careful examination of new compounds.

Experimental Section

X-ray Crystallography. $C_{20}H_{24}N_2O$, M_w = 308.43. Crystals obtained by slow evaporation of a solution in acetone–ether; orthorhombic, $P2_12_12_1$, a = 6.535 (1) Å, b = 12.484 (2) Å, c = 20.039 (5) Å, V = 1634.8 Å^3, d_c = 1.25 g cm^{-3}, Z = 4, I (Cu Kα) = 1.5418 Å, F(000) = 664, m, 5.3 cm^{-1} (absorption ignored). Data collected from a small crystal (0.3 × 0.3 × 0.4 mm) on a Cad-4 Nonius diffractometer, using graphite monochromated Cu Kα radiation and the q – 2q scan technique up to q = 68°. From the 3071 (hkl and $-hkl$) measured reflections, of which 1732 were unique (R_{sym} = 0.037), 1680 were considered as observed having $I > 3s(I)$, $s(I)$ from counting statistics, and kept in refinement calculations. The structure was solved by direct methods[16] and refined by full-matrix least-squares methods, minimizing the function $S(F_o - F_c)^2$.[17] Difference Fourier maps showed all the hydrogen atoms. They were refined and affected an isotropic thermal factor equivalent to that one of the bonded atom, plus 10%. Convergence was reached at R = 0.038, R_w = 0.039 (with $R_w = [Sw(F_o - F_c)^2/SWF_o^2]^{1/2}$ and $w = 1/s^2(F_o)$). No residual was higher than 0.22 e Å^{-3} in the final difference map. In the crystal, the molecules are linked by hydrogen bonds established between the hydrogen atom HN1 of one molecule and the oxygen atom O23 of another (d N1···O23 = 2.985 (19) Å, angle N1–H1–O23 = 145°).

Mass Spectrometry. Tandem mass spectrometry experiments were carried out on a triple quadrupole R-30-10 Nermag mass spectrometer. Ionization conditions: bombardment gas = xenon; FAB gun voltage = 9 kV; FAB matrix = glycerol. Collisionally activated dissociation (CAD) conditions: collision gas = argon; collision gas pressure = 4 × 10^{-6} Torr; collision energy (E_{lab}) between 0 and 30 eV. The values of lens potentials were optimized for obtaining maximum intensity of the MH$^+$ ion peaks before introduction of the collision gas.

Acknowledgment. We thank Professor J.-C. Tabet and Professor J. Bedin (Université Pierre et Marie Curie, Paris) for allowing us access to instrumental facilities for the mass spectrometry.

Registry No. (±)-1, 134779-80-9; 2, 57103-59-0; 5, 117611-47-9; 6, 117678-03-2.

Supplementary Material Available: Tables of atomic coordinates, anisotropic thermal parameters, bond lengths, and selected bond and torsion angles (4 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(16) Sheldrick, G. M. *SHELXS86. A Program for Solution of Crystal Structure from Diffraction Data*; University of Göttingen, Germany, 1986.
(17) Sheldrick, G. M. *SHELX76. Program for Crystal Structure determination*, University of Cambridge, United Kingdom, 1976.

On the Mechanism of Lewis Acid Promoted Ene Cyclizations of ω-Unsaturated Aldehydes

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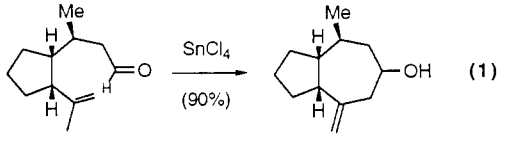
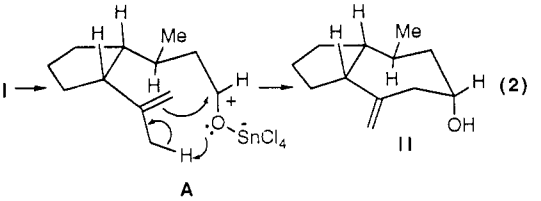
The diastereomerically labeled d_1 enals **1** and **2** were prepared from (*S*)-3-bromo-2-methylpropanol **5** by a sequence involving homologation to the allylic alcohol **13** and Sharpless epoxidation to either the α- or the β-epoxide diastereomers **14** or **15**. Reduction with $LiAlD_4$ afforded the diastereomerically deuterated diols **16** and **20**, respectively. Deoxygenation of the thionocarbonate derivatives **17** and **21** followed by THP ether cleavage and Swern oxidation afforded aldehydes **1** and **2**. The undeuterated aldehyde **28** was similarly prepared. Cyclization of **1** and **2** with Me_2AlCl afforded the *cis*-(*E*)-ethylidenecyclohexanols **3** and **4**, respectively, as the major products in accord with a mechanism involving internal proton or deuteron transfer from the vinylic CHD grouping to the aldehyde carbonyl. Product ratios (*E*:*Z*, cis:trans) from the two aldehydes were significantly different, indicative of a substantial isotope effect.

Some years ago we described a stereoselective synthesis of hydroazulenes through cyclization of ω-unsaturated aldehydes such as **I** (eq 1).[1] To account for the predominance of the trans product **II** and the absence of endocyclic double bond isomers we suggested a mechanism involving internal proton transfer as formulated for the ene reaction (eq 2). Subsequent studies by Snider and co-workers on Lewis acid cyclizations of 5-hexenals were consistent with this proposal.[2]



I II α-OH (major) III β-OH (minor)



A II

While transition state **A** nicely accounts for the stereochemistry and regiochemistry of these cyclizations, the alternative pathway **B** involving external proton transfer is also possible (eq 3).[3] In the case of aldehyde **I** only the

(1) Marshall, J. A.; Andersen, N. H.; Johnson, P. C. *J. Org. Chem.* 1970, *35*, 186.

(2) Johnston, M. I.; Kwass, J. A.; Beal, R. B.; Snider, B. B. *J. Org. Chem.* 1987, *52*, 5419. For a comprehensive review, see: Snider, B. B. in *Comprehensive Organic Synthesis*; Heathcock, C. H., Ed.; Pergamon Press: Oxford, 1991; Vol. 2, pp 527–562.

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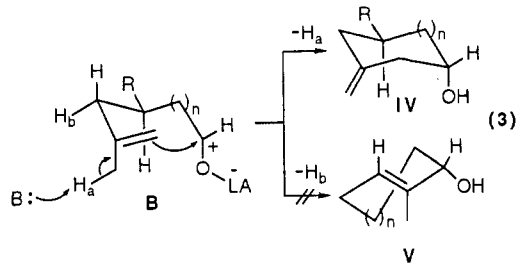
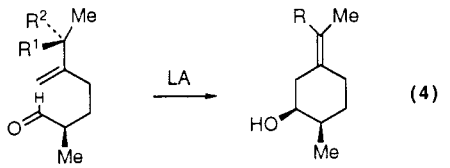


allylic CH_3 protons can attain a stereoelectronically favorable orientation for concerted cyclization via **A** or **B**. In the hexenyl cyclizations studied by Snider, H_b is also favorably aligned for concerted intermolecular loss.[2] However, this pathway is energetically disfavored as it would lead to a *trans*-cyclohexene (**V**). Thus, the exclusive formation of exocyclic olefinic products does not constitute proof for internal proton transfer.

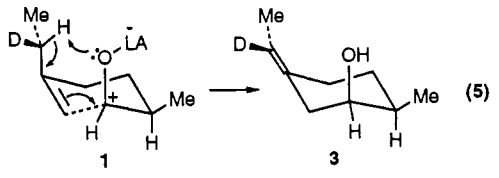
In connection with our recent findings that Lewis acid ene-type cyclizations can be employed for 12- and 14-membered ring formation, the question of internal vs external proton transfer became relevant to the design of suitable cyclization substrates.[4] We therefore decided to conduct studies that would distinguish these two reaction pathways.

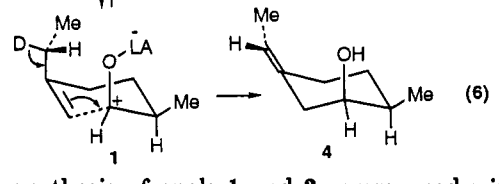
Our plan entailed the synthesis of diastereomerically deuterated enals **1** and **2** and their cyclization to the (*E*)-ethylidenecyclohexanols **3** and **4** (eq 4). As illustrated



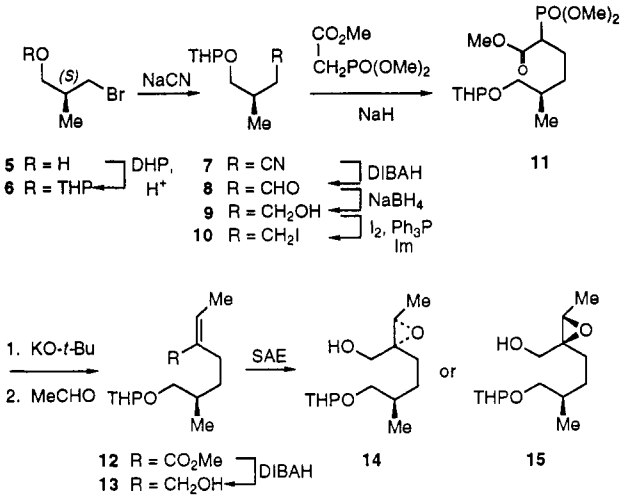
1 $R^1 = H, R^2 = D$ 3 R = D
2 $R^1 = D, R^2 = H$ 4 R = H

in eqs 5 and 6, aldehyde **1** would give rise to the (ethylidene-d_1)-cyclohexanol **3** by internal proton transfer or the d_0 analogue **4** by external deuterium abstraction. The opposite outcome would be expected for aldehyde **2**.

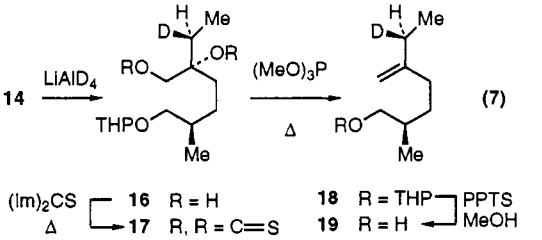




Our synthesis of enals **1** and **2** commenced with the (*S*)-bromo alcohol **5**.[5] Reaction of the THP derivative **6** with NaCN afforded the nitrile **7**. In sequential reduction–hydrolysis, reduction led to the alcohol **9**. The derived iodide[6] was converted to the phosphono ester **11** which underwent Wittig condensation with acetaldehyde leading to ester **12** as an 85:15 inseparable *E*:*Z* mixture.[7] Reduction of this mixture with DIBAH afforded the alcohol **13**, also an inseparable mixture, in 96% yield. Allylic alcohol **13** was subjected, as the mixture, to Sharpless epoxidation leading to **14** (D-(−)-DIPT reagent) or **15** (L-(+)-DIPT reagent).[8] Evaluation of the stereoisomeric purity of these epoxides was complicated by the presence of the THP grouping which caused a doubling of potentially diagnostic ^1H and ^{13}C NMR signals. Although each epoxide appeared homogeneous, it is likely that the minor isomer, arising from the 15% of (*Z*)-olefin present in **12** and **13**, escaped detection in each case. The presence of these isomers would eventually lead to contamination of **1** by **2** and vice versa assuming no differences in the ensuing Sharpless epoxidations of the *E* vs *Z* allylic alcohols.



Reduction of epoxide **14** with $LiAlD_4$ afforded diol **16**. Deoxygenation via the thionocarbonate **17**[9] and then THP cleavage gave rise to the unsaturated alcohol **19** (eq 7). An



analogous sequence was employed to convert epoxide **15** to the diastereomeric unsaturated alcohol **23** (eq 8). In a like manner the nondeuterated unsaturated alcohol **27** was prepared from epoxide **15** (eq 9).

The three unsaturated alcohols were oxidized to the corresponding aldehydes by the method of Swern.[10] Cyclization was effected by treatment with 1 equiv of Me_2AlCl in CH_2Cl_2 at −78 °C for 0.5 h. The undeuterated aldehyde **28** afforded an 85:15 mixture of cis, *E* and *cis*, *Z* products **4** and **29** with less than 5% of the trans isomers (eq 10).[11]

(3) Conceivably, **I** could cyclize through the alternative higher energy chair conformation in which the Me substituent adopts an axial and the $OSnCl_4$ an equatorial orientation with intermolecular proton transfer. Support for the preferential formation of axial alcohols, as in **A** → **II** and **B** → **IV**, comes from studies on cyclizations leading to rigid trans-fused ring systems. Andersen, N. H.; Uh, H.-S.; Smith, S. E.; Wuts, P. G. M. *J. Chem. Soc., Chem. Commun.* **1972**, 956.

(4) Marshall, J. A.; Andersen, M. W. *J. Org. Chem.* **1992**, *57*, 2766.

(5) Aldrich Chemical Co., Milwaukee, WI 53233, Catalogue 1992–1993, item no. 32,505-8.

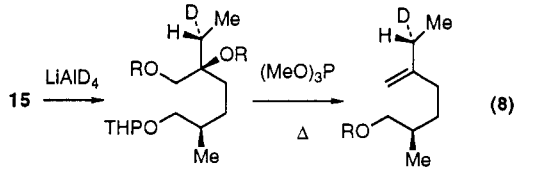
(6) Corey, E. J.; Pyne, S. G.; Su, W. *Tetrahedron Lett.* **1983**, *24*, 4883. Lange, G. L.; Gottardo, C. *Synth. Commun.* **1990**, *20*, 1473.

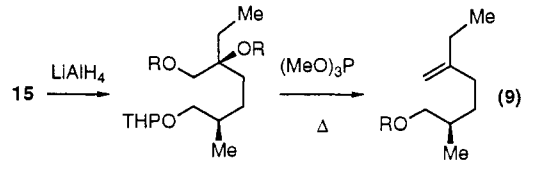
(7) Marshall, J. A.; DeHoff, B. S.; Cleary, D. G. *J. Org. Chem.* **1986**, *51*, 1735.

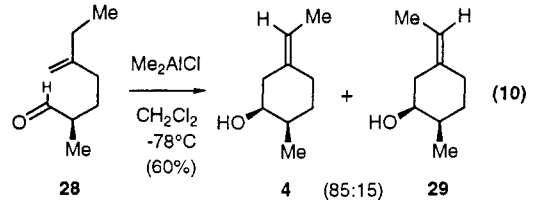
(8) Hanson, R. M.; Sharpless, K. B. *J. Org. Chem.* **1986**, *51*, 1922.

(9) Corey, E. J.; Carey, F. A.; Winter, R. A. E. *J. Am. Chem. Soc.* **1965**, *87*, 934. The ^1H NMR spectra of the thionocarbonates derived from **17** and **21** after hydrolysis of the THP grouping showed no distinctive ^1H NMR signals that could be used to evaluate their diastereomeric purity.

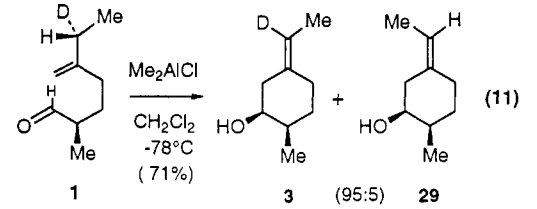
(10) Omura, K.; Swern, D. *Tetrahedron* **1978**, *34*, 1651.





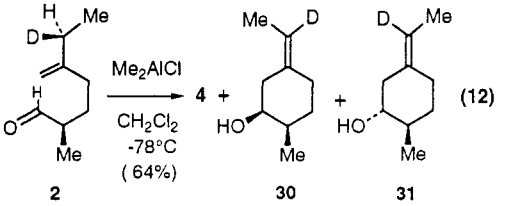


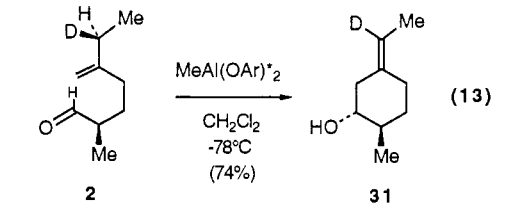
Under identical conditions the deuterated enal **1** gave a 95:5 mixture of *cis-E-*d_1 and *cis-Z-*d_0 products **3** and **29** (eq 11).[12] The diastereomeric deuterated enal **2**, on the



other hand, gave rise to a 5:3:1 mixture of *cis-E-*d_0**-4**, *cis-Z-*d_1**-30** and *trans-E-*d_1**-31** alcohols (eq 12).[13,14] An authentic sample of the latter alcohol was secured through cyclization of enal **2** with Yamamoto's MABR reagent (eq 13).[15,16]

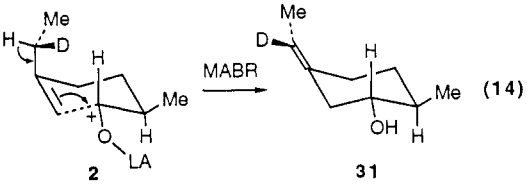
These results support an ene cyclization pathway involving internal proton transfer, as illustrated in eq 5. Comparison of product ratios for the three aldehydes **1**, **2**, and **28** reveals a significant deuterium isotope effect consistent with this conclusion.[12,13] Thus, less of the minor *cis-Z-***29** is formed from **1** (loss of D) than from **28** (loss of

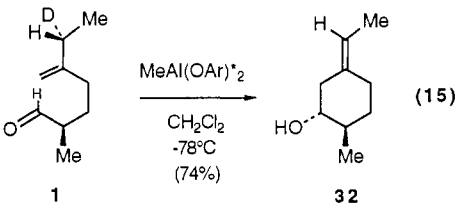




H). More dramatically, enal **2** gives rise to significantly greater amounts of *cis-Z-***30** (loss of H) and *trans-E-***31** (loss of H) products at the expense of the alcohol (loss of D) *cis-E-***4**.

The MABR-promoted cyclization of **2** (eq 13) must proceed by external proton transfer (eq 14).[17] In accord with this analysis, the diastereomeric enal **1** gave the trans, *E*, d_0 product **32** exclusively (after correcting for contamination by **2**) upon treatment with MABR (eq 15). Here the deuterium isotope effect, if operative, is evidently insufficient to perturb the preferred reaction pathway.





Me_2AlCl-promoted reactions appear to be more sensitive to subtle structural changes than the analogous MABR reactions. The magnitude of the deuterium isotope effect suggests a concerted nearly symmetrical transition state for the former cyclization.[18]

Experimental Section[19]

(*S*)-3-Bromo-2-methyl-1-[(tetrahydropyranyl)oxy]propane (6). To 12.4 g (81.0 mmol) of (*S*)-(+)-3-bromo-2-methyl-1-propanol (Aldrich, 97%)[5] at 0 °C was added 7.2 mL (81.0 mmol) of dihydropyran. An exothermic reaction ensued, and after several minutes TLC analysis indicated the reaction was complete. The reaction mixture was purified directly by flash chromatography (hexanes, then 10% ether/hexanes) affording 18 g (94%) of acetal **6** as a 1:1 mixture of diastereomers: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.57 (m, 1 H, acetal H), 3.83 (m, 1 H, CH_2Br), 3.69–3.61 (m, 1 H, CH_2OTHP), 3.54–3.43 (m, 3 H, CH_2Br, ring CH_2O), 3.33–3.24 (m, 2 H, CH_2OTHP), 2.12–2.05 (m, 1 H, CHMe), 1.80–1.48 (m,

(11) Under comparable conditions the desmethyl analogue of **28** yielded an 88:12 mixture of *E* and *Z* isomeric products.[2]

(12) Actually, a mixture of **3** (82%) plus **29** (4%), from **1**, and **4** (7%) plus **30** (7%), from the inseparable diastereomer **2**, was obtained according to integration of the ^{1}H NMR spectrum. By dividing the ratio of **29**:**4** (0.176), from **28**, by **29**:**3** (0.053), from **1**, an isotope effect of 3.3 can be calculated. This compares with a value of 2.4–2.8 for intermolecular thermal ene reactions. Song, Z.; Beak, P. *J. Am. Chem. Soc.* **1990**, *112*, 8126. See also: Song, Z.; Christophe, D. R.; Beak, P. *J. Org. Chem.* **1987**, *52*, 3938. Snider, B. B.; Ron, E. *J. Am. Chem. Soc.* **1985**, *107*, 8160.

(13) A mixture of **4** (57%) plus **30** (32%), from **2**, and **3** (11%), from the inseparable diastereomer **1**, was obtained accordingly to integration of the ^{1}H NMR spectrum. By dividing the ratio of **4**:**29** (5.67), from **28**, by **4**:**30** (1.77), from **2**, an isotope effect of 3.2 can be calculated.[12] The ratio of **4**:**30** shown in eq 12 is corrected for the 14% of trans product **31** removed by chromatography prior to the NMR analysis.

(14) Snider has shown that the vinyl methyl analogue of **28** affords a 90:10 mixture of cis- and trans-2-methyl-5-methylenecyclohexanols under comparable conditions.[2] Apparently the nature of the vinylic substituent (Me vs Et) as well as the isotope effect influence the cis/trans ratio of such cyclizations.

(15) Maruoka, K.; Saito, S.; Ooi, T.; Yamamoto, H. *Synlett* **1991**, 579. Maruoka, K.; Ooi, T.; Yamamoto, H. *J. Am. Chem. Soc.* **1990**, *112*, 9011.

(16) For a recent analysis of this reaction, see: Marshall, J. A. *Chemtracts: Org. Chem.* **1992**, *5*, 1.

(17) In MABR-promoted cyclizations leading to rigid trans-fused decalins, equatorial alcohols are strongly favored.[15,16]

(18) O'Ferral, R. A. M. *J. Chem. Soc. B.* **1970**, 785.

(19) For a summary of experimental protocols, see: Marshall, J. A.; Wang, X.-j. *J. Org. Chem.* **1991**, *56*, 960.

6 H, ring H), 1.02, 1.01 (2 diast, each d, J = 6.8, 6.8 Hz, 3 H, Me).

(*S*)-3-Methyl-4-[(tetrahydropyranyl)oxy]butanenitrile (7). To a slurry of dry NaCN (5.00 g, 91.9 mmol) in 75 mL of dry DMSO at 70 °C was added a solution of bromide **6** (18.0, 75.9 mmol) in 10 mL of DMSO. The reaction mixture was then heated for an additional 6 h and cooled to room temperature. The resulting solids were dissolved in ca. 200 mL of water and extracted with Et_2O. The combined organic extracts were washed with brine and dried over Na_2SO_4. Filtration and removal of the solvents followed by flash chromatography (50% Et_2O in hexanes) afforded 12 g (86%) of nitrile **7** as a colorless oil: IR (film) ν 2245 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.56 (m, 1 H, acetal H), 3.80 (m, 1 H, ring CH_2O), 3.72 (dd, J = 9.9, 4.9 Hz, 1 H, $CH^a_2OTHP_a$), 3.56 (dd, J = 9.9, 7.9 Hz, 1 H, $CH^b_2OTHP_a$), 3.52 (m, 1 H, ring CH_2O), 3.35 (dd, J = 9.9, 4.7 Hz, 1 H, $CH^a_2OTHP_b$), 3.18 (dd, J = 9.8, 8 Hz, 1 H, $CH^b_2OTHP_b$), 2.55–2.29 (m, 2 H, CH_2CN), 2.17–2.11 (m, 1 H, C*H*Me), 1.80–1.40 (m, 6 H, ring CH_2), 1.07, 1.06 (2 diast, each d, J = 6.8, 6.8 Hz, 3 H, Me). Anal. Calcd for $C_{10}H_{17}NO_2$: C, 65.54; H, 9.35. Found: C, 65.43; H, 9.33.

(*R*)-3-Methyl-4-[(tetrahydropyranyl)oxy]butan-1-ol (9). To a solution of 12.0 g (65.5 mmol) of the nitrile **7** in 350 mL of anhydrous Et_2O at −78 °C was added dropwise 98.2 mL of 1 M DIBAH in hexanes. The cooling bath was removed, and the reaction mixture was allowed to warm to room temperature for several minutes. The reaction mixture was then poured into 400 mL of a stirring solution of saturated aqueous sodium potassium tartrate. After the solution cleared (ca. 20 min) the mixture was extracted with Et_2O and the combined organic extracts were dried over Na_2SO_4. The dried extracts were filtered through a plug of silica gel under reduced pressure, and the solvents were removed under reduced pressure. The crude aldehyde was dissolved in 200 mL of dry MeOH, cooled to 0 °C, and treated with $NaBH_4$ (2.50 g, 65.5 mmol). The reaction mixture was allowed to slowly warm to room temperature over 2 h, quenched with ca. 200 mL of water, and extracted with ether. The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated. Purification by flash chromatography (ether) afforded 8.8 g (72% from nitrile **7**) of alcohol **9** as a clear colorless oil: IR (film) ν 3422 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.57 (m, 1 H, acetal H), 3.74–3.47 (m, 4 H, CH_2OR), 3.26 (dd, J = 9.6, 4.9 Hz, 1 H, $CH^a_2OTHP_a$), 3.19 (dd, J = 9.5, 7.4 Hz, 1 H, $CH^b_2OTHP_a$), 2.28 (bs, 1 H, OH), 1.92–1.77 (m, 1 H, C*H*Me), 1.77–1.50 (m, 8 H, ring H and CH_2CH_2OH), 0.94, 0.92 (2 diast, each d, J = 6.8 Hz, 3 H, Me). Anal. Calcd for $C_{10}H_{20}O_3$: C, 63.79; H, 10.71. Found: C, 63.75; H, 10.75.

(*R*)-3-Methyl-4-[(tetrahydropyranyl)oxy]-1-iodobutane (10). To a solution of 14.2 g (54.1 mmol) of PPh_3 in 300 mL of anhydrous CH_2Cl_2 at room temperature was added 3.70 g (54.1 mmol) of imidazole. After all the solids had dissolved, 13.7 g (54.1 mmol) of iodine was added. The resulting dark mixture was stirred for several minutes, and a solution of 8.5 g (45.2 mmol) of alcohol **9** in 75 mL of CH_2Cl_2 was added dropwise over 10 min. The reaction mixture was stirred an additional 10 min and then concentrated under reduced pressure. The crude oil was poured into 500 mL of stirring pentane and the resulting precipitate removed by filtration. The pentane extracts were next filtered through a plug of silica gel under reduced pressure, washing with 10% ether in hexanes to ensure complete elution of product. The organic extracts were concentrated under reduced pressure, affording 11 g (82%) of the crude iodide **10** as a yellow oil which was used directly without further purification: ^1H NMR (300 MHz, $CDCl_3$) δ 4.54 (m, 1 H, acetal H), 3.81 (m, 1 H, CH_2I), 3.60–3.50 (m, 1 H, CH_2OTHP), 3.48 (m, 1 H, CH_2I), 3.30–3.15 (m, 3 H, ring CH_2O and CH_2OTHP), 2.09–1.94 (m, 1 H, C*H*Me), 1.91–1.40 (m, 8 H, ring H and CH_2CH_2I), 0.92, 0.91 (2 diast, each d, J = 6.6, 6.7 Hz, 3 H, Me).

(*R*)-Methyl 2-(Dimethylphosphono)-5-methyl-6-[(tetrahydropyranyl)oxy]hexanoate (11). To a slurry of 1.80 g (72.5 mmol) of 95% NaH in 200 mL of dry DMSO at room temperature was added dropwise 19.2 mL (72.5 mmol) of trimethyl phosphonoacetate over 30 min. After an addition 30 min of stirring at room temperature a clear gray solution resulted and 11 g (60.4 mmol) of iodide **10** in 50 mL of DMSO was added dropwise. The reaction mixture was stirred an additional 12 h at room temperature and quenched with 500 mL of water. The aqueous mixture was extracted with ethyl acetate, and the combined extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography (ethyl acetate as eluent) providing 12 g (56%) of phosphonate **11** as a clear colorless oil: IR (film) ν 1735 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.52 (m, 1 H, acetal H), 3.79–3.74 (m, 9 H, 3 OMe), 3.53–3.46 (m, 2 H, CH_2O), 3.17–3.14 (m, 1 H, CH_2OR), 2.96–2.88 (m, 1 H, CH_2OR), 2.05–1.30 (m, 11 H, $CHCO_2Me$ and CH_2), 1.15 (m, 1 H, C*H*Me), 0.93–0.88 (m, 3 H, Me). Anal. Calcd for $C_{15}H_{29}O_7P$: C, 51.13; H, 8.30. Found: C, 51.05; H, 8.35.

(2*R*,5*E*)-2-Methyl-5-carbomethoxy-1-[(tetrahydropyranyl)oxy]-5-heptene (12). To a solution of 10.3 mL of 1 M potassium *tert*-butoxide in 50 mL of anhydrous THF at 0 °C was added a solution of phosphonate **11** (3.3 g, 9.4 mmol) in 10 mL of THF. The reaction was allowed to warm to room temperature for 30 min and cooled to −78 °C, and 1.1 mL (20 mmol) of freshly distilled acetaldehyde was added over several minutes. The reaction mixture was stirred 1 h at −78 °C, allowed to warm to room temperature, and partitioned between Et_2O and water. The aqueous phase was extracted with ether, and the combined organic extracts were dried over Na_2SO_4. Filtration and removal of the solvents under reduced pressure followed by flash chromatography (10% Et_2O in hexanes) afforded 1.9 g (84%) of ester **12** as an inseparable 85:15 mixture of E/Z isomers: IR (film) ν 1714, 1648 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.80 (q, J = 7.2 Hz, 1 H, vinyl H), 4.54 (m, 1 H, acetal H), 3.84 (m, 1 H, ring CH_2O), 3.70 (s, 3 H, CO_2Me), 3.60 (dd, J = 9.5, 6.1 Hz, 1 H, CH_2OTHP_a), 3.49 (m, 2 H, ring CH_2O and CH_2OTHP_b), 3.23 (dd, J = 9.5, 5.9 Hz, 1 H, CH_2OTHP_a), 3.16 (dd, J = 9.5, 6.5 Hz, 1 H, CH_2OTHP_b), 2.32–2.27 (m, 2 H, allylic H), 1.80–1.40 (m, 8 H, CH_2), 1.77 (d, J = 7.2 Hz, 3 H, vinyl Me), 1.19 (m, 1 H, C*H*Me), 0.97, 0.96 (2 diast, each d, J = 6.7, 6.7 Hz, 3 H, Me); Z isomer (partial) δ 6.80 (q, J = 7.1 Hz, 1 H, vinyl H), 1.92 (d, J = 7.2 Hz, 3 H, vinyl Me). Anal. Calcd for $C_{15}H_{26}O_4$: C, 66.63; H, 9.69. Found: C, 66.62; H, 9.73.

(2*R*,5*E*)-2-Methyl-5-(hydroxymethyl)-1-[(tetrahydropyranyl)oxy]-5-heptene (13). To a solution of 2.80 g (10.4 mmol) of ester **12** in 150 mL of anhydrous Et_2O at −78 °C was added dropwise 24 mL of 1 M DIBAH in hexanes. The reaction mixture was stirred an additional 10 min and then poured into 500 mL of dilute aqueous HCl. The aqueous mixture was shaken well to dissolve the salts and extracted with Et_2O. The combined organic extracts were dried over Na_2SO_4 and filtered through a plug of silica gel. Removal of the solvents under reduced pressure afforded the crude alcohol which was purified by flash chromatography (50% then 75% ether in hexanes), affording 2.4 g (96%) of allylic alcohol **13** as an inseparable 86:14 mixture of E/Z isomers: IR (film) ν 3411 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.47 (q, J = 6.7 Hz, 1 H, vinyl H), 4.54 (m, 1 H, acetal H), 4.00 (bs, 2 H, CH_2OH), 3.86–3.75 (m, 1 H, ring CH_2O), 3.62–3.45 (m, 2 H, ring CH_2O, CH_2OTHP), 3.20 (m, 1 H, CH_2OTHP), 2.11 (m, 2 H, allylic H), 1.80–1.30 (m, 8 H, CH_2), 1.23 (m, 1 H, C*H*Me), 0.95 (d, J = 6.7 Hz, 3 H, Me), 0.93 (d, J = 6.6 Hz, 3 H, Me); Z isomer (partial) δ 5.39 (q, vinyl H), 4.13 (s, CH_2OH). Anal. Calcd for $C_{14}H_{26}O_3$: C, 69.38; H, 10.81. Found: C, 69.45; H, 10.80.

(1*S*,2*S*)-1-Methyl-2-(hydroxymethyl)-2-[(*R*)-3-methyl-4-[(tetrahydropyranyl)oxy]butyl]oxirane (15). The method of Sharpless was followed.[8] To a suspension of 1 g of powdered 4A molecular sieves in 150 mL of anhydrous CH_2Cl_2 at 0 °C was added successively 0.20 mL (0.93 mmol) of L-(+)-diisopropyl tartrate and 0.19 mL (0.62 mmol) of titanium tetraisopropoxide. The resulting mixture was stirred for 30 min then cooled to −20 °C, and 2.3 mL of 5 M *tert*-butyl hydroperoxide in 2,2,4-trimethylpentane was added dropwise. After 30 min, 1.50 g (6.19 mmol) of alcohol **13** was added dropwise as a solution in 25 mL of CH_2Cl_2. The reaction mixture was stirred for 2.5 h at −20 °C whereupon TLC analysis indicated the reaction was complete. The mixture was warmed to 0 °C and treated successively with 20 mL of water and then 5 mL of aqueous 30% NaOH saturated with NaCl. The resulting biphasic suspension was stirred vigorously at room temperature for 1 h, suction filtered through a plug of Celite, and extracted with Et_2O. The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude epoxide was purified by flash chromatography (ether), affording 1.5 g (88%) of epoxide **15** (epimers at the THP acetal): ^1H NMR (300 MHz, $CDCl_3$) δ 4.52 (m, 1 H, acetal H), 3.73–3.12 (m, 7 H, CH_2OR and $CHOR$),

1.87–1.20 (m, 11 H, CH_2 and methine H), 1.30 (d, J = 5.6 Hz, Me), 0.93, 0.91 (2 diast, each d, J = 6.7, 6.5 Hz, 3 H, Me). Anal. Calcd for $C_{14}H_{26}O_4$: C, 65.08; H, 10.15. Found: C, 64.97; H, 10.14.

(1*R*,2*R*)-1-Methyl-2-(hydroxymethyl)-2-[(*R*)-3-methyl-4-[(tetrahydropyranyl)oxy]butyl]oxirane (14). The foregoing procedure was followed. From 2.00 g (8.25 mmol) of alcohol **13**, 0.27 mL (1.26 mmol) of D-(−)-DIPT, 0.25 mL (0.82 mmol) of titanium tetraisopropoxide, 1.5 g of 4A molecular sieves, and 3.1 mL of 5 M *tert*-butyl hydroperoxide in 170 mL of CH_2Cl_2 was obtained 2.0 g (95%) of epoxide **14** (epimers at the THP acetal). Epoxide **14** showed similar spectral properties to those of diastereomer **15**: partial ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.31, 1.29 (2 diast, each J = 5.6, 6.6 Hz, 3 H, Me). Anal. Calcd for $C_{14}H_{26}O_4$: C, 65.08; H, 10.15. Found: C, 64.84; H, 10.20.

(2*R*,5*R*)-5-Methyl-2-[(*R*)-1-deuterioethyl]-6-[(tetrahydropyranyl)oxy]-1,2-hexanediol (20). To a solution of epoxide **15** (1.20 g, 4.64 mmol) in 40 mL of anhydrous THF at −78 °C was added dropwise a freshly prepared solution of 0.40 g of $LiAlD_4$ (Aldrich, 98 atom %) in 10 mL of THF (canula). The cooling bath was removed, and the reaction mixture was allowed to warm to room temperature and stirred for an additional 30 min. The mixture was then cooled to 0 °C and carefully quenched with ca. 50 mL of saturated aqueous sodium potassium tartrate. After 1 h of stirring the suspension cleared and the mixture was extracted with ethyl acetate. The combined organic extracts were dried over Na_2SO_4 and filtered, and the solvents were removed under reduced pressure. Purification by flash chromatography (Et_2O) afforded 1.1 g (92%) of diol **20**: IR (film) ν 3411 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.51 (m, 1 H, acetal H), 3.83 (m, 1 H, CHOR), 3.50 (m, 4 H, CHOR), 3.21 (m, 1 H, CHOR), 2.10 (bs, 2 H, OH), 1.80–0.70 (m, 18 H). Anal. Calcd for $C_{14}H_{27}DO_4$: C, 64.33; H, 10.83. Found: C, 63.68; H, 10.91.

(2*S*,5*R*)-5-Methyl-2-[(*S*)-1-deuterioethyl]-6-[(tetrahydropyranyl)oxy]-1,2-hexanediol (16). The foregoing procedure was followed. From 2.0 g (7.74 mmol) of epoxide **14** and 0.65 g (15.5 mmol) of $LiAlD_4$ in 75 mL of THF was obtained 2 g of crude diol **16** which was used without further purification. Diol **16** showed similar spectral properties to those of diastereomer **20**.

(2*R*,5*R*)-5-Methyl-2-ethyl-6-[(tetrahydropyranyl)oxy]-1,2-hexanediol (24). The foregoing procedure was followed. From 0.20 g (0.77 mmol) of epoxide **15** and 1.6 mL of 1 M $LiAlH_4$ (THF) in 5 mL of THF was obtained 0.17 g (85%) of crude diol **24** which was used without further purification.

(2*R*,5*R*)-5-Methyl-2-[(*R*)-1-deuterioethyl]-6-[(tetrahydropyranyl)oxy]-1,2-hexanediol Thionocarbonate (21). A mixture of 1.10 g (4.21 mmol) of diol **20** and 1.00 g (5.47 mmol) of 1,1′-(thiocarbonyl)diimidazole (90%) in 5 mL of anhydrous toluene was heated at reflux temperature for 30 min. The resulting brown solution was cooled to room temperature and chromatographed directly (25% then 50% ether in hexanes), affording 1.10 g (87%) of thionocarbonate **21**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.51 (m, 1 H, acetal H), 4.32 (2 diast, AB = apparent, t, J = 10.8, 2 H, thionocarbonate ring CH_2), 3.80 (2 diast, m, 1 H THP ring CH_2O), 3.58, 3.55 (2 diast, each dd, J = 5.9, 6.9 and 9.6, 11.4 Hz, 1 H, CH_2OTHP), 3.49–3.45 (2 diast, m, 1 H, THP ring CH_2O), 3.20, 3.16 (2 diast, each dd, J = 5.7, 6.5 and 9.6, 11.3 Hz, 1 H, CH_2OTHP), 1.88–1.65 (m, 6 H, CH_2), 1.60–1.49 (m, 4 H, CH_2, CHD), 1.16 (m, 1 H, methine), 0.96 (2 diast, each d, J = 7.4 Hz, *Me*CHD), 0.92, 0.91 (2 diast, each d, J = 6.7, 6.7 Hz, 3 H, *Me*CH). Anal. Calcd for $C_{15}H_{25}DO_4S$: C, 59.37; H, 8.63; S, 10.57. Found: C, 59.43; H, 8.64; S, 10.61.

(2*S*,5*R*)-5-Methyl-2-[(*S*)-1-deuterioethyl]-6-[(tetrahydropyranyl)oxy]-1,2-hexanediol Thionocarbonate (17). The foregoing procedure was followed. From 2 g (7.65 mmol) of crude diol **16** and 1.5 g (7.65 mmol) of 1,1′-(thiocarbonyl)diimidazole in 25 mL of dry toluene was obtained 2.1 g (91% from epoxide **14**) of **17**. Spectral properties of **17** were similar to those of diastereomer **21**.

(2*S*,5*R*)-5-Methyl-2-ethyl-6-[(tetrahydropyranyl)oxy]-1,2-hexanediol Thionocarbonate (25). The foregoing procedure was followed. From 0.17 g (0.65 mmol) of crude diol **24** and 0.19 g (0.95 mmol) of (thiocarbonyl)diimidazole in 2 mL of dry toluene was obtained 0.19 g (85% from epoxide **15**) of **25**. Spectral properties were similar to those of the deuterated analogues **21** and **17**: partial ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.98 (2 diast, t, J = 7.4 Hz, 3 H, CH_2Me), 0.93, 0.91 (2 diast, each d, J = 6.8, 6.8 Hz, 3 H, CH*Me*).

(*R*)-5-Methyl-2-[(*R*)-1-deuterioethyl]-6-[(tetrahydropyranyl)oxy]-1-hexene (22). A solution of 1.10 g (3.64 mmol) of thionocarbonate **21** in 10 mL of trimethyl phosphite was refluxed under a nitrogen atmosphere for 72 h. The mixture was cooled to 0 °C, and ca. 20 mL of 0.5 N NaOH was added dropwise with stirring. After an additional 1 h of stirring at room temperature the mixture was extracted with ether. The combined organic extracts were dried over Na_2SO_4 and filtered, and the solvents were removed under reduced pressure. Purification by flash chromatography (hexanes then 10% ether/hexanes) afforded 0.72 g (87%) of olefin **22**: IR (film) ν 3073, 1637 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.68 (bs, 2 H, C=CH_2), 4.56 (m, 1 H, acetal H), 3.84 (m, 1 H, ring CH_2O), 3.59, 3.22 (2 diast, each dd, J = 6.2, 5.8 and 9.4, 9.4 Hz, 1 H, CH_2OTHP), 3.50, 3.13 (2 diast, each dd, J = 7.0, 6.5 and 9.4, 9.4 Hz, 1 H, CH_2OTHP), 3.50–3.44 (m, 1 H, ring CH_2O), 2.08–1.82 (m, 3 H, allylic H), 1.80–1.40 (m, 8 H, CH_2), 1.28 (m, 1 H, methine), 1.00, 0.98 (2 diast, each d, J = 7.4, 7.4 Hz, 3 H, *Me*CH), 0.924, 0.918 (2 diast, each d, J = 6.7, 6.7 Hz, 3 H, *Me*CHD). Anal. Calcd for $C_{14}H_{25}DO_2$: C, 73.96; H, 11.52. Found: C, 74.03; H, 11.50.

(*R*)-5-Methyl-2-[(*S*)-1-deuterioethyl]-6-[(tetrahydropyranyl)oxy]-1-hexene (18). The foregoing procedure was followed. From 2.0 g (6.61 mmol) of thionocarbonate **17** in 30 mL of trimethyl phosphite was obtained 1.3 g (87%) of alkene **18**. Spectral properties were similar to those of diastereomer **22**. Anal. Calcd for $C_{14}H_{25}DO_2$: C, 73.96; H, 11.52. Found: C, 74.01; H, 11.56.

(*R*)-5-Methyl-2-ethyl-6-[(tetrahydropyranyl)oxy]-1-hexene (26). The foregoing procedure was followed. From 0.15 g of thionocarbonate **25** in 2 mL of trimethyl phosphite was obtained 85 mg (77%) of alkene **26**. Spectral properties were similar to those of the deuterated analogues **18** and **22**: partial ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.00 (2 diast, t, J = 7.4 Hz, 3 H, CH_2Me), 0.93, 0.92 (2 diast, each d, J = 6.7, 6.7 Hz, 3 H, CH*Me*). Anal. Calcd for $C_{14}H_{26}O_2$: C, 74.28; H, 11.58. Found: C, 74.34; H, 11.55.

(*R*)-2-Methyl-5-[(*R*)-1-deuterioethyl]-5-hexen-1-ol (23). To a solution of 0.72 g (3.17 mmol) of THP ether **22** in 4 mL of methanol at room temperature was added 20 mg of PPTS. The mixture was stirred for 2 days at room temperature at which point TLC analysis indicated the reaction to be complete. The crude reaction mixture was chromatographed directly (10%, 25%, and then 50% ether in hexanes), affording 0.36 g (80%) of alcohol **23** as a volatile fragrant oil: $[\alpha]_D$ +10.7 (*c* 1.5, CH_2Cl_2); IR (film) ν 3357, 2125 (CD), 1643 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.69 (bs, 2 H, C=CH_2), 3.50 (dd, J = 10.5, 5.6 Hz, 1 H, CH_2OH), 3.42 (dd, J = 10.5, 6.2 Hz, 1 H, CH_2OH), 2.14–1.99 (m, 3 H, allylic H), 1.66–1.49 (m, 2 H, homoallylic CH_2), 1.40 (s, 1 H, OH), 1.28–1.18 (m, 1 H, methine), 1.00 (dt, J = 7.4, 1.0 Hz, 3 H, *Me*CHD), 0.92 (d, J = 6.7 Hz, 3 H, *Me*CH). Anal. Calcd for $C_9H_{17}DO$: C, 75.46; H, 12.66. Found: C, 75.61; H, 12.60. Mass spectral (EI) comparison of the deuterated sample **23** and its protio analogue **27** indicated d_1/d_0 = 96–97%.

(*R*)-2-Methyl-5-[(*S*)-1-deuterioethyl]-5-hexen-1-ol (19). The foregoing procedure was followed. From 1.3 g (5.75 mmol) of THP ether **18** and 70 mg of PPTS in 10 mL of MeOH was obtained 0.68 g (83%) of alcohol **19**. Spectral properties were similar to those of diastereomer **23**. Anal. Calcd for $C_9H_{17}DO$: C, 75.46; H, 12.66. Found: C, 75.40; H, 12.60.

(*R*)-2-Methyl-5-ethyl-5-hexen-1-ol (27). The foregoing procedure was followed. From 70 mg (0.31 mmol) of THP ether **26** and a catalytic amount of PPTS in 1.5 mL of MeOH was obtained 40 mg (91%) of alcohol **27**. Spectral properties were similar to those of deuterated analogues **23** and **19**: Partial ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.00 (t, J = 7.4 Hz, 3 H, *Me*CH_2), 2.14–1.97 (m, 4 H, allylic H). Anal. Calcd for $C_9H_{18}O$: C, 75.93; H, 12.75. Found: C, 75.97; H, 12.78.

(*R*)-2-Methyl-5-[(*R*)-1-deuterioethyl]-5-hexenal (1). To a solution of oxalyl chloride (0.23 mL, 2.63 mmol) in 10 mL of CH_2Cl_2 at −78 °C was added DMSO (0.25 mL, 3.50 mmol) dropwise. After 5 min, alcohol **23** (0.25 g, 1.75 mmol) was added as a solution in 2 mL of CH_2Cl_2. The resulting mixture was stirred for 30 min, and triethylamine (0.9 mL, 6.7 mmol) was added. The suspension was then warmed to 0 °C, diluted with 20 mL of ether, and washed with saturated aqueous ammonium chloride. The

aqueous phase was extracted with ether, and the combined organic extracts were washed with water and then brine and dried over Na_2SO_4. Filtration through a plug of silica gel and removal of solvents provided 0.23 g (93%) of aldehyde 1 as a fragrant volatile yellow oil which was used without further purification: IR (film) ν 3073, 1719, 1637 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.61 (d, J = 1.5 Hz, 1 H, CHO), 4.74 (s, 1 H, $=CH_2$), 4.70 (s, 1 H, $=CH_2$), 2.33 (m, 1 H, C*H*Me), 2.05–1.92 (m, 4 H, allylic H), 1.92–1.82 (m, 1 H, CH_2 homoallylic), 1.54–1.42 (m, 1 H, CH_2 homoallylic), 1.09 (d, J = 7.0 Hz, 3 H, *Me*CH), 1.00 (dt, J = 7.4, 1.0 Hz, 3 H, *Me*CHD).

(*R*)-2-Methyl-5-[(*S*)-1-deuterioethyl]-5-hexenal (2). The foregoing procedure was followed. From 250 mg (1.75 mmol) of alcohol **19**, 0.23 mL (2.63 mmol) of oxalyl chloride, 0.25 mL (3.50 mmol) of DMSO, and 0.90 mL (6.7 mmol) of triethylamine in 10 mL of CH_2Cl_2 was obtained 0.23 g (93%) of volatile aldehyde **2**. Spectral properties were similar to those of diastereomer 1.

(*R*)-2-Methyl-5-ethyl-5-hexenal (28). The foregoing procedure was followed. From 25 mg (0.18 mmol) of alcohol **27**, 23 μL (0.26 mmol) of oxalyl chloride, 25 μL (0.35 mmol) of DMSO, and 0.10 mL (0.70 mmol) of triethylamine in 1 mL of CH_2Cl_2 was obtained 15 mg (60%) of volatile crude aldehyde **28** which was used without further purification.

Me_2AlCl-Promoted Cyclizations. Aldehyde 1: (1*S*,2*R*,-*E*)-2-Methyl-5-ethylidenecyclohexanol (3). To a solution of freshly prepared aldehyde 1 (90 mg, 0.64 mmol) in 5 mL of anhydrous CH_2Cl_2 at −78 °C was added dropwise 0.64 mL of 1 M Me_2AlCl in hexane (Aldrich). The resulting yellow solution was stirred an additional 30 min, quenched with 2 mL of saturated aqueous $NaHCO_3$, and allowed to warm to room temperature. The reaction mixture was extracted with ether, and the combined organic extracts were dried over Na_2SO_4. Filtration and removal of the solvents under reduced pressure (then a stream of N_2) afforded the crude volatile alcohol. Subsequent purification by flash chromatography (25% then 50% ether in hexanes) gave 64 mg (71%) of an inseparable 95:5 mixture of E and Z isomers **3** and **29** (cis/trans > 95:5) after correction for the presence of ca. 14% of **4** and **30** from the diastereomeric impurity **2**:[12] $[\alpha]_D$ + 37.5 (c 3.2, CH_2Cl_2); IR (film) ν 3411, 2212 (CD), 1659 cm^{-1}; HRMS (EI) calcd for $C_9H_{15}DO$ 141.1264, found 141.1270.

***cis*-*E*-d_1-3**: ^1H NMR (300 MHz, $CDCl_3$) δ 3.72 (bs, 1 H, C*H*OH), 2.53 (bd fine coupling, J = 13.4 Hz, 1 H, ring allylic C*H*$^a_2$$CH_2$), 2.30 (bd, J = 13.5 Hz, 1 H, C*H*$^a_2$CHOH), 2.23 (ddd, J = 1.6, 3.9, 13.4 Hz, 1 H, C*H*$^b_2$CHOH), 1.74 (bdd, J = 4.6, 13.9 Hz, 1 H, ring allylic C*H*$^b_2$$CH_2$), 1.80–1.45 (m, 2 H, homoallylic CH_2), 1.59 (s, 3 H, =CD*Me*), 1.41 (bs, 1 H, OH), 1.23 (m, 1 H, C*H*Me), 0.94 (d, J = 6.8 Hz, 3 H, ring Me); ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.9, 120.16 (wk t), 72.1, 44.3, 36.9, 29.6, 27.3, 18.0, 13.2.

***cis*-*Z*-d_0-29** (partial): ^1H NMR (300 MHz, $CDCl_3$) δ 5.41 (q, J = 6.5 Hz, 1 H, vinyl H), 3.79 (bs, 1 H, C*H*OH), 2.68 (ddd, J = 1.7, 4.4, 13.8 Hz, 1 H, C*H*$^a_2$CHOH), 2.12 (bd, J = 13.5 Hz, 1 H, C*H*$^b_2$CHOH), 2.00 (m, 2 H, ring allylic CH_2CH_2), 1.25 (m, 1 H, C*H*Me); ^{13}C NMR (75 MHz, $CDCl_3$) δ 72.2, 35.8, 35.6, 30.6, 17.8, 13.1.

Aldehyde 2. The foregoing procedure was followed. From 110 mg of aldehyde **2** and 0.82 mL of Me_2AlCl in 10 mL of CH_2Cl_2 was obtained 70 mg (64%) of a mixture of **4**, **30**, and **31** from which the trans-deuterated isomer **31** (10 mg) was separable through column chromatography on silica gel. Analysis of the ^1H NMR spectrum of the remaining cis products showed 57% of **4**, 32% of **30**, and 11% of **3**, the latter arising from the inseparable diastereomeric impurity **1** in the starting aldehyde. A corrected ratio of 55:31:14 for **4**:**30**:**31** could thus be calculated.

***cis*-E-d_0-4**: similar to ***cis*-*E*-d_1-3**; partial ^1H NMR (300 MHz, $CDCl_3$) δ 5.26 (q, J = 6.8 Hz, 1 H, vinyl H), 1.59 (dt, J = 6.6, 1.4 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.01, 120.5, 72.1, 44.3, 36.9, 29.6, 27.3, 18.0, 13.3.

***cis*-*Z*-d_1-30**: similar to ***cis*-*Z*-d_0-29**; partial ^1H NMR (300 MHz, $CDCl_3$) δ 3.79 (bs, 1 H, CHOH), 2.68 (ddd, J = 1.7, 4.4, 13.8 Hz, 1 H, C*H*$_2$CHOH); partial ^{13}C NMR (75 MHz, $CDCl_3$) δ 72.2, 35.8, 35.6, 30.6, 17.8, 13.1.

***trans*-*E*-d_1-31**: see below.

Aldehyde 28. The foregoing procedure was followed. From 15 mg (0.11 mmol) of aldehyde **28** and 0.15 mL of Me_2AlCl in 2 mL of CH_2Cl_2 was obtained 9 mg (60%) of an 85:15 mixture of E and Z isomers **4** and **29**.

MABR-Promoted Cyclizations. Aldehyde 1: (1*R*,2*R*,-*E*)-2-Methyl-5-ethylidenecyclohexanol (32). To a solution of 0.99 g (3.48 mmol) of 2,6-di-*tert*-butyl-4-bromophenol (freshly chromatographed white powder) in 10 mL of dry CH_2Cl_2 at rt was added 0.90 mL (1.74 mmol) of 2 M trimethylaluminum in hexanes. The reaction mixture was stirred an additional 1 h at room temperature and cooled to −78 °C, and a solution of aldehyde 1 (80 mg, 0.57 mmol) in 4 mL of CH_2Cl_2 was added dropwise over several minutes. The reaction mixture was stirred an additional 1 h, quenched with 5 mL of saturated aqueous $NaHCO_3$, allowed to warm to room temperature, and extracted with ether. The combined organic extracts were dried over Na_2SO_4 and filtered, and the solvents were removed under reduced pressure (then a stream of N_2), affording the crude volatile alcohol. Subsequent purification by flash chromatography (25% then 50% ether in hexanes) gave 59 mg (74%) of alcohol **32** containing ca. 15% of **31** as evidenced by comparison of the integration for vinylic and carbinyl H signals. This isomer must come from the diastereomeric impurity **2** present in aldehyde **1**: $[\alpha]_D$ +29.7 (c 3.5, CH_2Cl_2); IR (film) ν 3346, 1659 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.19 (q, J = 6.7 Hz, 1 H, vinyl H), 3.12 (ddd, J = 4.5, 9.2, 10.2 Hz, 1 H, CHOH), 2.51–2.41 (m, 2 H, ring allylic CH_2), 1.98 (bt, J = 12.2 Hz, 1 H, ring allylic CH_2), 1.78–1.65 (m, 2 H, ring allylic CH_2), 1.54–1.37 (m, 2 H, homoallylic CH_2), 1.55 (dt, J = 6.6, 1.6 Hz, 3 H, vinyl Me), 1.00 (d, J = 6.5 Hz, 3 H, CH*Me*), 1.03–0.86 (m, 1 H, methine); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.3, 118.2, 77.0, 45.6, 40.3, 33.0, 27.2, 18.4, 13.2; HRMS (EI) calcd for $C_9H_{16}O$ 140.12012, found 140.12017. Anal. Calcd for $C_9H_{16}O$: C, 77.09; H, 11.50. Found: C, 77.05; H, 11.47.

Aldehyde 2. The foregoing procedure was followed. From 110 mg (0.78 mmol) of aldehyde **2**, 0.89 g (3.12 mmol) of 2,6-di-*tert*-butyl-4-bromophenol and 0.78 mL (1.56 mmol) of trimethylaluminum in 10 mL of CH_2Cl_2 was obtained 78 mg (71%) of alcohol **31** contaminated by ca. 10% of **32** as evidenced by the presence of a vinyl H quartet at 5.2 ppm in the ^1H NMR spectrum. This isomer must come from the diastereomeric impurity **1** present in aldehyde **2**. Spectral data were similar to those of ***trans*-*E*-d_0-32**.

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Supplementary Material Available: Selected ^1H NMR spectra (18 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.