use of $Bu_3SnAlEt_2$ instead of zinc powder to effect conversion of α-haloepoxides to allylic alcohols would also be advantageous because this reagent would be expected to show different chemoselectivity. Zinc powder in alcoholic solvents operates via electron transfer processes. Thus any functional group able to accept electrons from zinc is susceptable to this reagent. Since zinc powder reactions are performed using excessive zinc powder, selective reduction of one of several groups is difficult. In the case of $Bu_3SnAlEt_2$, high chemoselectivity can be expected. This reagent can be visualized as a dipolar moiety, consisting of tributyltin anion and diethylaluminum cation. The anionic tin is polarizable and thus would have a high affinity for bromine and iodine. The cationic aluminum is highly oxyphilic and thus would be expected to preferentially cleave or at least polarize C-O bonds. Therefore this reagent should exhibit high reactivity for those substrates wherein C-Br or C-I bonds are adjacent to C-O bonds.

RESULTS

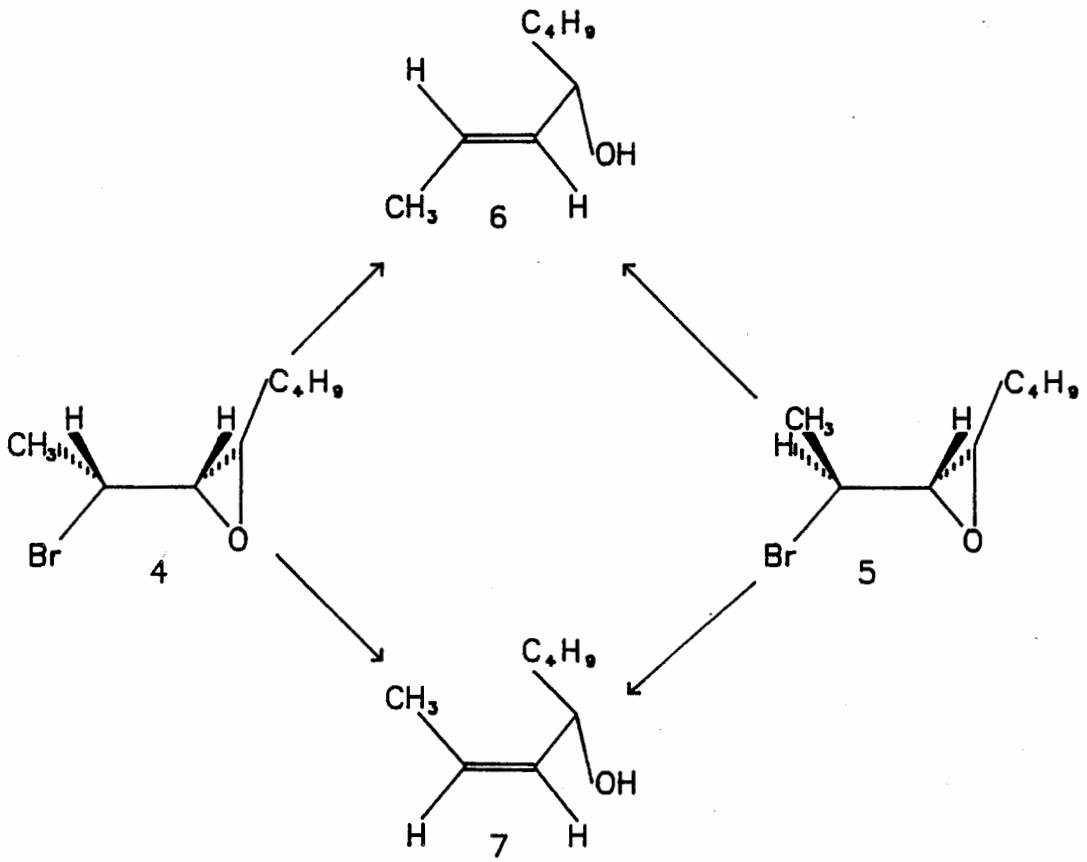
As a test of the strategies outlined in Scheme 2 and 3, we examined the reactions of zinc powder and $Bu_3SnAlEt_2$ with α-substituted epoxides 1, 2, 4, and 5.

The reaction of 1 with zinc powder and $Bu_3SnAlEt_2$ was examined to determine if the reagents would effect the conversion of 1 to 1-octen-3-ol, 3 (Scheme 8). This reaction is of interest because, if successful with either reagent, it would allow the conversion shown in Scheme 2 without generation of the corresponding halogen substrate. The reaction of 2 with $Bu_3SnAlEt_2$ was examined using (±)-2. This reaction was conducted to determine if $Bu_3SnAlEt_2$ would convert (±)-2 to 1-octen-3-ol, (±)-3. The reaction of chiral 2 with zinc powder was conducted to give chiral 3 which was required as a pheromone synergist for *Oryzaephilus mercator* and *O. surinamensis*.[10] The reactions of 4 and 5 with zinc powder and $Bu_3SnAlEt_2$ were conducted to determine the stereochemistry of these two substrates to allylic alcohols, 6 and 7 (Scheme 9).

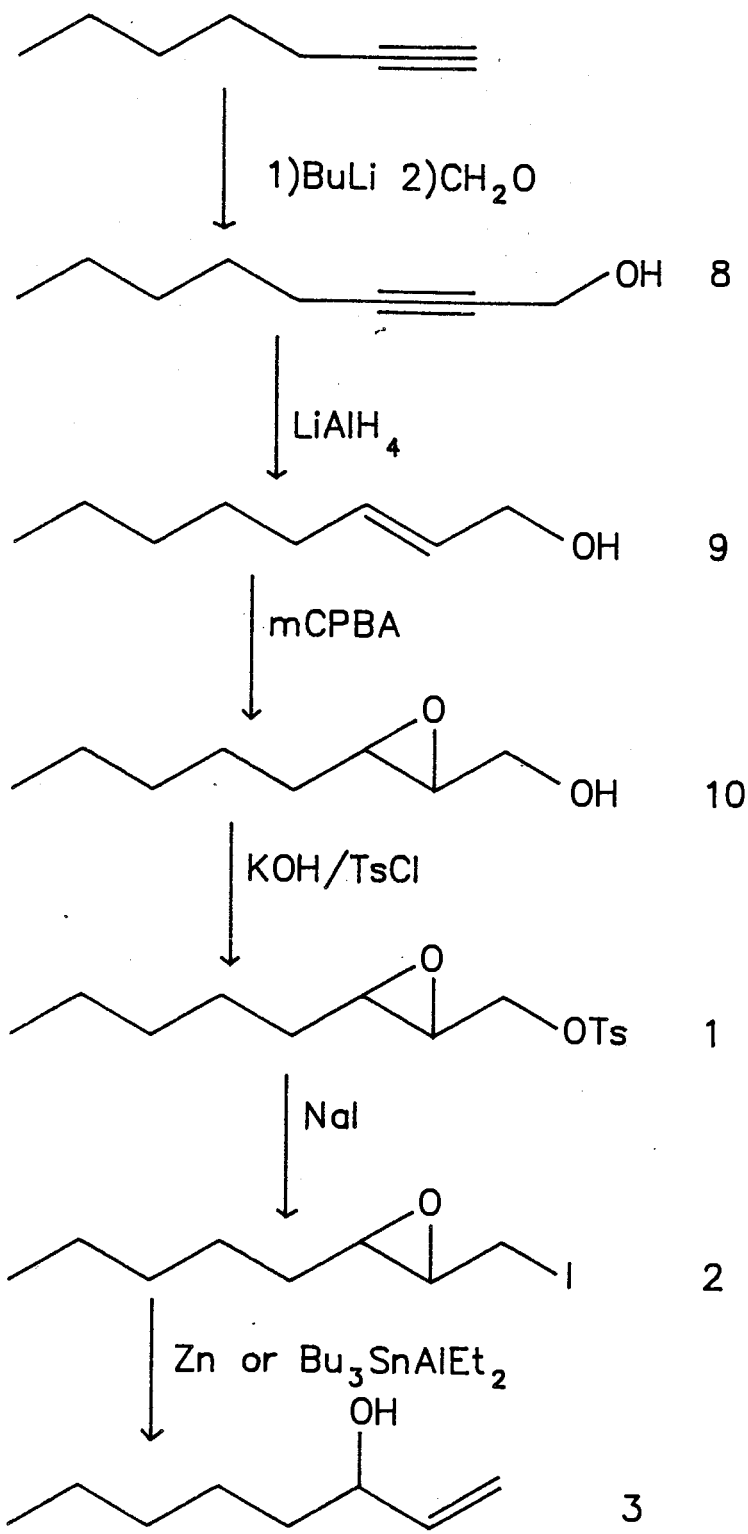
Preparation of (±)-3, (S)-3, and (*R*)-3 commenced with reaction of 1-heptynyllithium with paraformaldehyde to give 8 in 80% yield[11] (Scheme 10). Reduction of 8 with lithium tetrahydridoaluminate gave 9 in nearly quantitative yield.[12] Epoxidation of 9 with m-chloroperoxybenzoic acid (m-CPBA) gave (±)-10 in 87% yield.[13] The chiral enantiomers, (2*S*,3*S*)-10 and (2*R*,3*R*)-10, were prepared from 9 by reaction of 9 under Sharpless asymmetric epoxidation conditions using either (+) or (-) diisopropyl tartrate as the chiral auxillary ligand in 91% and 51% yield respectively.[3] Preparation of the Mosher ester ((+)-α-methoxy-α-trifloromethylphenylacetyl



Scheme 8



Scheme 9


1)BuLi 2)CH_2O
OH
8
$LiAlH_4$
OH
9
mCPBA
O
OH
10
KOH/TsCl
O
OTs
1
NaI
O
I
2
Zn or $Bu_3SnAlEt_2$
OH
3

Scheme 10

derivative)[14] of (2*S*,3*S*)-10 and (2*R*,3*R*)-10 followed by analysis of the resulting diastereoisomeric mixture by capillary GC revealed an enantiomeric excess of 90% for (2*S*,3*S*)-10 and 80% for (2*R*,3*R*)-10. (±)-10, (2*S*,3*S*)-10, and (2*R*,3*R*)-10 were each converted to the corresponding tosylates, (±)-1, (2*S*,3*S*)-1, and (2*R*,3*R*)-1, by treatment with p-toluenesulfonyl chloride and powdered potassium hydroxide in ether to yield 91%, 61%, and 98% respectively.[15] The tosylates, (±)-1, (2*S*,3*S*)-1, and (2*R*,3*R*)-1, were each converted to the corresponding iodides, (±)-2, (2*R*,3*S*)-2, and (2*S*,3*R*)-2, by reaction with sodium iodide in reagent grade acetone in yields of 91%, 90% and 96% respectively.[16]

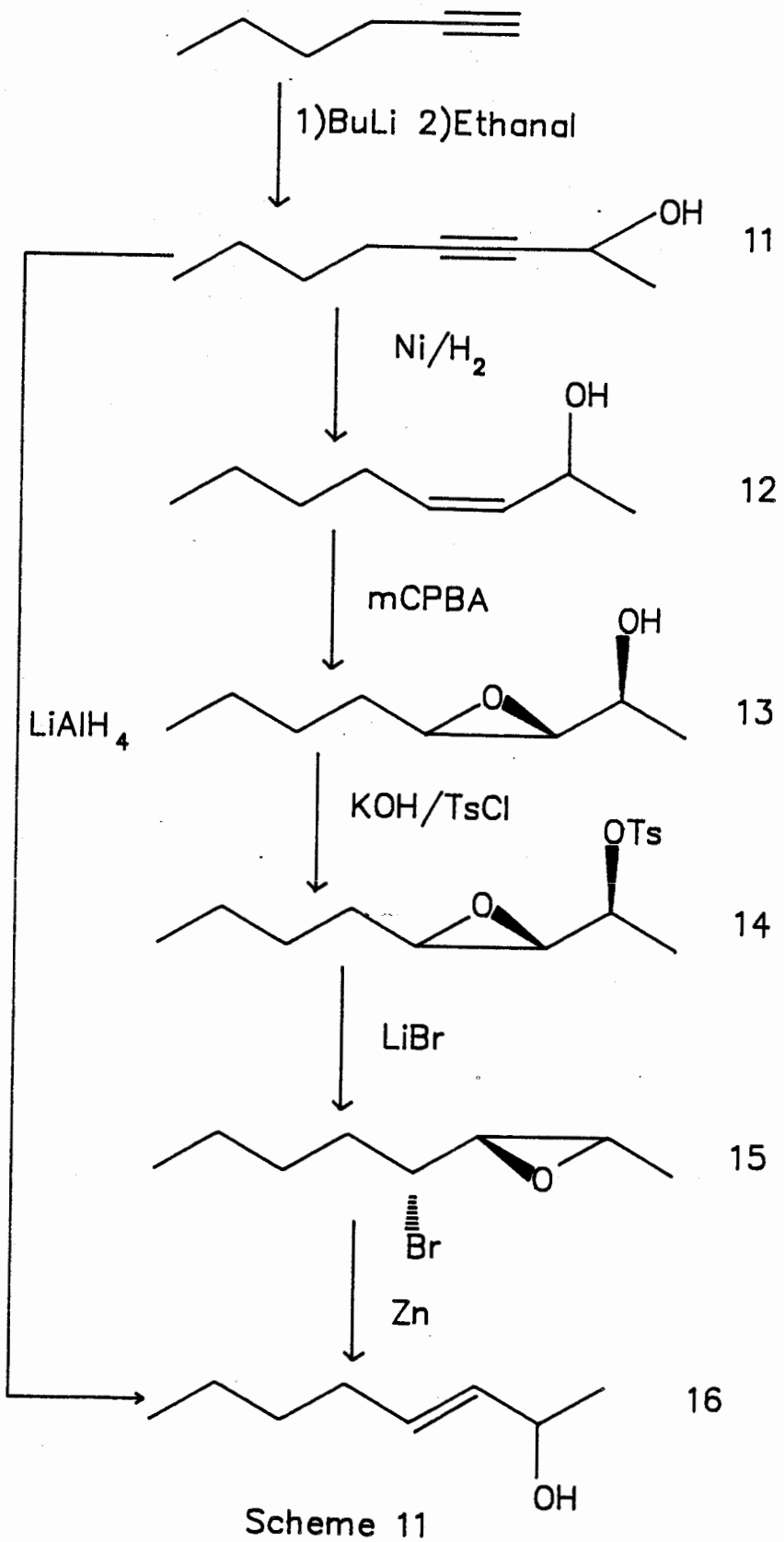
Reaction of (±)-1 with zinc powder failed to produce (±)-3. Reaction of (±)-2, (2*R*,3*S*)-2, and (2*S*,3*R*)-2, with zinc powder gave the corresponding products of (±)-3, (*S*)-3, and (*R*)-3 in good yields. In the case of the reaction of (2*R*,3*S*)-2, the chemical yield of the zinc mediated reaction was 85% and no diminution of chiral purity at C_3 was detected during the reaction. In the case of (2*S*,3*R*)-2, the chemical yield was 75% and a small reduction (1%) in chiral purity of C_3 was detected. This is within the limits of error for the determination of chiral purity by GC analysis of diastereoisomeric ratios of Mosher ester derivatives. We therefore conclude that the zinc mediated conversion of racemic and chiral 2 to racemic and chiral 3 proceeds without loss of chirality at C_3.

We next examined the reaction of various α-substituted epoxides with $Bu_3SnAlEt_2$. Of the several methods available to generate $Bu_3SnAlEt_2$,[17] we chose a route via formation of the tributyltin anion. The reaction of tributyltin hydride and lithium diisopropylamine gave tributyltin lithium. This was reacted with diethylaluminum chloride. This method has been shown

by Ms. S. Sharma in this laboratory to be the most efficient and clean route to $Bu_3SnAlEt_2$ of those reported.[17] Reaction of (±)-1 with $Bu_3SnAlEt_2$ in THF failed to give detectable amounts of 3. From this reaction, we recovered good yields of starting material. However, reaction of (±)-2 with $Bu_3SnAlEt_2$ successfully gave 3 in 74% yield.

To determine the stereochemistry of the zinc powder and $Bu_3SnAlEt_2$ mediated conversion of α-haloepoxides to allylic alcohols observed above, *cis-erythro*-2-bromo-3,4-epoxyoctane, 4, and *cis-threo*-2-bromo-3,4-epoxyoctane, 5, were prepared and subjected to reaction with each reagent (see Scheme 3 for a description of the possible stereochemical outcome of these reactions). The choice of the *cis* geometry in the epoxide group of these substrates was dictated by the reported *threo* selectivity of m-CPBA in the epoxidation of *Z* secondary allylic alcohols;[4] this reaction would easily allow access to *cis-threo*-3,4-epoxy-2-octanol, 13. The reported *erythro* selectivity of the reduction of α-ketoepoxides would allow access to the corresponding *cis-erythro*-3,4-epoxy-2-octanol, 19.[18]

The synthesis of 4 and 5 commenced with reaction of 1-hexynyllithium with ethanal[11] to give 11 in 49% yield (Scheme 11). Propargylic alcohol, 11, was reduced to the *Z* allylic alcohol 12 by P2 nickel in near quantitative yield.[19] Epoxidation of 12 with m-CPBA gave 13 which exhibited a ^1H NMR spectrum consistant with it being *cis-threo*-3,4-epoxy-2-octanol, ($J_{2,3}$ coupling of 8.0 Hz). Epoxide hydrogen coupling ($J_{3,4}$) of 4.3 Hz indicates a *cis* epoxide.[20] The tosylate, 14, was prepared by reaction of 13 with p-toluenesulfonyl chloride and potassium hydroxide in ether.[15] When 14 was reacted with lithium bromide in reagent grade acetone,[16] the expected product was not obtained; instead the S_N2' product, *cis-erythro*-4-bromo-


1)BuLi 2)Ethanal
OH
11
Ni/H2
OH
12
mCPBA
OH
O
LiAlH4
13
KOH/TsCl
OTs
O
14
LiBr
O
15
Br
Zn
16
OH

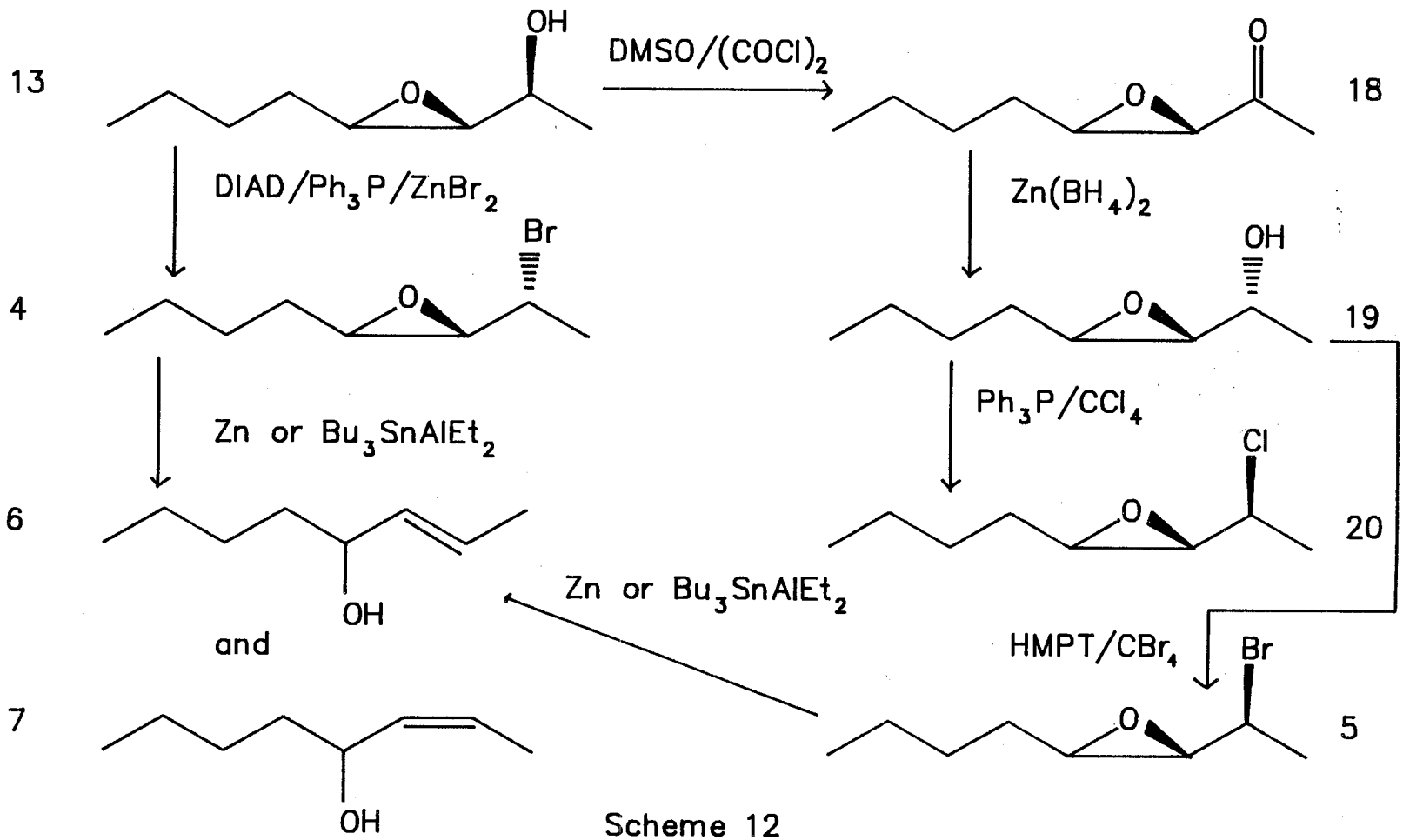
Scheme 11

2,3-epoxyoctane 15, was obtained in 41% yield.

The structure 15 was verified from the following ^{1}H NMR spectral information. The calculated chemical shifts for the hydrogens on the epoxide bearing carbons are δ 3.55 and 3.80 ppm, and for the hydrogen on the carbon bearing the bromide 4.23 ppm.[21] The chemical shifts observed were 3.14, 3.28, and 3.77 ppm with associated coupling which indicated that these hydrogens are on C_3, C_2, and C_4 respectively. The observed coupling of 4.1 Hz for $J_{2,3}$ indicates that 15 has the *cis* geometry.[20] Since it is probable that the bromide addition at C_4 proceeds with inversion and the tosylate displacement by oxygen at C_2 proceeds in a similar manner; the *erythro* product would be the resulting configuration of the product.

Reaction of 15 with zinc powder in methanol gave *E*-3-octen-2-ol, 16, in 81% yield which was independently generated by reduction of 11 by lithium tetrahydridoaluminate.[13] The conversion of 15 to 16 by zinc powder requires the transformation to proceed via an *anti* elimination of the leaving groups.

The conversion of 13 to *cis-erythro*-2-bromo-3,4-epoxyoctane, 4, was achieved using Mitsunobu conditions in 49% yield[22] (Scheme 12). These conditions allowed clean S_N2 replacement of the hydroxyl of 13 by bromide without the intervention of the S_N2' reaction observed when 14 was reacted with lithium bromide. The observed ^{1}H NMR coupling constant between the C_2 and C_3 hydrogens for 4 is 8.9 Hz. Reaction of 4 with zinc powder produced a 6:7 ratio of 95:5. The ratio of 6 to 7 was determined by ^{1}H NMR analysis of the isolated mixture and by GC analysis. There was approximately 5% of 18 in 13 and the same precentage of 5 would be found in 4. The reaction of 4 with $Bu_3SnAlEt_2$ produced a 6:7 ratio of 100:0 (^{1}H NMR, GC).


13
OH
O
DMSO/(COCl)2
O
O
18
DIAD/Ph3P/ZnBr2
Zn(BH4)2
Br
OH
4
O
O
19
Ph3P/CCl4
Zn or Bu3SnAlEt2
Cl
6
O
O
20
OH
Zn or Bu3SnAlEt2
and
HMPT/CBr4
Br
7
O
5
OH

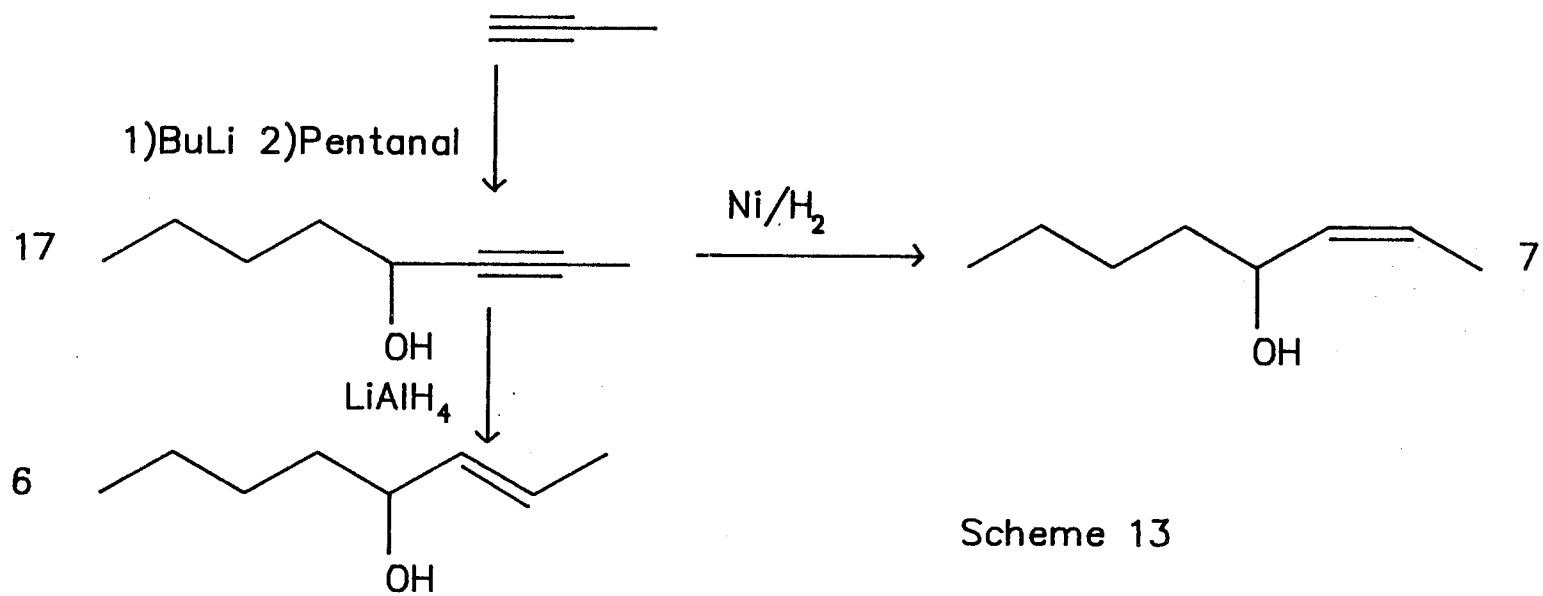
Scheme 12

Authentic samples of 6 and 7 were prepared independently. The syntheses of the isomers commenced by the reaction of propynyllithium and pentanal[11] (Scheme 13). This reaction yielded 2-octyn-4-ol, 17, in 90% yield which was reduced to 6 with lithium tetrahydridoaluminate in 62% yield.[13] Hydrogenation of 17 with P2 nickel gave 7 in 80% yield.[15]

To prepare *cis-threo*-2-bromo-3,4-epoxyoctane, 5, 13 was oxidized to *cis*-3,4-epoxy-2-octanone, 18, with oxalyl chloride in dimethylsulfoxide (DMSO) in 71% yield[23] (Scheme 12). *Erythro* selective reduction of 18 with zinc borohydride[18] gave 19 in 88% yield. This product was assigned the expected *erythro* stereochemistry on the basis of its ^{1}H NMR spectrum which exhibited a $J_{2,3}$ coupling of 7.7 Hz. Comparison of the ^{1}H NMR spectra of 13 and 19 revealed that the chemical shifts of the hydrogens on C_2, C_3, and C_4 are different. The signals for the C_3H of both isomers are visible in the spectra of both isomers and were used to determine the *thero:erythro* ratio of each isomer. The *threo:erythro* ratio for 13 is 93.6:6.4 and that for 19 is 4.4:95.6.

Conversion of 19 to the desired bromoepoxide, 5, proceeded poorly under a number of conditions (see Appendix A). We then converted 19 to the corresponding chloride, 20, by reaction with triphenylphosphine in carbon tetrachloride (CCl_4) in 62% yield.[24] Subsequent reactions of 20 with zinc powder and $Bu_3SnAlEt_2$ resulted in recovered starting material without a trace of the expected product.

cis-Threo-2-bromo-3,4-epoxyoctane, 5, was finally synthesized by Dr. M. Singh using hexamethylphosphorous triamide (HMPT) and carbon tetrabromide (CBr_4) at -78°C.[25] The observed coupling constant of 5 for $J_{2,3}$ is 9.4 Hz. Reaction of 5 with either zinc powder or $Bu_3SnAlEt_2$



Scheme 13

produced a 6:7 ratio of 9:1.

Since the product of reacting 5 with zinc powder or $Bu_3SnAlEt_2$ was not of the expected stereochemistry, a test for isomerization of 7 in ether with 1 N HCl was conducted. No isomerization under these workup mimicking conditions was observed. When 7 was dissolved in methanol with zinc powder at reflux for 2 hrs, no isomerization to 6 was found. When 7 was added to a solution of $Bu_3SnAlEt_2$ at 0°C for 2 hrs, a ratio of 6:7 of 1:1 was found. This would indicate that 7 could be formed in the reaction, but was isomerized to 6 before completion.

CONCLUSIONS

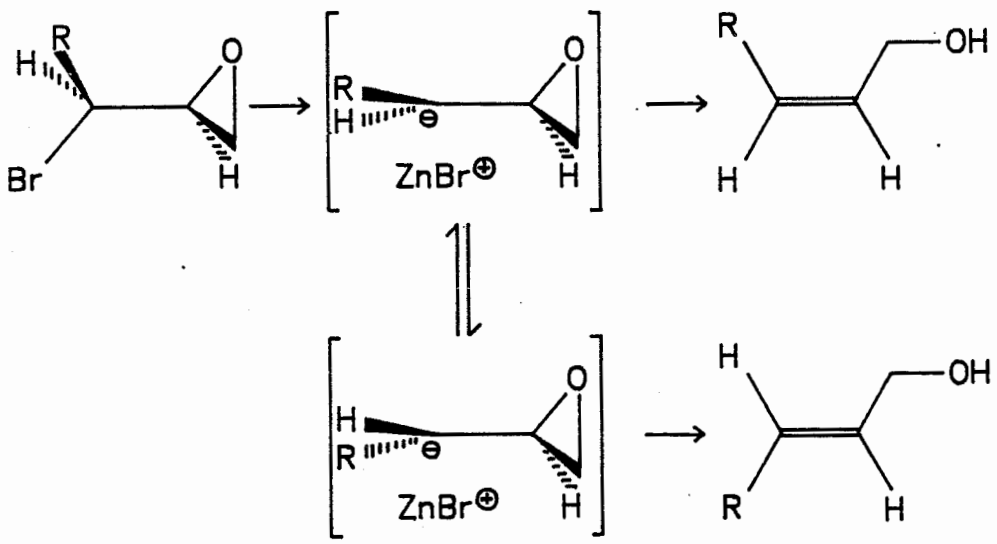
The results of the reactions of *cis-erythro*-2-bromo-3,4-epoxyoctane, 4, and *cis-threo*-2-bromo-3,4-epoxyoctane, 5, mediated with zinc powder or $Bu_3SnAlEt_2$ are given in Table 2. It is evident that the major product from these reactions is *E*-2-octen-4-ol, 6. The product of the reactions is determined by either the initial reaction or by isomerization after the product is formed. Isomerization of the product was checked by subjecting the product to the reaction conditions.

When 1 N HCl is mixed with a solution of 7, *Z*-2-octen-4-ol, in ether, the isomerization product, 6, is not detected by GC analysis after 24 hrs. This indicates that 6 is formed as the major product of the reaction of 4 or 5 with zinc powder and is not isomerized from 7 by 1 N HCl upon workup of the reactions. Since 7 did not isomerize with zinc powder in methanol, the products of the reaction of 4 and 5 must be derived from the initial reaction or isomerized by zinc bromide formed during the reductive elimination. Since isomerization of 7 to 6 with $Bu_3SnAlEt_2$ was noted under the reaction conditions, the stereochemistry of the reaction of 7 with $Bu_3SnAlEt_2$ is not certain at this time and could be the cyclic mechanism proposed earlier.

A possible mechanism that would produce the products of 6 and 7 as obtained by the reaction of 4 and 5 with zinc powder is given in Scheme 14. An electron from the zinc metal is transfered to the reagent, cleaving the C-Br bond. Rotation about the C_3-C_4 bond prior to C_3-O bond cleavage would yield isomeric products. It is known that the *E* isomer, which corresponds to 6, is more stable then the *Z* isomer, 7. If the rotation were allowed,

cis-2-bromo-3,4-epoxyoctane	6, *E*-2-octen-4-ol	7, *Z*-2-octen-4-ol
4, *erythro* with zinc powder	95	5
$Bu_3SnAlEt_2$	100	0
5, *threo* with zinc powder	90	10
$Bu_3SnAlEt_2$	89	11

Table 2: Products of the reaction of *cis*-2-bromo-3,4-epoxyoctane mediated by zinc powder or $Bu_3SnAlEt_2$



Scheme 14

more of 6 would be formed commencing from either 4 or 5. In a paper published by Stevens *et al*,[26] the elimination of bromine from a labeled sample of 1,1,2-tribromocyclohexane was studied using zinc powder and sodium iodide. It was found that NaI gave exclusively *anti* elimination and zinc powder gave 89% *anti* and 11% *syn*.

EXPERIMENTAL SECTION

General Procedures. Routine GC analyses were run on a Hewlett-Packard 5880A gas chromatograph using a DB-1 capillary column (0.2mm ID X 15m) and suitable temperature control programs. Infra red spectra were determined on a Perkin-Elmer 599B spectrophotometer. Samples were run as neat films between NaCl plates or as KBr pellets. The CH stretching and CH bending absorptions are not reported for IR spectra. ^1H NMR were recorded on a Bruker 400 WM NMR spectrometer in $CDCl_3$ using the residual $CHCl_3$ for internal standard. Low resolution mass spectra were obtained either via direct insertion or via GC inlet on a Hewlett-Packard 5985B coupled gas chromatograph/mass spectrometer. All samples were run using an electron impact ionization voltage of 70 eV. All reactions requiring anhydrous and/or oxygen free conditions were conducted with a positive pressure of argon or nitrogen in flame dried glassware. Tetrahydrofuran (THF) was freshly distilled from sodium or potassium metal with benzophenone as an indicator. Methylene chloride (CH_2Cl_2) was dried by distillation over P_2O_5 or CaH_2. Acetonitrile (CH_3CN) was dried by distillation from CaH_2 and stored over 4A molecular sieves. Pyridine (C_6H_5N) was dried by distillation and storing over KOH. Dimethyl formamide [$(CH_3)_2NCHO$] was dried by distillation and stored over 4A molecular sieves. All boiling points and melting points are uncorrected. The enantiomeric excess of the chiral alcohols were determined by GC analysis of the derivatives of (+)-α-methoxy-α-trifluoromethylphenylacetic acid (MPTA).

Preparation of 2-Octyn-1-ol, 8. To 25.0 g (255 mmol) of 1-heptyne in 250 mL of dry THF under argon at 0°C was added 100 mL of 2.6 M (260 mmol)

of BuLi. After 30 min, 10.5 g (350 mmol) of dry paraformaldehyde was added and stirred for 30 min. The reaction was refluxed for 3.5 hrs and quenched after the solution was cooled to rt by pouring into 200 mL of ice water. The organic layer was separated and the aqueous layer was extracted with (4 X 75mL) ether. The combined organic extract was dried over anhyd $MgSO_4$, filtered, and concentrated in vacuo to give a crude liquid. The liquid was distilled at 51°C (0.35 mmHg) [lit.[27] bp 46-47°C (0.1mmHg)] to yield 80% (20.1 g) of **8** from 1-heptyne. IR (film) 3330, 2290, 2220, 1140, 1010 cm^{-1}; mass spectrum, *m/e* (relative intensity) 95(32), 93(31), 83(38), 79(29), 77(13), 70(56), 69(39), 68(15), 67(57), 57(20), 56(15), 55(84), 53(27), 52(23), 51(15), 43(30), 42(31), 41(100); ^1H NMR ($CDCl_3$) δ 0.85 (3H, C_8, t, J=6.7 Hz), 1.29 (4H, C_7, C_6, m), 1.46 (2H, C_5, quint, J=6.8 Hz), 2.16 (2H, C_4, m), 2.60 (1H, OH, broad), 4.20 (2H, C_1, t, J=3.2 Hz). The ^1H NMR spectrum was previously reported.[27]

Preparation of *E*-2-Octen-1-ol, 9. To 20.0 g (159 mmol) of **8** in 200 mL of dry THF under argon was added 9.0 g (270 mmol, 1.5 eq) of $LiAlH_4$ and the solution was refluxed for 30 min. The reaction was quenched by sequential addition of 9 mL of H_2O, 9 mL of 15% NaOH, and 27 mL of H_2O with 10 min between each addition. The reaction was then filtered to remove the insoluble aluminum salts. The filtrate was extracted with (3 X 100mL) ether and the fractions combined. The combined organic extract was dried over anhyd $MgSO_4$, filtered, and concentrated in vacuo to give a crude liquid which distilled at 54°C (0.15 mmHg) [lit.[28] bp 70°C (2mmHg)] to yield 95% (19.0 g) of **9**. IR (film) 3325, 1000, 972 cm^{-1}; mass spectrum, *m/e* (relative intensity) 110(2.6), 82(14), 81(18), 69(15), 68(20), 67(20), 57(100), 56(14), 55(36), 54(14), 44(14), 43(36), 42(18), 41(52); ^1H NMR

($CDCl_3$) δ 0.89 (3H, C_8, t, J=6.7 Hz), 1.30 (4H, C_7, C_6, m), 1.38 (2H, C_5, m), 2.04 (2H, C_4, q, J=6.5 Hz), 4.08 (2H, C_1, t, J=6.5 Hz), 5.63 (2H, C_3, C_2, m). The ^1H NMR spectrum was previously reported.[27]

Alternative Preparation of 9. To 25 g (255 mmol) of 1-heptyne in 250 mL of dry THF at 0°C under argon was added 100 mL of 2.6 M (260 mmol) of BuLi. The solution was stirred for 30 min, then 10.5 g (350 mmol) of paraformaldehyde was added. The solution was heated to reflux for 3.5 hrs. The solution cooled to rt and 9.5 g (260 mmol) of $LiAlH_4$ added. After heating to reflux, GC analysis showed that the alkyne had been reduced. After cooling, the reaction was quenched by the sequential addition of 10 mL H_2O, 10 mL of 15% NaOH, and 30 mL of H_2O with 10 min between each addition. Insoluble aluminum salts were filtered and the filtrate extracted with (3 X 100mL) ether. The combined organic extract was dried over anhyd $MgSO_4$, filtered, and concentrated <u>in vacuo</u> to give a crude liquid which was distilled at 105°C (25 mmHg) to yield 84% (27.5 g) of **9**. The spectroscopic data was in agreement with that given above for **9**.

Preparation of *trans*-2,3-Epoxy-1-octanol, (±)-10. To 16.6 g (78.3 mmol) of 85% m-chloroperoxybenzoic acid in 200 mL of CH_2Cl_2 at 0°C was added 10.0 g (78.1 mmol) of **9** in 10 mL of CH_2Cl_2. The reaction was allowed to warm to rt and stirred for 2 hrs. The reaction was quenched by addition of 150 mL of a sat'd Na_2CO_3 soln and stirred for 1 hr. The organic layer was separated and the aqueous layer extracted with (4 X 50mL) ether. The combined organic extract was dried over anhyd $MgSO_4$, filtered, and concentrated <u>in vacuo</u> to give a crude liquid which was distilled at 55-65°C (0.25 mmHg) and crystallized upon refrigeration, mp 28-29°C [lit.[29] mp 33-34°C]. The yield of (±)-**10** was 87% (9.75 g). IR (film) 3330, 1727, 1292,

1260, 1080, 1035, 890, 755, 740 cm^{-1}; mass spectrum, *m/e* (relative intensity) 101(12), 83(100), 57(16), 55(73), 43(13), 41(15); ^1H NMR ($CDCl_3$) δ 0.91 (3H, C_8, t, J=6.7 Hz), 1.38 (4H, C_7, C_6, m), 1.46 (2H, C_5, m), 1.59 (2H, C_4, m), 2.93 (1H, C_1H_A, m), 2.97 (1H, C_1H_B, m), 3.64 (1H, C_3, dd, J=4.0, 13.3 Hz), 3.93 (1H, C_2, dd, J=2.7, 13.3 Hz).

Preparation of (2*S*,3*S*)-10. To 18.2 mL (19.1 g, 67.2 mmol) of $Ti[OCH(CH_3)_2]_4$ in 200 mL of dry CH_2Cl_2 at -23°C (dry ice/CCl_4 bath) under argon was added 18.3 mL (16.4 g, 70 mmol) of diisopropyl L(+) tartrate in 20 mL of dry CH_2Cl_2. After 10 min, 8.5 g (66.3 mmol) of 9 dissolved in 10 mL of dry CH_2Cl_2 was added to the solution followed by 135 mmol of dry t-butylhydroperoxide[30] in CH_2Cl_2 and stirred for 10 min. The reaction was placed in the freezer at -23°C until complete and quenched by dilution with 200 mL of ether and 18.2 mL of sat'd Na_2SO_4 solution. The quenched reaction mixture was filtered through a bed of Celite, and the filtrate was mixed with 100 mL of sat'd NaCl in 2 N NaOH. The organic layer was separated and the aqueous layer was extracted with (4 X 50mL) ether, dried over anhyd $MgSO_4$, filtered, and concentrated <u>in vacuo</u> to give a liquid which crystallized upon refrigeration to yield 91% (8.66 g) of (*S*,*S*)-10, mp 33-34.5°C. The spectroscopic data was in agreement with that given above for (±)-10. To 100 mg (0.69 mmol) of (2*S*,3*S*)-10 in 1 mL of CH_2Cl_2 was added 5 drops of dry C_6H_5N and 200 mg (0.79 mmol) of MTPA Cl. The solution was allowed to react overnight, then was washed with 1 mL of H_2O and GC analysis of the organic layer showed two diastereoisomers of the ester in the ratio of 95.2:4.8. The diastereoisomers were confirmed by CI on the GC mass spectrum.

Preparation of (2*R*,3*R*)-10. The procedure was identical to that

described above for the preparation of (2*S*,3*S*)-10 except that diisopropyl a D(-) tartrate was used. The crude product was purified by chromatography on Silica gel column using hexane:ethyl acetate (1:1) as eluent to yield 51% (4.4 g) of (*R*,*R*)-10 from 9, mp 34-35°C. The spectroscopic data was in agreement with that given above for (±)-10. To 100 mg (0.69 mmol) of (2*R*,3*R*)-10 in 1 mL of CH_2Cl_2 was added 5 drops of dry C_6H_5N and 200 mg (0.79 mmol) of MTPA Cl. The solution was allowed to stirred overnight, then was washed with 1 mL of H_2O. GC analysis of the organic layer showed two diastereoisomers of the ester in the ratio of 90.1:9.9. The diastereoisomers were confirmed by CI on the GC mass spectrum.

Preparation of *trans*-2,3-Epoxy-1-octanyl Tosylate, (±)-1. To 9.7 g (67.3 mmol) of (±)-10 in 150 mL of anhyd ether at -10°C was added 14.18 g (74.4 mmol, 1.1 eq) of p-toluenesulfonyl chloride and 47.5 g (338 mmol, 5 eq) of powdered KOH which was divided in 5 portions and added over 20 min, keeping the temperature below 0°C. The solution was stirred at 0°C for 30 min and then poured into 400 mL of ice water. The organic layer was separated and the aqueous layer was extracted with (3 X 75mL) ether. The combined organic extract was backwashed with (2 X 50mL) sat'd NaCl, dried over anhyd $MgSO_4$, filtered, and concentrated <u>in vacuo</u> to give a crystalline solid, mp 23-25°C. The yield of (±)-1 was 91% (18.3 g). IR (KBr pellet) 1360, 1180, 960, 815, 770, 670, 560 cm^{-1}; mass spectrum, *m/e* (relative intensity) 155(100), 91(57), 55(12); ^1H NMR ($CDCl_3$) δ 0.87 (3H, C_8, t, J=6.7 Hz), 1.28 (4H, C_7, C_6, m), 1.37 (2H, C_5, m), 1.50 (2H, C_4, m), 2.43 (3H, $ArCH_3$, s), 2.76 (1H, C_3, dt, J=2.1, 11.1 Hz), 2.93 (1H, C_2, ddd, J=2.1, 3.7, 6.0 Hz), 3.96 (1H, C_1H_A, dd, J=6.6, 12.0 Hz), 4.17 (1H, C_1H_B, dd, J=3.5, 12.0 Hz), 7.34 (2H, Ar, d, J=8.0 Hz), 7.78 (2H, Ar, d, J=8.0

Hz). Anal. Calcd for $C_{15}H_{22}O_3S$: C, 60.38; H, 7.43. Found: C, 60.43; H, 7.67.

Preparation of (2*S*,3*S*)-1. The procedure was identical to that described above for the preparation of (±)-1, except that (2*S*,3*S*)-10 was used. It was purified by chromatography on Silica gel using hexane:ethyl acetate (4:1) as eluent. The yield of (2*S*,3*S*)-1 was 61% (10 g) from (2*S*,3*S*)-10, mp 23.5-25°C. The spectroscopic data was in agreement with that given above for (±)-1.

Preparation of (2*R*,3*R*)-1. The procedure was identical to that described above for the preparation of (±)-1, except that (2*R*,3*R*)-10 was used. The yield of (2*R*,3*R*)-1 was 98% (8.7 g) from (2*R*,3*R*)-10, mp 23-25°C. The spectroscopic data was in agreement with that given above for (±)-1.

Reaction of (±)-1 with Zinc Powder. To 1 g (3.4 mmol) of (±)-1 in 20 mL of absolute methanol under argon was added 0.67 g (10.2 mmol) of zinc powder. The solution was refluxed for 3 hr. After cooling, 10 mL of ether and 20 mL of sat'd NaCl was added and the layers separated. The aqueous layer was washed with (3 X 10mL) ether. The ether fractions were combined and dried over anhyd $MgSO_4$. The solvent was removed in vacuo. GC analysis of the resulting concentrate did not reveal a component corresponding to (±)-3 but did reveal a component corresponding to (±)-1.

Reaction of (±)-1 with $Bu_3SnAlEt_2$. To 1.68 mL (12 mmol) diisopropylamine in 30 mL THF at 0°C was added 4.56 mL of 2.6 M (12 mmol) BuLi. After 30 min, the reaction was cooled to -78°C and 3.17 mL (12 mmol) of Bu_3SnH was added slowly to maintain the temperature below -60°C. After 2 hrs, 12 mL of 1 M (12 mmol) of Et_2AlCl was added and the reaction was allowed to warm to 0°C. After 1 hr, 2.98 g (10 mmol) of (±)-1 in 2 mL THF

was added slowly. After 1 hr, 10 mL of 1 N HCl was added to quench to reaction. The layers were separated and the aqueous layer was extracted with (3 X 20mL) pentane. The combined organic layer was dried over anhyd $MgSO_4$, filtered, and concentrated in vacuo. GC analysis of the resulting liquid did not reveal a component corresponding to (±)-3 although there was no component corresponding to (±)-1.

Preparation of *trans*-2,3-Epoxy-1-iodooctane, (±)-2. To 10.0 g (33.5 mmol) of (±)-1 in 200 mL of spectroscopic grade acetone was added 10.1 g (67 mmol, 2 eq) of dry NaI and the solution was stirred for 3 hrs. The solution was filtered and the filtrate concentrated to yield yellow crystals. The crystals were dissolved in a pentane:water (50 mL:50 mL) mixture. The organic layer was separated and the aqueous layer was extracted with (4 X 50mL) pentane. The combined organic extract was dried over anhyd $MgSO_4$, filtered, and concentrated in vacuo to give a liquid which crystallized upon refrigeration, mp 22.5-25°C. The yield of (±)-2 was 97% (8.2 g). IR (KBr pellet) 1723, 1250, 1180, 892, 815, 750, 670, 610, 560 cm^{-1}; mass spectrum, *m/e* (relative intensity) 127(87), 83(100), 57(32), 55(86), 41(19); ^1H NMR ($CDCl_3$) δ 0.93 (3H, C_8, t, J=6.7 Hz), 1.36 (4H, C_7, C_6, m), 1.47 (2H, C_5, m), 1.57 (2H, C_4, m), 2.81 (1H, C_3, dt, J=1.8, 5.5 Hz), 3.03 (2H, C_2, C_1H_A, m), 3.27 (1H, C_1H_B, dd, J=4.8, 8.9 Hz). Anal. Calcd for $C_8H_{15}IO$: C, 37.81; H, 5.95. Found: C, 38.07; H, 6.00.

Preparation of (2*R*,3*S*)-2. The procedure was identical to that described above for the preparation of (±)-2 except that (2*S*,3*S*)-1 was used. The yield of (2*R*,3*S*)-2 was 90% (6.9 g) from (2*S*,3*S*)-1, mp 23-25.5°C. The spectroscopic data was in agreement with that given above for (±)-2.

Preparation of (2*S*,3*R*)-2. The procedure was identical to that

described above for the preparation of (±)-2 except that (2*R*,3*R*)-1 was used. The yield of (2*S*,3*R*)-2 was 96% (6.9 g) from (2*R*,3*R*)-1, mp 23.5-26°C. The spectroscopic data was in agreement with that given above for (±)-2.

Preparation of 1-Octen-3-ol, (±)-3, by reaction of (±)-2 with Zinc. To 0.15 g (0.6 mmol) of (±)-2 in 3 mL of absolute methanol was added 0.12 g (1.8 mmol, 3 eq) of zinc powder and the solution was refluxed for 2 hrs, cooled and diluted with 15 mL of ether and washed with three 15 mL portions of sat'd NaCl. The organic layer was dried over anhyd $MgSO_4$, filtered, and concentrated in vacuo to give a crude liquid. The liquid was purified by Kugelrohl distillation at 50°C (0.25mmHg) [lit.[31] bp 62-65°C (1mmHg)] to yield 80% (61 mg) of (±)-3. IR (film) 3350, 3080, 1680, 1290, 1140, 1060, 1020, 990, 920, 725 cm^{-1}; mass spectrum, *m/e* (relative intensity) 127(41), 83(100), 67(12), 57(14), 55(47), 41(11); ^1H NMR ($CDCl_3$) δ 0.87 (3H, C_8, t, J=6.7 Hz), 1.30 (4H, C_7, C_6, m), 1.52 (2H, C_5, m), 1.60 (2H, C_4, m), 4.09 (1H, C_3, q, J=6.7 Hz), 5.09 (1H, *Z*-C_1H, dd, J=1.3, 10.7 Hz), 5.21 (1H, *E*-C_1H, dd, J=1.3, 17.3 Hz), 5.86 (1H, C_2, ddd, J=6.0, 10.7, 18.0 Hz). The ^1H NMR[32] and IR[33] spectra were previously reported.

Preparation of (*S*)-1-Octen-3-ol, (*S*)-3. To 6.5 g (25.6 mmol) of (2*R*,3*S*)-2 in 125 mL of absolute methanol was added 5.02 g (76.8 mmol, 3 eq.) of powdered zinc and the solution was refluxed for 3 hrs. After cooling, 125 mL of pentane was added and the solution was filtered, backwashed with (2 X 50mL) sat'd NaCl solution, dried over anhyd $MgSO_4$, filtered, and concentrated in vacuo to give 85% (2.8 g) of (*S*)-3 as a liquid. The spectroscopic data was in agreement with that given above for (±)-3, bp 62.5-63.5°C (1.25mmHg). To 100 mg (0.73 mmol) of (*S*)-3 in 1 mL of CH_2Cl_2 was added 5 drops of dry C_6H_5N and 200 mg (0.79 mmol) of MTPA Cl.

The solution was allowed to react overnight, then was washed with 1 mL of H_2O. GC analysis of the organic layer showed two diastereoisomers of the ester in the ratio of 95.5:4.5. The diastereoisomers were confirmed by CI on the GC mass spectrum.

Preparation of (*R*)-1-Octen-3-ol, (*R*)-3. The procedure was identical to that described above for the preparation of (*S*)-3, except that (2*S*,3*R*)-2 was used. The yield was 75% (2.6 g) of (*R*)-3. The spectroscopic data was in agreement with that given above for (±)-3, bp 65-66°C (1.25mmHg). To 100 mg (0.73 mmol) of (*R*)-3 in 1 mL of CH_2Cl_2 was added 5 drops of dry C_6H_5N and 200 mg (0.79 mmol) of MTPA Cl. The solution was allowed to react overnight, then was washed with 1 mL of H_2O. GC analysis of the organic layer showed two diastereoisomers of the ester in the ratio of 89.7:10.3. The diastereoisomers were confirmed by CI on the GC mass spectrum.

Preparation of 1-Octen-3-ol, (±)-3, by reaction of (±)-2 with $Bu_3SnAlEt_2$. To 1.4 mL (10 mmol) of diisopropylamine in 30 mL of dry THF and cooled to 0°C was added 3.8 mL of 2.6 M (10 mmol) of BuLi and stirred for 30 min. The solution was cooled to -78°C and 2.64 mL (10 mmol) of Bu_3SnH in 2.36 mL dry THF was added slowly to maintain the temperature below -70°C. The reaction was maintained at -78°C for 2 hrs and 10 mL of 1 M (10 mmol) of Et_2AlCl was slowly added. The temperature was increased to 0°C and maintained at this temperature for 1 hr.[34] At this point, 2.55 g (10 mmol) of (±)-2 in 5 mL of dry THF was added and the reaction was stirred for 1 hr. The reaction was quenched by addition of 10 mL of 1 N HCl with stirring for 1 hr. The organic layer was separated and the aqueous layer was extracted with (4 X 10mL) ether. The combined organic extract was dried over anhyd $MgSO_4$, filtered, and concentrated <u>in vacuo</u> to give a crude

liquid. The liquid was purified by chromatography on a Silica gel column using hexane:ethyl acetate (4:1) as eluent. The yield of (±)-3 was 74% (0.94 g). The spectroscopic data was in agreement with that given above for (±)-3.

Preparation of 3-Octyn-2-ol, 11. To 20.0 g (244 mmol) of 1-hexyne in 100 mL of dry THF at 0°C was added 10 mmol triphenylmethane and 94 mL of 2.6 M (244 mmol) of BuLi. The reaction was stirred for 1 hr, then 13.8 mL (245 mmol) of ethanal in 40 mL dry THF was slowly added to avoid localized boiling. The reaction was stirred for 2 hrs, then quenched by pouring into 200 mL of ice water. The organic layer was separated and the aqueous layer was extracted with (4 X 50mL) ether. The combined organic extract was backwashed with (2 X 50mL) of sat'd NH_4Cl, dried over anhyd $MgSO_4$, filtered, and concentrated <u>in vacuo</u> to give a crude liquid. The liquid was distilled at 87-88°C (17 mmHg). [lit.[35] bp 84-85°C (15mmHg)] to yield 49% (14.95 g) of 11. IR (film) 3350, 2255, 1342, 1295, 1160, 1080, 1010, 900 cm^{-1}; mass spectrum, *m/e* (relative intensity) 111(71), 97(100), 88(12), 86(21), 84(38), 83(18), 81(18), 79(21), 77(30), 69(78), 67(29), 55(46), 45(18), 43(71), 41(36); ^1H NMR ($CDCl_3$) δ 0.91 (3H, C_8, t, J=8.0 Hz), 1.43 (3H, C_1, d, J=7.5 Hz), 1.45 (4H, C_7, C_6, m), 1.73 (1H, OH, d, J=5.3 Hz), 2.20 (2H, C_5, dt, J=2.0, 7.0 Hz), 4.52 (1H, C_2, m). The IR spectrum was previously reported.[35]

Preparation of *Z*-3-Octen-2-ol, 12. To 2.64 g (10.6 mmol) of $Ni(OAc)_2 \kappa 4H_2O$ in 50 mL of 95% ethanol with H_2 purge was added 10 mL (14.2 mmol) of a solution containing 0.5 g of $NaBH_4$ in 12 mL of absolute ethanol and 0.65 mL of 2 N NaOH. After 5 min, 1.6 mL (23.9 mmol) of ethylenediamine was added, followed by 11.5 g (91.1 mmol) of 11. The

reaction was stirred for 4 hrs under H_2 purge and monitored by GC analysis of aliquots. Just prior to total conversion, the reaction was quenched by addition of 100 mL of sat'd NaCl and acidified with 1 N HCl (≈50 mL). The solution was extracted with (4 X 50mL) ether. The combined organic extract was backwashed with (2 X 50mL) of sat'd NaCl with 2 mL of 1 N HCl, dried over anhyd $MgSO_4$, filtered, and concentrated <u>in vacuo</u> to give 98% (11.5 g) of **12** as a liquid [lit.[35] bp 82°C (21mmHg)]. IR (film) 3360, 1712, 1280, 1110, 1055, 922, 740 cm^{-1}; mass spectrum, *m/e* (relative intensity) 113(31), 110(20), 71(100), 68(15), 58(32), 57(52), 45(29), 43(77), 41(33); ^1H NMR ($CDCl_3$) δ 0.91 (3H, C_8, t, J=6.7 Hz), 1.25 (3H, C_1, d, J=5.3 Hz), 1.35 (4H, C_7, C_6, m), 1.81 (1H, OH, broad), 2.08 (2H, C_5, m), 4.65 (1H, C_2, quint, J=6.7 Hz), 5.42 (2H, C_4, C_3, m). The IR spectrum was previously reported.[35]

Preparation of *cis-threo*-3,4-Epoxy-2-octanol, 13. To 18.2 g (85.8 mmol) of 85% m-chloroperoxybenzoic acid[4] in 200 mL of CH_2Cl_2 at 0°C was added 11 g (85.8 mmol) of **12** in 10 mL of CH_2Cl_2. The solution was warmed to rt and stirred for 2 hrs. The reaction was quenched by addition of 200 mL of sat'd Na_2CO_3 and stirred for 1 hr. The organic layer was separated and the aqueous layer extracted with (4 X 50mL) pentane. The combined organic extract was dried over anhyd $MgSO_4$, filtered, and concentrated <u>in vacuo</u> to give 95% (12.5 g) of **13** as a liquid, bp 60°C (0.2mmHg). IR (film) 3440, 1725, 1575, 1285, 1262, 1110, 1072, 900, 887, 828, 812, 758, 735 cm^{-1}; mass spectrum, *m/e* (relative intensity) 69(49), 58(100), 57(58), 55(18), 45(37), 43(49), 41(46); ^1H NMR ($CDCl_3$) δ 0.93 (3H, C_8, t, J=7.3 Hz), 1.28 (3H, C_1, d, J=7.0 Hz), 1.40 (4H, C_7, C_6, m), 1.57 (2H, C_5, m), 2.00 (1H, OH, broad), 2.89 (1H, C_3, dd, J=4.3, 8.0 Hz), 3.05 (1H, C_4, m), 3.67 (1H, C_2, d quint, J=1.5 7.0 Hz). From decoupling experiments, $J_{2,3}$=8.0 Hz.

Preparation of *cis-threo*-3,4-Epoxy-2-octanyl Tosylate, 14. To 11 g (76.3 mmol) of 13 in 150 mL of anhyd ether at -10°C was added 15.8 g (82.7 mmol, 1.1 eq) p-toluenesulfonyl chloride and 21.4 g (381 mmol, 5 eq) of powdered KOH divided in five portions which were added over 20 min. The solution was stirred for 1 hr and quenched by pouring into 500 mL of ice water. The organic layer was separated and the aqueous layer was extracted with (3 X 50mL) ether. The combined organic extract was backwashed with (2 X 25mL) of sat'd NaCl, dried over anhyd $MgSO_4$, filtered, and concentrated in vacuo without heating to give a liquid which crystallized upon refrigeration (mp 21-22°C). The yield of 14 was 83% (18.9 g). IR (KBr pellet) 1725, 1600, 1365, 1195, 1180, 910, 820, 790, 670, 580, 562 cm^{-1}; mass spectrum, *m/e* (relative intensity) 241(4.5), 212(4.8), 155(83), 127(19), 91(100), 69(43), 65(50), 57(24), 55(19), 43(45), 41(85); ^1H NMR ($CDCl_3$) δ 0.90 (3H, C_8, t, J=6.7 Hz), 1.38 (4H, C_7, C_6, m), 1.44 (3H, C_1, d, J=6.7 Hz, 2H, C_5, m), 2.44 (3H, $ArCH_3$, s), 2.92 (2H, C_4, C_5, m), 4.42 (1H, C_2, quint, J=6.7 Hz), 7.33 (2H, Ar, d, J=7.3 Hz), 7.83 (2H, Ar, d, J=7.3 Hz). Anal. Calcd for $C_{15}H_{22}O_3S$: C, 60.38; H, 7.43. Found: C, 60.34; H, 7.65.

Preparation of *cis-erythro*-4-Bromo-2,3-epoxyoctane, 15. To 3.11 g (10.4 mmol) of 14 in 50 mL of reagent grade acetone was added 7.22 g (83.3 mmol, 8 eq) of LiBr and the solution was stirred overnight in a darkened flask. Then 20 mL of water and 10 mL of pentane were added and the solution was stirred for 10 min. The organic layer was separated and the aqueous layer was extracted with (4 X 10mL) pentane. The combined organic extract was backwashed with (2 X 25mL) water, dried over anhyd $MgSO_4$ and concentrated in vacuo to give a liquid which was purified by chromatography

on a Silica gel column using hexane:ethyl acetate (6:1) as eluent. The yield of 15 was 55% (1.19 g). bp 45-46°C (0.01mmHg); IR (film) 1725, 1260, 1185, 1120, 1060, 980, 930, 825, 755, 740, 705, 645 cm^{-1}; mass spectrum, *m/e* (relative intensity) 127(75), 109(13), 85(22), 83(30), 71(13), 69(28), 67(15), 57(38), 55(100), 45(17), 43(30), 41(55); ^1H NMR ($CDCl_3$) δ 0.92 (3H, C_8, t, J=7.3 Hz), 1.30 (3H, C_1, d, J=5.6 Hz), 1.42 (4H, C_6, C_7, m), 1.83 (1H, C_5H_A, m), 1.91 (1H, C_5H_B, m), 3.14 (1H, C_3, dd, J=4.0, 9.6 Hz), 3.28 (1H, C_2, qd, J=4.1, 5.6 Hz), 3.77 (1H, C_4, ddd, J=5.5, 8.0, 9.6 Hz). Anal. Calcd for $C_{15}H_{22}BrO$: C, 46.39; H, 7.30. Found: C, 46.82; H, 7.60.

Preparation of *E*-3-Octen-2-ol, 16. To 0.50 g (2.41 mmol) of 15 in 10 mL of absolute methanol was added 0.47 g (7.23 mmol, 3 eq) of powdered zinc and the solution was refluxed for 5 hrs. The flask was cooled to rt then 5 mL of ether and 4 mL of 2 N HCl were added suquentially. The organic layer was separated and the aqueous layer was extracted with (3 X 10mL) ether. The combined organic extract was backwashed with (2 X 10mL) sat'd Na_2CO_3. The ether extract was dried over anhyd $MgSO_4$, filtered and concentrated <u>in vacuo</u> to give 81% (0.25 g) of 16 as a liquid, bp 79-81°C (12mmHg) [lit.[35] bp 82.3-83°C (15mmHg)]. IR (film) 3370, 1740, 1675, 1300, 1265, 1155, 1130, 1070, 975, 955, 927, 758, 745 cm^{-1}; mass spectrum, *m/e* (relative intensity) 128(0.4), 113(1.8), 110(0.6), 85(13), 71(100), 58(20), 57(38), 55(15), 45(15), 43(64), 41(37); ^1H NMR ($CDCl_3$) δ 0.84 (3H, C_8, t, J=8.1 Hz), 1.20 (3H, C_1, d, J=7.5 Hz), 1.29 (4H, C_6, C_7, m), 1.96 (2H, C_5, q, J=7.8 Hz), 4.19 (1H, C_2, quint, J=7.5 Hz), 5.45 (1H, C_3, tdd, J=1.5, 7.5, 15.3 Hz), 5.57 (1H, C_4, dtd, J=0.8, 7.5, 15.3 Hz). The infra red, ^1H NMR, and mass spectra obtained for the product of the hydrogenation of 11 using $LiAlH_4$ were identical to those obtained for 16 as prepared above. The IR spectrum

was previously reported.[35]

Preparation of *cis-erythro*-2-Bromo-3,4-epoxyoctane, 4. To 2.88 g (20 mmol) of 13 and 10.66 g (40 mmol, 2 eq) of triphenylphosphine in 100 mL of dry THF were added 2.25 g (10 mmol, 0.5 eq) of $ZnBr_2$ and 5.70 mL (40 mmol, 2 eq) of diisopropylazodicarboxylate in 50 mL of dry THF. The reaction was stirred for 3 hrs and then passed through a Silica gel column using hexane as eluent to remove the inorganic byproducts. The yield of 4 was 49% (2.01 g). bp 41-43°C (0.01mmHg); IR (film) 1780, 1270, 1250, 1175, 1005, 945, 920, 820, 810, 640 cm^{-1}; mass spectrum, *m/e* (relative intensity) 127(62), 71(38), 69(100), 57(18), 41(18); ^1H NMR ($CDCl_3$) δ 0.94 (3H, C_8, t, J=7.3 Hz), 1.85 (3H, C_1, d, J=6.8 Hz), 2.47 (6H, C_5, C_6, C_7, m), 3.06 (1H, C_4, td, J=4.5, 7.5 Hz), 3.13 (1H, C_3, dd, J=4.0, 9.5 Hz), 3.71 (1H, C_2, qd, J=6.5, 9.5 Hz). Anal. Calcd for $C_{15}H_{22}BrO$: C, 46.39; H, 7.30. Found: C, 46.61; H, 7.66.

Reaction of 4 with Zinc. To 0.50 g (2.41 mmol) of 4 in 15 mL of absolute methanol was added 0.47 g (7.23 mmol, 3 eq) of powdered zinc and the solution was refluxed for 3 hrs. The flask was cooled to rt and 5 mL of ether and 4 mL of 2 N HCl were added. The organic layer was separated and the aqueous layer was extracted with (3 X 10mL) ether. The combined organic extract was backwashed with (2 X 10mL) sat'd $NaHCO_3$. The ether extract was dried over anhyd $MgSO_4$, filtered and concentrated <u>in vacuo</u> to give 68% (0.21 g) of **6** as a liquid, bp 120°C (15mmHg) [lit.[36] bp 91°C (11mmHg)]. IR (film) 3370, 1680, 1320, 1150, 1080, 1050, 1030, 1010, 972, 905, 738 cm^{-1}; mass spectrum, *m/e* (relative intensity) 128(0.4), 113(2.0), 99(1.0), 95(1.5), 86(18), 71(100), 43(10); ^1H NMR ($CDCl_3$) δ 0.91 (3H, C_8, t, J=7.4 Hz), 1.34 (4H, C_7, C_6, m), 1.50 (3H, C_5, OH, m), 1.72 (3H, C_1, dd,

J=1.7, 7.4 Hz), 4.02 (1H, C_4, q, J=7.4 Hz), 5.48 (1H, C_3, qdd, J=1.7, 7.2, 15.4 Hz), 5.66 (1H, C_2, dqd, J=1.0, 7.4, 15.2 Hz). The ^{1}H NMR spectrum was previously reported.[37]

Reaction of 4 with $Bu_3SnAlEt_2$. To 0.56 mL (4 mmol) of diisopropylamine in 10 mL THF at 0°C was added 1.52 mL of 2.6 M (4 mmol) of BuLi. After 30 min, the solution was cooled to -78°C and 1.06 mL (4 mmol) of Bu_3SnH was added. After 90 min, 4.0 mL of 1.0 M (4 mmol) of Et_2AlCl was added and the temperature was increased to 0°C. After 1 hr, 0.414 g (2 mmol) of 4 was added and the reaction stirred for 1 hr. The reaction was quenched with 6 mL of 2 N HCl. The organic layer was separated and the aqueous layer was extracted with (3 X 20mL) hexane. The extracts were combined, dried over anhyd $MgSO_4$, filtered, and concentrated <u>in vacuo</u> to give a liquid which was distilled at 120°C (15mmHg) to give 60% (302 mg) of **6**. IR (film) 3380, 1740, 1680, 1050, 1030, 1010, 970 cm^{-1}; mass spectrum, *m/e* (relative intensity) ; ^{1}H NMR ($CDCl_3$) δ 0.93 (3H, C_8, t, J=7.3 Hz), 1.33 (4H, C_6, C_7, m), 1.55 (2H, C_5, m), 1.70 (3H, C_1, dd, J=1.6, 7.6 Hz), 3.53 (1H, OH, broad), 4.03 (1H, C_4, m broaden), 5.48 (1H, C_3, qdd, J=1.5, 8.1, 15.2 Hz), 5.65 (1H, C_2, dqd, J=1.1, 7.5, 15.3 Hz).

Preparation of Pentanal. To 32.32 g (150 mmol) of pyridinium chlorochromate in 500 mL of dry CH_2Cl_2 was added 12.25 mL (113 mmol, 10 g) of pentanol. By GC analysis of aliquots, the reaction was diluted with 500 mL ether after completion, filtered, and passed through a column of Forisil using ether as eluent. The eluent was concentrated at 70°C (1 atm) through a 12 in Vigreux column to yield 23% (2.2 g) of pentanal, bp 55°C (200mmHg) [lit.[38] 103°C (760mmHg)]. ^{1}H NMR ($CDCl_3$) δ 0.96 (3H, C_5, t, J=6.9 Hz), 1.48 (4H, C_3, C_4, m), 2.47 (2H, C_2, dt, J=2.0, 7.2 Hz), 9.75 (1H, C_1, t, J=2.0

Hz).

Preparation of (±)-2-Octyn-4-ol, 17. To 1.7 g (25 mmol) of propyne condensed in 50 mL THF at -78°C was slowly added 10 mL of 2.6 M (26 mmol) BuLi. After 30 min, 2.15 g (25 mmol) of pentanal in 10 mL THF was slowly added and the solution stirred for 1 hr at -78°C. After warming to rt, 10 mL of 1 N HCl was added. The layers were separated and the aqueous layer was extracted with (3 X 10mL) ether. The combined extract was backwashed with sat'd NH_4Cl, dried over anhyd $MgSO_4$, filtered, and concentrated <u>in vacuo</u> to yield 90% (2.49 g) of 17, bp 95-97°C (17mmHg) [lit.[37] bp 100-102°C (29mmHg)]. IR (film) 3360, 1340, 1155, 1110, 1045, 1010, 900 cm^{-1}; mass spectrum, *m/e* (relative intensity) 125(0.48), 111(10), 97(14), 84(14), 69(100), 41(26); ^1H NMR ($CDCl_3$) δ 0.92 (3H, C_8, t, J=6.4 Hz), 1.48 (6H, C_5, C_6, C_7, m), 1.85 (3H, C_1, t, J=2.3 Hz), 4.33 (2H, C_4, OH, broad). The ^1H NMR and IR spectra were previously reported.[37]

Preparation of *E*-2-Octen-4-ol, 6, from 17. To 1 g (7.9 mmol) of 17 in 30 mL THF was added 0.3 g (7.9 mmol) $LiAlH_4$. The reaction was heated to reflux for 1 hr, then cooled to rt, and quenched with 1 N HCl (20mL). The aqueous layer was extracted with (3 X 10mL) ether and the extracts were combined. The combined extract was backwashed with (2 X 10mL) sat'd NH_4Cl, dried over anhyd $MgSO_4$, filtered, and concentrated <u>in vacuo</u> to yield 62% (4.9 g) of **6**. IR (film) 3360, 1050, 1030, 1010, 975 cm^{-1}; mass spectrum, *m/e* (relative intensity) 128(0.36), 113(2.2), 99(1.2), 95(1.8), 86(20), 71(100), 58(12), 57(10), 53(13), 43(25), 41(22); ^1H NMR ($CDCl_3$) δ 0.90 (3H, C_8, dt, J=1.6, 7.6 Hz), 1.30 (4H, C_6, C_7, m), 1.50 (3H, C_5, OH, m), 1.71 (3H, C_1, dd, J=1.6, 7.5 Hz), 4.03 (1H, C_4, dq, J=1.0, 7.3 Hz), 5.48 (1H, C_3, qdd, J=1.7, 8.2, 15.4 Hz), 5.65 (1H, C_2, dqd, J=1.1, 7.5, 15.5 Hz). The

^{1}H NMR and IR spectra were previously reported.[37]

Preparation of *Z*-2-Octen-4-ol, 7, from 17. To 2.49 g (10 mmol) of $Ni(OAc)_2 \cdot 4H_2O$ in 50 mL of 95% ethanol with H_2 bubbling through the solution was added 10 mL of a solution comprised of 0.5 g $NaBH_4$, 12 mL 100% ethanol, and 0.65 mL 2 N NaOH. After 5 min, 1.6 mL (23.9 mmol) of ethylenediamine was added; this was followed by the addition of 1.0 g (7.92 mmol) of **17**. The reaction was followed by GC analysis of aliquots. After completion, the solution was diluted with 20 mL of sat'd NaCl, acidified with 2 N HCl and the layers were separated. The aqueous layer was extracted with (2 X 10mL) ether and the combined extract was backwashed with (2 X 10mL) sat'd NaCl, dried over anhyd $MgSO_4$, filtered, and concentrated <u>in vacuo</u> to yield 80 % (0.83 g) of **7**, bp 64.5-67°C (18mmHg) [lit.[37] bp 63-65°C (20mmHg)]. IR (film) 3380, 1720, 1170, 1050, 1025, 740 cm^{-1}; mass spectrum, *m/e* (relative intensity) 128(0.20), 113(1.6), 99(1.0), 95(1.6), 86(18), 71(100), 58(10), 57(13), 53(18), 43(37), 41(35); ^{1}H NMR ($CDCl_3$) δ 0.91 (3H, C_8, dt, J=1.2, 8.6 Hz), 1.33 (4H, C_6, C_7, m), 1.44 (1H, C_5H_A, m), 1.61 (1H, C_5H_B, m), 1.68 (3H, C_1, dd, J=1.7, 7.9 Hz), 2.09 (1H, OH, broad), 4.48 (1H, C_4, dq, 1.2, 7.6 Hz), 5.40 (1H, C_3, qdd, J=1.7, 7.8, 10.9 Hz), 5.58 (1H, C_2, dqd, J=1.2, 7.8, 10.8 Hz). The ^{1}H NMR and IR spectra were previously reported.[37]

Preparation of *cis*-3,4-Epoxy-2-octanone, 18. To 6.35 mL (69 mmol) of oxalyl chloride in 50 mL CH_2Cl_2 at -60°C was added 10.7 mL (138 mmol) of distilled DMSO in 10 mL CH_2Cl_2. After 2 min, 9 g (63 mmol) of **13** in 10 mL CH_2Cl_2 was slowly added. After 15 min, 50 mL (357 mmol) of Et_3N was added and the reaction stirred for 5 min. It was warmed to rt and diluted with 100 mL H_2O. The layers were separated and the aqueous layer was extracted with (2 X 30mL) hexane. The combined extract was washed with sat'd NaCl, 1

N HCl until acidic, H_2O, 5% Na_2CO_3 until basic, and finally H_2O. The organic layer was dried over anhyd $MgSO_4$, filtered, and concentrated in vacuo to give a liquid which distilled at 35°C (0.10mmHg) [lit.[39] bp 55-56°C (2mmHg)] to yield 71% (6.4 g) of **18**. IR (film) 1730, 1260, 1195, 1130, 1065, 1035, 965, 945, 915, 870, 780 cm^{-1}; mass spectrum, *m/e* (relative intensity) 141(0.44), 113(0.60), 99(10), 85(100), 57(40), 55(18), 43(94), 42(10), 41(27); ^1H NMR ($CDCl_3$) δ 0.91 (3H, C_8, t, J=7.3 Hz), 1.43 (6H, C_5, C_6, C_7, m), 2.25 (3H, C_1, s), 3.21 (1H, C_4, q, J=5.2 Hz), 3.57 (1H, C_3, d, J=5.0 Hz). The mass spectrum was previously reported.[40]

Preparation of *cis-erythro*-3,4-Epoxy-2-octanol, 19. To 6 g (42.2 mmol) of **18** in 40 mL ether at 0°C under argon was added 88.6 mL (≈21.1 mmol) of $Zn(BH_4)_2$.[41] The reaction was quenched with 20 mL of 1 M HCl and the organic layer was separated, dried over anhyd $MgSO_4$, filtered, and concentrated in vacuo to give 88% yield (5.35 g) of **19**, bp 66°C (0.45mmHg). IR (film) 3430, 1270, 1105, 1065, 955, 810 cm^{-1}; mass spectrum, *m/e* (relative intensity) 69(69), 58(100), 57(50), 55(18), 45(25), 43(32), 41(34); ^1H NMR ($CDCl_3$) δ 0.96 (3H, C_8, t, J=7.3 Hz), 1.37 (3H, C_1, d, J=7.0 Hz), 1.49 (7H, C_5, C_6, C_7, OH, m), 2.82 (1H, C_3, dd, J=4.1, 7.7 Hz), 3.01 (1H, C_4, ddd, J=4.0, 5.2, 7.0 Hz), 3.73 (1H, C_2, broaden, d quint, J=1.9, 6.5 Hz). From decoupling experiments, $J_{2,3}$=7.7 Hz.

Preparation of *cis-threo*-2-Chloro-3,4-epoxyoctane, 20. To 1.09 g (4.2 mmol) of triphenylphosphine in 10 mL of dry CH_3CN was added 1.01 mL (10.4 mmol) of CCl_4. After 30 min, 0.5 g (3.47 mmol) of **19** was added. The progress of the reaction was followed by GC analysis of aliquots. Upon completion, the reaction was diluted with dry ethyl ether (50 mL) and filtered to remove most of the triphenylphosphine oxide. The product was

concentrated and purified by Silica gel chromatography using hexane:ethyl acetate (6:1) as eluent. The yield of 20 was 97% (0.55 g). bp 52-54°C (0.1mmHg); IR (film) 1270, 1240, 1060, 1030, 995, 980, 915, 830, 815, 700 cm^{-1}; mass spectrum, *m/e* (relative intensity) 127(26), 87(10), 78(11), 76(28), 71(21), 69(100), 58(24), 57(20), 55(10), 43(10), 41(22). Anal. Calcd for $C_{15}H_{22}ClO$: C, 59.07; H, 9.30. Found: C, 59.28; H, 9.48.

Preparation of *cis-threo*-2-Bromo-3,4-epoxyoctane, 5. (Provided by Dr. S. M. Singh) To 0.4 g (2.77 mmol) of 19 and 0.92 g (2.77 mmol) of CBr_4 in 12 mL of THF at -78°C was added dropwise 4.5 mL (24.93 mmol) of HMPT. The reaction was stirred for 12 hrs at -78°C and was allowed to warm to rt overnight. Ice water (10 mL) was added to quench the reaction. The layers were separated and the aqueous layer was extracted with (5 X 20mL) pentane. The combined organic layer was backwashed with sat'd NaCl, dried with anhyd Na_2SO_4, filtered and concentrated <u>in vacuo</u>. The liquid was purified by Silica gel chromatography using hexane:ethyl acetate (90:10) as eluent to yield 74% (0.42 g) of 5. bp 42-44°C (0.01mmHg); IR (film) 1752, 1265, 1210, 1060, 1045, 1030, 990, 980, 918, 830, 815, 740, 655 cm^{-1}; mass spectrum, *m/e* (relative intensity) 127(67), 109(10), 71(38), 69(100), 57(19), 43(12), 41(27) CI 209(55), 207(53), 191(9), 189(10), 127(95), 109(100), 85(59); ^1H NMR ($CDCl_3$) δ 0.91 (3H, C_8, t, J=7.0 Hz), 1.46 (6H, C_5, C_6, C_7, m), 1.74 (3H, C_1, d, J=7.2 Hz), 3.14 (2H, C_3, C_4, m), 3.86 (1H, C_2, qd, J=7.0, 9.3 Hz). The ^1H NMR did not show any components corresponding to 4.

Reaction of 5 with Zinc. To 47 mg (0.72 mmol) of zinc powder in 5 mL absolute methanol was added 50 mg (0.24 mmol) of 5. The solution was refluxed for 5 hrs and then cooled to rt. The solution was diluted with 10 mL of ether and extracted with (3 X 10mL) sat'd NaCl. The organic layer was

dried with anhyd $MgSO_4$, filtered, and concentrated in vacuo to yield 75% (23 mg) of **6**. GC and ^1H NMR analysis indicated a composition of 10% **7** and 90% **6**.

Reaction of 5 with $Bu_3SnAlEt_2$. To 50 μL (0.36 mmol) of diisopropylamine in 10 mL THF at 0°C was added 0.14 mL of 2.6 M (0.36 mmol) of BuLi and stirred for 30 min. The solution was then cooled to -78°C and 96 μL (0.36 mmol) of Bu_3SnH was added slowly. After 1.5 hrs, 0.36 mL of 1 M (0.36 mmol) of Et_2AlCl was slowly added and the temperature was allowed to rise to 0°C for 1 hr. Then 50 mg (0.24 mmol) of **5** was added and stirred at 0°C for 2 hrs. The temperature was allowed to rise to rt and the reaction stirred for a further 16 hrs. The reaction was quenched with 2 mL of 1 N HCl. The layers were separated and 20 mL of sat'd NaCl was added to the aqueous layer and extracted with (2 X 10mL) ether. The combined organic layer was dried over anhyd $MgSO_4$, filtered, and concentrated in vacuo. The composition of the products of **6** and **7** 89:11 and a yield of 70% (21.5 mg).

Isomerization Test of 7 with 1 N HCl. To 2 μL of **7** in 1 mL of ether was added 0.2 mL of 1 N HCl and stirred for 24 hrs. GC analysis of the ether layer did not indicate a component corresponding to **6**.

Isomerization Test of 7 with Zinc. To 100 μL of **7** in 5 mL of absolute methanol was added 100 mg of zinc powder. The solution was stirred at reflux for 2 hrs. GC analysis of the organic liquid did not reveal a component corresponding to **6**.

Isomerization Test of 7 with $Bu_3SnAlEt_2$. To 140 μL (1 mmol) of diisopropylamine in 5 mL THF at 0°C was added 0.38 mL of 2.6 M (1 mmol) of BuLi and stirred for 30 min. The solution was then cooled to -78°C and 265 μL (1 mmol) of Bu_3SnH was added slowly. After 1 hr, 1 mL of 1 M (1 mmol)

of Et_2AlCl was slowly added and the temperature was allowed to rise to 0°C for 30 min. Then 128 mg (1 mmol) of 7 was added and stirred for 1 hr. The reaction was quenched with 1 mL of 1 N HCl and the layers separated. The aqueous layer was extracted with (3 X 5mL) ether and the combined layers was dried over $MgSO_4$, filtered, and concentrated in vacuo. GC analysis of the concentrate revealed a 6:7 ratio of 1:1 along with the tin byproducts.

APPENDIX A

The following seven procedures failed to produce 5, *cis-threo*-2-bromo-3,4-epoxyoctane, from *cis-erythro*-3,4-epoxy-2-octanol, 19:

1[22]-To 144 mg (1 mmol) of 19 in 4 mL of THF was added 524 mg (2 mmol) of triphenylphosphine. After 5 min, 113 mg (0.5 mmol) of $ZnBr_2$ and 142 mg (1 mmol) of diisopropylazodicarboxylate (DIAD) in 2 mL of THF were added. The solution was stirred for 1 hr, diluted with hexane (20 mL) and passed through a Silica gel column to remove the precipitates. Only 19 was detected by GC.

2[42]-To 2 mL of dry C_6H_5N was added 110 μL (1.1 mmol) of phosphorous tribromide. After cooling, 144 mg (1 mmol) of 19 was added and the reaction stirred for 7 hrs. The solution was then added to 2 mL of water and the layers separated. The aqueous layer was extracted with ether (3 X 5mL). Analysis of the ether extract by GC revealed no components eluting in the region expected for either the epoxy alcohol or the bromoepoxide.

3[43]-To 2 mL of dry $(CH_3)_2NCHO$ was added 110 μL (1.1 mmol) of phosphorous tribromide. After cooling to rt, 144 mg (1 mmol) of 19 in 2 mL of DMF was added and the reaction heated to 50°C for 7 hrs. The reaction was then cooled and poured into 10 mL H_2O, extracted with ether (3 X 5mL), dried over $MgSO_4$ and concentrated. GC analysis of the concentrated extract revealed only components eluting much later then expected for 5.

4[44]-To 289 mg (1.1 mmol) of triphenylphosphine in 5 mL of dry CH_3CN at 0°C was added 55 μL (1 mmol) of Br_2. After 10 min, the ice bath was removed and 144 mg (1 mmol) of 19 in 5 mL of CH_3CN was added. The solution was stirred for 1 hr and the solvent was removed in vacuo. The residue

decomposed upon distillation at 60°C (0.05mmHg). Use of CH_2Cl_2 as the solvent gave no improvement.

5[45]-To 178 mg (1 mmol) of N-bromosuccinimide in 5 mL of dry THF or CH_3CN was added dropwise 262 mg (1 mmol) of triphenylphosphine in 5 mL of the same solvent. After 10 min, 144 mg (1 mmol) of 19 was added and the reaction stirred for 1 hr. The solvent was evapourated in vacuo. Analysis by GC of the sticky mass which resulted gave no evidence of the desired product.

6[24]-To 315 mg (1.2 mmol) of triphenylphosphine in 5 mL of dry THF or CH_3CN was added 996 mg (3 mmol) of CBr_4. After 10 min, 144 mg (1 mmol) of 19 was added and the reaction stirred for 1 hr. The solvent was evapourated in vacuo. Analysis by GC of the sticky mass which resulted gave no evidence of the desired product.

7[46]-To 144 mg (1 mmol) of 19 in 3 mL of dry CH_3CN at 0°C was added 206 mg (2 mmol) of NaBr followed by 558 μL of 45% $BF_3 \kappa Et_2O$ (2 mmol). After 1 hr, water was added and the products were extracted with (3 X 5mL) ether. The combined ether layers was dried with anhyd $MgSO_4$, filtered and concentrated in vacuo. GC analysis showed that the major product eluated faster then 19 and could not be the desired product.

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