trifuging, washing with methanol, and drying (vacuum, 24 h) gave only 1.5 mg (1.6% yield) of orange powder.

Norbornene (0.75 g, 8.0 mmol, the sample used above, freshly distilled) in toluene (1 mL, the same as above, just passed through a short column of basic alumina) was dried and degassed over CaH_2 in three freeze–thaw cycles under high vacuum. After distillation onto the initiator (14.0 mg, 0.030 mmol) and sealing under vacuum, the mixture was warmed to room temperature. The color turned from orange to brown in 3 days. Pouring into ca. 10 mL of methanol gave no precipitate.

Effect of O_2 On Polymerization of Cyclopentene by 1. Cyclopentene (1.4 mL, 14.6 mmol, refluxed over CaH_2 and distilled just before) was passed through a column of basic alumina. By use of the apparatus described above in the experiment with **3** and O_2, it was dried and degassed over CaH_2 (three freeze–thaw cycles under high vacuum) and distilled onto **1** (48 mg, 0.098 mmol). Oxygen (0.1 mmol) was admitted, and the tube was then warmed at 43–45 °C. After ca. 1 h the original purple color had faded. After ca. 24 h the reaction mixture was still not noticeably viscous. Pouring into ca. 10 mL of CH_3OH at this point precipitated no polymer.

The same experiment was conducted simultaneously without oxygen. (The evacuated tube was simply sealed after the cyclopentene had been distilled onto the initiator.) The reaction mixture solidified in 3 h and after 24 h was dissolved in ca. 3 mL of $CHCl_3$ and precipitated with CH_3OH. After drying under vacuum for 12 h, the yield was 0.835 g (84%).

Acknowledgments. We are greatful to the National Science Foundation (Grant CHE-81-08998) and the U.S. Office of Naval Research for support and to Jim Frey and the Colorado State University Regional NMR Center, funded by the National Science Foundation (Grant CHE-82-08821), for the ^{13}C NMR spectrum in Figure 6.

Registry No. 3, 50726-27-7; **7**, 62342-88-5; poly(phenylacetylene), 25038-69-1; polypropyne, 28391-48-2; poly(*tert*-butylacetylene), 51730-68-8; poly(1-hexyne), 28827-85-2; poly(2-pentyne), 28904-75-8; poly(2-butyne), 25684-85-9; polyacetylene, 25067-58-7; poly(5-chloro-1-pentyne), 88996-53-6; poly(methyl 5-hexynoate), 88996-54-7; poly(5-cyano-1-pentyne), 88996-55-8; poly(methyl propargyl ether), 57884-03-4; poly(methyl propiolate), 27342-21-8; polynorbornene, 25038-76-0; polycyclopentene, 25103-85-9; polycyclooctene, 25267-51-0; polycycloheptene, 26426-65-3; $C_6H_5C{\equiv}W(CO)_4Cl$, 50726-26-6; $C_6H_5C{\equiv}W(CO)_4I$, 50726-28-8; polypentenamer, 28702-43-4; polyoctenamer, 28702-45-6; polyheptenamer, 28702-44-5; polynorbornenamer, 42813-64-9.

Supplementary Material Available: ^1H NMR spectrum of poly(*tert*-butylacetylene) prepared in experiment 4 of Table I, ^{13}C NMR spectrum of poly(acetylene) (experiment 9 in Table I), ^1H NMR and IR spectra of 4 samples of poly(pentadeuteriophenylacetylene), IR spectrum of poly(propyne) prepared in experiment 3, Table I, ^{13}C NMR spectra of poly(methyl 5-hexynoate) and poly(5-chloro-1-pentyne) prepared in experiments 10 and 11 in Table I, and ^1H NMR and IR spectra of poly(5-cyano-1-pentyne), prepared by repeating experiment 12 in Table I on a larger scale (11 pages). Ordering information is given on any current masthead page.

Stereocontrolled Synthesis of Trans-2,5-Disubstituted Tetrahydrofurans

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Abstract: A process is described for the stereospecific construction of trans-2,5-disubstituted tetrahydrofurans, involving 2,4,4,6-tetrabromo-2,5-cyclohexadienone-induced cyclization of γ,δ-unsaturated alcohols to the 3-bromotetrahydropyrans followed by ring contraction. Control over the side-chain stereochemistry can also be exerted, as exemplified by the sequence **6** → **7** → **8**. To probe the possibility that 1,3 relative asymmetric induction manifested by this strategy could prevail over an opposing 1,2 influence, construction of a model of the 2,3,5-trisubstituted tetrahydrofuran ring of ionophores such as monensin was investigated. In this instance, highly polarized olefins, such as (trimethylsilyl)methyl-substituted alkenes or methyl enol ethers, were required for Markovnikov orientation. Although the desired 2,3-cis-2,5-trans substitution pattern could be introduced, the cyclization reaction was not stereospecific in these instances.

The synthesis of polyether antibiotics remains a challenge, requiring methods for the stereocontrolled construction of oxacyclic rather than carbocyclic rings.[1] The 2,5-disubstituted tetrahydrofuran units, which are common to these natural products, are particularly troublesome since 1,3-interactions are weak in five-membered rings. Although electrophilic cyclization of γ,δ-unsaturated alcohols is one of the most direct routes to such systems,[2] these cyclizations generally proceed with only modest stereoselectivity.[3] As an example, 2-methyl-6-octen-3-ol (Z:E mixture, 1:3) is cyclized with 2,4,4,6-tetrabromo-2,5-cyclohexadienone (TBCO)[4] to give a 56:44 ratio of trans/cis tetrahydrofurans (71% yield); iodine (I_2, Na_2CO_3, acetonitrile) is only slightly more selective, giving a 75:25 ratio of trans/cis isomers (48% yield). We sought therefore a procedure for specific generation of the trans isomers, not only to overcome the limitations of direct cyclization but also as a complement to our previously reported strategy for the selective formation of cis-2,5-disubstituted tetrahydrofurans.[3b]

(1) Structures: (a) Westley, J. W. *Annu. Rep. Med. Chem.* **1975**, *10*, 246; *Adv. Appl. Microbiol.* **1977**, *22*, 172. Pressman, B.C. *Annu. Rev. Biochem.* **1976**, *45*, 501. Total syntheses: for references to initial work on lasalocid A, monensin, and nonactin, see: (b) Bartlett, P. A. *Tetrahedron* **1980**, *36*, 2. More recently: (c) Ireland, R. E.; Anderson, R. C.; Badoud, R.; Fitzsimmons, B. J.; McGarvey, G. J.; Thaisrivongs, S.; Wilcox, C. S. *J. Am. Chem. Soc.* **1983**, *105*, 1988. (d) Kishi, Y.; Hatakeyama, S.; Lewis, M.D. *Front. Chem. Plenary Keynote Lect.* IUPAC Congr., *28th*, **1981**, 237. Synthetic methods, inter alia: (e) Ireland, R. E.; Vevert, J.P. *J. Org. Chem.* **1980**, *45*, 4259. (f) Amouroux, R.; Folefoc, G.; Chastrette, F.; Chastrette, M. *Tetrahedron Lett.* **1981**, *22*, 2259. (g) Amouroux, R; Chastrette, F.; Chastrette, M. *J. Heterocycl. Chem.* **1981**, *18*, 565; (h) Fraser-Reid, B.; Sun, K. M.; Tam, T. F. *Bull. Soc. Chim. Fr.* **1981**, 238. (i) Williams, D. R.; Phillips, J. G.; Barner, B. A. *J. Am. Chem. Soc.* **1981**, *103*, 7398. (j) Walba, D. M.; Stoudt, G. S. *Tetrahedron Lett.* **1982**, *23*, 727.

(2) Bartlett, P. A. In "*Asymmetric Synthesis*"; Morrison, J. D.; Ed.; Academic Press: New York; Vol. 3, in press. Staninets, V. I.; Shilov, E. A. *Russ. Chem. Rev.* **1971**, *40*, 272.

(3) There are exceptions to this generalization. See, for examples: (a) Fukuyama, T.; Wang, C.-L. J.; Kishi, Y. *J. Am. Chem. Soc.* **1979**, *101*, 260. (b) Rychnovsky, S. D.; Bartlett, P. A. *Ibid.* **1981**, *103*, 3963. (c) Hosokawa, T.; Hirata, M.; Murahashi, S.; Sonoda, A. *Tetrahedron Lett.* **1976**, 1821. (d) Reference 1g.

(4) Kato, T.; Ichinose, I.; Hosogai, T.; Kitahara, Y. *Chem. Lett.* **1976**, 1187.

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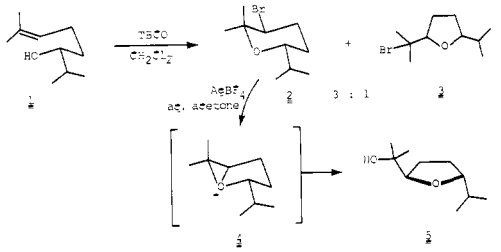
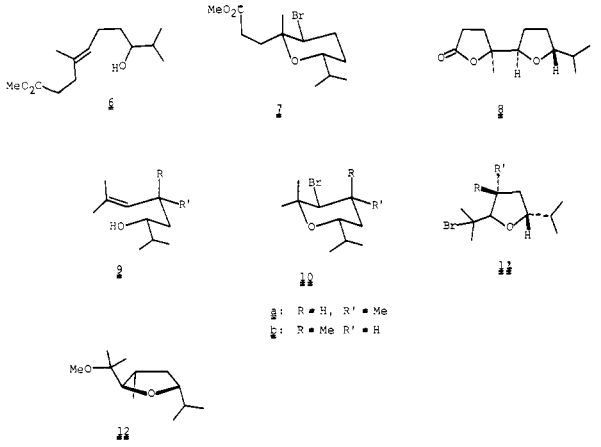
Since 1,3 relative asymmetric induction is more readily attained in six-membered rings than in five, we envisaged a sequence in which the desired stereochemical relationship would be introduced on cyclization to a tetrahydropyran and subsequently preserved on ring contraction to the desired tetrahydrofuran.[5] As illustrated by the conversion of **1** → **5**, this strategy is indeed successful.

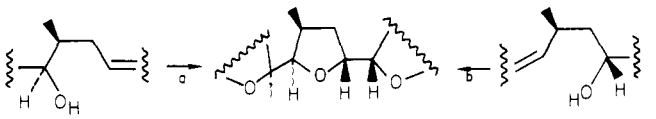


Cyclization of 2,7-dimethyl-6-octen-3-ol (**1**)[6] with TBCO leads to a separable mixture of the tetrahydropyran **2** and its tetrahydrofuran regioisomers **3** (78% yield). Although the byproduct **3** is obtained as a 1:1 mixture of stereoisomers, the desired ether **2** is essentially a single compound (>95% by 250–MHz NMR). A number of other electrophiles, including *N*-bromosuccinimide, *N*-iodosuccinimide, iodine, *N*-phenylselenophthalimide,[7] and mercuric nitrate/bromine[8] were investigated, but no improvement in regioselectivity was realized. Ring contraction of **2** with silver tetrafluoroborate in methanol gives the trans tetrahydrofuran **5** stereospecifically,[9] presumably via the bridged oxonium ion **4**.[5]

An added element in this process, the possibility of controlling the stereochemistry at a side-chain chiral center, was explored with the trans olefinic ester **6**.[11] TBCO-induced cyclization of this material is analogous to that of **1**, providing tetrahydropyran **7** and the tetrahydrofuran regioisomers in a 3:1 ratio (49% yield). Ring contraction in aqueous acetone gives lactone **8** in 75% yield, with clean inversion at the tertiary center.[12]

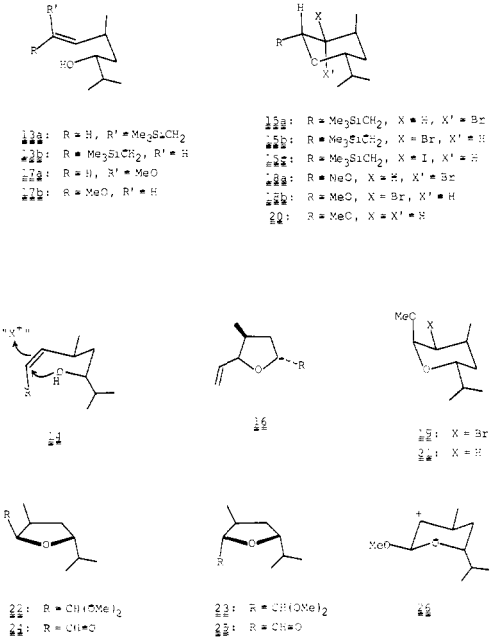


A common tetrahydrofuran substitution pattern in the polyethers is illustrated in the part structure below.[1a] Kishi demonstrated that the 2,5-trans stereochemistry of this trisubstituted ring can be introduced by direct cyclization when proceeding from left to right (path a).[3a] In this case, the methyl substituent acts in concert with the carbinol center to direct cyclization to the 2,5-trans product. The alternative cyclization mode (path b) would pit the stereodirecting influences of these two centers against each other and provide a measure of the efficacy of the cyclization/ring contraction sequence.



Cyclization of **9a**[13] provides the tetrahydropyran **10a** in 88% yield, along with 11% of the tetrahydrofuran **11a** (1.3:1 mixture); ring contraction of **10a** then affords tetrahydrofuran **12** in 83% yield. The lack of unfavorable 1,3-diaxial interactions undoubtedly explains why **10a** is formed so efficiently. In contrast, cyclization of the appropriate model for the polyether segment (isomer **9b**[13]) affords exclusively tetrahydrofuran **11b** (74% yield, 2:1 mixture of isomers). Clearly, Markovnikov selectivity is not sufficient to overcome the 1,3-steric interactions that would be generated in **10b**. A variety of other electrophilic reagents were investigated, but none led to tetrahydropyran.

We investigated the allylsilanes **13**[13,16] and enol ethers **17**[13] in an effort to increase the orientational bias of the double bond.



Cyclization of the cis allylsilane **13a** proceeds in 55% yield with relative asymmetric induction from the methyl substituent, via **14**, to afford axial bromide **15a**, which is not suitable for ring

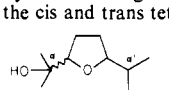
(5) Ring contractions of this sort are well precedented in carbohydrate chemistry: Grouiller, A.; Bazin, H.; Gagnieu, C. *Tetrahedron Lett.* **1982**, *23*, 2559. Hanessian, S. *Chem. Commun.* **1966**, 796. Stevens, C. L.; Glinski, R. P.; Taylor, K. G.; Sirokman, F. *J. Org. Chem.* **1970**, *35*, 592.

(6) Brown, E.; Guilmet, E.; Touet, J. *Tetrahedron* **1973**, *29*, 2589; Julia, M.; Julia, S.; Guegan, R. *Bull. Soc. Chim. Fr.* **1960**, 1072.

(7) Nicolaou, K. C. *Tetrahedron* **1981**, *37*, 4097.

(8) Hoye, T. R.; Kurth, M. J. *J. Am. Chem. Soc.* **1979**, *101*, 5065.

(9) The trans stereochemistry of **5** was assigned by ^{13}C NMR comparison with an authentic mixture of the cis and trans tetrahydrofurans i, obtained



i

from epoxidation of **1** and base-catalyzed cyclization. The cis isomer shows upfield signals for the C-α (84.66 vs. 85.08 ppm) and C-α'(32.70 vs. 33.13 ppm) resonances, similar to those observed for related compounds.[10]

(10) Thomas, A. F.; Thommen, W.; Willhalm, B.; Hagaman, E. W.; Wenkert, E. *Helv. Chim. Acta* **1974**, *57*, 2055.

(11) Prepared from 2-methyl-6-hepten-3-ol by benzylation, osmium tetraoxide cleavage, 2-propenylmagnesium bromide addition, orthoester Claisen rearrangement, and methanolysis.

(12) Peracid epoxidation of **6** and base-induced cyclization affords a 1:1 mixture of the two lactones with the *R*,S** relationship between the ring-connecting carbons. One of these proved to be identical with **7** by GC and high-field ^1H and ^{13}C NMR, confirming its stereochemical assignment.

(13) The diastereomeric mixture of **9a** and **9b** was prepared by coupling 2-acetoxy-4-methyl-3-pentene with the trimethylsilyl enol ether of 3-methyl-2-butanone,[14] followed by $LiAlH_4$ or L-Selectride (Aldrich) reduction. However, only isomer **9a** could be obtained pure by HPLC; **9b** was therefore prepared by the alkylation of γ-isopropyl-γ-butyro lactone, reduction to the lactol, and Wittig reaction. Reaction of this lactol with [(trimethylsilyl)-methylene]-[15] and (methoxymethylene)triphenylphosphorane afforded the allylsilanes **13** and enol ethers **17** respectively. The cis and trans isomers of **13** and **17** were separated chromatographically.

(14) Reetz, M. T.; Huttenhain, S.; Hubner, F. *Synth. Commun.* **1981**, 217.

(15) Fleming, I.; Patterson, I. *Synthesis* **1979**, 446.

(16) Colvin, E. "Silicon in Organic Chemistry"; Butterworths: London, 1981. Fleming, I. In "Comprehensive Organic Chemistry"; Barton, D., Ollis, W. D., Eds.; Pergamon Press: Oxford, 1979; Vol. 3, p 541.

contraction.[17] The trans isomer (**13b**), on treatment with either iodine or a brominating agent, affords small amounts of the desired tetrahydropyrans **15b** and **15c**[17] (10–20% yield) along with the halotetrahydrofurans. Using the less volatile cyclohexyl-substituted derivatives (**13**, c-C_6H_{11} instead of *i*-Pr), we found that the major products of these cyclizations are the vinyl-substituted tetrahydrofurans **16**, resulting from elimination of halotrimethylsilane.

Complete regioselectivity is achieved on cyclization of the enol ethers **17**.[18] The cis isomer **17a** affords the axial bromide **18a**[17] in 87% yield with either NBS or TBCO, in analogy with the cis olefin **13a**. The trans enol ether **17b**, however, gives the equatorial bromides **18b** and **19** (2:3 ratio) in 81% yield (NBS or TBCO). The strong stabilization exerted by the methoxy group must be responsible for the nonstereospecific nature of this cyclization. In addition to the NMR evidence for stereochemical assignments,[17] we showed that tri-*n*-butyltin hydride dehalogenation of **18a** and **18b** gives the same compound, **20**, which is different from the product (**21**) obtained from **19**. An authentic mixture of **20** and **21** was formed by acid-catalyzed cyclization of **17a** or **17b**.

Both tetrahydropyrans **18b** and **19** were expected to contract to the desired 2,3,5-trisubstituted tetrahydrofuran **22**. However, the axial anomer **19** affords exclusively the undesired diastereomer **23** with silver tetrafluoroborate in refluxing methanol (83% yield). Concerted ring contraction of **19** would generate exceptionally severe steric interactions in the transition state, hence the reaction must proceed in a nonconcerted manner via cation **26**. In contrast, treatment of tetrahydropyran **18b** under identical conditions proceeds as desired, giving a 9.5:1 ratio of **22** and the 2,5-cis isomer **23** in 80% yield. The isomeric products **22** and **23** are readily distinguished by ^{13}C NMR[19] and by the fact that alkaline equilibration of the derived aldehydes, **24** and **25**, strongly favors the latter isomer.

Although an entirely satisfactory solution to the challenge of 1,3- vs. 1,2-asymmetric induction was not devised, the cyclization/ring contraction strategy outlined here should prove to be valuable in a variety of other applications.

Experimental Section[20,21]

(3*R,6*S**)-3-Bromo-2,2-dimethyl-6-(1-methylethyl)tetrahydropyran (2) and (2*R**,5*S**)- and (2*R**,5*R**)-2-(1-Bromo-1-methylethyl)-5-(1-methylethyl)tetrahydrofuran (3).** To 400 mg (2.56 mmol) of 2,7-dimethyl-6-octen-3-ol in 40 mL of dry CH_2Cl_2 was added 1.05 g (2.56 mmol) of 2,4,4,6-tetrabromo-2,5-cyclohexadienone (TBCO). The resulting solution was stirred in the dark at 21 °C under nitrogen for 24 h. The solution was washed with 1 N NaOH and worked up[21] to give a crude product, which was purified by chromatography (silica gel/3% ether–hexane) to give 349 mg (58% yield) of **2** and 123 mg (20% yield) of **3** as oils.

2: IR 2950, 1360, 1240, 1150, 1120, 1060 cm^{-1}; ^1H NMR δ 0.84 (d, 3, J = 6.7 Hz), 1.34 (s, 6), 1.48–1.75 (m, 3), 1.98–2.27 (m, 2), 3.20–3.28 (m, 1), 3.91 (dd, 1, J = 5.0, 12.1 Hz). Anal. Calcd for $C_{10}H_{19}BrO$: C, 51.06; H, 8.16; Br, 33.98. Found: C, 51.31; H, 8.04; Br, 33.89.

3 (1:1 mixture of cis and trans isomers): IR ($CDCl_3$) 2975, 1380, 1080 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.83–0.99 (m, 6), 1.51–1.71 (m, 1), 1.71–1.75 (m, 6), 1.79–2.16 (m, 4), 3.55–3.72 (m, 1), 3.79–3.86 (m, 1). Anal. Calcd for $C_{10}H_{19}BrO$: C, 51.06; H, 8.16; Br, 33.98. Found: C, 50.89; H, 7.99; Br, 33.82.

(2*R,5*R**)-2-(1-Hydroxy-1-methylethyl)-5-(1-methylethyl)tetrahydrofuran (5).** To 145 mg (0.744 mmol) of $AgBF_4$ in 0.90 mL of acetone and 0.15 mL of water was added 175 mg (0.744 mmol) of bromide **2**. AgBr precipitated immediately; however, the resulting solution was stirred at 21 °C for 2 h. The AgBr was removed by filtration and washed with ether, the filtrate was worked up,[21] and the crude product was purified by chromatography (silica gel/25% ether–hexane) to give 112 mg (88% yield) of **5** as a colorless liquid: IR 3575, 2950, 1330, 1130 cm^{-1}; ^1H NMR δ 0.85 (d, 3, J = 6.8 Hz), 0.96 (d, 3, J = 6.6 Hz), 1.11 (s, 3), 1.22 (s, 3), 1.48–2.05 (m, 6), 3.56–3.65 (m, 1), 3.73 (dd, 1, J = 6.2, 9.4 Hz); ^{13}C NMR ($CDCl_3$) δ 17.85, 19.08, 23.59, 26.80, 26.94, 29.84, 33.13, 71.23, 85.08, 85.38. Anal. Calcd for $C_{10}H_{20}O_2$: C, 69.70; H, 11.72. Found: C, 69.57; H, 11.69.

Methyl (2*R,3*S**,6*R**)-3-Bromo-2-methyl-6-(1-methylethyl)tetrahydropyran-2-propanoate (7).** In a similar manner, 100 mg (0.438 mmol) of alcohol **6** was treated with 197 mg (0.482 mmol) of TBCO in 3 mL of dry CH_2Cl_2. The crude product was purified by chromatography (silica gel/10% ether–hexane) to give 49 mg (36% yield) of **7** and 17 mg (13% yield) of the tetrahydrofuran isomers as yellow liquids.

7: IR 2950, 1720, 1440, 1270, 1160 cm^{-1}; ^1H NMR δ 0.83 (d, 3, J = 9.8 Hz), 0.86 (d, 3, J = 9.7 Hz), 1.32 (s, 3), 1.25–1.44 (m, 1), 1.52 (q, 1, J = 6.7 Hz), 1.60–1.73 (m, 1), 1.86–1.98 (m, 1), 2.08–2.24 (m, 3), 2.38–2.48 (m, 2), 3.17–3.25 (m, 1), 3.67 (s, 3), 3.92 (dd, 1, J = 5.6, 11.5 Hz). Anal. Calcd for $C_{13}H_{23}O_3Br$: C, 50.81; H, 7.56; Br, 26.01. Found: C, 50.68; H, 7.55; Br, 26.08. Tetrahydrofuran regioisomers (cis and trans mixture): IR 2950, 1720, 1440, 1300, 1180 cm^{-1}; ^1H NMR δ 0.82–0.96 (m, 6), 1.51–1.78 (m, 5), 1.84–2.32 (m, 5), 2.48–2.79 (m, 2), 3.51–3.63 (m, 1), 3.69 (s, 3), 3.96 (m, 1).

(5*R)-5-Methyl-5[(2*S**,5*S**)-5-(1-methylethyl)tetrahydrofuran-2-yl]dihydrofuran-2-one (8).** A 186-mg sample (0.605 mmol) of bromide **7** was treated with 200 mg (1.03 mmol) of $AgBF_4$ in 0.30 mL of water and 1.80 mL of acetone as described above. The crude product was purified by chromatography (silica gel/50% ether–hexane) to give 97 mg (75% yield) of **8** as a light oil: IR 3000, 2900, 1770, 1470, 1380, 1260, 1160, 1070 cm^{-1}; ^1H NMR δ 0.84 (d, 3, J = 6.7 Hz), 0.94 (d, 3, J = 6.6 Hz), 1.34 (s, 3), 1.52–1.73 (m, 3), 1.78–2.10 (m, 3), 2.21–2.35 (m, 1), 2.46–2.78 (m, 2), 3.58 (q, 1, J = 7.2 Hz), 4.02 (t, 1, J = 7.4 Hz); ^{13}C NMR ($CDCl_3$) δ 18.11, 19.22, 22.98, 27.78, 28.55, 29.44, 29.90, 33.12, 83.21, 85.91, 88.25, 176.93. Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.88; H, 9.51. Found: C, 67.57; H, 9.53.

(2*R,3*R**,4*R**,6*S**)- and (2*R**,3*S**,4*S**,6*R**)-3-Bromo-2-methoxy-4-methyl-6-(1-methylethyl)tetrahydropyran (18b and 19).** To 2.20 g (12.79 mmol) of trans enol ether **17b** in 50 mL of dry CH_2Cl_2 at 0 °C under nitrogen in the dark were added 1.18 g (14.06 mmol) of $NaHCO_3$ and 2.50 g (14.06 mmol) of *N*-bromosuccinimide. The resulting mixture was allowed to warm slowly to 21 °C and was stirred for 12 h. The solvent was evaporated at reduced pressure, the residue was diluted with ether, and the organic layer was worked up.[21] The crude product was purified by chromatography (silica gel/1.5% ether–hexane then 2.5% ether–hexane) to give 1.53 g (48% yield) of **19** and 1.09 g (33% yield) of **18b** as colorless liquids.

19: IR 2980, 1470, 1390, 1110, 1050 cm^{-1}; ^1H NMR δ 0.90 (d, 3, J = 6.7 Hz), 1.01 (d, 3, J = 6.6 Hz), 1.22 (d, 3, J = 7.1 Hz), 1.35 (m, 1), 1.81 (dd, 1, J = 7.2, 14.0 Hz), 1.99 (ddd, 1, J = 5.1, 8.7, 13.7 Hz), 2.20 (m, 1), 3.39 (s, 3), 3.51 (ddd, 1, J = 3.8, 8.4, 8.4 Hz), 3.77 (dd, 1, J = 3.8, 7.9 Hz), 4.80 (d, 1, J = 3.7 Hz). Anal. Calcd for $C_{10}H_{19}BrO_2$: C, 47.81; H, 7.64; Br, 31.81. Found: C, 48.08; H, 7.54; Br, 31.69.

18b: IR 2980, 1470, 1390, 1220, 1140, 1050 cm^{-1}; ^1H NMR δ 0.89 (d, 3, J = 6.8 Hz), 0.98 (d, 3, J = 6.7 Hz), 1.24 (d, 3, J = 7.3 Hz), 1.70 (m, 3), 3.41 (m, 1), 3.52 (s, 3), 3.98 (dd, 1, J = 5.2, 8.6 Hz), 4.33 (d, 1, J = 8.4 Hz), 4.50 (d, 1, J = 8.6 Hz) at ratio 1:3. Anal. Calcd for $C_{10}H_{19}BrO_2$: C, 47.81; H, 7.64; Br, 31.81. Found: C, 47.49; H, 7.47; Br, 31.54.

(2*R,3*S**,5*R**)-2-(Dimethoxymethyl)-3-methyl-5-(1-methylethyl)-tetrahydrofuran (22).** To 75 mg (0.385 mmol) of dry $AgBF_4$ in 1 mL of dry methanol were added 88 mg (0.350 mmol) of bromide **18b** in 1 mL of dry methanol via syringe. The resulting solution was refluxed under nitrogen for 20 h and then cooled to 21 °C. The precipitated AgBr was removed by filtration through glass wool. The filtrate was diluted with CH_2Cl_2, washed with water, and worked up,[21] and the crude product was purified by chromatography (silica gel/10% ether–hexane) to give 57 mg (80% yield) of **22** as an oil: IR 2960, 1470, 1210, 1080 cm^{-1},; ^1H NMR δ 0.83 (d, 3, J = 6.7 Hz), 0.94 (d, 3, J = 6.7 Hz), 0.99 (d, 3, J = 7.1 Hz), 1.60–1.86 (m, 3), 2.37 (m, 1), 3.39 (s, 3), 3.42 (s, 3), 3.86

(17) 250-MHz ^1H NMR ($CDCl_3$): **15a**, δ 3.26 (ddd, 1, J = 2.2, 6.4, 12.0), 3.50 (dd, 1, J = 4.7, 9.3), 3.91 (br s, 1); **15b** δ 3.34 (ddd, 1, J = 2.7, 6.0, 8.6), 3.72 (ddd, 1, J = 2.9, 10.5, 10.5), 3.99 (dd, 1, J = 4.8, 10.1); **15c**, δ 3.47 (ddd, 1, J = 2.1, 5.9, 11.4), 3.90 (ddd, 1, J = 3.0, 10.6, 10.6), 4.36 (ddd, 1, J = 4.7, 10.3); **18a**, δ 3.35 (ddd, 1, J = 2.2, 7.3, 11.4), 3.99 (br s, 1, J < 1), 4.36 (br s, 1, $w_{1/2} \approx 5$ Hz); **18b** δ 3.41 (m, 1, obscured), 3.98 (dd, 1, J = 5.2, 8.6), 4.50 (d, 1, J = 8.6); **19**, δ 3.51 (ddd, 1, J = 3.8, 8.4, 8.4), 3.77 (dd, 1, J = 3.8, 7.9), 4.80 (d, 1, J = 3.7).

(18) Suzuki, K.; Mukaiyama, T. *Chem. Lett.* **1982**, 683.

(19) Compound **22** shows resonances at δ 14.3 and 103.2 for the 3-methyl and acetal carbons, respectively; the corresponding resonances for isomer **23** appear at δ 19.1 and 106.4.

(20) Representative experrimental procedures are given in this section; the remaining experimental details are available in the supplementary material.

(21) General: ^1H NMR and ^{13}C NMR spectra were acquired on 250-MHz Fourier transform instruments. Chemical shifts are reported in ppm on the δ scale relative to tetramethylsilane as 0 ppm. ^1H NMR data are presented as follows: chemical shift (multiplicity, number of protons, coupling constants in hertz). IR spectra were obtained on a Perkin-Elmer Model 1420 spectrophotometer. All spectra were obtained in $CDCl_3$ solvent. Unless otherwise indicated, all reaction workups culminated in washing the organic layer with brine, drying over $MgSO_4$, and concentration at reduced pressure on a rotary evaporator. Tetrahydrofuran was distilled from sodium/benzophenone immediately prior to use; methylene chloride was dried by distillation from P_2O_5. Combustion analyses were performed by the Microanalytical Laboratory, Department of Chemistry, University of California, Berkeley, Ca.

(m, 2), 4.18 (d, 1, J = 5.4 Hz) and 4.32 (d, 1, J = 8.0 Hz) at ratio 1.0:9.5 for **23**/**22**; ^{13}C NMR δ 14.28, 17.49, 19.02, 33.22, 35.20, 36.96, 52.27, 53.77, 79.29, 82.89, 103.17. Anal. Calcd for $C_{11}H_{22}O_3$: C, 65.29, H, 10.98. Found: C, 65.21; H, 10.99.

(2*R,3*R**,5*S**)-2-(Dimethoxymethyl)-3-methyl-5-(1-methylethyl)-tetrahydrofuran (23).** In a similar manner, 201 mg (0.800 mmol) of the isomeric bromide **19** was ring contracted with 171 mg (0.880 mmol) of $AgBF_4$. The crude product was purified by chromatography (silica gel/10% ether–hexane) to give 134 mg (83% yield) of **23** as a colorless liquid: IR 2960, 1470, 1220, 1080 cm^{-1}; ^{1}H NMR δ 0.84 (d, 3, J = 6.8 Hz), 0.95 (d, 3, J = 6.7 Hz), 1.07 (d, 3, J = 6.9 Hz), 1.47–1.84 (m, 3), 2.17 (m, 1), 3.43 (s, 3), 3.44 (s, 3), 3.38–3.57 (m, 1), 3.65 (dd, 1, J = 7.2, 7.2 Hz), 4.17 (d, 1, J = 5.9 Hz); ^{13}C NMR δ 18.10, 19.12, 19.21, 32.87, 34.67, 36.94, 54.05, 55.34, 83.74, 85.14, 106.42. Anal. Calcd for $C_{11}H_{22}O_3$: C, 65.29; H, 10.98. Found: C, 65.18; H, 11.05.

(2*R,3*S**,5*R**)-3-Methyl-5-(1-methylethyl)tetrahydrofuran-2-carboxaldehyde (24).** To 266 mg (1.32 mmol) of acetal in 2.5 mL of THF was added 2.5 mL of 1 N HCl. The resulting solution was refluxed for 6 h, then cooled, and neutralized with 2.5 mL of 1 N NaOH. The mixture was diluted with water and extracted with ether, and the organic layer was worked up.[21] The crude product was purified by chromatography (silica gel/15% ether–hexane) to give 130 mg (63% yield) of **23** as an oil: IR 2960, 1730, 1470, 1070 cm^{-1}; ^{1}H NMR δ 0.88 (d, 3, J = 6.7 Hz), 0.99 (d, 3, J = 6.6 Hz), 1.03 (d, 3, J = 7.2 Hz), 1.57–1.98 (m, 3), 2.70 (m, 1), 4.03 (dd, 1, J = 7.3, 7.3 Hz), 4.26 (dd, 1, J = 2.2, 6.7 Hz), 9.66 (d, 1, J = 2.7 Hz), 9.73 (d, 1, J = 2.2 Hz) at ratio 1.0:5.5 for **25**/**24**; ^{13}C NMR δ 14.83, 18.05, 18.89, 33.19, 36.88, 37.15, 84.80, 85.64, 203.87. Anal. Calcd for $C_9H_{16}O_2$: C, 69.18; H, 10.34. Found: C, 68.89; H, 10.22.

(2*R,3*R**,5*S**)-3-Methyl-5-(1-methylethyl)tetrahydrofuran-2-carboxaldehyde (24).** A 500-mg (2.47 mmol) sample of acetal **23** was hydrolyzed in a similar manner to afford a 78% yield of **25** as an oil: IR 2960, 1730, 1470, 1100 cm^{-1}; ^{1}H NMR δ 0.81 (d, 3, J = 6.8 Hz), 0.94 (d, 3, J = 6.6 Hz), 1.06 (d, 3, J = 6.8 Hz), 1.48–1.83 (m, 3), 2.31 (m, 1), 3.76 (dd, 1, J = 2.3, 6.5 Hz), 3.83 (dd, 1, J = 7.5, 7.5 Hz), 9.66 (d, 1, J = 2.3 Hz); ^{13}C NMR δ 17.82, 18.38, 19.02, 33.18, 35.95, 36.80, 85.31, 89.31, 202.58. Anal. Calcd for $C_9H_{16}O_2$: C, 69.18; H, 10.34. Found: C, 68.86; H, 10.37.

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Registry No. 1, 50735-59-6; **1** (benzyl ether), 89065-91-8; **1** (epoxide), 89065-89-4; **2**, 89065-44-1; *cis*-**3**, 89065-45-2; *trans*-**3**, 89065-46-3; **5**, 89065-47-4; **6**, 89065-48-5; **6**, 89065-92-9; (*R**,*S**,*S**)-**6** (epoxide), 89065-93-0; (*R**,*S**,*R**)-**6** (epoxide), 89104-57-4; **6** (ethyl ester, benzyl ether), 89065-90-7; **7**, 89065-49-6; **8**, 89065-50-9; **9a**, 89065-51-0; **9b**, 89065-52-1; **10a**, 89065-53-2; (*R**,*R**,*R**)-**11a**, 89065-54-3; (*R**,*S**)-**11a**, 89065-81-6; **12**, 89065-55-4; (*R**,*S**)-**13a**, 89065-83-8; (*R**,*R**)-**13a**, 89065-84-9; (*R**,*S**)-**13b**, 89065-86-1; (*R**,*R**)-**13b**, 89065-87-2; **15a**, 89065-95-2; **15b**, 89065-96-3; **15c**, 89065-97-4; (*R**,*S**,*R**)-**16**, 89065-71-4; (*S**,*S**,*R**)-**16**, 89065-75-8; (*R**,*S**)-**17a**, 89065-82-7; (*R**,*R**)-**17a**, 89065-62-3; (*R**,*S**)-**17b**, 89065-63-4; (*R**,*R**)-**17b**, 89065-64-5; **18a**, 89065-66-7; **18b**, 89065-76-9; **19**, 89065-77-0; **20**, 89065-65-6; **21**, 89104-51-8; **22**, 89065-78-1; **23**, 89065-79-2; **24**, 89065-80-5; **25**, 89065-67-8; (*R**,*R**)-i, 89065-47-4; (*R**,*S**)-i, 89065-88-3; TBCO, 20244-61-5; $(CH_3)_2C{=}CHCH(CH_3)CH_2COCH(CH_3)_2$, 89065-94-1; $(CH_3)_2C{=}CHCH(OAc)CH_3$, 54166-19-7; $(CH_3)_2CHC(OSiMe_3){=}CH_2$, 17510-45-1; $CH_3CH{=}CH(CH_2)_2CH(OH)CH(CH_3)_2$, 89065-85-0; (*R**,*S**)-(*E*)-$Me_3SiCH_2CH{=}CHCH(CH_3)CH_2$CH(OH)-c-$C_6H_{11}$, 89065-98-5; (*R**,*R**)-(*E*)-$Me_3SiCH_2CH{=}CHCH(CH_3)CH_2CH(OH)$-c-$C_6H_{11}$, 89065-99-6; triethyl orthoacetate, 78-39-7; (5*R**,2′*R**,5′*S**)-5-methyl-5-[5′-(1″-methylethyl)tetrahydrofuran-2-yl]-dihydrofuran-2-one, 89104-55-2; (5*R**,2′*R**,5′*R**)-5-methyl-5-[5′-(1″-methylethyl)tetrahydrofuran-2-yl]dihydrofuran-2-one, 89104-56-3; (3*R**,5*S**)-3-methyl-5-(1′-methylethyl)dihydrofuran-2-one, 89065-57-6; (3*r**,5*R**)-3-methyl-5-(1′-methylethyl)dihydrofuran-2-one, 89065-56-5; (2*R**,3*R**,5*S**)-3-methyl-5-(1′-methylethyl)tetrahydrofuran-2-ol, 89065-58-7; (2*R**,3*S**,5*R**)-3-methyl-5-(1′-methylethyl)tetrahydrofuran-2-ol, 89065-59-8; (2*R**,3*S**,5*S**)-3-methyl-5-(1′-methylethyl)-tetrahydrofuran-2-ol, 89065-60-1; (2*R**,3*R**,5*R**)-3-methyl-5-(1′-methylethyl)tetrahydrofuran-2-ol, 89065-61-2; isopropylbutyrolactone, 38624-29-2; (methoxymethyl)triphenylphosphonium chloride, 4009-98-7; 2-(1′-bromoethyl)-5-(1″-methylethyl)tetrahydrofuran, 89065-68-9; (1′*R**,2*R**,5*R**)-2-(1′-iodoethyl)-5-(1′-methylethyl)tetrahydrofuran, 89065-69-0; (1′*R**,2*R**,5*S**)-2-(1′-iodoethyl)-5-(1′-methylethyl)tetrahydrofuran, 89104-52-9; (1′*S**,2*R**,5*R**)-2-(1′-iodoethyl)-5-(1′-methylethyl)tetrahydrofuran, 89104-53-0; (1′*S**,2*R**,5*S**)-2-(1′-iodoethyl)-5-(1′-methylethyl)tetrahydrofuran, 89104-54-1; (2*R**,3*S**,4*R**,6*S**)-3-bromo-6-cyclohexyl-4-methyl-2-(trimethylsilylmethyl)tetrahydropyran, 89065-70-3; (2*R**,3*S**,4*S**,6*R**)-6-cyclohexyl-3-iodo-4-methyl-2-(trimethylsilylmethyl)tetrahydropyran, 89065-72-5; 2-trimethylsilylethyl)-3-methyltetrahydrofuran, 89065-73-6; (2*S**,2′*R**,3*S**,5*R**)-5-cyclohexyl-2-(1-iodo-2-trimethylsilylethyl)-3-methyltetrahydrofuran, 89065-74-7.

Supplementary Material Available: Experimental procedures, spectral data, and characterization of compounds not described in the Experimental Section (12 pages). Ordering information is given on any current masthead page.