product (0.097 g, 0.26 mmol) in methylene chloride (1.3 mL) at 25 °C under nitrogen was added DBU (0.072 mL, 0.51 mmol) dropwise. After 1.5 h, the mixture was diluted with methylene chloride and 5% hydrochloric acid. The crude product was isolated from the organic layer and was purified under nitrogen by flash chromatography (silica gel, 3% acetone/methylene chloride)[13] to give 0.071 g (81%) of **14c** as a yellow solid: mp 105–106 °C; TLC (3% acetone/methylene chloride) R_f 0.27 (single spot); ^{1}H NMR ($CDCl_3$) 7.71 (s, 1 H), 6.60 (s, 1 H), 3.80 (s, 3 H), 3.71 (s, 3 H), 1.6–2.8 (br m, 10 H); IR ($CHCl_3$) 3010, 2950, 1660, 1610, 1515, 1465 cm^{-1}; mass spectrum (70 eV), m/e 258.1248 (M^+, 258.1256 calcd for $C_{16}H_{18}O_3$).

The remaining compounds of this series were prepared by similar procedures on similar scales.

13. The crude product was purified by column chromatography (silica gel, 2% ethyl acetate/methylene chloride) or by recrystallization from 40% THF/hexane to give yellow crystals: mp 206–207 °C; TLC (silica gel, 5% ether/chloroform) R_f 0.40 (single spot); IR ($CHCl_3$) 5.9 μm; ^{1}H NMR ($CDCl_3$) 7.85 (s, 1 H), 6.3 (s, 1 H), 5.9 (s, 2 H), 3.25 (m, 8 H); ^{13}C NMR ($CDCl_3$) 205.9 (s), 172.78 (s), 146.16 (s), 147.5 (s), 134.75 (s), 128.57 (s), 122.98 (s), 108.40 (d), 105.15 (d), 100.88 (t), 35.84 (t), 28.98 (t), 27.91 (t), 27.14 (t); mass spectrum (70 eV), m/e 228.080 (M^+, 228.078 calcd for $C_{14}H_{12}O_3$).

14a. Purification was accomplished with high-performance LC (μ-Porasil, methylene chloride), affording a 67% yield of **14a** as a yellow solid: mp 64–66 °C; TLC (silica gel, methylene chloride) R_f 0.31 (single spot); ^{1}H NMR ($CDCl_3$) 7.90 (m, 1 H), 7.05 (m, 1 H), 1.70–2.80 (m, 10 H); IR ($CHCl_3$) 3010, 2950, 1660, 1595, 1485, 1450, 820 cm^{-1}; mass spectrum (70 eV), m/e 198.1047 (M^+, 198.1044 calcd for $C_{14}H_{14}O$). An analytically pure sample was obtained by repeating the high-performance LC purification as described above.

Anal. Calcd for $C_{14}H_{14}O$: C, 84.81; H, 7.12. Found: C, 84.78; H, 7.30.

14b. The usual isolation procedure provided a 90% yield (^{1}H NMR) of **14b** as a yellow solid which could be recrystallized (albeit with low recovery) from 40% THF/hexane at −25 °C to give yellow crystals: mp 100–102 °C; TLC (silica gel, 10% acetone/methylene chloride) R_f 0.59 (single spot); ^{1}H NMR 7.91 (d, J = 8.5 Hz, 1 H), 6.70 (m, 2 H), 3.61 (s, 3 H), 1.6–2.8 (br m, 10 H); IR ($CHCl_3$) 3010, 2950, 1660, 1605, 1495 cm^{-1}; mass spectrum (70 eV), m/e 228.1133 (M^+, 228.1151 calcd for $C_{15}H_{16}O_2$).

14d. The same procedure afforded an 83% yield (^{1}H NMR) of **14d** as a deep yellow solid which could be recrystallized (low recovery) from 40% THF/hexane to give yellow crystals: mp 80–81 °C; TLC (silica gel, 2% ethyl acetate/methylene chloride) R_f 0.45 (single spot); ^{1}H NMR ($CDCl_3$) 7.7 (s, 1 H), 6.65 (s, 1 H), 5.95 (s, 2 H), 2.8–2.2 (br m, 8 H), 2.05 (m, 2 H); IR ($CHCl_3$) 3010, 2950, 1660, 1590, 1500, 1480 cm^{-1}; mass spectrum (70 eV), m/e 242.0960 (M^+, 242.0943, calcd for $C_{15}H_{14}O_3$).

Preparation of Naphthocycloalkenones. The following sample procedure is given for one of these dehydrogenations.

15. Through a solution of **13** (0.143 g, 0.63 mmol), methylene chloride (3 mL), and DBU (0.192 g, 1.26 mmol) at 25 °C was bubbled oxygen for 4 h. After an additional 24 h at 25 °C, the solution was subjected to a standard workup to yield 0.114 g (80%) of **15** as yellow crystals: mp 168–170 °C; TLC (silica gel, 5% ether/chloroform) R_f 0.45 (single spot); IR ($CHCl_3$) 5.85 μm; ^{1}H NMR ($CDCl_3$) 8.6 (s, 1 H), 7.9–7.3 (AB, 2 H), 7.15 (s, 1 H), 6.08 (s, 2 H), 3.3–2.7 (A_2B_2, 4 H); ^{13}C NMR ($CDCl_3$) 207.44 (s), 156.06 (s), 150.26 (s), 147.82 (s), 134.50 (d), 130.90 (s), 130.48 (s), 129.75 (s), 122.31 (d), 104.36 (d), 101.42 (d), 101.23 (t), 36.92 (t), 25.75 (t, CH_2); mass spectrum (70 eV), m/e 226.061 (M^+, 226.063 calcd for $C_{14}H_{10}O_3$).

16. The application of the same procedure as above converted **14d** into **16** in 77% yield as yellow crystals: mp 98–100 °C; TLC (silica gel, 30% THF/hexane) R_f 0.45 (single spot); IR ($CHCl_3$) 6.0 μm; ^{1}H NMR ($CDCl_3$) 8.95, (s, 1 H), 7.8–7.1 (AB, 2 H), 7.08 (s, 1 H), 6.05 (s, 2 H), 3.08 (t, 2 H), 2.75 (t, 2 H), 2.2 (m, 2 H); ^{13}C NMR ($CDCl_3$) 200.48 (s), 150.39 (s), 146.99 (s), 144.89 (s), 133.06 (d), 130.19 (d), 128.53 (s), 126.77 (s), 125.35 (d), 104.19 (d), 103.95 (d), 41.21 (t), 31.49 (t), 23.08 (t); mass spectrum (70 eV), m/e 240.077 (M^+, 240.078 calcd for $C_{15}H_{12}O_3$).

Acknowledgment. The National Cancer Institute, DHEW, is gratefully acknowledged for providing the financial support for this research (Grant No. CA20701 and CA19689-01).

Registry No. 5d, 66003-47-2; **5e**, 75534-18-8; **5f**, 75534-19-9; **5g**, 75548-48-0; **5h**, 75534-20-2; **8**, 75534-21-3; **9**, 75534-22-4; **11**, 75534-23-5; **12a**, 75534-24-6; **12b**, 75534-25-7; **12c**, 75534-26-8; **12d**, 75534-27-9; **13**, 75534-28-0; **14a**, 54558-75-7; **14b**, 41624-53-7; **14c**, 75534-29-1; **14d**, 75534-30-4; **15**, 75534-31-5; **16**, 75534-32-6; *tert*-butyl mercaptan, 75-66-1; 3-bromocyclohexene, 1521-51-3; 3-(*tert*-butylthio)cyclohexene, 75534-33-7; 2,3-epoxycyclohexyl *tert*-butyl sulfone, 75534-34-8; *tert*-butyldimethylchlorosilane, 18162-48-6; 3-methoxyphenylacetic acid, 1798-09-0; 2-(3-methoxyphenyl)ethanol, 5020-41-7; 2-(2-bromo-5-methoxyphenyl)ethanol, 75534-35-9; 1,2,3,4,4a,9,10,10a-octahydro-6,7-dimethoxy-10a-[(1,1-dimethylethyl)sulfonyl]-4-phenanthrenol, 75534-36-0; 2,3,4a,9,10,10a-hexahydro-6,7-dimethoxy-10a-[(1,1-dimethylethyl)sulfonyl]-4(1*H*)-phenanthrenone, 75534-37-1.

(13) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923, 2925.

Regio- and Stereochemistry of Dialkylcuprate Additions to Selected Alkylidene Oxiranes

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The stereochemistry of the vinyloxiranes obtained by the treatment of several alkylidene cyclohexanones with dimethylsulfonium methylide is discussed. The structure and stereochemistry of the products produced by treatment of the vinyloxiranes with lithium dibutyl- or dimethylcuprate are discussed.

The regio- and stereochemical course of the reaction of dialkylcuprates with allyl[3] and propargyl esters,[4] allyl carbamates,[5] propargyl ethers,[6] and propargyl-[7] and vinyloxiranes[8] has been well documented. In general, ad-

(1) Career Development Awardee, National Institute of General Medical Sciences, 1973-78.

(2) Taken in part from the Ph.D. thesis of M.A.C., Yale University, 1979.

(3) (a) Rona, P.; Toekes, L.; Tremble, J.; and Crabbé, P. *Chem. Commun.* **1969**, 43. (b) Anderson, R. J.; Henrick, C. A.; Siddall, J. B. *J. Am. Chem. Soc.* **1970**, *92*, 735; **1972**, *94*, 5379. (c) Goering, H. L.; Singleton, V. D. *Ibid.* **1976**, *98*, 7854. (d) Kreft, A. *Tetrahedron Lett.* **1977**, 1035.

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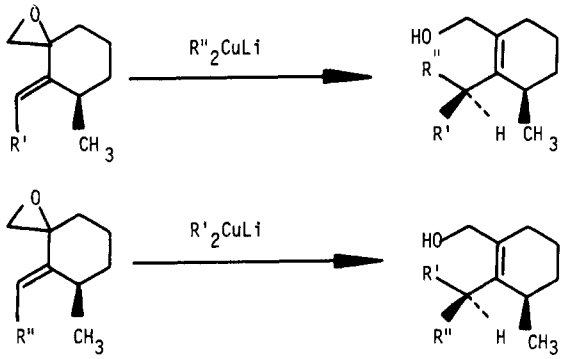
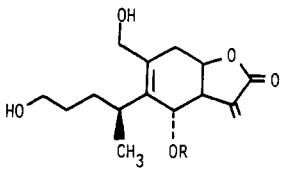
Scheme I



dition occurs anti to the leaving group, and the site of bond formation is governed by double bond substitution or steric factors. In the case of allylic carbamates (phenyl isocyanate derived), substitution occurs via an S_N2' syn addition.

We sought to determine both the regio- and stereochemical course of dialkylcuprate additions to alkylideneoxiranes of the general structural type illustrated in Scheme I, since the presence of the resultant allylic alcohol substitution pattern appears in the antileukemic lactones eriolanin **1a** and eriolangin **1b**.[9,10] If the $A^{1,3}$ interactions[11]



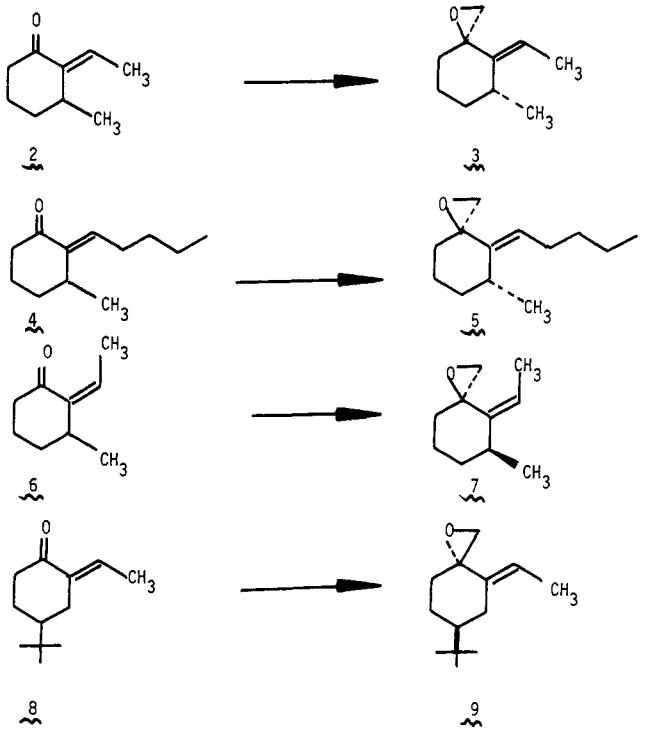
1a, R= α-methacryloyl
1b, R= angeloyl

(R′ = CH_3 and R″ = n-C_4H_9, Scheme I) were to force the ring methyl group into a β-axial conformation, then it might be anticipated that attack of the cuprate reagent would occur on the α face, providing a single diastereomer in each instance. Such a rationale would be dependent upon attainment of the appropriate overlap between the allylic C–O bond and the π orbitals of the double bond with each ring in a chairlike conformation.

Results and Discussion

Although the addition of dimethylsulfonium methylide to cyclohexanones has been shown to give predominately products derived from axial attack,[12] the mode of reaction of this reagent with alkylidene ketones is unknown. Enones **2**, **4**, and **6** were prepared (Scheme II) by the method of Smith[13] while enone **8** was prepared via the addition of

Scheme II



methylmagnesium bromide to the pyrrolidinomethylene derivative of 4-*tert*-butylcyclohexanone. The *E* configuration of **2**, **4**, and **8** was confirmed by the low-field shift of the vinylic protons at δ 6.58, 6.46, and 6.70, respectively, while the *Z* enone **6** displayed its vinylic proton at δ 5.65 ((*Z*)-**4** δ 5.51).

The methylenation of the enones proved to be highly stereoselective. Although we were unable to detect stereoisomers, the presence of which would have facilitated direct spectroscopic comparison (^1H, ^{13}C), we were nonetheless able to assign the stereochemistries depicted in Scheme II for **3**, **5**, and **9** by spectroscopic means.

The allylic methine proton in oxiranes **3** and **5** appears at δ 3.08 and 3.05, respectively, significantly downfield from the value of δ 2.16 for the same proton in **7**, indicating that the protons in the former cases are situated equatorially to the ring and, consequently, deshielded by the double bond. Moreover, the oxirane protons which are syn to the double bond in **3**, **5**, and **9** have chemical shifts upfield (δ 2.43, 2.43, and 2.41, respectively) relative to the shifts of their respective anti protons (δ 2.71, 2.71, and 2.63) due to the shielding effect of the double bond. The *syn*-oxirane protons in this trio display W coupling ($J \approx 1.5$ Hz, **9**) with their respective C-6 α protons, in accord with line broadening observed in oxiranes having an axial methylene group in cyclohexane systems.[15] The *anti*-oxirane proton of **7** has a chemical shift (δ 2.60) similar to that of its counterpart in **3**, **5**, and **9**, but the *syn*-proton is deshielded (δ 2.56) relative to the same signals in **3**, **5**, and **9** and does not show any discernible long-range coupling. The ^{13}C spectra of **3**, **5**, and **9** indicate that the oxirane methylene carbons all absorb within 0.5 ppm of each other, while the equivalent signal in **7** is shielded by 4 ppm.

These data argue that oxiranes **3**, **5**, and **9** have the stereochemistries indicated in Scheme II and are highly populated by a conformation having the oxirane methylene group axial and, in the former two cases, the ring methyl

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(10) For a synthesis of these substances, see: Grieco, P. A.; Oguri, T.; Gilman, S.; DeTitta, G. T. *J. Am. Chem. Soc.* **1978**, *100*, 1616.
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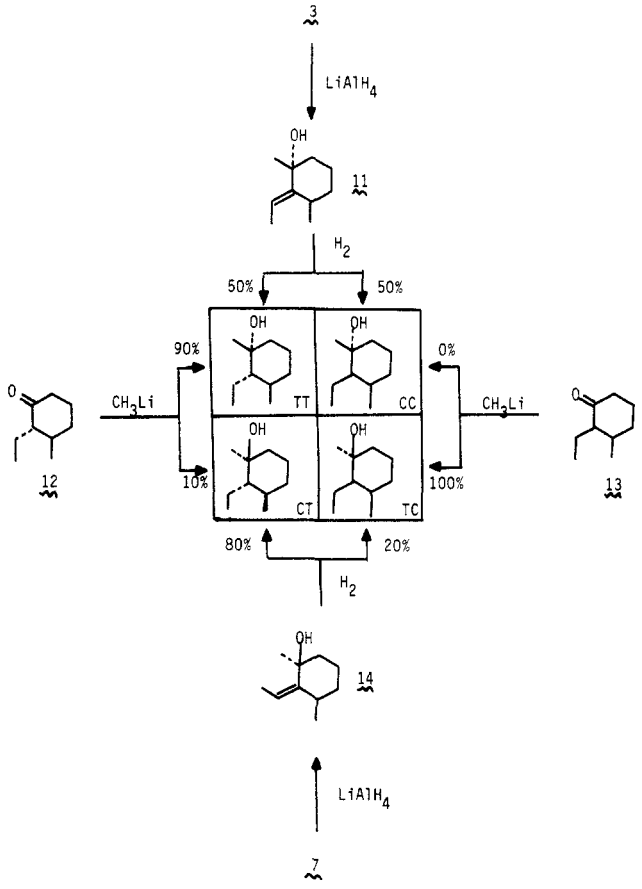
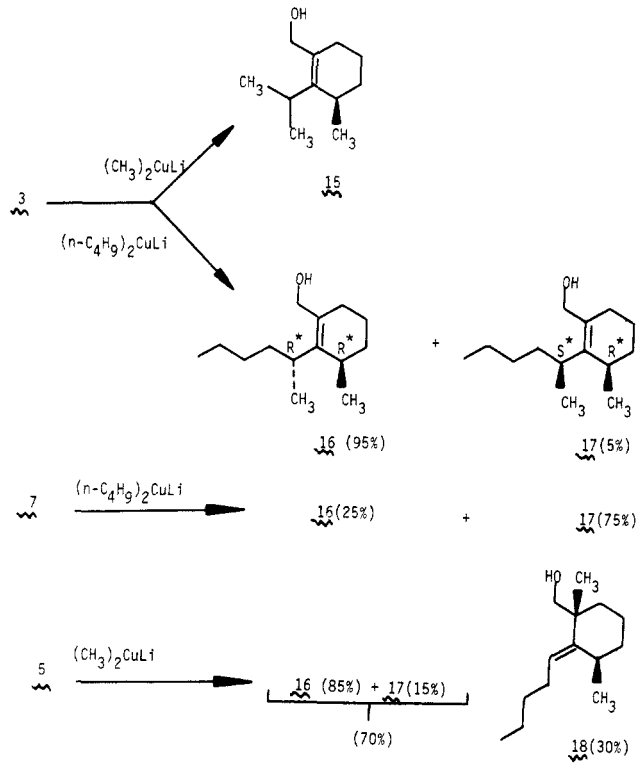
(15) Vary, M. W.; McBride, J. M.; Cady, M. A., Ziegler, F. E. *Cryst. Struct. Commun.* **1979**, *8*, 799.

Scheme III



Scheme IV



group axially oriented due to $A^{1,3}$ strain. Oxirane **7** exists in a preferred conformation which has the ring methyl in an equatorial position (methine proton, δ 2.16), but the relative stereochemistry of the oxirane and methyl could not be unambiguously assigned on spectroscopic grounds. This question was resolved by chemical means (Scheme III).

If oxiranes **3** and **7** differed only by the double bond geometry, then the sequence of reductions ($LiAlH_4$, H_2) would provide the same pair of saturated cyclohexanols (TT, CC) but not necessarily in the same ratios. On the other hand, if the relative stereochemistries at the asymmetric centers were different, a different pair of alcohols would be obtained (TT,CC and CT,TC).[16]

In accord with Scheme III, oxirane **3** was reduced with lithium aluminum hydride to provide **11** along with a minor amount of the conjugate reduction product. Hydrogenation of **11** (Pd/C, 1 atm of H_2) gave a 50/50 mixture of the TT and CC cyclohexanols. In a similar fashion, oxirane **7** provided an ill-resolved ~80/20 mixture of two alcohols with distinctly different retention times from those obtained via **3**. These alcohols were inferred to be the CT and TC isomers, pure samples of which were to be obtained in subsequent experiments. The lack of crossed contamination ruled out the possibility of prior double bond isomerization in the hydrogenation steps. These experiments clearly indicate that the configuration of **7** at the asymmetric centers is opposite to that present in **3**.

Further chemical correlation of these assignments was made in the following manner. Hydrogenation of a mixture of enones **2** and **6** followed by base-catalyzed equilibration of the mixture of cyclohexanones provided a 75/25 mixture of **12** and **13**, respectively.[17]

Treatment of the trans isomer **12** with methyllithium provided a 90/10 mixture of alcohols which were readily separated by GC. The preference for equatorial addition of Grignard and alkyllithium reagents to 2-methyl-, *trans*-3,4-dimethyl-, 3,3,5-trimethyl-, and 4-*tert*-butylcyclohexanone[18] permitted the assignment of the major component as the TT isomer and of the minor component as the CT isomer. This assignment was supported by their behavior on GC analysis (column A; see Experimental Section), since the retention time of the major component bearing an axial hydroxyl group was less than the retention time of the minor component having an equatorial hydroxyl group. The latter compound was identical (GC, 270-MHz NMR) with the major isomer from the successive reductions of **7**. Although not essential to the stereochemical analysis, cis ketone **13**, upon treatment with methyllithium, gave a single alcohol which was shown (GC and 270-MHz NMR) to be the TC isomer. By the various pathways described in Scheme III, the four diastereomeric trialkylcyclohexanols (M^+ with m/e 156) could be prepared under conditions which permitted them to be separated by gas chromatography and subsequently shown to have unique 270-MHz NMR spectra.

The mechanism of formation of the four oxiranes can be accommodated by assuming an axial approach of the reagent to the alkylidene ketones which is considered to be in a conformation which approaches a half chair, having C-1, C-2, C-3, and C-6 nearly planar. This geometry re-

(16) The symbol TC, for example, indicates that the alkyl groups at C_1–C_2 are trans while at C_2–C_3 they are cis.

(17) The NMR spectrum of *cis*-2,3-dimethylcyclohexanone displays the 3-methyl signal as a doublet at δ 0.83 while the trans isomer has a doublet at δ 1.05. Pfeffer, P. E.; Osman, S. F. *J. Org. Chem.* **1972**, *37*, 2425. These values are in excellent agreement with the data on ketones **12** and **13** (see Experimental Section). Moreover, the calculated equilibrium constant, K_{ee} (trans/cis), is 5.25 (84/16) at 27 °C. See: Eliel, E. L., Allinger, N. L.; Angyal, S. J.; Morrison, G. A. "Conformational Analysis"; Wiley-Interscience: New York, 1965; p 113.

(18) Nazarov, I. N.; Akhrem, A. A.; Kamernitzky, A. V. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1958**, 631. Kamernitzky, A. V.; Akhrem, A. A. *Zh. Obshch. Khim.* **1960**, *30*, 754; *Izv. Akad. Nauk. SSSR, Ser. Khim.* **1959**, 748.

duces the incipient 1,3-diaxial interaction in the transition state leading to 3 and 5.

The stereochemistries of 3 and 5 are clearly such that cuprate addition to these oxiranes could not be achieved through a chairlike transition state having both the ring methyl group and the C–O bond axially oriented (vide supra). Nonetheless, the stereochemical course of the reaction of cuprates with oxiranes 3, 5, and 7 was explored.

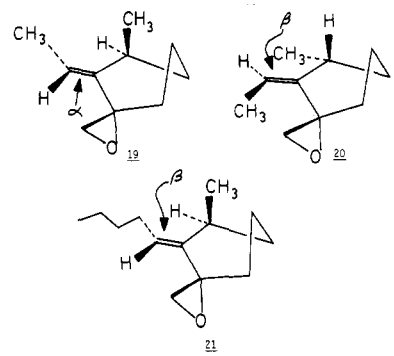
Oxirane 3, upon exposure to ethereal lithium dimethylcuprate at 0 °C, gave rise to a single allylic alcohol which was assigned structure 15 (Scheme IV) on the basis of spectroscopic data. The ^{1}H NMR spectrum displayed the isopropyl methine proton as a characteristic septet at δ 2.79 (J = 7 Hz) while the ring methine proton absorbed at δ 2.10. The decoupled ^{13}C NMR spectrum revealed the required 11 singlets with vinylic carbons absorbing at δ 144.42 and 129.03. This experiment confirmed the anticipated regiochemistry of addition of the cuprate to the less hindered (secondary vs. tertiary) position of the allylic residue. No product from direct S_N2 displacement at the oxirane methylene could be detected.

Treatment of oxirane 3 with lithium di-*n*-butylcuprate at −25 °C gave rise to what appeared to be a single regioisomer which was assignable to either structure 16 or 17 on the basis of its 270-MHz NMR spectrum. The one-proton multiplet at δ 2.58 was assigned to the chain methine proton while the one-proton multiplet at δ 2.26 was attributable to the ring methine proton in accord with the chemical shifts in alcohol 15. The decoupled ^{13}C spectrum of this substance revealed 13 of the required 14 singlets. The quaternary sp^2 carbons at δ 144.17 and 129.84 had weak signals (~5% intensity) immediately to the high-field and low-field sides of the respective signals. These weak absorptions were assumed to belong to the diastereomer 17, since the relative stereochemistry present in the major substance was shown to be *R**,*R**, as represented by structure 16, by means of a single-crystal, X-ray analysis of the *p*-bromophenylurethane.[15]

Exposure of the (*Z*)-oxirane 7 to lithium di-*n*-butylcuprate yielded both allylic alcohols 16 and 17 with the latter isomer, *R**,*S**, predominating. The 270-MHz NMR spectrum of this mixture revealed a new 1-proton multiplet at δ 2.45 for the chain methine proton of 17, upfield from the signal of its counterpart in 16. The ^{13}C NMR spectrum of the mixture displayed a pair of equal-intensity singlets at δ 144.37 and 130.00 with an interior pair of one-third the intensity at δ 144.04 and 130.21, the reverse of the pattern that was observed in the reaction of 3 with lithium di-*n*-butylcuprate. When a 2/1 mixture of enones 2 and 3, respectively, was converted to the oxiranes and subsequently treated with lithium di-*n*-butylcuprate, a mixture of diastereomers 16 and 17 was produced wherein the former isomer predominated as witnessed by the more intense interior signals for the olefinic carbons located at δ 144.20, 143.87, 129.80, and 129.58. It should be noted that there appears to be a concentration dependence upon the chemical shift of the two quaternary carbons, presumably associated with hydrogen bonding. However, the $\Delta\delta$ for each carbon in the diastereomers remains constant at 0.33 ppm for the lower field signal and 0.21 ppm for the other signal.

Treatment of 5 with lithium dimethylcuprate gave products derived from both modes of allylic addition to the vinyloxirane. Seventy percent of the reaction mixture consisted of an 85/15 ratio of isomers 16 and 17, while the remaining 30% consisted of a single olefinic alcohol, 18. The stereochemical assignment of 18 was made on the basis of the upfield shift (+0.44 ppm) of the vinyl proton upon oxidation of the alcohol to the aldehyde 19. This shift established not only the *E* configuration of the double bond but also the preferred conformation of 18, wherein the formyl group prefers to be equatorial to the ring.

The proton NMR evidence indicates that none of the three vinyloxiranes (3, 5, or 7) is in a preferred ground-state conformation which has both the allylic C–O bond overlapping with the p orbitals of the olefin and the ring in a chairlike conformation. Although such considerations can account for the results observed by Kreft,[3d] it is quite clear that the ring must be distorted to acquire the appropriate orbital overlap in the transition state. Thus, it can be argued that vinyloxirane 3 would exist in a twist conformation in the transition state (19) wherein the axial C–O bond maintains overlap and the $A^{1,3}$ interaction is avoided. The preferred mode of attack of the di-*n*-butylcuprate would occur from the α face of the double bond, syn to the oxygen.[19]



Oxirane 5 would preferentially react through the conformation 20. Although $A^{1,3}$ interactions must occur to some extent between the oxirane methylene and the ethylidene group, this difficulty must be sustained to attain overlap. The approach of the cuprate is favored on the β face in an anti mode distal to the ring methyl group.

The results obtained with the (*E*)-pentylideneoxirane are somewhat anomalous. Transition-state 21 would account for the appearance of the major regioisomers 16 and 18 via an anti approach to the vinyl oxirane system from the β face in spite of the "axial" methyl group. This disparity may well lie in the nature of the lithium dimethylcuprate which may be considered both less regiospecific and less sterically demanding than the dibutylcuprate reagent.

It can be seen that our original premise discussed at the beginning of the paper cannot be readily attained in this system by simply ordering the introduction of the alkyl residues. This condition has been met in part by inverting the stereochemistry of the double bond (7 vs. 3). However, this stereoselectivity is not simply achieved by a single operational inversion but rather by three: double bond isomerism, relative stereochemistry of the asymmetric centers, and mode of attack of the cuprate. Unless all of the three factors can be controlled, a high degree of selectivity cannot be attained.

Experimental Section

Melting points were determined on a Fisher-Johns apparatus and are corrected. Elemental analyses were performed by Atlantic Microlabs, Inc. and Olin Corp.

Proton nuclear magnetic spectra (^{1}H NMR) were recorded on a Perkin-Elmer R-32 (90 MHz) or Bruker HX-270 (270 MHz) spectrometer. Carbon-13 nuclear magnetic spectra (^{13}C NMR)

(19) This process is envisaged as an anti attack of the cuprate on the double bond to give a π-allyllike complex which transfers an alkyl group with retention of configuration. The complex, or facsimile thereof, is reasonable in view of Goering's results.[3c]

were recorded on a Varian CFT-20 (20 MHz) spectrometer. Chemical shifts are reported in parts per million (δ) downfield from tetramethylsilane. Infrared spectra were recorded on a Beckman IR 4250 spectrometer and are calibrated relative to the 1601-cm^{-1} stretch of polystyrene. Gas chromatography–mass spectra were determined on a Hewlett-Packard 5985A GC-MS-DS containing a 3 ft × $^1/_8$ in. 3% OV-101 column.

Gas chromatograms were recorded by employing a Varian 90-P or 1400 thermal conductive or Perkin-Elmer 3920-FID unit. The following columns were employed: A, 5 ft × $^1/_8$ in., 10% Carbowax 20M on Chromosorb W-HP (80/100); B, 5 ft × $^1/_8$ in. 1.5% OV-101 on Chromosorb GHP (100/120); C, 6 ft × $^1/_4$ in. 20% Carbowax 20M on Chromosorb W (40/60); D, 5 ft × $^1/_8$ in. 5% OV-1 on Chromosorb W-HP (80/100). Preparative liquid chromatography was accomplished on a Waters Prep LC/500 using a single silica gel cartridge.

Ether and tetrahydrofuran (THF) were dried over sodium–benzophenone ketyl, methanol was dried over $Mg(OCH_3)_2$, and dimethyl sulfoxide and methylene chloride were dried over CaH_2.

(*E*)-2-Ethylidene-3-methylcyclohexanone (2) and (*Z*)-2-Ethylidene-3-methylcyclohexanone (6). The method of Heng and Smith[13] was exmployed. A solution of crude aldol products (from 0.15 mmol of cyclohexenone) dissolved in 200 mL of benzene containing 2.03 g of *p*-toluenesulfonic acid was refluxed with azeotropic removal of water over a period of 3 h. The reaction mixture was cooled to room temperature, poured into saturated sodium bicarbonate solution, and extracted with ether. The organic layers were combined, dried, and concentrated in vacuo. The residue was distilled to give 11.4 g (55%) of the product as a colorless oil [bp 44 °C/(0.75 torr)] consisting of a 4:1 mixture of (*E*)- and (*Z*)-ethylidene enones **2** and **6**, respectively, as determined by GC analysis (column D) and NMR spectroscopy. Separation of the enone mixture was achieved on a Waters Prep LC/500 unit (5% ether/hexane). (*E*)-Ethylidene enone **2** had the following physical properties:[13] IR (CCl_4) 1683 and 1614 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.58 (1 H, q, J = 7 Hz), 3.13 (1 H, m), 2.49 (1 H, m), 2.27 (1 H, m), 2.05–1.57 (4 H, br m), 1.76 (3 H, d, J = 7 Hz), 1.05 (3 H, d, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 201.55, 142.44, 133.13, 39.96, 30.18, 29.66, 19.68, 18.47, 12.86. For (*Z*)-ethylidene enone **6**: IR (CCl_4) 1689 and 1631 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.65 (1 H, m), 2.55 (1 H, m), 2.46 (2 H, m), 2.06–1.79 (3 H, br m), 1.83 (3 H, d, J = 7 Hz), 1.51 (1 H, m), 1.08 (3 H, d, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 204.78, 143.41, 128.31, 42.63, 38.47, 32.78, 22.02, 19.24, 14.66.

3-Methyl-(*E*)-2-pentylidenecyclohexanone (4). By employment of the same scale reaction as above with *n*-valeraldehyde and dehydration in toluene, 17.6 g (65%) of a colorless liquid was obtained [bp 60 °C (0.02 torr)], which contained **4** (60%), its *Z* isomer (20%), and the β,γ-unsaturated isomer (20%). The *E* isomer could be separated from the latter two isomers (Waters LC-500, 5% ether/hexanes): bp 64 °C (0.02 torr); IR (CCl_4) 1684 and 1615 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.46 (1 H, t, J = 8 Hz), 3.10 (1 H, m), 2.56–1.26 (12 H, br m,), 1.04 (3 H, d, J = 7 Hz), 0.91 (3 H, t, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 202.09, 141.51, 138.81, 40.16, 30.76, 30.40, 30.20, 27.03, 22.35, 20.25, 18.56, 13.73.

Anal. Calcd for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 79.89; H, 11.05.

4-*tert*-Butyl-(*E*)-2-ethylidenecyclohexanone (8). A solution of 1.85 g (10.2 mmol) of 4-*tert*-butyl-2-(hydroxymethylene)-cyclohexanone[20] in 20 mL of dry ether at 0 °C under N_2 was treated dropwise with 1.30 mL (15.7 mmol) of dry pyrrolidine. After 5 min the ice bath was removed and the reaction mixture stirred at 25 °C for 1 h. Anhydrous magnesium sulfate was added and the mixture filtered and concentrated to give a yellow oil which was crystallized from hexane to give 2.0 g (83%) of 4-*tert*-butyl-2-(pyrrolidinomethylene)cyclohexanone as a pale yellow solid: mp 53–56 °C; IR (CCl_4) 1655, 1547 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.63 (1 H, br s), 3.71–3.41 (4 H, m), 3.03–2.73 (1 H, m), 2.48–1.17 (10 H, m), 0.91 (9 H, s). Anal. Calcd for $C_{15}H_{25}NO$: C, 76.54; H, 10.71; N, 5.95. Found: C, 76.76; H, 10.68; N, 6.04.

To a solution of 488 mg (2.07 mmol) of the vinylogous amide in 5 mL of ether at 0 °C was added dropwise 1.1 mL of 2.2 M ethereal methylmagnesium bromide. The cooling bath was removed, and stirring was continued for 1 h. The reaction mixture was decomposed with 10 mL of 10% H_2SO_4 and stirred 10 min. The aqueous layer was thoroughly extracted with ether, dried over $MgSO_4$, filtered, and concentrated to give 298 mg (80%) of **8** (>90% *E*) upon distillation: bp 85–90 °C (0.08 torr; Kugelrohr); IR (CCl_4) 1690, 1618 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.87–6.53 (*E* isomer), 5.69–5.39 (*Z* isomer, 1 H, m), 2.90–1.26 (7 H, m), 1.73 (3 H, d, J = 7 Hz), 0.95 (9 H, s). Anal. Calcd for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 79.65; H, 10.97.

(*E*)-Ethylideneoxirane 3. A dispersion of 0.58 g (12.0 mmol) of NaH (50%) was thoroughly washed with dry hexane (from CaH_2) under N_2 followed by removal of residual hexane with a stream of N_2. Dry dimethyl sulfoxide (20 mL, from dimsyl anion) was added and the mixture stirred at 70 °C until gas evolution ceased (1 h). To the cooled solution at 0 °C was added dropwise 2.48 g (12.0 mmol) of trimethylsulfonium iodide in 10 mL of dry Me_2SO. After the addition was complete, the mixture was stirred 5 min, followed by the dropwise addition of 552 mg (4.0 mmol) of enone **2** in 2 mL of THF. The reaction mixture was allowed to stir for 2 h at 0 °C and then for 18 h at 25 °C. The reaction mixture was diluted with an equal volume of water, extracted thoroughly with hexane, washed with saturated brine, dried, filtered, and concentrated to give a mixture of (*E*)-ethylideneoxirane **3** (80%) and enone **2** (20%). Recycling of the mixture gave complete conversion. Distillation afforded 390 mg (64%) of **3** as a colorless oil: bp 78 °C (1.0 torr); IR (CCl_4) 3035, 1450, 909 and 837 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.45 (1 H, q, J = 7 Hz), 3.08 (1 H, m), 2.71 (1 H, d, J = 6 Hz), 2.43 (1 H, br d, J = 6 Hz), 2.01–1.45 (5 H, br m), 1.58 (3 H, d, J = 7 Hz), 1.31 (1 H, m), 1.01–1.05 (3 H, d, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 140.70, 112.93, 57.43, 57.14, 34.61, 31.39, 30.22, 19.63, 17.96, 11.14; mass spectrum (70 eV), m/e (relative intensity) 152 (M^+, 38), 123 (82), 95 (61), 93 (43), 91 (45), 81 (100), 79 (47), 67 (78), 55 (64).

(*E*)-Pentylideneoxirane 5. The material was prepared on the scale described for **3** except that recycling was unnecessary. Distillation (Kugelrohr) gave 400 mg (84%) of **5**: bp 60 °C (0.02 torr); IR (CCl_4) 3029, 1450, 1187 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.37 (1 H, t, J = 8 Hz), 3.05 (1 H, m), 2.71 (1 H, d, J = 6 Hz), 2.43 (1 H, br d, J = 6 Hz), 2.11–1.56 (6 H, br m,), 1.54–1.24 (6 H, br m), 1.03 (3 H, d), 0.90 (3 H, t, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 140.00, 118.90, 57.12, 56.90, 34.61, 31.45 (2 C), 30.52, 25.52, 21.61, 19.48, 18.14, 13.18; mass spectrum (70 eV), m/e (relative intensity) 194 (M^+, 38), 149 (66), 137 (67), 133 (97), 109, (78), 105 (57), 95 (100), 93 (71), 91 (68), 81 (91), 79 (60), 67 (78), 57 (62), 55 (92).

(*Z*)-Ethylideneoxirane 7. This compound was prepared on a 9.0-mmol scale as described for **5** in 82% yield: bp 72 °C (4 torr); IR (CCl_4) 3034, 1453, 906, 854 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.16 (1 H, q, J = 7 Hz), 2.60 (1 H, d, J = 6 Hz), 2.56 (1 H, d, J = 6 Hz), 2.16 (1 H, m), 1.96–1.51 (4 H, br m), 1.77 (3 H, d, J = 7 Hz), 1.44–0.96 (2 H, br m), 1.04 (3 H, d, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 140.73, 115.19, 6067, 52.26, 38.70, 36.01, 35.69, 23.97, 17.65, 12.72; mass spectrum (70 eV), m/e (relative intensity) 152 (M^+, 2), 123 (5), 86 (18), 84 (8), 81 (6), 71 (10), 58 (6), 57 (100), 56 (70), 55 (13).

(*E*)-Ethylideneoxirane 9. This compound was prepared in 84% yield as described above without recycling: ^1H NMR ($CDCl_3$) δ 5.82 (1 H, q, J = 8 Hz), 2.82 (1 H, td, ABX, J_{AX} = 11 Hz, J_{BX} = 3 Hz, axial C-3 proton), 2.63 (1 H, d, J_{AB} = 6.5 Hz), 2.41 (1 H, dd, J_{AB} = 6.5 Hz, J_{AX} = 1.5 Hz), 2.30–1.00 (6 H, m), 1.50 (3 H, d, J = 8 Hz), 0.92 (9 H, s); ^{13}C NMR ($CDCl_3$) δ 136.73, 113.53, 60.20, 56.69, 47.65, 34.46, 32.25, 28.62, 27.94, 27.27, 26.54, 26.11, 11.66.

(*E*)-Ethylidenecyclohexanol 11. To a stirred solution of 260 mg (1.71 mmol) of (*E*)-ethylideneoxirane **3** in 10 mL of dry ether cooled in an ice–salt bath was added in small portions 280 mg (0.74 mmol) of lithium aluminum hydride. The resulting suspension was stirred for 1 h at 0 °C. Saturated sodium sulfate solution was added cautiously until all of the reducing agent was destroyed. The mixture was taken up in ether and dried. Concentration in vacuo afforded 230 mg (88%) of (*E*)-ethylidenecyclohexanol **11** as a colorless oil which crystallized upon being allowed to stand to give a low-melting solid but defied successful recrystallization: IR (CCl_4) 3775–3400, 1449, 1374, 1125, 952, 921 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.76 (1 H, q, J = 7 Hz), 3.03 (1 H, m), 1.84 (1 H, m), 1.73–1.44 (5 H, br m), 1.62 (3 H, d, J = 7 Hz), 1.37 (1 H, br m), 1.34 (3 H, s), 1.06 (3 H, d, J = 7 Hz); gas chromatograph–mass spectrum (70 eV), m/e (realative intensity) 154 (M^+,

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15), 139 (36), 136 (69), 121 (100), 107 (86), 105 (36), 93 (94), 91 (59), 79 (61), 77 (38).

Hydrogenation of (*E*)-Ethylidenecyclohexanol 11. A solution of 92 mg (0.6 mmol) of (*E*)-ethylidenecyclohexanol **11** in 10 mL of anhdrous methanol containing 30 mg of 10% palladium on charcoal was reduced under 1 atm of hydrogen at 23 °C. After the hydrogen uptake had ceased, the mixture was filtered through Celite 545 and concentrated, affording 80 mg (86%) of crude product as a colorless oil. GC analysis on column A indicated the presence of two alcohols in the ratio of 50:50. These isomers were separated by preparative gas chromatography on column B at 110 °C. The TT cyclohexanol (retention time 8.0 min, column A) had the following physical properties: IR (CCl_4) 3650–3240, 1457, 1375, 918 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.72–1.19 (10 H, br m), 1.21 (3 H, s), 0.97 (3 H, t, J = 8 Hz), 0.93 (3 H, d, J = 6 Hz), 0.69 (1 H, m); gas chromatograph–mass spectrum (70 eV), m/e (relative intensity) 156 (M^+, 13), 138 (24), 113 (23), 109 (34), 96 (25), 95 (31), 82 (16), 81 (26), 71 (100), 58 (19), 55 (16). For the CC cyclohexanol (retention time 11.3 min, column A): ^1H NMR ($CDCl_3$) δ 2.08 (1 H, m), 1.66–1.13 (10 H, br m), 1.20 (3 H, s), 0.97 (3 H, t, J = 8 Hz), 0.88 (3 H, d, J = 7 Hz); gas chromatograph–mass spectrum (70 eV), m/e (relative intensity) 156 (M^+, 9), 138 (22), 113 (20), 109 (40), 96 (25), 95 (28), 82 (17), 81 (32), 71 (100), 58 (18).

(*Z*)-Ethylidenecyclohexanol 14. This compound was prepared in 86% yield as described for **11**: IR (CCl_4) 3644–3200, 1454 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.18 (1 H, br q, J = 7 Hz), 2.08 (1 H, m), 1.94 (3 H, d, J = 7 Hz), 1.81–1.38 (6 H, br m), 1.38 (3 H, s), 1.03 (1 H, br m), 1.00 (3 H, d, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 147.34, 115.86, 75.85, 43.09, 35.58, 35.48, 27.37, 22.08, 19.15, 14.36; gas chromatograph–mass spectrum (70 eV), m/e (relative intensity) 154 (M^+, 37), 139 (100), 111 (44), 93 (37), 81 (59), 72 (43), 69 (37).

Hydrogenation of (*Z*)-Ethylidenecyclohexanol 14. Reduction was accomplished as described for **11** in 82% yield to provide a 4:1 ratio of the CT cyclohexanol (retention time 10.8 min) and the TC cyclohexanol (retention time 9.8 min), respectively, as determined by GC analysis on column A. The clean separation of these isomers was difficult. The pure CT isomer was prepared by another route (vide infra) and compared by GC retention times. The mixture could not be resolved by gas chromatography–mass spectroscopy (OV-101, 70 eV): m/e (relative intensity) 156 (M^+, 11), 138 (27), 113 (28), 109 (41), 96 (29), 95 (36), 82 (16), 81 (30), 71 (100).

***trans*- (12) and *cis*-2-Ethyl-3-methylcyclohexanone (13).** A solution of 1.28 g (9.3 mmol) of enone **3** in 20 mL of anhydrous methanol containing 12 mg of 10% Pd/C was reduced under 1 atm of hydrogen at 22 °C. After the uptake of hydrogen had ceased, the mixture was filtered through Celite 545. Concentration of the filtrate afforded 1.10 g (85%) of a mixture (~1:1) of ketones **12** and **13**. Stereochemical assignments were achieved by epimerization of this material with sodium methoxide (10 mol %) in anhydrous methanol to a 2:1 mixture of trans and cis isomers, respectively. These isomeric ketones were separated by preparative gas chromatography on column C. Trans ketone **12** had the following physical properties: IR (CCl_4) 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.42–2.21 (2 H, br m), 2.05–1.38 (8 H, br m), 1.04 (3 H, d, J = 7 Hz), 0.87 (3 H, t, J = 7 Hz); gas chromatograph–mass spectrum (70 eV), m/e (relative intensity) 140 (M^+, 20), 112 (28), 98 (15), 97 (100), 84 (11), 81 (15), 69 (31), 56 (16), 55 (24). For cis ketone **13**: IR (CCl_4) 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.32 (3 H, br m), 1.95–1.60 (6 H, br m), 1.28 (1 H, m), 0.85 (3 H, t, J = 7 Hz), 0.82 (3 H, d, J = 7 Hz); gas chromatograph–mass spectrum (70 eV), m/e (relative intensity) 140 (M^+, 18), 112 (29), 98 (14), 97 (100), 81 (14), 69 (33), 56 (17), 55 (25).

Reaction of Trans Ketone 12 with Methyllithium. To a stirred solution of 86 mg (0.6 mmol) of trans ketone **12** in 7 mL of dry ether cooled in an ice bath was added dropwise 2.0 mL (2.6 mmol) of 1.3 M methyllithium. After 1 h at 0 °C, the mixture was quenched with 10% NaH_2PO_4 solution, water was added, and the mixture was extracted with ether. The aqueous layer was washed with ether, and the combined organic layers were dried and concentrated in vacuo to give 85 mg (90%) of a 90:10 mixture (determined by VPC analysis on column A) of TT cyclohexanol and CT cyclohexanol, respectively, as a colorless oil. Separation of these isomers was accomplished by preparative gas chromatography on column A. The stereochemical assignment was supported by the behavior of the two isomers of column A (110 °C). The more polar equatorial alcohol (CT cyclohexanol) had a longer retention time (10.8 min) than its axial isomer (TT cyclohexanol, 8.0 min). The former compound was identical (GC retention time) with the major component (CT) formed by the hydrogenation of (*Z*)-ethylidenecyclohexanol **14**, while the major component had the retention time (8.0 min) of one of the components from hydrogenation of (*E*)-ethylidenecyclohexanol **11**. For the TT cyclohexanol: NMR ($CDCl_3$) δ 1.75–1.49 (5 H, br m), 1.48–1.15 (5 H, br m), 1.10 (3 H, s), 1.00 (3 H, t, J = 8 Hz), 0.95 (3 H, d, J = 7 Hz), 0.82 (m, 1 H); gas chromatograph–mass spectrum (70 eV), m/e (relative intensity) 156 (M^+, 11), 138 (25), 113 (27), 109 (36), 96 (29), 95 (35), 82 (19), 81 (25), 71 (100), 58 (17).

Reaction of Cis Ketone 13 with Methyllithium. In the manner described (vide supra), ketone **13** provided the TC cyclohexanol without any detectable trace (GC) of any other isomer, all of which have different retention times. The TC cyclohexanol (column A, retention time 9.8 min, 110 °C) agreed with the minor component from hydrogenation of (*Z*)-ethylidenecyclohexanol **14**. For the TC cyclohexanol: IR (CCl_4) 3640–3390, 1455, 1374, 930 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.93–1.14 (11 H, br m), 1.24 (3 H, s), 0.95 (3 H, d, J = 7 Hz), 0.94 (3 H, t, J = 7 Hz); gas chromatograph–mass spectrum (70 eV), m/e (relative intensity) 156 (M^+, 8), 138 (20), 113 (26), 109 (27), 96 (20), 95 (27), 82 (15), 81 (26), 71 (100), 67 (15), 58 (26), 55 (26).

Allylic Alcohol 15. To a stirred suspension of 2.8 g (15.0 mmol) of cuprous iodide in 45 mL of dry ether cooled to 0 °C was added dropwise 16.5 mL (30.0 mmol) of methyllithium. After 5 min, 850 mg (5.6 mmol) of (*E*)-ethylideneoxirane **3** was added in 9 mL of ether. After being stirred 30 min at 0 °C, the reaction mixture was poured into a saturated ammonium chloride solution containing ammonium hydroxide (pH 9). After the mixture was stirred for 10 min, the layers were separated, the aqueous layer was extracted with ether, and the organic layers were combined, washed with water, dried, and concentrated in vacuo. The residue was distilled (Kugelrohr) to give 810 mg (86%) of allylic alcohol **15** as a colorless oil: bp 60 °C (0.02 torr); IR (CCl_4) 3615, 3572–3200 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.11 (2 H, m), 2.79 (1 H, septet, J = 7 Hz), 2.30 (1 H, m), 2.10 (2 H, m), 1.73–1.36 (5 H, br m), 1.09–1.04 (br m, 9 H); ^{13}C NMR ($CDCl_3$) δ 144.42, 129.03, 62.59, 31.03, 30.37, 29.38, 27.83, 22.99, 21.33, 20.91, 17.60.

Anal. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, 78.36; H, 12.01.

Reaction of (*E*)-Ethylideneoxirane 3 with Lithium Di-*n*-butylcuprate. The scale and conditions were the same as those above except that the cuprate was prepared at −30 °C and the reaction was run at −25 °C. Distillation (Kugelrohr) afforded 940 mg (82%) of a 95/5 mixture of diasteromers **16** and **17**, respectively, as a colorless liquid: bp 60 °C (0.02 torr); IR (CCl_4) 3700–3200, 1456, 994 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.15 (1 H, d, J = 12 Hz), 4.04 (1 H, d, J = 12 Hz), 2.58 (1 H, m), 2.26 (1 H, m), 2.14 (2 H, m), 1.83–1.09 (11 H, br m), 1.05 (6 H, d, J = 7 Hz), 0.88 (3 H, t, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 144.17, 129.84, 63.00, 36.00, 35.21, 31.14, 30.55, 29.27, 27.89, 22.78, 21.21 (2 C), 17.63, 13.93.

Anal. Calcd for $C_{14}H_{26}O$: C, 79.93; H, 12.46. Found: C, 79.80; H, 12.43.

***p*-Bromophenylurethane of Alcohol 16.** To a stirred solution of 230 mg (1.1 mmol) of allylic alcohol **16** and 280 mg (1.4 mmol) of *p*-bromophenyl isocyanate in 30 mL of dry THF was added 340 mg (0.3 mmol) of 1,4-diazabicyclo[2.2.2]octane (Dabco). The resulting solution was allowed to stir at 25 °C under nitrogen for 18 h. The solvent was removed in vacuo, and the residue was taken up in either. A small amount of water was added, and the mixture was stirred for 10 min. The mixture was dried and concentrated in vacuo. Preparative layer chromatography of the residue with 50:50 ether–hexane as the eluant afforded 380 mg (85%) of the *p*-bromophenylurethane as a white crystalline solid. Evaporative crystallization from pentane afforded large needles suitable for single-crystal X-ray analysis:[15] mp 87–88 °C; IR (CCl_4) 3438, 1740, 1500, 1200 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.41 (2 H, m), 7.28 (2 H, m), 6.58 (1 H, br s), 4.70 (1 H, d, J = 12 Hz), 4.64 (1 H, d, J = 12 Hz), 2.59 (1 H, m), 2.29 (1 H, m), 2.09 (2 H, m), 1.79–1.11 (10 H, br m), 1.07 (6 H, d, J = 7 Hz), 0.87 (3 H, t, J = 7 Hz).

Reaction of (*Z*)-Ethylideneoxirane 7 with Lithium Di-*n*-butylcuprate. In the manner described above for the *E* isomer, a mixture of diastereomers **16** and **17** was produced in a 1/3 ratio, respectively. The infrared spectrum appeared identical with that of **16**, and the 270-MHz NMR spectrum had the following signals in addition to those present in the isomer **16**: ($CDCl_3$) δ 4.11 (2 H, br m), 2.45 (1 H, m), 1.03 (3 H, d, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 144.37 (**17**), 144.04 (**16**), 130.21 (**16**), 130.00 (**17**, olefinic carbons).

Reaction of (*E*)-Pentylideneoxirane with Lithium Dimethylcuprate. To a stirred suspension of 8.55 g (45 mmol) of cuprous iodide in 150 mL of dry ether cooled to 0 °C was added dropwise 69.2 mL (90.0 mmol; 0.77 M solution) of methyllithium. After 10 min, 3.0 g (15.5 mmol) of (*E*)-pentylideneoxirane **5** was added in 30 mL of ether. After 40 min at 0 °C the reaction mixture was poured into a saturated ammonium chloride solution containing ammonium hydroxide (~pH 9). After the mixture was stirred for 10 min, the layers were separated, the aqueous layer was extracted with ether, and the organic layers were combined, washed with water, dried, and concentrated in vacuo. The residue was distilled (Kugelrohr) to give 3.05 g (94%) of a colorless liquid [bp 70 °C (0.02 torr)] consisting of 70% of **16** and **17** and 30% of **18** (VPC). Isomers **16** and **17** were separated from **18** (Waters Prep LC/500, 5% ether/hexane). The ratio of **16**/**17** was 85/15 as determined by integration of the multiplets at δ 2.45 and 2.58, respectively. Pentylidene alcohol **18** had the following physical properties: bp 60 °C (0.02 torr); IR (CCl_4) 3650-3375, 1458, 1046 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.19 (1 H, t, J = 7 Hz), 3.75 (1 H, d, J = 10 Hz), 3.13 (1 H, d, J = 10 Hz), 2.90 (1 H, m), 2.23-1.87 (3 H, m), 1.86-1.17 (10 H, br m), 1.12 (3 H, d, J = 7 Hz), 1.00 (3 H, s), 0.91 (3 H, t, J = 6 Hz); ^{13}C NMR ($CDCl_3$) δ 145.07, 123.32, 70.40, 40.94, 34.85, 32.25, 31.73, 29.62, 26.78 (2 C), 22.37, 21.70, 16.72, 13.79. Anal. Calcd for $C_{14}H_{26}O$: C, 79.93; H, 12.46. Found: C, 79.83; H, 12.43.

(*E*)-Pentylidenealdehyde 19. To a stirred suspension of pyridinium chlorochromate (310 mg, 1.43 mmol) and anhydrous sodium acetate (117 mg, 1.43 mmol) in 6 mL of methylene chloride was added a solution of (*E*)-pentylidene alcohol **18** (150 mg, 0.71 mmol) in 5 mL of methylene chloride. After being stirred for 4 h at 25 °C, the reaction mixture was diluted with ether and filtered through a pad of Florisil over Celite 545. The solids were washed well with ether. Concentration of the organic layers afforded 140 mg (95%) of crude product as a colorless oil. Distillation afforded 130 mg (89%) of (*E*)-pentylidene aldehyde **19**: bp 50 °C (0.02 torr); IR (CCl_4) 2800, 2705, 1728, 1465, 1456 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.30 (1 H, s), 4.77 (1 H, t, J = 7 Hz), 2.95 (1 H, m), 2.22-1.92 (2 H, br m), 1.82-1.39 (6 H, br m), 1.31 (4 H, br m), 1.23 (3 H, s), 1.12 (3 H, d, J = 7 Hz), 0.91 (3 H, m); gas chromatograph-mass spectrum (70 eV), m/e (relative intensity) 208 (M^+, 2), 179 (90), 123 (100), 109 (75), 97 (22), 95 (56), 81 (65), 67 (23).

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Registry No. 2, 59697-64-2; **3**, 75731-75-8; (*E*)-**4**, 75731-76-9; (*Z*)-**4**, 75731-77-0; **5**, 75731-78-1; **6**, 43011-49-0; **7**, 75766-22-2; (*E*)-**8**, 75731-79-2; (*Z*)-**8**, 75731-80-5; **9**, 75731-81-6; **11**, 75731-82-7; **12**, 75731-83-8; **13**, 75731-84-9; **14**, 75766-23-3; **15**, 75731-85-0; **16**, 75731-86-1; **16** *p*-bromophenylurethane, 75731-87-2; **17**, 75731-88-3; **18**, 75731-89-4; (*trans*)-(*E*)-1,3-dimethyl-2-pentylidenecyclohexanecarboxaldehyde, 75750-99-1; 2-cyclohexenone, 960-68-7; *n*-valeraldehyde, 110-62-3; 4-*tert*-butyl-2-(hydroxymethylene)cyclohexanone, 22252-96-6; 4-*tert*-butyl-2-(pyrrolidinomethylene)cyclohexanone, 75731-90-7; methyl bromide, 74-83-9; *p*-bromophenyl isocyanate, 2493-02-9; (*TT*)-1,3-dimethyl-2-ethylcyclohexanol, 75731-91-8; (*CC*)-1,3-dimethyl-2-ethylcyclohexanol, 75766-24-4; (*CT*)-1,3-dimethyl-2-ethylcyclohexanol, 75766-25-5; (*TC*)-1,3-dimethyl-2-ethylcyclohexanol, 75766-26-6.

Reactions of α,β-Unsaturated Ketones with Hydrogen Sulfide. γ-Keto Sulfides or Tetrahydrothiopyranols?[1]

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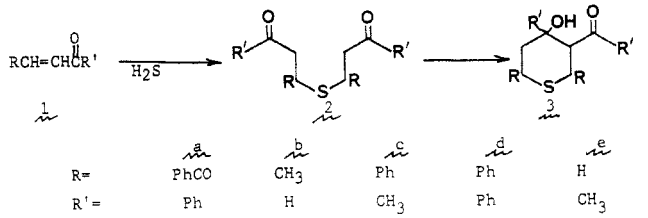
The reaction of several α,β-unsaturated ketones with H_2S under a variety of conditions has been investigated. With *trans*-1,2-dibenzoylethylene (**1a**) the tetrahydrothiopyranol **3a** is the only product, not the corresponding open-chain sulfide **2a** reported in the literature. The product from benzylideneacetone (**1c**) is the tetrahydrothiopyranol (**3c**) with the relative configuration at C-4 epimeric with that reported in the literature based on the observation of long-range coupling of the hydroxyl and C-5 axial hydrogen in one isomer. The "α-, β-, and γ-sulfides" reported from benzylideneacetophenone (**1d**) were shown to be (α-sulfide) a mixture of the diastereomeric sulfides **2d**, (β-sulfide) the tetrahydrothiopyranol **3d** with the stereochemistry **12**, once again based on long-range coupling of the OH and C-5 axial hydrogen, and (γ-sulfide) the tetrahydrothiophene **13**. From methyl vinyl ketone (**1e**) an authentic sample of the open-chain sulfide **2e** could be obtained with H_2S and cyclized with Na_2S to the tetrahydrothiopyranol **3e** as a mixture of epimers **21** and **22** whose structures were assigned from ^{13}C chemical shift data.

The base-catalyzed conjugate addition of H_2S to α,β-unsaturated ketones **1** to give γ-keto sulfides **2** appears to be a well-known reaction.[2] What is not well-known, however, is that sometimes sulfides such as **2** undergo a facile intramolecular aldol condensation to give tetra-



(1) Taken from the Ph.D. dissertation of D. Del Mazza, Texas Christian University, 1980.

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