Diastereodifferentiation in S_N2' Additions of Methylcuprates to Nonracemic Acyclic Vinyloxiranes

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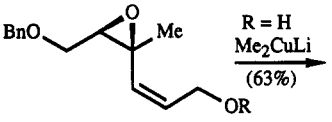
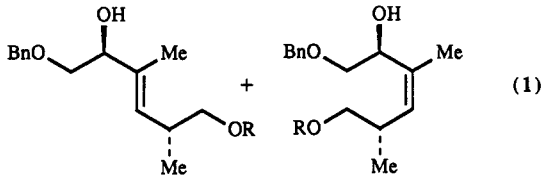
S_N2' additions of Me_2CuLi, MeCu(CN)Li, and $Me_2Cu(CN)Li_2$ to the 2*S* and 2*R* alkoxy *cis*-(*Z*)- and -(*E*)-vinyloxiranes **8**, **9**, **13**, and **14** were examined as possible routes to acyclic subunits of polypropionate natural products. Highest anti:syn ratios were found for the (2*S*)- and (2*R*)-hydroxy-(*E*)-vinyloxiranes **13a** and **14a** followed by the (2*R*)-MTM ether analogue **14c**. In both cases Me_2CuLi gave higher ratios than either of the cyanocuprates (>99:1 vs 14:1 for **13a**/**13b** and >40:1 vs ~24:1 for **14c**).

Recent studies have shown that appropriately substituted acyclic vinyloxiranes undergo highly anti selective S_N2' displacements with methylcuprates to afford allylic alcohols which can be further elaborated to subunits of polypropionate natural products.[1-4] For example, the *cis*-(*Z*)-vinyloxirane I affords the S_N2' products II and III with 99% anti stereoselectivity (eq 1).[1] Likewise, the



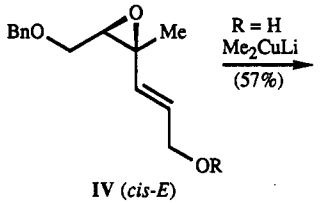
I (*cis*-*Z*)



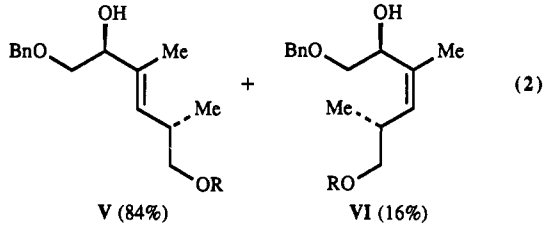
(1)

II (94%) III (6%)

cis-(*E*) isomer IV yields the analogous S_N2' products V and VI with 96% anti selectivity (eq 2). These reactions are



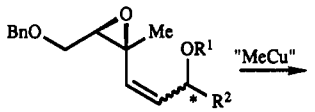
IV (*cis*-*E*)



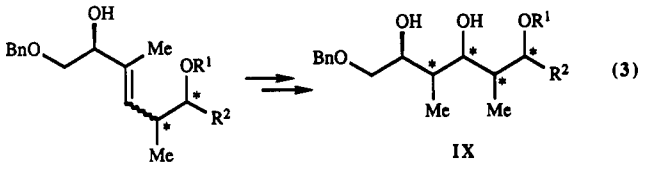
(2)

V (84%) VI (16%)

most efficient with the free alcohols (vs TBS ethers) suggestive of an OH directing effect. The present investigation was undertaken to examine the stereochemical role of allylic alcohol and ether substituents on the diastereoselectivity of S_N2' displacements in vinyloxiranes such as VII (eq 3). These studies set the stage for further applications of this methodology in the synthesis of macrolides and related natural products.[5]



VII (E or Z, * = *S* or *R*)



(3)

VIII IX

Representative vinyloxiranes were prepared as outlined in Scheme I starting from the known epoxy aldehyde **2**.[1] Corey–Fuchs Wittig condensation with CBr_4–Ph_3P afforded the vinylidene dibromide **3** in high yield.[6] This was subjected to sequential dehydrobromination–debromination according to Nicolaou.[7] Addition of acetaldehyde to the resulting lithio acetylide intermediate afforded the diastereomeric alcohols **5a** and **6a** as a 1:1 inseparable mixture. Enriched samples of the (2*S*)-alcohol **5a** could be secured through oxidation of the mixture to ketone **7** and reduction of **7** with (*S*)-BINAL-H[8] or *ent*-Chirald-LAH.[9] The resulting ca. 4:1 mixture of *S* and *R* alcohols **5a** and **6a** could not be separated. The corresponding TBS ethers **5b**/**6b** and MTM ethers **5c**/**6c** were likewise inseparable. Mixtures enriched in the 2*R* diastereomers **6a–c** (ca. 3:1) were secured through reduction of ketone **7** with (*R*)-BINAL-H[8] or Chirald-LAH[9] and subsequent ether formation. These mixtures were hydrogenated to the corresponding inseparable mixtures of (*Z*)-allylic alcohols and ethers **8** and **9**. The absolute stereochemistry of the carbinyl center was ascertained by ^1H NMR analysis of the *O*-methylmandelates.[10]

The (*E*)-vinyloxiranes **13-14** were readily prepared starting from enone **12**, the Horner–Emmons product of aldehyde **2**.[11] Reduction of this enone with (*S*)-BINAL-H

(1) Marshall, J. A.; Trometer, J. D.; Blough, B. E.; Crute, T. D. *J. Org. Chem.* **1988**, *53*, 4274.
(2) Marshall, J. A.; Trometer, J. D. *Tetrahedron* **1989**, *45*, 391.
(3) Marshall, J. A.; Blough, B. E. *J. Org. Chem.* **1990**, *55*, 1540.
(4) Marshall, J. A. *Chem. Rev.* **1989**, *89*, 1503.
(5) Cf.: Masamune, S. *Aldrichimica Acta* **1978**, *11*, 23. Hoffmann, R. W. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 489.
(6) Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972**, 3769.
(7) Nicolaou, K. C.; Prasad, C. V. C.; Somers, P. K.; Hwang, C.-K. *J. Am. Chem. Soc.* **1989**, *111*, 5330.
(8) Noyori, R.; Tomino, I.; Tanimoto, Y.; Nishizawa, M. *J. Am. Chem. Soc.* **1984**, *106*, 6709.
(9) Yamaguchi, S.; Mosher, H. S. *J. Org. Chem.* **1973**, *38*, 1870. Chirald is available from Aldrich Chemical Co., Milwaukee, WI. The enantiomer was obtained from Eli Lilly and Co. to whom we are grateful.
(10) Trost, B. M.; Belletire, J. L.; Godleski, S.; McDougal, P. G.; Balkovec, J. M.; Baldwin, J. J.; Christy, M. E.; Ponticello, G. S.; Varga, S. L.; Springer, J. D. *J. Org. Chem.* **1986**, *51*, 2370.
(11) Cf.: Blancheite, M. A.; Choy, W.; Davis, S. T.; Essenfield, A. P.; Masamune, S.; Roush, W. R.; Sakai, T. *Tetrahedron Lett.* **1984**, *25*, 2183.

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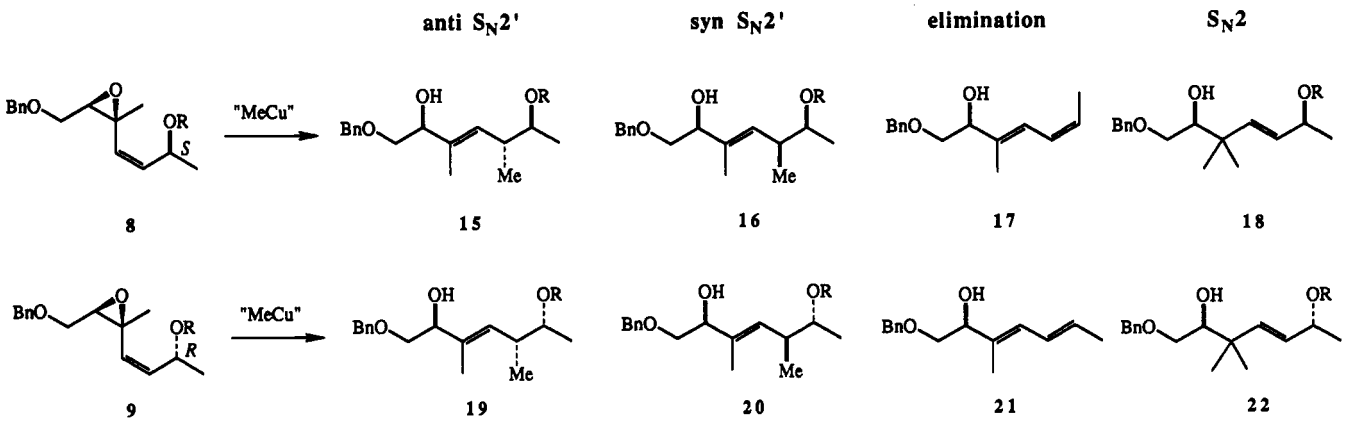
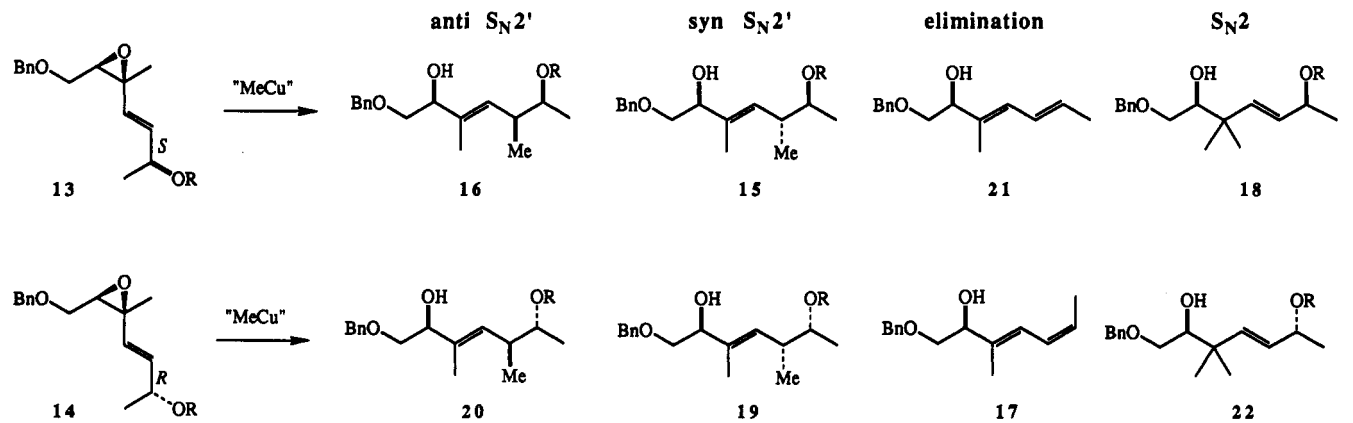
Table I. (*Z*)-Vinyloxiranes



entry	8:9	R	series	MeCu[a]	yield	elim (17/21)	S_N2 (18 or 22)	S_N2'	S_N2' products 15	16	19	20	anti/syn 8 (15:16)	9 (19:20)
1	19:81	TBS	b	B	100	–	–	100	17.4	2.0	35.8	44.7	8.7:1	0.8:1
2	80:20	TBS	b	B	94	–	–	100	72.1	8.4	11.2	8.3	8.6:1	1.3:1
3	80:20	TBS	b	C	96	95	–	5	–	–	–	–	–	–
4	76:24	MTM	c	B	97	7	6	87	61.2	14.9	11.2	12.7	4.1:1	0.9:1
5	12:88	MTM	c	C	97	32	3	65	12.3	<1	59.3	28.4	>12:1	2.1:1

[a] Starting material was recovered from reactions employing Me_2CuLi. B = MeCu(CN)Li in Et_2O. C = $Me_2Cu(CN)Li_2$ in Et_2O.

Table II. (*E*)-Vinyloxiranes



entry	13:14	R	series	MeCu[a]	yield	elim (17/21)	S_N2 (18 or 22)	S_N2'	S_N2' products 15	16	19	20	anti/syn 13 (16:15)	14 (20:19)
1	28:72	H	a	A	95	–	18	82	<1	28.5	<1	71.5	>99:1	>99:1
2	28:72	H	a	B	100	–	29	71	1.8	25.5	4.8	67.2	14.2:1	14.4:1
3	28:72	H	a	C	87	–	38	62	1.8	25.8	9.6	62.7	14.3:1	6.5:1
4	25:75	TBS	b	A	90	14	7	79	4.3	20.4	5.1	70.2	4.7:1	13.8:1
5	25:75	TBS	b	B	99	2	2	96	6.3	18.1	4.6	71.0	2.9:1	15.4:1
6	25:75	TBS	b	C	86	95	–	5	–	–	–	–	–	–
7	25:75	MTM	c	A	86	7	7	86	2.4	23.5	1.8	73.0	9.5:1	40.6:1
8	25:75	MTM	c	B	100	–	–	100	5.0	18.3	3.0	73.7	3.3:1	23.8:1
9	25:75	MTM	c	C	96	100	–	–	–	–	–	–	–	–

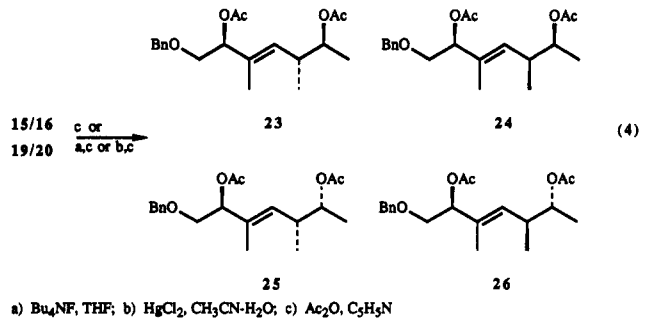
[a] A = Me_2CuLi in Et_2O–THF. B = MeCu(CN)Li in Et_2O. C = $Me_2Cu(CN)Li_2$ in Et_2O.

or *ent*-Chirald-LAH gave a mixture of alcohols enriched in the 2*S* isomer **13a** whereas (*R*)-BINAL-H or Chirald-LAH gave mainly the 2*R* alcohol **14a**.[8,9] Neither these alcohols nor the derived ethers **13b/14b** or **13c/14c** could be separated. The stereochemical purity of the alcohols could be increased by Sharpless kinetic resolution.[12] However, we were unable to secure completely pure samples without significant material loss. Eventually we discovered that the four diastereomeric S_N2' products **15**, **16**, **19**, and **20** (see Tables I and II) could be analyzed as their diacetate derivatives **23–26** (see eq 4) by gas chromatography after removal of the S_N2 and elimination products by column chromatography on silica gel. Consequently, we were able to establish syn/anti preferences for cuprate additions on mixtures of **8/9** and **13/14** of known composition. The identity of the elimination and S_N2 products was established from the ^1H NMR spectra of the separated mixtures.

Three cuprates were employed for these studies, Me_2CuLi, MeCu(CN)Li, and $Me_2Cu(CN)Li_2$ (Tables I and II).[13] None gave S_N2' products with the OH substituted (*Z*)-vinyloxiranes **8a/9a**. The 2,5-dihydrofurans **10/11**

(12) Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765.

(13) Cf.: Lipshutz, B. H. *Synthesis* **1987**, 325.

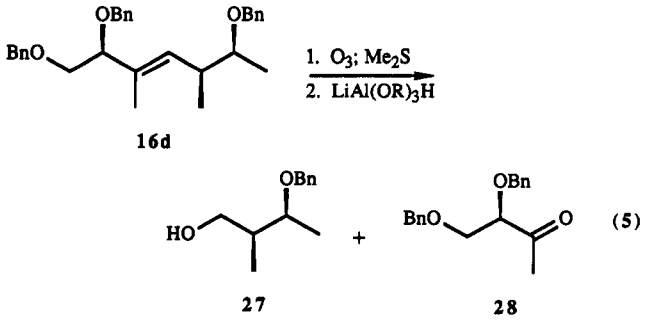


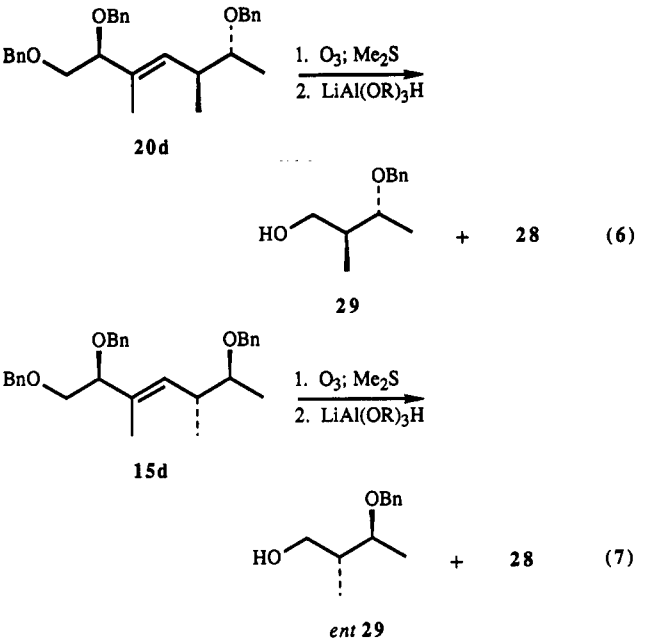
a) Bu_4NF, THF; b) $HgCl_2$, CH_3CN-H_2O; c) Ac_2O, C_5H_5N

were the sole isolable products (Scheme I). The Gilman cuprate (A) proved unreactive with the TBS and MTM derivatives **8b/9b** and **8c/9c**. Starting material was recovered in both cases. Best results were obtained with the TBS ether **8b** and the lower order cyanocuprate (B) which afforded an 8.7:1 mixture of anti and syn S_N2' adducts **15** and **16** (Table I, entry 1). An even higher ratio of these two products was obtained with the MTM ether **9c** and the higher order cyanocuprate (C). However, in this case the elimination and S_N2 products **17** and **18** accounted for 35% of the reaction (Table I, entry 5). The higher order cyanocuprate (C) gave nearly all elimination products **17/21** with the TBS ethers **8b/9b** (entry 3). Significantly, the 2*R* ethers **9b** and **9c** showed much lower anti:syn ratios than the 2*S* diastereomers **8b** and **8c**.

As a group, the (*E*)-vinyloxiranes **13/14a-c** were much better behaved than their *Z* counterparts (Table II). The highest anti:syn ratios were obtained from reaction of the Gilman cuprate with the OH substituted vinyloxiranes **13a** and **14a** (entry 1). These alcohols also showed high anti selectivity with the two cyanocuprate reagents (entries 2 and 3). Unfortunately, all three reactions produced significant amounts of S_N2 products **18** and **22**. S_N2' displacements on the TBS ethers **13b/14b** were moderately anti selective with the Gilman and lower order cyanocuprates (entries 4 and 5). The higher order reagent gave nearly total elimination products **17/21** with these epoxides (entry 6). The MTM ethers **13c/14c** behaved similarly (entry 9). The (2*R*)-MTM ether **14c** showed excellent anti selectivity in its reaction with the lower order cyanocuprate (entry 7). Only a small amount of elimination and S_N2 products were formed in this reaction. Overall, this combination offers the best potential for synthetic applications as the product **20c** is a *monoprotected* secondary diol, in contrast to **20a**, the product of anti S_N2' displacement of the OH substituted epoxide **14a**.

The stereochemistry of the three dominant S_N2' products **16a** (a 12:1 mixture of **16a:20a** secured by Sharpless kinetic resolution[12] of **13a/14a** followed by cuprate addition as in Table II, entry 1), **20a** (from Table II, entry 1), and **15b** (from Table I, entry 2) was ascertained by ozonolysis–reduction of the benzyl ether derivatives **16d**, **20d**, and **15d** to the syn and anti alcohols **27**, **29**, and *ent*-**29** of known configuration (Eqs 5, 6, and 7).





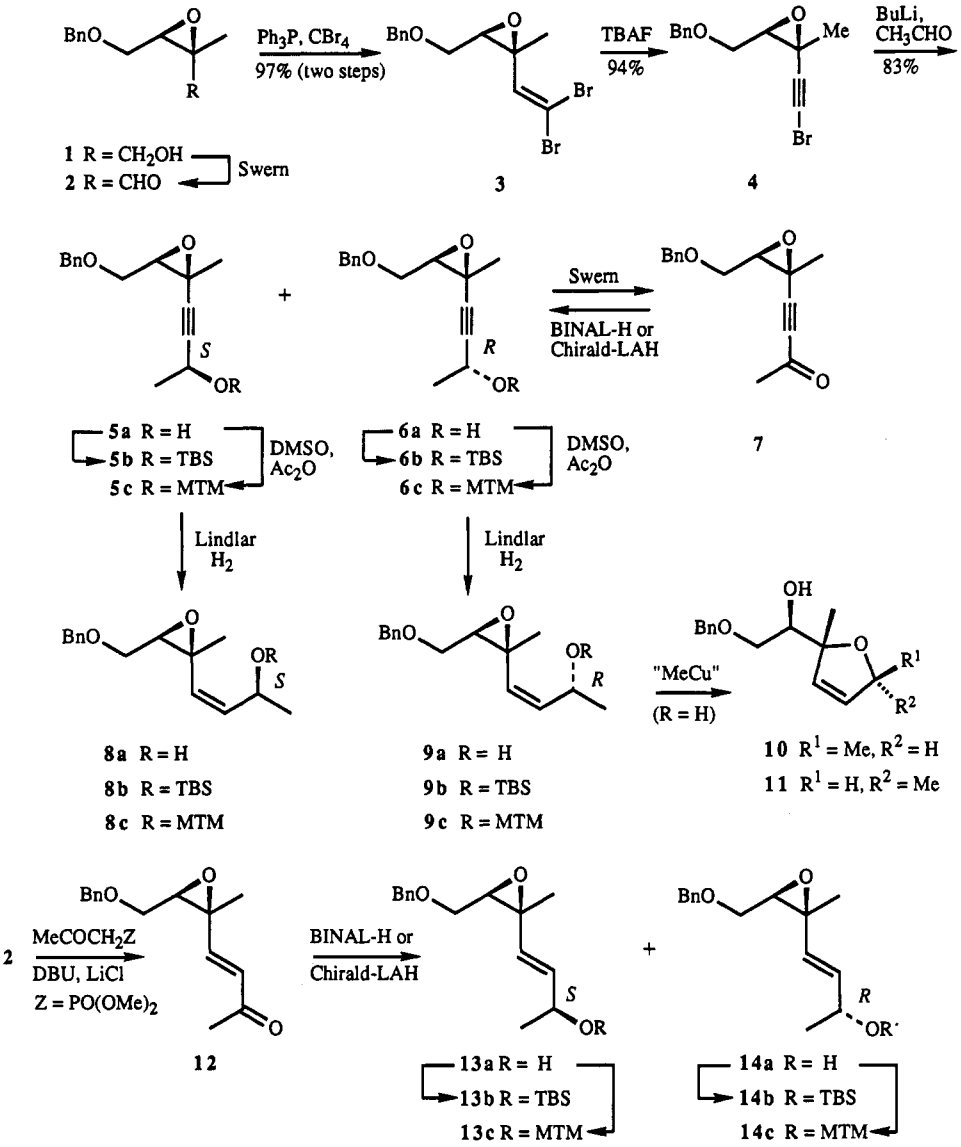
While these studies were in progress we discovered that the CuCN, employed in our earlier studies with vinyloxiranes I and IV,[1] was of poor quality. A more recently acquired sample of CuCN gave better product ratios reproducibly in reactions employing the lower order cyanocuprate.[14] Accordingly, we repeated those earlier experiments with pure CuCN. We also examined the previously unreported MTM ether derivatives Ic and IVc. These findings are summarized in Table III. The conclusions to be drawn from Table III are (1) the MTM grouping is less susceptible to elimination than TBS for the (*Z*)-vinyloxirane I (Table III, entry 8 vs 4), and (2) additions involving the lower order cyanocuprate reagent prepared from impure CuCN resemble those of the higher order cyanocuprate (entry 3 vs 6), especially in regard to elimination. Thus it appears likely that our earlier reported experiments with vinyloxiranes I and IV and lower order cyanocuprate (B) actually involved higher order cyanocuprate (C) or a mixture of the two.[1]

Several interesting contrasts can be seen between our present findings with **8/9**, **13/14**, and our previous studies on the primary alcohol analogues I and IV (eqs 1 and 2).[1] In particular, the primary *Z* allylic alcohol Ia gave only minor amounts of cyclization product whereas the secondary alcohol analogues **8a/9a** suffered total conversion to the 2,5-dihydrofurans **10/11** (Scheme I). Furthermore, the TBS ether derivative of both the *Z* and *E* primary allylic alcohols Ib and IVb gave 90–95% of elimination products and only trace quantities of S_N2' products with Me_2CuLi[1] and gave *mainly* S_N2' addition with MeCu(CN)Li derived from pure CuCN (entry 4). The secondary TBS analogues **8b/9b**, on the other hand (1) did not react with Me_2CuLi, and (2) gave *only* S_N2' products with MeCu(CN)Li (Table I, entries 1 and 2).

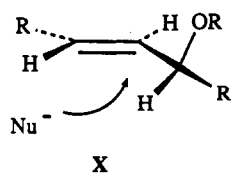
Except for the *E* allylic alcohols (Table II, entries 1 and 2), the stereoselectivity of S_N2' additions to the vinyloxiranes **8/9** and **13/14** showed a marked dependence on the configuration at C2. Of the ethers, the (2*R*)-MTM derivative **14c** showed the best internal matching of stereocenters for anti addition (Table II, entries 7 and 8). The general trends can be rationalized on the basis of

(14) Previous samples of CuCN were yellow to olive green in appearance. The most effective CuCN was obtained from Aldrich Chemical Co. as a white free-flowing solid.

Scheme I



stereoelectronic and steric effects as illustrated in Figure 1. The depicted conformations are derived from molecular mechanics calculations on the prototype systems R^1 = Me, R^2 = MTM.[15] Kahn and Hehre have suggested that nucleophilic additions to the 2-position of allylic alcohol derivatives proceed via a conformation in which the alkoxy grouping adopts an orientation perpendicular to the double bond and the nucleophile attacks anti to this grouping as illustrated in X.[16] A recent report by Nakamura and co-workers on S_N2' displacements of 4-alkoxy allylic halides with cuprates is consistent with this analysis.[17] According to Figure 1 all of the epoxy ethers should be able to attain the requisite geometry. Addition to **8**, **9**, and **13** can proceed anti to both the OR^2 grouping and the epoxide oxygen. Thus, in the absence of steric effects, these additions should be highly stereoselective. Addition to the 2*S* isomer **14**, on the other hand, must proceed syn to either the epoxide oxygen or to the allylic OR^2 substituent and stereoselectivity should therefore be diminished. It can be seen that our results are inconsistent with this analysis. The 2*S* isomer **14c** actually gives the best anti:syn ratio of S_N2' products.



X

Hanessian has shown that a proximal MTM ether can direct S_N2 displacements on secondary sulfonic esters by cuprate reagents.[18] An analogous directing effect may be operative for ether **14c**. However, the effect is probably small as other conformers with favorable OMTM orientations for directed additions, and differing in energy by less than 1 kcal/mol, were also found for **9c** and **13c**, but

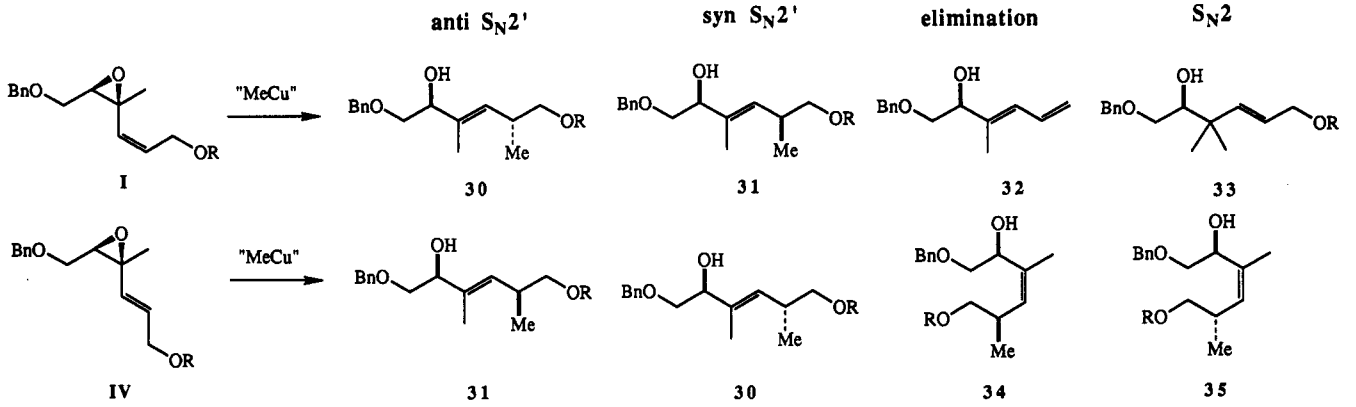
(15) MacroModel 3.0 was employed for these calculations. Each isomer was subjected to a Monte Carlo search routine of 2000 cycles with a 180° dihedral angle constraint on the vinyl-epoxide sigma bond to approximate the presumed transition state geometry. Each generated conformer was subjected to 50 interactions leading to an initial set of ca. 600 for **9c** and **14c** and ca. 300 conformers for **8c** and **13c**. Each set was further minimized with Batchmin V3.1b (250 iterations) to a final set of 15–40 conformers with average RMS of ca. 0.1. For a description of MacroModel, see: Mohamidi, F.; Richard, N.; Guida, W.; Liskamp, R.; Lipton, M.; Caufield, C.; Chang, G.; Hendrickson, T.; Still, W. *J. Computational Chem.* **1990**, *11*, 440.

(16) Kahn, S. D.; Hehre, W. J. *J. Org. Chem.* **1988**, *53*, 301.

(17) Nakamura, E.; Sekiya, K.; Arai, M.; Aoki, S. *J. Am. Chem. Soc.* **1989**, *111*, 3091.

(18) Hanessian, S.; Thavonekham, B.; DeHoff, B. *J. Org. Chem.* **1989**, *54*, 5831.

Table III. Cyanocuprate Additions to Vinyloxiranes I and IV

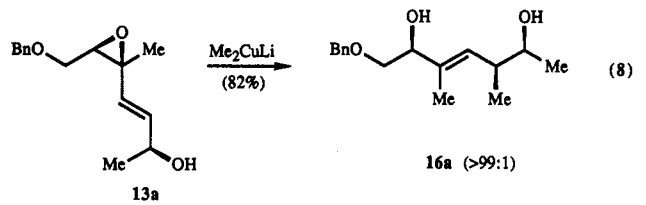


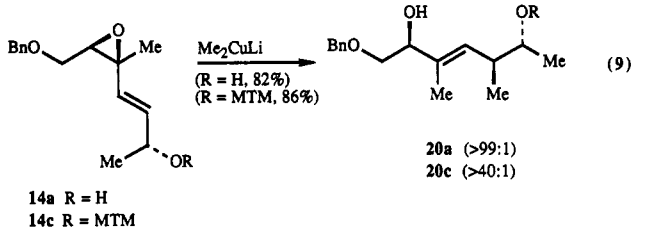
entry	epoxide	R	MeCu[a]	yield	elim (32)	S_N2 (33)	S_N2' (30, 31, 34, 35)	S_N2' products 30	S_N2' products 31	E/Z	anti/syn[d]
1	Ia	H	B[b]	74	0	18	82	99	1	>99:1	99:1
2	Ia	H	B[c]	66	0	16	84	97	3	>99:1	32:1
3	Ib	TBS	B[b]	100	95	0	5	98	0	49:1	>99:1
4	Ib	TBS	B[c]	96	20	0	80	75	25	>99:1	3:1
5	Ib	TBS	C[b]	98	100	0	0	0	0	-	-
6	Ib	TBS	C[c]	100	100	0	0	0	0	-	-
7	Ic	MTM	A	78	40	0	60	97	3	99:1	32:1
8	Ic	MTM	B[c]	85	0	0	100	79	21	>99:1	4:1
9	IVa	H	B[c]	72	0	23	77	15	85	24:1	5.7:1
10	IVb	TBS	B[c]	90	10	0	90	18	82	>99:1	4.5:1
11	IVc	MTM	B[c]	73	19	<1	80	22	78	>99:1	3.5:1

[a] A = Me_2CuLi in Et_2O–THF. B = MeCu(CN)Li in Et_2O. C = $Me_2Cu(CN)Li_2$ in Et_2O. [b] Impure CuCN. [c] Pure CuCN. [d] For *E* products.

not **8c**.[15] Conceivably, the MTM directing effect may be acting in opposition to the anti S_N2' stereoelectronic effect, thus diminishing stereoselectivity with **8c**, **9c**, and **13c**.

In conclusion, we have shown that methylcuprate additions to *cis*-(*E*)-vinyloxiranes **13** and **14** show good to excellent anti S_N2' diastereoselectivity. Addition of Me_2CuLi to alcohols **13a** and **14a** in particular affords only the (*E*)-anti addition products **16a** and **20a** (eqs 8 and 9),





along with minor amounts of S_N2 products. Of the protected alcohol derivatives, the (*R*)-MTM ether **14c** shows the highest anti:syn selectivity with Me_2CuLi as the preferred cuprate (eq 9). Differences in selectivity between the (*Z*)-(*S*)/(*R*) and (*E*)-(*S*)/(*R*) ethers **8b/c**, **9b/c**, **13b/c**, and **14b/c** can be ascribed to a combination of stereoelectronic (anti to epoxide oxygen) and steric factors (Figure 1). A directing effect may be operational with the MTM ethers. At present we have no satisfactory explanation for the exceedingly high selectivity observed with the (*E*)-(*S*)/(*R*) alcohols **13a** and **14a**. However, our findings indicate that S_N2' additions of cuprates to *cis*-(*E*)-vinyloxiranes such as **13** and **14** could be a useful route to subunits of polypropionate natural products, provided efficient methodology can be developed for controlling the allylic OH stereocenter. Work along these lines is in progress.

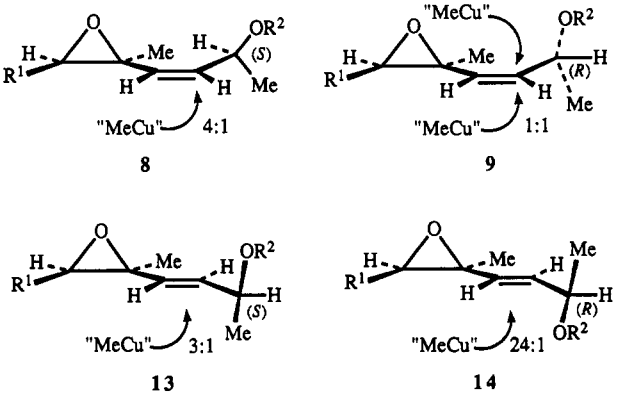


Figure 1. Diastereoselectivity in S_N2' additions to vinyloxiranes **8**, **9**, **13**, and **14**. Selectivity is indicated for R^2 = MTM.

Experimental Section[19]

(3*S*,4*R*)-5-(Benzyloxy)-1,1-dibromo-3,4-epoxy-3-methyl-

(19) The apparatus and methods described by G. W. Kramer, M. M. Midland, and A. B. Levy[20] were used to maintain an argon or nitrogen; atmosphere in the reaction flask. Anhydrous solvents were obtained by distillation from benzophenone ketyl (diethyl ether, THF, P_2O_5 (dichloromethane), calcium hydride (hexamethylphosphoramide), or sodium (benzene, toluene). Combustion microanalyses were performed by Atlantic Laboratories, Norcross, GA. Analytical thin-layer chromatography (TLC) on plates precoated with E. Merck silica gel 60 F254 of 0.25 mm thickness was routinely used to monitor reactions. E. Merck silica gel 60 (230–400 ASTM mesh) was employed for column chromatography according to the procedure of Still, Kahn, and Mitra.[21]

(20) Brown, H. C. *Organic Synthesis via Boranes*; Wiley: New York, 1975; pp 191–202.

(21) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

1-pentene (3). Aldehyde **2** was prepared from alcohol **1** by Swern oxidation[22] and used crude as described below in the prepartaion of enone **12**.

To a stirred solution of 7.45 g (28.4 mmol) of triphenylphosphine in 71 mL of dry CH_2Cl_2 at room temperature under argon was added 4.71 g (14.2 mmol) of carbon tetrabromide, whereupon the mixture turned orange.[6] After 15 min, 6.93 mL (49.7 mmol) of triethylamine was added, causing the mixture to turn dark red. The mixture was cooled to −78 °C, and 1.46 g (7.1 mmol) of crude aldehyde **2** was added in 20 mL of dry CH_2Cl_2. After stirring overnight with warming to 0 °C, the mixture was diluted with hexanes, and the resulting precipitate was filtered. The filtrate was concentrated under reduced pressure, and the residue was dissolved in a minimum amount of CH_2Cl_2. This procedure was repeated until no further precipitate was seen. The resulting oil was purified by flash chromatography on silica gel. Elution with 4:1 hexane–ether afforded 2.51 g (97%) of dibromo olefin **3**: IR (film) ν 2859, 1630, 1453, 1376, 1094, 900, 832, 737, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.36 (m, 5 H, phenyl H), 6.64 (s, 1 H, vinyl H), 4.62, 4.52 (AB q, 2 H, J = 11.8 Hz, $PhCH_2$), 3.81, 3.40 (AB of ABX, J_{AB} = 11.2 Hz, J_{AX} = 3.7 Hz, J_{BX} = 6.5 Hz, CH_2OBn), 3.18 (X of ABX, J_{AX} = 3.7 Hz, J_{BX} = 6.5 Hz, epoxy H), 1.51 (s, 3 H, epoxy CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.9, 136.0, 128.5 (2 C), 127.8 (3 C), 92.5, 73.4, 69.5, 62.6, 60.4, 21.0; $[\alpha]^{23}_D$ +4.2° (*c* 2.42, EtOH). Anal. Calcd for $C_{13}H_{14}O_2Br_2$: C, 43.13; H, 3.90; Br, 44.14. Found: C, 43.06; H, 3.90; Br, 44.21.

(3*S*,4*R*)-5-(Benzyloxy)-1-bromo-3,4-epoxy-3-methyl-1-pentyne (4). To a stirred solution of 1.86 g (5.13 mmol) of dibromo olefin **3** in 26 mL of THF was added 15.4 mL (15.4 mmol) of 1.0 M tetrabutylammonium fluoride in THF.[7] The mixture was stirred overnight, diluted with water, and extracted with ether. The combined extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The brown oil was purified by flash chromatography on silica gel. Elution with 3:1 hexane–ether afforded 1.35 g (94%) of acetylenic bromide **4**: IR (film) ν 2861, 2212, 1453, 1379, 1300, 1233, 1093, 1028, 838, 737, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.36 (m, 5 H, phenyl H), 4.59 (AB q, 2 H, J = 11.8 Hz, $PhCH_2$), 3.77, 3.66 (AB of ABX, J_{AB} = 11.3 Hz, J_{AX} = 5.0 Hz, J_{BX} = 5.5 Hz, CH_2OBn), 3.09 (X of ABX, 1 H, J = 5.25 Hz, epoxy H), 1.53 (s, 3 H, epoxy CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.9, 128.5 (2 C), 127.8 (3 C), 77.4, 73.5, 69.5, 62.6, 52.0, 45.4, 22.9; $[\alpha]^{23}_D$ −21.0° (*c* 2.14, $CHCl_3$); HRMS calcd for $C_{13}H_{13}O_2Br{\cdot}NH_4$ ($M + NH_4$) 298.0443, found *m/e* 298.0452. Anal. Calcd for $C_{13}H_{13}O_2Br$: C, 55.54; H, 4.66; Br, 28.42. Found: C, 55.59; H, 4.69; Br, 28.33.

(2*S*,5*S*,6*R*)-7-(Benzyloxy)-5,6-epoxy-5-methyl-3-heptyn-2-ol (5a). To a stirred solution of 6.22 mL (6.22 mmol) of 1.0 M lithium aluminum hydride in THF in 13 mL of dry THF under argon at room temperature was added 6.22 mL (6.22 mmol) of 1.0 M ethanol in THF dropwise over 30 min. The solution was stirred for 30 additional min, and then 1.28 g (6.22 mmol) of (*S*)-(−)-1,1′-biaphthol in 12.5 mL of dry THF was added dropwise over 1 h. The solution became milky white, and stirring was continued for 1 h. The mixture was cooled to −78 °C, a solution of 0.530 g (2.2 mmol) of ynone **7** in 5 mL of dry THF was added dropwise over 30 min, and the mixture was stirred for 4 h. The reaction was quenched with 3 mL of ethanol, and the mixture was stirred with 50 mL of saturated aqueous Rocelle's salts for 2 h. The aqueous layer was extracted with ether. The combined extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The clear oil was purified by flash chromatography on silica gel. Elution with 2:1 ether–hexane afforded 0.404 g (76%) of an inseparable 6.2:1 mixture of diastereomeric alcohols **5a** and **6a** as determined by ^1H NMR spectral analysis of the derived ethers **8b** and **9b**: ^1H NMR (300 MHz, $CDCl_3$) δ 7.32 (m, 5 H, phenyl H), 4.59, 4.53 (AB q, 2 H, J = 11.9 Hz, $PhCH_2$), 4.47 (q, 1 H, J = 6.6 Hz, CH_3CH), 3.76, 3.66 (AB of ABX, J_{AB} = 11.3, J_{AX} = 5.0, J_{BX} = 5.5 Hz, CH_2OBn), 3.10 (X of ABX, 1 H, J_{AX} = 5.2, J_{BX} = 5.3 Hz, epoxy H), 2.1 (bs, 1 H, OH), 1.52 (s, 3 H, epoxy H), 1.38 (d, 3 H, J = 6.6 Hz, CH_3CH); HRMS calcd for $C_{15}H_{18}O_3$ (M) 264.1604, found *m/e* 264.1600.

(2*S*,5*S*,6*R*)-7-(Benzyloxy)-2-[(*tert*-butyldimethylsilyl)oxy]-5,6-epoxy-5-methyl-3-heptyne (5b). To a stirred solution of 97.1 mg (0.394 mmol) of the foregoing 6.2:1 mixture of propargyl alcohols **5a** and **6a** in 2.0 mL of dry DMF at room temperature under nitrogen was added 85.9 mg (1.26 mmol) of imidazole and 95.1 mg (0.631 mmol) of *tert*-butyldimethylsilyl chloride. The mixture was stirred overnight, and the reaction was quenched with 2 mL of water. The aqueous layer was extracted with CH_2Cl_2. The combined extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The crude oil was purified by flash chromatography on silica gel. Elution with 3:1 hexane–ether afforded 138 mg (97%) of a 6.2:1 mixture of silyl ethers **5b** and **6b**: IR (film) ν 2931, 2858, 2362, 1472, 1317, 1253, 1101, 994, 838, 779, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.33 (m, 5 H, phenyl H), 4.62, 4.52 (AB q, 2 H, J = 11.8 Hz, $PhCH_2$), 4.48 (q, 1 H, J = 6.5 Hz, carbinyl H), 3.80, 3.63 (AB of ABX, J_{AB} = 11.3, J_{AX} = 4.5, J_{BX} = 5.7 Hz, CH_2OBn), 3.09 (X of ABX, J_{AX} = 4.5, J_{Bx} = 5.7 Hz, epoxy H), 1.51 (s, 3 H, epoxy CH_3), 1.35 (d, 3 H, J = 6.5 Hz, $CHCH_3$), 0.88 (s, 9 H, $SiC(CH_3)_3$), 0.09, 0.08 (s, 6 H, $SiCH_3$'s); ^{13}C NMR (75 MHz, $CDCl_3$) 138.4, 128.8 (2 C), 128.2 (2 C), 128.1, 87.4, 80.5, 73.7, 70.2, 63.1, 59.3, 51.5, 26.1 (3 C), 25.6, 23.6, 18.5, −4.2, −4.5 ppm; $[\alpha]^{23}_D$ −69.9° (*c* 1.15, $CHCl_3$). Anal. Calcd for $C_{21}H_{31}O_3Si$: C, 70.15; H, 8.69. Found: C, 69.87; H, 8.94.

(2*S*,5*S*,6*R*)-7-(Benzyloxy)-2-[(methylthio)methoxy]-5,6-epoxy-5-methyl-3-heptyne (5c). A solution of 48.0 mg (0.195 mmol) of a 6.2:1 mixture of alcohols **5a** and **6a** in 0.78 mL of dimethyl sulfoxide, 0.51 mL of acetic anhydride, and 0.16 mL of glacial acetic acid was stirred for 2 days. The reaction was quenched with saturated sodium bicarbonate, and the aqueous layer was extracted with ether. The combined extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The oil was purified by flash chromatography on silica gel. Elution with 3:1 hexane–ether afforded 29.8 mg (50%) of a 6.2:1 mixture of thioethers **5c** and **6c** and 22.3 mg (50%) of ynone **7**; IR (film) ν 2983, 2924, 2854, 2354, 2331, 1453, 1300, 1094, 757, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.33 (m, 5 H, phenyl H), 4.71, 4.63 (AB q, 2 H, J = 11.6 Hz, SCH_2O), 4.6 (m, 1 H, $CHCH_3$), 4.62, 4.54 (AB q, 2 H, J = 11.9 Hz, $PhCH_2$), 3.77, 3.64 (AB of ABX, J_{AB} = 11.3, J_{AX} = 4.8, J_{BX} = 5.6 Hz, CH_2OBn), 3.10 (X of ABX, 1 H, J_{AX} = 5.0, J_{BX} = 5.4 Hz, epoxy H), 2.12 (s, 3 H, CH_3S), 1.53 (s, 3 H, epoxy CH_3), 1.39 (d, 3 H, J = 6.7 Hz, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.8, 128.7 (2 C), 127.8 (3 C), 83.9, 82.2, 73.5, 72.7, 69.6, 62.6, 62.5, 61.4, 51.2, 31.6, 26.9, 23.2, 22.7, 21.6, 14.1, 14.0; $[\alpha]^{23}_D$ −169.8° (*c* 1.61, $CHCl_3$); HRMS calcd for $C_{17}H_{26}O_3S$ (M) 310.1603, found *m/e* 310.1615.

(2*R*,5*S*,6*R*)-7-(Benzyloxy)-5,6-epoxy-5-methyl-3-heptyn-2-ol (6a). To a stirred solution of 1.98 mL (1.98 mmol) of a 1.0 M solution of lithium aluminum hydride in THF in 76 mL of dry ether at room temperature under argon was added 1.29 g (4.56 mmol) of Chirald in 5 mL of dry ether. The solution was stirred for 3 min and cooled to −78 °C. The mixture became extremely thick upon cooling. To this slurry was added 0.371 g (1.52 mmol) of ynone **7** in 5 mL of dry ether dropwise over 30 min. The solution was stirred for 1 h and quenched with ethanol and Rochelle's salts. The aqueous layer was extracted with ether. The combined extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The thick oil was purified by flash chromatography on silica gel. Elution with 1:1 hexane–ether afforded 0.242 g (65%) of a 5.1:1 mixture of alcohols **6a** and **5a** by ^1H NMR spectral analysis of the derived ethers **9b** and **8b**: IR (film) ν 3406, 2980, 1453, 1079, 846, 740, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.32 (m, 5 H, phenyl H), 4.59, 4.53 (AB q, 2 H, J = 11.9 Hz, $PhCH_2$), 4.47 (q, 1 H, J = 6.6 Hz, CH_3CH), 3.76, 3.66 (AB of ABX, J_{AB} = 11.3, J_{AX} = 5.0, J_{BX} = 5.5 Hz, CH_2OBn), 3.10 (X of ABX, 1 H, J_{AX} = 5.2, J_{BX} = 5.3 Hz, epoxy H), 2.1 (bs, 1 H, OH), 1.52 (s, 3 H, epoxy H), 1.38 (d, 3 H, J = 6.6 Hz, CH_3CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.9, 128.5 (2 C), 127.8 (3 C), 86.6, 80.9, 73.4, 69.5, 62.6, 58.2, 51.3, 24.0, 23.1; $[\alpha]^{23}_D$ +25.7° (*c* 2.64, $CHCl_3$); HRMS calcd for $C_{15}H_{18}O_3{\cdot}NH_4$ ($M + NH_4$) 264.1604, found *m/e* 264.1600. Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 73.53; H, 7.74.

(2*R*,5*S*,6*R*)-7-(Benzyloxy)-2-[(*tert*-butyldimethylsilyl)oxy]-5,6-epoxy-5-methyl-3-heptyne (6b). The procedure described for TBS ether **5b** was employed with 53.9 mg (0.219 mmol) of a 5.1:1 mixture of alcohols **6a** and **5a** in 1.1 mL of DMF, 47.8 mg (0.70 mmol) of imidazole, and 52.8 mg (0.350 mmol) of *tert*-butyldimethylsilyl chloride. The product was purified by flash chromatography on silica gel. Elution with 4:1 hexane–ether

(22) Omura, K.; Swern, D. *Tetrahedron* **1978**, *34*, 1651.

afforded 61.3 mg (98%) of a 5.1:1 mixture of **6b** and **5b**: IR (film) ν 2930, 2857, 2231, 1472, 1317, 1252, 1101, 994, 837, 779, 735, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.33 (m, 5 H, phenyl H), 4.63, 4.54 (AB q, 2 H, J = 11.9 Hz, $PhCH_2$), 4.5 (q, 1 H, J = 6.5 Hz, CH_3CH), 3.80, 3.65 (AB of ABX, J_{AB} = 11.3, J_{AX} = 4.6, J_{BX} = 5.7 Hz, CH_2OBn), 3.09 (X of ABX, 1 H, J_{AX} = 4.7, J_{BX} = 5.6 Hz, epoxy H), 1.52 (s, 3 H, epoxy CH_3), 1.36 (d, 3 H, J = 6.5 Hz, CH_3CH), 0.89 (s, 9 H, $SiC(CH_3)_3$), 0.11, 0.09 (s, 3 H, $SiCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.0, 128.4 (3 C), 127.8 (2 C), 87.3, 80.1, 73.4, 69.8, 62.6, 58.9, 51.2, 18.1 (3 C), 25.3, 23.3, 18.2, -4.6, -4.9, $[\alpha]^{23}_D$ +27.2° (c 2.71, $CHCl_3$); HRMS calcd for $C_{21}H_{32}O_3Si$ (M) 360.2121, found m/e 360.2118.

(2*R*,5*S*,6*R*)-7-(Benzyloxy)-2-[(methylthio)methoxy]-5,6-epoxy-5-methyl-3-heptyne (6c). The procedure described for thioether **5c** was employed with 69.1 mg (0.280 mmol) of a 5.1:1 mixture of alcohols **6a** and **5a** in 1.12 mL of dimethyl sulfoxide, 0.74 mL of acetic anhydride, and 0.22 mL of glacial acetic acid. The product was purified by flash chromatography on silica gel. Elution with 4:1 hexane–ether afforded 46.6 mg (54%) of a 5.1:1 mixture of thioethers **6c** and **5c** and 21.0 mg (31%) of ynone **7**: IR (film) δ 2985, 2922, 2862, 1747, 1453, 1300, 1094, 1049, 859, 739, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.33 (m, 5 H, phenyl H), 4.71, 4.64 (AB q, 2 H, J = 11.4 Hz, SCH_2O), 4.61, 4.53 (AB q, 2 H, J = 11.7 Hz, $PhCH_2$), 4.56 (q, 1 H, J = 6.7 Hz, $CHCH_3$), 3.76, 3.64 (AB of ABX, J_{AB} = 11.3, J_{AX} = 4.8, J_{BX} = 5.6 Hz, CH_2OBn), 3.10 (X of ABX, 1 H, J_{AX} = 5.1, J_{BX} = 5.3 Hz, epoxy H), 2.11 (s, 3 H, SCH_3), 1.52 (s, 3 H, epoxy CH_3), 1.39 (d, 3 H, J = 6.7 Hz, $CHCH_3$); $[\alpha]^{23}_D$ + 158.3° (c 2.33, $CHCl_3$); HRMS calcd for $C_{17}H_{26}O_3S$ (M) 310.1603, found m/e 310.1615.

(5*S*,6*R*)-7-(Benzyloxy)-5,6-epoxy-5-methyl-3-heptyn-2-one (7). To a stirred solution of 1.32 g (4.7 mmol) of acetylenic bromide **4** in 23.0 mL of dry THF at -78 °C under argon was added 2.0 mL (5.16 mmol) of 2.6 M n-butyllithium in hexanes dropwise.[7] The mixture was stirred for 20 min and quenched with 5.6 mL (5.6 mmol) of 1.0 M ethanol in THF. To ensure complete quenching, the mixture was stirred for 30 min at -78 °C and then 2.3 mL (6.10 mmol) of 2.6 M n-butyllithium in hexanes was added and the mixture was stirred an additional 30 min. To this solution was added 0.784 mL (14.1 mmol) of acetaldehyde. The mixture was stirred for 5 h with warming to room temperature and then it was diluted with water, and the aqueous layer was extracted with ether. The combined extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The yellow oil was purified by flash chromatography on silica gel. Elution with 2:1 hexane–ether afforded 0.954 g (83%) of a 1:1 mixture of alcohols **5** and **6** and 0.159 g (17%) of the terminal acetylene (**4**, H in place of Br). The alcohol mixture was used directly without further purification.

To a stirred solution of 0.954 g (3.9 mmol) of a 1:1 mixture of alcohols **5a** and **6a** in 19.3 mL of dry CH_2Cl_2 at room temperature under argon was added 2.14 g (5.0 mmol) of the Dess–Martin periodinane reagent.[23] The cloudy solution was stirred overnight and poured into 50 mL of sat. sodium bicarbonate containing 5 g of sodium thiosulfate. The aqueous layer was extracted with CH_2Cl_2, and the combined extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The crude oil was purified by flash chromatography on silica gel. Elution with 2:1 hexane–ether afforded 0.885 g (94%) of ynone **7**: IR (film) ν 2863, 2219, 1681, 1453, 1359, 1305, 1251, 1190, 1092, 845, 740, 669 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.36 (m, 5 H, phenyl H), 4.64, 4.53 (AB q, 2 H, J = 11.9 Hz, $PhCH_2$), 3.75, 3.65 (AB of ABX, J_{AB} = 11.3 Hz, J_{AX} = 4.9 Hz, J_{BX} = 5.5 Hz, CH_2OBn), 3.20 (X of ABX, 1 H, J_{AX} = 5.1 Hz, J_{BX} = 5.3 Hz, epoxy H), 2.28 (s, 3 H, $COCH_3$), 1.53 (s, 3 H, epoxy CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 183.6, 137.6, 128.5 (2 C), 127.9, 127.8 (2 C), 87.6, 82.8, 73.5, 69.2, 63.1, 50.6, 32.6, 22.2; $[\alpha]^{23}_D$ -3.3° (c 2.97, $CHCl_3$); HRMS calcd for $C_{15}H_{16}O_3$ (M) 243.1021, found m/e 243.1019.

(*Z*)-(2*R*,3*S*,6*S*)-1-(Benzyloxy)-6-[(*tert*-butyldimethylsilyl)oxy]-2,3-epoxy-3-methyl-4-heptene (8b). To a round-bottom flask was added 30.8 mg (0.0854 mmol) of a 6.2:1 mixture of alkynes **5b** and **6b**, 6.2 mg of Lindlar's catalyst and 85 μL of dry benzene. The flask was flushed with hydrogen, and a balloon filled with hydrogen was placed on the flask. The dark slurry was stirred vigorously for 1.5 h whereupon the mixture was filtered through a plug of Celite and concentrated under reduced pressure affording 30.9 mg (100%) of a 6.2:1 mixture of alkenes **8b** and **9b**: ^1H NMR (300 MHz, $CDCl_3$) δ 7.33 (m, 5 H, phenyl H), 5.58 (dd, 1 H, J = 7.7, 11.7 Hz, vinyl H), 5.31 (d, 1 H, J = 11.7 Hz, vinyl H), 4.94 (m, 1 H, carbinyl H), 4.58, 4.46 (AB q, 2 H, J = 11.8 Hz, $PhCH_2$), 3.50 (m, 2 H, CH_2OBn), 3.06 (t, 1 H, J = 5.4 Hz, epoxy H), 1.38 (s, 3 H, epoxy CH_3), 1.20 (d, 3 H, J = 6.3 Hz, CH_3CH), 0.86 (s, 9 H, $SiC(CH_3)_3$), 0.38 (s, 3 H, $SiCH_3$), 0.007 (s, 3 H, $SiCH_3$); HRMS calcd for $C_{21}H_{34}O_3Si$ (M - CH_3) 362.2277, found m/e 362.2267.

(*Z*)-(2*S*,5*S*,6*R*)-7-(Benzyloxy)-2-[(methylthio)methoxy]-5,6-epoxy-5-methyl-3-heptene (8c). Hydrogenation of 32.2 mg (0.105 mmol) of a 6.2:1 mixture of thioethers **5c** and **6c** in 105 μL of benzene and 1 drop of quinoline over 8 mg of Lindlar's catalyst was carried out as described above. The crude product was purified by flash chromatography on silica gel. Elution with 2:1 hexane–ether afforded 24.2 mg (75%) of a 6.2:1 mixture of the Z olefins **8c** and **9c**: IR (film) ν 2968, 2922, 2854, 1750, 1453, 1367, 1292, 1065, 736, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.33 (m, 5 H, phenyl H), 5.57 (d, 1 H, J = 11.6 Hz, vinyl H), 5.47 (dd, 1 H, J = 11.6, 9.5 Hz, vinyl H), 4.83 (m, 1 H, CHOMTM), 4.59, 4.48 (AB q, 2 H, J = 11.8 Hz, $PhCH_2$), 4.54, 4.43 (AB q, 2 H, J = 11.3 Hz, SCH_2O), 3.53, 3.47 (AB of ABX, J_{AB} = 10.9, J_{AX} = 5.3, J_{BX} = 5.6 Hz, CH_2OBn), 3.08 (X of ABX, 1 H, J_{AX} = 5.4, J_{BX} = 5.5 Hz, epoxy H), 2.12 (s, 3 H, CH_3S), 1.41 (s, 3 H, epoxy CH_3), 1.22 (d, 3 H, J = 6.4 Hz, CH_3CH); HRMS calcd for $C_{17}H_{24}O_3S$ (M) 308.1446, found m/e 308.1459.

(*Z*)-(2*R*,5*R*,6*R*)-7-(Benzyloxy)-5,6-epoxy-5-methyl-3-hepten-2-ol (9a). The procedure described for epoxyheptene **8b** was employed with 5.0 mg (20.3 μmol) of an 8.6:1 mixture of propargylic alcohols **6a** and **5a** in 20 μL of ethyl acetate and 1 mg of Lindlar's catalyst. The flask was flushed with hydrogen and fitted with a hydrogen-filled balloon. The slurry was stirred for 2.5 h, filtered through a plug of silica gel, and concentrated under reduced pressure. The oil was purified by flash chromatography on silica gel. Elution with 2:1 ether–hexane afforded 4.8 mg (96%) of an 8.6:1 mixture of vinyloxiranes **9a** and **8a** according to ^1H NMR spectral analysis: ^1H NMR (300 MHz, $CDCl_3$) δ 7.35 (m, 5 H, phenyl H), 5.58–5.44 (m, 2 H, vinyl H), 4.60 (m, 1 H, carbinyl H), 4.55 (s, 2 H, $PhCH_2$), 3.62, 3.39 (AB of ABX, 2 H, J_{AB} = 10.7, J_{AX} = 4.7, J_{BX} = 7.3 Hz, CH_2OBn), 3.08 (X of ABX, 1 H, J_{AX} = 4.7, J_{BX} = 7.3 Hz, CH_2CH), 2.83 (bs, 1 H, alcohol), 1.42 (s, 3 H, epoxy CH_3), 1.21 (d, 3 H, J = 6.4 Hz, $CHCH_3$). Anal. Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.69; H, 8.01.

(*Z*)-(2*R*,5*S*,6*R*)-7-(Benzyloxy)-2-[(*tert*-butyldimethylsilyl)oxy]-5,6-epoxy-5-methyl-3-heptene (9b). The procedure described for epoxyheptene **8b** was employed with 54.3 mg (0.151 mmol) of a 5.0:1 mixture of alkynes **6b** and **5b**, 0.15 mL of dry benzene, and 14.0 mg of Lindlar's catalyst. The crude product was purified by flash chromatography on silica gel. Elution with 5:1 hexane–ether afforded 46.5 mg (85%) of a 5.0:1 mixture of alkenes **9b** and **8b**: IR (film) ν 2928, 2854, 1724, 1472, 1362, 1255, 1078, 995, 836, 776, 697 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.32 (m, 5 H, phenyl H), 5.46 (dd, 1 H, J = 11.6, 8.6 Hz, vinyl H), 5.31 (d, 1 H, J = 11.6 Hz, vinyl H), 4.87 (m, 1 H, CH_3CH), 4.57, 4.47 (AB q, 2 H, J = 11.9, $PhCH_2$), 3.51, 3.37 (AB of ABX, J_{AB} = 11.0, J_{AX} = 4.8, J_{BX} = 6.0 Hz, CH_2OBn), 2.98 (X of ABX, 1 H, J_{AX} = 4.8, J_{BX} = 6.0 Hz, epoxy H), 1.40 (s, 3 H, epoxy CH_3), 1.09 (d, 3 H, J = 6.2 Hz, CH_3CH), 0.87 (s, 9 H, $SiC(CH_3)_3$), 0.06, 0.05 (s, 6 H, $SiCH_3$s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.2, 137.9, 128.4 (2 C), 127.8 (3 C), 122.9, 73.3, 69.1, 65.7, 60.6, 59.7, 25.9 (3 C), 24.0, 23.2, 18.2, -4.4, -4.3; $[\alpha]^{23}_D$ -24.1° (c 1.35, $CHCl_3$); HRMS calcd for $C_{21}H_{34}O_3Si$ (M - CH_3) 362.2277, found m/e 362.2276.

(*Z*)-(2*R*,5*S*,6*R*)-7-(Benzyloxy)-2-[(methylthio)methoxy]-5,6-epoxy-5-methyl-3-heptene (9c). The procedure described for epoxyheptene **8b** was employed with 46.6 mg (0.152 mmol) of a 5.1:1 mixture of alkynes **6c** and **5c** in 0.152 mL of benzene, 12 mg of Lindlar's catalyst, and 1 drop of quinoline. The product was purified by flash chromatography on silica gel. Elution with 4:1 hexane–ether afforded 33.9 mg (73%) of a 5.1:1 mixture of alkenes **9c** and **8c**: IR (film) ν 2975, 2922, 2856, 1726, 1453, 1375, 1299, 1067, 875, 737, 698 cm^{-1}; ^1H NMR (300 MHz,

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$CDCl_3$) δ 7.31 (m, 5 H, phenyl H), 5.60 (d, 1 H, J = 11.5 Hz, vinyl H), 5.36 (dd, 1 H, J = 9.2, 11.5 Hz, vinyl H), 4.86 (m, 1 H, CH_3CH), 4.63, 4.50 (AB_q, 2 H, J = 11.3 Hz, SCH_2O), 4.57, 4.48 (AB q, 2 H, J = 11.9 Hz, $PhCH_2$), 3.52, 3.38 (AB of ABX, J_{AB} = 11.0, J_{AX} = 4.8, J_{BX} = 6.0 Hz, CH_2OBn), 3.02 (X of ABX, 1 H, J_{AX} = 4.9, J_{BX} = 5.9 Hz, epoxy H), 2.13 (s, 3 H, CH_3S), 1.42 (s, 3 H, epoxy CH_3), 1.14 (d, 3 H, J = 6.3 Hz, CH_3CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.6, 135.7, 128.4 (2 C), 128.1, 127.8 (2 C), 127.8, 73.3, 72.0, 69.2, 69.0, 60.8, 59.4, 23.4, 20.6, 13.9; $[\alpha]^{23}_D$ +90.0° (c 1.02, $CHCl_3$); HRMS calcd for $C_{17}H_{24}O_3S$ (M) 308.1446, found m/e 308.1459.

(5*S*,6*R*)-7-(Benzyloxy)-5,6-epoxy-5-methyl-3-hepten-2-one (12). To a solution of 0.63 mL (7.2 mmol) of oxalyl chloride in 12 mL of dry CH_2Cl_2 under argon at −78 °C was added 1.02 mL (14.4 mmol) of dimethyl sulfoxide. The mixture was allowed to stir for 20 min, and then 1.0 g (4.8 mmol) of alcohol 1 in 5 mL of dry CH_2Cl_2 was added and stirring was continued for 1.5 h. The reaction was quenched with 3.35 mL (24.0 mmol) of triethylamine and warmed to 0 °C with stirring. The thick mixture was diluted with 20 mL of water, and the phases were separated. The organic phase was washed with water, dried over Na_2SO_4, and concentrated under reduced pressure. The residual aldehyde 2 was used directly in the next step.

To a stirred solution of 0.966 g (5.82 mmol) of dimethyl 2-oxopropylphosphonate in 48 mL of dry acetonitrile under argon was added 0.247 g (5.82 mmol) of freshly dried lithium chloride, followed by 0.683 mL (4.85 mmol) of 1,8-diazabicyclo[5.4.0]-7-undecene and then the foregoining crude aldehyde 2 in 5 mL of dry acetonitrile.[11] The solution was stirred overnight and quenched with water. The aqueous phase was extracted with ether, and the combined extracts were dried over $MgSO_4$. The yellow oil was purified by flash chromatography on silica gel. Elution with 2:1 hexane–ether afforded 1.0 g (84%) of enone 12: IR (film) ν 2980, 2933, 2870, 1675, 1625, 1360, 1255, 1090, 980, 735, 700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.3 (m, 5 H, phenyl H), 6.62 (d, 1 H, J = 16.1 Hz, vinyl H), 6.20 (d, 1 H, J = 16.1, vinyl H), 4.59, 4.54 (AB q, 2 H, J = 4.4 Hz, $PhCH_2$), 3.53, 3.49 (AB of ABX, 2 H, J_{AB} = 11.1, J_{AX} = 5.6, J_{BX} = 5.1 Hz, CH_2OHBn), 3.24 (t, 1 H, J = 5.3 Hz, epoxide H), 2.18 (s, 3 H, $OCCH_3$), 1.46 (s, 3 H, epoxide CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.3, 137.6, 132.1, 128.5 (2 C), 127.9 (2 C), 127.8 (2 C), 73.3, 67.6, 64.2, 59.1, 27.7, 21.2; $[\alpha]^{23}_D$ +27.1° (c 2.23, $CHCl_3$); HRMS calcd for $C_{15}H_{18}O_3$ (M) 246.1256, found m/e 246.1254.

(*E*)-(2*R*,5*R*,6*R*)-7-(Benzyloxy)-5,6-epoxy-5-methyl-3-hepten-2-ol (14a). The procedure described for alcohol **6a** was employed with 0.217 g (0.882 mmol) of enone 12. The product was purified by flash chromatography on silica gel. Elution with 1:1 hexane–ether afforded 0.154 g (71%) of a 3:1 mixture of alohols **14a** and **13a**: IR (film) ν 3430, 3000, 2980, 1740, 1460, 1285, 1105, 1085, 985, 765, 710 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.32 (m, 5 H, phenyl H), 5.76 (dd, 1 H, J = 15.7, 5.8 Hz, vinyl H), 5.54 (d, 1 H, J = 15.7 Hz, vinyl H), 4.60, 4.47 (AB q, 2 H, J = 12.1 Hz, $PhCH_2$), 4.26 (m, 1 H, $CHOH$), 3.53 (d, 2 H, J = 5.4 Hz, CH_2OBn), 3.15 (t, 1 H, J = 5.4 Hz, epoxy H), 2.14 (d, 1 H, J = 5.0 Hz, OH), 1.42 (s, 3 H, epoxy CH_3), 1.20 (d, 3 H, J = 6.4 Hz, CH_3CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.9, 137.8, 128.4 (3 C), 127.8 (2 C), 126.6, 73.1, 68.1, 67.9, 63.6, 59.3, 23.3, 21.9; $[\alpha]^{23}_D$ +10.8° (c, $CHCl_3$). Anal. Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.23; H, 8.15.

(*E*)-(2*R*,5*S*,6*R*)-7-(Benzyloxy)-2-[(*tert*-butyldimethylsilyl)oxy]-5,6-epoxy-5-methyl-3-heptene (14b). The procedure described for TBS ether **5b** was employed with 100.5 mg (0.405 mmol) of a 3:1 mixture of alcohols **14a** and **13a** in 2 mL of dry DMF, 88.2 mg (1.30 mmol) of imidazole, and 97.6 mg (0.648 mmol) of *tert*-butyldimethylsilyl chloride. The product was purified by flash chromatography on silica gel. Elution with 4:1 hexane–ether afforded 124.1 mg (85%) of a 3:1 mixture of silyl ethers **14b** and **13b**: IR (film) ν 2928, 2856, 1726, 1471, 1360, 1312, 1255, 1150, 1093, 973, 917, 835, 777, 736, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.32 (m, 5 H, phenyl H), 5.75 (dd, 1 H, J = 4.7, 15.6 Hz, vinyl H), 5.54 (d, 1 H, J = 15.6 Hz, vinyl H), 4.59, 4.48 (AB q, 2 H, J = 11.9 Hz, $PhCH_2$), 4.30 (m, 1 H, $CHCH_3$), 3.60, 3.50 (AB of ABX, J_{AB} = 11.1, J_{AX} = 4.8, J_{BX} = 5.9 Hz, CH_2OBn), 3.14 (X of ABX, 1 H, J_{AX} = 4.7, J_{BX} = 5.9 Hz, epoxy H), 1.41 (s, 3 H, epoxy CH_3), 1.15 (d, 3 H, J = 6.4 Hz, CH_3CH), 0.87 (s, 9 H, $SiC(CH_3)_3$), 0.03, 0.02 (s, 6 H, $SiCH_3$s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.4, 137.9, 128.4(2C), 127.8 (2 C), 127.7, 125.3, 73.2, 68.4, 63.7, 59.3, 53.4, 25.9 (3 C), 24.4, 22.0, 18.3, −4.7, −4.8; $[\alpha]^{23}_D$ +9.8° (c 1.97, $CHCl_3$). Anal. Calcd for $C_{21}H_{34}O_3Si$: C, 70.00; H, 9.88. Found: C, 69.61; H, 10.03.

(*E*)-(2*R*,5*S*,6*R*)-7-(Benzyloxy)-2-[(methylthio)methoxy]-5,6-epoxy-5-methyl-3-heptene (14c). To a stirred solution of 154.4 mg (0.62 mmol) of a 3:1 mixture of alcohols **14a** and **13a** in 2 mL of 1,2-dimethoxyethane at room temperature under argon was added 37 mg (0.933 mmol) of 60% sodium hydride in mineral oil. The slurry was stirred for 1 h, 57 μL (0.684 mmol) of chloromethyl methyl sulfide and 102.5 mg (0.684 mmol) of sodium iodide were added, and the solution was stirred overnight. The reaction was quenced with sodium bicarbonate, and the aqueous layer was extracted with ether. The combined extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The product was purified by flash chromatography on silical gel. Elution with 1:1 ether–hexane afforded 110.3 mg (58%) of a 3:1 mixture of thioethers **14c** and **13c**: ^1H NMR (300 MHz, $CDCl_3$) δ 7.32 (m, 5 H, phenyl H), 5.58 (m, 2 H, vinyl H), 4.59, 4.42 (AB q, 2 H, J = 11.4 Hz, SCH_2O), 4.58, 4.48 (AB q, 2 H, J = 11.9 Hz, $PhCH_2$), 4.25 (m, 1 H, CH_3CH), 3.57, 3.51 (AB of ABX, J_{AB} = 11.1 Hz, J_{AX} = 5.0 Hz, J_{BX} = 5.7 Hz, CH_2OBn), 3.15 (X of ABX, 1 H, J_{AX} = 5.2 Hz, J_{BX} = 5.5 Hz, epoxy H), 2.12 (s, 3 H, SCH_3), 1.42 (s, 3 H, epoxy CH_3), 1.22 (d, 3 H, J = 6.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.8, 134.8, 129.7, 128.4 (3 C), 127.8 (2 C), 73.3, 72.0 (2 C), 68.2, 63.6, 59.2, 21.8, 21.2, 13.8; $[\alpha]^{23}_D$ +78.4° (c 3.59, $CHCl_3$). Anal. Calcd for $C_{15}H_{20}O_3$: C, 66.21; H, 7.84. Found: C, 66.30; H, 7.95.

Representative Cuprate Additions to Vinyloxiranes: A. Gilman Cuprate. To a stirred slurry of 41.5 mg (0.219 mmol) of copper(I) iodide in 0.55 mL of dry THF under argon at −20 °C was added 0.314 mL (0.438 mmol) of 1.4 M methyllithium in ether. The solution became clear and was stirred for 0.5 h. A solution of 15.9 mg (0.0439 mmol) of a 3:1 mixture of vinyloxiranes **14b** and **13b** in dry THF was added dropwise, and the mixture was stirred overnight with warming to 0 °C. The reaction was quenched with 2 mL of 1:1 3% aqueous ammonium hydroxide–saturated aqueous ammonium chloride. The solution was stirred until the copper salts were completely dissolved into the aqueous layer. The aqueous layer was extracted with ether, and the combined extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was filtered through a plug of silica gel with ether and concentrated under reduced pressure affording 14.9 mg (90%) of a mixture of addition products.

B. Lower Order Cyano Cuprate. To a stirred slurry of 17.3 mg (0.193 mmol) of copper(I) cyanide[14] in 0.5 mL of dry ether under argon at −23 °C was added 0.138 mL (0.193 mmol) of 1.4 M methyllithium in ether dropwise. The solution became clear and was stirred for 0.5 h. A solution of 14.0 mg (0.0386 mmol) of a 3:1 mixture of vinyloxiranes **14b** and **13b** in 0.3 mL of ether was added dropwise, and the solution was stirred overnight with warming to 0 °C. The product mixture was isolated as described in part A, affording 14.4 mg (99%) of a mixture of addition products.

C. Higher Order Cyano Cuprate. To a stirred slurry of 14.8 mg (0.165 mmol) of copper(I) cyanide[14] in 0.8 mL of dry ether under argon at −23 °C was added 0.236 mL (0.331 mmol) of 1.4 M methyllithium dropwise. The solution became clear and was stirred for 0.5 h. A solution of 10.2 mg (0.0331 mmol) of a 6:1 mixture of vinyloxiranes **9c** and **8c** in 0.2 mL of ether was added dropwise, and the solution was stirred overnight with warming to 0 °C. The product mixture was isolated as described in part A, affording 9.7 mg (91%) of a mixture of addition products.

Cuprate Products. 15b: ^1H NMR (300 MHz, $CDCl_3$) δ 7.3 (m, 5 H, aryl H), 5.38 (d, 1 H, J = 9.7 Hz, vinyl H), 4.56 (s, 2 H, benzyl H), 4.23 (X of ABX, 1 H, J_{AX} = 3.8 Hz, J_{BX} = 8.7 Hz, carbinyl H), 3.67 (m, 1 H, CHOTBS), 3.51, 3.41 (AB of ABX, J_{AB} = 9.5 Hz, J_{AX} = 3.5 Hz, J_{BX} = 8.6 Hz, CH_2OBn), 2.38 (m, 2 H, OH and CHC=C), 1.61 (s, 3 H, vinyl CH_3), 1.01 (d, 3 H, J = 6.2 Hz, CH_3CH), 0.90 (d, 3 H, J = 6.8 Hz, CH_3CH), 0.86 (s, 9 H, $SiC(CH_3)_3$), 0.05, 0.01 (s, 6 H, $Si(CH_3)_2$); HRMS calcd for $C_{22}H_{38}O_3SiNH_4$ (M + NH_4) 396.2934, found m/e 396.2939.

20a: ^1H NMR (300 MHz, $CDCl_3$) δ 7.32 (m, 5 H, aryl H), 5.34 (d, 1 H, J = 10.0 Hz, vinyl H), 4.55 (s, 2 H, benzyl H), 4.25 (m, 1 H, $BnOCH_2CH$), 3.51 (m, 1 H, carbinyl H), 3.51, 3.39 (AB of ABX, J_{AB} = 9.4 Hz, J_{AX} = 4.1 Hz, J_{BX} = 8.1 Hz, CH_2OBn), 2.43 (m, 2 H, OH and CHC=C), 1.64 (s, 3 H, vinyl CH_3), 1.41 (bs, 1

H, OH), 1.15 (d, 3 H, J = 6.2 Hz, CH_3CH), 0.94 (d, 3 H, J = 6.8 Hz, CH_3CH); HRMS calcd for $C_{16}H_{24}O_3NH_4$ (M + NH_4) 282.2059, found m/e 282.2072.

20b: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 (m, 5 H, aryl H), 5.37 (d, 1 H, J = 9.6 Hz, vinyl H), 4.55 (s, 2 H, benzyl H), 4.22 (m, 1 H, $BnOCH_2CH$), 3.66 (dq, 1 H, J = 4.4, 6.1 Hz, TBSOCH), 3.51, 3.43 (AB of ABX, J_{AB} = 9.4 Hz, J_{AX} = 3.4 Hz, J_{BX} = 8.7 Hz, CH_2OBn), 2.37 (m, 2 H, OH and CHC=C), 1.64 (s, 3 H, vinyl CH_3), 0.99 (d, 3 H, J = 6.2 Hz, $CH_3CHOTBS$), 0.91 (d, 3 H, J = 6.8 Hz, CH_3CH), 0.85 (s, 9 H, $SiC(CH_3)_3$), 0.01 (s, 6 H, $Si(CH_3)_2$); HRMS calcd for $C_{22}H_{38}O_3SiNH_4$ (M + NH_4) 396.2934, found m/e 396.2943.

20c: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 (m, 5 H, aryl H), 5.39 (d, 1 H, J = 9.5 Hz, vinyl H), 4.64, 4.55 (AB q, 2 H, J = 11.4 Hz, SCH_2O), 4.55 (s, 2 H, benzyl H), 4.23 (m, 1 H, $BnOCH_2CH$), 3.65 (dq, 1 H, J = 5.1, 7.0 Hz, MTMOCH), 3.51, 3.42 (AB of ABX, J_{AB} = 9.4 Hz, J_{AX} = 3.3 Hz, J_{BX} = 8.5 Hz, CH_2OBn), 2.55 (m, 1 H, CHC=C), 2.40 (bs, 1 H, OH), 2.11 (s, 3 H, SCH_3), 1.62 (s, 3 H, vinyl CH_3), 1.04 (d, 3 H, J = 6.2 Hz, $CH_3CHOMTM$), 0.96 (d, 3 H, J = 6.9 Hz, CH_3CH); HRMS calcd for $C_{18}H_{28}O_3SNH_4$ (M + NH_4) 342.2103, found m/e 342.2101.

Analysis of the Product Mixtures. The mixtures were analyzed by gas chromatography of the derived diacetates on a 30 M Superox column. These were prepared by stirring the cuprate product mixture with an excess of tetrabutylammonium fluoride in THF followed by aqueous workup. The MTM group was removed by stirring this crude product with 1.5 equiv (based on the starting vinyloxiranes) of mercuric chloride in 4:1 acetonitrile–water and then filtering the slurry through a plug of Celite and $MgSO_4$. The diacetates **23–26** were formed by dissolving the crude diols in a minimal amount of dry CH_2Cl_2 followed by the addition of excess acetic anhydride and pyridine. The vials were then placed in a cleaning sonocator and sonocated for 2 h. The volatiles were removed by blowing nitrogen into the vial.

(2*S*,3*S*)-3-(Benzyloxy)-2-methyl-1-butanol (27). To a stirred solution of 24.2 mg (96 μmol) of diol mixture **16a/20a** (12:1) in 1 mL of dry benzene was added 34.3 μL (0.289 mmol) of benzyl bromide, 32.4 mg (0.577 mmol) of crushed KOH, and 3 drops of TDA-1. This slurry was stirred vigorously overnight. The reaction was quenched with 1 mL of water, and the aqueous layer was extracted with ether. The combined extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The oil was purified by flash chromatography on silica gel. Elution with 6:1 hexane–ether afforded 10.3 mg of starting diols, 4.5 mg (30%) of dibenzylated triol, and 9.4 mg (50% based on recovered starting material) of tribenzylated triol, mainly **16d**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29 (m, 15 H, aryl H), 4.57, 4.40 (AB q, 2 H, J = 11.6 Hz, benzyl H), 4.56, 4.32 (AB q, 2 H, J = 12.0 Hz, benzyl H). 4.50 (s, 2 H, benzyl H), 3.94 (X of ABX, J_{AX} = 5.2 Hz, J_{BX} = 6.8 Hz, C=CCHOBn), 3.59, 3.49 (AB of ABX, J_{AB} = 10.2 Hz, J_{AX} = 5.3 Hz, J_{BX} = 6.6 Hz, CH_2OBn), 3.26 (dq, 1 H, J = 6.5, 6.8 Hz, $BnOCHCH_3$), 2.59 (m, 1 H, $CHCH_3$), 1.61 (s, 3 H, vinyl CH_3), 1.11 (d, 3 H, J = 6.0 Hz, $CHCH_3$), 1.06 (d, 3 H, J = 6.8 Hz, $BnOCHCH_3$); HRMS calcd for $C_{30}H_{36}O_3NH_4$ (M + NH_4) 462.3008, found m/e 462.3028.

Into a stirred solution of 9.4 mg (21.1 μmol) of tribenzyl ether **16d** in 0.53 mL of dry CH_2Cl_2 at −78 °C was bubbled ozone until a blue color persisted. Argon was then bubbled through the solution until the blue color disappeared whereupon 7.8 μL (105.7 μmol) of dimethyl sulfide was added dropwise. The mixture was stirred for 0.5 h, and 42 μL (21 μmol) of 0.5 M lithium tris(1,1-diethylpropyloxy)aluminum hydride in THF was added dropwise.[26] The solution was stirred an additional 15 min, ethanol was added, and the mixture was stirred with saturated aqueous Rochelle's salt until two distinct layers were apparent. The aqueous layer was extracted with CH_2Cl_2, and the combined extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The clear oil was purified by flash chromatography on silica gel. Elution with 2:1 hexane–ether afforded 2.1 mg (47%) of alcohol **27** without detection of the diastereomer and 2.6 mg (45%) of ketone **28**.

27: $[\alpha]^{25}_D$ +35.4° (*c* 0.21, $CHCl_3$); IR (film) ν 3402, 2935, 1452, 1377, 1278, 1116, 1027, 788, 713 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31 (m, 5 H, aryl H), 4.61, 4.45 (AB q, 2 H, J = 11.8 Hz, benzyl H), 3.60 (m, 2 H, $HOCH_2$ and CHOBn), 2.00 (m, 1 H, CH_3CH), 1.60 (m, 1 H, alcohol H), 1.19 (d, 3 H, J = 6.4 Hz, CH_3CHOBn), 0.87 (d, 3 H, J = 7.1 Hz, CH_3CHCH_2) [reported[24] ^{1}H NMR (250 MHz) 7.36 (s), 4.62, 4.46 (AB q, J = 12 Hz), 3.71 (m), 3.56 (dd, J = 4.5, 11 Hz), 2.37 (s, OH), 2.00 (m), 1.18 (d, J = 6), 0.86 (d, J = 7 Hz).

28: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 (m, 10 H, aryl H), 4.65, 4.58 (AB q, 2 H, J = 12.0 Hz, benzyl H), 4.53 (d, 2 H, J = 2.9 Hz, benzyl H), 3.97 (t, 1 H, J = 4.6 Hz, CHOBn), 3.73 (d, 2 H, J = 4.6 Hz, CH_2OBn), 2.22 (s, 3 H, $COCH_3$).

(2*S*,3*R*)-3-(Benzyloxy)-2-methyl-1-butanol (29). Benzylation of 44.0 mg (0.26 mmol) of diol mixture **20a/16a** (5.1:1) as described above afforded, after 3 days of stirring, 30.8 mg (52%) of dibenzylated and 20.5 mg (28%) of tribenzylated product **20d**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29 (m, 15 H, aryl H), 5.40 (d, 1 H, J = 9.4 Hz, vinyl H), 4.58, 4.32 (AB q, 2 H, J = 12.1 Hz, benzyl H), 4.56, 4.44 (AB q, 2 H, J = 11.9 Hz, benzyl H), 4.50 (s, 2 H, benzyl H), 3.97 (X of ABX, J_{AX} = 4.8 Hz, J_{BX} = 7.2 Hz, CH_2CHOBn), 3.62, 3.50 (AB of ABX, J_{AB} = 10.4 Hz, J_{AX} = 4.8 Hz, J_{BX} = 7.2 Hz, CH_2CHOBn), 3.41 (dq, 1 H, J = 4.7, 6.2 Hz, $BnOCHCH_3$), 2.67 (m, 1 H, $CHCH_3$), 1.59 (s, 3 H, vinyl CH_3), 1.09 (d, 3 H, J = 6.3 Hz, $CHCH_3$), 1.03 (d, 3 H, J = 6.8 Hz, $BnOCHCH_3$); HRMS calcd for $C_{30}H_{36}O_3NH_4$ (M + NH_4) 462.3008, found m/e 462.3015.

Ozonolysis of **20d**, as described above, afforded 4.1 mg (43%) of a 5:1 mixture of alcohols **29** and **27**: $[\alpha]^{25}_D$ −24.0° (*c* 0.41, $CHCl_3$); IR (film(ν 3418, 2928, 1452, 1377, 1316, 1276, 1115, 1027, 788, 710 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 (m, 2 H, aryl H), 4.65, 4.40 (AB q, 2 H, J = 11.5 Hz, benzyl H), 3.58 (m, 2 H, $HOCH_2$), 3.47 (dq, 1 H, J = 6.1, 7.2 Hz, CHOBn), 1.76 (m, 1 H, $CHCH_3$), 1.24 (d, 3 H, J = 6.1 Hz, CH_3CHOBn), 0.89 (d, 3 H, J = 7.0 Hz, CH_3CH) [reported[25] ^{1}H NMR (360 MHz) 7.35 (m), 4.67, 4.40 (AB q, J = 12 Hz), 3.61 (m), 3.50 (dq, J = 6, 6 Hz), 1.78 (m), 1.25 (d, J = 6 Hz), 0.90 (d, J = 6 Hz).

(3*S*,2*R*)-3-(Benzyloxy)-2-methyl-1-butanol (*ent*-29). Benzylation of 13.6 mg (0.052 mmol) of diol mixture **15a/16a/19a/20a** (78:8:11:9) as described above afforded, after 10 days of stirring, 18.6 mg (81%) of tribenzylated product **15d/20d/19d/20d**.

Ozonolysis, as described above, afforded 4.6 mg (54%) of alcohol mainly *ent*-**29**; $[\alpha]^{25}_D$ +15.2° (*c* 0.46, $CHCl_3$).

(*Z*)-(4*R*,5*R*)-6-(Benzyloxy)-4,5-epoxy-4-methyl-1-[(methylthio)methoxy]-2-hexene (Ic). To a stirred solution of 63.1 mg (0.269 mmol) of vinyloxirane Ia and 0.158 mL (2.15 mmol) of dimethyl sulfide in 1.1 mL of dry acetonitrile at 0 °C was added 261 mg (1.08 mmol) of benzoyl peroxide in 4 portions over 1 h. The solution was stirred for 4 h and quenched with 3 mL of saturated sodium bicarbonate. The aqueous layer was extracted with ether, and the combined extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The crude oil was purified by flash chromatography on silica gel. Elution with 3:1 hexane–ether afforded 42.7 mg (54%) of vinyloxirane Ic and 14.4 mg of dihydrofuran resulting from cyclization: IR (film) ν 2968, 2921, 2855, 1454, 1292, 1073, 951, 737, 700 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 (m, 5 H, aryl H), 5.61 (m, 2 H, vinyl H), 4.60 (s, 2 H, SCH_2O), 4.58, 4.48 (AB q, 2 H, J = 11.9 Hz, benzyl H), 3.54 (d, J = 11.0 Hz, CH_2OMTM), 3.54, 3.41 (AB of ABX, J_{AB} = 11.0 Hz, J_{AX} = 4.9 Hz, J_{BX} = 5.9 Hz, $BnOCH_2$), 3.09 (X of ABX, J_{AX} = 5.0 Hz, J_{BX} = 5.9 Hz, epoxy H), 2.12 (s, 3 H, SCH_3), 1.41 (s, 3 H, epoxy CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.0, 130.2 (2 C), 128.4 (3 C), 128.0 (2 C), 74.9, 73.3, 69.4, 64.6, 61.9, 59.3, 23.2, 14.0; $[\alpha]^{23}_D$ +22.0° (*c* 2.14, $CHCl_3$). Anal. Calcd for $C_{16}H_{22}O_3S$: C, 65.28; H, 7.53. Found: C, 65.46; H, 7.60.

(*E*)-(4*R*,5*R*)-6-(Benzyloxy)-4,5-epoxy-4-methyl-1-[(methylthio)methoxy]-2-hexene (IVc). To a stirred solution of 21.3 mg (0.091 mmol) of vinyloxirane IVc in 0.2 mL of dry dimethoxyethane at 0 °C was added 7.3 mg (0.182 mmol) of 60% sodium hydride as a dispersion in oil. The solution was stirred for 0.5 h, whereupon 15 mg (0.1 mmol) of dry sodium iodide and 10 mL (0.1 mmol) of chloromethyl methyl sulfide were added. The solution was stirred for 6 h with warming to room temperature. The reaction was quenched with 2 mL of water, and the aqueous layer was extracted with ether. The combined extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The crude oil was purified by flash chromatography on silica gel. Elution

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with 3:1 hexane–ether afforded 15.2 mg (57%) of vinyloxirane IVc: IR (film) ν 2968, 2922, 2854, 1453, 1383, 1300, 1071, 765, 738, 698 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 (m, 5 H, aryl H), 5.82 (dt, 1 H, J = 5.6, 15.8 Hz, vinyl H), 5.64 (d, 1 H, J = 15.8 Hz, vinyl H), 4.61 (s, 2 H, SCH_2O), 4.59, 4.48 (AB q, 2 H, J = 11.9 Hz, benzyl H), 4.05 (d, 2 H, J = 5.5 Hz, C=CHCH_2), 3.58, 3.51 (AB of ABX, J_{AB} = 11.1 Hz, J_{AX} = 5.0 Hz, J_{BX} = 5.8 Hz, CH_2OBn), 3.15 (X of ABX, 1 H, J_{AX} = 5.0 Hz, J_{BX} = 5.7 Hz, CH_2CH), 2.13 (s, 3 H, SCH_3), 1.43 (s, 3 H, epoxy CH_3); $[\alpha]^{23}_D$ +11.2° (c 1.52, $CHCl_3$). Anal. Calcd for $C_{16}H_{22}O_3S$: C, 65.28; H, 7.53. Found: C, 65.22; H, 7.38.

(*E*)-(2*R*,5*S*)-6-(Benzyloxy)-2,4-dimethyl-5-hydroxy-1-[(methylthio)methoxy]-3-hexene (30c). The lower order cyanocuprate, prepared as described from 8.7 mg (0.097 mmol) of copper cyanide[14] and 0.07 mL (0.097 mmol) of 1.4 M methyllithium in diethyl ether, was added to 5.7 mg (0.020 mmol) of vinyloxirane Ic, affording 5.1 mg (85%) of allylic alcohol **30c**: IR (film) ν 3448, 2958, 2921, 2861, 1496, 1454, 1302, 11163, 1073, 9056, 735, 698, 680 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 (m, 5 H, aryl H), 5.33 (d, 1 H, J = 9.2 Hz, vinyl H), 4.59 (s, 2 H, SCH_2O), 4.55 (s, 2 H, benzyl H), 4.21 (d, 1 H, J = 5.4 Hz, carbinyl H), 3.6–3.2 (m, 4 H, $BnOCH_2$ and $MTMOCH_2$), 2.69 (m, 1 H, CHCH$_3$), 2.42 (bs, 1 H, OH), 2.10 (s, 3 H, SCH_3), 1.63 (s, 3 H, vinyl CH_3), 0.97 (d, 3 H, J = 6.7 Hz, CHCH_3); $[\alpha]^{24}_D$ −24° (c 0.80, $CHCl_3$); HRMS Calcd for $C_{17}H_{26}O_3SNH_4$ (M + NH_4) 328.1946, found m/e 328.1957.

(*E*)-(2*S*,5*S*)-6-(Benzyloxy)-2,4-dimethyl-5-hydroxy-1-[(methylthio)methoxy]-3-hexene (31c). The lower order cyanocuprate prepared as described from 23.1 mg (0.258 mmol) of copper cyanide,[14] and 0.19 mL (0.258 mmol) of 1.4 M methyllithium in diethyl ether was added to 15.2 mg (0.052 mmol) of vinyloxirane IVc, affording 11.6 mg (73%) of allylic alcohol **31c**: IR (film) ν 3454, 2921, 1454, 1071, 734 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 (m, 5 H, aryl H), 5.33 (d, 1 H, J = 9.2 Hz, vinyl H), 4.58 (s, 2 H, SCH_2O), 4.55 (s, 2 H, benzyl H), 4.21 (X of ABX, 1 H, J_{AX} = 3.0 Hz, J_{BX} = 8.5 Hz, carbinyl H), 3.51, 3.39 (AB of ABX, J_{AB} = 9.5 Hz, J_{AX} = 3.2 Hz, J_{BX} = 8.6 Hz, CH_2OBn), 3.35, 3.30 (AB of ABX, J_{AB} = 8.0 Hz, J_{AX} = 5.5 Hz, J_{BX} = 6.9 Hz, CH_2OMTM), 2.69 (m, 1 H, CHCH$_3$), 2.47 (bs, 1 H, OH), 2.09 (s, 3 H, SCH_3), 1.63 (s, 3 H, vinyl CH_3), 0.97 (d, 3 H, J = 6.7 Hz, CHCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.9, 134.2, 130.0, 128.5 (2 C), 127.8, 127.7 (2 C), 75.4, 75.2, 73.6, 73.3, 72.8, 32.4, 17.6, 13.8, 12.8; $[\alpha]^{24}_D$ +15.4° (c 1.87, $CHCl_3$); HRMS calcd for $C_{17}H_{26}O_3SNH_4$ (M + NH_4) 328.1946, found m/e 328.1939.

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Supplementary Material Available: ^{1}H NMR spectra for **5a,c, 6a–c, 7, 12, 20a–c, 30c, 31c** and Chem 3D structures for the six lowest energy conformers of **8c, 9c, 13c,** and **14c** as calculated by MacroModel V3.0 (28 pages). Ordering information is given on any current masthead page.

Notes

Regio- and Stereoselective Iodofluorination of Alkenes with Bis(pyridine)iodonium(I) Tetrafluoroborate

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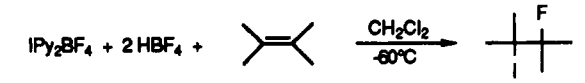
Selectively fluorinated compounds are a subject of current interest.[1] A classical preparation is the addition of fluoride to alkanes[2] and, in this way, mixed halogens have been challenging species. Iodine monofluoride[3] is particularly attractive, although it must be synthesized in situ. To do that, different combinations of reagents have been proposed.[4]

Scheme I



Recently, we have reported[5] that when cyclohexene was treated with bis(pyridine)iodonium(I) tetrafluoroborate (IPy_2BF_4) in the presence of tetrafluoroboric acid at −30 °C, in methylene dichloride, *trans*-1-fluoro-2-iodocyclo-

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(3) Iodine monofluoride has been described in a very few publications. No reports of the reactivity of isolated IF toward organic compounds have been published. It is known the tendency of this compound to disproportionate giving rise to hypervalent iodine species (IF_3 and IF_5). See, for instance: Schmeisser, M.; Sartori, P.; Naumann, D. *Chem. Ber.* **1979**, *103*, 880. Pyridine complexes of IF can be isolated: Schmidt, H.; Meinert, H. *Angew. Chem.* **1959**, *71*, 126.

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