STEREO AND REGIOSELECTIVE OPENINGS OF CHIRAL 2,3-EPOXY ALCOHOLS,
VERSATILE ROUTES TO OPTICALLY PURE NATURAL PRODUCTS AND DRUGS,
UNUSUAL KINETIC RESOLUTIONS

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Abstract A diverse selection of new synthetic applications of the titanium-
catalyzed asymmetric epoxidation (AE) process is described. These include
asymmetric syntheses of (+)-Darvon[R] Alcohol, (-)-bestatin, (+)-2-methyl
bestatin, (-)-propranolol, (-)-α-amino-β-hydroxybutyric acid, and (-)- and
(+)-frontalin. The kinetic resolution mode of the AE process was used to
prepare chiral insect pheromones in very high (>99% e.e.) optical purity;
these include (+)-and (-)-α-caprolactone, (-)-exobrevicomin, (-)-endobrevi-
comin, (+)-and (-)-ipsdienol, and (+)-trans-verbenol. A number of unusual
kinetic resolutions based on the AE process are presented; these include
resolutions of allenic alcohols, α-acetylenic carbinols, β-hydroxy sulfides,
and a dienol.

Almost two years ago we first reported on the titanium-catalyzed asymmetric epoxidation
process shown in Scheme I.[1a] In the interim this new chiral catalyst system has rapidly
become accepted as one of the best means for synthesizing a great variety of optically pure

SCHEME I

D-(-)-diethyl tartrate (unnatural)
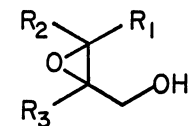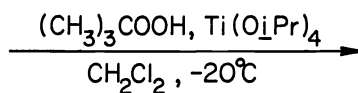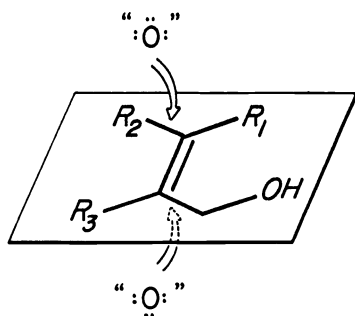
L-(+)-diethyl tartrate (natural)

$(CH_3)_3COOH, Ti(O\underline{i}Pr)_4$
CH_2Cl_2 , -20°C

70-87% yields,
⪈ 90% e.e.

organic substances. Among the primary reasons for rapid adoption of the method are:
1) simplicity - all the ingredients are inexpensive and commercially available.
2) reliability - it succeeds with most allylic alcohols, however, bulky substituents at R_1
    are deleterious.[2]
3) high optical purity - generally >90% e.e. and usually >95%e.e. (99.5% e.e. was the
    highest measured accurately to date).
4) absolute stereochemistry is predictable - so far no exceptions to the rules laid down in
    Scheme I (provided one is dealing with a prochiral allylic alcohol, vide infra).
5) relatively insensitive to preexisting chirality - in allylic alcohols with preexisting
    chiral centers, the diastereofacial preference of the chiral titanium-tartrate catalyst
    is often strong enough to over-ride diastereofacial preferences inherent in the chiral
    olefinic substrate (exceptions and general guidelines discussed later, vide infra).
6) versatility of 2,3-epoxy alcohols as intermediates - new selective transformations are
    rapidly being discovered.

     This lecture will concentrate on unpublished results from our laboratory regarding:
1) selective reactions of 2,3-epoxy alcohols and related derivatives; 2) syntheses of
diverse types of drugs and natural products; 3) and some unusual kinetic resolutions.

1) Selective Transformations of 2,3-Epoxy Alcohols and Derivatives
     Although barely studied until the past few years, the 2,3-epoxy alcohol moiety (e.g. 1)
abounds with possibilities for nucleophilic openings exhibiting high regio- and stereo-
chemical control.[50] In epoxy alcohol 1 positions 2 and 3 are obvious sites for nucleophilic
attack and methods now exist for directing attack to either C-2 or C-3. We will return to
selective C-2 and C-3 openings, but first let us explore a less obvious mode in which nucleo-
philes can react with 2,3-epoxy alcohols.
     (a) Opening at C-1
     In collaboration with Professor Satoru Masamune's group[3] we have found that certain
2,3-epoxy alcohols (1) can be selectively substituted at C-1 by virtue of the Payne Re-
arrangement[4] in which an equilibrium is established between 1 and its 1,2-epoxy alcohol
isomer 2. In many cases C-1 in epoxide isomer 2 is by far the most reactive site toward

SCHEME II. Payne Rearrangement/Opening Processes
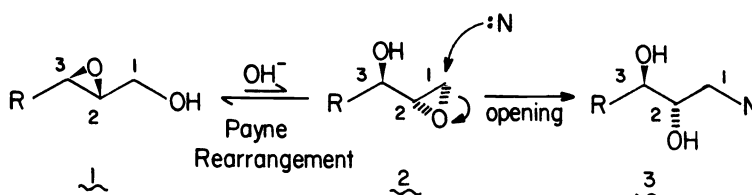
nucleophiles, with the result that the Payne Equilibrium (1 ⇌ 2) is siphoned off to afford
diol 3 as the major, if not the exclusive, product (Scheme II). When the nucleophile is
PhS⁻ the opening process leads to 3 (N = SPh), and these diol thiophenyl ethers are key
intermediates in the iterative sequence developed by the Masamune and Sharpless groups[3] for
synthesizing higher saccharides of any relative or absolute configuration.

     We have examined the efficacy of several other interesting nucleophiles in this novel
Payne Rearrangement/Opening sequence. A few highlights of these experiments are shown in
Scheme III. From the examples given for BH_4^- as nucleophile some general trends for these
rearrangement/opening processes are apparent. Cis-epoxy alcohols give cleaner C-1 attack

than trans-epoxy alcohols (in the cis cases more of the 1,2-epoxide is present at equili-
brium[4]). A C-4 alkoxy substituent (i.e. carbohydrate cases) has a deactivating effect on
C-3 and favors the desired C-1 product (thus the method provides a route to omega-deoxy-
sugars). Simple 2,3-epoxy alcohols (i.e. R in 1 is saturated) are poor substrates as one
gets substantial attack at C-3 and C-2 as well as C-1. Geraniol-2,3-epoxide (in which C-3
is 3°) is not reduced at C-3, and the major product is the desired 2,3-diol but some
1,3-diol also results. Triol (resulting from ⁻OH acting as :N in Scheme II) is also formed
but with the better substrates it is a very minor product. The various factors outlined
here for BH_4^- as nucleophile, should be useful guides when contemplating applications of
these rearrangement/opening processes involving other nucleophiles.

Cyanide was only briefly examined and the yields need to be improved substantially
(triol was a major by-product). However, the reaction shown in Scheme III does suggest that
an attractive one carbon homologation process could be developed (in this case a protected
L-2-deoxy-ribono-1,4-lactone was isolated in 35% yield).

The last example in Scheme III demonstrates that nitrogen nucleophiles are also
effective. The process offers a new route to omega-aminosugars. The sequence should also
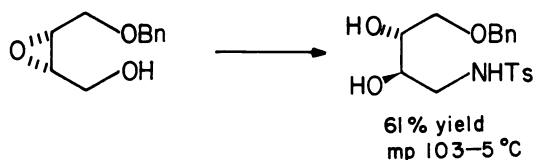work with mono-alkylated sulfonamide anions (e.g. TsN^-CH_2Ph).

<p align="center">SCHEME III</p>

(a) BH_4^- as Nucleophile (NaOH, H_2O, t-BuOH, reflux)
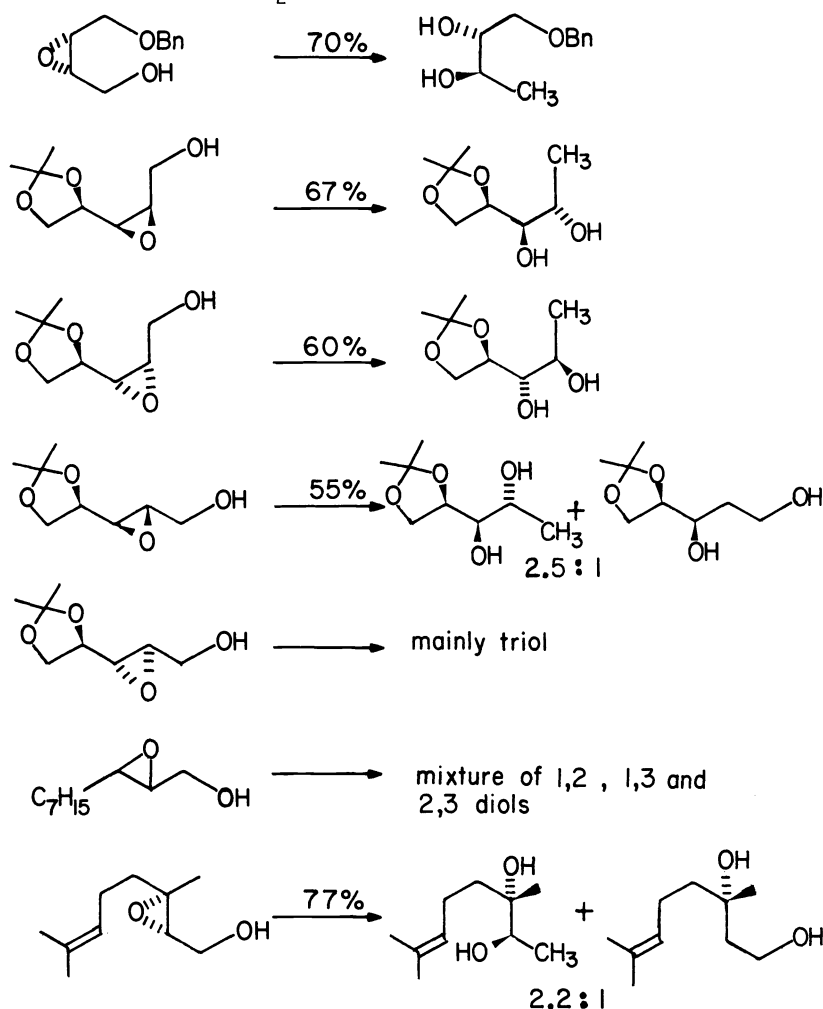
(b) ⁻CN as Nucleophile (NaOH, H₂O, dioxane, 80°C)

35% yield
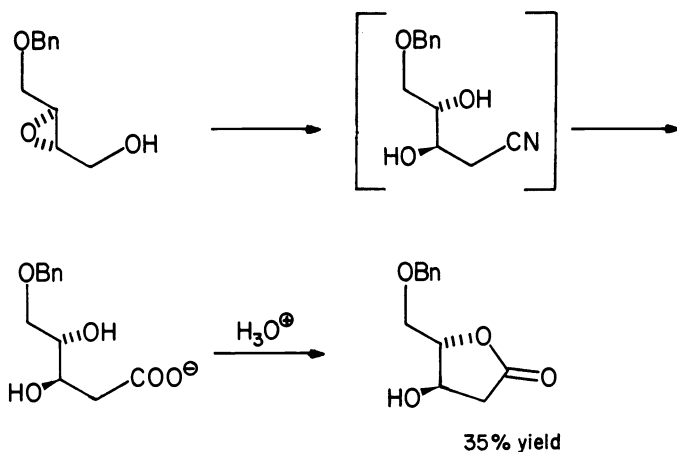
(c) TsNH⁻ as Nucleophile (NaOH, H₂O, dioxane, 60°C)

61% yield
mp 103–5 °C

Other strategies for substitutions at C-1 can leave the 2,3-epoxide moiety intact. As revealed in Scheme IV, conversion of the 2,3-epoxy alcohol to the mesylate or tosylate leads (in some cases via the corresponding iodide or bromide) to substitution of various nucleophiles (e.g. H⁻,[1] R⁻,[5,6] ⁻SPh[7]).

SCHEME IV

M = S or Se
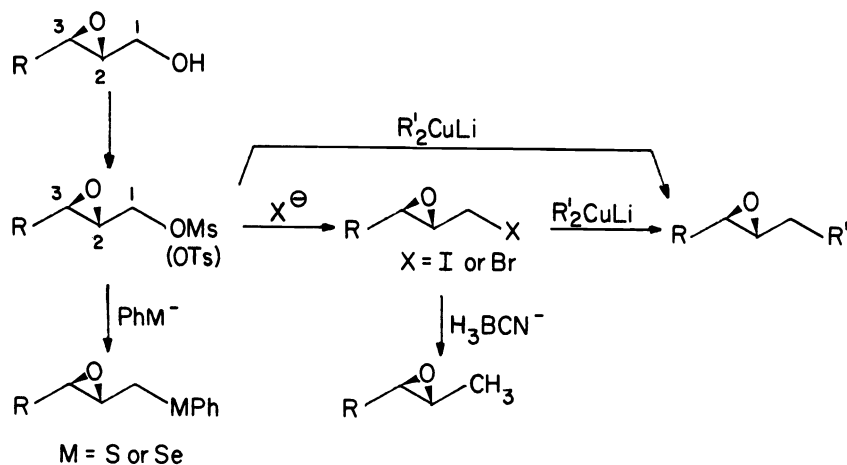
When C-1 substitution was recently attempted with malonate on the epoxy tosylate 4, a further interesting transformation ensued:

4   5 , 65% yield
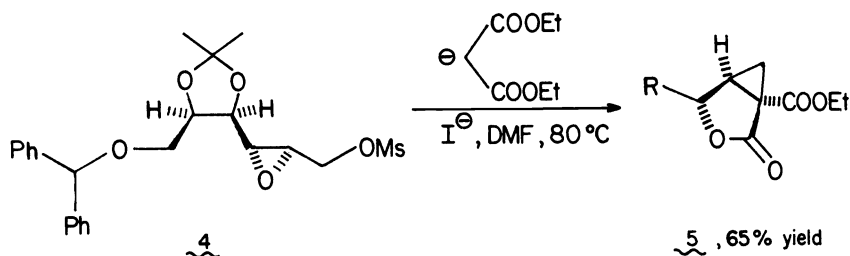
This is likely to prove a fairly general route to chiral cyclopropanes related to 5. This type of cyclopropane forming process is well precedented[8] but access to the appropriate epoxy carbanion intermediates had previously been indirect. Furthermore, we were unable to locate an example (such as ours) involving an epoxy malonate intermediate. The facile γ-lactone formation has the virtue of distinguishing between the malonate ester groups, and thereby also providing a new chiral center.

   (b) Opening at C-2 or C-3.

   Simple epoxy alcohols or their ether derivatives (e.g. 6) are known to open selectively

      6a, R = H   7   8a, R = H
      6b, R = Bn   8b, R = Bn
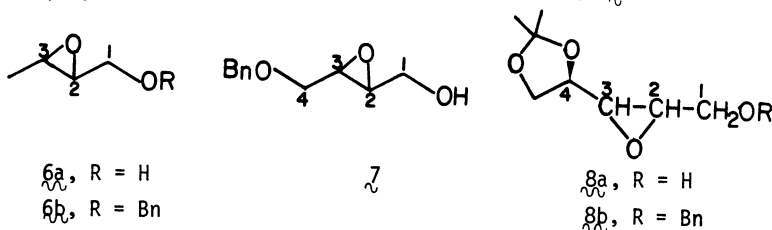
at C-3 with carbon[9], nitrogen[10], and oxygen[11] nucleophiles; This selectivity is presumably controlled by electronic effects (the steric environments at C-2 and C-3 in 6 are comparable). When the electronic and steric effects at C-2 and C-3 are roughly equivalent, as they are in 7, we have observed almost equal attack at C-2 and C-3 with both N_3^- and PhS^- as nucleophiles (Payne Rearrangement suppressed by the use of buffered conditions).

   We[12] and others[11,13] have found that certain reagents which are delivered intramolecularly by virtue of attachment to the hydroxyl, in for example 6a and 7, can exhibit high selectivity for C-2. However, we recently discovered another set of circumstances which favors attack at C-2. This new type of selectivity was first observed with the carbohydrate-like epoxy alcohols 8a. Note that carbons 2 and 3 are electronically similar in 7 and 8a, but that 8a has an added steric liability on the C-3 side. All four diastereomers (at C-2 and C-3) of 8a have been opened with N_3^- in NH_4Cl buffered methoxyethanol and in each case good (worst case is 7:1 in favor of C-2) to excellent selectivity for C-2 opening is observed.[14] Similar C-2 selectivity is seen with PhS^- and $PhSe^-$ and 8a. Thus the modest steric bias in 8a appears to significantly favor the avenue for external nucleophilic attack (even with the slender azide nucleophile) which leads to C-2 substitution. That the C-1 hydroxyl is not important in directing these azide openings is suggested by the fact that the C-2 selectivity is intact in the benzyl ether derivatives 8b.[14] If this intermolecular selectivity for C-2 proves general in these carbohydrate cases (e.g. 8), it greatly expands the range of nucleophiles for attack at C-2. The intramolecular C-2 substitution processes requiring the hydroxyl as a binding site place an inherent and fairly serious constraint on the nature of the nucleophile.

Lest one get the impression that all the major factors influencing these epoxy alcohol openings are now well understood, we offer the examples in Scheme V for your perusal. With one exception the entries in Scheme V are consonant with expectations based on our under-
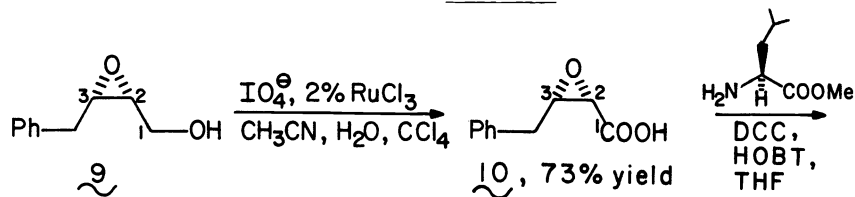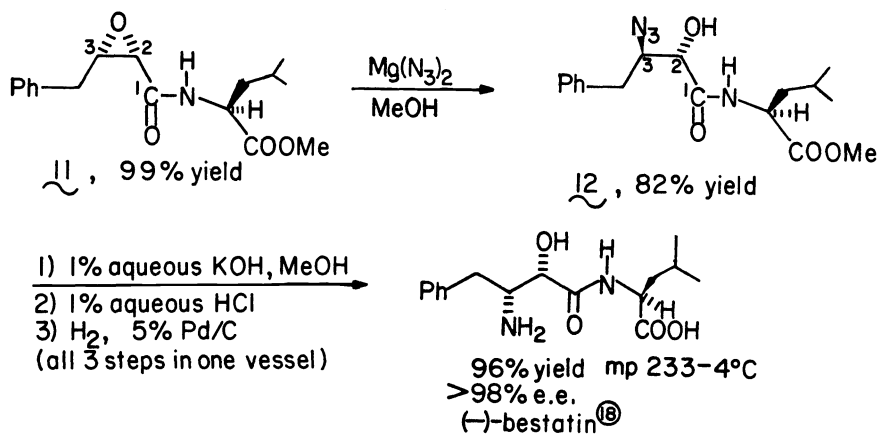
SCHEME V.   Methyl Cuprate Openings*
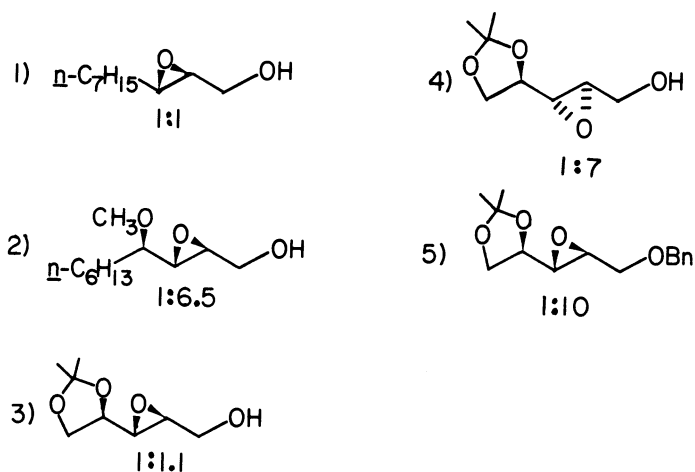
*5 equivalents Me_3CuLi_2, Et_2O, -40°C; C-3:C-2 ratios are indicated.

standing of these epoxy alcohol openings and on literature precedents[15] for related methyl cuprate openings. The glaring exception is entry 3 which exhibits almost no selectivity for C-2 over C-3 [note however that C-2 selectivity is reestablished in the benzyl ether derivative (entry 5)]. An explanation for this anomalous result eludes us at present, but it does reveal that current understanding may be inadequate for making reliable predictions when complex nucleophiles are involved.

As already mentioned selective nucleophilic attack at C-3 can be managed in simple epoxy alcohols such as 6, but this selectivity vanishes in carbohydrate-like cases such as 7 and 8. Another strategy for controlling C-2 versus C-3 attack becomes available upon oxidation of the 2,3-epoxy alcohols to their glycidic acid analogues. The best means for effecting this oxidation involves an improved catalytic RuO_4 system developed recently in our laboratory (in our experience this improved procedure offers advantages over older ones in most all applications involving RuO_4).[16] As shown in Scheme VI epoxy alcohol 9 is oxidized to the glycidic acid 10. As noted by Still and Ohmizu with an epoxy alcohol related to 9, only the

SCHEME VI
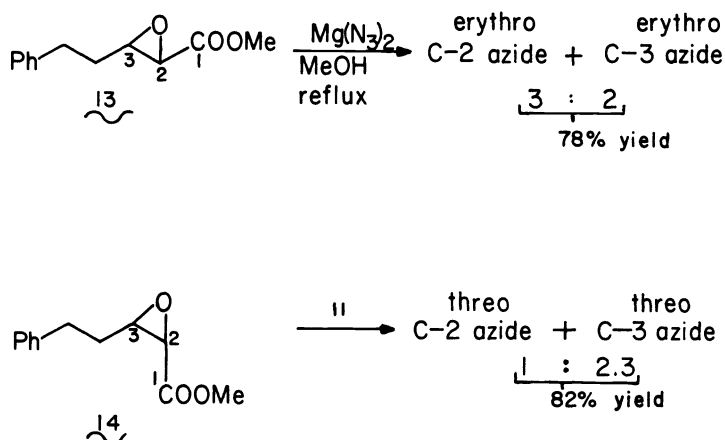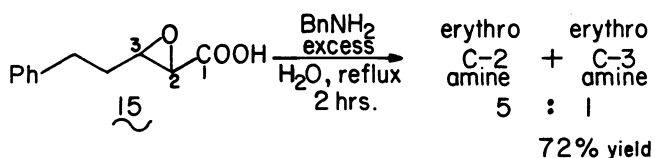
11 , 99% yield → 12 , 82% yield

1) 1% aqueous KOH, MeOH
2) 1% aqueous HCl
3) H$_2$, 5% Pd/C
(all 3 steps in one vessel)

96% yield mp 233-4°C
>98% e.e.
(—)-bestatin®

new RuO$_4$ procedure gave a good result although many oxidants were tried.[17] DCC coupling afforded the 2,3-epoxy amide 11, which opened exclusively at C-3 with azide to give 12.[18] There is substantial precedent in the work of Martynov for nucleophilic openings of 2,3-epoxy amides at C-3.[19] The factors directing C-3 attack of nucleophiles in such epoxy amides are very strong and even completely override geminal substitution at C-3.[19] We are presently testing whether this effect is strong enough to direct attack to C-3 even in saccharide 2,3-epoxy amides where C-4 bears an alkoxy substituent.
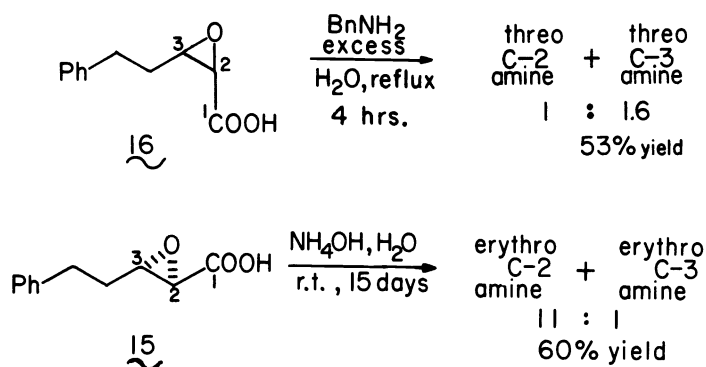
In sharp contrast to the behavior of glycidic amides, the inherent directing effects in

13 $\xrightarrow[\text{MeOH reflux}]{\text{Mg(N}_3)_2}$ erythro C-2 azide + erythro C-3 azide

3 : 2,
78% yield

14 $\xrightarrow{\text{11}}$ threo C-2 azide + threo C-3 azide

1 : 2.3,
82% yield

openings of glycidic esters are very weak, if the azide openings of 13 and 14 are any indication. These striking differences between the epoxy esters and epoxy amides are being studied further. In the meantime, if one wishes to direct a nucleophile to C-3 the epoxy amide derivative is clearly the candidate most likely to succeed.

There are a few intriguing reports in the literature that simple glycidic acids undergo selective opening at C-2 with basic amines as the nucleophiles.[20] This attracted our interest since it suggested a means of directing attack to either C-3 (epoxy amide already demonstrated to be highly effective) or to C-2 (if the free epoxy acid were employed). Unfortunately, the C-2 directing effect proved to be quite weak in our hands:

15 $\xrightarrow[\text{H}_2\text{O, reflux 2 hrs.}]{\text{BnNH}_2 \text{ excess}}$ erythro C-2 amine + erythro C-3 amine

5 : 1
72% yield

Notice that the C-2/C-3 ratio is much better for the trans-epoxy acid 15 than for the cis-epoxy acid 16 (a trend reported earlier by Harada and coworkers[20b,20c]). When 15 is exposed to NH_4OH (instead of benzylamine) for 11 days at room temperature the C-2/C-3 product ratio improves to 11:1. The benzylamine openings of the 2-methyl-substituted analogs of both 15 and 16 were also examined, but not surprisingly C-3 attack predominated in each case (recall that with the epoxy amides an additional C-3 substituent did not thwart highly selective attack at C-3). It is obvious, but worth mentioning, that additional electronic and/or steric factors (in the glycidic acid substrate) which work against C-3 can be expected to favor better C-2 selectivities than those seen with 15 and 16. For example, the glycidic acid analogs of 7 and 8 should open very selectively at C-2 with amine and other nucleophiles.

In spite of the fair to poor selectivities for attack at C-2 by amine nucleophiles on simple glycidic acids such as 15 and 16, we have a recent result which suggests other nucleophiles may be more promising:
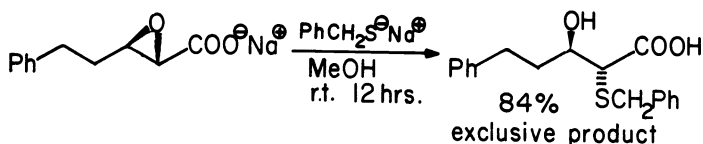
From the foregoing discussion it is apparent that 2,3-epoxy alcohols and their derivatives are emerging as chiral intermediates with unique potential for further stereo- and regioselective transformations. This statement is also supported by the numerous practical applications in which the process has played a key role in a synthetic sequence.

2) Syntheses of Diverse Types of Chiral Natural Products and Drugs.

The AE process was used in the following published syntheses:
disparlure,[1b,5] leukotriene derivatives,[1b,21,22,23,24] saltmarsh caterpillar pheromone,[5] Comstock mealy bug pheromone,[25] aklavinone,[26] maytansine,[27] methymycin,[1b] erythromycin,[1b] virginiamycin M,[28] squalene-2,3-epoxide,[29] sphingosine derivatives,[10b,10c] rifamycin S,[30] narasin,[31] salinomycin,[31] sirodesmin A,[32] verrucarin A,[17] alditols,[3a,13a] deoxyalditols,[12a,13a,33] aminodeoxyalditols,[33,13a,14] the four D-pentoses,[3b] the eight L-hexoses,[34] 2,6-dideoxy-D-arabino-hexose,[33] 2,6-dideoxy-D-ribo-hexose,[33] α-D-and β-D-C-glycopyranosides,[35] and chiral 1,2-disubstituted trans-cyclodecenes.[36]

In addition to these published cases we wish to disclose some unpublished applications in a highly abbreviated manner. In general only the key epoxy alcohol (along with yield and % e.e. for AE step) and the final product (with overall yield from epoxy alcohol) will be indicated. Occassionally an interesting intermediate step will be shown. The following syntheses will eventually be described in more detail elsewhere.
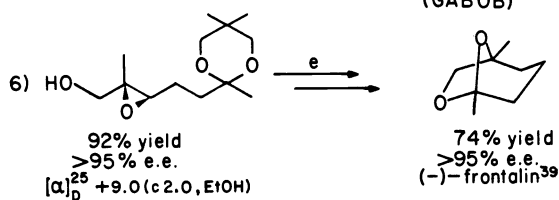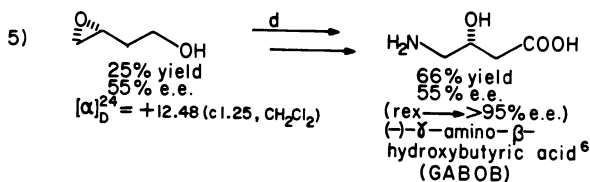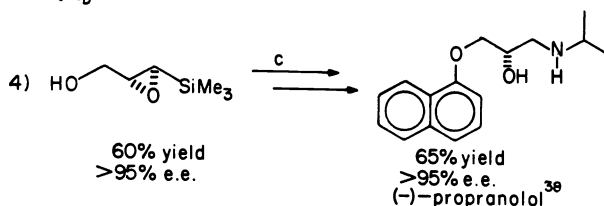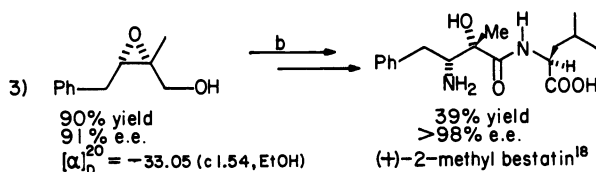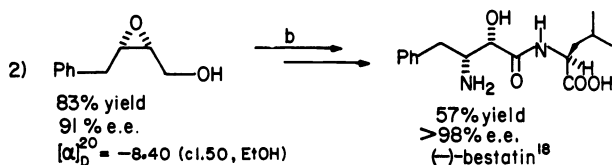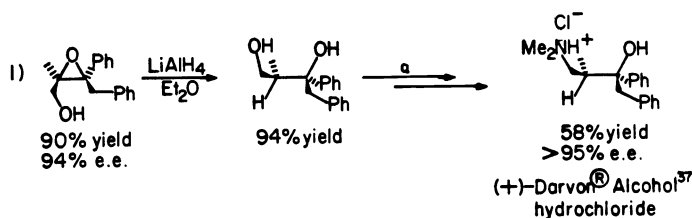
(a) TsCl, pyr.; Me$_2$NH, DMSO; HCl, Et$_2$O. (b) RuO$_4$[16]; L-leucine methyl ester hydrochloride, DCC, HOBT, N-methyl morpholine, THF; NaN$_3$, MgSO$_4$ MeOH; 1% KOH, H$_2$O, MeOH; 1% HCl, H$_2$O; H$_2$, 5% Pd/C, MeOH, H$_2$O; see also Scheme VI. (c) MsCl, Et$_3$N, CH$_2$Cl$_2$, -20°C; ArO$^-$Na$^+$, DMF; Bu$_4$N$^+$F$^-$, DMSO, THF: i-PrNH$_2$, H$_2$O. (d) RuO$_4$[16]; NH$_4$OH, THF. (e) LiAlH$_4$, Et$_2$O; CHCl$_3$, cat. TsOH(H$_2$O).

In the six examples given above a prochiral allylic alcohol was employed. We and others are also finding that the kinetic resolution (KR) of racemic allylic alcohols can be a practical route to chiral substances.[33] Some examples are outlined below where the chiral allylic alcohol (obtained from the racemic allylic alcohol by the KR mode[45] of the AE process in usually >99% e.e.) and the pheromone derived from it are shown.

1)
Ph—CH=CH—CH(OH)—CH₂CH₃

$[\alpha]_D^{25} = -3.68$ (c 1.5, EtOH)

$$\xrightarrow[\substack{63\% \\ (ref. 40)}]{a}$$

Ethyl lactone structure, **R** configuration, H

Trogoderma granarium

attractant

2)
Ph—CH₂CH₂—CH(OH)—CH=CH₂

$[\alpha]_D^{25} = -0.89$ (c 1.25, EtOH)

$$\xrightarrow[\substack{60\% \\ (refs. 40,41)}]{a}$$

lactone structure, **S** configuration

3)
dioxolane—CH₂CH₂CH₂—CH(OH)—CH=CH₂

$[\alpha]_D^{23} = +12.0$ (c 3.28, MeOH)

$$\xrightarrow[\substack{60\% \\ (ref. 39)}]{b}$$

bicyclic ketal with CH₃ and ethyl, H

(−)-exobrevicomin

4)
dioxolane—CH₂CH₂CH₂—CH(OH)—CH=CH₂

$$\xrightarrow[\substack{20\% \\ (ref. 39)}]{c}$$

bicyclic ketal with CH₃, ethyl, H

(−)-endobrevicomin

(a) H_2, PtO_2, EtOAc; Ac_2O, pyr.; RuO_4[16]; K_2CO_3, MeOH; conc. HCl.
(b) MCPBA, CH_2Cl_2; Ac_2O, pyr. [proceed with ($\underline{S}$)-threo-epoxy acetate after separation from erythro isomer by silica gel chromatography]; Me_2CuLi, Et_2O, 0°C; 10% H_2SO_4/pentane (1:1). (c) Same as in (b) except proceed with ($\underline{S}$)-erythro-epoxy acetate.

Racemic ipsdienol is commercially available.[42] The (R)-(-)-enantiomer is an attractant
for Ips pini and the (S)-(+)-enantiomer for Ips paraconfusus. Both the R and S enantiomers
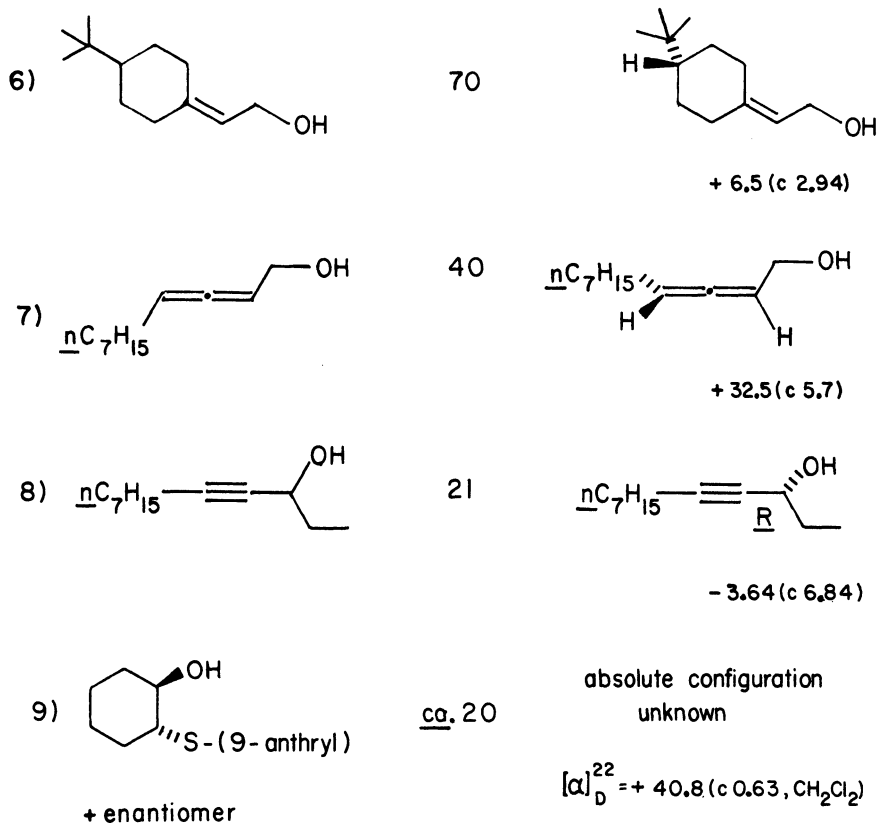

ipsdienol

(S)-trans-verbenol

were prepared in high (> 99% e.e.) optical purity by running the kinetic resolution to 90%
conversion using the appropriate tartrate ester [(+)-DIPT → R, (-)-DIPT → S]. Trans-verbenol
is also commercially available.[42] It is partially enriched in the desired (S)-enantiomer,[43]
but much higher purity material was obtained by running the KR process using (+)-DIPT.[44]

3) Unusual Kinetic Resolutions

Since our original publication[45] on the kinetic resolution (KR) process, we have ex-
amined a wide variety of potential substrates. As revealed by the new results shown in the
Table the KR process is not restricted to secondary allylic alcohols in which the chirality
resides at the carbinol carbon. Entries 1 through 5 probe the sensitivity to chiral centers
at various positions in primary allylic alcohols. Entries 6 and 7 are novel in that they
involve kinetic resolution of molecules possessed of axial chirality. Entry 8 reveals that
even acetylenic alcohols undergo kinetic resolution, albeit very inefficiently. Entry 9 is
an example of a β-hydroxysulfide undergoing kinetic resolution,[46] but at such a low level
that it can only be regarded as a curiosity.

TABLE. Unusual Kinetic Resolutions*

Racemic Substrate	% e.e. of Recovered Substrate	Recovered Substrate

1) Ph ... OH   6   Ph R ... OH   + 6.3 (c 1.57)

2) Ph ... OH   >95   Ph S ... OH   + 98.0 (c 3.2)

3) Ph ... OH   80   Ph S ... OH   + 113.0 (c 3.7)

4)   + enantiomer   85   + 116.5 (c 5.02)

5)   47.8**

6)

70

+ 6.5 (c 2.94)

7) nC_7H_{15}

40

+ 32.5 (c 5.7)

8) nC_7H_{15}

21

− 3.64 (c 6.84)

9)   S-(9-anthryl)

+ enantiomer

ca. 20

absolute configuration
unknown

$[\alpha]_D^{22} = + 40.8 (c\ 0.63, CH_2Cl_2)$

(*) (+)-DIPT was employed in all cases, and most reactions were run to
about 60% conversion (± 10%) at -20°C. Reaction times generally
ranged from 15h to 2 days, but the acetylenic carbinol (entry 8)
required 7 days. The rotations ($[\alpha]_D^{25}$ in absolute ethanol unless
otherwise indicated) are given for each recovered (and chromato-
graphically purified) substrate. The absolute configurations were
secured by correlations with molecules of known configuration.

(**) This is a calculated result based on Woodard's[47a] carefully de-
termined relative rates for the two enantiomers of perillyl
alcohol [with (+)-DIPT at -20° k(R)/k(S) = 2.98] and assuming
60% conversion. See footnote 9 in reference 45 for the equation
used in such calculations.

The Table indicates the absolute configuration of the slow reacting (i.e. recovered) en-
antiomer. In most all cases the outcome is nicely rationalized by the detailed mechanism
which we currently favor for the AE process.[47] Certain cases (i.e. entries 4, 6, and 7) are
trivial to rationalize based only on the enantioface selection rule (see Scheme I). By con-
trast, explication of the especially interesting and important results embodied in entries 1,
2, and 3, requires recourse to our detailed picture of the transition state for the pro-
cess.[48] It is gratifying that this mechanistic model easily predicts not only which en-
antiomers will react faster but also the approximate magnitude of the rate difference for
entries 1, 2, and 3. You may well ask how one could predict the small (6% e.e.) effect seen
for the trans-allylic alcohol isomer in entry 1. The point is that the favored mechanism

predicted very little or no kinetic resolution in this case; this expectation was confirmed by the negligible (6% e.e.) kinetic resolution observed. We and others have grown to depend on this insensitivity of the AE process to chirality in the E-β-vinyl substitutent, for it allows one to expect the enantioface selection rule to strongly override diastereofacial inclinations existing in the chiral substrate. On the other hand, we[3a] and others[13a] have learned to expect serious departures from the enantioface selection rules when the chiral center is in the Z-β-vinyl position (e.g. entry 3). The dramatic kinetic resolution seen in entry 2 leads to the prediction that similar loss of control over facial-selection may arise when the α-vinyl carbon center is chiral. The simple rule to remember is that if your allylic alcohol has a chiral atom attached to the olefinic unit in the E-β-position you can expect the AE process to access either diastereoface selectively. However, if the chiral atom is in either the Z-β-position or the α-position, the AE process will likely give selective access to only one of the diastereofaces.

Perhaps the most dramatic result to date illustrating the remarkable selectivity inherent in these chiral titanium-tartrate epoxidation catalysts is that shown in Scheme VII for epoxidation of the racemic hexadienol 17.

SCHEME VII
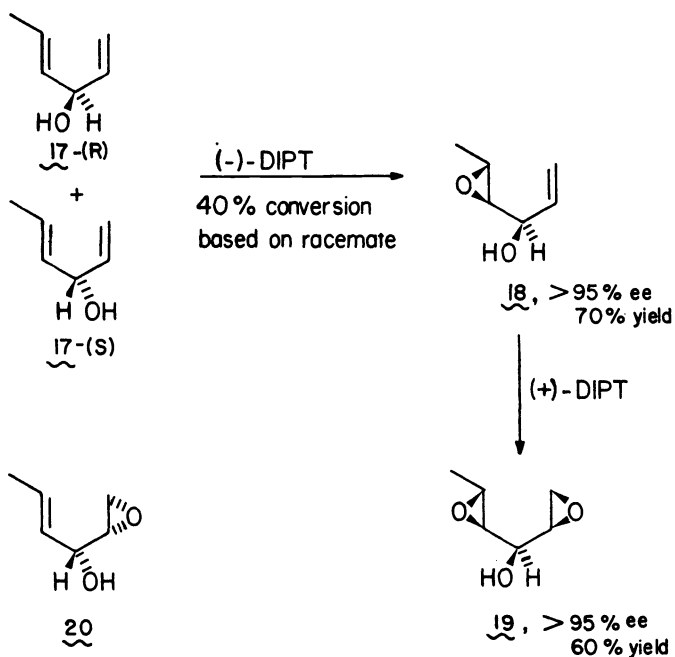
Each enantiomer of 17 offers four distinct olefinic faces for epoxidation, hence there are eight possible monoepoxides. However, two facts enabled us to predict that a single epoxy alcohol, namely 18, should form at less than 50% conversion using (-)-DIPT. The KR selection rule alone can not in this case predict the outcome.[49] The problem is that each enantiomer of 17 possesses a "fast reacting" enantioface for either tartrate chirality. This curious situation is an obvious consequence of the carbinol center bearing two vinylic substituents. Thus both 18 and another erythro-epoxy alcohol 20 could arise based on the KR selection rule alone (eight possibilities is reduced to two). However, due to the fairly extensive kinetic studies on these epoxidations performed by Woodard,[47a] we knew that the (E)-propenyl substituent in 17 would be about 70 to 100 times more reactive than the vinyl substituent. Crossing this large relative rate difference (70 to 100) with the large KR

selection factor (the k fast/k slow ratio for chiral $\underline{E}$-propenylcarbinols is about 100[45]) allows the correct prediction, namely that epoxy alcohol 18 will be formed very selectively. Another way of tracing the selection factors which reduce the eight possibilities to one involves three binary decisions:

1) with ($\underline{E}$)-propenyl and vinyl carbinols only erythro-epoxy alcohols are formed (8 → 4);

2) with (-)-DIPT only erythro-isomers 18 and 20 are possible (4 → 2); and finally

3) the ($\underline{E}$)-propenyl moiety is much more reactive than the vinyl moiety (2 → 1).

As expected and shown in Scheme VII, when 18 is subjected to another AE step using the tartrate of opposite chirality [i.e. (+)-DIPT] the bisepoxy alcohol 19 is produced.

Two very important aspects of these asymmetric epoxidations which have been ignored in this lecture are: 1) the mechanism of the process; and 2) the practical experimental details which facilitate execution of the process in the laboratory. These two subjects will be covered extensively in a review scheduled to appear during August of 1983 in Volume 16 (Issue No. 3) of Aldrichimica Acta.[48,50]

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41. The starting allylic alcohol for case 2 was subjected to our KR process on a one mole scale with no difficulty. This resolved allylic alcohol along with a variety of chiral epoxy alcohols (made using the AE process) are sold by Reaction Design Corp., 100 Hoffman Place, Hillside, N.J., 07205.

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43. Interupts response of <u>Dendroctonus brevicomis</u> (western pine beetle) to its attractant pheromones.

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