Acknowledgment. We are grateful to the National Institutes of Health for financial support. Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for the partial support of this research. We thank Claudia P. Cartaya-Marin for experimental assistance. Preliminary experiments were carried out by Gary B. Phillips.

Registry No. 1, 1655-07-8; 2, 53750-52-0; 3, 81763-01-1; 4, 84433-95-4; 5, 91781-66-7; 6, 91781-67-8; 7, 91781-68-9; 8, 91781-69-0; 9, 91781-70-3; 10, 91781-71-4; 11, 91781-72-5; 12, 3197-68-0; 12 (tosylate), 3399-72-2; 13, 82201-80-7; 14, 91781-73-6; 15, 91781-74-7; 16, 91781-75-8; 17, 91781-76-9; 18, 91781-77-0; 19, 91781-78-1; 20, 91781-79-2; 21, 91781-80-5; 22, 91781-81-6; 23, 91781-82-7; 24, 35944-13-9; 25, 75685-75-5; 26, 91781-83-8; 27, 91781-84-9; 28, 91781-85-0; 29, 91781-86-1; 30, 87887-29-4; 31, 91781-87-2; 32, 71203-75-3; (*E*)-33, 71203-75-3; (*Z*)-33, 91781-98-5; 34, 91781-89-4; 35a, 91781-90-7; 35b, 91781-91-8; 35c, 91781-92-9; 36, 91781-93-0; 37, 91781-94-1; 38a, 91781-95-2; 38b, 91781-96-3; 39a, 91781-97-4; 39b, 76519-80-7; Me_2AlCl, 1184-58-3; $Me_{1.5}AlCl_{1.5}$, 12542-85-7; $MeAlCl_2$, 917-65-7; HCHO, 50-00-0; $EtAlCl_2$, 563-43-9; cyclohexanone, 108-94-1; cyclopentanone, 120-92-3; cyclobutanone, 1191-95-3; 4-*tert*-butylcyclohexanone, 98-53-3; acetophenone, 98-86-2; benzophenone, 119-61-9; 2-methylcyclohexanone, 583-60-8; methyl cyclopropyl ketone, 10472-24-9; methyl 2-oxocyclopentanecarboxylate, 10472-24-9; 2-acetylbutyrolactone, 517-23-7; methyl acetoacetate, 105-45-3; methylenecyclopentane, 1528-30-9; ethylidenecyclopentane, 2146-37-4; 2-ethyl-1-butene, 760-21-4; methylenecyclohexane, 1192-37-6; 5-iodo-2-methyl-1-pentene, 73541-16-9; 6-iodo-2-methyl-2-hexene, 63588-94-3; 5-methyl-4-hexen-1-ol, 42272-94-6; 5-methyl-4-hexen-1-ol tosylate, 61755-53-1.

Synthetic and Biological Studies of Compactin and Related Compounds. 2. Synthesis of the Lactone Moiety of Compactin[1]

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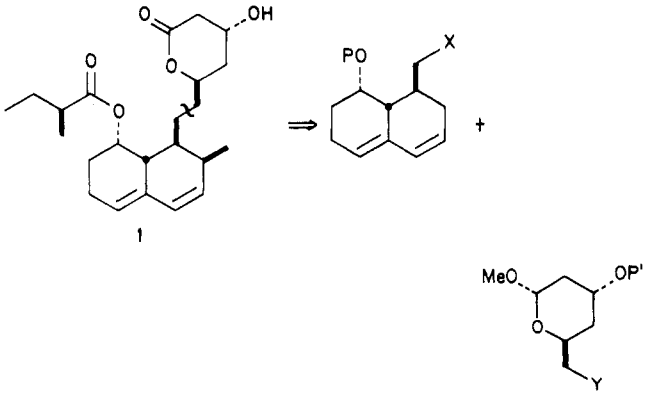
Received March 26, 1984

Several optically active synthons for the lactone portion of compactin have been prepared. Lithium aluminum hydride opening of epoxide **23** affords a 92:8 mixture of axial alcohol **27** and regioisomer **28** in 96% yield. Silylation of this material followed by removal of the trityl group with sodium in ammonia gives primary alcohol **31**. Tosylation of **31** (90%) followed by iodide displacement furnishes iodide **36** (96%). Sulfone **49** is obtained (31%) accompanied by **36** (55%) upon treatment of tosylate **35** with sodium benzenesulfinate and tetra-*n*-butylammonium iodide. Oxidation of **31** by the Swern method affords aldehyde **37** (93%) which reacts with ylide **43** to give coupled product **44** (54%). Hydrogenation of **44** (100%) followed by acidic hydrolysis gives hydroxy hemiacetals **47** (69%). The hemiacetal functionality is selectively oxidized with Fetizon's reagent to obtain β-hydroxy-δ-lactone **48** (70%).

Introduction

In 1976, Endo and co-workers isolated a potent inhibitor of HMG CoA reductase, named ML236B, from the metabolites of *Penicillium citrinium*.[3] This compound proved to be identical with a compound isolated from *P. breviocompactum* and named compactin (1) by Brown and co-workers at Beecham Pharmaceuticals.[4] Since that time, several other naturally occurring mevinic acids, compounds possessing a highly functionalized hexalin or octalin unit and a β-hydroxy-δ-lactone portion which are linked by an ethylene bridge, have been isolated.[5] The potential utility of this class of compounds as hypocholesterolemic agents[6] and their interesting structural features have prompted extensive synthetic investigations.[1,7,8]



1

(1) For Part 1, see: Heathcock, C. H.; Taschner, M. J.; Rosen, T.; Thomas, J. A.; Hadley, C. R.; Popják, G. *Tetrahedron Lett.* **1982**, *23*, 4747.

(2) Current address: Department of Chemistry, University of Akron, Akron, OH 44325.

(3) (a) Endo, A.; Kuroda, M.; Tsujita, Y. *J. Antibiot.* **1976**, *29*, 1346. (b) Endo, A.; Kuroda, M.; Tanzawa, K. *FEBS Lett.* **1976**, *72*, 323. (c) Endo, A.; Tsujita, Y.; Kuroda, M.; Tanzawa, K. *Eur. J. Biochem.* **1977**, *77*, 31.

(4) Brown, A. G.; Smale, T. C.; King, T. J.; Hasenkamp, R.; Thompson, R. H. *J. Chem. Soc., Perkin Trans. 1* **1976**, 1165.

(5) Mevinolin: (a) Alberts, A. W.; Chen, J.; Kuraon, G.; Hunt, V.; Huff, J.; Hoffman, C.; Rothrock, J.; Lopez, M.; Joshua, H.; Harris, E.; Patchett, A.; Monaghan, R.; Currie, S.; Stapley, E.; Albers-Schonberg, G.; Hensens, O.; Hirshfield, J.; Hoogsteen, K.; Liesch, J.; Springer, J. *Proc. Natl. Acad. Sci. USA* **1980**, *77*, 3957. (b) Endo, A. *J. Antibiot.* **1979**, *32*, 852. Dihydrocompactin: Lam, Y. K. T.; Gullo, V. P.; Goegelman, R. T.; Jorn, D.; Huang, L.; DeRiso, C.; Monaghan, R. L.; Putter, I. *J. Antibiot.* **1981**, *34*, 614. Dihydromevinolin: Albers-Schonberg, G.; Joshua, H.; Lopez, M. B.; Hensens, O. D.; Springer, J. P.; Chen, J.; Ostrove, S.; Hoffman, C. H.; Alberts, A. W.; Patchett, A. A. *J. Antibiot.* **1981**, *34*, 507.

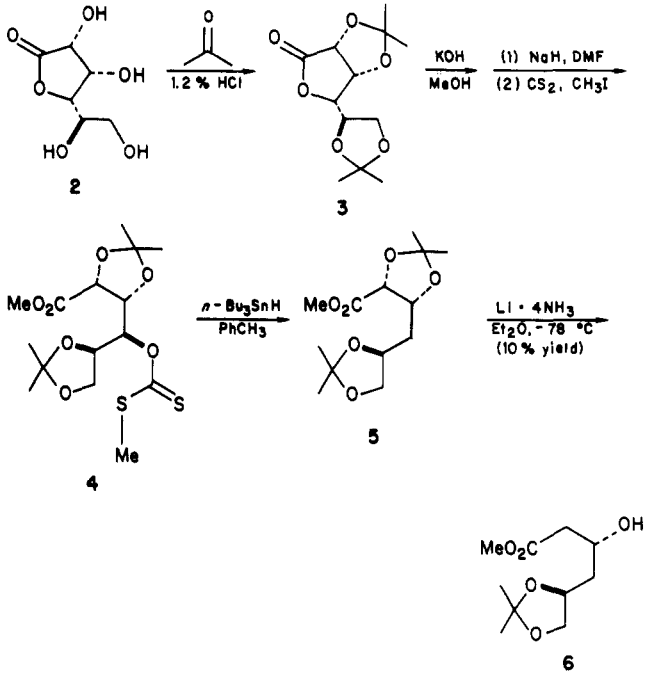
(6) Mabuchi, H.; Haba, T.; Tatami, R.; Miyamoto, S.; Sakai, Y.; Wakasugi, T.; Watanabe, A.; Koizumi, J.; Takeda, R. *N. Engl. J. Med.* **1981**, *305*, 478.

(7) Total syntheses: Compactin: (a) Wang, N. Y.; Hsu, C. T.; Sih, C. J. *J. Am. Chem. Soc.* **1981**, *103*, 6358. (b) Hirama, M.; Uei, M. *Ibid.* **1982**, *104*, 4251. (c) Grieco, P. A.; Zelle, R. E.; Lis, R.; Finn, J. *Ibid.* **1983**, *105*, 1403. (d) Girotra, N. N.; Wendler, N. L. *Tetrahedron Lett.* **1982**, *23*, 5501. (e) Girotra, N. N.; Wendler, N. L. *Ibid.* **1983**, *24*, 3687. Mevinolin: Hirama, M.; Iwashita, M. *Tetrahedron Lett.* **1983**, *24*, 1811.

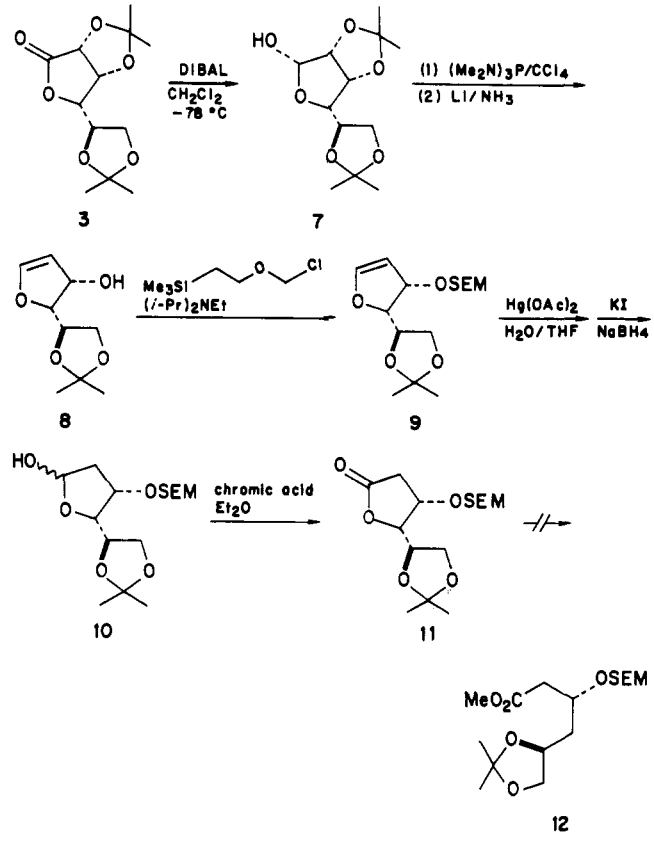
(8) Synthetic studies: (a) Danishefsky, S.; Kerwin, J. F., Jr.; Kobayashi, S. *J. Am. Chem. Soc.* **1982**, *104*, 358. (b) Funk, R. L.; Zeller, W. E. *J. Org. Chem.* **1982**, *47*, 180. (c) Deutsch, E. A.; Snider, B. B. *Ibid.* **1982**, *47*, 2682. (d) Prugh, J. D.; Deana, A. A. *Tetrahedron Lett.* **1982**, *23*, 281. (e) Yang, Y.-L.; Falck, J. R. *Ibid.* **1982**, *23*, 4305. (f) Lee, T.-J.; Holtz, W. J.; Smith, R. L. *J. Org. Chem.* **1982**, *47*, 4750. (g) Anderson, P. C.; Clive, D. L. J.; Evans, C. F. *Tetrahedron Lett.* **1983**, *24*, 1373. (h) Kuo, C. H.; Patchett, A. A.; Wendler, N. L. *J. Org. Chem.* **1983**, *48*, 1991. (i) Deutsch, E. A.; Snider, B. B. *Tetrahedron Lett.* **1983**, *24*, 3701.

0022-3263/84/1949-3994$01.50/0

Scheme I



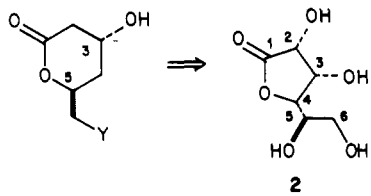
Scheme II



Our general approach to 1 is outlined above. We envisioned the assembly of an appropriately substituted hexalin unit[1] and a lactone synthon which could then be coupled to afford a masked compactin molecule. We recently reported our preliminary work on the synthesis of the lactone moiety of 1.[9] Herein, we report in detail the synthesis of several synthons for the lactone portion of 1 and the requisite technology for subsequent elaboration to the β-hydroxy lactone functionality.

Results and Discussion

Retrosynthetic analysis of the lactone unit of compactin (1) suggests that it may be derived from a suitable carbohydrate precursor. D-Gulono-γ-lactone (2) appeared to



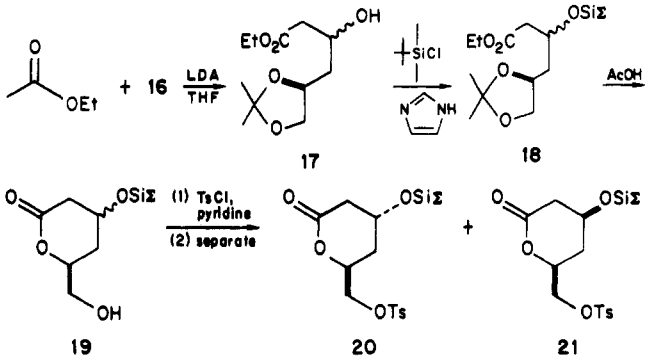
be an attractive educt for this strategy. It possesses the necessary absolute configuration at the 3- and 5-positions and requires deoxygenation at the 2- and 4-positions. Thus, γ-lactone 2 is first converted to the known bis(acetonide) 3 in a yield of 70%.[10] Saponification of lactone 3 with KOH in methanol gives the corresponding hydroxy carboxylate which is converted directly to xanthate ester 4. Heating a toluene solution of 4 and tri-*n*-butyl tin hydride furnishes the 4-deoxy product (5) in an efficient overall yield of 70% from lactone 3.[11] Unfortunately, reductive removal of the oxygen functionality at C-2 could not be accomplished. Numerous unsuccessful attempts were made to achieve this end. Treatment of 5 with lithium–bronze does afford the desired alcohol (6) but in an unsatisfactory yield of only 10% (Scheme I).[12]

In the hope of circumventing this problem, the feasibility of deoxygenating C-2 of compound 3 and then applying the Barton procedure for deoxygenation at the 4-position was investigated. The first aspect of this strategy is accomplished utilizing the procedure of Ireland.[13] Reduction of γ-lactone 3 with diisobutylaluminum hydride furnishes crystalline hemiacetal 7 in a yield of 90%. Compound 7 is converted to unsaturated alcohol 8 by treatment with hexamethylphosphorous triamide and carbon tetrachloride followed by immediate lithium/ammonia reduction of the resulting phosphonium chloride adduct (80% yield).[13] Alcohol 8 is protected as its [2-(trimethylsilyl)ethoxy]methyl (SEM) ether (9).[14] Hydroxylation[15] of 9 (74% yield) and subsequent oxidation of the resulting epimeric mixture of hemiacetals using the Brown protocol (aqueous chromic acid, ether)[16] affords lactone 11 in 53% yield. However, deoxygenation of the 4-position using the Barton procedure is unsuccessful. Treatment of 11 with potassium hydroxide in methanol followed by attempted xanthate formation results in structural decomposition (Scheme II).

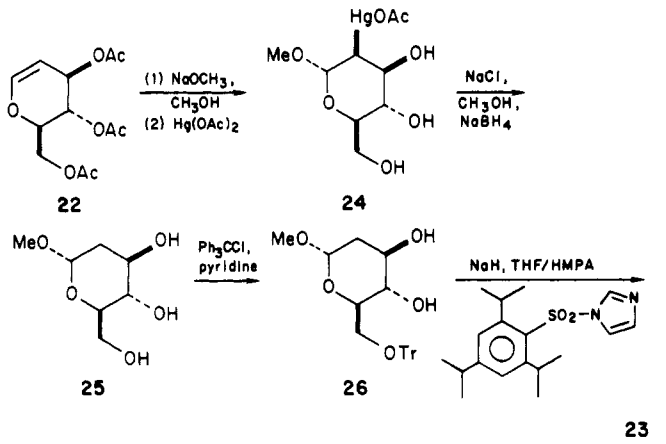
Because of these difficulties, we examined the use of optically active aldehyde 16,[17] derived from L-malic acid (13), as the chiral building block for elaboration of the lactone synthon. The hydroxy diacid (13) is first converted to the known monoprotected triol 14.[18] Acetonide formation proceeds smoothly to give compound 15[17] in 61%

(9) Heathcock, C. H.; Taschner, M. J.; Thomas, J. A. "Abstracts of Papers", 183rd National Meeting of the American Chemical Society, Las Vegas, NV, March, 1982; American Chemical Society: Washington, D.C., 1982; ORGN13.
(10) Hulyalkar, R. K.; Jones, J. K. N. *Can. J. Chem.* **1963**, *41*, 1898.
(11) Barton, D. H. R.; McCombie, S. W. *J. Chem. Soc., Perkin Trans 1* **1975**, 1574.
(12) Mueller, R. H.; Gillick, J. G. *J. Org. Chem.* **1978**, *43*, 4647.
(13) Ireland, R. E.; Thaisrivongs, S.; Vanier, N.; Wilcox, C. S. *J. Org. Chem.* **1980**, *45*, 48.
(14) Lipshutz, B. H.; Pegram, J. J. *Tetrahedron Lett.* **1980**, *21*, 3343.
(15) Corey, E. J.; Goto, G. *Tetrahedron Lett.* **1980**, *21*, 3463.
(16) Brown, H. C.; Garg, C. P.; Liu, K.-T. *J. Org. Chem.* **1971**, *36*, 387.
(17) Corey, E. J.; Shirahama, H.; Yamamoto, H.; Terashima, S.; Venkateswarlu, A.; Schaaf, T. K. *J. Am. Chem. Soc.* **1971**, *93*, 1490.
(18) Feit, P. W.; Nielsen, O. T. *J. Med. Chem.* **1966**, *9*, 416.

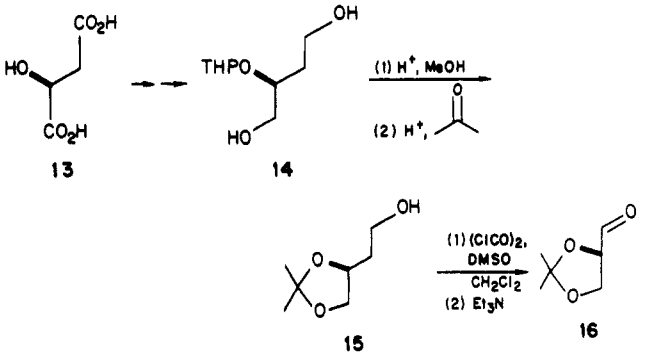
Scheme III



Scheme IV. Corey's Synthesis of Epoxide 23

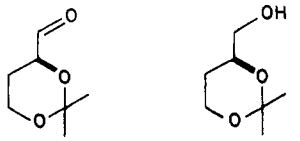


yield for the one-pot sequence.[19] Swern oxidation[20] of alcohol **15** affords aldehyde **16**[17,19] in 74% yield.



Addition of the lithium enolate of ethyl acetate to aldehyde **16** furnishes a 1:1 mixture of aldols **17** in 58% yield. The mixture is then protected as the corresponding *tert*-butyldimethylsilyl ethers[21] **18** in 88% yield. Heating a solution of **18** in 80% acetic acid affords lactones **19** in 60% yield, after recrystallization. Treatment of **19** with *p*-toluenesulfonyl chloride in pyridine gives an easily separable mixture of the desired crystalline tosylate **20** (47% yield) and its epimer **21** (44% yield) (Scheme III).

(19) The material obtained in this manner contains 10% of the corresponding six-membered acetonide isomer and was used as such.

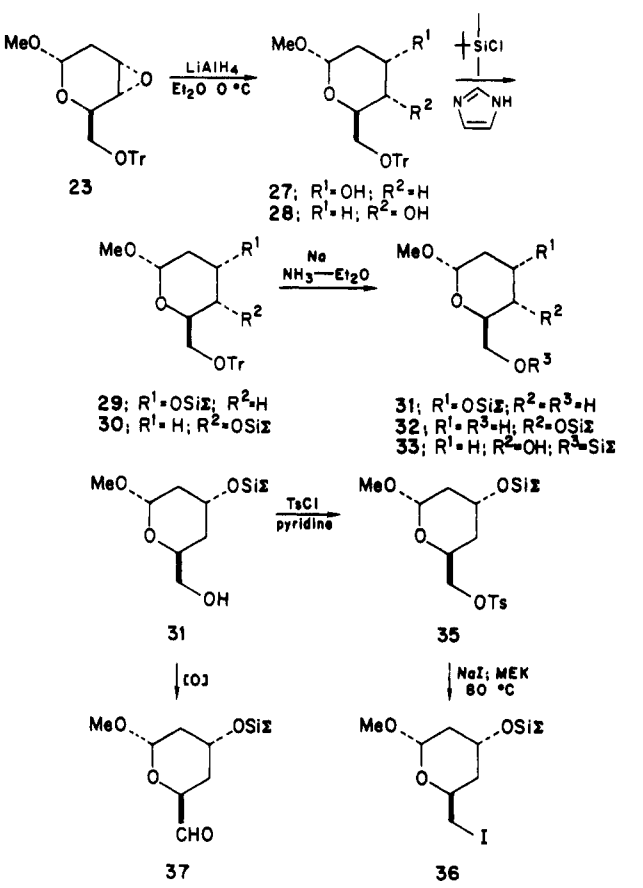


See: Meyers, A. I.; Lawson, J. P. *Tetrahedron Lett.* **1982**, *23*, 4883.

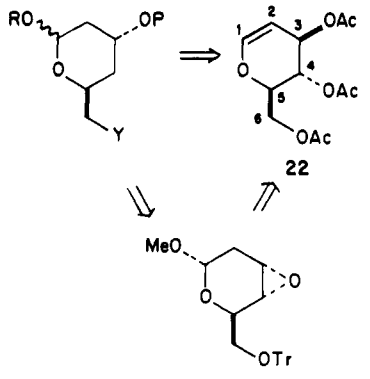
(20) Mancuso, A. J.; Huang, S.-L.; Swern, D. *J. Org. Chem.* **1977**, *43*, 2480.

(21) Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190.

Scheme V



Although compound **20** is a potentially useful synthon for the lactone portion of **1**, the inefficiency of having to perform such an isomer separation led us to pursue a third approach to the system. Once again, we chose a carbohydrate precursor. Tri-*O*-acetyl-D-glucal (**22**) requires



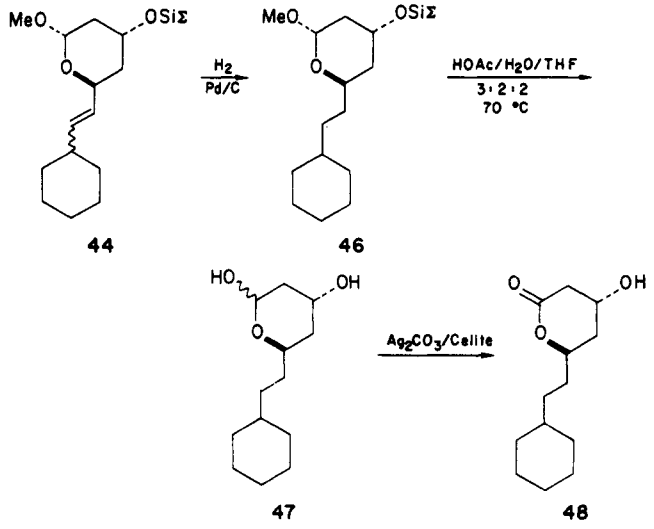
three basic manipulations for this purpose. (1) Oxygen functionality must be introduced at C-1, (2) C-3 must be inverted, and (3) the acetoxy group at C-4 must be removed. The synthesis of epoxide **23** (Scheme IV), an intermediate in Corey's synthesis of (−)-*N*-methylmaysenine,[22] accomplishes requirements 1 and 2. Thus **23** was prepared by the method of Corey.[23] Treatment of **23** with lithium aluminum hydride affords a 92:8 mixture of the desired axial[24] alcohol **27** and regioisomer **28**

(22) Corey, E. J.; Wiegel, L. O.; Chamberlin, A. R.; Lipshutz, B. H. *J. Am. Chem. Soc.* **1980**, *102*, 1439.

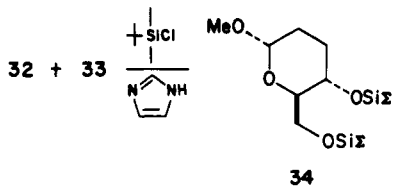
(23) Full details for the preparation of **23**[22] are given in the Experimental Section.

(24) Plattner, A.; Heusser, H.; Kulkarni, A. B. *Helv. Chim. Acta* **1948**, *31*, 1822, 1885.

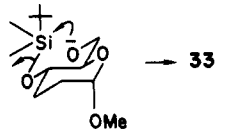
Scheme VI



in 96% yield.[25] The alcohols are protected as the corresponding *tert*-butyldimethylsilyl ethers (**29** and **30**, 93% yield),[21] and the trityl group is removed[26] to obtain alcohol **31** and an inseparable (silica gel column chromatography) mixture of **32** and another isomer, presumably **33**. Sily-

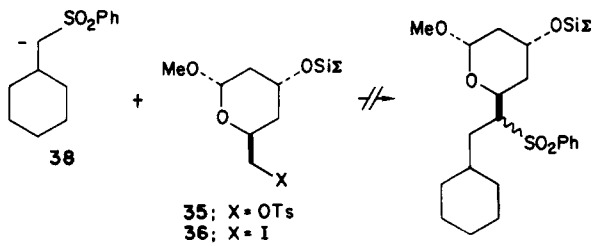


lation of the mixture furnishes a single product, compound **34**. The presence of compound **33** is rationalized readily by an intramolecular silyl migration in the intermediate alkoxide. Alcohol **31** is converted to tosylate **35** in the

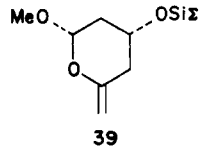


standard manner (90% yield) and this material is transformed into iodide **36** (95% yield). Alcohol **31** is also oxidized by Swern's method[20] to obtain aldehyde **37** in 93% yield (Scheme V).

With lactone synthons **35**–**37** in hand, we examined several model reactions for formation of the ethylene bridge linking the hexalin and lactone portions of **1**. Numerous attempts to displace iodide or tosylate with sulfone anion **38** were unsuccessful. One isolates either recovered

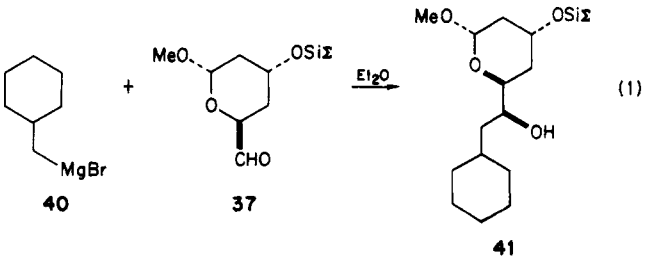


starting material or what appears to be elimination product **39**, on the basis of its ^{1}H NMR spectrum.[27] The lack of



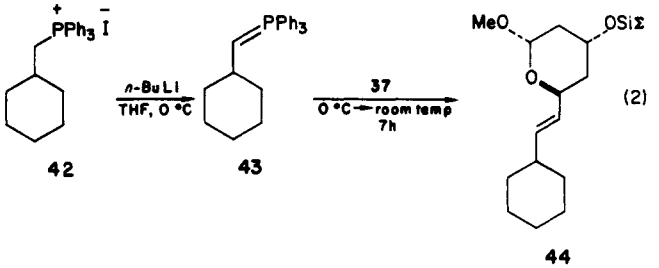
any coupled product is apparently due to the sterically congested transition state required for its formation. In addition, the S_N2 mechanism is well-known to be retarded by proximal electron-withdrawing groups.[28]

We next investigated the stoichiometric reaction of aldehyde **37** and Grignard reagent **40** (eq 1). This reaction

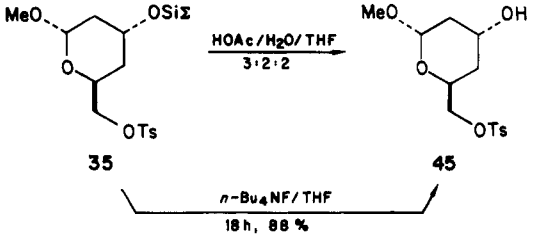


affords adduct **41** but in a rather low yield (27%). The ^{1}H NMR spectrum of the coupled product indicates that it is a single compound. The indicated stereochemical configuration at the carbinol center of **41** is that predicted by Cram's chelation control model for additions to aldehydes.[29] However, there is no direct evidence for the stereochemical assignment at this center.

The Wittig reaction of ylide **43** and aldehyde **37** furnishes olefin **44** in 54% yield (eq 2). Compound **44** is



hydrogenated to obtain compound **46** (quantitative yield) which was utilized to study the specific conditions required to unmask the latent β-hydroxy-δ-lactone moiety. Treatment of tosylate **35** with tetra-*n*-butylammonium fluoride in tetrahydrofuran[30] or with mild aqueous acid affords alcohol **45**. This observation suggests that the silyl



ether in compound **46** is not stable to the conditions required for the hydrolysis of the methyl glycoside linkage (note the acid stability of the silyl ether function in the transformation **18** → **19**). Thus, there are two alternatives for obtaining **48**: (1) conversion of **46** to the corresponding hydroxy hemiacetal and selective oxidation of the hemiacetal or (2) use of a less labile protecting group[31] on the

(25) This result is consistent with those obtained by another group: Wareing, J. R.; Fuller, C. E.; Kathavvala, F. G. "Abstracts of Papers", 185th National Meeting of the American Chemical Society, Seattle, WA., March, 1983; American Chemical Society: Washington, D.C., 1983; ORGN11.

(26) Kovac, P.; Bauer, S. *Tetrahedron Lett.* **1972**, 2349.

(27) Compound **39**: ^{1}H NMR ($CDCl_3$) δ 0.09 (s, 6), 0.90 (s, 9), 3.50 (s, 3), 4.20 (d, 1, J = 2), 4.48 (d, 1, J = 2), 4.50 (dd, 1, J = 3, 8).

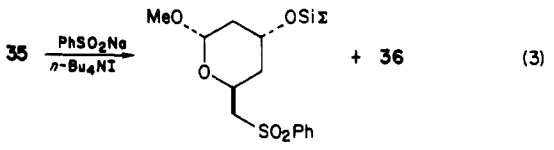
(28) For example, see: Hine, J.; Brader, W. H., Jr. *J. Am. Chem. Soc.* **1953**, *75*, 3964. Bordwell, F. G.; Brannen, W. T., Jr. *Ibid.* **1964**, *86*, 4645.

(29) Cram, D. J.; Kopecky, K. R. *J. Am. Chem. Soc.* **1959**, *81*, 2737.

(30) Corey, E. J.; Snider, B. B. *J. Am. Chem. Soc.* **1972**, *94*, 2549.

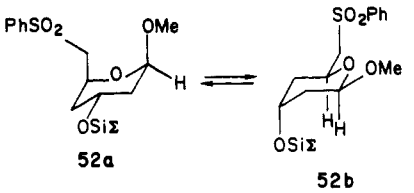
secondary alcohol. The former strategy is successful. Heating **46** in a THF solution of aqueous acetic acid gives hemiacetals **47** in 69% yield. The epimeric mixture is oxidized with silver carbonate on Celite[32] to obtain the desired crystalline lactone **48** in 70% yield (Scheme VI).

We also investigated the possibility of forming the ethylene linkage in a reaction in which the masked lactone appendage is the nucleophile and the hexalin portion is the alkylating agent. Treatment of tosylate **35** with sodium benzenesulfinate and tetra-*n*-butylammonium iodide in refluxing tetrahydrofuran gives sulfone **49** (31% yield) and iodide **36** (55% yield) (eq 3). Generation of the anion of



49

49 followed by the addition of iodide **50**[33] gives, upon workup, recovered **50** and an approximate equimolar mixture of **49** and a diastereomer which is assigned stereostructure **51** on the basis of ^{1}H NMR decoupling experiments. The proton on the anomeric carbon of **51**, H_A, appears as a broad doublet at 4.7 ppm. The coupling constant of 2.8 Hz clearly indicates that the methoxy group is axial. Thus, the new diastereomer cannot arise simply as a result of epimerization at the carbon bearing the (phenylsulfonyl)methyl group, as this process would give a compound in which the three substituents are all equatorial. Furthermore, H_C must be axial, 4.36 ppm (tt, J = 5, 10). It is mechanistically conceivable that the new diastereomer could be compound **52** (conformer **52a**, axial

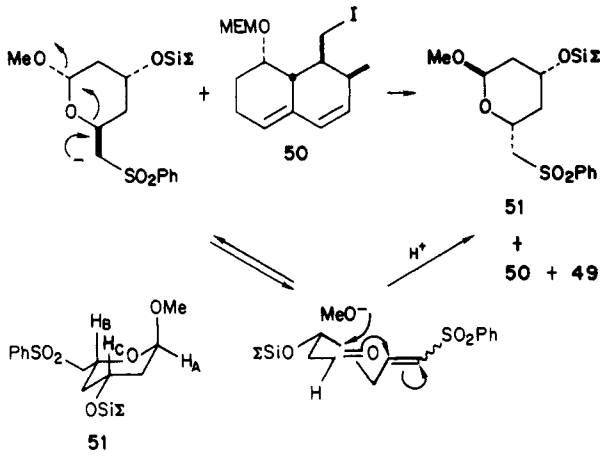


52a **52b**

methoxy group). However, this possibility is eliminated by ^{1}H NMR spectral evidence. The two protons adjacent to the phenylsulfonyl group each appear as double doublets: 3.15 ppm (J = 3.4, 14.6), 3.43 ppm (J = 8.1, 14.6). Irradiation of the signal at 3.43 ppm causes the signal for ring proton H_B (4.36 ppm) to collapse to a doublet of multiplets with the large coupling constant being 8–9 Hz, which is consistent with an axial–axial coupling. Therefore, the proton on C-5 must be axial and the new diastereomer must be compound **51**. A mechanistic interpretation of the genesis of **51** is suggested in Scheme VII. Fragmentation of the anion resulting from deprotonation of **49** (β-elimination) gives the unsaturated sulfone aldehyde. Addition of methoxide to the carbonyl group provides a hemiacetal anion, which undergoes Michael addition to the α,β-unsaturated sulfone moiety. The result is epimerization at two positions, C-1 and C-5. The alternative interpretation, epimerization at C-3, is mechanistically untenable.

In conclusion, lactone synthons **35–37** are prepared quite efficiently from the readily available epoxide **23**. Acidic hydrolysis followed by selective oxidation of the resulting hydroxy hemiacetal with silver carbonate on Celite unmasks the β-hydroxy-δ-lactone moiety. These synthons are useful not only for synthetic studies of the naturally occurring mevinic acids but also for the preparation of analogues designed for biological investigation which incorporate this structural unit.[34]

Scheme VII



Experimental Section

General Methods. Unless otherwise noted, materials were obtained from commercial suppliers and used without further purification. Ether and tetrahydrofuran were distilled from sodium/benzophenone immediately prior to use. Hexamethylphosphoric triamide (HMPA) was distilled from calcium hydride and stored over 4-Å molecular sieves. Dichloromethane was distilled from phosphorus pentoxide. Oxalyl chloride was distilled and stored at −15 °C. Boiling points and melting points are uncorrected. Infrared (IR) spectra were determined with a Perkin-Elmer Model 297 infrared recording spectrophotometer. ^{1}H NMR spectra were determined on the following spectrometers: Varian EM 390, UCB 200, or UCB 250 (super-conducting, FT instruments operating at 200 and 250 MHz, respectively). ^{13}C NMR spectra were measured at 25.14 MHz with a Nicolet TT-23 spectrometer or at 62.89 MHz with the UCB 250. All NMR spectra were determined with deuteriochloroform as the solvent. Chemical shifts are expressed in ppm downfield from internal tetramethylsilane. Significant ^{1}H NMR data are tabulated in order: multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet), number of protons, coupling constant(s) in Hz. Mass spectra were obtained with Atlas MS-12, Consolidated 12-110B, or Kratos MS-50 mass spectrometers. Gravity column chromatography was done with Merck silica gel 60 (70–230 mesh ASTM), and flash chromatography[35] was done with MN silica gel 60 (230–400 mesh ASTM). Thin-layer chromatography (TLC) was performed with Analtech silica gel GF TLC plates (250 microns) and compound visualization was effected with a 5% solution of 12-molybdophosphoric acid in ethanol or a solution of 10% vanillin and 5% sulfuric acid in 95% ethanol. Elemental analyses were performed by the Microanalytical Laboratory, operated by the College of Chemistry, University of California, Berkeley, CA.

2,3:5,6-Di-*O*-isopropylidene-D-gulono-γ-lactone (3).[10] To a 1.2% (by weight) solution of HCl in acetone was added 11.72 g (65.8 mmol) of D-gulono-γ-lactone. The reaction mixture was stirred at room temperature for 18 h and solid K_2CO_3 was added. The mixture was filtered, and the solvent was removed with a rotary evaporator. The crude product was recrystallized from 100% ethanol to furnish 11.9 g (46 mmol, 70%) of **3** as a white crystalline solid, mp 152–154 °C (lit.[10] 153–154 °C).

(31) For an excellent treatise on this subject, see: Greene, T. W. "Protective Groups in Organic Synthesis", Wiley: New York, 1981.
(32) Fetizon, M.; Golfier, M. *Hebd. Seances Acad. Sci.* **1968**, *267*, 900.
(33) Details of the synthesis of this compound will appear shortly.
(34) For the synthesis and biological activity of several β-hydroxy-β-methyl-6-lactone (mevalonolactone) derivatives, see: Sato, A.; Ogiso, A.; Noguchi, N.; Mitsui, S.; Kaneko, I.; Shimada, Y. *Chem. Pharm. Bull.* **1980**, *28*, 1509.
(35) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
(36) Hayashi, H.; Nakanishi, K.; Brandon, C.; Marmur, J. *J. Am. Chem. Soc.* **1973**, *95*, 8749.

2,3:5,6-Di-*O*-isopropylidene-4-*O*-(*S*-methyldithiocarbonyl)-D-gulonic Acid Methyl Ester (4). To a 0.50 M solution of 11.8 g (45.7 mmol) of lactone **3** in CH_3OH was added 3.03 g (46 mmol) of solid KOH. The solution was stirred at room temperature for 18 h. The CH_3OH was removed with a rotary evaporator. Residual CH_3OH was removed under high vacuum. The resulting hydroxy carboxylate was dissolved in 50 mL of DMF and added slowly to a stirring suspension of 1.15 g (68.6 mmol) of oil free NaH in 25 mL of DMF. The reaction mixture was stirred at room temperature until hydrogen evolution ceased (ca. 1 h). To the resulting solution was added 5.50 mL (6.95 g, 91.5 mmol) of CS_2 followed by 8.54 mL (19.5 g, 137 mmol) of CH_3I. The reaction mixture was stirred at room temperature for 8 h. The solution was poured into 100 mL of NH_4Cl/NH_4OH pH 7 buffer solution, and the mixture was extracted with ether (3 × 200 mL). The combined ether extracts were washed with H_2O (2 × 100 mL) and brine and dried ($MgSO_4$), and the solvent was removed with a rotary evaporator. The crude product was purified by chromatography on silica gel (30/1) with 15:85 ether/hexane as the eluant to obtain 14.6 g (38.3 mmol, 84%) of **4** as a light yellow oil: ^1H NMR δ 1.35 (s, 3), 1.40 (s, 3), 1.46 (s, 3), 1.61 (s, 3), 2.57 (s, 3), 3.75 (s, 3), 3.98 (dd, 1, J = 6.8, 8.6), 4.14 (dd, 1, J = 6.1, 8.6), 4.56 (dt, 1, J = 4.6, 6.4), 4.71 (d, 1, J = 7), 4.80 (dd, 1, J = 3.7, 7), 6.03 (t, 1, J = 4.1); ^{13}C NMR δ 18.66, 25.10, 25.26, 25.92, 26.31, 52.13, 65.12, 73.53, 75.16, 75.46, 77.57, 109.56, 110.92, 169.34, 215.32. Anal. Calcd for $C_{15}H_{24}O_7S_2$: C, 47.35; H, 6.36. Found: C, 47.72; H, 6.38.

2,3:5,6-Di-*O*-isopropylidene-4-deoxy-D-gulonic Acid Methyl Ester (5). A solution of 2.20 g (5.8 mmol) of xanthate **4** in 30 mL of toluene was added dropwise to a refluxing solution of 2.29 mL (2.53 g, 8.7 mmol) of n-Bu_3SnH in 50 mL of toluene over a period of 1 h. After the addition was complete, the solution was heated at reflux for 18 h. The solution was concentrated with a rotary evaporator and the crude product was purified by chromatography on silica gel (30/1) with 1:9 ether/hexane as the eluant to obtain 1.35 g (4.92 mmol, 85%) of **5** as a colorless oil: ^1H NMR δ 1.37 (s, 3), 1.40 (s, 3), 1.43 (s, 3), 1.60 (s, 3), 1.84 (m, 2), 3.66 (t, 1, J = 7.7), 3.76 (s, 3), 4.07 (dd, 1, J = 5.9, 8), 4.27 (quintet, 1, J = 6), 4.43 (ddd, 1, J = 5.3, 6.6, 8), 4.63 (d, 1, J = 6.6); ^{13}C NMR δ 25.43, 26.64, 33.44, 51.45, 68.70, 72.74, 74.21, 75.72, 77.07, 108.60, 110.47, 170.25. Anal. Calcd for $C_{13}H_{22}O_6$: C, 56.92; H, 8.08. Found: C, 56.89; H, 8.09.

2,3:5,6-Di-*O*-isopropylidene-α-D-*gulono*-furanose (7). To a 0.50 M solution of 1.29 g (5.0 mmol) of lactone **3** in CH_2Cl_2 at −78 °C was added 7.5 mL (7.5 mmol) of diisobutylaluminum hydride (1 M solution in hexane). The solution was stirred at −78 °C for 3 h and was then poured into a vigorously stirring mixture of 25 g of ice, 8 mL of acetic acid, and 50 mL of CH_2Cl_2. This mixture was stirred vigorously for 30 min, the layers were separated, and the organic phase was washed with saturated aqueous $NaHCO_3$ (2 × 25 mL) and brine. The CH_2Cl_2 solution was dried ($MgSO_4$), and the solvent was removed with a rotary evaporator. The crude product was recrystallized from hexane to afford 1.17 g (4.5 mmol, 90%) of **7** as a white crystalline solid: mp 113 °C; ^1H NMR δ 1.29 (s, 3), 1.40 (s, 3), 1.44 (s, 6), 3.75 (m, 1), 4.18 (m, 2), 4.37 (m, 1), 4.65 (m, 2), 5.45 (br s, 1). Anal. Calcd for $C_{12}H_{20}O_6$: C, 55.37; H, 7.74. Found: C, 55.62; H, 7.72.

1,4-Anhydro-2-deoxy-5,6-*O*-isopropylidene-D-*ribo*-hex-1-enitol (8). To a 0.25 M solution of 13.1 g (50.4 mmol) of hemiacetal **7** and 5.84 mL (9.31 g, 60.5 mmol) of CCl_4 in THF at −78 °C was added 9.61 mL (8.63 g, 52.9 mmol) of hexamethylphosphorous triamide. The solution was stirred at −78 °C for 30 min and allowed to warm to 0 °C. The reaction mixture was stirred at 0 °C for 5 min and then transferred by canula to a stirring solution of 10.6 g (1.51 mol) of lithium in 1.0 L of NH_3 at −78 °C. The mixture was allowed to warm to −33 °C (refluxing NH_3) and stirred at −33 °C for 3 h. To the system was added carefully 93.6 g (1.75 mol) of solid NH_4Cl, followed by 1.0 L of ether, and the NH_3 was allowed to evaporate. The mixture was filtered, and the solvent was removed under reduced pressure. The crude product was purified by chromatography on silica gel (30/1) with 3:7 ethyl acetate/hexane as the eluant to obtain 7.50 g (40.3 mmol, 80%) of **8** as a colorless oil: IR (film) 3450, 1610 cm^{-1}; ^1H NMR δ 1.40 (s, 3), 1.46 (s, 3), 3.88 (dd, 1, J = 6.9, 8.5), 4.24 (m, 2), 4.51 (q, 1, J = 6.7), 4.85 (m, 1), 5.22 (t, 1, J = 2.7), 6.62 (d, 1, J = 2.7); ^{13}C NMR δ 25.07, 26.11, 66.29, 73.13, 74.37, 85.00, 104.02, 109.25, 149.70. Anal. Calcd for $C_9H_{14}O_4$: C, 58.05; H, 7.58. Found: C, 58.22; H, 7.51.

1,4-Anhydro-2-deoxy-5,6-*O*-isopropylidene-3-*O*-[[2-(trimethylsilyl)ethoxy]methyl]-D-*ribo*-hex-1-enitol (9). To a 0.50 M solution of 0.75 g (4.03 mmol) of alcohol **8** and 2.81 mL (2.08 g, 16.1 mmol) of *N,N*-diisopropylethylamine in CH_2Cl_2 was added 1.92 mL (2.01 g, 12.1 mmol) of [2-(trimethylsilyl)ethoxy]methyl chloride (SEM–Cl). The reaction mixture was stirred at room temperature for 12 h, diluted with ether, and filtered through a pad of silica gel. The silica gel was rinsed well with ether, and the filtrate was concentrated with a rotary evaporator. The crude product was purified by chromatography on silica gel (30/1) with 1:9 ethyl acetate/hexane as the eluant to obtain 0.89 g (2.82 mmol, 70%) of **9** as a colorless oil: IR (film) 1610 cm^{-1}; ^1H NMR δ 0.00 (s, 9), 0.88 (m, 2), 1.38 (s, 3), 1.45 (s, 3), 3.52 (m, 2), 3.66 (m, 1), 5.22 (t, 1, J = 2.7), 6.58 (d, 1, J = 2.7). Anal. Calcd for $C_{15}H_{28}O_5Si$: C, 56.93; H, 8.92. Found: C, 57.11; H, 8.87.

2-Deoxy-5,6-*O*-isopropylidene-3-*O*-[[2-(trimethylsilyl)ethoxy]methyl]-α,β-D-*xylo*-furanose (10). To a solution of 0.83 g (0.263 mmol) of enol ether **9** in 20 mL of THF and 5 mL of H_2O at 0 °C was added 0.92 g (2.89 mmol) of $Hg(OAc)_2$. The solution was stirred at 0 °C for 30 min, and 2.18 g (13.2 mmol) of KI in 3 mL of H_2O was added. The resulting solution was stirred at 0 °C for 30 min. The system was cooled to −10 °C and 0.10 g (2.63 mmol) of $NaBH_4$ was added. The reaction mixture was stirred at −10 °C for 5 min and filtered through a pad of Celite, and the Celite was rinsed with ether. The combined fractions were washed with H_2O and brine, dried ($MgSO_4$), and concentrated with a rotary evaporator to afford 0.65 g (1.93 mmol, 74%) of **10**: ^1H NMR δ 0.00 (s, 9), 0.90 (m, 2), 1.35 (s, 3), 1.40 (s, 3), 5.50 and 5.70 (two m, 1).

3-*O*-[[2-(Trimethylsilyl)ethoxy]methyl]-2-deoxy-5,6-*O*-isopropylidene-D-gulono-γ-lactone (11). To a solution of 0.10 g (0.30 mmol) of hemiacetal **10** in 4 mL of ether was added 0.15 mL of chromic acid solution.[16] The reaction mixture was stirred vigorously for 2 h at room temperature. To the two-phase mixture was added 5 mL of H_2O and the layers were separated. The aqueous phase was extracted with ether (2 × 15 mL). The combined organic fractions were washed with saturated aqueous $NaHCO_3$ and brine, dried ($MgSO_4$), and concentrated with a rotary evaporator. The crude product was purified by chromatography on silica gel (30/1) with 4:6 ethyl acetate/hexane as the eluant to obtain 0.05 g (0.16 mmol, 53%) of lactone **11** as a colorless oil: IR (film) 1780 cm^{-1}; ^1H NMR δ 0.03 (s, 9), 0.93 (m, 2), 1.39 (s, 3), 1.43 (s, 3), 2.69 (dd, 1, J = 6.7, 17.5), 2.81 (dd, 1, J = 5.7, 17.2), 3.62 (m, 2), 3.86 (m, 1), 4.13 (m, 1), 4.50 (m, 3), 4.71 (s, 2).

(*S*)-2,2-Dimethyl-1,3-dioxolane-4-ethanol (15).[17] To a 0.50 M solution of 125 g (658 mmol) of **14**[18] in CH_3OH was added 1.30 g of PTSA·H_2O. The solution was stirred at room temperature for 18 h, and the CH_3OH was removed with a rotary evaporator. To the system was added 2.0 L of acetone and 0.65 g of PTSA·H_2O, and the reaction mixture was stirred at room temperature for 24 h. Solid $NaHCO_3$ was added, the mixture was filtered, and the filtrate was concentrated with a rotary evaporator. The crude product was distilled at reduced pressure to obtain 59.5 g (407 mmol, 62%) of **15**: bp 86 °C (20 mm) [lit.[36] 87 °C (22 torr)]; IR (film) 3450 cm^{-1}; ^1H NMR δ 1.37 (s, 3), 1.42 (s, 3), 1.82 (dd, 2, J = 6.3, 12.1), 3.60 (t, 1, J = 8), 3.78 (t, 2, J = 5.7), 4.09 (dd, 1, J = 6, 7), 4.27 (quintet, 1, J = 6.5).

(*S*)-2,2-Dimethyl-1,3-dioxolane-4-ethanal (16).[17] To a solution of 4.80 mL (6.99 g, 55 mmol) of oxalyl chloride in 125 mL of CH_2Cl_2 at −60 °C was added a solution of 7.8 mL (8.58 g, 110 mmol) of Me_2SO in 25 mL of CH_2Cl_2 over a period of 5 min. The solution was stirred at 60 °C for 2 min, and a solution of 7.3 g (50 mmol) of **15** in 50 mL of CH_2Cl_2 was added over a period of 5 min. The reaction mixture was stirred at −60 °C for 15 min. To the system was added 34.8 mL (25.2 g, 250 mmol) of triethylamine. The mixture was stirred at −60 °C for 5 min and allowed to warm to room temperature. To the system was added 250 mL of H_2O and the layers were separated. The aqueous phase was extracted with 250 mL of CH_2Cl_2. The combined CH_2Cl_2 fractions were washed successively with 100 mL of 1% aqueous HCl, 100 mL of saturated aqueous $NaHCO_3$, 100 mL of H_2O, and 100 mL of brine, dried (Na_2SO_4), and concentrated with a rotary evaporator to obtain 5.34 g (37 mmol, 74%) of aldehyde **16**, which was used without further purification in the next reaction:[19] IR

(film) 1725 cm^{-1}; ^1H NMR δ 1.37 (s, 3), 1.42 (s, 3), 2.67 (dd, 1, J = 2, 6, 17), 2.86 (ddd, 1, J = 2, 6, 17), 3.60 (dd, 1, J = 6, 7.5), 4.20 (dd, 1, J = 6, 7.5), 4.55 (quintet, 1, J = 6), 9.80 (s, 1).

Ethyl (3*R*,5*S*)- and (3*S*,5*S*)-5,6-*O*-Isopropylidene-3,5,6-trihydroxyhexanoate (17). To a solution of 6.52 mL (4.67 g, 46.2 mmol) of diisopropylamine in 35 mL of THF at −78 °C was added 30.8 mL (46.2 mmol) of *n*-butyllithium (1.5 M solution in hexane) and the solution was stirred at −78 °C for 15 min. To the system was added 4.51 mL (4.07 g, 46.2 mmol) of ethyl acetate dropwise over a period of 5 min. The reaction mixture was stirred at −78 °C for 15 min, and 5.34 g (37 mmol) of aldehyde **16** in 10 mL of THF was added. The mixture was stirred at −78 °C for 5 min, and the reaction was then quenched with 5.29 mL (5.55 g, 92.5 mmol) of acetic acid. The system was allowed to warm to 0 °C and 25 mL of H_2O was added. The mixture was extracted with ether (2 × 100 mL). The combined extracts were washed with 1% aqueous HCl, saturated aqueous $NaHCO_3$, and brine and dried ($MgSO_4$), and the solvent was removed with a rotary evaporator to obtain 6.20 g (26.7 mmol, 58%) of **17** as a light yellow oil: IR (film) 3500, 1725 cm^{-1}; ^1H NMR δ 1.25 (t, 3, J = 7), 1.35 (s, 3), 1.40 (s, 3), 1.75 (m, 2), 2.51 (d, 2, J = 6), 3.59 (t, 1, J = 7), 4.20 (m, 5). Anal. Calcd for $C_{11}H_{20}O_5$: C, 56.88; H, 8.68. Found: C, 56.65; H, 8.48.

Ethyl (3*R*,5*S*)- and (3*S*,5*S*)-3-*O*-(*tert*-Butyldimethylsilyl)-5,6-*O*-isopropylidene-3,5,6-trihydroxyhexanoate (18). To a 1.0 M solution of 6.20 g (26.7 mmol) of alcohol **17** in DMF was added 3.63 g (53.4 mmol) of imidazole and 4.83 g (32 mmol) of *tert*-butylchlorodimethylsilane. The mixture was stirred at 50 °C for 2 h, cooled to room temperature, and poured into 200 mL of H_2O. The resulting mixture was extracted with hexane (3 × 100 mL). The combined hexane extracts were washed with H_2O and brine and dried (Na_2SO_4), and the solvent was removed with a rotary evaporator to obtain 8.12 g (23.5 mmol, 88%) of **18** as a colorless oil: IR (film) 1740 cm^{-1}; ^1H NMR δ 0.05, 0.07, 0.08, 0.10 (4s, 6), 0.87 and 0.88 (2s, 9), 1.26 (t, 3, J = 7.2), 1.33 and 1.34 (2s, 3), 1.39 (s, 3), 1.74 (m, 2), 2.51 (dd, 2, J = 6.1, 9.2), 3.50 (dd, 1, J = 7.7, 16.4), 4.17 (m, 5); ^{13}C NMR δ −4.77, 14.10, 17.90, 25.70, 26.91, 41.19, 41.72, 42.24, 43.59, 60.08, 67.05, 69.79, 72.50, 72.72, 108.64, 170.92, 171.17. Anal. Calcd for $C_{17}H_{34}O_5Si$: C, 58.92; H, 9.89. Found: C, 58.84; H, 9.73.

(3*R*,5*S*)- and (3*S*,5*S*)-3-*O*-(*tert*-Butyldimethylsilyl)-3,5,6-trihydroxyhexanoic Acid δ-Lactone (19). A solution of 1.61 g (4.85 mmol) of acetonide **18** in 4 mL of 80% acetic acid was heated at 100 °C for 1 h. The reaction mixture was cooled to room temperature, diluted with 10 mL of H_2O, and extracted with CH_2Cl_2 (3 × 25 mL). The combined extracts were washed with saturated aqueous $NaHCO_3$ and brine and dried (Na_2SO_4), and the solvent was removed with a rotary evaporator. The crude product was recrystallized from hexane to obtain 0.95 g (3.64 mmol, 60%) of **19** as a white crystalline solid: mp 74–75 °C; IR ($CHCl_3$) 3600, 3450, 1730 cm^{-1}; ^1H NMR δ 0.09 (s, 6), 0.88 (s, 9), 1.93 (m, 2), 2.50 (m, 1.5), 2.82 (dd, 0.5, J = 5.6, 17.2), 3.77 (m, 2), 4.30 (m, 1.5), 4.79 (m, 0.5); ^{13}C NMR δ −5.01, 17.81, 25.58, 32.02, 34.13, 39.16, 40.03, 63.54, 64.48, 76.77, 78.23, 170.23, 170.05. Anal. Calcd for $C_{12}H_{24}O_4Si$: C, 55.35; H, 9.29. Found: C, 55.27; H, 9.06.

(3*R*,5*S*)- and (3*S*,5*S*)-3-*O*-(*tert*-Butyldimethylsilyl)-6-(*p*-tolylsulfonyl)-3,5,6-trihydroxyhexanoic Acid δ-Lactone (20 and 21). To a solution of 0.24 g (0.92 mmol) of alcohol **19** in 1.0 mL of pyridine at 0 °C was added 0.18 g (0.93 mmol) of *p*-toluenesulfonyl chloride. The reaction mixture was allowed to warm slowly to room temperature. The mixture was stirred at room temperature for 12 h, diluted with ether, and washed with cold 5% aqueous HCl, H_2O, saturated aqueous $NaHCO_3$, and brine. The ether solution was dried ($MgSO_4$), and the solvent was removed with a rotary evaporator. The crude product was purified by chromatography on silica gel (30/1) with 1:1 ether/hexane as the eluant to obtain 0.18 g (0.43 mmol, 47%) of **20** as a white crystalline solid, mp 108–109 °C, and 0.17 g (0.41 mmol, 44%) of **21** as a colorless oil.

Compound **20**: IR (film) 1740, 1600 cm^{-1}; ^1H NMR δ 0.06 (s, 6), 0.86 (s, 9), 1.87 (m, 2), 2.46 (s, 3), 2.55 (d, 2, J = 3.2), 4.18 (t, 2, J = 3.6), 4.29 (m, 1), 4.86 (m, 1), 7.36 (d, 2, J = 8.2), 7.79 (d, 2, J = 8.2). Anal. Calcd for $C_{19}H_{30}O_6SSi$: C, 55.04; H, 7.29. Found: C, 54.95; H, 6.99.

Compound **21**: IR (film) 1740, 1600 cm^{-1}; ^1H NMR δ 0.06 (s, 6), 0.86 (s, 9), 1.75 (m, 2), 2.42 (dd, 1, J = 7.5, 17.4), 2.46 (s, 3), 2.76 (dd, 1, J = 5.4, 17.3), 4.16 (d, 2, J = 4.6), 4.46 (m, 1), 7.36 (d, 2, J = 8.2), 7.80 (d, 2, J = 8.3).

Methyl 2-(Acetoxymercurio)-2-deoxy-α-D-mannopyranoside (24).[22] To a solution of 0.42 g (18 mmol) of sodium in 600 mL of CH_3OH was added 50.0 g (184 mmol) of triacetate **22**. After stirring for 1.5 h, 58.6 g (184 mmol) of $Hg(OAc)_2$ was added and stirring was continued for an additional period of 2.5 h. The mixture was filtered through a pad of Celite and concentrated under reduced pressure to approximately one quarter of the original volume. The solution was allowed to stand at room temperature until crystallization began at which time it was placed in a −15 °C freezer. After 3 h, the crystals were filtered and washed with cold CH_3OH and ether. The above procedure was repeated with the mother liquor. The combined crystals were dried under high vacuum to afford 63.6 g (146 mmol, 79%) of mercurial **24**.

Methyl 2-Deoxy-α-D-*arabino*-hexopyranoside (25).[22] To a suspension of 63.6 g (146 mmol) of mercurial **24** in 150 mL of CH_3OH at room temperature was added 12.8 g (219 mmol) of NaCl. The suspension was stirred until the mercurial dissolved (ca. 30 min). The solution was cooled to 0 °C and 5.82 g (153 mmol) of $NaBH_4$ was added in portions over a period of 30 min. The reaction mixture was stirred at 0 °C for 30 min after the last addition of $NaBH_4$. The mixture was filtered through a Celite pad and the Celite was rinsed with CH_3OH. The filtrate was concentrated with a rotary evaporator, and the residue was suspended in 500 mL of ethyl acetate. This suspension was brought to pH ~4 with 12 N HCl and then neutralized with solid $NaHCO_3$. The mixture was dried over 4-Å molecular sieves, and the liquid portion was decanted from the solids and filtered through Celite. The solids were leached three times with 400-mL portions of boiling ethyl acetate. The leachings were filtered through Celite. The combined ethyl acetate fractions were concentrated with a rotary evaporator. The residue was dried over P_2O_5 under high vacuum at room temperature for 48 h, at 55 °C for 20 h, and at 100 °C for 1 h to obtain 20.0 g (112 mmol, 77%) of triol **25**.

Methyl 2-Deoxy-6-*O*-(triphenylmethyl)-α-D-*arabino*-hexopyranoside (26).[22] To a solution of 20 g (112 mmol) of triol **25** in 40 mL of pyridine at room temperature was added 32.8 g (118 mmol) of triphenylmethyl chloride. The reaction mixture was stirred at room temperature for 16 h, poured into 500 mL of ethyl acetate, and washed with cold 5% aqueous HCl (3 × 75 mL), H_2O, saturated aqueous $NaHCO_3$, and brine. The ethyl acetate solution was dried ($MgSO_4$), and the solvent was removed with a rotary evaporator. The crude product was recrystallized from benzene/hexane to afford 40 g (95.2 mmol, 85%) of diol **26** as a white crystalline solid, mp 143–144 °C (lit.[22] mp 142–144 °C).

Methyl 3,4-Anhydro-2-deoxy-6-*O*-(triphenylmethyl)-α-D-*ribo*-hexopyranoside (23).[22] To a suspension of 0.83 g (34.3 mmol) of oil free NaH in 40 mL of THF was added 2.98 mL (3.07 g, 17.1 mmol) of HMPA. To the cooled (0 °C) solution was added 3.6 g (8.57 mmol) of diol **26**. The system was warmed to room temperature and stirred for 30 min. The system was cooled to −23 °C, and 3.15 g (9.43 mmol) of 2,4,6-triisopropylbenzenesulfonyl imidazole was added. The reaction mixture was stirred at −23 °C for 1 h, slowly warmed to 0 °C over a period of 1 h, and stirred at 0 °C for 1 h. The resulting suspension was diluted with ether and filtered through Celite. The Celite was rinsed with ether and the filtrate was washed with water (4 × 50 mL) and brine. The organic solution was dried ($MgSO_4$), and the solvent was removed with a rotary evaporator. The crude product was recrystallized from ether/hexane. The mother liquor was concentrated and the residue purified by chromatography on silica gel (10/1) with 1:3 ether/hexane as the eluant. This procedure furnished a total of 3.30 g (8.21 mmol, 96%) of epoxide **23** as a white crystalline solid: mp 103–104 °C (lit.[22] 101–102 °C); IR ($CHCl_3$) 1600 cm^{-1}; ^1H NMR δ 2.15 (m, 2), 3.24 (m, 2), 3.33 (s, 3), 3.39 (m, 2), 4.12 (t, 1, J = 5.4), 4.71 (t, 1, J = 3.5), 7.30 (m, 9), 7.47 (m, 6); ^{13}C NMR δ 29.31, 47.85, 51.29, 55.63, 64.52, 67.95, 86.87, 95.88, 127.06, 127.81, 128.69, 143.84; $[\alpha]^{25}_D$ +40.6 ($CHCl_3$, c 4.22) [lit.[22] $[\alpha]^{25}_D$ +40 ($CHCl_3$, c 4.22)]. Anal. Calcd for $C_{26}H_{26}O_4$: C, 77.59; H, 6.51. Found: C, 77.46, H, 6.48.

Methyl 2,4-Dideoxy-6-*O*-(triphenylmethyl)-α-D-*erythro*-hexopyranoside (27). To a solution of 5.34 g (13.3 mmol) of epoxide **23** in 40 mL of ether was added 1.01 g (26.6 mmol) of $LiAlH_4$ in portions over a period of 15 min. The reaction mixture

was stirred at 0 °C for 1.5 h and then treated sequentially with 1.01 mL of H_2O, 1.01 mL of 15% aqueous NaOH, and 3.03 mL of H_2O. The mixture was stirred at room temperature until the precipitate became white and granular. $MgSO_4$ was added, the mixture was filtered, and solids were washed with ether, and the filtrate was concentrated with a rotary evaporator. The crude product was purified by chromatography on silica gel (20/1) with 1:3 ether/hexane as the eluant to obtain 5.16 g (12.8 mmol, 96%) of a 92:8 mixture[37] of alcohols **27** and **28** as a white crystalline solid, mp 102 °C (from hexane).

Compound **27**: IR ($CHCl_3$) 3500, 1600 cm^{-1}; ^1H NMR δ 1.53 (m, 1), 1.84 (m, 3), 3.05 (dd, 1, J = 4, 9.6), 3.25 (dd, 1, J = 6.4, 9.5), 3.44 (s, 3), 3.62 (m, 1), 4.05 (br s, 1), 4.20 (m, 1), 4.89 (s, 1), 7.30 (m, 9), 7.45 (m, 6); ^{13}C NMR δ 35.06, 35.22, 54.88, 63.06, 63.94, 67.10, 86.53, 99.16, 126.93, 127.70, 128.77, 144.20. Anal. Calcd for $C_{26}H_{28}O_4$: C, 77.20; H, 6.98. Found: C, 77.42; H, 7.07.

Methyl 3-*O*-(*tert*-Butyldimethylsilyl)-2,4-dideoxy-6-*O*-(triphenylmethyl)-α-D-*erythro*-hexopyranoside (29). To a solution of 5.16 g (12.8 mmol) of alcohol **28** in 10 mL of DMF was added 1.91 g (28.2 mmol) of imidazole and 2.32 g (15.4 mmol) of *tert*-butyldimethylchlorosilane. The stirring mixture was heated at 50 °C for 8 h, cooled to room temperature, poured into 40 mL of H_2O, and extracted with hexane (3 × 50 mL). The combined hexane extracts were washed with H_2O and brine and dried (Na_2SO_4), and the solvent was removed with a rotary evaporator. The crude product was recrystallized from CH_3OH to afford 6.17 g (11.9 mmol, 93%) of **29**[37] as a white crystalline solid: mp 100 °C; IR (film) 1600 cm^{-1}; ^1H NMR δ 0.02 (s, 3), 0.03 (s, 3), 0.86 (s, 9), 1.55 (m, 1), 1.70 (m, 3), 3.00 (dd, 1, J = 4.4, 9.5), 3.16 (dd, 1, J = 6.4, 9.4), 3.38 (s, 3), 4.05 (t, 1, J = 4), 4.34 (m, 1), 4.74 (m, 1), 7.30 (m, 9), 7.45 (m, 6). Anal. Calcd for $C_{32}H_{42}O_4Si$: C, 74.09; H, 8.16. Found: C, 74.32; H, 8.04.

Methyl 3-*O*-(*tert*-Butyldimethylsilyl)-2,4-dideoxy-6-hydroxy-α-D-*erythro*-hexopyranoside (31). Under a nitrogen atmosphere, into a flame-dried 200-mL three-necked round-bottom flask equipped with a gas inlet adapter, a dry ice condenser, a glass stopper, and a magnetic stirring bar immersed in a dry ice/acetone cooling bath was condensed 44 mL of ammonia. To the system was added 44 mL of ether followed by 807 mg (35.1 mmol) of sodium. To the stirring deep blue mixture was added 6.29 g of **29** in 17 mL of ether. The cold bath was removed, and the deep red mixture was stirred for 20 min. To the system was cautiously added 2.52 g of ammonium chloride, the ammonia was allowed to evaporate, $MgSO_4$ was added, and the mixture was suction filtered. The colorless filtrate was concentrated with a rotary evaporator, and the resulting solid/oil mixture was purified by flash chromatography[35] to obtain 2.30 g (69% yield) of pure **31** and 360 mg (11%) of a mixture of **31** and isomers **32** and **33** (~1.7:1 **31**/**32** and **33**). Compound **31**: IR (film) 3450 cm^{-1}; ^1H NMR δ 0.02 (s, 3), 0.05 (s, 3), 0.89 (s, 9), 1.48 (dt, 1, J = 3, 13.2), 1.64 (m, 1), 1.78 (m, 2), 3.33 (s, 3), 3.53 (m, 1), 3.66 (m, 1), 4.11 (quintet, 1, J = 3.6), 4.23 (ddd, 1, J = 3, 6.6, 13.6), 4.76 (t, 1, J = 3.6); ^{13}C NMR δ 6.96, 37.55, 46.64, 48.45, 66.52, 75.47, 76.64, 77.64, 110.27. Anal. Calcd for $C_{13}H_{28}O_4Si$: C, 56.48; H, 10.21. Found: C, 56.65; H, 10.12. Isomers **32** and **33** were obtained as a mixture uncontaminated by **31** after a second chromatographic purification and possessed the following properties: IR (film) 3425 (broad), 2940, 2860, 1455, 1250 cm^{-1}; ^1H NMR δ 0.04, 0.06 (s, 6), 0.85, 0.87 (s, 9), 1.80 (m, 5), 3.36 (s, 3), 3.51–3.90 (complex, 4), 4.64, 4.67 (d, 1, J = 2.5, 2.8). Anal. Calcd for $C_{13}H_{28}O_4Si$: C, 56.48; H, 10.21. Found: C, 56.61; H, 10.14.

Methyl 3-*O*-(*tert*-Butyldimethylsilyl)-2,4-dideoxy-6-*O*-(*p*-tolylsulfonyl)-α-D-*erythro*-hexopyranoside (35). To a solution of 1.63 g (5.90 mmol) of alcohol **31** in 11 mL of pyridine at 0 °C was added 1.35 g (7.09 mmol) of *p*-toluenesulfonyl chloride. The reaction mixture was allowed to warm slowly to room temperature and was stirred for 24 h. The mixture was poured into 100 mL of ether and washed with cold 10% aqueous HCl. The aqueous layer was extracted with ether (2 × 25 mL), and the combined organic extracts were washed with 2% aqueous HCl, H_2O, saturated aqueous $NaHCO_3$, and brine. The ether solution was dried (Na_2SO_4) and filtered, and the solvent was removed with a rotary evaporator. The crude product was purified by chromatography on silica gel (20/1) with 1:9 ethyl acetate/hexane as the eluant to obtain 2.28 g (5.30 mmol, 90%) of tosylate **35** as a colorless oil: IR (film) 1600 cm^{-1}; ^1H NMR δ 0.03 (s, 6), 0.87 (s, 9), 1.52 (m, 2), 1.75 (m, 2), 2.45 (s, 3), 3.24 (s, 3), 4.04 (d, 2, J = 4.7), 4.08 (m, 1), 4.32 (m, 1), 4.67 (m, 1), 7.34 (d, 2, J = 8.1), 7.81 (d, 2, J = 8.3); ^{13}C NMR δ −4.85, 21.46, 25.64, 34.76, 36.22, 54.75, 62.07, 63.24, 72.49, 98.28, 127.88, 129.69, 144.54; $[\alpha]^{25}_D$ 54.4 ($CHCl_3$, c 1.67). Anal. Calcd for $C_{20}H_{34}O_6SSi$: C, 55.78; H, 7.96. Found: C, 55.63; H, 7.93.

Methyl 3-*O*-(*tert*-Butyldimethylsilyl)-2,4-dideoxy-6-iodo-α-D-*erythro*-hexopyranoside (36). To a solution of 0.60 g (1.40 mmol) of tosylate **35** in methyl ethyl ketone was added 2.10 g (14 mmol) of NaI. The stirring mixture was heated at 80 °C for 4.5 h. The resulting suspension was cooled to room temperature, diluted with 50 mL of ether, and washed with H_2O, 10% aqueous $NaHSO_3$, and brine. The ether solution was dried ($MgSO_4$), and the solvent was removed with a rotary evaporator. The crude product was purified by chromatography on silica gel (10/1) with 1:19 ether/hexane as the eluant to obtain 0.51 g (1.33 mmol, 95%) of iodide **36** as a colorless oil: IR (film) 2950, 1260 cm^{-1}; ^1H NMR δ 0.03 (s, 3), 0.05 (s, 3), 0.89 (s, 9), 1.56 (m, 1), 1.75 (m, 3), 3.18 (dd, 1, J = 7.2, 10.3), 3.26 (dd, 1, J = 4.4, 10.3), 3.88 (s, 3), 4.10 (m, 1), 4.76 (m, 1); ^{13}C NMR δ −4.82, 10.14, 17.97, 25.70, 36.34, 39.20, 55.07, 63.82, 98.75. Anal. Calcd for $C_{13}H_{27}IO_3Si$: C, 40.42; H, 7.04; I, 32.85. Found: C, 40.27; H, 7.04; I, 33.03.

Methyl 3-*O*-(*tert*-Butyldimethylsilyl)-2,4-dideoxy-6-oxo-α-D-*erythro*-hexopyranoside (37). To a solution of 0.105 mL (0.15 g, 1.20 mmol) of oxalyl chloride in 3.0 mL of CH_2Cl_2 at −60 °C was added a solution of 0.17 mL (0.186 g, 2.39 mmol) of Me_2SO in 0.5 mL of CH_2Cl_2 dropwise over a period of ca. 1 min. The solution was stirred for 2 min at −60 °C, and a solution of 0.30 g (1.09 mmol) of alcohol **31** in 2.0 mL of CH_2Cl_2 was added. The mixture was stirred at −60 °C for 15 min, and 0.76 mL (0.55 g, 5.45 mmol) of triethylamine was added. After stirring for 15 min at −60 °C, the mixture was warmed to room temperature, diluted with CH_2Cl_2, and washed with H_2O, 1% aqueous HCl, H_2O, saturated aqueous $NaHCO_3$, and brine. The CH_2Cl_2 solution was dried (Na_2SO_4) and the solvent was removed with a rotary evaporator. The crude product was purified by chromatography on silica gel (20/1) with 1:9 ether/hexane as eluant to obtain 0.28 g (1.01 mmol, 93%) of aldehyde **37** as a colorless oil: IR (film) 1740 cm^{-1}; ^1H NMR δ 0.05 (s, 3), 0.06 (s, 3), 0.89 (s, 9), 1.80 (m, 4), 4.77 (t, 1, J = 3.6), 9.72 (s, 1); $[\alpha]^{25}_D$ +94.35 ($CHCl_3$, c 1.47). Anal. Calcd for $C_{13}H_{26}O_4Si$: C, 56.90; H, 9.55. Found: C, 56.94; H, 9.47.

Methyl 2,3-Dideoxy-4,6-bis-*O*-(*tert*-butyldimethylsilyl)-α-D-*erythro*-hexopyranoside (34). Under a nitrogen atmosphere, into a 10-mL round-bottomed flask equipped with a reflux condenser and a magnetic stirring bar was placed 9.4 mg (0.034 mmol) of a mixture of **32** and **33** in 0.1 mL of DMF. To the stirring solution was added 6.3 mg (0.093 mmol) of imidazole and 7.7 mg (0.051 mmol) of *tert*-butylchlorodimethylsilane, and the mixture was heated at 60 °C for 4.5 h. The system was cooled to room temperature, 5 mL of water was added, and the mixture was extracted with hexanes. The hexane extracts were washed with brine and dried over $MgSO_4$, and the solvent was removed with a rotary evaporator. The resulting crude material (13.5 mg) was purified by column chromatography (1 g of silica gel) with 1:3 ether/hexanes as the eluant to obtain 5.4 mg (41% yield) of **34** as a pale yellow oil: IR (film) 2930, 2860, 1260 cm^{-1}; ^1H NMR δ 0.02 (s, 6), 0.03 (s, 6), 0.84 (s, 9), 0.86 (s, 9), 1.75 (m, 4), 3.36 (s, 3), 3.49 (m, 2), 3.65 (dd, 1, J = 6.4, 11), 3.89 (d, 1, J = 11), 4.66 (d, 1, J = 2.4); HRMS calcd for $C_{15}H_{33}O_4Si_2$ (parent − C_4H_9) 333.1917, found 333.1915.

(6*S*)-Methyl 3-*O*-(*tert*-Butyldimethylsilyl)-2,4-dideoxy-6-(cyclohexylmethyl)-6-hydroxy-α-D-*erythro*-hexopyranoside (41). Under an argon atmosphere, into a flame-dried 10-mL round-bottomed flask equipped with a rubber septum and a magnetic stirring bar was placed 13.1 mg (0.54 mmol) of magnesium.[38] The system was flamed gently, and after cooling to room temperature the flask was charged with 0.16 mL of ether. To the stirring suspension was added 67.7 mg (0.42 mmol) of cyclo-

(37) The ratio **27**:**28** is determined from integration of the ^1H NMR signals for the carbinol protons of the two alcohols. Compound **27**: 4.89 ppm. Compound **28**: 4.62 ppm. The mixture of alcohols (**27** and **28**) is silylated to give the corresponding mixture of **29** and **30**. After removal of the trityl protecting group, chromatography affords pure alcohol **31**.

(38) Magnesium was filed from a triply sublimed chunk.

hexylmethyl bromide in 0.13 mL of ether. After 1 min, an exotherm occurred. When the reaction mixture ceased boiling, the syringe which delivered the bromide was rinsed with two 0.2-mL portions of ether (added to reaction mixture), and the system was flamed gently. The system was cooled to −20 °C, charged with 105 mg (0.38 mmol) of aldehyde **37** in 0.13 mL of ether, and allowed to warm to room temperature over a period of 1 h. The reaction was quenched with 1 mL of aqueous NH_4Cl/NH_4OH pH 7 buffer solution, ether was added, and the layers were separated. The organic phase was washed with brine, and the combined aqueous fractions were extracted with ether. The combined organic fractions were dried over $MgSO_4$, and the solvent was removed with a rotary evaporator. The resulting yellow oil (120 mg) was purified by column chromatography (4 g of silica gel) with 1:6 ether/hexanes as the eluant, to obtain 21.2 mg (15% yield) of **41** as a colorless viscous oil. An additional 41.9 mg of a 2.1:1 mixture of aldehyde **37** and **41** (12% yield) was also obtained.

Compound **41**: IR (film) 3475, 2940, 2850, 1250 cm^{-1}; ^1H NMR δ 0.03 (s, 3), 0.04 (s, 3), 0.89 (s, 9), 1.10–1.87 (complex, 17), 2.28 (d, 1, J = 4.7), 3.32 (s, 3), 3.55 (m, 1), 3.91 (ddd, 1, J = 2.9, 5.7, 10.8), 4.08 (m, 1), 4.75 (dd, 1, J = 2.5, 4.4). Anal. Calcd for $C_{20}H_{40}O_4Si$: C, 64.46; H, 10.82. Found: C, 64.12; H, 10.77.

(Cyclohexylmethyl)triphenylphosphonium Iodide (42). A 1.0 M benzene solution of 2.24 g (10 mmol) of cyclohexylmethyl iodide and 2.62 g (10 mmol) of triphenylphosphine was heated at reflux for 48 h. The resulting salt was filtered, washed with ether, and dried under high vacuum to obtain 2.28 g (4.70 mmol, 47%) of **42** as a white crystalline solid, mp 275 °C. Anal. Calcd for $C_{25}H_{28}IP$: C, 61.74; H, 5.80. Found: C, 61.83; H, 5.72.

Coupling of Phosphonium Salt 42 and Aldehyde 37. To a suspension of 0.13 g (0.26 mmol) of phosphonium salt **42** in 1.0 mL of THF at 0 °C was added 0.175 mL (0.26 mmol) of *n*-butyllithium (1.5 M solution in hexane). The reaction mixture was stirred at 0 °C for 20 min, at which time no solids remained. To the red-orange solution was added a solution of 72 mg (0.26 mmol) of aldehyde **37** in 1.0 mL of THF. After stirring at 0 °C for 1 h, the mixture was warmed to room temperature and allowed to stir for 6 h. The mixture was diluted with 10 mL of hexane and filtered, and the filtrate was concentrated with a rotary evaporator. The crude product was purified by chromatography on silica gel (10/1) with 1:19 ether/hexane as the eluant to obtain 50 mg (0.14 mmol, 54%) of olefin **44**: IR (film) 2950, 1260 cm^{-1}; ^1H NMR δ 0.03 and 0.06 (2s, 6), 0.89 and 0.92 (2s, 9), 3.34 and 3.35 (2s, 3), 4.08 (m, 1), 4.72 (m, 1), 4.98 (m, 1), 5.33 (m, 2). Anal. Calcd for $C_{20}H_{38}O_3$: C, 67.74; H, 10.80. Found: C, 67.65; H, 10.81.

Methyl 3-*O*-(*tert*-Butyldimethylsilyl)-2,4,6-trideoxy-6-(cyclohexylmethyl)-α-D-*erythro*-hexopyranoside (46). Into a 25-mL round-bottomed flask equipped with a rubber septum and magnetic stirring bar was placed 53.9 mg (0.15 mmol) of alkene **44** in 1.6 mL of ethyl acetate. To this solution was added 16 mg of 10% palladium on carbon, the reaction flask was connected to an atmospheric hydrogenation apparatus, and the mixture was stirred for 160 min at room temperature. The reaction mixture was diluted with ether, the catalyst was removed by suction filtration through a Celite pad, and the solvent was removed with a rotary evaporator to obtain 54.2 mg (quantitative yield) of pure **46** as a colorless oil. This material was used in subsequent transformations without further purification: IR (film) 2920, 2850, 1445, 1360, 1250, 1195 cm^{-1}; ^1H NMR δ 0.03 (s, 3), 0.04 (s, 3), 0.88 (s, 9), 1.09–1.87 (m, 19), 3.31 (s, 3), 4.04 (m, 2), 4.71 (t, 1); ^{13}C NMR δ −4.9, −4.7, 18.0, 25.7, 26.4, 26.7, 32.8, 33.26, 33.34, 33.4, 37.1, 37.7, 39.1, 54.8, 64.0, 64.6, 98.1. Anal. Calcd for $C_{20}H_{40}O_3Si$: C, 67.38; H, 11.31. Found: C, 67.47; H, 11.17.

Methyl 2,4-Dideoxy-6-*O*-(*p*-tolylsulfonyl)-α-D-*erythro*-hexopyranoside (45). Under a nitrogen atmosphere, into a 25-mL round-bottomed flask equipped with a rubber septum and magnetic stirring bar was placed 72.4 mg (0.17 mmol) of silyl ether **35**. To the stirring solution was added 0.17 mL (0.17 mmol) of 1 M tetra-*n*-butylammonium fluoride in THF. The mixture was stirred at room temperature for 18 h, diluted with ether, and washed with aqueous sodium bicarbonate and brine. The combined aqueous washings were extracted with ether, the combined organic fractions were dried over $MgSO_4$, and the solvent was removed with a rotary evaporator. The crude material was purified by column chromatography (3 g of silica gel) with 5:3 ether/hexanes as the eluant to obtain 46.6 mg (88% yield) of **45** as a pale yellow oil which was judged to be pure from its ^1H NMR spectrum: IR (film) 3550, 2925, 1600, 1355, 1170 cm^{-1}; ^1H NMR δ 1.22–1.97 (complex, 5), 2.45 (s, 3), 3.34 (s, 3), 3.52 (d, 1, J = 9.5), 4.05 (m, 2), 4.22 (m, 1), 4.81 (d, 1, J = 3.0), 7.34 (d, 2, J = 8.2), 7.80 (d, 2, J = 8.2); HRMS calcd for $C_{14}H_{20}O_6S$ 316.0981, found 316.0986.

Acid-Catalyzed Hydrolysis of Methyl 3-*O*-(*tert*-Butyldimethylsilyl)-2,4,6-trideoxy-6-(cyclohexylmethyl)-α-D-*erythro*-hexopyranoside (46). Under a nitrogen atmosphere, into a 10-mL round-bottomed flask equipped with a reflux condenser and magnetic stirring bar was placed 25.2 mg (0.071 mmol) of acetal **46** in 1 mL of a 3:2:2 mixture of acetic acid, tetrahydrofuran, and water. The stirring solution was heated at 70 °C for 160 min, diluted with 15 mL of ether, and washed with water, two portions of saturated aqueous sodium bicarbonate, and brine (all portions were 5 mL). The combined aqueous washings were extracted with ether, the combined organic fractions were dried over $MgSO_4$, and the solvent was removed with a rotary evaporator. The crude yellow oil was purified by column chromatography (1 g of silica gel) with 3:1 ether/hexanes as the eluant to obtain 11.1 mg (69% yield) of **47** as a colorless oil: IR ($CHCl_3$) 3540, 2940, 2850 cm^{-1}; ^1H NMR δ 0.80–2.20 (complex, 19), 2.81–5.44 (complex, 5); HRMS calcd for $C_{13}H_{24}O_3$ 228.1726, found 228.1730.

(4*R*,6*R*)-6-(2-Cyclohexylethyl)-4-hydroxytetrahydropyran-2-one (48). Under a nitrogen atmosphere, into a 100-mL round-bottomed flask equipped with a reflux condenser and magnetic stirring bar was placed 19.5 mg (0.086 mmol) of hydroxy hemiacetal **47** in 0.75 mL of benzene. To the stirring solution was added 374 mg (approximately 0.62 mmol) of silver carbonate on Celite, and the suspension was heated at 65–80 °C for 3 h. An additional 60 mg (0.1 mmol) of silver carbonate on Celite and 0.2 mL of benzene was added to the system, and the mixture was heated at 80 °C for 2.5 h. The reaction mixture was diluted with ether and suction filtered through a Celite pad. The solids were rinsed well with ether, and the filtrate was concentrated to afford 15.7 mg of an off-white solid. The crude material was purified by column chromatography (0.5 g of silica gel) with 4:1 ether/hexanes as the eluant to obtain 13.5 mg (70% yield) of hydroxy lactone **48** as a waxy white solid. This material could be recrystallized from hexanes: mp 72–73 °C (lit.[8e] mp 65–67 °C); IR ($CHCl_3$) 3620, 3440, 2940, 2850, 1720 cm^{-1}; ^1H NMR δ 0.80–2.20 (complex, 20), 2.61 (m, 1), 2.75 (dd, 1, J = 5.0, 18), 4.40 (m, 1), 4.65 (m, 1); HRMS calcd for $C_{13}H_{23}O_3$ (parent + H) 227.1648, found 227.1647.

Methyl 3-*O*-(*tert*-Butyldimethylsilyl)-2,4,6-trideoxy-6-(phenylsulfonyl)-α-D-*erythro*-hexopyranoside (49). Into a 10-mL round-bottomed flask fitted with a reflux condenser and magnetic stirring bar and under a nitrogen atmosphere was placed 277 mg (0.644 mmol) of *p*-toluenesulfonate ester **35** in 3.5 mL of THF. To the stirring solution was added 845 mg (5.15 mmol) of sodium benzenesulfinate and 1.42 g (3.86 mmol) of tetrabutylammonium iodide. The mixture was heated at reflux for ca. 8 h, diluted with ether, and washed with water and brine. The aqueous washings were extracted with ether, the combined organic fractions were dried over $MgSO_4$, and the solvent was removed with a rotary evaporator. The crude product mixture was purified by column chromatography (2 g of silica gel) with 1:9 ethyl acetate/hexanes as the initial eluant and gradually increasing the solvent polarity to obtain 138 mg (55%) of iodide **36** and 80.5 mg (31%) of sulfone **49**, both as light yellow oils. Compound **49**: IR (film) 3070, 2930, 2860, 1445, 1360, 1310, 1255, 1195 cm^{-1}; ^1H NMR δ −0.01 (s, 3), 0.01 (s, 3), 0.86 (s, 9), 1.64 (m, 4), 3.14 (dd, 1, J = 4.6, 14.6), 3.24 (s, 3), 3.38 (dd, 1, J = 7.3, 14.6), 4.04 (t, 1, J = 3.5), 4.61 (m, 2), 7.60 (m, 3), 7.94 (d, 2, J = 7.0). The ^1H NMR spectrum of **36** was identical with that of the material prepared earlier.

Reaction of the Anion of Sulfone 49 with Iodide 50. Under a nitrogen atmosphere into an oven-dried, 10-mL, round-bottomed flask equipped with a rubber septum and a magnetic stirring bar was placed 74.5 mg (0.186 mmol) of sulfone **49** in 0.2 mL of THF. To the stirring solution, at −78 °C, was added 0.12 mL (0.19 mmol) of 1.5 M *n*-BuLi in hexanes. The system was stirred at −78 °C for a period of 10–15 min. To the resulting clear yellow solution was added 67.4 mg (0.172 mmol) of iodide **50** in 0.2 mL of THF. The mixture was stirred at −78 °C for a period of 1.5 h. The cold bath was removed, and the mixture was allowed to stir at room

temperature for a period of 1 day. The brown product mixture was partitioned between water and ether. The layers were separated, and the organic phase was washed with two 15-mL portions of water (small emulsion broken up with solid sodium chloride). The aqueous washings were extracted with two 10-mL portions of ether. The combined organic fractions were dried over $MgSO_4$. The solvent was removed with a rotary evaporator, and the resulting yellow oil was subjected to silica gel column chromatography to obtain ca. 55 mg (82%) of recovered iodide **50**, 12 mg (16%) of recovered sulfone **49**, 11.4 mg (15%) of sulfone **51**, and 8.9 mg of unidentified materials. Compound **51**: IR (film) 3060, 2925, 2850, 1440, 1375, 1305, 1250, 1140, 1110 cm^{-1}; ^1H NMR δ 0.04 (s, 6), 0.85 (s, 9), 1.34 (m, 2), 1.89 (m, 2), 3.15 (dd, 1, J = 3.4, 14.6), 3.32 (s, 3), 3.43 (dd, 1, J = 8.1, 14.6), 4.06 (m, 1), 4.36 (tt, 1, J = 5, 10), 4.70 (d, 1, J = 2.9), 7.57 (m, 3), 7.94 (d, 2, J = 7.0). Anal. Calcd for $C_{19}H_{32}O_5SSi$: C, 56.96; H, 8.05. Found: C, 57.04; H, 7.99.

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Registry No. **1**, 73573-88-3; **2**, 6322-07-2; **3**, 67642-42-6; **3** hydroxycarboxylate deriv., 91312-46-8; **4**, 91312-47-9; **5**, 91312-48-0; **7**, 78039-08-4; **8**, 68198-85-6; **9**, 91312-49-1; **10** α-D-gulo deriv., 91312-50-4; **10** β-D-gulo deriv., 91312-51-5; **11**, 91312-52-6; **14**, 5055-09-4; **15**, 32233-43-5; **16**, 32233-44-6; (3*R*)-**17**, 91312-53-7; (3*S*)-**17**, 91312-54-8; (3*R*)-**18**, 91312-55-9; (3*S*)-**18**, 91312-56-0; (3*R*)-**19**, 91312-57-1; (3*S*)-**19**, 91312-58-2; **20**, 91312-59-3; **21**, 91327-64-9; **22**, 2873-29-2; **23**, 73541-95-4; **24**, 73573-78-1; **25**, 13145-22-7; **26**, 73541-94-3; **27**, 86030-92-4; **28**, 91312-60-6; **29**, 91312-61-7; **31**, 91312-62-8; **32**, 91312-63-9; **33**, 91312-64-0; **34**, 91312-65-1; **35**, 91312-66-2; **36**, 91312-67-3; **37**, 91312-68-4; **41**, 91312-69-5; **42**, 91312-70-8; (*E*)-**44**, 91327-65-0; (*Z*)-**44**, 91383-94-7; **45**, 91312-71-9; **46**, 91312-72-0; **47** (isomer 1), 91312-73-1; **47** (isomer 2), 91383-67-4; **48**, 86031-05-2; **49**, 91312-74-2; **50**, 91312-75-3; **51**, 91312-76-4; CS_2, 75-15-0; SEM-Cl, 76513-69-4; ethyl acetate, 141-78-6; cyclohexylmethyl bromide, 2550-36-9; cyclohexylmethyl iodide, 5469-33-0.

1-Oxa-4-decalone Derivatives. Synthesis and Structure

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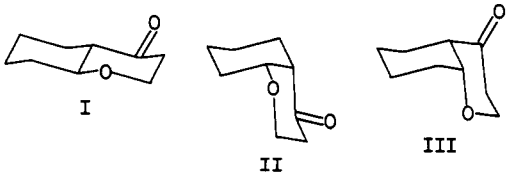
The synthesis of some 1-oxa-4-decalone derivatives is described. Both epimers at C-4a were isolated and their configurations and conformations were inferred by ^1H and ^{13}C NMR studies.

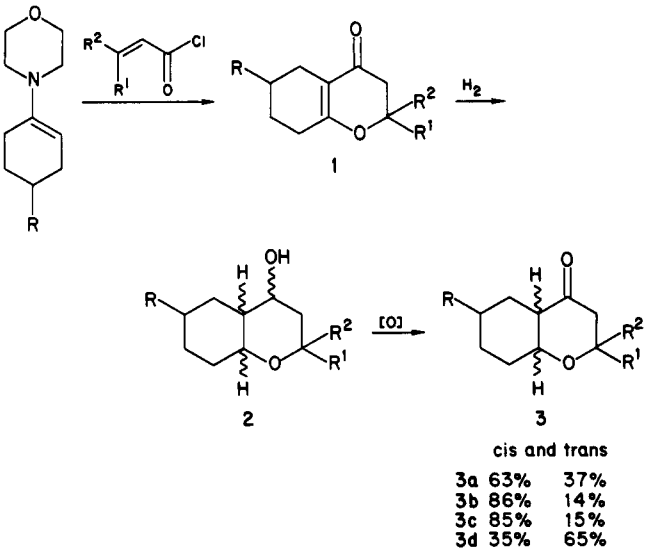
Our purpose was to synthesize a series of 1-oxa-4-decalone derivatives (octahydrobenzo-4-pyranones) **3** in an effort to investigate by ^1H and ^{13}C NMR spectroscopy both their configurations and their preferred conformations. These compounds are nearly unknown. *cis*- and *trans*-1-oxa-4-decalones, and some 6- and 7-methoxycarbonyl derivatives, have been prepared and identified by ^1H NMR.[1]

It is generally accepted that tetrahydro-4-pyranones exist in a chair form.[2,3] However, tetrahydropyran has a chair conformation that is slightly flattened from the shape of cyclohexane. The somewhat larger C–O–C bond angle and shorter C–O bond length cause this distorsion.[4] Chair-like conformations of 1-oxa-4-decalone derivatives could be anticipated by analogy with *cis*- and *trans*-decalones.[5] Thus the trans compounds are uncomplicated since they can all be expected to be based on conformation I. In the cis series, the two possible conformations II and



III have to be considered. However, II is clearly less favorable than III because of the greater 1,3-diaxial interactions in the former.[6]

Scheme I[a]



	cis	trans
3a	63%	37%
3b	86%	14%
3c	85%	15%
3d	35%	65%

[a] a, R = H; R¹ = R² = H; b, R = H; R¹ = Me; R² = H; c, R = H; R¹ = R² = Me; d, R = *t*-Bu, R¹ = R² = Me.

1-Oxa-4-decalones Synthesis. Path A. Earlier, we reported on the synthesis of 2,3,5,6,7,8-hexahydrobenzo-

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