Tetrahedron Vol. 45, No. 2, pp. 391 to 402, 1989
Printed in Great Britain.

0040-4020/89 $3.00+.00

STEREOSELECTIVE S_N2' ADDITIONS OF ORGANOCUPRATES TO HOMOCHIRAL ACYCLIC VINYLOXIRANES

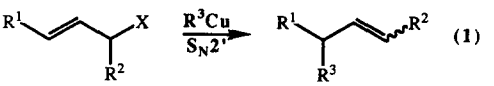
James A. Marshall, Joseph D. Trometer and Darryl G. Cleary

Department of Chemistry, University of South Carolina
Columbia, South Carolina 29208

(*Received in USA* 31 *May* 1988)

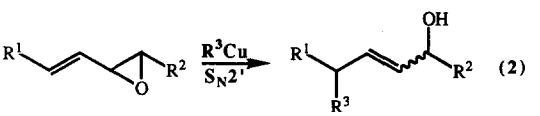
Abstract. Additions of various methylcopper reagents to the homochiral acyclic vinyloxiranes **A14**, **A15**, **B6-B9**, and **C5**, **C6** were performed in order to evaluate *E*/*Z* and syn/anti preferences. The unsubstituted oxiranes **A14** and **A15** gave a mixture of S_N2 and S_N2' substitution products with the four reagents examined, $LiMe_2Cu$, LiMeCuCN, $BrMgMe_2Cu$, and LiMeCuI • BF_3. The more highly substituted systems **B6-B9** derived from geraniol and **C5**, **C6** derived from nerol yielded only S_N2' products. The (*Z*)-allylic alcohol derivatives **B8** and **C6** and LiMeCuCN gave the best anti/syn ratios (99:1 and 97:3, respectively). In both cases the newly formed double bond was exclusively *E*.

S_N2' alkylations of allylic esters, ethers and halides by organocopper reagents are a well documented class of synthetically useful reactions (eq. 1).[1] In recent years significant attention has been directed to



(1)

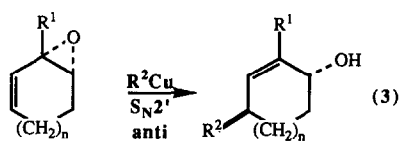
the stereochemistry of such displacements in both cyclic and homochiral acyclic allylic derivatives.[2] Vinyloxiranes, a subset of the foregoing allylic systems, also undergo S_N2' alkylation by organocopper reagents (eq. 2). These reactions are of particular interest as they give rise to allylic alcohols, themselves



(2)

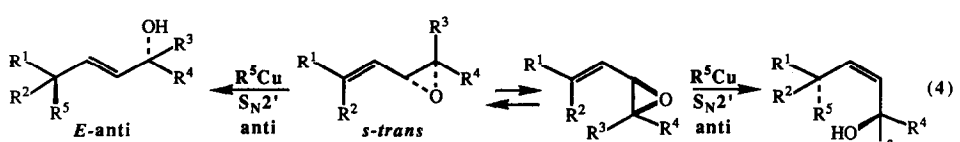
valuable synthetic intermediates. Although the initial observation of the reaction was made with acyclic vinyloxiranes,[3] all subsequent studies have employed systems in which the double bond and/or the epoxide are part of a five or six membered ring.[4] Acyclic cases have not heretofore been examined.

In general, S_N2' displacements on allylic alcohol derivatives (eq. 1) and cyclic vinyloxiranes (eq. 3) by organocopper reagents have been found to proceed with inversion (anti pathway).[2,4,5] Acyclic vinyloxi-



(3)

ranes would expectedly follow an analogous course. However, unlike their cyclic counterparts, the acyclic systems can react via either *s-cis* or *s-trans* conformers and thus yield mixtures of *E* and *Z* S_N2' products (eq. 4).[6]

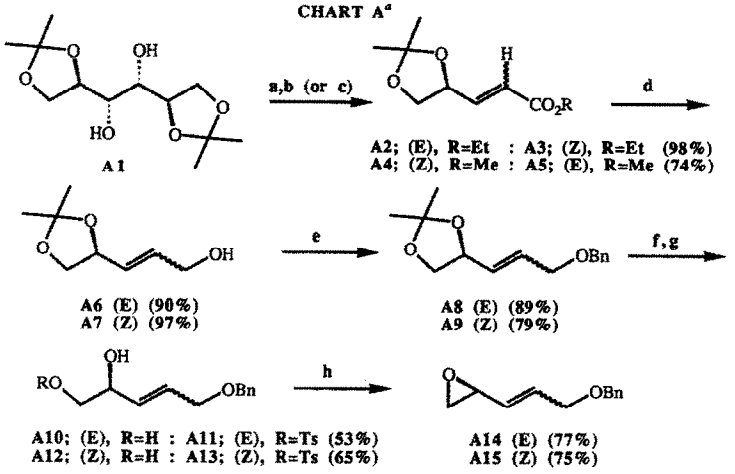


(4)

The present investigation was undertaken to examine the sp^2 and sp^3 stereochemistry of these acyclic S_N2' additions with a view toward developing routes to homochiral allylic alcohols.[7]

Our initial studies were carried out on the (*E*) and (*Z*)-vinyloxiranes **A14** and **A15** derived from glyceraldehyde acetonide prepared *in situ* by $NaIO_4$ cleavage of 1,2:5,6-di-*O*-isopropylidene-D-mannitol (**A1**) as described by Takano, *et al.*[8] Condensation with triethyl α-phosphonoacetate afforded predominately the (*E*)-conjugated ester **A2** as reported,[8] whereas addition of methyl α-(triphenylphosphoryliden)acetate in methanol yielded mainly the (*Z*)-conjugated ester **A4**.[9] The *E* and *Z* isomers were purified by column chromatography and each was reduced to the corresponding *E* and *Z*-allylic alcohol **A6** and **A7** with DIBAH. Benzylation then afforded the benzyl ethers **A8** and **A9**. Hydrolysis of the acetonide groupings followed by selective tosylation and base treatment completed the sequence.

CHART A[a]



[a] a) $NaIO_4$, 5% $NaHCO_3$, room temperature, 1 h; b) $(EtO)_2POCH_2CO_2Et$, 6*M* K_2CO_3, room temperature, 24 h, 48:1 E:Z; c) Ph_3PCHCO_2Me, MeOH, 0°C, 24 h, 7:1 Z:E; d) *i*-Bu_2AlH, CH_2Cl_2, -78°C, 2 h; e) *n*-BuLi, HMPA, $PhCH_2Br$, THF, -78°C, 6 h; f) 1*M* HCl, MeOH, room temperature, 2 h; g) *p*-TsCl, pyridine, CH_2Cl_2, 0°C, 18 h; h) NaH, THF, 0°C, 1 h.

Vinyloxiranes **A14** and **A15** were treated with a number of methylcopper reagents in order to find conditions favoring S_N2' additions (Table 1). The major products were identified by ^1H NMR analysis and product compositions were measured by capillary gc analysis. Diene **1.5** was not isolable but its formation was deduced by the production of benzyl alcohol. With the cuprate reagents the (*Z*)-vinyloxirane gave higher ratios of S_N2'/S_N2 products than the *E* isomer. The lower order cyanocuprate (method B) proved most satisfactory.[10] A considerable amount of elimination product (benzyl alcohol) was produced with the Gilman cuprate both in ether (method E) and THF-ether (method A).[11] The relative amount of this product increased with lower temperature. The (*Z*)-vinyloxirane **A15** afforded only the (*E*)-allylic alcohol **1.1** with each of the methylcopper reagents. The *E* isomer **A14**, on the other hand, gave mixtures of *E* and *Z* S_N2' products **1.1** and **1.2** with all but the Gilman cuprate (methods A and E). Yamamoto's BF_3 complexed methylcopper reagent (method D)[12] showed an unusual preference for the *Z* S_N2' product **1.2** with the (*E*)-vinyloxirane **A14** but the *Z* isomer **A15** yielded only the *E* product **1.1** under these conditions. Both this reagent and the MeMgBr reagent C cleanly afforded S_N2 products without *E*/*Z* isomerization, unlike the cuprates A, B and E.

The *E* and *Z* S_N2' products **1.1** and **1.2** have previously been prepared in high optical purity.[13] Unfortunately, these isomers could neither be separated from each other nor from the S_N2 products **1.3** and **1.4** so evaluation of the S_N2' stereoselectivity could not be made directly. However, selective oxidation of the allylic alcohol components **1.1** and **1.2** of the product mixtures with MnO_2 gave the related conjugated aldehydes (eq. 5) which were readily separated from unreacted alcohols **1.3** and **1.4**.

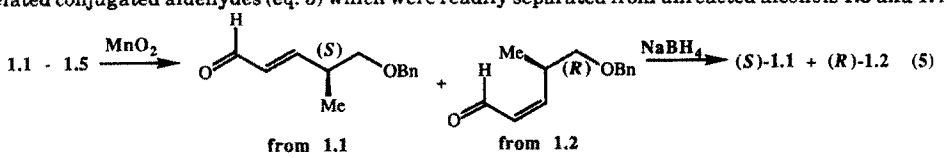
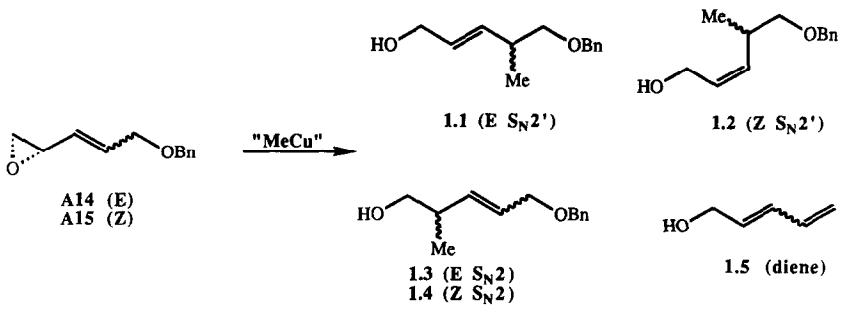


Table 1. Cuprate Additions to Vinyloxiranes **A14** and **A15**



				S_N2'		S_N2			
entry	substrate	method[1]	yield[2]	1.1 (*E*)	1.2 (*Z*)	1.3 (*E*)	1.4 (*Z*)	diene[3]	S_N2'/S_N2
1	**A14** (*E*)	A	50	10.5	0	47.0	1.9	40.6	0.2
2	**A15** (*Z*)	A	55	35.4	0	15.0	13.4	36.2	1.2
3	**A14** (*E*)	B	87	69.5	7.3	11.8	0	11.4	5.6
4	**A15** (*Z*)	B	83	81.0	0	2.9	6.1	10.0	9.0
5	**A14** (*E*)	C	94	47.2[4]	9.5	16.9	0	26.4	3.4
6	**A15** (*Z*)	C	88	76.3[5]	0	0	12.9	10.8	5.9
7	**A14** (*E*)	D	76	28.2	60.6	11.2	0	0	7.9
8	**A15** (*Z*)	D	78	82.2	0	0	11.8	6.0	7.0
9	**A14** (*E*)	E	71	24.6	0	33.6	0	41.8	0.7
10	**A15** (*Z*)	E	68	78.9	0	2.7	8.0	10.4	7.4

[1] **A**: $LiMe_2Cu$, THF/Et_2O (4:1), 0°C; **B**: LiMeCuCN, Et_2O, 0°C; **C**: CuBr • Me_2S, MeMgBr, Me_2S, THF, 0°C; **D**: CuI, MeLi, BF_3 • Et_2O, THF/Et_2O (5:1), -78° → 25°C; **E**: $LiMe_2Cu$, Et_2O, 0°C. [2] Yield of total crude products calculated as alcohols. [3] as determined by benzyl alcohol content. [4] anti/syn ~6:1. [5] anti:syn >4.5:1.

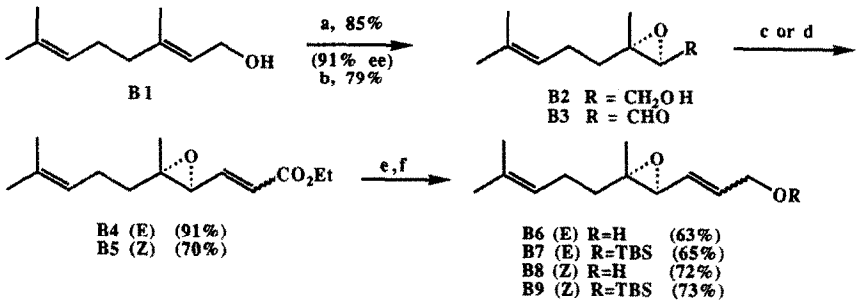
Reduction of the purified enals then gave the allylic alcohol mixture **1.1** and **1.2** whose *E/Z* composition was determined by gc analysis. The optical rotation of this mixture was used to calculate the ee, assuming both alcohols are formed by the same pathway (inversion or retention), and correcting for the optical purity of the starting esters **A2** and **A4**.[14] In this manner, we were able to estimate anti/syn preferences of 4.5 to 6:1 for reactions involving vinyloxiranes **A14** and **A15** with the MeMgBr-CuBr • Me_2S reagent.

In view of the indirect nature of the foregoing analysis we turned our attention to other vinyloxiranes in which stereochemical preferences might be more readily discerned. The geraniol related systems **B6** and **B8** seemed well suited on several counts. In the first place, the oxirane methyl substituent should increase the energy of s-cis conformers thereby diminishing the amounts of *Z*-S_N2' products. Secondly, the presence of additional substituents on the oxirane ring would expectedly disfavor S_N2 product formation. Finally, anti and syn S_N2' displacements would lead to diastereoisomers whose analysis would not depend upon assumptions regarding optical purity.

Vinyloxiranes **B6** and **B8** were prepared as outlined in Chart B from the known Sharpless epoxidation product **B2**[15] of geraniol (**B1**) through Swern oxidation[16] followed by Horner-Emmons,[13] or Still-Horner-Emmons condensation[8b] and reduction. Addition of the Gilman cuprate[11] in THF-ether (method A) to the (*E*)-vinyloxirane **B6** afforded an 84:16 mixture of the two *E* S_N2' products **2.1** (anti addition) and **2.2** (syn addition) as determined by capillary gc analysis of the derived mono TBS ethers. The (*Z*)-vinyloxirane **B8**, on the other hand, yielded a 3:97 mixture of isomers **2.1** (syn addition) and **2.2** (anti addition) under the same conditions. In neither case were S_N2 or elimination by-products detected.

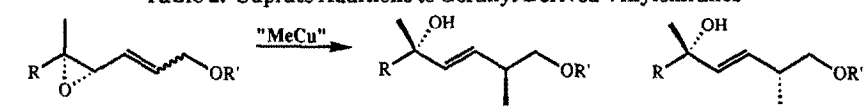
The relative stereochemistry of diols **2.1** and **2.2** was deduced through ozonolysis-reduction of the mono TBS ethers (R' = TBS) to the known *R* or *S* mono TBS ether of 2-methyl-1,3-propanediol (eq. 6).[15] The

CHART B[a]



[a] a) *L*-(+)-diethyl tartrate (7%), Ti(O*i*-Pr)$_4$ (5%), *t*-BuOOH, 3Å molecular sieves, CH_2Cl_2, -23°C, 2.5 h; b) $(ClCO)_2$, DMSO, Et_3N, CH_2Cl_2, -78°C, 2 h; c) $(EtO)_2POCH_2CO_2Et$, NaH, THF, 6 h; d) $(TFEO)_2POCH_2CO_2Et$, 18-crown-6, KHMDS, THF, -78°C, 6 h; e) *i*-Bu_2AlH, CH_2Cl_2, -78°C, 30 min; f) *t*-$BuMe_2SiCl$, Et_3N, DMAP, CH_2Cl_2, 25°C, 16 h.

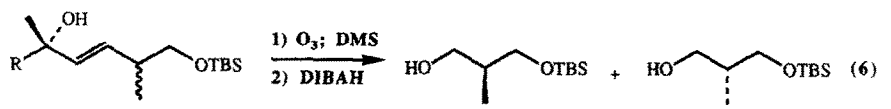
Table 2. Cuprate Additions to Geranyl Derived Vinyloxiranes



				products[2,3]		mode of addition
epoxide	R'	method[1]	yield	anti-*E*[4]	syn-*E*[5]	anti/syn
B6 (*E*)	H	A	81	84	16	5.2
B8 (*Z*)	H	A	75	3	97	32
B6 (*E*)	H	B	84	88	12	7.3
B8 (*Z*)	H	B	88	1	99	99
B7 (*E*)	TBS	A	77	70	30	2.3
B9 (*Z*)	TBS	A	78	18	82	4.5
B7 (*E*)	TBS	B	81	75	25	3.0
B9 (*Z*)	TBS	B	79	16	84	5.2

[1] Methods: A: $LiMe_2Cu$, THF/Et_2O (4:1), 0°C; B: LiMeCuCN, Et_2O, 0°C. [2] Product distribution of derived silyl ethers. [3] Typical result selected from several trials varying by ± 5% (absolute yield). [4] Produced through anti addition to **B6/B7** or syn addition to **B8/B9**. [5] Produced through anti addition to **B8/B9** or syn addition to **B6/B7**.

absolute configuration at the newly introduced methyl center could be ascertained from the rotation of these TBS ethers.



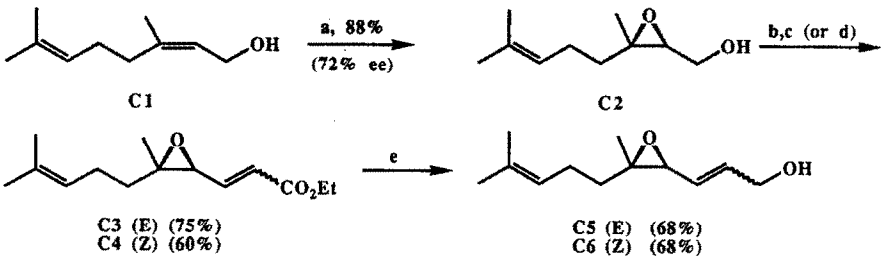
In both cases, the observed rotation of the TBS ethers correlated well with the ratio of diastereomeric starting alcohols **2.1** and **2.2** as measured by gc, after correction for the ee of the starting epoxy alcohol **B2**.

The lower order methylcyanocuprate reagent (method B) showed similar but slightly higher stereoselectivity with vinyloxiranes **B6** and **B8** compared to the Gilman cuprate (Table 2). Both reagents afforded the syn-*E* product **2.2** almost exclusively with the (*Z*)-vinyloxirane **B8**.

The TBS ethers **B7** and **B9**, derived from epoxy allylic alcohols **B6** and **B8**, exhibited a comparable, albeit somewhat lower, propensity toward anti S_N2' addition of both the Gilman and the lower order cyanocuprate reagents (Table 2). The strikingly high proportion of anti S_N2' product observed with the (*Z*)-allylic alcohol system **B8** as opposed to the silyl ether **B9** or the (*E*)-allylic alcohol and ether **B6** and **B7** suggests the possible involvment of an O-heterocuprate in the allyl complexation step.[7]

As a further test of the methodology we examined the addition of methylcuprates to the (*E*) and (*Z*)-*cis*-vinyloxiranes **C5** and **C6**, prepared from nerol (**C1**) by a sequence analogous to that employed for the isomers **B6** and **B8**. Addition of $LiMe_2Cu$ or LiMeCuCN proceeded with high anti *s-trans* selectivity

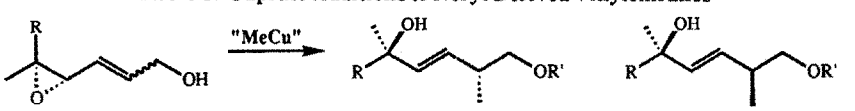
CHART C[a]



[a] a) *L*-(+)-diethyl tartrate (15%), $Ti(Oi\text{-}Pr)_4$ (10%), *t*-BuOOH, 3Å molecular sieves, CH_2Cl_2, -23°C, 2.5 h; b) $(ClCO)_2$, DMSO, Et_3N, CH_2Cl_2, -78°C, 2 h; c) $(EtO)_2POCH_2CO_2Et$, NaH, THF, 6 h; d) $(TFEO)_2POCH_2CO_2Et$, 18-crown-6, KHMDS, THF, -78°C, 6 h; e) *i*-Bu_2AlH, CH_2Cl_2, -78°C, 30 min.

(Table 3) in accord with previous observations on the trans oxirane isomers **B6** and **B8**. As before, reaction of the cyanocuprate with the (*Z*)-allylic alcohol oxirane showed the highest selectivity. It should be noted that the S_N2' products **3.1** and **3.2** are enantiomeric with **2.1** and **2.2** obtained from **B6** and **B8**.

Table 3. Cuprate Additions to Neryl Derived Vinyloxiranes



C5 (E)
C6 (Z)

3.1 Anti-E

3.2 Syn-E

			products[2,3]		mode of addition
epoxide	method[1]	yield	anti-*E*[4]	syn-*E*[5]	anti/syn
C5 (*E*)	A	95	14	86	6.3
C6 (*Z*)	A	93	95	5	19
C5 (*E*)	B	90	10	90	9.0
C6 (*Z*)	B	95	97	3	32

[1] Methods: A: $LiMe_2Cu$, THF/Et_2O (4:1), 0°C; B: LiMeCuCN, Et_2O, 0°C. [2] Product distribution of derived silyl ethers. [3] Typical result selected from several trials varying by ± 5% (absolute yield). [4] Produced through syn addition to **C5** or anti addition to **C6**. [5] Produced through syn addition to **C6** or anti addition to **C5**.

Thus through proper choice of cuprate and vinyloxirane, it is possible to prepare S_N2' adducts of high diastereomeric and enantiomeric purity. In the present study this point is best demonstrated by the 99:1

ratio of syn-*E* (**2.2**) to anti-*E* (**2.1**) products from vinyloxirane **B8** and LiMeCuCN and the 97:3 ratio of anti-*E* (**3.1**) to syn-*E* (**3.2**) products from vinyloxirane **C6** and the same cuprate. The anti-*E* and the syn-*E* isomers **2.1** and **3.2** could expectedly be obtained equivalently from the enantiomeric vinyloxiranes which, in turn, could be prepared through use of *D*-(-)-diethyl tartrate in the initial Sharpless epoxidation of geraniol or nerol.

The higher preference for *E* S_N2' products in cuprate additions to the geranyl and neryl systems **B6-B9** and **C5,C6** as opposed to the unsubstituted vinyloxiranes **A14,A15** stems in part from unfavorable 1,5-steric interactions imposed by the *Z* vinylic substituent and the remote oxirane cis substituent (R^2 and R^3 in eq. 4) in the stereoelectronically favored coplanar transition state conformation. Where such effects are minimal, as in the case of vinyloxirane **A14** (*cf.* eq. 4, $R^2 = R^3 = H$), the cuprate reagent also plays a role in directing *E*/*Z* selectivity (Table 1, compare entries 1, 3, 5, 7 and 9).

Goering has reported a striking contrast in regioselectivity for substitution reactions with $LiMe_2Cu$ *vs.* LiMeCuCN in sterically unbiased allylic acetates and mesitoates.[5c] The cyanocuprate reagent gives nearly exclusive S_N2' (gamma) substitution whereas the Gilman cuprate affords a nearly equal mixture of S_N2 (alpha) and S_N2' products. It is suggested that an initial cuprate-olefin complex is formed which leads to an anti-gamma σ-allyl cuprate complex (oxidative addition, see Figure 1). The cyano substituted σ-copper complex undergoes rapid reductive elimination to the S_N2' product whereas the dimethylcuprate σ-complex equilibrates via a π-allyl species before reductive elimination. An analogous, though less dramatic, trend is discernible with vinyloxirane **A15** (Table 1, entry 2 *vs.* 4). When ether is employed as the solvent both cuprates give mainly S_N2' products with the (*Z*)-vinyloxirane **A15** (Table 1, entries 4 and 10). The (*E*)-vinyloxirane **A14**, however, shows a preference for S_N2 over S_N2' substitution with the Gilman cuprate (entries 1 and 9). The analysis is complicated by the formation of substantial diene **1.5** of undetermined stereochemistry. Possible reaction pathways to the various products based on Goering's proposal for allylic acetates[5c] are traced in Figure 1. The formation of *Z* S_N2 product **1.4** from the (*Z*)-vinyloxirane **A15** but not from the *E* isomer **A14** suggests that direct S_N2 attack at the allylic position occurs to some extent (Table 1, entries 2, 4, 6, 8 and 10). On the other hand, the formation of *E* S_N2 product **1.3** from (*Z*)-vinyloxirane **A15** (entries 2, 4, and 10) requires interconversion of *Z* and *E* allyl Cu intermediates as shown in Fig. 1.

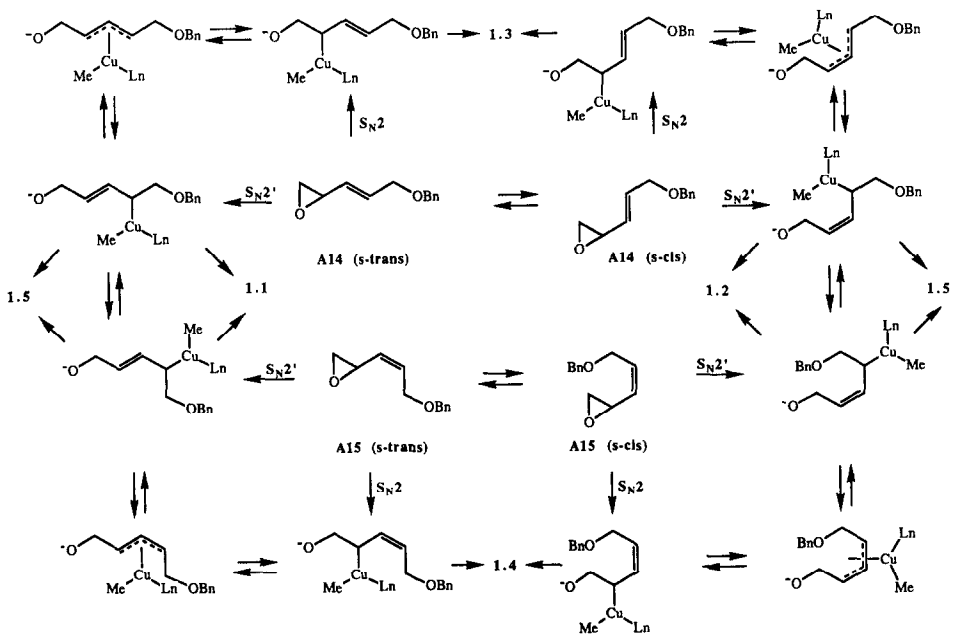


Figure 1. Product forming pathways for cuprate additions to vinyloxiranes **A14** and **A15**

In sharp contrast to the relatively unpromising product distributions obtained with vinyloxiranes **A14** and **A15**, the geranyl and neryl systems **B6**-**B9** and **C5**,**C6** show neither S_N2 nor elimination products. Here steric effects would disfavor S_N2 products. Although elimination would expectedly occur less readily with an alcohol than an alkoxide substituent, the absence of such products from TBS ethers **B7** and **B9** indicates that additional factors may be operative.

List of Abbreviations. Bn = $PhCH_2$, DIBAH = *i*-Bu_2AlH, DMAP = 4-(*N*,*N*-dimethylamino)pyridine, DMS = Me_2S, DMSO = Me_2SO, HMPA = $(Me_2N)_3PO$, KHMDS = $KN(SiMe_3)_2$, TBS = *t*-$BuSiMe_2$, TFE = CF_3CH_2, *p*-Ts = *p*-$CH_3C_6H_4SO_2$.

Acknowledgements. Support from the National Science Foundation (CHE-8615569 and CHE-8411172) is gratefully acknowledged.

Experimental[18]

(4*S*),(*E*) and (*Z*)-Ethyl 4,5-(Isopropylidenedioxy)-2-pentenoate (A2 and A3). To a slurry of 6.3 g (24 mmol) of 1,2:5,6-di-*O*-isopropylidene-D-mannitol (**A1**) in 50 mL of 5% aqueous $NaHCO_3$ at 0°C was added dropwise a solution of 6.3 g (29.5 mmol) of $NaIO_4$ in 50 mL of water. The bath was removed and the mixture was stirred for 1 h. The mixture was cooled to 0°C followed by the addition of 22.6 g (100 mmol) of triethyl α-phosphonoacetate and 150 mL of 6 *M* K_2CO_3. The resulting mixture was allowed to warm to room temperature and was stirred for 24 h. The reaction mixture was extracted four times with CH_2Cl_2 and the combined extracts were dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford 9.73 g of a pale yellow oil. Flash chromatography on silica gel with hexane-50% ether-hexanes gradient afforded 9.31 g (96%) of the (*E*)-isomer **A2** and 0.21 g (2%) of the (*Z*)-isomer **A3**.

(*E*)-isomer A2: IR (film) ν 3000, 2960, 2880, 1735, 1625, 1430, 1410, 1400, 1395, 1215, 1190, 1090, 1010, 890, 840 cm^{-1}. ^1H NMR δ 1.27 (t, J = 7.1 Hz, 3H, $OCH_2\underline{CH_3}$), 1.39 (s, 3H, $C(CH_3)_2$), 1.43 (s, 3H, $C(CH_3)_2$), 3.66 (dd, A of ABX, J = 7.1, 8.3 Hz, 1H, $ROCH_2CH$), 4.16 (dd, B of ABX, J = 6.6, 8.3 Hz, 1H, $ROCH_2CH$), 4.18 (q, J = 7.1 Hz, 2H, $O\underline{CH_2}CH_3$), 4.66 (m, X of ABX, 1H, CH_2CHOR), 6.08 (dd, A of ABX, J = 1.4, 15.6 Hz, 1H, vinyl H), 6.86 (dd, B of ABX, J = 5.7, 15.6 Hz, 1H, vinyl H). $[\alpha]_D^{23}$ 38.1° (*c* 2.94, $CHCl_3$) [lit. $[\alpha]_D^{17}$ 43.3° (*c* 0.5, $CHCl_3$)].[8]

(*Z*)-isomer A3: IR (film) ν 2950, 2920, 2850, 1720, 1650, 1435, 1380, 1370, 1305, 1260, 1220, 1170, 1070, 980, 850 cm^{-1}. ^1H NMR δ 1.27 (t, J = 7.1 Hz, 3H, $OCH_2\underline{CH_3}$), 1.37 (s, 3H, $C(CH_3)_2$), 1.43 (s, 3H, $C(CH_3)_2$), 3.61 (m, 1H, $ROCH_2CH$), 4.15 (q, J = 7.1 Hz, 2H, $O\underline{CH_2}CH_3$), 4.35 (m, 1H, $ROCH_2CH$), 5.48 (m, X of ABX, 1H, CH_2CHOR), 5.82 (dd, A of ABX, J = 1.7, 11.6 Hz, 1H, vinyl H), 6.34 (dd, B of ABX, J = 6.5, 11.6 Hz, 1H, vinyl H). $[\alpha]_D^{23}$ 108.1° (*c* 1.85, $CHCl_3$) [lit. $[\alpha]_D^{17}$ 124.3° (*c* 0.54, $CHCl_3$)].[8]

(4*S*),(*Z*) and (*E*)-Methyl 4,5-(Isopropylidenedioxy)-2-pentenoate (A4 and A5). To a slurry of 11.5 g (0.043 mol) of 1,2:5,6-di-*O*-isopropylidene-D-mannitol (**A1**) in 200 mL of a 5% $NaHCO_3$ solution (4:1 MeOH/H_2O) at 0°C was added dropwise 12.1 g (0.057 mol) of $NaIO_4$ in 60 mL of a 1:1 MeOH/H_2O solution. The mixture was stirred at room temperature for 2 h and cooled to 0°C. To this cooled mixture was added a slurry of 42 g (0.126 mol) of methyl α-(triphenylphosphoranylidene)acetate in 100 mL of methanol. The mixture was stirred at 0°C for 24 h and extracted four times with 200 mL of CH_2Cl_2. The combined extracts were dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford a viscous yellow oil. This oil was taken up in 400 mL of 80% hexane-ether solution, the precipitated triphenylphosphine oxide was filtered, and the filtrate was concentrated under reduced pressure to afford a pale yellow oil. Flash chromatography on silica gel with hexanes-50% ether-hexanes gradient afforded 10.55 g (65%) of (*Z*)-isomer **A4** and 1.42 g (9%) of (*E*)-isomer **A5**.

(*Z*)-isomer A4: IR (film) ν 3000, 2960, 2880, 1735, 1625, 1430, 1410, 1400, 1395, 1215, 1190, 1090, 1010, 890, 840 cm^{-1}. ^1H NMR δ 1.37 (s, 3H, $C(CH_3)_2$), 1.43 (s, 3H, $C(CH_3)_2$), 3.60 (dd, A of ABX, J = 6.7, 8.2 Hz, 1H, $ROCH_2CH$), 3.70 (s, 3H, $COCH_3$), 4.36 (dd, B of ABX, J = 6.9, 8.2 Hz, 1H, $ROCH_2CH$), 5.47 (apparent dq, X of ABX, J = 1.7, 6.8 Hz, 1H, CH_2CHOR), 5.83 (dd, J = 1.7, 11.6 Hz, 1H, vinyl H), 6.35 (dd, J = 6.6, 11.6 Hz, 1H, vinyl H). $[\alpha]_D^{22}$ 120.9° (*c* 3.54, $CHCl_3$). *Anal.* Calcd for $C_9H_{14}O_4$: C, 58.05; H, 7.58. Found: C, 58.06; H, 7.59.

(*E*)-isomer A5: IR (film) ν 2950, 2920, 2850, 1720, 1650, 1435, 1380, 1370, 1305, 1260, 1220, 1170, 1070, 980, 850 cm^{-1}. ^1H NMR δ 1.38 (s, 3H, $C(CH_3)_2$), 1.42 (s, 3H, $C(CH_3)_2$), 3.65 (dd, A of ABX, J = 7.1, 8.2 Hz, 1H, $ROCH_2CH$), 3.72 (s, 3H, $COCH_3$), 4.16 (dd, B of ABX, J = 6.6, 8.2 Hz, 1H, $ROCH_2CH$), 4.64 (apparent q, X of ABX, J = 5.7, 12.3 Hz, 1H, CH_2CHOR), 6.18 (dd, J = 1.4, 15.6 Hz, 1H, vinyl H), 6.87 (dd, J = 5.6, 15.6 Hz, 1H, vinyl H). $[\alpha]_D^{22}$ 46.4° (*c* 3.97, $CHCl_3$). *Anal.* Calcd for $C_9H_{14}O_4$: C, 58.05; H, 7.58. Found: C, 57.97; H, 7.55.

(4*S*),(*E*)-4,5-(Isopropylidenedioxy)-2-penten-1-ol (A6). To a stirred solution of 5.99 g (29.9 mmol) of ester **A2** in 150 mL of dry CH_2Cl_2 at -78°C was added 75 mL (75 mmol) of DIBAH (1 *M* in hexanes) over 30 min. The mixture was stirred at -78°C for 2 h, quenched with 5 mL of water and treated with 150 mL of saturated aqueous Rochelle's salt. The mixture was allowed to warm to room temperature and the phases were separated. The organic phase was washed twice with Rochelle's salt and the combined aqueous phases were extracted three times with CH_2Cl_2. The combined extracts were dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford 4.56 g of a cloudy oil. Flash chromatography on silica gel with hexanes-75% ether-hexanes gradient afforded 4.25 g (90%) of allylic alcohol **A6**. IR (film) ν 3450, 2990, 2940, 2880, 1455, 1380, 1370, 1245, 1215, 1155, 1055, 945, 855, 790 cm^{-1}. ^1H NMR δ 1.36 (s, 3H, $C(CH_3)_2$), 1.40 (s, 3H, $C(CH_3)_2$), 1.80 (bs, 1H, $CH_2\underline{OH}$), 3.57 (t, A of ABX, J = 7.9 Hz, 1H, $ROCH_2CH$), 4.07 (dd, B of ABX, J = 6.1, 8.2 Hz, 1H, $ROCH_2CH$), 4.13 (bs, 2H, $C\underline{H_2}OH$), 4.50 (apparent q, X of ABX, J = 7.0

Hz, 1H, CH_2CHOR), 5.68 (ddt, J = 1.6, 7.4, 15.4 Hz, 1H, vinyl H), 5.93 (dt, J = 5.1, 15.4 Hz, 1H, vinyl H). $[\alpha]_D^{21}$ 33.3° (*c* 3.87, $CHCl_3$). *Anal.* Calcd for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 60.65; H, 8.94.

(4*S*),(*Z*)-4,5-(Isopropylidenedioxy)-2-penten-1-ol (A7). To a solution of 60 mL (60 mmol) of DIBAH (1 *M* in hexanes) in 150 mL of dry CH_2Cl_2 at -78°C was added a solution of 4.60 g (24.7 mmol) of (*Z*)-ester **A4** in 20 mL of dry CH_2Cl_2 over 20 min. The resulting mixture was stirred at -78°C for 2 h, quenched with 2 mL of water and treated with 200 mL of saturated aqueous Rochelle's salt. The mixture was allowed to warm to room temperature and the phases were separated. The organic phase was washed twice with Rochelle's salt and the combined aqueous phases were extracted three times with CH_2Cl_2. The combined extracts were dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford 3.98 g of a cloudy oil. Flash chromatography on silica gel with hexanes-75% ether-hexanes afforded 3.80 g (97%) of alcohol **A7**. IR (film) ν 3430, 2990, 2960, 2880, 1455, 1380, 1370, 1295, 1250, 1215, 1155, 1060, 1030, 945, 900, 860, 790 cm^{-1}. ^1H NMR δ 1.33 (s, 3H, $C(CH_3)_2$), 1.36 (s, 3H, $C(CH_3)_2$), 2.65 (bs, 1H, CH_2OH), 3.50 (t, A of ABX, J = 8.0 Hz, 1H, $ROCH_2CH$), 4.03 (dd, B of ABX, J = 6.1, 8.1 Hz, 1H, $ROCH_2CH$), 4.19 (m, 2H, CH_2OH), 4.80 (apparent q, X of ABX, J = 7.5 Hz, 1H, CH_2CHOR), 5.48 (m, 1H, vinyl H), 5.76 (m, 1H, vinyl H). $[\alpha]_D^{21}$ 13.2° (*c* 3.81, $CHCl_3$). *Anal.* Calcd for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 60.51; H, 8.77.

(4*S*),(*E*)-1-Benzyloxy-4,5-(isopropylidenedioxy)-2-pentene (A8). A stirred solution of 4.68 g (29.6 mmol) of allylic alcohol **A6** in 35 mL of dry THF containing a few crystals of 1,10-phenanthroline was cooled to -78°C and *n*-BuLi (8.5 *M* in hexanes) was added until the end point was reached. This dark red mixture was stirred at -78°C for 10 min and 7.0 mL (40.2 mmol) of HMPA was added. To this mixture was added 4.8 mL (40.4 mmol) of benzyl bromide over 10 min. The yellow solution was stirred at -78°C for 1 h and then at room temperature for 5 h. The mixture was washed twice with water and the organic layer was dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford 6.83 g of a yellow oil. Flash chromatography on silica gel with hexanes-70% ether-hexanes gradient afforded 6.54 g (89%) of benzyl ether **A8**. IR (film) ν 3090, 3070, 3040, 2990, 2950, 2870, 1500, 1460, 1380, 1370, 1250, 1220, 1160, 1125, 1070, 1035, 975, 915, 865, 745, 705 cm^{-1}. ^1H NMR δ 1.37 (s, 3H, $C(CH_3)_2$), 1.41 (s, 3H, $C(CH_3)_2$), 3.58 (t, A of ABX, J = 8.0 Hz, 1H, $ROCH_2CH$), 4.03 (d, J = 5.3 Hz, 2H, CH_2OBn), 4.08 (dd, B of ABX, J = 6.1, 8.2 Hz, 1H, $ROCH_2CH$), 4.51 (s, 2H, OCH_2Ph), 4.52 (m, X of ABX, 1H, CH_2CHOR), 5.72 (ddt, J = 1.4, 7.3, 15.5 Hz, 1H, vinyl H), 5.90 (dt, J = 5.4, 15.5 Hz, 1H, vinyl H), 7.32 (s, 5H, phenyl H). $[\alpha]_D^{22}$ 28.5° (*c* 2.96, $CHCl_3$). *Anal.* Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.45; H, 8.14.

(4*S*),(*Z*)-1-Benzyloxy-4,5-(isopropylidenedioxy)-2-pentene (A9). Benzylation as described for ether **A8** was performed on 3.18 g (20.1 mmol) of alcohol **A7** in 30 mL of dry THF with 20.1 mmol of *n*-BuLi, 5.0 mL of HMPA and 4.0 mL (33.6 mmol) of benzyl bromide. After aqueous workup, drying over $MgSO_4$ and filtration, the mixture was concentrated under reduced pressure to afford 4.13 g of a dark amber oil. Flash chromatography on silica gel with hexanes-50% ether-hexanes gradient afforded 3.96 g (79%) of ether **A9**. IR (film) ν 3100, 3070, 3040, 2990, 2940, 2880, 1500, 1455, 1385, 1375, 1250, 1160, 1060, 1030, 860, 795, 740, 700 cm^{-1}. ^1H NMR δ 1.36 (s, 3H, $C(CH_3)_2$), 1.41 (s, 3H, $C(CH_3)_2$), 3.52 (t, A of ABX, J = 8.0 Hz, 1H, $ROCH_2CH$), 4.03 (dd, B of ABX, J = 6.1, 8.0 Hz, 1H, $ROCH_2CH$), 4.10 (d, J = 6.4 Hz, 2H, CH_2OBn), 4.50 (AB, J_{AB} = 11.8 Hz, Δν = 10.2 Hz, 2H, OCH_2Ph), 4.77 (apparent q, X of ABX, J = 7.0 Hz, 1H, CH_2CHOR), 5.64 (m, 1H, vinyl H), 5.80 (m, 1H, vinyl H), 7.32 (s, 5H, phenyl H). $[\alpha]_D^{23}$ -5.92° (*c* 4.59, $CHCl_3$). *Anal.* Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.41; H, 8.05.

(2*S*),(*E*)-5-Benzyloxy-3-pentene-1,2-diol (A10). To a solution of 4.89 g (19.7 mmol) of ether **A8** in 30 mL of methanol at room temperature was added 60 mL of 1.0 *M* HCl. The resulting mixture was stirred at room temperature for 4 h. The mixture was extracted with CH_2Cl_2 until the organic layer showed no diol present according to TLC analysis. The combined extracts were dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford 3.61 g of a yellow oil. Flash chromatography on silica gel with hexanes-90% ether-hexanes gradient afforded 3.24 g (80%) of diol **A10**. IR (film) ν 3380, 3100, 3080, 3040, 2930, 2870, 1500, 1455, 1365, 1250, 1210, 1110, 1070, 1030, 975, 880, 745, 705 cm^{-1}. ^1H NMR δ 3.01 (m, 1H, CH_2OH), 3.20 (d, J = 4.3 Hz, 1H, CHOH), 3.51 (m, 2H, CH_2OH), 3.99 (d, J = 5.5 Hz, 2H, CH_2OBn), 4.20 (bs, 1H, CHOH), 4.49 (s, 2H, OCH_2Ph), 5.70 (dd, J = 5.7, 15.6 Hz, 1H, vinyl H), 5.87 (dt, J = 5.6, 15.6 Hz, 1H, vinyl H), 7.31 (s, 5H, phenyl H). $[\alpha]_D^{22}$ 2.32° (*c* 1.98, $CHCl_3$). *Anal.* Calcd for $C_{12}H_{16}O_3$: C, 69.20; H, 7.75. Found: C, 68.89; H, 7.61.

(2*S*),(*E*)-5-Benzyloxy-1-tosyloxy-3-penten-2-ol (A11). To a solution of 2.78 g (13.3 mmol) of diol **A10** in 20 mL of pyridine at 0°C was added 2.76 g (14.5 mmol) of *p*-toluenesulfonyl chloride. The mixture was stirred at 0°C for 18 h and poured into 100 mL of EtOAc. The mixture was washed twice with water followed by aqueous $CuSO_4$ until there was no color change in the aqueous layer. The extracts were dried over Na_2SO_4, filtered and concentrated under reduced pressure to afford 3.94 g of a yellow oil. Flash chromatography on silica gel with hexanes-90% ether-hexanes gradient afforded 3.17 g (66%) of tosylate **A11**. IR (film) ν 3400, 3060, 3030, 2860, 1610, 1510, 1470, 1370, 1320, 1310, 1230, 1210, 1190, 1140, 1120, 1090, 1040, 990, 920, 850, 830, 800, 760 cm^{-1}. ^1H NMR δ 2.15 (bs, 1H, CHOH), 2.42 (s, 3H, phenyl CH_3), 3.87 (dd, A of ABX, J = 7.5, 10.2 Hz, 1H, OCH_2CH), 3.98 (d, J = 5.3 Hz, 2H, CH_2OBn), 4.03 (dd, B of ABX, J = 3.4, 10.2 Hz, 1H, OCH_2CH), 4.40 (m, X of ABX, 1H, CH_2CHOH), 4.48 (s, 2H, OCH_2Ph), 5.64 (dd, J = 5.7, 15.6 Hz, 1H, vinyl H), 5.91 (dt, J = 5.3, 15.6 Hz, 1H, vinyl H), 7.31 (s, 5H, phenyl H), 7.55 (m, 4H, phenyl H). *Anal.* Calcd for $C_{19}H_{22}O_5S$: C, 62.96; H, 6.12; S, 8.85. Found: C, 62.78; H, 6.09; S, 8.55.

(2*S*),(*Z*)-5-Benzyloxy-3-pentene-1,2-diol (A12). The hydrolysis as described for diol **A10** was performed on 7.89 g (31.7 mmol) of acetonide **A9** in 50 mL of methanol with 100 mL of 1 *M* HCl at room temperature. Following extraction of the reaction mixture with CH_2Cl_2, the combined extracts were dried over Na_2SO_4, filtered and concentrated under reduced pressure to afford 5.98 g of a viscous oil. Flash chromatography on silica gel with hexanes-90% ether-hexanes gradient afforded 5.60 g (85%) of diol **A12**. IR (film) ν 3370, 3060, 3030, 2940, 2860, 1510, 1470, 1390, 1330, 1230, 1090, 1040, 890 cm^{-1}. ^1H NMR δ 2.20 (bs, 1H, $HOCH_2CH$), 2.71 (bs, 1H, CH_2CHOH), 3.50 (m, 2H, $HOCH_2CH$), 4.09 (m, 2H, CH_2OBn), 4.47 (m, 1H, CH_2CHOH), 4.52 (s, 2H, OCH_2Ph), 5.61 (m, 1H, vinyl H), 5.77 (m, 1H, vinyl H), 7.33 (s, 5H, phenyl H). *Anal.* Calcd for $C_{12}H_{16}O_3$: C, 69.20; H, 7.75. Found: C, 69.05; H, 7.71.

(2*S*),(*Z*)-5-Benzyloxy-1-tosyloxy-3-penten-2-ol (A13). The reaction as described for tosylate **A11** was performed on 4.62 g (22.2 mmol) of diol **A12** in 30 mL of dry pyridine at 0°C with 4.51 g (23.6 mmol) of *p*-toluenesulfonyl chloride. After an aqueous workup, the organic extracts were dried over Na_2SO_4, filtered and concentrated under reduced pressure to afford 6.33 g of a dark oil. Flash chromatography on silica gel with hexanes-90% ether-hexanes gradient afforded 6.23 g (77%) of tosylate **A13**. IR (film) ν 3400, 3060, 3040, 2860, 1610, 1520, 1470, 1380, 1320, 1300, 1230, 1210, 1190, 1150, 1120, 1080, 1040, 990, 920, 850, 830, 760 cm^{-1}. ^{1}H NMR δ 2.42 (s, 3H, phenyl CH_3), 2.53 (d, J = 4.0 Hz, 1H, CHO<u>H</u>), 4.05 (m, 4H, CH_2OBn and CH_2OTs), 4.47 (s, 2H, OC<u>H</u>$_2$Ph), 4.65 (m, 1H, C<u>H</u>OH), 5.50 (m, 1H, vinyl H), 5.77 (m, 1H, vinyl H), 7.30 (s, 5H, phenyl H), 7.54 (m, 4H, phenyl H). *Anal.* Calcd for $C_{19}H_{22}O_4S$: C, 62.96; H, 6.12; S, 8.85. Found: C, 62.82; H, 6.18; S, 8.79.

(2*S*),(*E*)-5-Benzyloxy-1,2-epoxy-3-pentene (A14). To a stirred solution of 0.50 g (1.37 mmol) of tosylate **A11** in 15 mL of dry THF at 0°C was added 0.16 g (6.67 mmol) of NaH. The resulting mixture was stirred at 0°C for 1 h and then at room temperature for 2 h. The excess NaH was quenched with water and the mixture was diluted with 100 mL of ether. The phases were separated and the organic phase was washed twice with water. The combined aqueous phases were extracted three times with ether and the combined extracts were dried over Na_2SO_4, filtered and concentrated under reduced pressure to afford 0.21 g of a pale yellow oil. Flash chromatography on silica gel (deactivated with 5-10% Et_3N) with hexanes-30% ether-hexanes gradient afforded 0.20 g (77%) of epoxide **A14**. IR (film) 3040, 2990, 2930, 2870, 1510, 1470, 1410, 1380, 1270, 1230, 1190, 1150, 1130, 1090, 1050, 990, 950, 870, 760 cm^{-1}. ^{1}H NMR δ 2.65 (dd, A of ABX, J = 2.7, 5.2 Hz, 1H, OC<u>H</u>$_2$CH), 2.95 (dd, B of ABX, J = 4.1, 5.2 Hz, 1H, OC<u>H</u>$_2$CH), 3.36 (m, X of ABX, 1H, C<u>H</u>$_2$CHO), 4.03 (dd, J = 1.5, 5.6 Hz, 2H, CH_2OBn), 4.51 (s, 2H, OC<u>H</u>$_2$Ph), 5.50 (ddt, J = 1.5, 8.0, 15.6 Hz, 1H, vinyl H), 6.06 (dt, J = 5.6, 15.6 Hz, 1H, vinyl H), 7.32 (s, 5H, phenyl H). $[\alpha]_D^{21}$ 5.61° (*c* 2.21, $CHCl_3$). *Anal.* Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.69; H, 7.45.

(2*S*),(*Z*)-5-Benzyloxy-1,2-epoxy-3-pentene (A15). The reaction as described for epoxide **A14** was performed on 6.19 g (17.1 mmol) of tosylate **A13** in 100 mL of dry THF with 0.45 g (18.8 mmol) of NaH. After an aqueous workup, the organic phase was dried over Na_2SO_4, filtered and concentrated under reduced pressure to afford 2.56 g of a yellow oil. Flash chromatography on silica gel (deactivated with 5-10% Et_3N) with hexanes-30% ether-hexanes afforded 2.45 g (75%) of epoxide **A15**. IR (film) ν 3050, 2990, 2950, 2870, 1510, 1470, 1420, 1390, 1270, 1230, 1200, 1160, 1130, 1090, 1050, 990, 950, 870, 760 cm^{-1}. ^{1}H NMR δ 2.63 (dd, A of ABX, J = 2.6, 5.3 Hz, 1H, OC<u>H</u>$_2$CH), 2.96 (dd, B of ABX, J = 4.1, 5.3 Hz, 1H, OC<u>H</u>$_2$CH), 3.57 (m, 1H, C<u>H</u>$_2$CHO), 4.22 (d, J = 6.4 Hz, 2H, CH_2OBn), 4.54 (AB, J_{AB} = 11.9 Hz, Δν = 6.4 Hz, 2H, OC<u>H</u>$_2$Ph), 5.20 (m, 1H, vinyl H), 5.89 (m, 1H, vinyl H), 7.33 (s, 5H, phenyl H). $[\alpha]_D^{20}$ -10.2° (*c* 4.39, $CHCl_3$). *Anal.* Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.66; H, 7.39.

(2*S*,3*S*)-3,7-Dimethyl-2,3-epoxy-6-octen-1-ol (B2). To a slurry of 0.8 g of 3Å molecular sieves in 50 mL of dry CH_2Cl_2 at -5°C was added 1.0 mL (4.75 mmol) of *L*-(+)-diethyl tartrate and 1.0 mL (3.35 mmol) of titanium (IV) isopropoxide. The mixture was stirred for 5 min and cooled to -23°C. To this cooled mixture was added 15.0 mL of *t*-butyl hydroperoxide (6.52 *M* in isooctane) with stirring. After 25 min, a solution of 11 mL (63.4 mmol) of geraniol (**B1**) in 10 mL of CH_2Cl_2 was added over 15 min. The resulting mixture was stirred at -23°C for 2.5 h and allowed to warm to 0°C. The mixture was quenched with 35 mL of water and allowed to stir for 45 min while warming to room temperature. To this suspension was added 10 mL of 30% NaOH in saturated brine and stirring was continued for 20 min. The phases were separated and the aqueous phase was extracted three times with CH_2Cl_2. The extracts were dried over Na_2SO_4, filtered and concentrated under reduced pressure to afford 13.4 g of a cloudy, viscous oil. Flash chromatography on silica gel with hexanes-40% ether-hexanes gradient afforded 9.20 g (85%) of epoxy alcohol **B2**. IR (film) ν 3430, 2970, 2930, 2860, 1450, 1385, 1075, 1035, 865 cm^{-1}. ^{1}H NMR δ 1.27 (s, 3H, epoxide CH_3), 1.44 (m, 1H), 1.58 (s, 3H, C(<u>C</u>H$_3$)$_2$), 1.65 (s, 3H, C(<u>C</u>H$_3$)$_2$), 1.66 (m, 1H), 1.95 (m, 1H, CH_2O<u>H</u>), 2.06 (m, 2H), 2.95 (m, 1H, epoxide H), 3.65 (m, 1H, C<u>H</u>$_2$OH), 3.80 (m, 1H, C<u>H</u>$_2$OH), 5.05 (t, J = 1.4 Hz, 1H, vinyl H). $[\alpha]_D^{22}$ -5.34° (*c* 3.24, $CHCl_3$) [lit. $[\alpha]_D^{22}$ -5.89 ($CHCl_3$), 91% ee].[15]

(2*S*,3*S*)-3,7-Dimethyl-2,3-epoxy-6-octenal (B3). To a solution of 11.0 mL (0.126 mol) of oxalyl chloride in 200 mL of dry CH_2Cl_2 at -78°C was added 18.0 mL (0.253 mol) of DMSO. The mixture was stirred at -78°C for 10 min and 16.33 g (0.095 mol) of alcohol **B2** (87% ee) in 25 mL of dry CH_2Cl_2 was added over 20 min. The white mixture was stirred at -78°C for 1 h and 70 mL (0.502 mol) of Et_3N was added over 30 min. The mixture was warmed to room temperature, diluted with 200 mL of ether and washed twice with water. The combined aqueous phases were extracted with ether and the combined extracts were dried over Na_2SO_4, filtered and concentrated under reduced pressure to afford a crude yellow oil. Flash chromatography on silica gel with hexanes-40% ether-hexanes gradient afforded 12.8 g (79%) of aldehyde **B3**. IR (film) ν 2970, 2920, 2860, 1725, 1450, 1405, 1380, 1240, 1110, 1075 cm^{-1}. ^{1}H NMR δ 1.42 (s, 3H, epoxide CH_3), 1.53 (m, 1H), 1.58 (s, 3H, C(<u>C</u>H$_3$)$_2$), 1.67 (s, 3H, C(<u>C</u>H$_3$)$_2$), 1.74 (m, 1H), 2.08 (m, 2H), 3.17 (d, J = 5.0 Hz, 1H, epoxide H), 5.04 (m, 1H, vinyl H), 9.44 (d, J = 5.0 Hz, 1H, CHO). $[\alpha]_D^{24}$ 104.4° (*c* 2.16, $CHCl_3$). *Anal.* Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.58. Found: C, 71.18; H, 9.53.

(4*S*,5*S*),(*E*)-Ethyl 5,9-Dimethyl-4,5-epoxy-2,8-decadienoate (B4). To a solution of 28.2 g (126 mmol) of triethyl phosphonoacetate in 100 mL of dry THF at 0°C was added 3.0 g (126 mmol) of NaH. The mixture was stirred at room temperature for 1 h and then cooled to -78°C. To this cooled mixture was added 6.52 g (38.7 mmol) of aldehyde **B3** (derived from alcohol **B2** of 87% ee) in 10 mL THF over 10 min. The mixture was stirred at -78°C for 6 h and allowed to warm to room temperature. The mixture was poured into 200 mL of 1:1 ether-NH_4Cl and the phases were separated. The organic layer was washed with water and the combined aqueous phases were extracted three times with ether. The combined extracts were dried over Na_2SO_4, filtered and concentrated under reduced pressure to afford 34.6 g of a yellow oil. Flash chromatography on silica gel with hexanes-15% ether-hexanes gradient afforded 8.43 g (91%) of (*E*)-ester **B4**. IR (film) ν 2980, 2940, 1720, 1655, 1450, 1390, 1370, 1305, 1265, 1180, 1040, 980 cm^{-1}. ^{1}H NMR δ 1.24 (s, 3H, epoxide CH_3), 1.26 (t, J = 7.2 Hz, 3H, OCH$_2$C<u>H</u>$_3$), 1.57 (s, 3H, C(<u>C</u>H$_3$)$_2$), 1.65 (s, 3H, C(<u>C</u>H$_3$)$_2$), 1.77-1.44 (m, 2H), 2.07 (m, 2H), 3.28 (d, J = 6.4 Hz, 1H, epoxide H), 4.18 (q, J = 7.2 Hz, 2H, OC<u>H</u>$_2$CH$_3$), 5.04 (t, J = 7.1 Hz, 1H, vinyl H), 6.05 (d, J = 15.7 Hz, 1H, vinyl H), 6.78 (dd, J = 6.4, 15.7

Hz, 1H, vinyl H). $[\alpha]_D^{22}$ 1.69° (*c* 3.47, $CHCl_3$). *Anal.* Calcd for $C_{14}H_{22}O_3$: C, 70.56; H, 9.30. Found: C, 70.50; H, 9.38.

(4*S*,5*S*),(*Z*)-Ethyl 5,9-Dimethyl-4,5-epoxy-2,8-dienoate (B5). To a solution of 4.0 mL (0.046 mol) of oxalyl chloride in 200 mL of CH_2Cl_2 at -78°C was added 6.5 mL (0.092 mol) of DMSO. The mixture was stirred for 10 min and a solution of 6.02 g (0.035 mol) of alcohol **B2** (91% ee) in 10 mL of CH_2Cl_2 was added over 10 min. The mixture was stirred for 1 h at -78°C then was quenched with 25 mL (0.179 mol) of Et_3N, allowed to warm to room temperature, diluted with 300 mL of ether and filtered through a pad of $MgSO_4$. The filtrate was concentrated under reduced pressure to afford aldehyde **B3** as a yellow oil which was used without further purification.

To a solution of 14.1 g (0.042 mol) of ethyl *bis*-(2,2,2-trifluoroethyl)phosphonoacetate and 25 g (0.095 mol) of 18-crown-6 in 1 L of dry THF at -78°C was added 85 mL (0.042 mol) of KHMDS (0.5 *M* in toluene). The mixture was stirred for 10 min and a solution of crude aldehyde **B3** in 10 mL of dry THF was added over 10 min. The mixture was stirred at -78°C for 2 h, allowed to warm to room temperature, and was diluted with 500 mL of EtOAc. The mixture was washed twice with saturated NH_4Cl and the combined aqueous phases were extracted with EtOAc. The combined extracts were dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford a viscous amber oil. The oil was dissolved in 100 mL of ether and filtered through a pad of silica gel with ether to remove most of the 18-crown-6. The filtrate was concentrated under reduced pressure to afford an amber oil. Flash chromatography on silica gel with hexanes-40% ether-hexanes afforded 5.82 g (70%) of (*Z*)-ester **B5**. IR (film) ν 2960, 2920, 2860, 1720, 1640, 1435, 1380, 1280, 1220, 1195, 1175, 1110, 1070, 995, 920, 880, 845 cm^{-1}. ^1H NMR δ 1.25 (s, 3H, epoxide CH_3), 1.28 (t, J = 7.1 Hz, 3H, $OCH_2\underline{CH_3}$), 1.60 (s, 3H, vinyl H), 1.66 (s, 3H, vinyl CH_3), 1.58-1.70 (m, 2H), 2.1 (m, 2H), 4.17 (q, J = 7.1 Hz, 2H, $O\underline{CH_2}CH_3$), 4.22 (d, J = 5.6 Hz, 1H, epoxide H), 5.09 (m, 1H, vinyl H), 5.99 (m, 2H, vinyl H). $[\alpha]_D^{22}$ 136.9° (*c* 3.25, $CHCl_3$). *Anal.* Calcd for $C_{14}H_{22}O_3$: C, 70.56; H, 9.30. Found: C, 70.21; H, 9.25.

(4*S*,5*S*),(*E*)-5,9-Dimethyl-4,5-epoxy-2,8-decadien-1-ol (B6). To a solution of 1.46 g (6.10 mmol) of ester **B4** (derived from alcohol **B2** of 86% ee) in 50 mL of dry CH_2Cl_2 at -78°C was added 15 mL (15 mmol) of DIBAH (1 *M* in hexanes) over 15 min. The resulting colorless solution was stirred at -78°C for 3 h and was quenched by the addition of 2 mL of water over 5 min. The mixture was treated with 50 mL of saturated aqueous Rochelle's salt and allowed to warm to room temperature. The phases were separated and the organic layer was washed three times with Rochelle's salt. The combined aqueous phases were extracted with CH_2Cl_2 and the combined extracts were dried over Na_2SO_4, filtered and concentrated under reduced pressure to obtain a crude yellow oil. Flash chromatography on silica gel with hexanes-80% ether-hexanes gradient afforded 0.755 g (63%) of alcohol **B6** as a colorless oil. IR (film) ν 3420, 2970, 2930, 2860, 1450, 1380, 1100, 1075, 1005, 960 cm^{-1}. ^1H NMR δ 1.25 (s, 3H, epoxide CH_3), 1.46 (m, 1H), 1.58 (s, 3H, $C(CH_3)_2$), 1.66 (s, 3H, $C(CH_3)_2$), 1.69 (m, 1H), 1.76 (m, 1H, $CH_2\underline{OH}$), 2.07 (m, 2H), 3.21 (d, J = 7.5 Hz, 1H, epoxide H), 4.16 (m, 2H, $C\underline{H_2}OH$), 2.06 (m, 1H, vinyl H), 5.59 (ddt, J = 1.6, 7.5, 15.6 Hz, 1H, vinyl H), 6.01 (dt, J = 5.2, 15.6 Hz, 1H, vinyl H). $[\alpha]_D^{23}$ -5.69° (*c* 3.51, $CHCl_3$). *Anal.* Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.25; H, 10.18.

(4*S*,5*S*),(*Z*)-5,9-Dimethyl-4,5-epoxy-2,8-decadien-1-ol (B8). The reduction was carried out as described for alcohol **B6** with 2.03 g (9.06 mmol) of ester **B5** (derived from alcohol **B2** of 86% ee) in 50 mL of CH_2Cl_2 at -78°C and 20 mL (20 mmol) of DIBAH (20% wt/wt in hexanes). After an aqueous workup, drying over Na_2SO_4 and filtration, the mixture was concentrated under reduced pressure to obtain a cloudy yellow oil. Flash chromatography on silica gel with hexanes-80% ether-hexanes gradient afforded 1.28 g (72%) of alcohol **B8**. IR (film) ν 3120, 2970, 2920, 2860, 1450, 1380, 1250, 1030, 820 cm^{-1}. ^1H NMR δ 1.24 (s, 3H, epoxide CH_3), 1.46 (m, 2H), 1.58 (s, 3H, $C(CH_3)_2$), 1.66 (s, 3H, $C(CH_3)_2$), 1.87 (m, 1H, $CH_2O\underline{H}$), 2.06 (m, 2H), 3.40 (d, J = 7.1 Hz, 1H, epoxide H), 4.29 (m, 2H, $C\underline{H_2}OH$), 5.06 (m, 1H, vinyl H), 5.40 (m, 1H, vinyl H), 5.88 (m, 1H, vinyl H). $[\alpha]_D^{23}$ 37.7° (*c* 2.64, $CHCl_3$). *Anal.* Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.33; H, 10.20.

Reaction of (2*S*),(*E*)-5-Benzyloxy-1,2-epoxy-3-pentene (A14) with $LiMe_2Cu$ (Method A). To a slurry of 434 mg (2.27 mmol) of CuI[20] in 20 mL of dry THF at 0°C was added 3.2 mL of MeLi (1.4 *M* in Et_2O). The mixture was stirred at 0°C for 10 min and a solution of 103 mg (0.54 mmol) of ether **A14** in 1 mL of THF was added over 1 min. The mixture was stirred at 0°C for 12 h and was quenched with aqueous saturated NH_4Cl. The mixture was stirred for 1 h at room temperature and the phases were separated. The organic phase was diluted with 50 mL of EtOAc and washed with NH_4Cl until there was no color change in the aqueous layer. The combined aqueous phases were extracted twice with EtOAc and the combined extracts were dried over Na_2SO_4, filtered and concentrated under reduced pressure to afford a dark amber oil. Flash chromatography on silica gel with 60% ether-hexanes afforded 52.5 mg (50%) of mixed alcohols. GC analysis indicated 40.6% benzyl alcohol (from elimination product), 1.9% S_N2-*Z*, 10.5% S_N2'-*E* and 47.0% S_N2-*E* products.

Reaction of (2*S*),(*E*)-5-Benzyloxy-1,2-epoxy-3-pentene (A14) with LiMeCuCN (Method B). To a slurry of 904 mg (10.1 mmol) of CuCN[20] in 25 mL of Et_2O at 0°C was added 7.2 mL of MeLi (1.4 *M* in Et_2O). The mixture was stirred at 0°C for 10 min and a solution of 154 mg (0.81 mmol) of ether **A14** in 2 mL of Et_2O was added over 1 min. The mixture was stirred at 0°C for 12 h and was quenched with aqueous NH_4Cl. The mixture was stirred at room temperature for 1 h and the phases were separated. The organic phase was diluted with 100 mL of EtOAc and washed with NH_4Cl until the aqueous layer remained colorless. The combined washes were extracted twice with EtOAc and the combined extracts were dried over Na_2SO_4, filtered and concentrated under reduced pressure. Flash chromatography on silica gel with 60% ether-hexanes afforded 157 mg (87%) of mixed alcohols. GC analysis indicated 11.4% benzyl alcohol (from elimination product), 6.1% S_N2'-*Z*, 69.5% S_N2'-*E* and 11.8% S_N2-*E* products.

Reaction of (2*S*),(*E*)-5-Benzyloxy-1,2-epoxy-3-pentene (A14) with CuBr • Me_2S and MeMgBr (Method C). To a slurry of 233 mg (2.33 mmol) of CuBr • Me_2S complex in 15 mL of dry THF at 0°C was added 0.5 mL of Me_2S and 4.0 mL of MeMgBr (3 *M* in Et_2O). The mixture was stirred for 20 min and a

solution of 102 mg (0.536 mmol) of ether **A14** in 2 mL of THF was added over 1 min. The mixture was stirred at 0°C for 10 h and was quenched with saturated aqueous NH_4Cl. The mixture was stirred at room temperature for 1 h and the phases were separated. The organic phase was diluted with 50 mL of EtOAc and washed with NH_4Cl until the aqueous layer remained colorless. The combined washes were extracted twice with EtOAc and the combined extracts were dried over Na_2SO_4, filtered and concentrated under reduced pressure. Flash chromatography on silica gel with 60% ether-hexanes afforded 104 mg (94%) of mixed alcohols. GC analysis indicated 26.4% benzyl alcohol (from elimination product), 9.5% S_N2'-*Z*, 47.2% S_N2'-*E* and 16.9% S_N2-*E* products.

Reaction of (2*S*),(*E*)-5-Benzyloxy-1,2-epoxy-3-pentene (A14) with CuI, MeLi and $BF_3 \cdot Et_2O$ (Method D). To a slurry of 231 mg (1.21 mmol) of CuI[20] in 10 mL of dry THF-Et_2O (5:1) at -5°C was added 0.85 mL of MeLi (1.4 *M* in Et_2O). The mixture was stirred at -5°C for 20 min, cooled to -78°C and charged with 0.22 mL (1.78 mmol) of $BF_3 \cdot Et_2O$. This mixture was stirred at -78°C for 30 min and a solution of 70.5 mg (0.37 mmol) of ether **A14** in 2 mL of Et_2O was added over 1 min. The mixture was stirred at -78°C for 1 h and allowed to slowly warm to room temperature. The mixture was stirred at room temperature for 1 h, cooled to 0°C and quenched with saturated aqueous NH_4Cl. The mixture was stirred for 1 h at room temperature and the phases were separated. The organic phase was diluted with 50 mL of EtOAc and washed with aqueous NH_4Cl until the aqueous phase remained colorless. The combined washes were extracted twice with EtOAc and the combined extracts were dried over Na_2SO_4, filtered and concentrated under reduced pressure. Flash chromatography on silica gel with 60% ether-hexanes afforded 57 mg (76%) of mixed alcohols. GC analysis indicated 60.6% S_N2'-*Z*, 28.2% S_N2'-*E* and 11.2% S_N2-*E* products.

Reaction of (2*S*),(*E*)-5-Benzyloxy-1,2-epoxy-3-pentene (A14) with $LiMe_2Cu$ in Et_2O (Method E). To a slurry of 303 mg (1.59 mmol) of CuI[20] in 15 mL of Et_2O at -5°C was added 2.3 mL of MeLi (1.4 *M* in Et_2O). The mixture was stirred at -5°C for 10 min and a solution of 73 mg (0.383 mmol) of ether **A14** in 2 mL of Et_2O was added over 2 min. The mixture was stirred at 0°C for 12 h and quenched with saturated aqueous NH_4Cl. The mixture was stirred at room temperature for 1 h and the phases were separated. The organic phase was diluted with 50 mL of EtOAc and washed with aqueous NH_4Cl until the aqueous phase remained colorless. The combined washes were extracted twice with EtOAc, and the combined extracts were dried over $NaSO_4$, filtered and concentrated under reduced pressure. Flash chromatography on silica gel with 60% ether-hexanes afforded 56.1 mg (71%) of mixed alcohols. GC analysis indicated 41.8% benzyl alcohol (from elimination product), 24.6% S_N2'-*E* and 33.6% S_N2-*E* products.

Reaction of (4*S*,5*S*),(*E*)-5,9-Dimethyl-4,5-epoxy-2,8-decadien-1-ol (B6) with $LiMe_2Cu$ (Method A). The reaction as described for **A14** was followed with 1.04 g (5.45 mmol) of epoxide **B6**, 4.11 g (21.5 mmol) of CuI[20] and 30 mL of MeLi (1.4 *M* in Et_2O) in 100 mL of dry THF. After aqueous workup, flash chromatography afforded 0.801 g (81%) of mixed alcohols. $[\alpha]_D^{23}$ -5.64° (*c* 3.79, $CHCl_3$). Monosilylation by the method of Chaudhary and Hernandez[19] as described below afforded 0.997 g (83%) of mixed ethers. GC analysis indicated 16% of the syn-*E* and 84% of the anti-*E* products.

Reaction of (4*S*,5*S*),(*E*)-5,9-Dimethyl-4,5-epoxy-2,8-decadien-1-ol (B6) with LiMeCuCN (Method B). The reaction as described for **A14** was followed with 151 mg (0.77 mmol) of epoxide **B6**, 1.10 g (11.3 mol) of CuCN[20] and 8.0 mL of MeLi (1.4 *M* in Et_2O). After aqueous workup, flash chromatography afforded 137 mg (84%) of mixed diols. Monosilylation by the method of Chaudhary and Hernandez[19] as described below afforded 181 mg (86%) of mixed ethers. GC analysis indicated 12% of the syn-*E* and 88% of the anti-*E* products.

Reaction of (4*S*,5*S*),(*Z*)-5,9-Dimethyl-4,5-epoxy-2,8-decadien-1-ol (B8) with $LiMe_2Cu$ (Method A). The reaction as described for **A14** was followed with 0.45 g (2.32 mmol) of epoxide **B8**, 1.84 g (2.82 mmol) of CuI[20] and 6.5 mL of MeLi (1.4 *M* in Et_2O) in 40 mL of dry THF. After aqueous workup, flash chromatography afforded 369 g (75%) of mixed alcohols. $[\alpha]_D^{23}$ 22.3° (*c* 1.48, $CHCl_3$). Monosilylation by the method of Chaudhary and Hernandez[19] as described below afforded 0.66 g (73%) of mixed ethers. GC analysis indicated 97% of the syn-*E* and 3% of the anti-*E* products.

Reaction of (4*S*,5*S*),(*Z*)-5,9-Dimethyl-4,5-epoxy-2,8-decadien-1-ol (B8) with LiMeCuCN (Method B). The reaction as described for **A14** was followed with 123 mg (0.626 mmol) of epoxide **B8**, 843 mg (9.41 mmol) of CuCN[20] and 6.7 mL of MeLi (1.4 *M* in Et_2O). After aqueous workup, flash chromatography afforded 117 mg (88%) of mixed diols. Monosilylation by the method of Chaudhary and Hernandez[19] as described below afforded 163 mg (90%) of mixed ethers. GC analysis indicated 1% of the syn-*E* and 99% of the anti-*E* products.

Reaction of (4*S*,5*R*),(*Z*)-5,9-Dimethyl-4,5-epoxy-2,8-decadien-1-ol (C6) with $LiMe_2Cu$ (Method A). The reaction as described for **A14** was followed with 114 mg (0.58 mmol) of epoxide **C6**, 480 mg (2.52 mmol) of CuI[20] and 3.6 mL of MeLi (1.4 *M* in Et_2O) in 15 mL of dry THF. After aqueous workup, flash chromatography afforded 120 mg (93%) of mixed diols. Mono silyl ethers were prepared by the method of Chaudhary and Hernandez[19] in which a solution of 120 mg (0.58 mmol) of the above diols in 5 mL of dry CH_2Cl_2 at room temperature was treated with 119 mg (0.79 mmol) of *t*-butyldimethylsilyl chloride, 0.2 mL (1.44 mmol) of Et_3N and catalytic DMAP. The mixture was stirred at room temperature for 6 h, diluted with 50 mL of ether and washed with water. The organic phase was dried over Na_2SO_4, filtered and concentrated under reduced pressure. Flash chromatography on silica gel with hexanes-30% ether-hexanes gradient afforded 171 mg (90%) of mixed ethers. GC analysis of the silyl ethers indicated 5% syn-*E* and 95% anti-*E* products.

Reaction of (4*S*,5*R*),(*Z*)-5,9-Dimethyl-4,5-epoxy-2,8-decadien-1-ol (C6) with LiMeCuCN (Method B). The reaction as described for **A14** was followed with 152 mg (0.78 mmol) of epoxide **C6**, 1.107 g (12.3 mmol) of CuCN[20] and 8.8 mL of MeLi (1.4 *M* in Et_2O). After aqueous workup, flash chromatography afforded 158 mg (95%) of mixed diols. $[\alpha]_D^{21}$ 13.2° (*c* 7.91, $CHCl_3$). Monosilylation by the

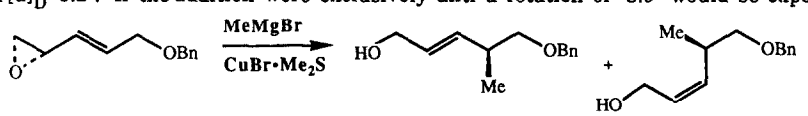
method of Chaudhary and Hernandez[19] as described above afforded 221 mg (94%) of mixed ethers. GC analysis indicated 3% of the syn-*E* and 97% of the anti-*E* products.

Reaction of (4*S*,5*R*),(*E*)-5,9-Dimethyl-4,5-epoxy-2,8-decadien-1-ol (C5) with $LiMe_2Cu$ (Method A). The reaction as described for **A14** was followed with 122 mg (0.62 mmol) of epoxide **C5**, 538 mg (2.82 mmol) of CuI[20] and 4.0 mL of MeLi (1.4 *M* in Et_2O) in 20 mL of dry THF. After aqueous workup, flash chromatography afforded 126 mg (95%) of mixed alcohols. Monosilylation by the method of Chaudhary and Hernandez[19] as described above afforded 185 mg (96%) of mixed ethers. GC analysis indicated 86% of the syn-*E* and 14% of the anti-*E* products.

Reaction of (4*S*,5*R*),(*E*)-5,9-Dimethyl-4,5-epoxy-2,8-decadien-1-ol (C5) with LiMeCuCN (Method B). The reaction as described for **A14** was followed with 136 mg (0.69 mmol) of epoxide **C5**, 959 mg (10.7 mmol) of CuCN[20] and 7.5 mL of MeLi (1.4 *M* in Et_2O) in 15 mL of dry ether. After aqueous workup, flash chromatography afforded 136 mg (90%) of mixed alcohols. $[\alpha]_D^{22}$ -15.6° (*c* 6.23, $CHCl_3$). Monosilylation by the method of Chaudhary and Hernandez[19] as described above afforded 188 mg (90%) of mixed ethers. GC analysis indicated 90% of the syn-*E* and 10% of the anti-*E* products.

References and Notes

1. For a comprehensive review, see Magid, R. M. *Tetrahedron* **1980**, *36*, 1901.
2. (a) allylic esters: Tseng, C. C.; Paisley, S. D.; Goering, H. L. *J. Org. Chem.* **1986**, *51*, 2884 and references cited to earlier papers in the series. (b) allylic lactones: Trost, B. M.; Klun, T. P. *J. Org. Chem.* **1980**, *45*, 4256. (c) allylic mesylates: Ibuka, T.; Nakao, T.; Nishii, S.; Yamamoto, Y. *J. Am. Chem. Soc.* **1986**, *108*, 7420. (d) allylic carbamates: Gallina, C.; Ciattini, P. G. *J. Am. Chem. Soc.* **1979**, *101*, 1035.
3. Anderson, R. J. *J. Am. Chem. Soc.* **1970**, *92*, 4978. Herr, R. W.; Johnson, C. R. *J. Am. Chem. Soc.* **1970**, *92*, 4979.
4. (a) Marino, J. P.; Fernandez de la Pradella, R.; Laborde, E. *J. Org. Chem.* **1987**, *52*, 4898 and references therein. (b) Wender, P. A.; Erhardt, J. M.; Letendre, L. J. *J. Am. Chem. Soc.* **1981**, *103*, 2114. (c) Ziegler, F. E.; Cady, M. A. *J. Org. Chem.* **1981**, *46*, 122.
5. For some exceptions, see (a) Marshall, J. A.; Audia, V. H. *J. Org. Chem.* **1987**, *52*, 1106. (b) Goering, H. L.; Tseng, C. C. *J. Org. Chem.* **1985**, *50*, 1597. (c) Goering, H. L.; Kantner, S. S. *J. Org. Chem.* **1984**, *49*, 422. (d) Goering, H. L.; Kantner, S. S.; Tseng, C. C. *J. Org. Chem.* **1983**, *48*, 715.
6. In a study involving S_N2' additions of cuprates to γ-vinyl-γ-lactones Trost and Klun showed that substituents, through their effect on acyclic conformation, play an important role in determining *E*/*Z* product ratios.[2b]
7. For a preliminary report, see Marshall, J. A.; Trometer, J. D. *Tetrahedron Lett.* **1987**, *28*, 4985.
8. (a) Takano, S.; Kurotaki, A.; Takahashi, M.; Ogasawara, K. *Synthesis* **1986**, 403. (b) Still, W. C.; Gennari, C. *Tetrahedron Lett.* **1983**, *24*, 4405.
9. *Cf.* Katsuki, T.; Lee, A. W. M.; Ma, P.; Martin, V. S.; Masamune, S.; Sharpless, K. B.; Tuddenham, D.; Walker, F. J. *J. Org. Chem.* **1982**, *47*, 1373.
10. Marino, J. P.; Jaen, J. C. *J. Am. Chem. Soc.* **1982**, *104*, 3165.
11. For a review of cuprates, see Lipshutz, B. H.; Wilhelm, R. S.; Kozlowski, J. A. *Tetrahedron* **1984**, *40*, 5005. Lipshutz, B. H.; Kozlowski, J. A.; Breneman, C. M. *J. Am. Chem. Soc.* **1985**, *107*, 3197.
12. *Cf.* Yamamoto, Y.; Yamamoto, S.; Yatagai, H.; Ishihara, Y.; Maruyama, K. *J. Org. Chem.* **1982**, *47*, 119.
13. Nagaoka, H.; Kishi, Y. *Tetrahedron* **1981**, *37*, 3873.
14. Based on the work of Nagaoka and Kishi, the rotation of (*S*)-**1.1** is -9.9° and that of (*R*)-**1.2** is -1.3°.[13] An 88:12 mixture of **1.1** and **1.2**, obtained from the (*E*)-vinyloxirane **A14** by method C (Table 1), showed $[\alpha]_D$ -6.2°. If the addition were exclusively anti a rotation of -8.9° would be expected



A14 88% (*S*)-**1.1**, $[\alpha]_D$ -9.9° 12% (*R*)-**1.2**, $[\alpha]_D$ -1.3°

assuming both products are formed by the same pathway. Accordingly, a *minimum* anti/syn preference of *ca.* 6:1 can be calculated. Similarly, the (*Z*)-vinyloxirane **A15** was calculated to favor anti S_N2' displacement with the foregoing cuprate by 4.5:1. These calculations assume (1) no racemization in the two-step selective oxidation-reduction sequence required for removal of the S_N2 by-product and (2) 90% optical purity for vinyloxiranes **A14** and **A15** as judged by optical rotation.
15. Gao, Y.; Hanson, R. M.; Klunder, J. A.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765.
16. Omura, K.; Swern, D. *Tetrahedron* **1978**, *34*, 1651.
17. Roush, W. R.; Palkowitz, A. D.; Palmer, M. A. J. *J. Org. Chem.* **1987**, *52*, 316.
18. The experimental procedures for **C2**-**C6** are not included owing to space limitations. These compounds were prepared by the same procedures employed for **B2**-**B8**.
19. Chaudhary, S. K.; Hernandez, O. *Tetrahedron Lett.* **1979**, 99.
20. CuI was purchased from Alfa and purified by Soxhlet extraction with THF. CuCN was stirred in water overnight, filtered and washed with ethanol. The ethanol was removed from the solid by azeotropic distillation with toluene and the resulting powder was thoroughly dried under vacuum.