(s), 755 (s), 720 (s), 690 (s); NMR (CH_2Cl_2, 4.72 τ ref) τ 2.8 (aromatic multiplet, 5 protons), 6.27, 6.44 (CH_3O doublet, J_{POCH} = 10 Hz, 6 protons); mass spectrum (70 eV), *m/e* (rel intensity) 248 (2), 187 (1.5), 186 (17.3), 185 (2.5), 156 (1.2), 155 (23.5), 140 (1.5), 108 (3.2), 107 (2.0), 94 (9.5), 93 (100), 91 (6.5), 90 (2.2), 79 (2.1), 78 (5.5), 77 (27), 66 (3.5), 65 (11.5), 64 (2.5), 63 (16.5), 51 (11), 50 (4.5), 47 (8), 45 (10), 39 (13).

Preparation of Phosphite Ozonides. Dry ozonized oxygen was bubbled through anhydrous dichloromethane in a three-necked flask refrigerated at −78 °C for triphenyl phosphite or methyl diphenyl phosphite, or at −88 °C for phenyl dimethyl phosphite. The appropriate phosphite was dissolved in methylene chloride and added from a dropping funnel at such a rate that the blue color of the solution in the flask persisted throughout the addition. After the phosphite addition was complete, the ozone was bubbled through the solution for another 5–15 min, and the solution was then purged with oxygen prior to its use in a decomposition run. The yield of ozonide obtained determined the yield of oxygen from decomposition of the sample. In the case of triphenyl phosphite, yields of the ozonide were from 70 to 100% and the sample could be kept at −78 °C for 7 days; with methyl diphenyl phosphite the yields were only 25–35% under the same conditions, and the storage lifetime at −78 °C was limited to 6 h. The ozonide of phenyl dimethyl phosphite, prepared in 45–50% yielded at −88 °C, had to be used immediately.

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Registry No. 1, 29833-83-8; **2**, 84812-10-2; **3**, 84812-11-3; methanol, 67-56-1; pyridine, 110-86-1; diphenyl methyl phosphate, 115-89-9; sodium phenoxide, 139-02-6; methyl phosphorodichloridate, 677-24-7; dimethyl phenyl phosphate, 10113-28-7; phenyl phosphorodichloride, 770-12-7; diphenyl methyl phosphite, 3577-87-5; phenol, 108-95-2; dimethyl phenyl phosphite, 18351-42-3; phenyl phosphorodichloridite, 3426-89-9; triphenyl phosphite, 101-02-0.

The Total Synthesis of Ionophore Antibiotics. A Convergent Synthesis of Lasalocid A (X537A)[1]

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Abstract: The construction of both the left-side aldehyde **2** and the right-side ketone **3** available from the reverse aldol reaction with lasalocid A (X537A) is described. For each synthesis chiral starting materials are used. For the aldehyde **2**, (*R*)-(−)-citronellene is the source of the lone asymmetric center and the aromatic ring is prepared by a Diels–Alder reaction between the pyrone **22** and 1-(dibenzylamino)-1-propyne. For the ketone **3**, carbohydrate precursors serve as the source of the furanoid and pyranoid subunits. These subunits are then joined through the use of the ester enolate Claisen rearrangement. Details for the aldol condensation between the aldehyde **2** and the zinc enolate of the ketone **3** are presented, and the formation of the natural ionophore from this process completes the highly convergent total synthesis.

The recently characterized[7] polyether ionophore antibiotics[8] represent a broad new class of biologically potent compounds that have rapidly found commercial value as coccidiostats[9] and anabolic agents[10] in animal medicine. In addition, the demonstration of their powerful cardiotonic activity[11] and apparent tissue selectivity[11] in mammalian systems holds promise for their use in human pharmacology. In light of these results, it is not surprising that the synthesis of these molecules has attracted the concern of numerous research groups, and several representatives of this class have yielded to total synthesis.[12] One such effort resulting in the total synthesis of lasalocid A (X537A) (**1**) is described herein.[13]

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(2) NRC (Canada) Postdoctoral Fellow, 1978–1979; NSERC (Canada)–NATO Postdoctoral Fellow, 1979–1980.

(3) Fonds National Suisse de la Recherche Scientifique Postdoctoral Fellow, 1979–1980.

(4) NSERC (Canada) Predoctoral Studentship, 1979–1982.

(5) Postdoctoral Fellow of the National Cancer Institute, USPHS, 1978–1979.

(6) Upjohn Co. Predoctoral Fellow, 1978–1980. For further details of this work, see: Thaisrivongs, S. Ph.D. Thesis, California Institute of Technology, 1980.

(7) Lasalocid A: Isolation—Berger, J.; Rochlin, A. I.; Scott, W. E.; Steinbach, L. H.; Goldberg, M. W. *J. Am. Chem. Soc.* **1951**, *73*, 5295–5298. Structure—Westley, J. W.; Evans, R. H., Jr.; Pruess, D. L.; Stempel, A. *Chem. Commun.* **1970**, 1467–1468. Johnson, S. M.; Herrin, J.; Liu, S. J.; Paul, I. C. *J. Am. Chem. Soc.* **1970**, *92*, 4428–4435.

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(12) (a) Calcimycin: Evans, D. A.; Sacks, C. E.; Kleschick, W. A.; Tabor, T. R. *J. Am. Chem. Soc.* **1979**, *101*, 6789–6791. Grieco, P. A.; Williams, E.; Tanaka, H.; Gilman, S. *J. Org. Chem.* **1980**, *45*, 3537–3539. (b) Lasalocid A: Nakata, T.; Schmid, G.; Vranesic, B.; Okigawa, M.; Smith-Palmer, T.; Kishi, Y. *J. Am. Chem. Soc.* **1978**, *100*, 2933–2935. (c) Monensin: Fukuyama, T.; Akasaka, K.; Karanewsky, D. S.; Wang, C.-L. J.; Schmid, G.; Kishi, Y. *Ibid.* **1979**, *101*, 259–263. Still, W. C.; McDonald, J.; Collum, D. *Ibid.* **1980**, *102*, 2117–2121.

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The basic design for this synthesis was predicated on a desire to define a synthetic strategy that could be generally applied to the construction of numerous members of the polyether ionophore class as well as to potentially important nonnatural analogues. Due to the structural complexity and chemical sensitivity of the naturally occurring polyether ionophores, it may only be through efficient total syntheses that a wider range of biologically informative structural variants will become available in useful quantities for evaluation. This total synthesis of lasalocid A (X537A) then represents not only an important objective in its own right, but also a reasonable milieu in which to evaluate the potential generality of the overall synthetic scheme.

A striking structural feature of most of the polyether ionophores is the chain of substituted tetrahydrofuran and tetrahydropyran rings. One of the simplest member of this group is lasalocid A (X537A) which contains one tetrahydrofuran and one tetrahydropyran ring in sequence. It was the objective of this work to develop a methodology to generate the polyether skeleton in a building block manner by joining individually performed tetrahydrofuran and/or tetrahydropyran rings. Not only is such a convergent approach potentially logistically efficient, but it also offers the opportunity for a flexible combination of the oxygen-heterocyclic building blocks with possible wide structural variation.

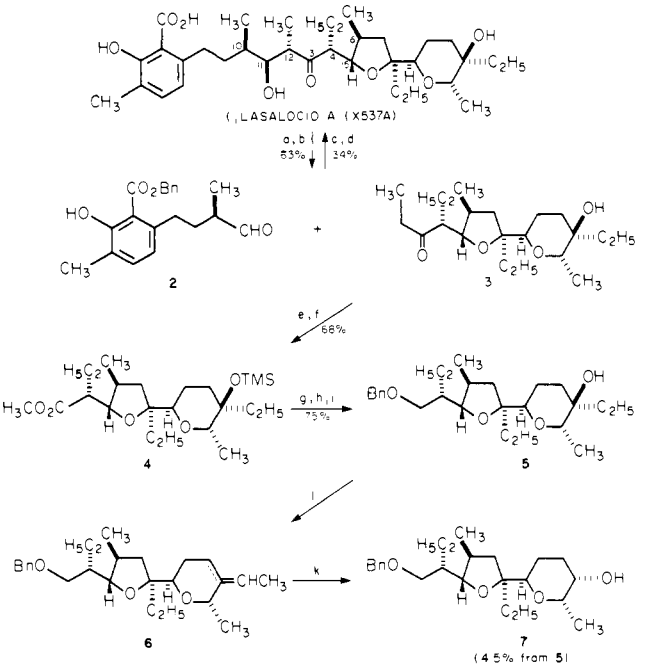
Another structural feature that is prevalent in these polyether ionophores and also central to lasalocid A (X537A) is the aldol-type linkage. In the antithetic sense, the C10,11 bond of lasalocid A (X537A) becomes the ideal point at which to divide the molecule. Technology gained through a process in which this particular aldol-type linkage can be reestablished from condensation of the left-side aldehyde **2** and the right-side ketone **3** should apply directly to other members of this class.

These objectives and basic concepts then form the basis of a broad synthetic program directed toward polyether ionophores, the first achievement in which is the total synthesis of lasalocid A (X537A). The current effort may be divided into three distinct segments. First, degradative work with the natural product itself[14] led quickly to the realization that the aldol-type condensation was indeed a viable approach for the construction of lasalocid A (X537A), and several key structures for comparison were also prepared from the right-side ketone **3**. Second, a synthesis of the chiral left-side aldehyde **2** from the readily available terpenoid precursor (*R*)-(−)-citronellene **8** and nonaromatic substrates was developed. Third, a strategy for the convergent synthesis of the right-side ketone **3** was realized through the application of the ester enolate Claisen rearrangement to appropriate tetrahydrofuranoid and tetrahydropyranoid intermediates derived from readily available monosaccharides.

I. Degradation and Aldol-Type Reconstitution of Lasalocid A (X537A) (1). The initial degradation of lasalocid A (X537A) (**1**) (Scheme I) through the reverse aldol-type reaction followed previously reported[14] conditions. After formation of the benzyl ester of the ionophore, pyrolysis led to the aldehyde **2** and the ketone **3** in good yield. This reverse aldol-type reaction provided optically pure samples of both partners in contrast to a previous report,[15] which indicated that the right-side ketone **3** was epimerized at C14.[16] In the present investigation, only a single diastereomer was observed in the ^{13}C NMR spectrum of compound **3**. For this purpose the pyrolytic process is obviously superior to the basic condition which also will effect the cleavage but leads to racemization of the aldehyde **2** and epimerization of the ketone **3**.

After much experimentation with a variety of conditions, it was found that the reconstruction of lasalocid A (X537A) (**1**) as its benzyl ester could be accomplished through the aldol-type reaction between 2 equiv of the aldehyde **2** and one of the zinc enolate[17] of the ketone **3**. The isomeric composition of the products obtained in 62% yield based on the ketone **3** used (95% based on unrecovered ketone **3**) was 54:32:10:4. No conditions were found that would duplicate the previously reported[12b] results in which aldehyde **2** of significantly lower optical purity was used. Chromatography of this isomeric mixture resulted in the isolation of the desired benzyl ester in isomerically pure form in a 34% yield, and hydrogenolysis then freed the natural product itself.

Scheme I. Degradation and Aldol-Type Reconstitution of Lasalocid A (X537A)[a]



[a] (a) Na salt of lasalocid A (X537A), BnBr, dioxane; (b) 230 °C (0.01 mmHg); (c) LDA, ether, −78 °C; $ZnCl_2$, 0 °C; RCHO, 0 °C, 5 min, (d) H_2, Pd/C, EtOH; (e) $KN(Me_3Si)_2$, THF; $(Me_3Si)Cl$; (f) O_3, CH_3OH–CH_2Cl_2; $NaBH_4$; CH_2N_2, Et_2O; (g) $LiAlH_4$, Et_2O; (h) *n*-Bu_4NF, THF; (i) KH, THF, BnBr; (j) KH, CS_2, CH_3I, THF; heat; (k) O_3, CH_3OH–CH_2Cl_2; $NaBH_4$.

While this aldol-type condensation effects the desired reconstitution of the ionophore and thereby assures the success of any synthetic scheme that can generate the two partners, the efficiency of the process is less than ideal, and further modifications are in order. However, the current results are sufficient to warrant a shift of attention to syntheses of the aldehyde **2** and the ketone **3**. In this connection, intermediate comparison samples were desired for the stereochemically more demanding synthesis of the ketone **3**. Particularly useful would be a naturally derived system representative of a stage in the synthesis shortly after the union of the tetrahydrofuran and tetrahydropyran rings. The degradation of the ketone **3** outlined in Scheme I was explored.

From the previous aldol-type reaction experiments, it was known that kinetic enolization of the ketone **3** generated the less substituted enolate. This was trapped with trimethylchlorosilane and then the resulting silyl enol ether was ozonized. Esterification of the acid formed led to the ester **4**, which was subsequently converted to the benzyl ether **5**. Since the planned synthetic scheme left the introduction of the tertiary alcohol in the tetrahydropyran ring until last, it would be advantageous to remove this substitution in the current degradation. Unfortunately, this could only be accomplished in poor yield, since dehydration of this tertiary alcohol invariably led to predominate formation of the endocyclic olefin. Only the described xanthate pyrolysis formed small but workable amount of the exocyclic olefin **6**.

(13) For preliminary reports of this work, see: Ireland, R. E.; Thaisrivongs, S.; Wilcox, C. S. *J. Am. Chem. Soc.* **1980**, *102*, 1155–1157. Ireland, R. E.; McGarvey, G. J.; Anderson, R. C.; Badoud, R.; Fitzsimmons, B. J.; Thaisrivongs, S. *Ibid.* **1980**, *102*, 6178–6180.

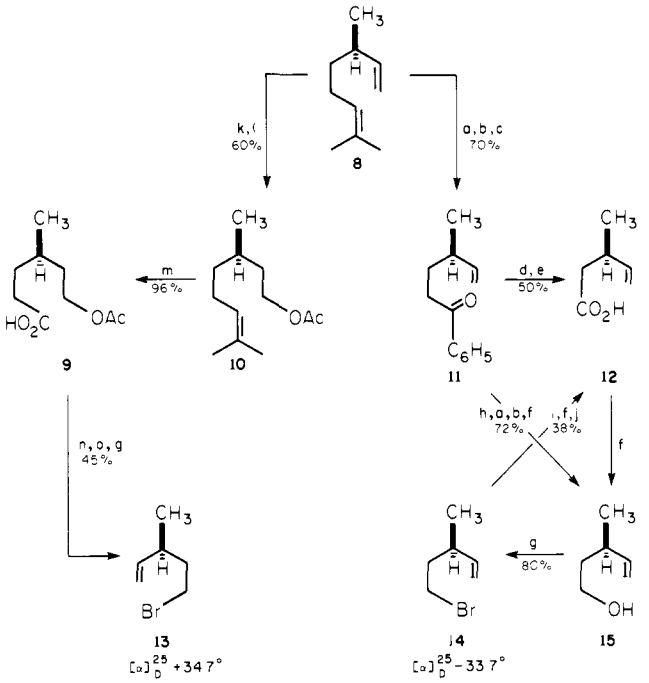
(14) Westley, J. W.; Evans, R. H., Jr.; Williams, T.; Stempel, A. *J. Org. Chem.* **1973**, *38*, 3431–3433.

(15) Westley, J. W.; Pitcher, R. G.; Seto, H. J. *J. Antibiot.* **1978**, *31*, 289–293.

(16) Lasalocid A numbering system is used throughout this discussion for clarity.

(17) Original conditions of House et al. (House, H. O.; Crumrine, D. S.; Teranishi, A. Y.; Olmstead, H. D. *J. Am. Chem. Soc.* **1973**, *95*, 3310–3324).

Scheme II. Synthesis of the Enantiomeric Bromopentenes **13** and **14**[a]



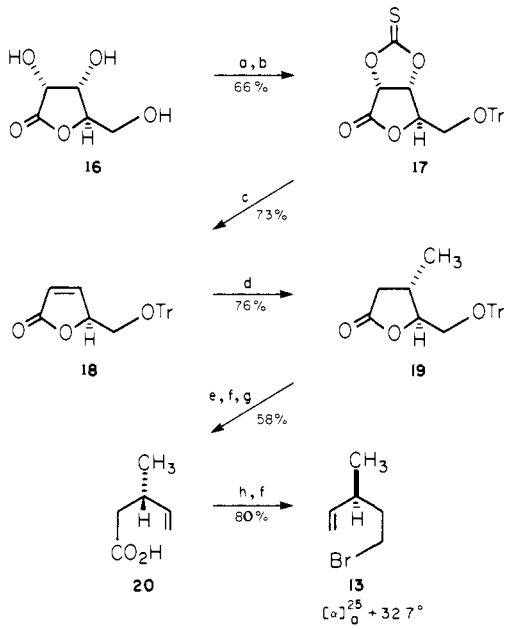
[a] (a) MCPBA, CH_2Cl_2; (b) H_5IO_6, Et_2O; C_6H_5MgBr, Et_2O; (c) PCC, CH_2Cl_2; (d) $HCO_2C_2H_5$, $NaOCH_3$; (e) $NaIO_4$, aqueous CH_3OH; (f) $LiAlH_4$, Et_2O; (g) MsCl, Et_3N, CH_2Cl_2; LiBr, acetone; (h) LDA, THF, -78 °C; Me_3SiCl; (i) $AgBF_4$, Me_2SO; (j) 8 N H_2CrO_4, acetone; (k) 9-BBN, THF; H_2O_2, OH^-; (l) AcCl, Et_3N; (m) O_3; 8 N H_2CrO_4, acetone; (n) $Pb(OAc)_4$, $Cu(OAc)_2$, C_6H_6-pyr.; (o) $NaOCH_3$, CH_3OH.

Ozonolysis, reduction, and then chromatography of the mixture of these olefins led to the isolation of the alcohol **7**. The physical and spectral constants of this alcohol proved to be invaluable in the definition of the stereochemical outcome of the ensuing synthetic effort.

II. Synthesis of the Chiral Left-Side Aldehyde 2. For the synthesis of the aldehyde **2**, an approach was chosen that entailed the construction of the aromatic ring system from aliphatic precursors. The more apparent approach that relied on the substitution of a preformed aromatic ring seemed fraught with difficulty by virtue of the tetrasubstituted pattern. The first focus for this scheme is the generation of a suitable side-chain unit that can serve as a latent aldehyde and carries the lone asymmetric center of the system. While initial successful exploration of this synthesis was done in a racemic model series, this report is confined to a discussion of the results with enantiomerically pure compounds.

The chiral unit chosen as starting material for this work was the monoterpene (*R*)-(−)-citronellene **8** (Scheme II). By suitable modification of the reaction sequences, it was possible to convert *either* olefinic arm of this terpene to the required bromoethyl residue *at will*. Thus, operation first by peracid oxidation resulted in preferential attack at the trisubstituted olefin and thence ultimate conversion to the bromopentane **14** required for the synthesis of the aldehyde **2** from naturally occurring lasalocid A (X537A) (**1**). In this work two procedures were developed for the degradative cleavage of the phenylketone **11**; one leads through the acid **12** to the alcohol **15** and the other provides the same alcohol **15** directly. The bromide **14** obtained from the latter approach was then reoxidized to the acid **12** for comparison purposes. In each case, when the enantiomeric purity of the acid **12** was checked by analysis of its ^1H NMR spectrum with a chiral shift reagent,[18] only one enantiomer could be detected (>95%).

Scheme III. Alternate Synthesis of the Bromopentene **13**[a]

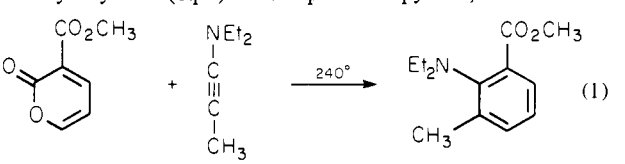


[a] (a) $(C_6H_5)_3CCl$, pyridine; (b) S=C(imid)$_2$, acetone; (c) Ni(Ra), acetone; (d) $LiMe_2Cu$, ether; (e) 5% Pd/C, ethanol, H_3O^+; (f) MsCl, Et_3N, CH_2Cl_2; LiBr, THF; (g) Li, NH_3(l), THF; (h) $LiAlH_4$, Et_2O.

As an alternative means to check this point and as well to provide access to the enantiomeric aldehyde **2**, initial hydroboration of (*R*)-(−)-citronellene **8** was investigated as a means to modify the less substituted olefinic arm (Scheme II). After conversion of the hydroboration product to the acid **9** by ozonization with an oxidative workup, Kochi decarboxylative oxidation[19] converted the carboxyl-bearing arm to the vinyl group, and ultimately the enantiomeric bromide **13** became available. The optical rotation of this bromide was equal in magnitude, but opposite in sign, to that of the bromide **14**. This result clearly demonstrated that no partial racemization had occurred during these reaction sequences and was a satisfying classical support for the optical purity of the two enantiomers. Thus, from the same chiral starting material, *both* enantiomers of the aliphatic side chain of the aldehyde **2** are readily available.

In contrast to material obtained elsewhere[12b] through attempted resolution of racemic acid **12**, the high enantiomeric purity of the bromide **14** in this investigation was confirmed *independently* from another synthesis of the bromide **13** from D-(+)-ribonic acid, γ-lactone (**16**), as shown in Scheme III. A single isomer resulted from addition of lithium dimethyl cuprate to the unsaturated lactone **18**. The acid **20**, which is enantiomeric to the acid **12**, was obtained via a reductive fragmentation of the bromide derivative of the lactone **19**. The specific rotation of the bromide **13** secured from this synthetic route was in excellent agreement with that derived from (*R*)-(−)-citronellene.

For the construction of the aromatic ring, the Diels–Alder reaction between a carbomethoxy-α-pyrone and an acetylenic reagent was chosen. Such an aromatic ring synthesis was reported earlier by Bryson[20] (eq 1) for the parent α-pyrone, and the sub-



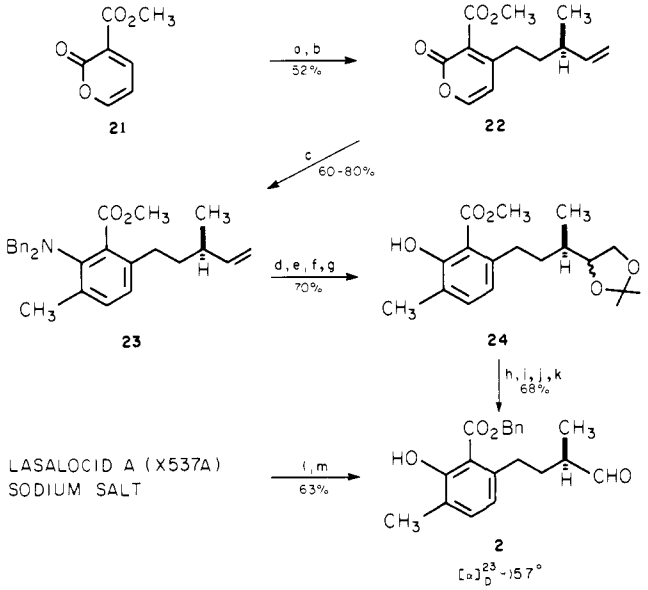
(1)

stitution pattern of the resulting aromatic ring was attractively similar to that of the desired aldehyde **2**. For the case at hand, it was first necessary to construct an α-pyrone that bore the alkyl side chain prepared above and then to explore the possibility that

(18) Tris[3-(heptafluoropropylhydroxymethylene)-*d*-camphorato]europium(III).

(19) Bacha, J. D.; Kochi, J. K. *Tetrahedron* **1968**, *24*, 2215–2226.
(20) Bryson, T. A.; Donelson, D. M. *J. Org. Chem.* **1977**, *42*, 2930–2931.

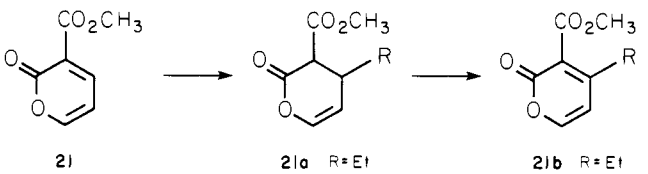
Scheme IV. Construction of the Chiral Aldehyde 2[a]



[a] (a) $BrMgCH_2CH_2CH(CH_3)CH=CH_2$ from **14**, THF; (b) MnO_2, CH_2Cl_2; (c) $Bn_2NC{\equiv}CCH_3$, C_6H_6; (d) OsO_4, NMO, aqueous CH_3COCH_3; (e) H_2, Pd/C, EtOH; (f) *i*-AmONO, HBF_4, EtOH; H_2O, Δ; (g) $(CH_3)_2C(OCH_3)_2$, H^+, CH_3COCH_3; (h) KH, $CH_3OCH_2CH_2OCH_2Cl$; (i) *n*-C_3H_7SLi, HMPA; BnBr; (j) H_3O^+; (k) $NaIO_4$, aqueous CH_3OH; (l) BnBr, dioxane; (m) 230 °C (0.01 mmHg).

an oxygen-substituted rather than nitrogen-substituted acetylenic system could be used in the Diels–Alder reaction. A solution to the former problem was readily found, but an extensive search for oxygen-substituted dienophiles proved fruitless. As a result, a synthesis of the aldehyde **2** was built around the utilization of an ynamine in the Diels–Alder reaction with the substituted α-pyrone (Scheme IV).

A noteworthy facet of this synthesis was the initial transformation of the α-pyrone **21** to its substituted derivative **22**. It was proposed that the preferred mode of organometallic conjugate addition to the α-pyrone **21** would be 1,4-addition rather than 1,6-addition by virtue of the deactivation of the 6-position by the ether oxygen. Rearomatization of the resulting 1,4 adduct was then to be accomplished by dehydrogenation. In model experiments, on addition of the α-pyrone **21** to lithium dimethyl cuprate



or cupric acetate/ethylmagnesium bromide solution, the reaction mixture turned purple, and after varying reaction times and temperatures, workup led to *no* desired adduct. On the premise that these results were the consequences of initial electron transfer from an incipient cuprate to the aromatic α-pyrone, the addition of ethylmagnesium bromide itself in the absence of copper salt was investigated. It was gratifying to find that the yield of the 1,4 adduct **21a** under these conditions was 90%. This result underscores the difference in character between these two organometallic reagents.

The dehydrogenation of the 1,4 adduct **21a** also proved to be an initial obstacle. Several standard reagents, such as sulfur, DDQ, and chloranil, were ineffective, and activated manganese dioxide, while effective, was capricious. In this model series, dehydrogenation was most efficiently (65% yield) effected by nickel peroxide which gave the model substituted α-pyrone **21b**.

When these experiences were applied to the preparation of the desired α-pyrone **22** in which both the racemic and optically active bromopentenes **14** were used, the conjugated 1,4-addition was similarly observed in good yield with the derived organomagnesium reagent. The nickel peroxide dehydrogenation procedure, however, was now ineffectual. It was presumed that the nickel reagent complexes with the terminal olefin of the dihydro-α-pyrone and is then inactivated. After further experimentation, again with a wide variety of reagents, it was found that only activated (Attenburrow[21]) manganese dioxide gave a reasonable yield of the desired α-pyrone **22**. Thus, in both series this α-pyrone was routinely available in moderate yield on a large scale and attention was turned to the Diels–Alder reaction.

The results reported earlier by Bryson[20] suggested that the Diels–Alder condensation between a 3-carbomethoxy-α-pyrone and a heterosubstituted acetylene would lead to an aromatic ring with the desired regiochemistry for the synthesis of the aldehyde **2**. Since in the present situation a phenol derivative is desired rather than the aniline system obtained in the earlier work,[20] considerable effort was expended to condense the substituted 3-carbomethoxy-α-pyrones to 1-methoxy-1-propyne, 1,1-diethoxy-1-propene, *tert*-butyldimethylsilyl keteneacetal of methyl propionate,[22] and *tert*-butyldimethylsilyl ketneaminal of *N,N*-dimethylpropionamide.[22] In no case was any [4 + 2] adduct or aromatic system detected in a complex reaction product. In order to accomplish the desired cycloaddition reaction, the reaction between the α-pyrone **21b** and *N,N*-diethyl-1-amino-1-propyne was investigated and found to produce the expected aromatic system in high (89%) yield exothermically when the reactants were mixed in benzene at room temperature. Happily, substitution of either the racemic or optically active substituted α-pyrone **22** and *N,N*-dibenzyl-1-amino-1-propyne did not alter these results, and in each case the aniline derivative **23** was obtained in high yield.

The choice of the *N,N*-dibenzyl-1-amino-1-propyne was predicated by the necessity to replace the nitrogen by oxygen through diazotization of the aniline derivative obtainable after hydrogenolysis of the initial aromatic product **23**. This process was efficiently accomplished as shown in Scheme IV, and the major skeletal and functional synthetic problems presented by the aldehyde **2** were solved. Further cosmetic work to exchange the methyl for a benzyl ester and to ummask the aldehyde function led to the desired aldehyde **2**. The necessity to exchange the methyl for the benzyl ester was dictated by the observation that the methyl ester was highly resistant to hydrolysis, and particularly after aldol-type condensation with the right-side ketone **3**, the methyl ester could not be removed without severe degradation of the system.

The identity of the chiral synthetic aldehyde **2** was established by comparison of its physical and spectral data with those observed on sample of the aldehyde **2** derived from natural lasalocid A (X537A) (**1**). A reliable (20% from α-pyrone **21** and 8% from (*R*)-(−)-citronellene (**8**)) synthesis of the chiral aldehyde **2** was thus available[23] and construction of the polyether ketone **3** was pursued.

III. Construction of the Polyether Right-Side Ketone 3. The basic concept for the synthesis of the right-side ketone **3** is presented in Scheme V. The heart of this highly convergent approach is the union of the furanoid acid **25** to the pyranoid glycal **26** through application of the ester enolate Claisen rearrangement.[24] Such an approach allows for the stereochemical control

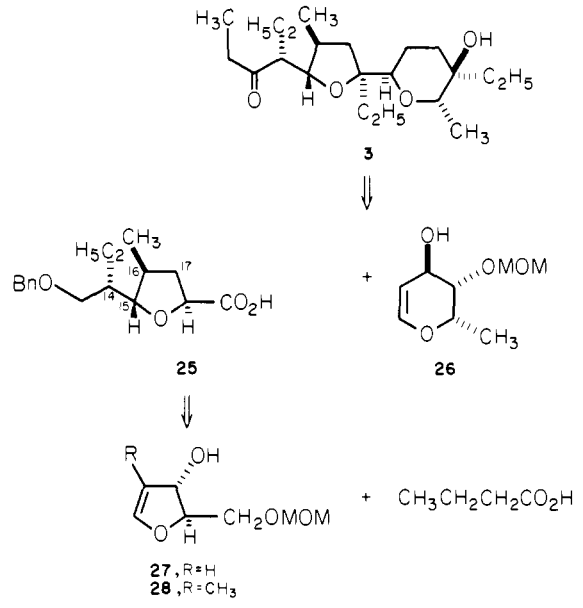
(21) Attenburrow, J.; Cameron, A. F. B.; Chapman, J. H.; Evans, R. M.; Hems, B. A.; Jansen, A. B. A.; Walker, T. *J. Chem. Soc.* **1952**, 1094–1111. Fatiadi, A. J. *Synthesis* **1976**, 65–104.

(22) Prepared by LDA enolization and then enolate trapping of methyl propionate or *N,N*-dimethylpropionamide.

(23) An initially unsettling feature of this work was the lack of correspondence between the optical rotations observed for common intermediates and the aldehyde **2** in this work and that of Kishi and co-workers.[12b] Since the optical purity of the acid **12** was verified by the use of chiral shift reagents in ^1H NMR experiments, both antipodes of the bromopentenes **13** and **14** were prepared, and the optical rotation of both synthetic and naturally derived aldehyde **2** was identical, the optical purity of the systems reported here is believed to be on a firm basis. The previously reported[12b] values for these systems seem, therefore, to represent the observations made on partially racemic material.

(24) Ireland, R. E.; Mueller, R. H.; Willard, A. K. *J. Am. Chem. Soc.* **1976**, *98*, 2868–2877.

Scheme V. Basic Design for Synthesis of Ketone 3



of the formation of the central carbon–carbon bond in an *intramolecular* reaction after the two partners have been joined in an efficient *intermolecular* esterification process. The known potential for stereochemical control during the Claisen rearrangement[25] is augmented in the ester enolate version through the possibility that either the *erythro* or *threo* product is accessible from the same precursor[26,27] by choice of enolization conditions.

Carbohydrate precursors were especially suitable for the construction of the chiral furanoid **25** and pyranoid **26** subunits. In an earlier report, the preparation[28] of various glycals and subsequent model studies[29] for ester enolate Claisen rearrangement were presented. For this synthesis, the pyranoid subunit **26** could be secured with minor modification of the existing sequence.[29,30] It remained to prepare the furanoid subunit **25** in order to explore the remaining features of this synthetic scheme.

The basic strategy for the construction of this subunit entailed the application of the ester enolate Claisen rearrangement technology to the butyrate of either glycal **27** or **28**. In the former case, it would then be necessary to introduce the C16 methyl group,[16] while in the latter situation, synthetic success depends on the stereoselective hydrogenation of a C16,17 double bond.[16]

An additional stereochemical point was uncertain at the outset. While it was known[24] that enolization of an ester produces predominately either isomeric enolate and hence the silyl keteneacetal by suitable solvent modification, the character (boat-like vs. chair-like) of the transition sate for the subsequent Claisen rearrangement of a cyclic allylic ester was not understood at the time.[31] Therefore, it was not possible to predict in advance which enolate geometry would lead to the desired *S* configuration at C14[16] in subunit **25**. On the other hand, the correct chirality at C15[16] was assured by the choice of furanoid glycal. Thus, while synthetic success was certain by virtue of the availability of both the 14*R* and 14*S* configurations[16] from the appropriate enolates, the correct conditions could not be defined until the four diastereomers **7** and **56–58** were prepared and compared with material obtained from degradation of the natural product itself. On the assumption that the stereochemical result of the enolization of the butyrate of the glycals **27** and **28** is the same as that for acyclic esters established earlier,[24] the later comparison revealed that the preferred transition state for this Claisen rearrangement was boat-like. Therefore, the 14*S* configuration[16] in subunit **25** would be derived from the (*Z*)-ketene acetal via enolization in 23% HMPA in THF.

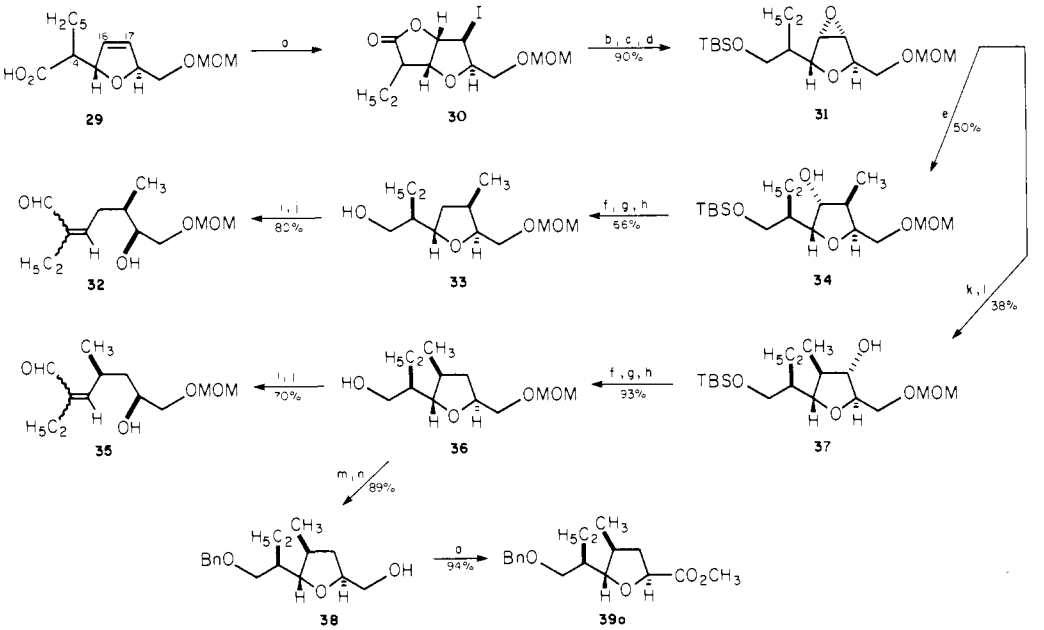
The construction of the acid **25** was first approached through the glycal **27**[29] from which the acid **29** was prepared (Scheme VI) as a mixture of C14 isomers[16] (LDA/THF: 73%; ratio[32] 81:19 and LDA/HMPA–THF: 60%; ratio[32] 21:79) as described earlier.[29] The problem was now the introduction of the C16 methyl group,[16] and for this exploration the more conveniently available LDA/THF isomeric mixture **29** was used. This acid mixture was converted to the α-oriented epoxides **31** in 90% overall yield through the intermediate iodolactone **30**. Reaction of this α-epoxide mixture with lithium dimethyl cuprate in ether/pentane resulted in the introduction of a β-oriented methyl group, and after chromatographic separation, the alcohol **34**, along with 12% of its C14 epimer,[16] was obtained. Removal of the hydroxyl group and silyl ether cleavage led to the isomerically pure primary alcohol **33**. In order to ascertain the location of the newly introduced ring methyl group, this alcohol was converted to the unsaturated aldehyde **32**. The ^{1}H NMR spectrum of this aldehyde revealed that the resonance due to the olefinic hydrogen was a triplet. Methylation at the desired C16 position[16] should give rise to an unsaturated aldehyde in which this olefinic hydrogen is only a doublet. The possibility of this signal being a pair of doublets, due to the possible formation of olefin isomers during base elimination, was ruled out by examination of the spectrum at different field strengths. This result showed that cuprate cleavage had occurred at the undesired C17 position.[16]

Since the methylation had taken place at the more hindered C17 position[16] with lithium dimethyl cuprate, it was hypothesized that the cleavage entailed prior complexation of the organometallic reagent with the adjacent methoxymethylene blocking group. To avoid this effect, the α-epoxide mixture **31** was treated with lithiated 1,3-dithiane.[33] Desulfurization of the resulting products then provided a new methylated alcohol **37** in moderate yield. In order to verify that this new alcohol was indeed the result of epoxide cleavage at the C16 position,[16] it was converted to the unsaturated aldehyde **35**, using the same sequence as described above. In this instance, the resonance due to the olefinic hydrogen in the ^{1}H NMR spectrum was the expected doublet. With the assurance that the structure of the furan ring was now correct, the intermediate primary alcohol **36** was converted to the anticipated furanoid subunit as its methyl ester **39a**.

The overall yield of this construction was disappointing and prompted an exploration into an alternate approach through a branched-chain carbohydrate precursor. For this purose, "α"-D-glucosaccharinic acid, γ-lactone (**40**),[34] was the ideal substrate. Available on large scale by the treatment of invert sugar with aqueous calcium hydroxide,[34] this branched-chain sugar fit the previously described technology (Scheme VII). Systematic application of the previous sequence[29] led in good yield to the mixture of unsaturated esters **43** in which either the *R* or *S* epimer at C14[16] could be made to predominate. It was somewhat surprising, but gratifying, to discover that catalytic hydrogenation of C16,17 double bond[16] in esters **43** gave a readily separable mixture of two saturated esters that were *only* epimeric at the earlier C14 pos-

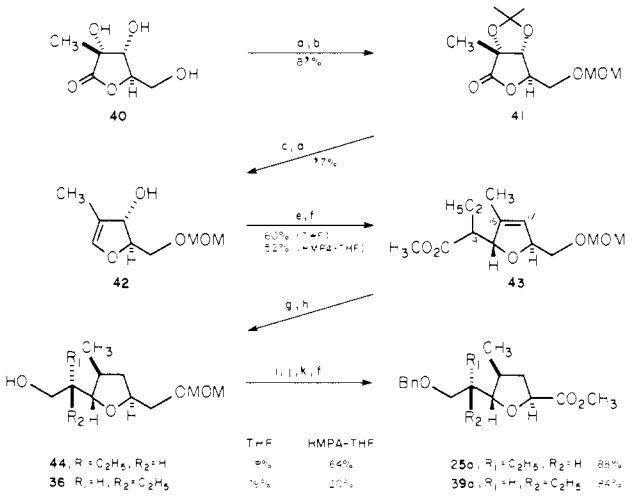
(25) von E. Doering, W.; Roth, W. R. *Tetrahedron* **1962**, *18*, 67–74.
(26) Ireland, R. E.; Wilcox, C. S. *Tetrahedron Lett.* **1977**, 2839–2842.
(27) In the ester enolate Claisen rearrangement, two factors determine the stereochemical outcome of the single carbon–carbon bond formation: the geometry of the enolate and the chair/boat character of the transition state. Enolate formation of straight chain esters can be readily controlled and predicted;[24] however, such is not the case with α-substituted esters. In the latter situation, the geometry of the enolate formed may be specific, but experimental reversal of the enolate geometry may not be possible. Moreover, reasonably accurate prediction of enolate geometry is possible only in the case of most α-heterosubstituted esters.
(28) Ireland, R. E.; Wilcox, C. S.; Thaisrivongs, S. *J. Org. Chem.* **1978**, *43*, 786–787.
(29) Ireland, R. E.; Thaisrivongs, S.; Vanier, N.; Wilcox, C. S. *J. Org. Chem.* **1980**, *45*, 48–61.
(30) Ireland, R. E.; Wilcox, C. S. *J. Org. Chem.* **1980**, *45*, 197–202.
(31) Subsequent to the current work, a definitive determination for the boat-like character for the transition state for rearrangement of glycal silyl ketene acetals was made through the synthesis of the (+)- and (−)-nonactic acids (Ireland, R. E.; Vevert, J.-P. *Can. J. Chem.* **1981**, *59*, 572–583).
(32) Ratios were determined from the corresponding hydrogenated methyl esters by GLPC (4% SE-30, 120 °C, $^1/_4$ in. × 6 ft).
(33) Yamashita, A.; Rosowsky, A. *J. Org. Chem.* **1976**, *41*, 3422–3425.
(34) Whistler, R. L.; BeMiller, J. N. *Meth. Carbohydr. Chem.* **1963**, *2*, 484–485.

Scheme VI. Synthesis of Epimeric Furanoid Subunit 39[a]



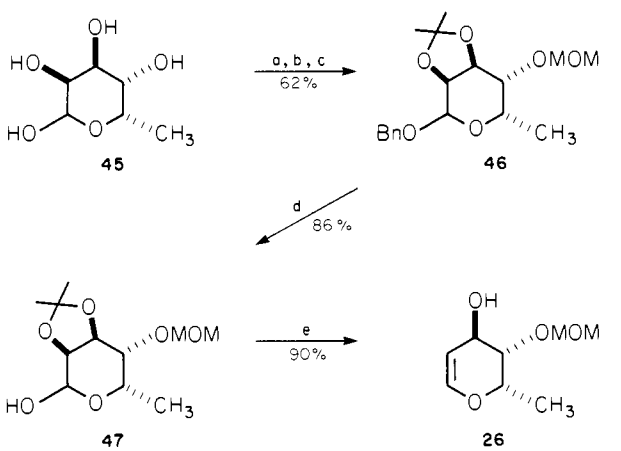
[a] (a) KI, I_2, aqueous $NaHCO_3$; (b) AlH_3, THF; (c) Na_2CO_3, CH_3OH; (d) TBSCl, imidazole, DMF; (e) $LiMe_2Cu$, ether–pentane; (f) NaH, CS_2, CH_3I, THF; (g) *n*-Bu_3SnH, toluene, Δ; (h) *n*-Bu_4NF, THF; (i) PCC, NaOAc, CH_2Cl_2; (j) KO-*t*-Bu, THF; (k) $C_4H_7S_2Li$, THF; (l) Ni(Ra), EtOH; (m) KH, $C_6H_5CH_2Br$, THF; (n) 10% HCl, THF; (o) Pt, O_2, aqueous $NaHCO_3$; CH_2N_2.

Scheme VII. Synthesis of Furanoid Subunit 25a[a]



[a] (a) CH_3COCH_3, H_2SO_4; (b) KH, $ClCH_2OCH_3$, THF; (c), DIBAL, ether, −78 °C; (d) $P(NMe_2)_3$, CCl_4, THF, 0 °C; Li, NH_3(l), then NH_4Cl; (e) *n*-C_3H_7COCl; LDA, THF (HMPA); Me_3SiCl; OH^-; (f) CH_2N_2, ether; (g) H_2, 10% Pt/C, EtOAc; (h) $LiAlH_4$, ether; (i) KH, $C_6H_5CH_2Br$, THF; (j) 10% HCl, THF; (k) Pt, O_2, aqueous $NaHCO_3$.

Scheme VIII. Synthesis of the Glycal 26[a]



[a] (a) BnOH, AcCl, (b) $(CH_3)_2C(OCH_3)_2$, H^+, acetone; (c) KH, $ClCH_2OCH_3$, THF; (d) Li, NH_3(l), THF; (e) $P(NMe_2)_3$, CCl_4, THF; 0 °C; Li, NH_3(l), then NH_4Cl.

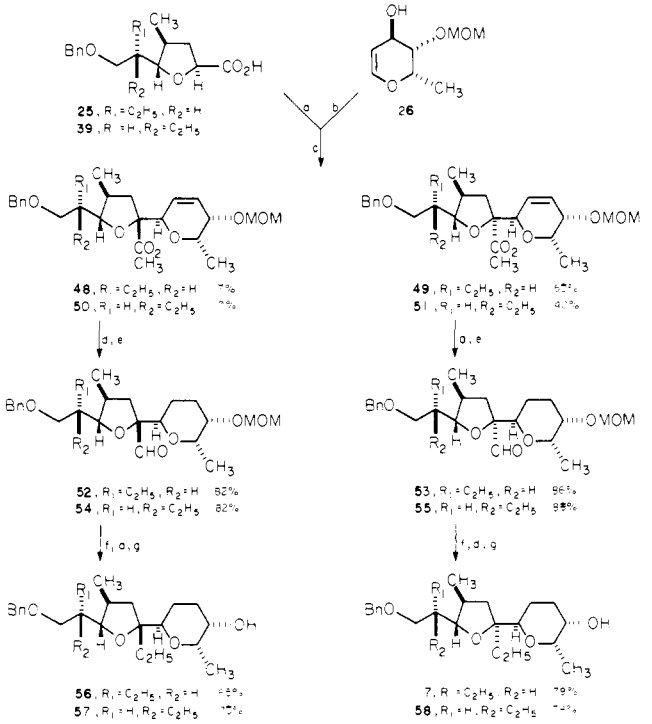
ition.[16] Hydrogenation had taken place in a highly stereoselective manner and in the desired α sense. Hydride reduction of the 14*S* ester[16] led to the previously formed (Scheme VI) alcohol **36**, while reduction of the 14*R* ester[16] gave the alcohol **44**. Both alcohols were readily transformed to the esters **25a** and **39a**. While the basis for the stereoselectivity of the catalytic hydrogenation of the esters **43** is not obvious, the outcome greatly increased the efficiency of the synthetic route for these furanoid subunits.

The construction of the alcohol **26** started with 6-deoxy-L-gulose (**45**)[30] as shown in Scheme VIII. The hydroxyl groups were differentiated as benzyl glycoside, *O*-isopropylidene, and methoxymethyl ether in compound **46**. Removal of the benzyl ether then led to the lactol **47** which was converted to the desired glycal **26** by the previously described procedure.[29]

The building blocks (acids **25** and **39** and the glycal **26**) of the right-side ketone **3** were now in hand, together with the necessary technology for their union.[29] It was the intention to generate all four possible diastereoisomers **7** and **56–58** from the connection of the pyranoid subunit **26** to both epimers of the furanoid acids **25** and **39** and to correlate the resultant stereoisomers with the natural degradation product **7**.

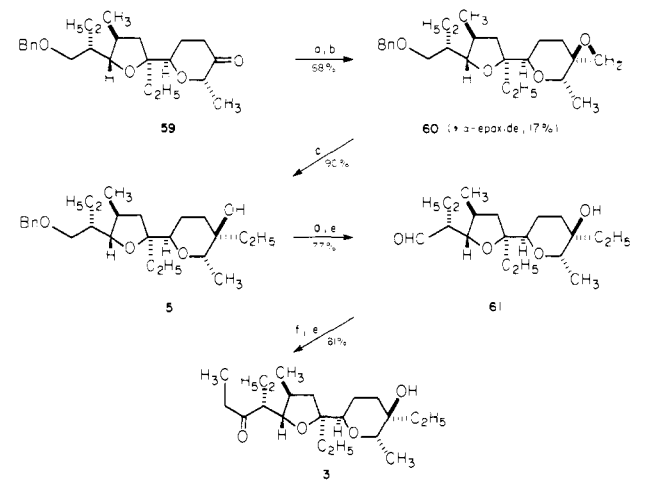
As described previously,[29] it was not possible to alter dramatically the stereochemical outcome of the enolization of α-heterosubstituted esters, and hence the more convenient THF conditions were used in these ester enolate Claisen rearrangements (Scheme IX). In this manner, the acid **25** resulted in the formation of the readily separable isomeric esters **48** and **49**, while the C14 epimer **39**[16] afforded the isomeric esters **50** and **51**. Although the yields of even the major diastereoisomers **49** and **51** were modest, this crucial step lent credability to the convergent synthetic scheme. Subsequent transformation of these esters individually to the projected alcohols **7** and **56–58** proceeded in excellent yields. With all four of the diastereoisomers in hand, it was now possible, through comparison to the natural degradation product **7**, to define completely their stereochemistry. The synthetic stereoisomer that was identical with the degradation product **7** is that derived from the major Claisen isomer **49** from the furanoid acid **25** which itself was the major Claisen isomer when

Scheme IX. Synthesis of the Degradation Product 7[a]



[a] (a) $(COCl)_2$, C_6H_6, DMF(cat); (b) *n*-BuLi, THF; (c) LDA, THF, Me_3SiCl; OH^-; CH_2N_2, ether; (d) H_2, Ni(Ra), EtOAc; (e) DIBAL, ether; -78 °C; (f) $(C_6H_5)_3P{=}CH_2$, THF; (g) 10% HCl, THF.

Scheme X. Completion of the Synthesis of Right-Side Ketone 3[a]



[a] (a) $(C_6H_5)_3P{=}CH_2$, THF; (b) MCPBA, CH_2Cl_2; (c) $LiMe_2Cu$, ether-pentane; (d) Li, NH_3(l); NH_4Cl; (e) PCC, NaOAc, CH_2Cl_2; (f) C_2H_5MgBr, THF.

the glycal **42** butyrate was enolized in HMPA/THF. Since the naturally derived material **7** is the syn isomer, its minor companion **56** must be from the anti series, as shown. The materials derived from the acid **39** which is formed by ester enolate Claisen rearrangement of the glycal **42** butyrate in THF will be epimeric with those from the acid **25** at C14[16] only, and thus, the major isomer must be the syn alcohol **58** and the minor is the anti alcohol **57**. This correlation served to assign the stereochemical outcome of all of these synthetic transformations and also defined the desired pathway for the construction of intermediate alcohol **7** for use in the completion of the synthesis of the ketone **3**.

The final stages of the ketone **3** synthesis (Scheme X) entailed essentially the introduction of two ethyl groups. The first of these, which transformed the secondary alcohol of the pyran ring of the intermediate **7** to the designated tertiary alcohol, required some attention to stereochemistry. Direct addition of organometallic reagents to the derived ketone **59** (Me_2SO, $(COCl)_2$, Et_3N, CH_2Cl_2; 94%) led as expected to a mixture of tertiary alcohols in which the undesired equatorial hydroxyl group predominated.[35] Thus, intermolecular attack of the carbonyl group takes place on the β-face of the pyran ring so as to avoid the steric hindrance of the adjacent axial methyl group. On the other hand, when the ketone **59** was first converted to the exo methylene olefin, oxidation with *m*-chloroperbenzoic acid then afforded a mixture of epoxides in which the β-epoxide **60** was the major component. Subsequent cleavage of this isomer then led to the axial tertiary alcohol **5** which was identical with the same intermediate obtained during degradation of lasalocid A (X537A). Transformation of this alcohol **5** to the ketone **3** followed standard protocol and provided the last link for the total synthesis of lasalocid A (X537A). Modification and adaptation of this synthetic strategy for the construction of other polyether antibiotics as well as some of their potentially therapeutically interesting analogues is under active investigation.

Experimental Section[36]

I. Degradation and Aldol-Type Reconstitution of Lasalocid A (X537A). Pyrolysis of Benzyl Lasalocid A. Benzyl 6-[(4-oxo-3(*R*)-methyl)butyl]-2-hydroxy-3-methylbenzoate (2) and 4(*R*)-[5(*S*)-Ethyl-3-(*S*)-methyl-5-(5(*R*)-ethyl-5-hydroxy-6(*S*)-methyl-2(*R*)-tetrahydro-

(35) Unpublished results from this laboratory by L. Courtney.

(36) Boiling points are uncorrected. Melting points were determined with a Hoover capillary melting point apparatus and are uncorrected. Infrared (IR) spectra were determined on a Perkin-Elmer 237B, 737B, 1310, or a Beckman 4210 infrared spectrometer. Proton nuclear magnetic resonance (^1H NMR) spectra were recorded on Varian T-60, EM-390, or Bruker WM-500 spectrometers. Chemical shifts are reported as δ values in parts per million relative to tetramethylsilane (δ 0.0) as an internal standard. Optical rotations were measured in 1-dm cells of 1-mL capacity, using a Perkin-Elmer Model 141 or a JASCO Model DIP-181 polarimeter. Chloroform, when used as a solvent for optical rotation determinations, was filtered through neutral alumina immediately prior to use. Analytical vapor-phase chromatographic (VPC) analyses were performed on a Hewlett-Packard 5750 gas chromatograph, equipped with a flame ionization detector, using helium carrier gas at a flow rate of 2 mL/min, preparative VPC on a Varian 930, equipped with a thermal conductivity detector, at a flow rate of 60 mL/min. The indicated liquid phase was absorbed on 60–80 mesh Chromosorb W AM DMCS. Analytical thin-layer chromatography (TLC) was conducted on 2.5 × 10 cm precoated TLC plates, silica gel 60 F-254, layer thickness 0.25 mm, manufactured by E. Merck and Co., Darmstadt, Germany. Preparative TLC was conducted on 20 × 20 cm glass plates coated in this laboratory with a 0.6-mm thickness of silica gel G "for TLC acc. to Stahl" (5–25 μm) manufactured by E. Merck and Co., Darmstadt, Germany. Silica gel columns for chromatography utilized E. Merck "Silica Gel 60", 70–230 mesh ASTM; flash chromatography used 230–400 mesh ASTM. Alumina refers to the Brockmann Activity I-Neutral material manufactured by M. Woelm. "Dry" solvents were distilled shortly before use from an appropriate drying agent. Ether and tetrahydrofuran (THF) were distilled under dry argon from sodium metal in the presence of benzophenone. *n*-Pentane was distilled from sodium metal under argon. Benzene and toluene were distilled from phosphorus pentoxide. Methanol was distilled from magnesium methoxide. Hexamethylphosphoramide (HMPA) was distilled at ~1.0 mm of Hg from pulverized calcium hydride. Triethylamine and diisopropylamine were distilled under argon from sodium benzophenone immediately prior to use. Pyridine and hexamethyldisilazane were all distilled before use from calcium hydride. Ammonia was distilled from the tank and then from a blue lithium solution. Other reagents were purified as follows: oxalyl chloride was distilled under argon; *n*-butanoyl chloride was heated at reflux for 3 h with phosphorus pentachloride and then distilled, and the distillate was treated with quinoline and redistilled; methyl iodide was distilled from phosphorus pentoxide immediately before use; tris(dimethylamino)phosphine (TDAP) was distilled under argon before use; chloromethyl methyl ether was dried for several hours over anhydrous calcium chloride, decanted and stirred briefly with anhydrous potassium carbonate, and then distilled under argon from anhydrous calcium chloride. Ammonium chloride was dried at 75 °C under vacuum (1 mmHg) over phosphorus pentoxide for at least 12 h. All other reactants and solvents were "Reagent Grade" unless described otherwise. "Ether" refers to anhydrous diethyl ether which is supplied by Mallinckrodt and Baker. "Petroleum ether" refers to the Analyzed Reagent grade hydrocarbon fraction, bp 35–60 °C, which is supplied by J. T. Baker Co., Phillipsburg, NJ, and was not further purified. Reactions were run under an argon atmosphere arranged with a mercury bubbler so that the system could be alternately evacuated and filled with argon and left under a positive pressure. Syringes and reaction flasks were dried at least 12 h in an oven (at 120–140 °C) and cooled in a desiccator over anhydrous $CaSO_4$ prior to use. Mass spectral analyses were performed by Dr. Kai Fang, UCLA, Los Angeles, CA, or Susan Rottschaefer, Caltech, Pasadena, CA. Elemental combustion analyses were performed by Spang Microanalytical Laboratory, Eagle Harbor, MI, or Jan Mitchell, Caltech, Pasadena, CA.

pyranyl)-2(*S*)-tetrahydrofuryl]hexan-3-one (3). Evaporative distillation of 2.77 g (3.7 mmol) of benzyl lasalocid A at 0.01 mmHg pressure (Kugelrohr oven temperature at 210–220 °C) gave a clear oil which was flash chromatographed on 100 g of silica gel with 10% ethyl acetate in petroleum ether to give 0.9 g (74%) of the aldehyde (**2**) and 1.1 g (84%) of the ketone (**3**).

Aldehyde **2**: $[\alpha]^{23}_D$ −15.4° (*c* 1.00, $CHCl_3$); IR ($CHCl_3$) 1715, 1660, 1620, 1465, 1420, 1390, 1300, 1250, 1150 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.92 (d, 3 H, *J* = 7 Hz, CH_3), 2.20 (s, 3 H, $ArCH_3$), 2.81 (bt, 2 H, *J* = 7 Hz, $ArCH_2C$), 5.36 (s, 3 H, CO_2CH_2), 6.56, 7.14 (2d, 2 H, *J* = 7.5 Hz, 2 ArH), 9.37 (d, 1 H, *J* = 1.5 Hz, CHO), 11.43 (s, 1 H, OH). Anal. Calcd for $C_{20}H_{22}O_4$: C, 73.60; H, 6.79. Found: C, 73.56; H, 6.70.

Ketone **3**: $[\alpha]^{24}_D$ −19.6° (*c* 1.02, $CHCl_3$); IR ($CHCl_3$) 3600, 1710, 1460, 1385, 1135, 1100, 1060, 960 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.20 (d, 3 H, *J* = 6 Hz, CH_3CHOC), 3.74 (q, 1 H, *J* = 6 Hz, $CHCH_3OC$); ^{13}C NMR ($CDCl_3$) δ 6.10, 7.08, 7.73, 12.15, 13.84, 16.37, 20.79, 20.98, 28.33, 29.04, 30.15, 36.64, 36.84, 40.41, 57.11, 70.57, 72.65, 76.55, 84.08, 85.58, 213.28. Anal. Calcd for $C_{21}H_{38}O_4$: C, 71.15; H, 10.80. Found: C, 71.14; H, 10.71.

Benzyl Lasalocid A. To a stirred solution of 0.3 mmol of LDA in 0.5 mL of dry ether at −78 °C under an argon atmosphere was added dropwise a solution of 35.5 mg (0.1 mmol) of the right-half ketone **3** in 0.7 mL of dry ether. After 5 min, the pale yellow solution was allowed to warm to 0 °C. After 10 min, 430 μL (0.3 mmol) of a 0.7 M solution of anhydrous zinc chloride in ether was added dropwise and the resulting heterogeneous mixture was stirred for 20 min at 0 °C. A solution of 65.3 mg (0.2 mmol) of the left-half aldehyde **2** in 0.4 mL of ether was then added rapidly through a cannula. A voluminous white precipitate was immediately formed. The resulting mixture was stirred for 5 min at 0 °C and then quenched by the addition of a mixture of saturated aqueous NH_4Cl and ether. The aqueous phase was separated and then extracted 3 times with ether, and the combined ethereal phases were washed with saturated aqueous NaCl and dried ($MgSO_4$). Removal of the solvent under reduced pressure and high-pressure liquid chromatography of the residue on silica gel with a solvent gradient of 5–10% ethyl acetate in petroleum ether allowed the separation of four aldol products in a combined yield of 62.4% (95% based on unrecovered ketone **3**) and a ratio of 54:32:10:4.

First Aldol Product: 23.0 mg (33.8%); R_f 0.22 (20% ethyl acetate in petroleum ether); ^1H NMR ($CDCl_3$) δ 2.19 (s, 3 H, Ar CH_3), 5.38 (s, 2 H, CO_2CH_2), 6.60, 7.11 (2d, 2 H, *J* = 8 Hz, 2 ArH), 11.31 (s, 1 H, ArOH); identical with authentic benzyl lasalocid A.

Second Aldol Product: 13.5 mg; R_f 0.16 (same eluent); ^1H NMR ($CDCl_3$) δ 2.19 (s, 3 H, $ArCH_3$), 5.39 (s, 2 H, CO_2CH_2), 6.62, 7.13 (2d, 2 H, *J* = 8 Hz, 2 ArH), 11.28 (s, 1 H, OH).

Third Aldol Product: 4.3 mg; R_f 0.10 (same eluent); ^1H NMR ($CDCl_3$) δ 2.21 (s, 3 H, $ArCH_3$), 5.40 (s, 2 H, CO_2CH_2), 6.62, 7.13 (2d, 2 H, *J* = 8 Hz, 2 ArH), 11.31 (s, 1 H, OH).

Fourth Aldol Product: 1.7 mg; R_f 0.06 (same eluent).

When only 1.1 equiv of aldehyde **2** was used and the reaction time was 4 min at 0 °C, the yield of the aldol products was 46.3% and the ratio 53:28:12:6.

Lasalocid A (1). To a stirred solution of 290 mg (0.43 mmol) of benzyl lasalocid A in 5 mL of absolute ethanol was added 30 mg of 10% palladium on carbon. The resulting mixture was stirred at room temperature under hydrogen atmosphere for 3 h. The catalyst was then removed by filtration and washed with three 5-mL portions of dichloromethane. The combined filtrates were concentrated under reduced pressure.

The above residue was dissolved in 5 mL of dichloromethane and 300 mg of solid Na_2CO_3 was added. The resulting mixture was stirred at room temperature for 10 h and then filtered. Concentration of the filtrate under reduced pressure gave 260 mg (100%) of the sodium salt of lasalocid A.

The spectral properties of this compound were identical with those of the authentic sodium salt of lasalocid A.

4(*R*)-[5(*S*)-Ethyl-3(*S*)-methyl-5-(5(*R*)-ethyl-5-(trimethylsiloxy)-6-(*S*)-methyl-2(*R*)-tetrahydropyranyl)-2(*S*)-tetrahydrofuryl]-3-(trimethylsiloxy)hex-2-ene. To a stirred solution of 11.22 mmol of potassium hexamethyldisilazide in 20 mL of dry THF at −78 °C under argon was added a solution of 1.325 g (3.74 mmol) of the ketone **3** in 3 mL of dry THF. After 10 min the reaction mixture was treated with 2.8 mL (11.2 mmol of Me_3SiCl) of the supernatant centrifugate from a mixture of 4.2 mL of trimethylchlorosilane and 1.4 mL of dry triethylamine. Cooling was then discontinued and the resulting mixture was stirred at room temperature for 90 min, diluted with 300 mL of ether, washed with two 80-mL portions of water and 40 mL of saturated aqueous NaCl, and then dried (Na_2SO_4). Removal of the solvents under reduced pressure and evaporative distillation of the residue afforded 1.76 g (94%) of the silyl enol ether: evaporative distillation 190 °C (0.05 mmHg); $[\alpha]^{22}_D$ +13.0° (*c* 1.30, $CHCl_3$); IR ($CHCl_3$) 1680, 1465, 1255, 1060, 845 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.15 (s, 9 H, $(CH_3)_3SiOC{=}$), 0.20 (s, 9 H, $(CH_3)_3SiOCC_3$), 0.87 (bt, 9 H, *J* = 7 Hz, CH_3CH_2), 0.92 (d, 3 H, *J* = 7 Hz, CH_3CHCC), 1.15 (d, 3 H, *J* = 7 Hz, CH_3CHOC), 1.50 (d, 3 H, *J* = 7 Hz, $CH_3CH{=}$), 3.83 (q, 1 H, *J* = 7 Hz, CH_3CHOC), 4.57 (q, 1 H, *J* = 7 Hz, $CH_3CH{=}$). Anal. Calcd for $C_{27}H_{54}O_4Si_2$: C, 65.00; H, 10.91. Found: C, 64.93; H, 10.85.

Methyl 2(*R*)-[5(*S*)-ethyl-3(*S*)-methyl-5-(5(*R*)-ethyl-5-(trimethylsiloxy)-6(*S*)-methyl-2(*R*)-tetrahydropyranyl)-2(*S*)-tetrahydrofuryl]butanoate (4). A solution of 0.96 g (1.92 mmol) of the above silyl enol ether in 25 mL of dry methanol and 4 mL of dry dichloromethane at −78 °C was treated with ozone until it was faintly blue. The reaction mixture was then treated with two 1.2-g (31.7 mmol) portions of sodium borohydride. Cooling was then discontinued, and the resulting suspension was stirred at room temperature for 2 h and then concentrated under reduced pressure. The residue was taken up in 50 mL of saturated aqueous NH_4Cl and then acidified (pH ≃ 2) with 10% aqueous HCl. The aqueous phase was extracted with four 40-mL portions of dichloromethane and the combined organic extracts were dried (Na_2SO_4) and then concentrated under reduced pressure. Treatment of the residue with diazomethane in ether, and then chromatography of the resulting ester on 50 g of silica gel with 10% ether–petroleum ether gave 599 mg (72%) of the methyl ester **4**: evaporative distillation 140–145 °C (0.001 mmHg); $[\alpha]^{22}_D$ −6.3° (*c* 1.01, $CHCl_3$) δ 0.020 (s, 9 H, $(CH_3)_3Si$), 0.83 (bt, 9 H, *J* = 7 Hz, CH_3CH_2), 0.90 (d, 3 H, *J* = 6 Hz, CH_3CHCC), 1.15 (d, 3 H, *J* = 7 Hz, CH_3CHOC), 3.67 (s, 3 H, CO_2CH_3), 3.83 (q, 1 H, *J* = 7 Hz, CH_3CHOC). Anal. Calcd for $C_{23}H_{44}O_5Si$: C, 64.44; H, 10.35. Found: C, 64.40; H, 10.26.

2(*S*)-[5(*S*)-Ethyl-3(*S*)-methyl-5-(5(*R*)-ethyl-5-(trimethylsiloxy)-6-(*S*)-methyl-2(*R*)-tetrahydropyranyl)-2(*S*)-tetrahydrofuryl]butan-1-ol. To a stirred ice-cooled solution of 600 mg (1.4 mmol) of the methyl ester **4** in 4 mL of dry ether under argon was added 160 mg (16.8 mmol of hydride) of lithium tetrahydridoaluminate. After 1 h the reaction mixture was cautiously treated with 0.16 mL of water, 0.16 mL of 15% aqueous NaOH, and then 0.48 mL of water, stirred for 0.5 h and then filtered. Removal of the solvent under reduced pressure afforded 557 mg (99%) of the corresponding primary alcohol: evaporative distillation 150–155 °C (0.001 mmHg); $[\alpha]^{22}_D$ +7.83° (*c* 1.06, $CHCl_3$); IR ($CHCl_3$) 3520, 1460, 1255, 1100, 1050, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.13 (s, 9 H, $(CH_3)_3Si$), 0.87 (bt, 9 H, *J* = 7 Hz, CH_3CH_2), 0.93 (d, 3 H, *J* = 6 Hz, CH_3CHCC), 1.17 (d, 3 H, *J* = 7 Hz, CH_3CHOC), 3.80 (q, 1 H, *J* = 7 Hz, CH_3CHOC). Anal. Calcd for $C_{22}H_{44}O_4Si$: C, 65.95; H, 11.07. Found: C, 66.00; H, 11.06.

2(*S*)-[5(*S*)-Ethyl-3(*S*)-methyl-5-(5(*R*)-ethyl-5-hydroxy-6(*S*)-methyl-2(*R*)-tetrahydropyranyl)-2(*S*)-tetrahydrofuryl]butan-1-ol. To a stirred solution of 264 mg (0.66 mmol) of the above alcohol in 8 mL of dry THF was added a solution of 430 mg (1.64 mmol) of tetra-*n*-butylammonium fluoride in 3.2 mL of dry THF. After 4 h, the reaction mixture was diluted with 70 mL of ether, then washed with two 30-mL portions of saturated aqueous $NaHCO_3$ and 30 mL of saturated aqueous NaCl, and then dried ($MgSO_4$). Removal of the solvents and chromatography of the residue on 10 g of silica gel with 35% ethyl acetate in cyclohexane afforded 196 mg (92%) of the corresponding diol: mp 74–75 °C (hexane); $[\alpha]^{24}_D$ +14.2° (*c* 1.16, $CHCl_3$); IR ($CHCl_3$) 3600, 3500, 1460, 1380, 1100, 1050, 950 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.96 (d, 3 H, *J* = 6 Hz, CH_3CHCC), 1.22 (d, 3 H, *J* = 6 Hz, CH_3CHOC). Anal. Calcd for $C_{19}H_{36}O_4$: C, 69.47; H, 11.05. Found: C, 69.37; H, 10.96.

Benzyl 2(*S*)-[5(*S*)-Ethyl-3(*S*)-methyl-5-(5(*R*)-ethyl-5-hydroxy-6-(*S*)-methyl-2(*R*)-tetrahydropyranyl)-2(*S*)-tetrahydrofuryl]butyl Ether (5). To a stirred suspension of 22 mg (0.6 mmol) of potassium hydride in 2 mL of dry THF at 0 °C under argon was added a solution of 164 mg (0.5 mmol) of the above diol in 1 mL of dry THF and then 0.09 mL (0.75 mmol) of benzyl bromide. The resulting mixture was stirred for 2 h at room temperature, treated with 5 mL of saturated aqueous $NaHCO_3$, and then diluted with 60 mL of ether. The organic phase was separated and washed with two 20-mL portions of saturated aqueous $NaHCO_3$ and 20 mL of saturated aqueous NaCl and then dried ($MgSO_4$). After removal of the solvents at reduced pressure, chromatography of the residue on 20 g of silica gel with 35% ether–petroleum ether provided 172 mg (82%) of the monobenzyl ether **5**: evaporative distillation 180–190 °C (0.005 mmHg); $[\alpha]^{22}_D$ +21.8° (*c* 1.40, $CHCl_3$); IR ($CHCl_3$) 3580, 1460, 1380, 1120, 1100, 1050, 960 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.96 (d, 3 H, *J* = 6 Hz, CH_3CHCC), 1.18 (d, 3 H, *J* = 6 Hz, CH_3CHOC), 3.76 (q, 1 H, *J* = 6 Hz, $CHCH_3OC$), 4.47 (s, 2 H, $C_6H_5CH_2$), 7.33 (b s, 5 H, C_6H_5). Anal. Calcd for $C_{26}H_{42}O_4$: C, 74.60; H, 10.11. Found: C, 74.50; H, 10.01.

Benzyl 2(*S*)-[5(*S*)-Ethyl-3(*S*)-methyl-5-(5(*S*)-hydroxy-6(*S*)-methyl-2(*R*)-tetrahydropyranyl)-2(*S*)-tetrahydrofuryl]butyl Ether (7). To a stirred solution of 60 mg (0.30 mmol) of potassium hydride in 0.5 mL of dry THF under argon was added a solution of 85 mg (0.20 mmol)

of the alcohol **5** in 0.5 mL of dry THF, followed by 0.06 mL (1.0 mmol) of carbon disulfide. After 5 h, the reaction mixture was treated with 0.025 mL (0.4 mmol) of methyl iodide and after an additional 30 min, the mixture was diluted with 40 mL of ether, washed with three 15-mL portions of water and 15 mL of saturated aqueous NaCl, and then dried ($MgSO_4$). Removal of the solvents gave a yellow oil which on preparative gas chromatography (column: 4%, SE-30, 0.25 in. × 6 ft, 220 °C, injector port 300 °C) as a 50% solution in ether gave 38 mg of the olefin mixture (exo:endo = 1:5) **6**.

A solution of the above residue in 20 mL of dry methanol and 2 mL of dry dichloromethane at −78 °C was treated with ozone until it was faintly blue. The reaction mixture was then treated with two 100-mg (2.6 mmol) portions of sodium borohydride. Cooling was then discontinued and the resulting suspension was stirred at room temperature for 10 h and then concentrated under reduced pressure. The residue was taken up in 30 mL of saturated aqueous NH_4Cl. The aqueous phase was separated and then extracted with three 15-mL portions of ether. The combined ethereal phases were washed with 15 mL of saturated aqueous NaCl and then dried ($MgSO_4$). Removal of the solvent and chromatography of the residue on 10 g of silica gel with 25% ethyl acetate–petroleum ether provided 3.5 mg (4.5%) of the alcohol **7**: evaporative distillation 140–150 °C (0.005 mmHg); $[\alpha]^{24}_D$ +25.8° (*c* 0.96, $CHCl_3$); IR ($CHCl_3$) 3650, 3480, 1470, 1400, 1120, 1080 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.83, 0.92 (2t, 6 H, J = 6 Hz, CH_3CH_2), 0.97 (d, 3 H, J = 6 Hz, CH_3CHCC), 1.17 (d, 3 H, J = 6 Hz, CH_3CHOC), 4.46 (s, 2 H, $C_6H_5CH_2$), 7.32 (b s, 5 H, C_6H_5). Anal. Calcd for $C_{24}H_{38}O_4$: C, 73.81; H, 9.81. Found: C, 73.76; H, 9.79.

II. Synthesis of the Left-Side Aldehyde 2. Citronellyl Acetate (10). To a stirred solution of 435 mL of 0.5 M 9-BBN in THF (0.2175 mol) at 0 °C was added 30.0 g (0.217 mol) of (*R*)-(−)-citronellene over 45 min. The resulting solution was allowed to warm to room temperature; after 2 h, 130 mL of absolute ethanol and 43.5 mL of 6 N aqueous NaOH were added. The resulting mixture was cooled to 0 °C and 84 mL of 30% H_2O_2 added over 30 min. The resulting mixture was refluxed for 1 h and then cooled to 0 °C, and the aqueous phase saturated with 200 g of K_2CO_3. The organic phase was separated and then dried ($MgSO_4$). Removal of solvent under reduced pressure, gave a residue which upon distillation (110–115 °C (25 mmHg)) gave 24.1 g of a mixture of citronellol and 1,5-cyclooctadiol.

The above mixture was dissolved in 600 mL of dry dichloromethane, and the resulting solution cooled to 0 °C. To this stirred solution was added 25.9 mL of triethylamine and 13.1 mL of acetyl chloride. After 1 h, 400 mL of saturated aqueous $NaHCO_3$ was added, and the organic phase separated and then dried ($MgSO_4$). Removal of solvent under reduced pressure and flash chromatography of the residue with 10% ethyl acetate in petroleum ether gave a residue which upon evaporative distillation (150 °C (25 mmHg)) gave 23.6 g of citronellyl acetate **10** (54% from citronellene): ^1H NMR ($CDCl_3$) δ 0.91 (d, 3 H, J = 5.5 Hz, CH_3CH); 1.62 and 1.68 (2s, 3 H (2×), $=C(CH_3)_2$), 2.03 (s, 3 H, CH_3CO_2), 4.10 (t, 2 H, J = 6 Hz, CH_2OAc), 5.10 (m, 1 H, $=CH$).

6-Acetoxy-4(*R*)-methyl Hexanoic Acid (9). A solution of 10.0 g (50 mmol) of citronellyl acetate (**10**) in 500 mL of dichloromethane was cooled to −78 °C and a stream of ozone in oxygen bubbled in until the solution remained blue for 10 min. The solution was then purged with a stream of nitrogen to remove excess ozone and the solvent removed under reduced pressure. The residual ozonide was dissolved in 250 mL of acetone and the resulting solution cooled to 0 °C. A solution of 8 N H_2CrO_4 in acetone was then added slowly until the solution remained brown. The reaction mixture was then poured into 800 mL of water and the resulting mixture extracted with 500-, 300-, and 200-mL portions of dichloromethane. The combined organic phases were dried ($MgSO_4$) and concentrated under reduced pressure. Evaporative distillation of the residue (160 °C (0.5 mmHg)) gave 7.4 g (78%) of the title acid. The yield on a 5-mmol scale was 96%: evaporative distillation 150–160 °C (0.5 mmHg); $[\alpha]^{25}_D$ +2.61° (c 3.52, $CHCl_3$); IR (neat) 3200, 1740, 1710, 1380, 1250 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.93 (s, 3 H, J = 5 Hz, CH_3CH), 1.2–1.9 (m, 5 H, CH_2CHCH_2), 2.01 (s, 3 H, CH_3CO), 2.37 (t (dd), 2 H, J = 7 Hz, CH_2CO_2H), 4.10 (t (dd), 2 H, J = 6 Hz, CH_2OAc). Anal. Calcd for $C_9H_{16}O_4$: C, 57.43; H, 8.57. Found: C, 57.45; H, 8.62.

3(*S*)-Methyl-4-pentenyl Acetate. To a solution of 3.002 g (15.94 mmol) of the acid **9** in 105 mL of benzene and 0.47 mL of pyridine were added 710 mg (3.56 mmol) of cupric acetate monohydrate and 12.84 g (28.96 mmol) of lead tetraacetate. The resulting mixture was refluxed for 16 h, and 6.0 g (13.53 mmol) of lead tetraacetate was then added and refluxing continued. After 6 h, the reaction mixture was cooled to room temperature and then poured into 150 mL of water. The organic phase was then separated, washed with three 150-mL portions of water, extracted with two 100-mL portions of saturated aqueous $NaHCO_3$, and then dried ($MgSO_4$). Removal of solvent at atmospheric pressure through a 30-cm Vigreux column gave a residue which was fractionally distilled (100–105 °C (25 mmHg)) to give 1.518 g (67%) of the 3(S)-methyl-4-pentenyl acetate: $[\alpha]^{25}_D$ +19.9° (*c* 1.18, $CHCl_3$); IR (neat) 2990, 1742, 1380, 1245, 1080, 920 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.00 (d, 3 H, J = 6.5 Hz, CH_3CH), 1.63 (d t, 2 H, J = J' = 5.5 Hz, $HCHCH_2CH_2O$), 2.00 (s, 3 H, CH_3CO), 2.25 (m (dtq), 1 H, $=CHCH(CH_3)CH_2$), 4.07 (t, 2 H, J = 6 Hz, CH_2CH_2O), 4.95 (m, 2 H, $CH=CH_aH_b$), 5.70 (m, 1 H, $HCCH=CH_aH_b$). Anal. Calcd for $C_8H_{14}O_2$: C, 67.57; H, 9.92. Found: C, 67.63; H, 9.89.

The bicarbonate extracts were acidified to pH 2 and extracted with two 100-mL portions of dichloromethane. The combined extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Evaporative distillation of the residue (100 °C (0.005 mmHg)) gave 759 mg (26%) of the acid 9.

3(*S*)-Methyl-4-penten-1-ol. To a stirred solution of 4.69 g (33 mmol) of the above acetate in 28 mL of methanol was added 30 mg of sodium methoxide, and the resulting solution stirred at room temperature. After 8 h, the reaction mixture was poured into 150 mL of ether and the resulting mixture washed with two 50-mL portions of water and then dried ($MgSO_4$). Removal of solvent by distillation at atmospheric pressure through a 30-cm Vigreux column gave a residue which upon evaporative distillation (80 °C (25 mmHg)) gave 3.26 g (99%) of the corresponding alcohol: $[\alpha]^{25}_D$ +29.22° (*c* 1.54, $CHCl_3$); IR (neat) 3350, 1655, 1060, 1005, 920 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.01 (d, 3 H, J = 4.5 Hz, CH_3), 1.53 (dt, 2 H, J = J' = 4.5 Hz, $HCCH_2CH_2$), 2.28 (m, 1 H, $=CH=CH(CH_3)CH_2$), 4.97 (m, 2 H, $CH=CH_aH_b$), 5.70 (m, 1 H, $CH=CH_aH_b$).

5-Bromo-3(*S*)-methyl-1-pentene (13). To a stirred solution of 4.504 g (44.97 mmol) of the above alcohol in 100 mL of dichloromethane at 0 °C were added 3.8 mL (49.1 mmol) of methanesulfonyl chloride and 6.91 mL (49.6 mmol) of triethylamine sequentially, and the resulting mixture stirred at 0 °C for 15 min. The reaction mixture was then poured into 100 mL of saturated aqueous $NaHCO_3$ and the resulting mixture stirred vigorously for 10 min. The organic phase was separated, dried ($MgSO_4$), and then concentrated under reduced pressure. The residue was dissolved in 130 mL of dry THF and 5.87 g (67.6 mmol) of anhydrous lithium bromide was added. The resulting mixture was refluxed for 4 h and then cooled to room temperature. It was poured into 300 mL of pentane, and the organic phase washed with two 100-mL portions of saturated $NaHCO_3$ and five 100-mL portions of water and then dried ($MgSO_4$). Solvent was removed by distillation through a 30-cm Vigreux column at atmospheric pressure. Evaporative distillation of the residue (70 °C (80 mmHg)) gave 6.28 g (86%) of the bromide **13**: $[\alpha]^{25}_D$ +32.7° (*c* 2.74, CH_3OH); IR (neat) 1655, 1470, 1435, 1270, 1015, 925 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.01 (d, 3 H, J = 5 Hz, CH_3), 1.80 (dt, 2 H, J = J' = 5 Hz, CH_2CH_2Br), 2.35 (m, 1 H, J = 5 Hz, $=CHCH(CH_3)CH_2$), 3.36 (t, 2 H, J = 5 Hz, CH_2CH_2Br), 5.02 (m, 2 H, $HC=CH_aH_b$), 5.64 (m, 1 H, $HCCH=CH_aH_b$).

1,1-Dimethyl-2-(3(*R*)-methyl-4-pentenyl)oxirane. To a stirred mixture of 18.99 g (110 mmol) of *m*-chloroperbenzoic acid and 15.19 g (180 mmol) of sodium bicarbonate in 450 mL of CH_2Cl_2 at 0 °C was added, in one portion, 12.5 g (90.4 mmol) of (*R*)-(−)-citronellene. The reaction mixture was stirred for 1.5 h at 0 °C and was then quenched by the addition of 150 mL of 10% aqueous Na_2SO_3. The resulting mixture was stirred for 15 min and then 25 g of $NaHCO_3$ in 50 mL of water was added. The organic layer was separated and then washed with two 200-mL portions of water and then dried ($MgSO_4$). The solvent was removed under reduced pressure to give a residue which was evaporatively distilled (150 °C (25 mmHg)) to give 11.2 g (80%) of the oxiranes: ^1H NMR ($CDCl_3$) δ 1.00 (d, 3 H, J = 6 Hz, $CHCH_3$), 1.25 (s, 3 H, CH_3), 1.30 (s, 3 H, CH_3), 1.47 (m, 4 H, $CHCH_2CH_2CHO$), 2.15 (m, 1 H, $H_2C=CHCH$), 2.80 (m, 1 H, CH_2CHO), 4.93 (m, 2 H, $H_2C=CH$), 5.70 (m, 1 H, $H_2C=CHCH$). Anal. Calcd for $C_{10}H_{18}O$: C, 77.87; H, 11.76. Found: C, 77.81; H, 11.65.

1-Oxo-1-phenyl-4(*R*)-methyl-5-hexene (11). To a stirred solution of 15.0 g (97.24 mmol) of the above epoxides in 450 mL of ether at 0 °C was added, in portions over 1.5 h, 26.6 g (116.7 mmol) of paraperiodic acid. The reaction mixture was then allowed to warm to room temperature. After 5 h, 23 g of $NaHCO_3$ was added and the mixture was stirred for 2 h. The reaction mixture was then dried ($MgSO_4$) and filtered.

The ethereal solution obtained above was cooled to 0 °C, and 200 mL of a 2.0 M solution of phenylmagnesium bromide in ether was slowly added. The reaction mixture was stirred at 0 °C for 1 h and then at room temperature overnight. It was then quenched by the careful addition of 50 mL of saturated aqueous NH_4Cl solution, followed by 300 mL of water and enough 3 N aqueous HCl to dissolve all the precipitated salts. The ethereal layer was separated and then washed consecutively with a 200-mL portion of each of the following: saturated aqueous NH_4Cl solution, saturated aqueous $NaHCO_3$ solution, saturated aqueous NaCl.

The organic layer was dried ($MgSO_4$) and then the solvent was removed under reduced pressure to give an oily residue.

To a stirred solution of the above oily residue in 450 mL of CH_2Cl_2 were added 2.6 g of sodium acetate and 74 g of a 1:1 (w/w) mixture of Celite and pyridinium chlorochromate. The reaction mixture was stirred at room temperature for 5 h, poured into 1.2 L of dry ether, and then filtered through Celite. Removal of the solvent under reduced pressure and flash chromatography of the residue on 100 g of silica gel with 10% ether in pentane gave 12.2 g (67%) of the phenyl ketone **11**: evaporative distillation 60 °C (1 mmHg); $[\alpha]^{25}_D$ +10.1° (*c* 1.76, $CHCl_3$); IR ($CHCl_3$) 1690, 1610, 1590, 1460, 920 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.05 (d, 3 H, J = 7.5 Hz, $CHCH_3$), 1.73 (m, 2 H, $CHCH_2CH_2$), 2.16 (m, 1 H, $H_2C{=}CHCH$), 2.90 (t, 2 H, J = 7.5 Hz, $COCH_2CH_2$), 4.92 (m, 2 H, $H_2C{=}CH$), 5.67 (m, 1 H, $H_2C{=}CHCH$), 7.4 (m, 3 H, Ar*H*), 7.92 (m, 2 H, Ar*H*). Anal. Calcd for $C_{13}H_{16}O$: C, 82.94; H, 8.57. Found: C, 83.08; H, 8.45.

3(*R*)-Methyl-4-penten-1-ol (15) (Method A). A solution of 8.0 g (42.5 mmol) of the ketone **11** and 8.5 g (157 mmol) of sodium methoxide in 250 mL of dry ethyl formate was stirred at room temperature overnight and then acidified to pH 4 with acetic acid. The reaction mixture was diluted with 1 L of ether and then extracted with two 400-mL portions of a 5% aqueous NaOH solution. The combined aqueous extracts were acidified to pH 2 with 6 N aqueous HCl and then extracted with two 400-mL portions of ether. The solvent was then removed under reduced pressure to give an oily residue.

The above residue was dissolved in 175 mL of methanol and 175 mL of pH 4 buffer and then 24.5 g (115 mmol) of sodium metaperiodate was added. The reaction mixture was stirred at room temperature for 7 days and then extracted with three 100-mL portions of dichloromethane. The organic extracts were combined and then washed with three 100-mL portions of 5% aqueous NaOH solution. The combined aqueous extracts were acidified to pH 2 with 6 N aqueous HCl and then extracted with three 100-mL portions of dichloromethane. These final organic extracts were dried ($MgSO_4$), and then the solvent was removed under reduced pressure to afford a residue containing the desired acid and benzoic acid.

The mixture of acids was dissolved in 400 mL of dry ether and 2 g (52.7 mmol) of lithium tetrahydridoaluminate was added. The reaction mixture was stirred at room temperature for 24 h and then 2 mL of water, 2 mL of 15% aqueous NaOH, and 6 mL of water were added successively. After being stirred vigorously for 20 min, the reaction mixture was dried ($MgSO_4$) and then the solvent was removed by atmospheric distillation through a Vigreux column. The residue was then fractionally distilled (60 °C (30 mmHg)) to give 2.107 g (49%) of the alcohol **15**: $[\alpha]^{25}_D$ −28.92° (*c* 2.5, $CHCl_3$); IR (neat) 3350, 1655, 1060, 1005, 920 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.01 (d, 3 H, J = 4.5 Hz, $CHCH_3$), 1.53 (dt, 2 H, J = 4.5 Hz, 4.5 Hz, $CHCH_2CH_2$), 2.28 (m, 1 H, $CHCH_3$), 4.97 (m, 2 H, $H_2C{=}CH$), 5.70 (m, 1 H, $H_2C{=}CH$). Anal. Calcd for $C_6H_{12}O$: C, 71.95; H, 12.08. Found: C, 71.83; H, 12.00.

3(*R*)-Methyl-4-penten-1-ol (15) (Method B). To a stirred solution of 90.51 mmol of LDA in 300 mL of dry THF at −78 °C was added 14.20 g (75.42 mmol) of the ketone **11** in 40 mL of dry THF. The reaction mixture was stirred at −78 °C for 0.5 h and then 19.2 mL of the centrifugate obtained from 30 mL of trimethylsilyl chloride and 10 mL of dry triethylamine were added. After the mixture was stirred at room temperature for 2 h, the reaction mixture was diluted with 1 L of pentane and then washed with two 500-mL portions of water and 500 mL of saturated aqueous NaCl. The organic layer was dried (K_2CO_3, Na_2SO_4), and then the solvent was removed under reduced pressure to give a colorless residue.

The above residue was dissolved in 300 mL of CH_2Cl_2 and cooled to 0 °C. To this solution was added 14.3 g (82.96 mmol) of *m*-chloroperbenzoic acid and 12.6 g (150.84 mmol) of $NaHCO_3$. The resulting mixture was stirred for 1 h at 0 °C and then for 3 h at room temperature. At this time, 1.4 g (8.2 mmol) of *m*-chloroperbenzoic acid was added. The reaction mixture was stirred at room temperature for another 3 h and then quenched by the addition of 100 mL of 10% aqueous Na_2SO_3 and 100 mL of a saturated $NaHCO_3$ solution. The organic layer was separated, washed with two 150-mL portions of water, and then dried ($MgSO_4$). Removal of solvent under reduced pressure gave a colorless residue.

The above residue was dissolved in 350 mL of cold ether and 22.4 g (98.05 mmol) of paraperiodic acid was added. The reaction mixture was stirred at 0 °C for 1 h and then at room temperature for 3 h. The ethereal solution was then washed with two 200-mL portions of a saturated $NaHCO_3$ solution and 200 mL of saturated aqueous NaCl and then dried ($MgSO_4$).

The above ethereal solution was cooled to 0 °C, and then 5.7 g (150.8 mmol) of lithium tetrahydridoaluminate was carefully added. The resulting mixture was stirred at 0 °C for 1 h and was then treated consecutively with 5.7 mL of water, 5.7 mL of a 15% aqueous NaOH solution, and 18 mL of water. The mixture was stirred vigorously for 15 min and then dried ($MgSO_4$). The solvent was removed by atmospheric distillation through a 15-cm Vigreux column, and the resulting residue was evaporatively distilled (up to 120 °C (27 mmHg)) to give 5.44 g (72%) of the alcohol (**15**).

5-Bromo-3(*R*)-methyl-1-pentene (14). To a stirred solution of 21.85 g (218 mmol) of the alcohol **15** and 45.58 mL of dry triethylamine in 520 mL of dry CH_2Cl_2 at 0° was added dropwise 18.56 mL (240 mmol) of methanesulfonyl chloride over a 10–15-min period. The reaction mixture was then stirred for 15 min at 0 °C and then poured into 500 mL of water. The aqueous layer was separated and then extracted with three 250-mL portions of dichloromethane. The organic fractions were dried ($MgSO_4$) and concentrated under reduced pressure to give an oily residue.

The above residue was dissolved in 600 mL of dry THF and then 26.06 g (300 mmol) of lithium bromide was added. The reaction mixture was heated at reflux for 4 h and then poured into 500 mL of water. This was extracted with three 250-mL portions of ether which were then combined and washed with 250 mL of saturated aqueous NaCl. The ethereal layer was dried ($MgSO_4$), and then the solvent was removed by atmospheric distillation through a 25-cm Vigreux column. The residue was then distilled under reduced pressure (68–69 °C (60 mmHg)) to give 25.72 g (77%) of the colorless bromide **14**: $[\alpha]^{25}_D$ −33.7° (*c* 2.76, CH_3OH); IR (neat) 1655, 1470, 1435, 1270, 1015, 925 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.01 (d, 3 H, J = 5 Hz, $CHCH_3$), 1.80 (dt, 2 H, J = 5 Hz, 5 Hz, CH_2CH_2Br), 2.35 (m, 1 H, J = 5 Hz, $CHCH_3$), 3.36 (t, 2 H, J = 5 Hz, CH_2Br), 5.02 (m, 2 H, $H_2C{=}CH$), 5.64 (m, 1 H, $H_2C{=}CH$).

3(*R*)-Methyl-4-pentenoic Acid (12). To a solution of 164 mg (0.84 mmol) of silver tetrafluoroborate in 0.8 mL of Me_2SO was added 123 mg (0.70 mmol) of the bromide **14**. The reaction mixture was stirred at room temperature for 24 h and then 80 μL of dry triethylamine was added. This was stirred for 1 h and then diluted with 20 mL of ether. The mixture was filtered through Celite and the filtrate was washed with three 10-mL portions of water and 10 mL of saturated aqueous NaCl. The organic layer was dried ($MgSO_4$) and then the volume was brought up to 30 mL by the addition of dry ether. To this ethereal solution at 0 °C was added 261 mg (6.9 mmol) of lithium tetrahydridoaluminate. The reaction mixture was stirred at 0 °C for 1.5 h and then 261 μL of water, 261 μL of a 15% aqueous NaOH solution, and 783 μL of water were added consecutively. The mixture was stirred vigorously for 20 min and then dried ($MgSO_4$). Solvent was removed by atmospheric distillation through a Vigreux column to give an oily residue.

The above residue was dissolved in 10 mL of acetone, and then enough Jones reagent was added to give the solution a brown tinge which persisted for longer than 15 min. The reaction mixture was then treated with 20% aqueous NaOH to pH 14 and then diluted with 20 mL of water. The aqueous layer was washed with three 10-mL portions of dichloromethane and then acidified with 6 N aqueous HCl to pH 2. The aqueous layer was extracted with three 10-mL portions of dichloromethane, and then the extracts were combined and dried ($MgSO_4$). The solvent was removed by atmospheric distillation through a Vigreux column and then the residue was evaporatively distilled (80–100 °C (27 mmHg)) to give 30 mg (38%) of the acid **12**: $[\alpha]^{23}_D$ −13.97° (*c* 2.90, $CHCl_3$); IR ($CHCl_3$) 3200, 1710, 1410, 1300, 930 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.12 (d, 3 H, J = 7 Hz, $CHCH_3$), 2.37 (ABXM, 2 H, CH_2CO_2H), 2.6 (m, 1 H, $CHCH_3$), 5.02 (m, 2 H, $H_2C{=}CH$), 5.80 (m, 1 H, $H_2C{=}CH$). Anal. Calcd for $C_6H_{10}O_2$: C, 63.14; H, 8.83. Found: C, 63.21; H, 8.85.

5-*O*-(Triphenylmethyl)-D-ribono-1,4-lactone. To a stirred solution of 8.15 g (55 mmol) of D-ribonic acid, γ-lactone in 400 mL of dry pyridine was added 18.6 g (66.7 mmol) of chlorotriphenylmethane. The resulting solution was heated at 70 °C for 16 h. The cooled reaction mixture was diluted with 600 mL of dichloromethane, washed with three 300-mL portions of 10% aqueous HCl and two 100-mL portions of saturated aqueous $NaHCO_3$, and then dried ($MgSO_4$). Removal of the solvents and chromatography of the residue on 300 g of silica gel with 50% ethyl acetate in petroleum ether afforded 18 g (84%) of the triphenylmethyl ether: IR ($CHCl_3$) 3590, 3020, 1790, 1490, 1450, 1125, 1095 cm^{-1}; ^1H NMR (CD_3COCD_3) δ 3.40 (ABX (ddd), 2 H, $J_{4,5} \simeq J_{4,5'}$ = 3 Hz), 4.27 (d, 1 H, J = 5 Hz, H-3), 4.47 (dd, 1 H, $J \simeq J'$ = 3 Hz, H-4), 4.77 (d, 1 H, J = 5 Hz, H-2), 7.33 (m, 15 H, Ph_3).

2,3-*O*-(Thiocarbonyl)-5-*O*-(triphenylmethyl)-D-ribono-1,4-lactone (17). To a stirred solution of 4 g (10 mmol) of the above diol in 500 mL of dry acetone was added 2.74 g (15.4 mmol) of *N*,*N*′-thiocarbonyldiimidazole. The resulting solution was heated to reflux for 3.5 h. The cooled reaction mixture was concentrated under reduced pressure to half the original volume and then poured into 500 mL of water. The resulting mixture was extracted with three 200-mL portions of dichloromethane. The combined organic phases were washed with two 200-mL portions of saturated aqueous $NaHCO_3$ and two 200-mL portions of water and then dried ($MgSO_4$). Removal of solvents and chromatography of the residue

on 200 g of silica gel with 20% ethyl acetate in petroleum ether afforded 3.5 g (79%) of compound **17**: mp 189–190 °C; $[\alpha]^{25}_D$ −8.9° (*c* 1.7, $CHCl_3$); IR ($CHCl_3$) 1820, 1505, 1460, 1315, 1190, 1010 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.2 (d, 1 H, *J* = 13 Hz, H-2), 3.85 (dd, 1 H, J_1 = 13 Hz, J_2 = 2 Hz, H-3), 4.8 (m, 1 H, H-4), 5.3 (ABX, 2 H, H-5's), 7.3 (s, 15 H, Ph_3). Anal. Calcd for $C_{25}H_{20}O_5S$: C, 69.43; H, 4.66; S, 7.41. Found: C, 69.41; H, 4.71; S, 7.43.

4(*S*)-Hydroxy-5-(triphenylmethoxy)-2-pentenoic Acid 1,4-Lactone (18). A suspension of 25 g of W-4 Raney nickel in 125 mL of acetone was heated to reflux overnight. The solid obtained was resuspended in 300 mL of tetrahydrofuran and 3.08 g (7.1 mmol) of the thiocarbonate **17** was added. The vigorously stirred mixture was heated to reflux for 24 h. The cooled mixture was then filtered and the solid residue washed with two 50-mL portions of tetrahydrofuran. The combined filtrates were concentrated under reduced pressure to give a solid residue which was crystallized from ethyl acetate–hexane to give 1.8 g (73%) of compound **18**: mp 151–153 °C; $[\alpha]^{25}_D$ −50.2° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 1510, 1465, 1180, 1105 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.3 (d, 2 H, *J* = 5 Hz, H-5's), 4.55 (m, 1 H, H-4), 4.95 (m, 1 H, H-3), 6.1 (dd, 1 H, J_1 = 9 Hz, J_2 = 2.5 Hz, H-2), 7.3 (m, 15 H, Ph_3). Anal. Calcd for $C_{24}H_{20}O_3$: C, 80.88; H, 5.66. Found: C, 80.69; H, 5.69.

4(*S*)-Hydroxy-3(*S*)-methyl-5-(triphenylmethoxy)pentanoic Acid 1,4-Lactone (19). To a stirred suspension of 4.97 g (23.5 mmol) of cuprous bromide–dimethyl sulfide complex in 150 mL of ether at 0 °C under argon was slowly added 21.85 mL (40.2 mmol) of a 1.84 M solution of methyllithium in ether. After 15 min, a solution of 1.19 g (3.35 mmol) of the butenolide **18** in 30 mL of benzene was added. After 1 h, the reaction mixture was washed with three 100-mL portions of NH_4Cl/NH_4OH pH 8 buffer and two 100-mL portions of water. The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue on 75 g of silica gel with 20% ethyl acetate in petroleum ether afforded 0.94 g (76%) of the lactone **19**: $[\alpha]^{25}_D$ +22.3° (*c* 2.8, $CHCl_3$); IR ($CHCl_3$) 2950, 1770, 1500, 1450, 1160, 1100 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.98 (d, 3 H, *J* = 6 Hz, CH_3), 2.1 (dd, 1 H, J_1 = 6 Hz, J_2 = 17 Hz, H-2), 2.35 (m, 1 H, H-3), 2.75 (dd, 1 H, J_1 = 5 Hz, J_2 = 17 Hz, H-2a), 4.1 (m, 1 H, H-5), 7.3 (m, 15 H, Ph_3). Anal. Calcd for $C_{25}H_{24}O_3$: C, 80.62; H, 6.49. Found: C, 80.73; H, 6.39.

4(*S*),5-Dihydroxy-3(*S*)-methylpentanoic Acid 1,4-Lactone. To a stirred solution of 0.94 g (2.5 mmol) of the triphenylmethyl ether **19** in 50 mL of ethanol was added 20 mg of 5% palladium on carbon and 2 drops of concentrated sulfuric acid. The resulting suspension was stirred at room temperature under a hydrogen atmosphere for 24 h, and then 0.5 g of solid $NaHCO_3$ was added. The mixture was filtered and the filtrate concentrated under reduced pressure. Chromatography of the residue on 20 g of silica gel with 50% ethyl acetate in petroleum ether afforded 0.25 g (76%) of the corresponding alcohol: evaporative distillation 90 °C (0.01 mmHg); $[\alpha]^{25}_D$ +81.7° (*c* 0.3, $CHCl_3$); IR ($CHCl_3$) 3600, 2950, 1790, 1470, 1170, 1110, 1030 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.05 (d, 3 H, *J* = 6 Hz, CH_3), 2.0–3.0 (m, 3 H, H-2's, H-3), 3.35 (b s, 1 H, OH), 3.75 (m, 2 H, H-5's), 4.15 (m, 1 H, H-4). Anal. Calcd for $C_6H_{10}O_3$: C, 55.37; H, 7.75. Found: C, 55.50; H, 7.72.

5-Bromo-4(*S*)-hydroxy-3(*S*)-methylpentanoic Acid 1,4-Lactone. By the procedure described for the preparation of the bromide **14**, 525 mg (4.03 mmol) of the above alcohol in 25 mL of dichloromethane with 1.56 mL (20 mmol) of methanesulfonyl chloride and 2.79 mL (20 mmol) of triethylamine gave the corresponding mesylate. This intermediate in 25 mL of tetrahydrofuran with 5 g of lithium bromide gave 685 mg (88%) of the desired bromide after evaporative distillation at 105 °C (0.025 mmHg): ^1H NMR ($CDCl_3$) δ 1.2 (d, 3 H, *J* = 6 Hz, CH_3), 2.1–3.0 (m, 3 H, H-2's, H-3), 3.05 (m, 2 H, H-5's), 4.3 (m, 1 H, H-4).

3(*S*)-Methyl-4-pentenoic Acid (20). To a solution of 0.1 g (14 mmol) of lithium in 40 mL of liquid ammonia at −78 °C was added a solution of 275 mg (1.4 mmol) of the above bromide in 10 mL of dry tetrahydrofuran. After 2 h, excess dry NH_4Cl was added and ammonia allowed to evaporate. The residue was diluted with 100 mL of water and the resulting aqueous phase was acidified and then extracted with three 20-mL portions of ether. The combined organic phases were dried ($MgSO_4$) and then concentrated under reduced pressure. Evaporative distillation of the residue at 90 °C (0.01 mmHg) gave 140 mg (86%) of the acid **20**: $[\alpha]^{24}_D$ +13.55° (*c* 3.3, $CHCl_3$); IR ($CHCl_3$) 3200, 1710, 1410, 1300, 930 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.12 (d, 3 H, *J* = 7 Hz, CH_3), 2.37 (ABX m, 2 H, $HCCH_aH_bCO_2H$), 2.6 (m, 1 H, $=CHCH(CH_3)CH_2$), 5.02 (m, 2 H, $CH=CH_aH_b$), 5.80 (m, 1 H, $CHCH=CH_aH_b$). Anal. Calcd for $C_6H_{10}O_2$: C, 63.14; H, 8.83. Found: C, 63.21; H, 8.85.

3-Carbomethoxy-4-(3(*R*)-methyl-5-pentenyl)-3,4-dihydro-2*H*-pyran-2-one. To 33 mL of 0.80 M THF solution (26.4 mmol) of the Grignard reagent derived from the bromide **14** was added 3.699 g (24 mmol) of α-pyrone **21** in 20 mL of dry THF over a period of 10 min. The resulting red-orange solution was stirred for 15 min at 0 °C and then poured into 250 mL of cold 10% aqueous HCl with vigorous stirring. The layers were separated and the aqueous layer was extracted with three 100-mL portions of dichloromethane. The combined organic layers were dried ($MgSO_4$), and then the solvent was removed under reduced pressure. The residue was evaporatively distilled (110–120 °C (1 mmHg)) to afford 4.956 g (87%) of the pale yellow adducts: IR (neat) 1775, 1745, 1660, 1215 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.98 (d, 3 H, *J* = 4 Hz, $CHCH_3$), 2.11 (m, 1 H, $CHCH_3$), 2.94 (m, 1 H, $CHCH{=}CHO$), 3.44 (d, 1 H, *J* = 5 Hz, $CHCO_2CH_3$), 3.74 (s, 3 H, CO_2CH_3), 4.95 (2 b s, 2 H, $CH{=}CH_2$), 5.28 (dd, 1 H, *J* = 3, 4 Hz, $CH{=}CHO$), 5.40–5.85 (m, 1 H, $CH{=}CH_2$), 6.49 (dd, 1 H, *J* = 1, 4 Hz, $CH{=}CHO$). Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.56; H, 7.60.

3-Carbomethoxy-4-(3(*R*)-methyl-5-pentyl)-2*H*-pyran-2-one (22). To a solution of 5.00 g (21 mmol) of the above dihydropyrones in 1 L of dichloromethane was added 100 g of activated MnO_2. The reaction mixture was stirred vigorously at room temperature for 3 h. The mixture was filtered through a pad of Celite which was then thoroughly washed with fresh dichloromethane. The filtrate was dried ($MgSO_4$) and the solvent was subsequently removed under reduced pressure to give 2.979 g (60%) of the α-pyrone **22**: evaporative distillation 105–110 °C (0.5 mmHg); $[\alpha]^{22}_D$ +3.3° (*c* 1.00, $CHCl_3$); IR (neat) 1730, 1640, 1555, 1250 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.00 (d, 3 H, *J* = 4 Hz, $CHCH_3$), 3.86 (s, 3 H, CO_2CH_3), 4.86 (b s, 1 H, $CH{=}CHH$), 5.03 (b s, 1 H, $CH{=}CHH$), 5.64 (ddd, 1 H, *J* = 5, 6, 12 Hz, $CH_2{=}CH$), 6.11 (d, 1 H, *J* = 3.5 Hz, $CH{=}CHO$), 7.42 (d, 1 H, *J* = 3.5 Hz, $CH{=}CHO$). Anal. Calcd for $C_{13}H_{16}O_4$: C, 66.09; H, 6.83. Found: C, 66.25; H, 6.74.

1-(Dibenzylamino)-2-propyne. To a solution of 17.0 mL (88.3 mmol) of freshly distilled *N*,*N*-dibenzylamine in 75 mL of ether was added 21.0 g (176.51 mmol) of freshly distilled propargyl bromide. The reaction mixture was stirred at room temperature for 15 min, heated at 40 °C for 12 h, and then cooled to room temperature and treated with 11.5 g of KOH in 50 mL of water. After the resulting mixture was vigorously stirred until all of the solids had dissolved, the layers were separated and the aqueous phase was extracted with 100 mL of ether. The ethereal fractions were washed with 100 mL of saturated aqueous NaCl and then dried (K_2CO_3). Removal of the solvent under reduced pressure and flash chromatography on 100 g of silica gel with 10% ethyl acetate in petroleum ether of the residue gave 13.0 g (63%) of the crystalline propyne: mp 42–43.5 °C; IR ($CHCl_3$) 3300, 1600, 1490, 1450, 1330, 1120 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.22 (t, 1 H, $C{\equiv}CH$), 3.23 (d, 2 H, $C{\equiv}CCH_2$), 3.67 (s, 4 H, $2{\times}NCH_2Ph$), 7.30 (m, 10 H, $2{\times}NPh$). Anal. Calcd for $C_{17}H_{17}N$: C, 86.77; H, 7.28; N, 5.95. Found: C, 86.74; H, 7.26; N, 5.85.

1-(Dibenzylamino)-1-propyne. To a solution of 5.0 g (21.25 mmol) of the above propyne in 3 mL of dry Me_2SO was added a solution of 100 mg (0.91 mmol) of potassium *tert*-butoxide in 0.75 mL of dry Me_2SO. The reaction mixture was stirred at room temperature for 1 h and then the solvent was removed by evaporative distillation under reduced pressure (0.01 mmHg) with the oven temperature being increased rapidly to 100 °C. The residue was then rapidly evaporatively distilled (130–190 °C (0.01 mmHg)) to give the desired ynamine. This ynamine could be stored in a freezer for up to 2 weeks if protected from moisture but was always evaporatively redistilled immediately before use: ^1H NMR ($CDCl_3$) δ 1.80 (s, 3 H, CH_3), 3.95 (s, 4 H, $2{\times}NCH_2Ph$), 7.28 (m, 10 H, $2{\times}NPh$).

2-(Dibenzylamino)-3-methyl-6-(3(*R*)-methyl-4-pentenyl)benzoic Acid, Methyl Ester (23). To a solution of 503.3 mg (2.13 mmol) of the α-pyrone **22** in 5 mL of dry benzene was added 551.4 mg (2.34 mmol) of the freshly distilled ynamine in 2 mL of dry benzene. The reaction mixture was heated at reflux for 1 h and then cooled to room temperature and poured into 15 mL of water. The resultant mixture was extracted with two 25-mL portions of dichloromethane, and the organic fractions were dried ($MgSO_4$). Removal of the solvents under reduced pressure and column chromatography of the residue on 30 g of silica gel with 2.5% ether in petroleum ether afforded 542.2 mg (60%) of the aromatic ester **23**: evaporative distillation 165–175 °C (0.005 mmHg); $[\alpha]^{22}_D$ +4.1° (*c* 1.18, $CHCl_3$); IR (neat) 1715, 1275, 1135, 750, 695 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.00 (d, 3 H, *J* = 4 Hz, $CHCH_3$), 1.93 (s, 3 H, $ArCH_3$), 3.78 (s, 3 H, CO_2CH_3), 4.10 (s, 4 H, $2{\times}NCH_2Ph$), 5.00 (m, 2 H, $CH{=}CH_2$), 5.70 (ddd, 1 H, *J* = 5, 6, 12 Hz, $CH{=}CH_2$), 6.94 (dd, 2 H, *J* = 5 Hz, 5 Hz, Ar*H*), 7.23 (s, 10 H, $2{\times}NCH_2Ph$). Anal. Calcd for $C_{29}H_{33}NO_2$: C, 81.46; H, 7.78; N, 3.28. Found: C, 81.41; H, 7.65; N, 3.27.

2-(Dibenzylamino)-3-methyl-6-(3(*R*)-methyl-4,5-*O*-isopropylidenepentyl)benzoic Acid, Methyl Ester. To a solution of 4.233 g (9.92 mmol) of the aromatic olefin **23** and 1.676 g (12.4 mmol) of 4-methylmorpholine 4-oxide in 4.41 mL of water and 2.20 mL of acetone was added 1.9 mL (0.019 mmol) of a solution of 0.01 M osmium tetroxide in *tert*-butyl alcohol. The reaction mixture was stirred for 24 h at room temperature and then quenched by the addition of a slurry of 50 mg of $Na_2S_2O_4$ and 2 g of Florisil in 1 mL of water. After being stirred for 5 min, the mixture was filtered through a pad of Celite with thorough washing of

the filter pad with acetone. The volume of the filtrate was brought to about 200 mL by the addition of acetone, and to this was added 150 mL of 10% aqueous HCl and the resulting solution was allowed to stand at room temperature for 15 min. The solution was then extracted with three 200-mL portions of dichloromethane, and the combined organic extracts were dried ($MgSO_4$). The solvent was removed under reduced pressure to give a residue which was flash chromatographed on 100 g of silica gel with 20% ethyl acetate in petroleum ether to afford 4.510 g (91%) of an inseparable mixture of the desired aromatic compounds: evaporative distillation 180–195 °C (0.005 mmHg); IR (neat) 1735, 1280, 1230, 1145, 1065, 710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.84, 1.00 (2d, 3 H, J = 4 Hz, $CHCH_3$), 1.30, 1.35 (2s, 6 H, $C(CH_3)_2$), 1.90 (s, 3 H, $ArCH_3$), 3.77 (s, 3 H, CO_2CH_3), 4.09 (s, 4 H, $2\times NCH_2Ph$), 6.91 (m, 2 H, Ar*H*), 7.19 (s, 10 H, $2\times NCH_2Ph$). Anal. Calcd for $C_{32}H_{39}NO_4$: C, 76.61; H, 7.84; N, 2.79. Found: C, 76.82; H, 7.83; N, 2.74.

2-Amino-3-methyl-6-(3(*R*)-methyl-4,5-*O*-isopropylidenepentyl)benzoic Acid, Methyl Ester. A mixture of 5.156 g (10.3 mmol) of the above dibenzylamino compounds and 516 mg of 10% palladium on carbon in 103 mL of absolute ethanol was shaken under a 50 psi atmosphere of hydrogen on a Parr hydrogenator for 10 h. The reaction mixture was then filtered and the filtrate was diluted with 300 mL of water. This mixture was extracted with three 150-mL portions of dichloromethane which were then combined and dried ($MgSO_4$). Removal of the solvents under reduced pressure gave a resident containing the desired amines and the vicinal diols. This mixture could be conveniently used in the subsequent reactions or separated by flash chromatography on 100 g of silica gel with ethyl acetate to give 518 mg of the aminodiols and 2.489 g of the amines (93% corrected total yield): evaporative distillation 135–140 °C (0.008 mmHg); IR (neat) 3490, 3390, 1690, 1615, 860, 805 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90, 1.02 (2d, 3 H, J = 4 Hz, $CHCH_3$), 1.30, 1.35 (2s, 6 H, $C(CH_3)_2$), 2.02 (s, 3 H, $ArCH_3$), 3.82 (s, 3 H, CO_2CH_3), 4.90 (b s, 2 H, NH_2), 6.47 (dd, 1 H, J = 5.5 Hz, 5.5 Hz, Ar*H*), 6.97 (d, 1 H, J = 5.5 Hz, Ar*H*). Anal. Calcd for $C_{18}H_{27}NO_4$: C, 67.26; H, 8.47; N, 4.36. Found: C, 67.12; H, 8.37; N, 4.27.

3-Methyl-6-(3(*R*)-methyl-4,5-dihydroxypentyl)salicylic Acid, Methyl Ester. To a stirred solution of 2.389 g (7.45 mmol) of the above amines and 7.45 mL of 48–50% tetrafluoroboric acid in 74.5 mL of absolute ethanol at 0 °C was added, in a dropwise manner, 1.50 mL (11.2 mmol) of isoamyl nitrite, and the resulting colorless solution was stirred for 30 min at 0 °C. At this time the reaction mixture was concentrated under reduced pressure and then the concentrate was dissolved in 125 mL of water. The resulting solution was then heated at 80 °C until 15 min past the cessation of gas evolution as monitored by a bubbler. The reaction mixture was then extracted with three 100-mL portions of dichloromethane and the combined extracts were then dried ($MgSO_4$). Removal of the solvent under reduced pressure gave a residue which afforded 1.779 g (85%) of the phenols after column chromatography on 100 g of silica gel with ethyl acetate: evaporative distillation 165–170 °C (0.01 mmHg); IR (neat) 3500, 1665, 1420, 1255, 1155, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.97 (2d, 3 H, J = 4 Hz, $CHCH_3$), 2.19 (s, 3 H, $ArCH_3$), 3.93 (s, 3 H, CO_2CH_3), 6.62, 7.16 (2d, 2 H, J = 5.5 Hz, 5.5 Hz, Ar*H*), 11.24 (bs, 1 H, ArO*H*). Anal. Calcd for $C_{15}H_{22}O_5$: C, 63.81; H, 7.85. Found: C, 63.82; H, 7.90.

3-Methyl-6-(3(*R*)-methyl-4,5-*O*-isopropylidenepentyl)salicylic Acid, Methyl Ester (24). A mixture of 2 mL of 2,2-dimethoxypropane, 2 mL of acetone, 179.7 mg (0.636 mmol) of the above diols, and a catalytic amount of *p*-toluenesulphonic acid was stirred at room temperature for 15 min. The reaction mixture was then taken up in 40 mL of ether, and this was washed with two 20-mL portions of a saturated $NaHCO_3$ solution and 20 mL of saturated aqueous NaCl and then dried ($MgSO_4$). Removal of the solvent under reduced pressure gave 201.5 mg (98%) of the essentially pure acetonides **24**: evaporative distillation 95–105 °C (0.003 mmHg); IR (neat) 1660, 1255, 1150, 1075, 870, 810 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.87, 1.03 (2d, 3 H, J = 6 Hz, $CHCH_3$), 1.33, 1.34 (2s, 6 H, $C(CH_3)_2$), 2.18 (s, 3 H, $ArCH_3$), 3.95 (s, 3 H, CO_2CH_3), 6.63 (dd, 1 H, J = 2.2, 7.5 Hz, Ar*H*), 7.18 (d, 1 H, J = 7.5 Hz, Ar*H*), 11.53 (s, 1 H, ArO*H*). Anal. Calcd for $C_{18}H_{26}O_5$: C, 67.06; H, 8.13. Found: C, 67.17; H, 7.93.

2-(β-Methoxyethoxymethyl)-3-methyl-6-(3(*R*)-methyl-4,5-*O*-isopropylidenepentyl)salicylic Acid, Methyl Ester. To a stirred suspension of 2.88 mmol of potassium hydride in 5 mL of dry THF at 0 °C was added 93.0 mg (0.288 mmol) of the phenols 24 in 1 mL of dry THF. The reaction mixture was stirred for 20 min at 0 °C and then 0.33 mL (2.88 mmol) of β-methoxyethoxymethyl chloride was added. The resulting mixture was stirred at 0 °C for 1 h and then at room temperature for 0.5 h. The reaction mixture was carefully quenched by the addition of a few drops of water and then diluted with 30 mL of ether which was then washed with two 10-mL portions of water and 10 mL of saturated aqueous NaCl. The organic layer was dried ($MgSO_4$) and then solvents were removed under reduced pressure to give quantitatively the essentially pure methyl esters: evaporative distillation 135–155 °C (0.003 mmHg); IR ($CHCl_3$) 1730, 1250, 1220, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88, 1.01 (2d, 3 H, $CHCH_3$), 1.33, 1.38 (2s, 6 H, $C(CH_3)_2$), 2.27 (s, 3 H, $ArCH_3$), 3.40 (s, 3 H, CH_2OCH_3), 3.92 (s, 3 H, CO_2CH_3), 5.07 (s, 2 H, OCH_2O), 6.90 (dd, 1 H, J = 3, 7.5 Hz, Ar*H*), 7.18 (d, 1 H, J = 7.5 Hz, Ar*H*). Anal. Calcd for $C_{22}H_{34}O_7$: C, 64.37; H, 8.35. Found: C, 64.52; H, 8.32.

2-(β-Methoxyethoxymethyl)-3-methyl-6-(3(*R*)-methyl-4,5-*O*-isopropylidenepentyl)salicylic Acid, Benzyl Ester. To a stirred solution of 0.52 mL (5.76 mmol) of *n*-propanethiol in 5 mL of dry pentane at 0 °C was added 1.25 mL (2.88 mmol) of a solution of 2.3 M butyllithium in hexane. The mixture was stirred at 0 °C for 15 min and then concentrated under reduced pressure. The resultant salt was dissolved in 4 mL of dry HMPA and this was cooled to 0 °C. To this solution 118.4 mg (0.288 mmol) of the above methyl esters in 2 mL of dry HMPA was added and the reaction mixture was stirred at 0 °C for 10 min and then at room temperature for 45 min. At this time, 0.69 mL (5.76 mmol) of benzyl bromide was added and the reaction mixture was stirred at room temperature for 2 h and then quenched by the addition of 4 mL of 10% aqueous HCl and 40 mL of ether. The ethereal layer was then consecutively washed with three 20-mL portions of 10% aqueous HCl, 20 mL of a saturated aqueous $NaHCO_3$, and 20 mL of saturated aqueous NaCl. The organic phase was then dried ($MgSO_4$). Removal of the solvent under reduced pressure gave a residue that was chromatographed on 10 g of silica gel with 20% ethyl acetate in petroleum ether to give 119.0 mg (85%) of the benzyl esters: evaporative distillation 180–195 °C (0.001 mmHg); IR (neat) 1738, 1250, 1140, 1040, 740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.75, 0.90 (2d, 3 H, $CHCH_3$), 1.32, 1.35 (2s, 6 H, $C(CH_3)_2$), 2.27 (s, 3 H, $ArCH_3$), 3.33 (s, 3 H, OCH_3), 4.97 (s, 2 H, OCH_2O), 5.33 (s, 2 H, OCH_2Ph), 6.87 (dd, 1 H, J = 3.7, 7.5 Hz, Ar*H*), 7.13 (d, 1 H, J = 7.5 Hz, ar*H*), 7.38 (m, 5 H, OCH_2Ph). Anal. Calcd for $C_{28}H_{38}O_7$: C, 69.11; H, 7.87. Found: C, 69.17; H, 7.94.

3-Methyl-6-(3(*R*)-methyl-4,5-dihydroxypentyl)salicylic Acid, Benzyl Ester. A mixture of 0.75 mL of 10% aqueous HCl, 3 mL of THF, and 89.5 mg (0.184 mmol) of the above benzyl esters was stirred at room temperature for 4 h and then heated at 50 °C for 7 h. The reaction mixture was diluted with 30 mL of ethyl acetate which was then washed with three 15-mL portions of saturated aqueous NaCl and dried ($MgSO_4$). Removal of the solvent under reduced pressure gave quantitatively the desired dihydroxy phenols: evaporative distillation 165–185 °C (0.003 mmHg); IR ($CHCl_3$) 3610, 1670, 1430, 1260, 1160 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.78 (b d, 3 H, J = 6 Hz, $CHCH_3$), 2.20 (s, 3 H, $ArCH_3$), 5.38 (s, 2 H, CO_2CH_2Ph), 6.60 (d, 1 H, J = 7.5 Hz, Ar*H*), 7.17 (d, 1 H, J = 7.5 Hz, Ar*H*), 7.42 (b s, 5 H, CO_2CH_2Ph), 11.33 (b s, 1 H, ArO*H*). Anal. Calcd for $C_{21}H_{26}O_5$: C, 70.37; H, 7.31. Found: C, 70.28; H, 7.27.

3-Methyl-6-(3(*R*)-formylbutyl)salicylic Acid, Benzyl Ester (2). To a solution of 66.0 mg (0.184 mmol) of the above diols in 4 mL of methanol was added 47.2 mg (0.221 mmol) of sodium metaperiodate in 1.5 mL of water. The reaction mixture was stirred for 2 h at room temperature and then diluted with 15 mL of water and extracted with two 15-mL portions of dichloromethane. The organic extracts were combined and dried ($MgSO_4$). Removal of the solvent under reduced pressure and chromatography of the residue on 10 g of silica gel with 5% ethyl acetate in petroleum ether gave 48.0 mg (80%) of the desired "left-half" aldehyde **2**.

***tert*-Butyldimethylsilyl-2(*R*)- and -2(*S*)-(3(*R*),4(*S*)-epoxy-5(*S*)-(methoxymethylenoxymethyl)-2(*R*)-tetrahydrofuryl)butyl Ether (31).** To a stirred solution of 1.17 g (5.07 mmol) of the acids **29** in 50 mL of 0.5 M aqueous $NaHCO_3$ was added a 25 mL aqueous solution of 8.4 g (50.6 mmol) of potassium iodide and 3.85 g (15.2 mmol) of iodine. The resulting mixture was stirred at room temperature in the dark for 12 h, then treated with 100 mL of 10% aqueous Na_2SO_3, and then extracted with three 60-mL portions of dichloromethane. The combined organic phases were washed with 40 mL of saturated aqueous $NaHCO_3$ and then dried ($MgSO_4$). Removal of the solvent under reduced pressure gave the crude iodolactones **30**.

To a stirred solution of 108 mg (2.85 mmol) of lithium tetrahydridoaluminate in 4 mL of dry THF at 0 °C under argon was added 0.08 mL of 90% sulfuric acid. After 1 h, a solution of 746 mg (2.09 mmol) of the above iodolactones **30** in 3 mL of dry THF was added to the reaction mixture. After an additional hour, the mixture was treated successively with 0.08 mL of water, 0.08 mL of 15% aqueous NaOH, and 0.24 mL of water. After another 15 min, the suspension was filtered and the filtrate concentrated under reduced pressure.

To a stirred solution of this residue in 10 mL of methanol was added 443 mg (4.18 mmol) of Na_2CO_3. After 24 h, the mixture was concentrated under reduced pressure and then taken up in 20 mL of saturated aqueous $NaHCO_3$ and 60 mL of dichloromethane. The organic phase was then washed with 20 mL of saturated aqueous NaCl and then dried

(K_2CO_3 and Na_2SO_4). Removal of the solvents under reduced pressure gave the crude epoxy alcohols.

To a stirred solution of this residue in 4 mL of dry DMF was added 427 mg (6.3 mmol) of imidazole and 472 mg (3.1 mmol) of *tert*-butyldimethylchlorosilane. After 16 h, the reaction mixture was diluted with 60 mL of ether, washed with 20 mL of saturated aqueous $NaHCO_3$ and 20 mL of saturated aqueous NaCl, and then dried (K_2CO_3 and Na_2SO_4). Removal of the solvent and chromatography of the residue on 60 g of silica gel with 10% ethyl acetate–cyclohexane afforded 631.1 mg (90%) of the epoxy silyl ethers **31** as a mixture of diastereomers: evaporative distillation 95–105 °C (0.005 mmHg); IR ($CHCl_3$) 1485, 1475, 1260, 1160, 1120, 1040, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.02 (s, 6 H, $(CH_3)_2Si$), 0.87 (s, 9 H, $(CH_3)_3C$), 3.30 (s, 3 H, OCH_3), 3.53 (d, 2 H, J = 5 Hz, CCH_2O), 4.57 (s, 2 H, OCH_2O). Anal. Calcd for $C_{17}H_{34}O_5Si$: C, 58.92; H, 9.89. Found: C, 58.98; H, 9.88.

***tert*-Butyldimethylsilyl-2(*R*)- and -2(*S*)-(3(*R*)-hydroxy-5(*S*)-methoxymethylenoxymethyl-4(*S*)-methyl-2(*R*)-tetrahydrofuryl)butyl Ether (34 and Epi-34).** To a stirred suspension of 1.8 g (9.45 mmol) of cuprous iodide in 20 mL of dry *n*-pentane at 0 °C under argon was 10 mL of a 1.8 M solution of methyllithium in ether. After 15 min, a solution of 631 mg (1.8 mmol) of the epoxides **31** in 4 mL of *n*-pentane was added to the reaction mixture. After 3 h, the mixture was treated with 10 mL of saturated aqueous NH_4Cl, diluted with 60 mL of ether, washed with two 20-mL portions of saturated aqueous NH_4Cl and 20 mL of saturated aqueous NaCl, and then dried ($MgSO_4$). Removal of the solvents under reduced pressure and chromatography of the residue on 50 g of silica gel with 25% ethyl acetate–cyclohexane afforded 334 mg (50%) of the alcohol **34** and 80 mg (12%) of the alcohol epi-**34**. Alcohol **34**: evaporative distillation 110–120 °C (0.005 mmHg); $[\alpha]^{22}_D$ +4.0° (*c* 0.93, $CHCl_3$); IR ($CHCl_3$) 3360, 1480, 1470, 1260, 1040, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.08 (s, 6 H, $(CH_3)_2Si$), 0.90 (s, 9 H, $(CH_3)_3C$), 0.94 (d, 3 H, J = 8 Hz, $CHCH_3$), 3.30 (s, 3 H, OCH_3), 4.57 (s, 2 H, OCH_2O). Anal. Calcd for $C_{18}H_{38}O_5Si$: C, 59.63; H, 10.56. Found: C, 59.65; H, 10.62. Alcohol epi-**34**: evaporative distillation 100–120 °C (0.005 mmHg); $[\alpha]^{23}_D$ +11.7° (*c* 1.02, $CHCl_3$); IR ($CHCl_3$) 3430, 1460, 1260, 1040, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.10 (s, 6 H, $(CH_3)_2Si$), 0.93 (s, 9 H, $(CH_3)_3C$), 3.33 (s, 3 H, OCH_3), 4.62 (s, 2 H, OCH_2O). Anal. Calcd for $C_{18}H_{38}O_5Si$: C, 59.63; H, 10.56. Found: C, 59.64; H, 10.50.

***tert*-Butyldimethylsilyl-2(*R*)-(5(*S*)-(methoxymethylenoxymethyl)-4(*S*)-methyl-3(*R*)-(methylthiothiocarbonyloxy)-2(*R*)-tetrahydrofuryl)butyl Ether.** To a stirred suspension of 26.5 mg (1.1 mmol) of sodium hydride in 1 mL of dry THF at 0 °C under argon was added a solution of 334 mg (0.92 mmol) of the alcohol **34** in 1 mL of dry THF. After 1 h, 0.28 mL (4.7 mmol) of carbon disulfide was added, and after an additional hour, 0.12 mL (1.93 mmol) of methyl iodide was added. The mixture was stirred for 3 h and then diluted with 70 mL of ether. It was then washed with two 30-mL portions of saturated aqueous $NaHCO_3$, 20 mL of saturated aqueous NaCl, and then dried ($MgSO_4$). Removal of the solvents gave 425 mg (100%) of the corresponding xanthate: evaporative distillation 130–140 °C (0.005 mmHg); $[\alpha]^{22}_D$ −3.5° (*c* 1.50, $CHCl_3$); IR ($CHCl_3$) 1480, 1230, 1070, 1050, 850 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.03 (s, 6 H, $(CH_3)_2Si$), 0.87 (s, 9 H, $(CH_3)_3C$), 1.05 (d, 3 H, J = 7 Hz, $CHCH_3$), 2.53 (s, 3 H, SCH_3), 3.35 (s, 3 H, OCH_3), 4.63 (s, 2 H, OCH_2O), 5.67 (d, 1 H, J = 4 Hz, S_2COCH). Anal. Calcd for $C_{20}H_{40}O_5Si$: C, 53.06; H, 8.91; S, 14.16. Found: C, 53.27; H, 8.91; S, 14.11.

***tert*-Butyldimethylsilyl-2(*R*)-(5(*S*)-(methoxymethylenoxymethyl)-4(*R*)-methyl-2(*S*)-tetrahydrofuryl)butyl Ether.** To a stirred solution of 425 mg (0.92 mmol) of the above xanthate in 9 mL of dry toluene at reflux under argon was added 0.3 mL (1.14 mmol) of tri-*n*-butyltin hydride. After 24 h, the reaction mixture was concentrated under reduced pressure and chromatography of the residue on 30 g of silica gel with 5% ethyl acetate–cyclohexane afforded 255 mg (80%) of the desoxysilyl ether: evaporative distillation 75–85 °C (0.005 mmHg); $[\alpha]^{24}_D$ −11.91° (*c* 1.055, $CHCl_3$); IR ($CHCl_3$) 1480, 1260, 1100, 1040, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.03 (s, 6 H, $(CH_3)_2Si$), 0.89 (s, 9 H, $(CH_3)_3C$), 0.95 (d, 3 H, J = 7 Hz, $CHCH_3$), 3.33 (s, 3 H, OCH_3), 3.52 (d, 2 H, J = 6 Hz, CCH_2O), 3.63 (d, 2 H, J = 5 Hz, $SiOCH_2$), 4.60 (s, 2 H, OCH_2O). Anal. Calcd for $C_{18}H_{38}O_4Si$: C, 62.38; H, 11.05. Found: C, 62.26; H, 11.05.

2(*R*)-(5(*S*)-(Methoxymethylenoxymethyl)-4(*R*)-methyl-2(*S*)-tetrahydrofuryl)butan-1-ol (33). To a stirred solution of 223.5 mg (0.645 mmol) of the above silyl ether in 3.2 mL of dry THF was added a solution of 430 mg (1.64 mmol) of tetra-*n*-butylammonium fluoride in 3.2 mL of dry THF. After 4 h, the reaction mixture was diluted with 70 mL of ether, washed with two 30-mL portions of saturated aqueous $NaHCO_3$ and 30 mL of saturated aqueous NaCl, and then dried ($MgSO_4$). Removal of the solvents and chromatography of the residue on 10 g of silica gel with 35% ethyl acetate–cyclohexane afforded 123 mg (82%) of the alcohol **33**: evaporative distillation 60–70 °C (0.005 mmHg); $[\alpha]^{23}_D$ −21.0° (*c* 1.405, $CHCl_3$); IR ($CHCl_3$) 3460, 1470, 1160, 1110, 1050 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.96 (d, 3 H, J = 7 Hz, $CHCH_3$), 3.33 (s, 3 H, OCH_3), 3.53 (d, 2 H, J = 6 Hz, CCH_2OC), 4.60 (s, 2 H, OCH_2O). Anal. Calcd for $C_{12}H_{24}O_4$: C, 62.04; H, 10.41. Found: C, 62.16; H, 10.48.

2(*S*)-(5(*S*)-(Methoxymethylenoxymethyl)-4(*R*)-methyl-2(*S*)-tetrahydrofuryl)butanal. To a stirred solution of 78 mg (0.336 mmol) of the alcohol **33** in 1.7 mL of dry dichloromethane was added 11 mg (0.134 mmol) of anhydrous sodium acetate and 145 mg (0.673 mmol) of pyridinium chlorochromate. After 2 h, the reaction mixture was diluted with 20 mL of dry ether and then stirred for 15 min. the resultant suspension was filtered and the solid was washed by trituration with three 20-mL portions of ether. Removal of the solvents and chromatography of the residue on 7 g of silica gel with 25% ethyl acetate–cyclohexane afforded 67 mg (85%) of the corresponding aldehyde: evaporative distillation 60–70 °C (0.005 mmHg); $[\alpha]^{23}_D$ +22.5° (*c* 1.11, $CHCl_3$); IR ($CHCl_3$) 2750, 1725, 1475, 1260, 1220, 1040, 920 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.91 (t, 3 H, J = 6 Hz, CH_3CH_2), 1.00 (d, 3 H, J = 7 Hz, $CHCH_3$), 3.33 (s, 3 H, OCH_3), 3.53 (d, 2 H, J = 6 Hz, CCH_2OC), 4.07 (dd, 1 H, J = 6, 12 Hz, OCHCC), 4.33 (dd, 1 H, J = 7, 14 Hz, OCHCC), 4.60 (s, 2 H, OCH_2O), 9.72 (d, 1 H, J = 4 Hz, CHO). Anal. Calcd for $C_{12}H_{22}O_4$: C, 62.58; H, 9.63. Found: C, 62.56; H, 9.66.

2-Ethyl-6(*S*)-hydroxy-7-(methoxymethylenoxy)-5(*R*)-methylhept-2-enal (32). To a stirred solution of 50 mg (0.217 mmol) of the above aldehyde in 4.4 mL of dry THF was added 5 mg of potassium *tert*-butoxide. The suspension was heated at 70 °C for 20 h, allowed to cool to room temperature, and then diluted with 30 mL of ether. The ethereal phase was washed with two 10-mL portions of saturated aqueous $NaHCO_3$ and 10 mL of saturated aqueous NaCl, and then dried ($MgSO_4$). Removal of solvents and chromatography of the residue on a silica gel TLC plate with 35% ethyl acetate–cyclohexane gave 25 mg of the β-elimination product **32**: evaporative distillation 80–90 °C (0.005 mmHg); IR ($CHCl_3$) 3600, 3450, 1680, 1460, 1160, 1120, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.93 (t, 3 H, J = 6 Hz, CH_3CH_2), 0.96 (d, 3 H, J = 7 Hz, $CHCH_3$), 3.33 (s, 3 H, OCH_3), 4.61 (s, 2 H, OCH_2O), 6.42 (t, 1 H, J = 8 Hz, C=CH), 9.40 (s, 1 H, CHO). Anal. Calcd for $C_{12}H_{22}O_4$: C, 62.58; H, 9.63. Found: C, 62.24; H, 9.71.

***tert*-Butyldimethylsilyl-2(*R*)- and -2(*S*)-[3(*S*)-(1,3-dithian-2-yl)-4(*S*)-hydroxy-5(*R*)-(methoxymethylenoxymethyl)-2(*R*)-tetrahydrofuryl]butyl Ether.** To a stirred solution of 1.46 g (12.2 mmol) of 1,3 dithiane in 12 mL of dry THF at −20 °C under argon was added, dropwise, 4.8 mL (12 mmol) of a 2.5 M solution of *n*-butyllithium in *n*-hexane. After 90 min, a solution of 840 mg (2.42 mmol) of the epoxides **26** in 4.5 mL of dry THF was slowly added into the reaction mixture, which was then kept at 5 °C for 2 days. The mixture was diluted with 60 mL of ether, washed with two 25-mL portions of water, 25 mL of saturated aqueous $NaHCO_3$, and 25 mL of saturated aqueous NaCl, and then dried ($MgSO_4$). Removal of the solvents under reduced pressure and chromatography of the residue on 50 g of silica gel with 25% ethyl acetate–cyclohexane afforded 509 mg (45%) of the dithioacetal of the 2*R*-isomer and 110 mg (10%) of the dithioacetal of the 2*S*-isomer. 2*R*-Isomer: evaporative distillation 160–170 °C (0.005 mmHg); $[\alpha]^{23}_D$ +18.0° (*c* 0.255, $CHCl_3$); IR ($CHCl_3$) 3600, 3450, 1480, 1470, 1260, 1040, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.09 (s, 6 H, $(CH_3)_2Si$), 0.92 (s, 9 H, $(CH_3)_3C$), 3.33 (s, 3 H, OCH_3), 4.63 (s, 2 H, OCH_2O). Anal. Calcd for $C_{21}H_{42}O_5S_2Si$: C, 54.04; H, 9.07; S, 13.74. Found: C, 54.26; H, 9.08; S, 13.78. 2*S*-Isomer: evaporative distillation 160–170 °C (0.005 mmHg); $[\alpha]^{22}_D$ +22.1° (*c* 1.095, $CHCl_3$); IR ($CHCl_3$) 3450, 1480, 1470, 1260, 1080, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.13 (s, 6 H, $(CH_3)_2Si$), 0.93 (s, 9 H, $(CH_3)_3C$), 3.33 (s, 3 H, OCH_3), 4.60 (s, 2 H, OCH_2O). Anal. Calcd for $C_{21}H_{42}O_5S_2Si$: C, 54.04; H, 9.07; S, 13.74. Found: C, 53.86; H, 8.92; S, 13.54.

(*tert*-Butyldimethylsilyl)-2(*R*)-(4(*S*)-hydroxy-5(*R*)-(methoxymethylenoxymethyl)-3(*S*)-methyl-2(*S*)-tetrahydrofuryl)butyl Ether (37). A solution of 640 mg (1.37 mmol) of the 2*R*-dithioacetal in 20 mL of ethanol was added to a slurry of W-4 Raney nickel (freshly made[37] from 20 g of Ni alloy) in 50 mL of ethanol at 90 °C and stirred for 5 h. The catalyst was then removed by filtration and washed with three 20-mL portions of ethanol. Removal of the solvent from the combined filtrates under reduced pressure and chromatography of the residue on 30 g of silica gel with 30% ethyl acetate–cyclohexane afforded 421 mg (85%) of the desulfurized compound **37**: evaporative distillation 110–120 °C (0.005 mmHg); $[\alpha]^{23}_D$ +9.4° (*c* 1.04, $CHCl_3$); IR ($CHCl_3$) 3350, 1480, 1260, 1040, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.07 (s, 6 H, $(CH_3)_3Si$), 0.90 (s, 9 H, $(CH_3)_3C$), 1.10 (d, 3 H, J = 7 Hz, $CHCH_3$), 3.38 (s, 3 H, OCH_3), 4.67 (s, 2 H, OCH_2O). Anal. Calcd for $C_{18}H_{38}O_5Si$: C, 59.63;

(37) W-4: Adkins, H.; Pavlic, A. A. *J. Am. Chem. Soc.* **1946**, *68*, 1471; **1947**, *69*, 3039–3041.

H, 10.56. Found: C, 59.71; H, 10.57.

***tert*-Butyldimethylsilyl-2(*R*)-(5(*R*)-(methoxymethylenoxymethyl)-3(*S*)-methyl-4(*S*)-(methylthiothiocarbonyloxy)-2(*S*)-tetrahydrofuryl)butyl Ether.** By the procedure described for the preparation of the xanthate of the 4*R*-methyl series, 421 mg (1.16 mmol) of the alcohol **37**, 41.8 mg (1.74 mmol) of sodium hydride in 9 mL of dry THF, 0.35 mL (5.82 mmol) of carbon disulfide, and 0.18 mL (2.89 mmol) of methyl iodide afforded, after chromatography on 40 g of silica gel with 5% ethyl acetate–cyclohexane, 496 mg (95%) of the corresponding xanthate: evaporative distillation 130–140 °C (0.005 mmHg); $[\alpha]^{22}_D$ +1.1° (*c* 1.32, $CHCl_3$); IR ($CHCl_3$) 1475, 1465, 1220, 1060, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.04 (s, 6 H, $(CH_3)_2Si$), 0.90 (s, 9 H, $(CH_3)_3C$), 2.53 (s, 3 H, SCH_3), 3.33 (s, 3 H, OCH_3), 4.63 (s, 2 H, OCH_2O), 5.67 (dd, 1 H, J = 4 Hz, 4 Hz, S_2COCH). Anal. Calcd for $C_{20}H_{40}O_5Si$: C, 53.06; H, 8.91; S, 14.61. Found: C, 53.00; H, 8.89; S, 13.99.

***tert*-Butyldimethylsilyl-2(*R*)-(5(*S*)-(methoxymethylenoxymethyl)-3(*S*)-methyl-2(*S*)-tetrahydrofuryl)butyl Ether.** By the procedure described for the preparation of the silyl ether of the 4*R*-methyl series, 470 mg (1.04 mmol) of the above xanthate in 10.4 mL of dry toluene with 0.41 mL (1.55 mmol) of tri-*n*-butyltin hydride afforded, after chromatography on 30 g of silica gel with 5% ethyl acetate–cyclohexane, 353 mg (98%) of the corresponding silyl ether: evaporative distillation 70–80 °C (0.005 mmHg); $[\alpha]^{23}_D$ +10.4° (*c* 1.15, $CHCl_3$); IR ($CHCl_3$) 1470, 1460, 1260, 1100, 1040, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.03 (s, 6 H, $(CH_3)_2Si$), 0.88 (s, 9 H, $(CH_3)_3C$), 3.33 (s, 3 H, OCH_3), 4.63 (s, 2 H, OCH_2O). Anal. Calcd for $C_{18}H_{38}O_4Si$: C, 62.38; H, 11.05. Found: C, 62.46; H, 11.07.

2(*R*)-(5(*S*)-(Methoxymethylenoxymethyl)-3(*S*)-methyl-2(*S*)-tetrahydrofuryl)butan-1-ol (36). By the procedure described for the preparation of the alcohol **33**, 340 mg (1.01 mmol) of the above silyl ether in 5 mL of dry THF with 530 mg (2 mmol) of tetra-*n*-butylammonium fluoride afforded, after chromatography on 20 g of silica gel with 35% ethyl acetate–cyclohexane, 236 mg (100%) of the alcohol **36**: evaporative distillation 60–70 °C (0.005 mmHg); $[\alpha]^{22}_D$ +5.4° (*c* 1.025, $CHCl_3$); IR ($CHCl_3$) 3490, 1460, 1110, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.96 (t, 3 H, J = 6 Hz, CH_3CH_2), 1.05 (d, 3 H, J = 6 Hz, CH_3CHCC), 3.34 (s, 3 H, OCH_3), 4.62 (s, 2 H, OCH_2O). Anal. Calcd for $C_{12}H_{24}O_4$: C, 62.04; H, 10.41. Found: C, 62.12; H, 10.32.

2(*S*)-(5(*S*)-(Methoxymethylenoxymethyl)-3(*S*)-methyl-2(*S*)-tetrahydrofuryl)butanal. By the procedure described for the preparation of the aldehyde of the 4*R*-methyl series, 130 mg (0.56 mmol) of the alcohol **36** in 3 mL of dry dichloromethane, 18 mg (0.22 mmol) of anhydrous sodium acetate, and 240 mg (1.11 mmol) of pyridinium chlorochromate afforded, after chromatography on 10 g of silica gel with 25% ethyl acetate–cyclohexane, 90 mg (70%) of the corresponding aldehyde: evaporative distillation 60–70 °C (0.005 mmHg); $[\alpha]^{22}_D$ +19.5° (*c* 1.435, $CHCl_3$); IR ($CHCl_3$) 1720, 1480, 1110, 1040, 920 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.93 (t, 3 H, J = 6 Hz, CH_3CH_2), 1.05 (d, 3 H, J = 6 Hz, $CHCH$), 3.36 (s, 3 H, OCH_3), 3.52 (d, 2 H, J = 5 Hz, CCH_2OC), 3.70 (dd, 1 H, J = 4 Hz, 8 Hz, O=CCCH), 4.62 (s, 2 H, OCH_2O), 9.77 (d, 1 H, J = 6 Hz, CHO). Anal. Calcd for $C_{12}H_{22}O_4$: C, 62.58; H, 9.63. Found: C, 62.67; H, 9.68.

2-Ethyl-6(*S*)-hydroxy-7-(methoxymethylenoxy)-4(*S*)-methylhept-2-enal (35). By the procedure described for the preparation of the β-elimination product **32**, 62 mg (0.27 mmol) of the above aldehyde in 2.5 mL of dry THF and 8 mg of potassium *tert*-butoxide afforded, after preparative silica gel TLC with 35% ethyl acetate–cyclohexane, 25 mg of the β-elimination product **35**: evaporative distillation 80–90 °C (0.005 mmHg); IR ($CHCl_3$) 3500, 1680, 1460, 1150, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.00 (t, 3 H, J = 7 Hz, CH_3CH_2), 1.12 (d, 3 H, J = 6 Hz, $CHCH_3$), 3.40 (s, 3 H, OCH_3), 4.67 (s, 2 H, OCH_2O), 6.27 (d, 1 H, J = 10 Hz, C=CH), 9.36 (s, 1 H, CHO). Anal. Calcd for $C_{12}H_{22}O_4$: C, 62.58; H, 9.63. Found: C, 62.65; H, 9.53.

Benzyl 2(*R*)-(5(*S*)-(Methoxymethylenoxymethyl)-3(*S*)-methyl-2-(*S*)-tetrahydrofuryl)butyl Ether. By the procedure described for the preparation of the benzyl ether **5**, 97.9 mg (0.42 mmol) of the alcohol **31**, 20 mg (0.5 mmol) of potassium hydride, and 0.075 mL (0.6 mmol) of benzyl bromide in 4 mL of dry THF afforded, after chromatography on 10 g of silica gel with 15% ethyl acetate–cyclohexane, 122.8 mg (91%) of the corresponding benzyl ether: evaporative distillation 100–110 °C (0.005 mmHg); $[\alpha]^{21}_D$ +9.9° (*c* 0.97, $CHCl_3$); IR ($CHCl_3$) 1450, 1380, 1365, 1120, 1100, 1030 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90 (t, 3 H, J = 6 Hz, CH_3CH_2), 1.01 (d, 3 H, J = 6 Hz, CH_3CHCC), 3.33 (s, 3 H, OCH_3), 4.43 (s, 2 H, $C_6H_5CH_2$), 4.61 (s, 2 H, OCH_2O), 7.30 (b s, 5 H, C_6H_5). Anal. Calcd for $C_{19}H_{30}O_4$: C, 70.77; H, 9.38. Found: C, 70.61; H, 9.15.

Benzyl 2(*R*)-(5(*S*)-(Hydroxymethyl)-3(*S*)-methyl-2(*S*)-tetrahydrofuryl)butyl Ether (38). To a stirred solution of 82.8 mg (0.26 mmol) of the methoxymethyl ether above in 4 mL of THF was added 1 mL of 10% aqueous HCl. The resulting solution was heated at 50 °C for 16 h, cooled to room temperature and then diluted with 50 mL of ether. The organic phase was washed with 20 mL of water, 20 mL of saturated aqueous $NaHCO_3$, and 20 mL of saturated aqueous NaCl and then dried ($MgSO_4$). After removal of the solvent at reduced pressure, chromatography of the residue on 10 g of silica gel with 35% ethyl acetate–cyclohexane afforded 70 mg (98%) of the alcohol **38**: evaporative distillation 100–110 °C (0.005 mmHg); $[\alpha]^{21}_D$ +26.9° (*c* 1.005, $CHCl_3$); IR ($CHCl_3$) 3600, 3460, 1460, 1385, 1370, 1100, 1030 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.94 (t, 3 H, J = 6 Hz, CH_3CH_2), 1.04 (d, 3 H, J = 6 Hz, CH_3CHCC), 4.49 (s, 2 H, $C_6H_5CH_2$), 7.36 (b s, 5 H, C_6H_5). Anal. Calcd for $C_{17}H_{26}O_3$: C, 73.35; H, 9.41. Found: C, 73.42; H, 9.40.

Benzyl 2(*R*)-(5(*S*)-Carbomethoxy-3(*S*)-methyl-2(*S*)-tetrahydrofuryl)butyl Ether (39a). To a stirred 5 mL aqueous solution of Adam's catalyst (freshly prepared from 200 mg of 84% platinum oxide) was added 30 mg (0.36 mmol) of solid $NaHCO_3$ and then a solution of 70 mg (0.25 mmol) of the alcohol **38** in 1 mL of acetone. After complete addition, oxygen was bubbled through this mixture at 50 °C for 4 h. The catalyst was then removed from the cooled reaction mixture by filtration and subsequently washed with two 20-mL portions of 0.2 M aqueous Na_2HPO_4. The combined filtrates were washed with 20 mL of ether and then acidified to pH ~2. The aqueous phase was extracted with four 20-mL portions of ether, and the combined ethereal extracts were washed with 20 mL of saturated aqueous NaCl and then dried ($MgSO_4$). Removal of the solvent at reduced pressure gave 68.8 mg (94%) of the corresponding acid epi-**25**.

A portion of this material was treated with diazomethane in ether and then chromatography of the resulting methyl ester **39a** on silica gel with 10% ethyl acetate–cyclohexane provided the analytical sample: evaporative distillation 100–110 °C (0.005 mmHg); IR ($CHCl_3$) 1740, 1460, 1385, 1370, 1100 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.93 (t, 3 H, J = 6 Hz, CH_3CH_2), 1.00 (d, 3 H, J = 6 Hz, CH_3CHCC), 3.70 (s, 3 H, CO_2CH_3), 4.43 (s, 2 H, $C_6H_5CH_2$), 7.31 (s, 5 H, C_6H_5). Anal. Calcd for $C_{18}H_{26}O_4$: C, 70.56; H, 8.55. Found: C, 70.58; H, 8.45.

2-Methyl-2,3-*O*-(1-methylethylidene)-D-ribonic Acid, γ-Lactone. To a stirred suspension of 67.0 mg (0.41 mol) of D-glucosaccharinic acid, γ-lactone[34] (**40**) in 815 mL of dry acetone at room temperature was added 8.15 mL of 96% sulfuric acid. After 30 h, the reaction mixture was adjusted to pH ~8 with aqueous ammonia. The resulting mixture was filtered and the filtrate concentrated under reduced pressure. The residual oil was dissolved in 800 mL of ether and washed with 500 mL of water. The aqueous layer was then extracted with three 100-mL portions of ether. The combined organic phases were washed with 300 mL of saturated aqueous NaCl and then dried ($MgSO_4$). Removal of solvent under reduced pressure and flash chromatography of the residue on 800 g of silica gel with 85% ether in petroleum ether afforded 77.9 g (94%) of the corresponding ketal, mp 60–61 °C (lit.[38] mp 61–61.5 °C).

2-Methyl-2,3-*O*-(1-methylethylidene)-5-*O*-(methoxymethyl)-D-ribonic Acid, γ-Lactone (41). To a stirred suspension of 1.3 g (32.4 mmol) of potassium hydride in 90 mL of dry THF at 0 °C under argon was added a solution of 5.03 g (24.86 mmol) of the 2,3-acetonide of D-glucosaccharinic acid, γ-lactone in 20 mL of dry THF, and then 3 mL (39.5 mmol) of chloromethyl methyl ether was added. The resulting mixture was stirred at room temperature for 8 h, treated with 20 mL of saturated aqueous $NaHCO_3$, and then diluted with 400 mL of ether. The organic phase was separated and then washed with two 200-mL portions of saturated aqueous $NaHCO_3$, 200 mL of saturated aqueous NaCl, and then dried ($MgSO_4$). After removal of solvents under reduced pressure, chromatography of the residue on 200 g of silica gel with 50% ether in petroleum ether provided 5.70 g (93%) of the methoxymethyl ether **41**: evaporative distillation 90–100 °C (0.005 mmHg); $[\alpha]^{22}_D$ −22.4° (*c* 1.32, $CHCl_3$); IR ($CHCl_3$) 1780, 1380, 1220, 1160, 1105, 1060, 1020 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.42 (s, 6 H, $C(CH_3)_2$), 1.62 (s, 3 H, CH_3), 3.33 (s, 3 H, OCH_3), 3.74 (d, 2 H, J = 3 Hz, CCH_2O), 4.47 (s, 1 H, H3), 4.59 (b s, 2 H, OCH_2O). Anal. Calcd for $C_{11}H_{18}O_6$: C, 53.65; H, 7.37. Found: C, 53.67; H, 7.25.

2-Methyl-2,3-*O*-(1-methylethylidene)-5-*O*-(methoxymethyl)-D-ribose. To a stirred solution of 5.70 g (23.1 mmol) of the lactone **41** in 100 mL of dry ether under argon at −78 °C was added, dropwise over 30 min, 35 mL of a 1 M solution of diisobutylaluminum hydride in hexane. After 1 h, the reaction mixture was cautiously treated with 2 mL of methanol, allowed to warm to room temperature, and then diluted with 500 mL of ether. This solution was washed with three 70-mL portions of saturated aqueous sodium potassium tartarate solution and 70 mL of saturated aqueous NaCl and then dried ($MgSO_4$). After removal of the solvent under reduced pressure, chromatography of the residue on 200 g of silica gel with 75% ether in petroleum ether afforded 5.76 g (100%) of the

(38) Utkin, L. M.; Grabilina, G. O. *Dokl. Akad. Nauk SSSR* **1953**, *93*, 301. Sowden, J. C.; Blair, M. G.; Kuenne, D. J. *J. Am. Chem. Soc.* **1957**, *79*, 6450–6454.

corresponding lactol as a mixture of anomers: evaporative distillation 90–100 °C (0.005 mmHg); $[\alpha]^{22}_D$ +17.9° (*c* 1.17, $CHCl_3$); IR ($CHCl_3$) 3600, 3450, 1460, 1380, 1210, 1160, 1105, 1060, 1030 cm^{-1}; ^1H NMR ($CDCl_3$) δ (minor anomer, major anomer) 3.31, 3.34 (s, 3 H, OCH_3), 3.59, 3.63 (d, 2 H, *J* = 2 Hz, CCH_2O), 4.58, 4.64 (s, 2 H, OCH_2O), 5.00, 5.17 (d, 1 H, *J* = 11 Hz, H-1). Anal. Calcd for $C_{11}H_{20}O_6$: C, 53.22; H, 8.12. Found: C, 53.06; H, 8.05.

1,4-Anhydro-2-deoxy-2-methyl-5-*O*-(methoxymethyl)-D-erythropent-1-enitol (42). To a stirred solution of 6.52 g (26.26 mmol) of the above lactol and 3.1 mL (32 mmol) of carbon tetrachloride in 100 mL of dry THF at −78 °C under argon was added 5.1 mL (28 mmol) of tris(dimethylamino)phosphine. After 45 min, the reaction mixture was allowed to warm to 0 °C and was then added, via a double-tipped needle, to a stirred solution of 52 cm (317 mmol) of lithium wire in 400 mL of anhydrous liquid ammonia at −78 °C under argon. Cooling was then discontinued (ammonia reflux), and after 2 h, 18.7 g (350 mmol) of anhydrous ammonium chloride was cautiously added to the reaction mixture. The resulting colorless mixture was diluted with 500 mL of ether and the ammonia was allowed to evaporate. The resulting ethereal suspension was filtered, and then concentration of the filtrate under reduced pressure afforded a crude mixture of the glycal **42**, the tetrahydrofuran reduction byproduct[28,29] and HMPA. After rapid passage of this crude product through 50 g of silica gel with 75% ether in petroleum ether, concentration of the eluate at reduced pressure and then distillation [Kugelrohr, 110 °C (0.01 mmHg)] of the residue gave 4.694 g of a mixture of the glycal **42** and the byproduct. Analysis of this mixture by ^1H NMR spectroscopy revealed a ratio of 4:1 for glycal to byproduct. Chromatography of a small portion of this mixture on silica gel with 75% ether–petroleum ether provided pure product for analysis: evaporative distillation 60–70 °C (0.005 mmHg); $[\alpha]^{23}_D$ +206.1° *c* 1.11, $CHCl_3$); IR ($CHCl_3$) 3590, 3450, 1675, 1460, 1380, 1210, 1150, 1100, 1020 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.69 (d, 3 H, *J* = 2 Hz, CH_3), 3.37 (s, 3 H, OCH_3), 3.56 (d, 2 H, *J* = 6 Hz, CCH_2O), 5.08 (s, 2 H, OCH_2O), 6.22 (b s, 1 H, HC=C). Anal. Calcd for $C_8H_{14}O_4$: C, 55.16; H, 8.10. Found: C, 55.11; H, 8.03.

Methyl 2(*R*)- and 2(*S*)-(2,5-dihydro-5(*S*)-(methoxymethylenoxymethyl)-3-methyl-2(*R*)-furyl)butanoates (43). A. From the Glycal 42 by Deprotonation in THF. To a stirred solution of 4.6 g (19.8 mmol of the glycal **42**) of the 4:1 mixture of the glycal **42** and the byproduct in 57 mL of dry THF at −78 °C under argon was added 8 mL (19.8 mmol) of a 2.48 M solution of *n*-butyllithium in hexane, and then after 5 min, 2.1 mL (20.2 mmol) of *n*-butyryl chloride was added. After 10 min at 0 °C, the reaction mixture was taken up in an argon flushed syringe and added dropwise to a stirred solution of 24.8 mmol of LDA in 57 mL of dry THF at −78 °C under argon. After 10 min, the reaction mixture was treated with 6.4 mL (37.8 mmol of Me_3SiCl) of the supernatant centrifugate from a 3:1 mixture of trimethylchlorosilane and triethylamine. After 2 h at room temperature, the reaction mixture was diluted with 100 mL of 1 N aqueous NaOH and stirred for 15 min. The organic phase was separated and extracted with three 50-mL portions of 1 N aqueous NaOH, and then the combined aqueous base phases were washed with 50 mL of ether, acidified (pH ~2) and extracted with four 100-mL portions of ether. The combined ethereal extracts were washed with 50 mL of saturated aqueous NaCl and then dried ($MgSO_4$). Removal of the solvent under reduced pressure afforded a mixture of the diastereomeric acids which was esterified with ethereal diazomethane. Chromatography of the resulting methyl esters on 300 g of silica gel with 30% ether in petroleum ether afforded 3.07 g (60%) of the methyl esters **43**. ^1H NMR analysis revealed a ratio of 9:1 for the two diastereomeric methyl esters: evaporative distillation 60–70 °C (0.005 mmHg); IR ($CHCl_3$) 1730, 1460, 1440, 1150, 1110, 1080, 1030 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.33 (s, 3 H, OCH_3), 3.49 (d, 2 H, *J* = 4 Hz, CCH_2O), 3.60, 3.68 (s, 3 H, CO_2CH_3), 4.60 (s, 2 H, OCH_2O), 5.50 (b s, 1 H, C=CH). Anal. Calcd for $C_{13}H_{22}O_5$: C, 60.45; H, 8.58. Found: C, 60.47; H, 8.49.

B. From the Glycal 42 by Deprotonation in HMPA–THF. By the same procedure as described in part A above, 17.87 mmol of the glycal **42** with 10.5 mL (24.15 mmol) of 2.3 M solution of *n*-butyllithium in hexane, 2.6 mL (25 mmol) of *n*-butyryl chloride in 70 mL of dry THF, and 10 mL of dry HMPA, added to 28.5 mmol of LDA in 64 mL of dry THF and 16 mL of dry HMPA, followed by 59 mmol of trimethylchlorosilane, afforded, after treating the diastereomeric acids with ethereal diazomethane and chromatography of the resulting methyl esters on 200 g of silica gel with 30% ether in petroleum ether, 2.4 g (52%) of the isomeric methyl esters **43**. ^1H NMR analysis revealed a ratio of 1:3 for the two diastereomeric methyl esters.

Methyl 2(*R*)- and 2(*S*)-(5(*S*)-(Methoxymethylenoxymethyl)-3(*S*)-methyl-2(*S*)-tetrahydrofuryl)butanoate. To a stirred solution of 2.4 g (9.3 mmol) of the diastereomeric methyl esters **43** (from HMPA/THF reaction) in 93 mL of ethyl acetate was added 240 mg of 10% platinum on carbon. The reaction mixture was stirred at room temperature under a hydrogen atmosphere for 3 h. The catalyst was then removed by filtration and washed with three 25-mL portions of ethyl acetate. Removal of the solvent from the combined filtrates and chromatography of the residue on 200 g of silica gel with 25% ethyl acetate in cyclohexane afforded 1.6 g (66%) of the 2*R* methyl ester and 0.53 g (21%) of the epimeric 2*S* methyl ester. 2*S* Methyl ester: evaporative distillation 80–90 °C (0.005 mmHg); $[\alpha]^{25}_D$ +16.2° (*c* 1.01, $CHCl_3$); IR ($CHCl_3$) 1730, 1460, 1390, 1110, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90 (t, 3 H, *J* = 6 Hz, CH_3CH_2), 1.06 (d, 3 H, *J* = 6 Hz, CH_3CHCC), 3.36 (s, 3 H, OCH_3), 3.52 (d, 2 H, *J* = 5 Hz, CCH_2O), 3.69 (s, 3 H, CO_2CH_3), 4.61 (s, 2 H, OCH_2O). Anal. Calcd for $C_{13}H_{24}O_5$: C, 59.98; H, 9.29. Found: C, 59.92; H, 9.31. 2*R* Methyl ester: evaporative distillation 80–90 °C (0.005 mmHg); $[\alpha]^{25}_D$ +5.4° (*c* 1.16, $CHCl_3$); IR ($CHCl_3$) 1730, 1460, 1275, 1220, 1160, 1105, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88 (t, 3 H, *J* = 6 Hz, CH_3CH_2), 0.99 (d, 3 H, *J* = 6 Hz, CH_3), 3.36 (s, 3 H, OCH_3), 3.51 (d, 2 H, *J* = 5 Hz, CCH_2O), 3.68 (s, 3 H, CO_2CH_3), 4.62 (s, 2 H, OCH_2O). Anal. Calcd for $C_{13}H_{24}O_5$: C, 59.98; H, 9.29. Found: C, 59.93; H, 9.12.

2(*R*)-(5(*S*)-(Methoxymethylenoxymethyl)-3(*S*)-methyl-2(*S*)-tetrahydrofuryl)butan-1-ol (36). By the procedure described for the preparation of the corresponding alcohol of compound **4**, 530 mg (2.0 mmol) of the 2*S* methyl ester above in 10 mL of dry ether with 80 mg of lithium tetrahydridoaluminate (8.4 mmol of hydride) afforded, after chromatography on 40 g of silica gel with 40% ethyl acetate in cyclohexane, 440 mg (95%) of an alcohol, the ^1H NMR spectrum of which was identical with that of compound **36**.

2(*S*)-(5(*S*)-(Methoxymethylenoxymethyl)-3(*S*)-methyl-2(*S*)-tetrahydrofuryl)butan-1-ol (44). By the procedure described for the preparation of the corresponding alcohol of compound **4**, 1.67 g (6.4 mmol) of the 2*R* methyl ester above in 32 mL of dry ether with 240 mg of lithium tetrahydridoaluminate (25.6 mmol of hydride) afforded, after chromatography on 100 g of silica gel with 50% ethyl acetate in cyclohexane, 1.45 g (97%) of the alcohol **44**: evaporative distillation 60–70 °C (0.005 mmHg); $[\alpha]^{25}_D$ +27.4° (*c* 1.265, $CHCl_3$); IR ($CHCl_3$) 3650, 3500, 1460, 1230, 1150, 1105, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.93 (t, 3 H, *J* = 6 Hz, CH_3CH_2), 1.01 (d, 3 H, *J* = 6 Hz, CH_3), 2.67 (dd, 1 H, *J* = 5, 6 Hz, $CHCH_3$), 3.33 (s, 3 H, OCH_3), 3.47 (d, 2 H, *J* = 5 Hz, CCH_2O), 4.60 (s, 2 H, OCH_2O). Anal. Calcd for $C_{12}H_{24}O_4$: C, 62.04; H, 10.41. Found: C, 62.01; H, 10.32.

Benzyl 2(*S*)-(5(*S*)-(Methoxymethylenoxymethyl)-3(*S*)-methyl-2-(*S*)-tetrahydrofuryl)butyl Ether. By the procedure described for the preparation of the benzyl ether **5**, 1.45 g (6.22 mmol) of the alcohol **44** with 300 mg (7.48 mmol) of potassium hydride and 1.2 mL (9.6 mmol) of benzyl bromide in 30 mL of dry THF afforded, after chromatography on 100 g of silica gel with 15% ethyl acetate in cyclohexane, 2.0 g (97%) of the corresponding benzyl ether: evaporative distillation 100–110 °C (0.005 mmHg); $[\alpha]^{25}_D$ +18.7° (*c* 1.71, $CHCl_3$); IR ($CHCl_3$) 1460, 1380, 1120, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.92 (t, 3 H, *J* = 6 Hz, CH_3CH_2), 1.02 (d, 3 H, *J* = 6 Hz, CH_3), 3.33 (s, 3 H, OCH_3), 3.47 (d, 4 H, *J* = 5 Hz, CCH_2O), 4.43 (s, 2 H, $C_6H_5CH_2$), 4.60 (s, 2 H, OCH_2O), 7.28 (b s, 5 H, C_6H_5). Anal. Calcd for $C_{19}H_{30}O_4$: C, 70.77; H, 9.38. Found: C, 70.58; H, 9.22.

Benzyl 2(*S*)-(5(*S*)-(Hydroxymethyl)-3(*S*)-methyl-2(*S*)-tetrahydrofuryl)butyl Ether. By the procedure described for the preparation of the alcohol **38**, 2.0 g (6.2 mmol) of the above methoxy methyl ether in 48 mL of THF and 12 mL of 10% aqueous HCl afforded, after chromatography on 100 g of silica gel with 35% ethyl acetate in cyclohexane, 1.7 g (99%) of the corresponding alcohol: evaporative distillation 100–110 °C (0.005 mmHg); $[\alpha]^{25}_D$ +49.3° (*c* 1.07, $CHCl_3$); IR ($CHCl_3$) 3600, 3450, 1460, 1380, 1220, 1100, 1080, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.93 (t, 3 H, *J* = 6 Hz, CH_3CH_2), 1.02 (d, 3 H, *J* = 6 Hz, CH_3), 3.47 (d, 2 H, *J* = 6 Hz, CCH_2O), 4.48 (s, 2 H, $C_6H_5CH_2$), 7.33 (b s, 5 H, C_6H_5). Anal. Calcd for $C_{17}H_{26}O_3$: C, 73.35; H, 9.41. Found: C, 73.46; H, 9.36.

Benzyl 2(*S*)-(5(*S*)-Carbomethoxy-3(*S*)-methyl-2(*S*)-tetrahydrofuryl)butyl Ether (25a). By the procedure described for the preparation of the methyl ester **34a**, 1.7 g (6.12 mmol) of the above alcohol in 60 mL of water with 643 mg (7.7 mmol) of solid $NaHCO_3$ and freshly prepared Adam's catalyst (from 2 g of 88% platinum oxide) afforded 1.63 g (91%) of the acid **25**. A portion of this material was treated with diazomethane in ether and chromatography of the resulting methyl ester on silica gel with 10% ethyl acetate in cyclohexane provided the analytical sample of the methyl ester **25a**: evaporative distillation 100–110 °C (0.005 mmHg); $[\alpha]^{24}_D$ +1.4° (*c* 1.11, $CHCl_3$); IR ($CHCl_3$) 1740, 1460, 1370, 1220, 1100, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.93 (t, 3 H, *J* = 6 Hz, CH_3CH_2), 1.01 (d, 3 H, *J* = 6 Hz, CH_3), 3.49 (d, 2 H, *J* = 6 Hz, CCH_2O), 3.70 (s, 3 H, CO_2CH_3), 3.80 (dd, 1 H, *J* = 5, 8 Hz, OCHCC), 4.38 (t, 1 H, *J* = 7 Hz, $CHCO_2CH_3$), 4.47 (s, 2 H, $C_6H_5CH_2$), 7.32 (b s, 5 H, C_6H_5). Anal. Calcd for $C_{18}H_{26}O_4$: C, 70.56; H, 8.55. Found: C, 70.54; H, 8.52.

Benzyl-6-deoxy-α- and -β-L-gulose. To a stirred solution of 1.5 g (9.14 mmol) of 6-deoxy-L-gulose (**45**) in 18 mL of benzyl alcohol was added 0.35 mL of acetyl chloride. After 2 days, the reaction mixture was diluted with 40 mL of chloroform and then neutralized with 10 g of barium carbonate. The resulting suspension was filtered and the solid residue washed with three 25-mL portions of chloroform. The combined filtrates were concentrated at 50 °C (0.01 mmHg) and the residue was chromatographed on 200 g of silica gel with ethyl acetate to give 1.8 g (77%) of the benzyl glycosides (α:β = 1:2). α-Glycoside: mp 134.5–135.5 °C (ethyl acetate–hexane); $[\alpha]^{23}_D$ −118.1° (*c* 1.135, $CHCl_3$); IR ($CHCl_3$) 3600, 3500, 1220, 1105, 1080, 1040, 1000 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.23 (d, 3 H, *J* = 6 Hz, CH_3), 4.54 (d, 1 H, *J* = 12 Hz, C_6H_5CH*H*), 4.73 (d, 1 H, *J* = 12 Hz, C_6H_5C*H*H), 4.93 (b s, 1 H, H-1), 7.38 (b s, 5 H, C_6H_5). Anal. Calcd for $C_{13}H_{18}O_5$: C, 61.41; H, 7.14. Found: C, 61.33; H, 7.18. β-Glycoside: evaporative distillation 130–140 °C (0.005 mmHg); $[\alpha]^{25}_D$ +117.9° (*c* 0.585, $CHCl_3$); IR ($CHCl_3$) 3600, 3450, 1220, 1175, 1080, 1060, 1000 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.27 (d, 3 H, *J* = 6 Hz, CH_3), 4.53 (d, 1 H, *J* = 11 Hz, C_6H_5CH*H*), 4.62 (d, 1 H, *J* = 8 Hz, H-1), 4.89 (d, 1 H, *J* = 11 Hz, C_6H_5C*H*H), 7.34 (b s, 5 H, C_6H_5). Anal. Calcd for $C_{13}H_{18}O_5$: C, 61.41; H, 7.14. Found: C, 61.39; H, 7.18.

Benzyl-6-deoxy-2,3-*O*-(1-methylethylidene)-α- and -β-L-gulose. To a stirred solution of 1.8 g (7.08 mmol) of the above benzyl glycosides in 70 mL of dry acetone was added 70 mg (0.37 mmol) of *p*-toluenesulfonic acid monohydrate and 1.1 mL (8.9 mmol) of 2,2-dimethoxypropane. After 12 h, the reaction mixture was neutralized with barium carbonate. The resulting suspension was filtered and the solid residue then washed with three 50-mL portions of acetone. The combined filtrates were concentrated under reduced pressure and the residue chromatographed on 100 g of silica gel with 25% ethyl acetate–petroleum ether to give 1.94 g (93%) of the corresponding ketals. α-Glycoside: mp 79–80 °C (hexane); $[\alpha]^{23}_D$ −62.8 °C (*c* 0.955, $CHCl_3$); IR ($CHCl_3$) 3970, 3460, 1380, 1240, 1160, 1100, 1030 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.19 (d, 3 H, *J* = 6 Hz, CH_3), 1.36, 1.50 (s, 6 H, $C(CH_3)_2$), 4.56 (d, 1 H, *J* = 12 Hz, C_6H_5CH*H*), 4.71 (d, 1 H, *J* = 12 Hz, C_6H_5C*H*H), 4.87 (b s, 1 H, H1), 7.33 (b s, 5 H, C_6H_5). Anal. Calcd for $C_{16}H_{22}O_5$: C, 65.29; H, 7.53. Found: C, 65.26; H, 7.51. β-Glycoside: evaporative distillation 100–110 °C (0.005 mmHg); $[\alpha]^{23}_D$ +105.5° (*c* 0.55, $CHCl_3$); IR ($CHCl_3$) 3560, 3350, 1390, 1230, 1180, 1120, 1060 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.30 (d, 3 H, *J* = 6 Hz, CH_3), 1.31, 1.40 (s, 6 H, $C(CH_3)_2$), 4.73 (d, 1 H, *J* = 4 Hz, H-1), 4.58 (d, 1 H, *J* = 12 Hz, C_6H_5CH*H*), 4.84 (d, 1 H, *J* = 12 Hz, C_6H_5C*H*H), 7.33 (b s, 5 H, C_6H_5). Anal. Calcd for $C_{16}H_{22}O_5$: C, 65.29; H, 7.53. Found: C, 65.31; H, 7.48.

Benzyl-6-deoxy-2,3-*O*-(1-methylethylidene)-4-*O*-(methoxymethyl)-α- and -β-L-gulose (46). By the procedure described for the preparation of the methoxymethyl ether **41**, 1.94 g (6.6 mmol) of a mixture of the above alcohols, 0.34 g (8.5 mmol) of potassium hydride and 1 mL (13.2 mmol) of chloromethyl methyl ether in 22 mL of dry THF afforded, after chromatography on 100 g of silica gel with 25% ethyl acetate–petroleum ether, 1.91 g (86%) of the methoxymethyl ethers **46**. α-Glycoside: evaporative distillation 120–130 °C (0.005 mmHg); $[\alpha]^{24}_D$ −41.3° (*c* 0.75, $CHCl_3$); IR ($CHCl_3$) 1380, 1240, 1150, 1100, 1020 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.20 (d, 3 H, *J* = 6 Hz, CH_3), 1.36, 1.51 (s, 6 H, $C(CH_3)_2$), 3.40 (s, 3 H, OCH_3), 4.57 (b s, 1 H, H-1), 7.34 (b s, 5 H, C_6H_5). Anal. Calcd for $C_{18}H_{26}O_6$: C, 63.89; H, 7.74. Found: C, 64.03; H, 7.75. β-Glycoside: evaporative distillation 100–110 °C (0.005 mmHg); $[\alpha]^{24}_D$ +147.8° (*c* 0.565, $CHCl_3$); IR ($CHCl_3$) 1390, 1230, 1155, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.40 (s, 3 H, OCH_3), 4.57 (d, 1 H, *J* = 12 Hz, H-1), 7.30 (b s, 5 H, C_6H_5). Anal. Calcd for $C_{18}H_{26}O_6$: C, 63.89; H, 7.74. Found: C, 63.83; H, 7.57.

6-Deoxy-2,3-*O*-(1-methylethylidene)-4-*O*-(methoxymethyl)-L-gulose (47). To a stirred solution of 3 cm (18.3 mmol) of lithium wire in 50 mL of anhydrous ammonia at −78 °C under argon was added a solution of 1.91 g (5.64 mmol) of the mixture of benzyl glycosides **46** in 10 mL of dry THF. Cooling was then discontinued (ammonia reflux), and after 1 h, 1.1 g (20.6 mmol) of anhydrous ammonium chloride was cautiously added to the reaction mixture. The resulting mixture was then diluted with 50 mL of ether and the ammonia was allowed to evaporate. The resulting suspension was filtered, and the solid was then washed by trituration with four 20-mL portions of ether. Removal of the solvent from the combined filtrates gave 1.2 g (86%) of the crystalline lactol **47**: mp 139 °C (ethyl acetate–hexane); $[\alpha]^{23}_D$ +61.7° (*c* 1.215, $CHCl_3$); IR ($CHCl_3$) 3600, 3460, 1390, 1230, 1160, 1100, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.27 (d, 3 H, *J* = 6 Hz, CH_3), 1.33, 1.47 (s, 6 H, $C(CH_3)_2$), 3.40 (s, 3 H, OCH_3), 3.57 (d, 1 H, *J* = 6 Hz, OH), 3.63 (dd, 1 H, *J* = 3 Hz, 3 Hz, H-4), 4.00 (dq, 1 H, *J* = 3 Hz, 6 Hz, H-5), 4.03 (dd, 1 H, *J* = 6 Hz, 6 Hz, H-2), 4.33 (dd, 1 H, *J* = 3 Hz, 6 Hz, H-3), 4.63 (d, 1 H, *J* = 6 Hz, OCH*H*O), 4.77 (d, 1 H, *J* = 6 Hz, OC*H*HO), 4.87 (dd, 1 H, *J* = 6 Hz, 6 Hz, H-1). Anal. Calcd for $C_{11}H_{20}O_6$: C, 53.22; H, 8.12. Found: C, 53.12; H, 8.21.

1,5-Anhydro-2,6-dideoxy-4-*O*-(methoxymethyl)-L-*xylo*-hex-1-enitol (26). By the procedure described for the preparation of the glycal **42**, 437.4 mg (1.76 mmol) of the lactol **47**, 0.22 mL (2.28 mmol) of carbon tetrachloride, 0.34 mL (1.87 mmol) of tris(dimethylamino)phosphine in 7 mL of dry THF with 3.5 cm (21.3 mmol) of lithium wire in 30 mL of anhydrous ammonia and 1.4 g (26.2 mmol) of anhydrous ammonium chloride afforded, after passage through 5 g of silica gel with 50% ethyl acetate–petroleum ether and distillation [Kugelrohr, 60 °C (0.1 mmHg)], 280 mg (90%) of the glycal **26**: $[\alpha]^{23}_D$ −206.4° (*c* 0.59, $CHCl_3$); IR ($CHCl_3$) 3620, 3450, 1640, 1240, 1150, 1090, 1030, 940 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.36 (d, 3 H, *J* = 6 Hz, CH_3), 3.40 (s, 3 H, OCH_3), 3.56 (m, 1 H, H-4), 4.10 (m, 2 H, H-3 and H-5), 4.66 (d, 1 H, *J* = 6 Hz, OCH*H*O), 4.73 (d, 1 H, *J* = 6 Hz, OC*H*HO), 4.89 (m, 1 H, H-2), 6.50 (d, 1 H, *J* = 6 Hz, H-1). Anal. Calcd for $C_8H_{14}O_4$: C, 55.16; H, 8.10. Found: C, 55.27; H, 8.20.

Benzyl 2(*R*)-[5(*R*)- and 5(*S*)-Carbomethoxy-3(*S*)-methyl-5-(5,6-dihydro-5(*S*)-(methoxymethylenoxy)-6(*S*)-methyl-2(*R*)-pyranyl)-2(*S*)-tetrahydrofuryl]butyl Ether (50 and 51). By the part A procedure described for the preparation of the methyl esters **43**, 272 mg (1.56 mmol) of the glycal **26** with 0.71 mL (1.63 mmol) of 2.3 M solution of *n*-butyllithium in hexane and 1.61 mmol of the acid chloride of the acid **39** in 6 mL of dry THF, added to 3.45 mmol of LDA in 7 mL of dry THF, followed by 5.1 mmol of trimethylchlorosilane, afforded, after treatment with ethereal diazomethane and chromatography on 30 g of silica gel with 20% ethyl acetate–cyclohexane, 125.7 mg of the methyl ester **50** and 283.4 mg of the methyl ester **51**, or a 30:70 ratio of a 57% combined yield. Methyl ester **50**: evaporative distillation 150–160 °C (0.005 mmHg); $[\alpha]^{24}_D$ +135.7° (*c* 1.915, $CHCl_3$); IR ($CHCl_3$) 1740, 1460, 1390, 1160, 1100, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.93 (t, 3 H, *J* = 6 Hz, CH_3CH_2), 0.97 (d, 3 H, *J* = 6 Hz, CH_3CHCC), 1.20 (d, 3 H, *J* = 6 Hz, CH_3CHOC), 3.37 (s, 3 H, OCH_3), 3.73 (s, 3 H, CO_2CH_3), 4.44 (b s, 2 H, $C_6H_5CH_2$), 4.60 (d, 1 H, *J* = 7 Hz, OCH*H*O), 4.71 (d, 1 H, *J* = 7 Hz, OC*H*HO), 5.63–6.13 (m, 2 H, HC=CH), 7.33 (b s, 5 H, C_6H_5). Anal. Calcd for $C_{26}H_{38}O_7$: C, 67.51; H, 8.28. Found: C, 67.70; H, 8.33. Methyl ester **51**: evaporative distillation 150–160 °C (0.005 mmHg); $[\alpha]^{24}_D$ +159.5° (*c* 0.845, $CHCl_3$); IR ($CHCl_3$) 1745, 1730, 1460, 1380, 1140, 1090, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.87 (t, 3 H, *J* = 6 Hz, CH_3CH_2), 0.96 (d, 3 H, *J* = 6 Hz, CH_3CHCC), 1.13 (d, 3 H, *J* = 6 Hz, CH_3CHOC), 3.33 (s, 3 H, OCH_3), 3.64 (s, 3 H, CO_2CH_3), 4.41 (b s, 2 H, $C_6H_5CH_2$), 4.57 (d, 1 H, *J* = 6 Hz, OCH*H*O), 4.70 (d, 1 H, *J* = 6 Hz, OC*H*HO), 6.00 (m, 2 H, HC=CH), 7.30 (b s, 5 H, C_6H_5). Anal. Calcd for $C_{26}H_{38}O_7$: C, 67.51; H, 8.28. Found: C, 67.61; H, 8.35.

Benzyl 2(*S*)-[5(*R*)- and 5(*S*)-Carbomethoxy-3(*S*)-methyl-5-(5,6-dihydro-5(*S*)-(methoxymethylenoxy)-6(*S*)-methyl-2(*R*)-pyranyl)-2(*S*)-tetrahydrofuryl]butyl Ether (48 and 49). By the part A procedure described for the preparation of the methyl esters **43**, 381 mg (2.18 mmol) of the glycal **26** with 1 mL (2.3 mmol) of 2.3 M solution of *n*-butyllithium in hexane and 2.45 mmol of the acid chloride of the acid **25** in 5 mL of dry THF, added to 4.6 mmol of LDA in 5 mL of dry THF, followed by 9.5 mmol of trimethylchlorosilane, afforded, after treatment with ethereal diazomethane and chromatography on 50 g of silica gel with 20% ethyl acetate–cyclohexane, 178 mg of the methyl ester **48** and 504 mg of the methyl ester **49**, or a 26:74 ratio of a 67% combined yield. Methyl ester **48**: evaporative distillation 150–160 °C (0.005 mmHg); $[\alpha]^{23}_D$ +148.6° (*c* 1.22, $CHCl_3$); IR ($CHCl_3$) 1740, 1460, 1215, 1160, 1100, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.92 (t, 3 H, *J* = 6 Hz, CH_3CH_2), 0.97 (d, 3 H, *J* = 6 Hz, CH_3CHCC), 1.18 (d, 3 H, *J* = 6 Hz, CH_3CHOC), 3.34 (s, 3 H, OCH_3), 3.73 (s, 3 H, CO_2CH_3), 4.47 (b s, 2 H, $C_6H_5CH_2$), 4.62 (d, 1 H, *J* = 7 Hz, OCH*H*O), 4.71 (d, 1 H, *J* = 7 Hz, OC*H*HO), 5.67–6.17 (m, 2 H, HC=CH), 7.33 (b s, 5 H, C_6H_5). Anal. Calcd for $C_{26}H_{38}O_7$: C, 67.51; H, 8.28. Found: C, 67.70; H, 8.39. Methyl ester **49**: evaporative distillation 150–160 °C (0.005 mmHg); $[\alpha]^{23}_D$ +178.8° (*c* 1.30, $CHCl_3$); IR ($CHCl_3$) 1750, 1730, 1460, 1385, 1155, 1100, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90 (t, 3 H, *J* = 6 Hz, CH_3CH_2), 0.97 (d, 3 H, *J* = 6 Hz, CH_3CHCC), 1.16 (d, 3 H, *J* = 6 Hz, CH_3CHOC), 2.50 (q, 1 H, *J* = 6 Hz, CH_3CHCC), 3.34 (s, 3 H, OCH_3), 3.68 (s, 3 H, CO_2CH_3), 4.43 (s, 2 H, $C_6H_5CH_2$), 4.57 (d, 1 H, *J* = 6 Hz, OCH*H*O), 4.70 (d, 1 H, *J* = 6 Hz, OC*H*HO), 5.31 (b s, 2 H, HC=CH), 7.32 (b s, 5 H, C_6H_5). Anal. Calcd for $C_{26}H_{38}O_7$: C, 67.51; H, 8.28. Found: C, 67.43; H, 8.27.

Benzyl 2(*R*)-[5(*R*)-Carbomethoxy-3(*S*)-methyl-5-(5(*S*)-(methoxymethylenoxy)-6(*S*)-methyl-2(*R*)-tetrahydropyranyl)-2(*S*)-tetrahydrofuryl]butyl Ether. To a stirred solution of 140 mg (0.30 mmol) of the methyl ester **50** in 5 mL of ethyl acetate was added 0.1 mL of Raney nickel catalyst suspension.[37] The reaction mixture was stirred at room temperature under hydrogen atmosphere for 3 h. The catalyst was then removed by filtration and washed with three 5-mL portions of ethyl acetate. The combined filtrates were concentrated under reduced pressure, and chromatography of the resulting residue on 10 g of silica gel

with 15% ethyl acetate in petroleum ether gave 120 mg (85%) of the saturated methyl ester: evaporative distillation 150–160 °C (0.005 mmHg); $[\alpha]^{26}_D$ +3.4° (*c* 0.83, $CHCl_3$); IR ($CHCl_3$) 1730, 1460, 1380, 1100, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.93 (t, 3 H, *J* = 6 Hz, CH_3CH_2), 0.94 (d, 3 H, *J* = 6 Hz, CH_3CHCC), 1.20 (d, 3 H, *J* = 6 Hz, CH_3CHOC), 3.31 (s, 3 H, OCH_3), 3.69 (s, 3 H, CO_2CH_3), 4.43 (b s, 3 H, $C_6H_5CH_2$), 4.58 (b s, 2 H, OCH_2O), 7.30 (b s, 5 H, C_6H_5). Anal. Calcd for $C_{26}H_{40}O_7$: C, 67.22; H, 8.68. Found: C, 67.46; H, 8.67.

Benzyl 2(*R*)-[5(*S*)-Carbomethoxy-3(*S*)-methyl-5-(5(*S*)-(methoxymethylenoxy)-6(*S*)-methyl-2(*R*)-tetrahydropyranyl)-2(*S*)-tetrahydrofuryl]butyl Ether. By the procedure described above, 340 mg (0.74 mmol) of the methyl ester **51** in 5 mL of ethyl acetate with 0.2 mL of Raney nickel catalyst suspension[37] afforded, after chromatography on 30 g of silica gel with 20% ethyl acetate in petroleum ether, 300 mg (88%) of the saturated methyl ester: evaporative distillation 150–160 °C (0.005 mmHg); $[\alpha]^{25}_D$ +19.3° (*c* 0.56, $CHCl_3$); IR ($CHCl_3$) 1745, 1730, 1460, 1385, 1210, 1140, 1105, 1030 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.93 (t, 3 H, *J* = 6 Hz, CH_3CH_2), 0.97 (d, 3 H, *J* = 6 Hz, CH_3CHCC), 1.12 (d, 3 H, *J* = 6 Hz, CH_3CHOC), 3.30 (s, 3 H, OCH_3), 3.63 (s, 3 H, CO_2CH_3), 4.40 (b s, 2 H, $C_6H_5CH_2$), 4.57 (b s, 2 H, OCH_2O), 7.30 (s, 5 H, C_6H_5). Anal. Calcd for $C_{26}H_{40}O_7$: C, 67.22; H, 8.68. Found: C, 67.23; H, 8.69.

Benzyl 2(*S*)-[5(*R*)-Carbomethoxy-3(*S*)-methyl-5-(5(*S*)-(methoxymethylenoxy)-6(*S*)-methyl-2(*R*)-tetrahydropyranyl)-2(*S*)-tetrahydrofuryl]butyl Ether. By the same hydrogenation procedure, 168 mg (0.36 mmol) of the methyl ester **48** in 5 mL of ether acetate with 0.1 mL of Raney nickel catalyst suspension[37] afforded, after chromatography on 20 g of silica gel with 15% ethyl acetate–cyclohexane, 150 mg (89%) of the saturated methyl ester: evaporative distillation 150–160 °C (0.005 mmHg); $[\alpha]^{24}_D$ +3.5° (*c* 1.255, $CHCl_3$); IR ($CHCl_3$) 1730, 1460, 1380, 1110, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.93 (t, 3 H, *J* = 6 Hz, CH_3CH_2), 0.95 (d, 3 H, *J* = 6 Hz, CH_3CHCC), 1.17 (d, 3 H, *J* = 6 Hz, CH_3CHOC), 3.33 (s, 3 H, OCH_3), 3.70 (s, 3 H, CO_2CH_3), 4.47 (b s, 2 H, $C_6H_5CH_2$), 4.59 (b s, 2 H, OCH_2O), 7.33 (b s, 5 H, C_6H_5). Anal. Calcd for $C_{26}H_{40}O_7$: C, 67.22; H, 8.68. Found: C, 67.02; H, 8.69.

Benzyl 2(*S*)-[5(*S*)-Carbomethoxy-3(*S*)-methyl-5-(5(*S*)-(methoxymethylenoxy)-6(*S*)-methyl-2(*R*)-tetrahydropyranyl)-2(*S*)-tetrahydrofuryl]butyl Ether. By the above procedure, 494 mg (1.07 mmol) of the methyl ester **49** in 8 mL of ethyl acetate with 0.3 mL of Raney nickel catalyst suspension[37] afforded, after chromatography on 40 g of silica gel with 20% ethyl acetate–cyclohexane, 420 mg (85%) of the saturated methyl ester: evaporative distillation 150–160 °C (0.005 mmHg); $[\alpha]^{23}_D$ +33.0° (*c* 1.03, $CHCl_3$); IR ($CHCl_3$) 1750, 1730, 1460, 1390, 1110, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90 (t, 3 H, *J* = 6 Hz, CH_3CH_2), 0.94 (d, 3 H, *J* = 6 Hz, CH_3CHCC), 1.12 (d, 3 H, *J* = 6 Hz, CH_3CHOC), 2.39 (q, 1 H, *J* = 6 Hz, CH_3CHCC), 3.32 (s, 3 H, OCH_3), 3.67 (s, 3 H, CO_2CH_3), 4.47 (b s, 2 H, $C_6H_5CH_2$), 4.60 (b s, 2 H, OCH_2O), 7.33 (b s, 5 H, C_6H_5). Anal. Calcd for $C_{26}H_{40}O_7$: C, 67.22; H, 8.68. Found: C, 67.31; H, 8.72.

Benzyl 2(*R*)-[5(*R*)-Formyl-3(*S*)-methyl-5-(5(*S*)-(methoxymethylenoxy)-6(*S*)-methyl-2(*R*)-tetrahydropyranyl)-2(*S*)-tetrahydrofuryl]butyl Ether (54). To a stirred solution of 100 mg (0.22 mmol) of the saturated methyl ester from the ester **50** in 2 mL of dry ether under argon at −78 °C was added dropwise over 10 min 0.7 mL of a 1 M hexane solution of diisobutylaluminum hydride. After 1 h, the reaction mixture was cautiously treated with 0.1 mL of methanol, allowed to warm to room temperature, and then diluted with 30 mL of ether. This solution was washed with three 10-mL portions of saturated aqueous sodium tartarate and 10 mL of saturated aqueous NaCl and then dried ($MgSO_4$). After removal of the solvent under reduced pressure, chromatography of the residue on 10 g of silica gel with 20% ethyl acetate in petroleum ether gave 90 mg (96%) of the aldehyde **54**: evaporative distillation 150–160 °C (0.005 mmHg); $[\alpha]^{24}_D$ +6.2° (*c* 1.015, $CHCl_3$); IR ($CHCl_3$) 1735, 1460, 1385, 1110, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.93 (t, 3 H, *J* = 6 Hz, CH_3CH_2), 0.94 (d, 3 H, *J* = 6 Hz, CH_3CHCC), 1.17 (d, 3 H, *J* = 6 Hz, CH_3CHOC), 3.33 (s, 3 H, OCH_3), 4.46 (b s, 2 H, $C_6H_5CH_2$), 4.60 (b s, 2 H, OCH_2O), 7.33 (b s, 5 H, C_6H_5), 9.57 (s, 1 H, CHO). Anal. Calcd for $C_{25}H_{38}O_6$: C, 69.10; H, 8.81. Found: C, 69.06; H, 8.78.

Benzyl 2(*R*)-[5(*S*)-Formyl-3(*S*)-methyl-5-(5(*S*)-(methoxymethylenoxy)-6(*S*)-methyl-2(*R*)-tetrahydropyranyl)-2(*S*)-tetrahydrofuryl]butyl Ether (55). By the procedure described above, 206 mg (0.44 mmol) of the saturated methyl ester from methyl ester **51** in 4 mL of dry ether with 1.4 mL of 1 M solution of diisobutylaluminum hydride in hexane afforded, after chromatography on 20 g of silica gel with 20% ethyl acetate in petroleum ether, 190 mg (98%) of the aldehyde **55**: evaporative distillation 150–160 °C (0.005 mmHg); $[\alpha]^{24}_D$ +30.7° (*c* 0.95, $CHCl_3$); IR ($CHCl_3$) δ 0.92 (t, 3 H, *J* = 6 Hz, CH_3CH_2), 3.32 (s, 3 H, OCH_3), 4.41 (b s, 2 H, $C_6H_5CH_2$), 4.59 (b s, 2 H, OCH_2O), 7.30 (b s, 5 H, C_6H_5), 9.67 (s, 1 H, CHO). Anal. Calcd for $C_{25}H_{38}O_6$: C, 69.10; H, 8.81. Found: C, 69.11; H, 8.91.

Benzyl 2(*S*)-[5(*R*)-Formyl-3(*S*)-methyl-5-(5(*S*)-(methoxymethylenoxy)-6(*S*)-methyl-2(*R*)-tetrahydropyranyl)-2(*S*)-tetrahydrofuryl]butyl Ether (52). By the procedure described above, 139 mg (0.30 mmol) of the saturated methyl ester from methyl ester **48** in 3 mL of dry ether with 0.9 mL of 1 M solution of diisobutylaluminum hydride in hexane afforded, after chromatography on 20 g of silica gel with 20% ethyl acetate in cyclohexane, 120 mg (92%) of the aldehyde **52**: evaporative distillation 150–160 °C (0.005 mmHg); $[\alpha]^{23}_D$ +18.7° (*c* 1.55, $CHCl_3$); IR ($CHCl_3$) 1730, 1460, 1390, 1100, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.93 (t, 3 H, *J* = 6 Hz, CH_3CH_2), 0.93 (d, 3 H, *J* = 6 Hz, CH_3CHCC), 1.17 (d, 3 H, *J* = 6 Hz, CH_3CHOC), 3.33 (s, 3 H, OCH_3), 4.47 (b s, 2 H, $C_6H_5CH_2$), 4.60 (b s, 2 H, OCH_2O), 7.33 (b s, 5 H, C_6H_5), 9.60 (s, 1 H, CHO). Anal. Calcd for $C_{25}H_{38}O_6$: C, 69.10; H, 8.81. Found: C, 69.08; H, 8.73.

Benzyl 2(*S*)-[5(*S*)-Formyl-3(*S*)-methyl-5-(5(*S*)-(methoxymethylenoxy)-6(*S*)-methyl-2(*R*)-tetrahydropyranyl)-2(*S*)-tetrahydrofuryl]butyl Ether (53). By the procedure described above, 407 mg (0.88 mmol) of the saturated methyl ester from methyl ester **49** in 5 mL of dry ether with 2.7 mL of 1 M solution of diisobutylaluminum hydride in hexane afforded, after chromatography on 30 g of silica gel with 20% ethyl acetate in cyclohexane, 363 mg (95%) of the aldehyde **53**: evaporative distillation 150–160 °C (0.005 mmHg); $[\alpha]^{23}_D$ +50.8° (*c* 1.00, $CHCl_3$); IR ($CHCl_3$) 1735, 1460, 1380, 1110, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90 (t, 3 H, *J* = 6 Hz, CH_3CH_2), 0.94 (d, 3 H, *J* = 6 Hz, CH_3CHCC), 1.12 (d, 3 H, *J* = 6 Hz, CH_3CHOC), 2.33 (q, 1 H, *J* = 6 Hz, CH_3CHCC), 3.30 (s, 3 H, OCH_3), 4.46 (b s, 2 H, $C_6H_5CH_2$), 4.57 (b s, 2 H, OCH_2O), 7.30 (b s, 5 H, C_6H_5), 9.67 (s, 1 H, CHO). Anal. Calcd for $C_{25}H_{38}O_6$: C, 69.10; H, 8.81. Found: C, 69.06; H, 8.80.

Benzyl 2(*R*)-[5(*S*)-Vinyl-3(*S*)-methyl-5-(5(*S*)-(methoxymethylenoxy)-6(*S*)-methyl-2(*R*)-tetrahydropyranyl)-2(*S*)-tetrahydrofuryl]butyl Ether. To a stirred solution of 161 mg (0.45 mmol) of methyltriphenylphosphonium bromide in 1 mL of dry THF at −78 °C under argon was added 0.185 mL (0.43 mmol) of a 2.3 M solution of *n*-butyllithium in hexane. Cooling was then discontinued and the reaction mixture was stirred at room temperature for 1 h and then cooled to −78 °C. A solution of 80 mg (0.18 mmol) of the aldehyde **54** in 1 mL of dry THF was added and the reaction mixture allowed to warm to room temperature, after 10 h, the reaction mixture was treated with 1 mL of saturated aqueous $NaHCO_3$, diluted with 40 mL of ether, washed with 20 mL of saturated aqueous $NaHCO_3$ and 20 mL of saturated aqueous NaCl, and then dried ($MgSO_4$). Removal of the solvents at reduced pressure and chromatography of the residue on 10 g of silica gel with 8% ethyl acetate in petroleum ether afforded 64 mg (80%) of the adduct: evaporative distillation 140–150 °C (0.005 mmHg); $[\alpha]^{26}_D$ −2.8° (*c* 1.04, $CHCl_3$); IR ($CHCl_3$) 1470, 1390, 1110, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.92 (t, 3 H, *J* = 6 Hz, CH_3CH_2), 0.93 (d, 3 H, *J* = 6 Hz, CH_3CHCC), 1.13 (d, 3 H, *J* = 6 Hz, CH_3CHOC), 3.31 (s, 3 H, OCH_3), 4.44 (b s, 2 H, $C_6H_5CH_2$), 4.58 (b s, 2 H, OCH_2O), 4.96 (dd, 1 H, *J* = 3, 11 Hz, HC=CH*H*(c)), 5.19 (dd, 1 H, *J* = 3, 18 Hz, CH=C*H*H(t)), 5.87 (dd, *J* = 11, 18 Hz, *H*C=CH_2), 7.31 (b s, 5 H, C_6H_5). Anal. Calcd for $C_{26}H_{40}O_5$: C, 72.19; H, 9.32. Found: C, 72.11; H, 9.20.

Benzyl 2(*R*)-[5(*R*)-Vinyl-3(*S*)-methyl-5-(5(*S*)-(methoxymethylenoxy)-6(*S*)-methyl-2(*R*)-tetrahydropyranyl)-2(*S*)-tetrahydrofuryl]butyl Ether. By the procedure described above, 180 mg (0.41 mmol) of the aldehyde **55** in 4 mL of dry THF with 0.85 mmol of methylenetriphenylphosphorane afforded, after chromatography on 20 g of silica gel with 8% ethyl acetate in petroleum ether, 160 mg (89%) of the adduct: evaporative distillation 140–150 °C (0.005 mmHg); $[\alpha]^{26}_D$ +42.1° (*c* 0.96, $CHCl_3$); IR ($CHCl_3$) 1460, 1380, 1100, 1030 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.93 (t, 3 H, *J* = 6 Hz, CH_3CH_2), 0.97 (d, 3 H, *J* = 6 Hz, CH_3CHCC), 1.20 (d, 3 H, *J* = 6 Hz, CH_3CHOC), 3.33 (s, 3 H, OCH_3), 4.44 (b s, 2 H, $C_6H_5CH_2$), 4.59 (b s, 2 H, OCH_2O), 5.00 (dd, 1 H, *J* = 3, 11 Hz, HC=CH*H*(c)), 5.13 (dd, 1 H, *J* = 3, 18 Hz, HC=CH*H*(t)), 5.87 (dd, 1 H, *J* = 11, 18 Hz, *H*C=CH_2), 7.30 (b s, 5 H, C_6H_5). Anal. Calcd for $C_{26}H_{40}O_5$: C, 72.19; H, 9.32. Found: C, 72.01; H, 9.20.

Benzyl 2(*S*)-[5(*S*)-Vinyl-3(*S*)-methyl-5-(5(*S*)-(methoxymethylenoxy)-6(*S*)-methyl-2(*R*)-tetrahydropyranyl)-2(*S*)-tetrahydrofuryl]butyl Ether. By the procedure described above, 109.5 mg (0.25 mmol) of the aldehyde **52** in 2 mL of dry THF with 0.57 mmol of methylenetriphenylphosphorane afforded, after chromatography on 10 g of silica gel with 7% ethyl acetate in cyclohexane, 90 mg (83%) of the adduct: evaporative distillation 140–150 °C (0.005 mmHg); $[\alpha]^{23}_D$ +2.8° (*c* 0.905, $CHCl_3$); IR ($CHCl_3$) 1460, 1380, 1205, 1110, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.93 (t, 3 H, *J* = 6 Hz, CH_3CH_2), 0.93 (d, 3 H, *J* = 6 Hz, CH_3CHCC), 1.14 (d, 3 H, *J* = 6 Hz, CH_3CHOC), 3.33 (s, 3 H, OCH_3), 4.44 (b s, 2 H, $C_6H_5CH_2$), 4.61 (b s, 2 H, OCH_2O), 4.93 (dd, 1 H, *J* = 3, 11 Hz, HC=CH*H*(c)), 5.13 (dd, 1 H, *J* = 3, 18 Hz, HC=CH*H*(t)), 5.90 (dd, 1 H, *J* = 11, 18 Hz, *H*C=CH_2), 7.33 (b s, 5 H, C_6H_5). Anal. Calcd for $C_{26}H_{40}O_5$: C, 72.19; H, 9.32. Found: C, 72.10; H, 9.29.

Benzyl 2(*S*)-[5(*R*)-Vinyl-3(*S*)-methyl-5-(5(*S*)-(methoxymethylenoxy)-6(*S*)-methyl-2(*R*)-tetrahydropyranyl)-2(*S*)-tetrahydrofuryl]butyl Ether. By the procedure described above, 353.4 mg (0.81 mmol) of the aldehyde **53** in 5 mL of dry THF with 1.72 mmol of methylenetriphenylphosphorane afforded, after chromatography on 30 g of silica gel with 7% ethyl acetate in cyclohexane, 310 mg (88%) of the adduct: evaporative distillation 140–150 °C (0.005 mmHg); $[\alpha]^{23}_D$ +51.4° (*c* 0.97, $CHCl_3$); IR ($CHCl_3$) 1460, 1380, 1100, 1030 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.91 (t, 3 H, *J* = 6 Hz, CH_3CH_2), 0.94 (d, 3 H, *J* = 6 Hz, CH_3CHCC), 1.20 (d, 3 H, *J* = 6 Hz, CH_3CHOC), 3.32 (s, 3 H, OCH_3), 4.47 (b s, 2 H, $C_6H_5CH_2$), 4.59 (b s, 2 H, OCH_2O), 5.02 (dd, 1 H, *J* = 3, 10 Hz, HC=CH*H*(c)), 5.20 (dd, 1 H, *J* = 3, 18 Hz, HC=CH*H*(t)), 5.87 (dd, 1 H, *J* = 10, 18 Hz, *H*C=CH_2), 7.32 (b s, 5 H, C_6H_5). Anal. Calcd for $C_{26}H_{40}O_5$: C, 72.19; H, 9.32. Found: C, 72.26; H, 9.15.

Benzyl 2(*R*)-[5(*R*)-Ethyl-3(*S*)-methyl-5-(5(*S*)-(methoxymethylenoxy)-6(*S*)-methyl-2(*R*)-tetrahydropyranyl)-2(*S*)-tetrahydrofuryl]butyl Ether. By the procedure described for the hydrogenation of ester **48**, 55 mg (0.13 mmol) of the adduct from aldehyde **54** in 2 mL of ethyl acetate with 0.05 mL of Raney nickel catalyst suspension[37] afforded, after chromatography on 10 g of silica gel with 7% ethyl acetate in petroleum ether, 49.5 mg (90%) of the saturated compound: evaporative distillation 140–150 °C (0.005 mmHg); $[\alpha]^{25}_D$ +14.0° (*c* 0.97, $CHCl_3$); IR ($CHCl_3$) 1460, 1380, 1100, 1035 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.20 (d, 3 H, *J* = 6 Hz, CH_3CHOC), 3.33 (s, 3 H, OCH_3), 4.52 (b s, 2 H, $C_6H_5CH_2$), 4.61 (b s, 2 H, OCH_2O), 7.33 (b s, 5 H, C_6H_5). Anal. Calcd for $C_{26}H_{42}O_5$: C, 71.85; H, 9.74. Found: C, 71.88; H, 9.74.

Benzyl 2(*R*)-[5(*S*)-Ethyl-3(*S*)-methyl-5-(5(*S*)-(methoxymethylenoxy)-6(*S*)-methyl-2(*R*)-tetrahydropyranyl)-2(*S*)-tetrahydrofuryl]butyl Ether. By the procedure described for the hydrogenation of ester **48**, 141 mg (0.33 mmol) of the adduct from aldehyde **55** in 3 mL of ethyl acetate with 0.1 mL of Raney nickel catalyst suspension[37] afforded, after chromatography on 15 g of silica gel with 7% ethyl acetate in petroleum ether, 130 mg (92%) of the saturated compound: evaporative distillation 140–150 °C (0.005 mmHg); $[\alpha]^{25}_D$ +14.3° (*c* 0.955, $CHCl_3$); IR ($CHCl_3$) 1460, 1385, 1105, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.20 (d, 3 H, *J* = 6 Hz, CH_3CHOC), 3.33 (s, 3 H, OCH_3), 4.43 (b s, 2 H, $C_6H_5CH_2$), 4.60 (b s, 2 H, OCH_2O), 7.30 (b s, 5 H, C_6H_5). Anal. Calcd for $C_{26}H_{42}O_5$: C, 71.85; H, 9.74. Found: C, 71.82; H, 9.88.

Benzyl 2(*S*)-[5(*R*)-Ethyl-3(*S*)-methyl-5-(5(*S*)-(methoxymethylenoxy)-6(*S*)-methyl-2(*R*)-tetrahydropyranyl)-2(*S*)-tetrahydrofuryl]butyl Ether. By the procedure described for the hydrogenation of ester **48**, 77.4 mg (0.18 mmol) of the adduct from aldehyde **52** in 3 mL of ethyl acetate with 0.1 mL of Raney nickel catalyst suspension[37] afforded, after chromatography on 10 g of silica gel with 7% ethyl acetate in cyclohexane, 65 mg (84%) of the saturated compound: evaporative distillation 140–150 °C (0.005 mmHg); $[\alpha]^{23}_D$ +27.0° (*c* 1.565, $CHCl_3$); IR ($CHCl_3$) 1460, 1380, 1210, 1110, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.17 (d, 3 H, *J* = 6 Hz, CH_3CHOC), 3.33 (s, 3 H, OCH_3), 4.44 (b s, 2 H, $C_6H_5CH_2$), 4.57 (b s, 2 H, OCH_2O), 7.33 (b s, 5 H, C_6H_5). Anal. Calcd for $C_{26}H_{42}O_5$: C, 71.85; H, 9.74. Found: C, 71.68; H, 9.58.

Benzyl 2(*S*)-[5(*S*)-Ethyl-3(*S*)-methyl-5-(5(*S*)-(methoxymethylenoxy)-6(*S*)-methyl-2(*R*)-tetrahydropyranyl)-2(*S*)-tetrahydrofuryl]butyl Ether. By the procedure described for the hydrogenation of ester **48**, 300 mg (0.69 mmol) of the adduct from aldehyde **53** in 5 mL of ethyl acetate with 0.1 mL of Raney nickel catalyst suspension[37] afforded, after chromatography on 25 g of silica gel with 7% ethyl acetate in cyclohexane, 270 mg (90%) of the saturated compound: evaporative distillation 140–150 °C (0.005 mmHg); $[\alpha]^{24}_D$ +28.3° (*c* 1.03, $CHCl_3$); IR ($CHCl_3$) 1460, 1390, 1100, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.82, 0.90 (2t, 6 H, *J* = 6 Hz, CH_3CH_2), 0.94 (d, 3 H, *J* = 6 Hz, CH_3CHCC), 1.18 (d, 3 H, *J* = 6 Hz, CH_3CHOC), 3.32 (s, 3 H, OCH_3), 4.46 (b s, 2 H, $C_6H_5CH_2$), 4.59 (b s, 2 H, OCH_2O), 7.30 (b s, 5 H, C_6H_5). Anal. Calcd for $C_{26}H_{42}O_5$: C, 71.85; H, 9.74. Found: C, 71.88; H, 9.59.

Benzyl 2(*R*)-[5(*R*)-Ethyl-3(*S*)-methyl-5-(5(*S*)-hydroxy-6(*S*)-methyl-2(*R*)-tetrahydropyranyl)-2(*S*)-tetrahydrofuryl]butyl Ether (57). By the procedure described for the preparation of the alcohol **38**, 40 mg (0.09 mmol) of the methoxymethyl ether from aldehyde **54** in 3 mL of THF and 0.75 mL of 10% aqueous HCl afforded, after chromatography on 7 g of silica gel with 25% ethyl acetate in petroleum ether, 35 mg (97%) of the alcohol **57**: evaporative distillation 140–150 °C (0.005 mmHg); $[\alpha]^{25}_D$ +11.6° (*c* 0.93, $CHCl_3$); IR ($CHCl_3$) 3620, 3450, 1460, 1380, 1100, 1070 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.14 (d, 3 H, *J* = 6 Hz, CH_3CHOC), 4.44 (s, 2 H, $C_6H_5CH_2$), 7.32 (b s, 5 H, C_6H_5). Anal. Calcd for $C_{24}H_{38}O_4$: C, 73.81; H, 9.81. Found: C, 73.79; H, 9.70.

Benzyl 2(*R*)-[5(*S*)-Ethyl-3(*S*)-methyl-5-(5(*S*)-hydroxy-6(*S*)-methyl-2(*R*)-tetrahydropyranyl)-2(*S*)-tetrahydrofuryl]butyl Ether (58). By the procedure described for the preparation of the alcohol **38**, 120 mg (0.28 mmol) of the methoxymethyl ether from aldehyde **55** in 4 mL of THF and 1 mL of 10% aqueous HCl afforded, after chromatography on 10 g of silica gel with 25% ethyl acetate in petroleum ether, 105 mg (97%) of the alcohol **58**: evaporative distillation 140–150 °C (0.005 mmHg); $[\alpha]^{25}_D$ +9.7° (*c* 0.96, $CHCl_3$); IR ($CHCl_3$) 3640, 3450, 1460, 1380, 1105, 1070 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.96 (d, 3 H, *J* = 6 Hz, CH_3CHCC), 1.17 (d, 3 H, *J* = 6 Hz, CH_3CHOC), 4.42 (s, 2 H, $C_6H_5CH_2$), 7.32 (b s, 5 H, C_6H_5). Anal. Calcd for $C_{24}H_{38}O_4$: C, 73.81; H, 9.81. Found: C, 73.91; H, 9.73.

Benzyl 2(*S*)-[5(*R*)-Ethyl-3(*S*)-methyl-5-(5(*S*)-hydroxy-6(*S*)-methyl-2(*R*)-tetrahydropyranyl)-2(*S*)-tetrahydrofuryl]butyl Ether (56). By the procedure described for the preparation of the alcohol **38**, 54.8 mg (0.13 mmol) of the methoxymethyl ether from aldehyde **52** in 4 mL of THF and 1 mL of 10% aqueous HCl afforded, after chromatography on 10 g of silica gel with 20% ethyl acetate–cyclohexane, 45 mg (92%) of the alcohol **56**: evaporative distillation 140–150 °C (0.005 mmHg); $[\alpha]^{23}_D$ +19.8° (*c* 2.0, $CHCl_3$); IR ($CHCl_3$) 3650, 3450, 1460, 1380, 1100, 1070 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.17 (d, 3 H, *J* = 6 Hz, CH_3CHOC), 4.47 (s, 2 H, $C_6H_5CH_2$), 7.33 (b s, 5 H, C_6H_5). Anal. Calcd for $C_{24}H_{38}O_4$: C, 73.81; H, 9.81. Found: C, 73.72; H, 9.72.

Benzyl 2(*S*)-[5(*S*)-Ethyl-3(*S*)-methyl-5-(5(*S*)-hydroxy-6(*S*)-methyl-2(*R*)-tetrahydropyranyl)-2(*S*)-tetrahydrofuryl]butyl Ether (7). By the procedure described for the preparation of the alcohol **38**, 265 mg (0.62 mmol) of the methoxymethyl ether from aldehyde **53** in 8 mL of THF and 2 mL of 10% aqueous HCl afforded, after chromatography on 20 g of silica gel with 25% ethyl acetate in petroleum ether, 240 mg (100%) of the alcohol **7**. The spectral characteristics of this material were identical with those of the alcohol derived from degradation of lasalocid A.

Benzyl 2(*S*)-[5(*S*)-Ethyl-3(*S*)-methyl-5-(6(*S*)-methyl-5-oxo-2(*R*)-tetrahydropyranyl)-2(*S*)-tetrahydrofuryl]butyl Ether (59). To a stirred solution of 0.06 mL of oxalyl chloride (0.69 mmol) in 2 mL of dry dichloromethane at −60 °C under argon was added 0.11 mL (1.55 mmol) of dimethyl sulfoxide. After 10 min, a solution of 240 mg (0.61 mmol) of the alcohol **7** in 1.5 mL of dry dichloromethane was added to the reaction mixture. After 15 min, the reaction mixture was treated with 0.44 mL (3.16 mmol) of dry triethylamine, allowed to warm to room temperature, and then diluted with 40 mL of ether. This mixture was washed with 15 mL of water, 15 mL of saturated aqueous $NaHCO_3$, and 15 mL of saturated aqueous NaCl, and then dried ($MgSO_4$). Removal of the solvents at reduced pressure and chromatography of the residue on 20 g of silica gel with 10% ethyl acetate in cyclohexane afforded 225 mg (94%) of the ketone **59**: evaporative distillation 120–130 °C (0.005 mmHg); $[\alpha]^{24}_D$ −5.9° (*c* 0.95, $CHCl_3$); IR ($CHCl_3$) 1720, 1460, 1380, 1110 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.27 (d, 3 H, *J* = 6 Hz, CH_3CHOC), 4.30 (q, 1 H, *J* = 6 Hz, $CHCO$), 4.44 (s, 2 H, $C_6H_5CH_2$), 7.33 (b s, 5 H, C_6H_5). Anal. Calcd for $C_{24}H_{36}O_4$: C, 74.19; H, 9.34. Found: C, 74.02; H, 9.35.

Benzyl 2(*S*)-[5(*S*)-Ethyl-3(*S*)-methyl-5-(6(*S*)-methyl-5-methylene-2(*R*)-tetrahydropyranyl)-2(*S*)-tetrahydrofuryl]butyl Ether. By the procedure described for the preparation of the adduct of aldehyde **54**, 214.5 mg (0.55 mmol) of the ketone **59** in 4 mL of dry THF with 1.38 mmol of methylenetriphenylphosphorane afforded, after chromatography on 20 g of silica gel with 4% ethyl acetate in cyclohexane, 200 mg (94%) of the corresponding exomethylene olefin: evaporative distillation 120–130 °C (0.005 mmHg); $[\alpha]^{24}_D$ +7.9° (*c* 1.205, $CHCl_3$); IR ($CHCl_3$) 1460, 1380, 1120, 1080 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.83, 0.93 (2t, 6 H, *J* = 6 Hz, CH_3CH_2), 0.97 (d, 3 H, *J* = 6 Hz, CH_3CHCC), 1.30 (d, 3 H, *J* = 6 Hz, CH_3CHOC), 4.43 (q, 1 H, *J* = 6 Hz, CHC=C), 4.47 (s, 2 H, $C_6H_5CH_2$), 4.67 (b s, 2 H, C=CH_2), 7.31 (b s, 5 H, C_6H_5). Anal. Calcd for $C_{25}H_{38}O_3$: C, 77.68; H, 9.91. Found: C, 77.64; H, 10.03.

Benzyl 2(*S*)-[5(*S*)-Ethyl-3(*S*)-methyl-5-(3(*R*)-1,5-dioxo-4(*S*)-methylspiro[2.5]-6(*R*)-octyl)-2(*S*)-tetrahydrofuryl]butyl Ether (60). To a stirred solution of 191 mg (0.49 mmol) of the above olefin in 5 mL of dry dichloromethane at 0 °C under argon were added 160 mg (1.9 mmol) of solid $NaHCO_3$ and 160 mg (0.74–0.83 mmol) of 80–90% *m*-chloroperbenzoic acid. Cooling was then discontinued, and the reaction mixture was stirred at room temperature for 3 h. After treatment of this mixture with 2 mL of 10% aqueous Na_2SO_3, the resulting mixture was diluted with 60 mL of ether, washed with two 20-mL portions of saturated aqueous $NaHCO_3$ and 20 mL of saturated aqueous NaCl, and then dried ($MgSO_4$). Removal of the solvents and chromatography of the residue on 20 g of silica gel with 10% ethyl acetate in petroleum ether afforded 141 mg of the epoxide **60** and 40 mg of the epimeric epoxide (ratio of 3.5:1 of 91% combined yield). Epoxide **60**: evaporative distillation 130–140 °C (0.005 mmHg); $[\alpha]^{24}_D$ −4.4° (*c* 1.03, $CHCl_3$); IR ($CHCl_3$) 1460, 1380, 1120, 1080 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.86, 0.93 (2t, 6 H, *J* = 6 Hz, CH_3CH_2), 0.97 (d, 3 H, *J* = 6 Hz, CH_3CHCC), 1.27 (d, 3 H, *J* = 6 Hz, CH_3CHOC), 2.52 (d, 1 H, *J* = 4 Hz, CCH*H*O), 2.59 (d, 1 H, *J* = 4 Hz, CC*H*HO), 4.47 (s, 2 H, $C_6H_5CH_2$), 7.33 (b s, 5 H, C_6H_5). Anal. Calcd for $C_{25}H_{38}O_4$: C, 74.59; H, 9.51. Found: C, 74.50; H, 9.46. Epi-epoxide **60**: evaporative distillation 130–140 °C (0.005 mmHg); $[\alpha]^{24}_D$ +7.8° (*c* 1.02, $CHCl_3$); IR ($CHCl_3$) 1460, 1380, 1120,

1080 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.86, 0.93 (2t, 6 H, J = 6 Hz, CH_3CH_2), 0.97 (d, 3 H, J = 6 Hz, CH_3CHCC), 1.24 (d, 3 H, J = 6 Hz, CH_3CHOC), 2.58 (d, 1 H, J = 5 Hz, CCH*H*O), 2.71 (d, 1 H, J = 5 Hz, CC*H*HO), 4.47 (s, 2 H, $C_6H_5CH_2$), 7.31 (b s, 5 H, C_6H_5). Anal. Calcd for $C_{25}H_{38}O_4$: C, 74.59; H, 9.51. Found: C, 74.39; H, 9.36.

Benzyl 2(*S*)-[5(*S*)-Ethyl-3(*S*)-methyl-5-(5(*R*)-ethyl-5-hydroxy-6(*S*)-methyl-2(*R*)-tetrahydropyranyl)-2(*S*)-tetrahydrofuryl]butyl Ether (5). By the procedure described for the preparation of the alcohols **34**, 120 mg (0.30 mmol) of the epoxide **60** in 3 mL of dry *n*-pentane with 320 mg (1.56 mmol) of copper(I) bromide-dimethyl sulfide complex and 1.4 mL (3.08 mmol) of 2.2 M methyllithium in ether afforded, after chromatography on 10 g of silica gel column with 15% ethyl acetate in petroleum ether, 120 mg (90%) of the alcohol **5**. The spectral characteristics of this material were identical with those of the alcohol derived from degradation of lasalocid A.

2(*S*)-[5(*S*)-Ethyl-3(*S*)-methyl-5-(5(*R*)-ethyl-5-hydroxy-6(*S*)-methyl-2(*R*)-tetrahydropyranyl)-2(*S*)-tetrahydrofuryl]butan-1-ol. To a stirred solution of 0.5 cm (3 mmol) of lithium wire in 10 mL of anhydrous liquid ammonia at -78 °C under argon was added a solution of 54 mg (0.13 mmol) of the monobenzyl ether **5** in 1 mL of dry THF. Cooling was then discontinued (ammonia reflux) and after 1 h, 250 mg (4.7 mmol) of anhydrous ammonium chloride was cautiously added to the reaction mixture. The resulting mixture was then diluted with 20 mL of ether and the ammonia was allowed to evaporate. The resulting suspension was filtered and the solid was washed by trituration with four 10-mL portions of ether. Removal of the solvent at reduced pressure from the combined filtrates and then chromatography of the residue on 10 g of silica gel with 40% ethyl acetate in petroleum ether afforded 42 mg (98%) of the corresponding diol. The spectral characteristics of this material were identical with those of the diol derived from degradation of lasalocid A.

2(*R*)-[5(*S*)-Ethyl-3(*S*)-methyl-5-(5(*R*)-ethyl-5-hydroxy-6(*S*)-methyl-2(*R*)-tetrahydropyranyl)-2(*S*)-tetrahydrofuryl]butanal (61). By the procedure described for the oxidation of the alcohol **33**, **80** mg (0.24 mmol) of the above diol in 3 mL of dry dichloromethane with 10 mg (0.12 mmol) of anhydrous sodium acetate and 133 mg (0.62 mmol) of pyridinium chlorochromate afforded, after chromatography on 10 g of silica gel with 40% ether in petroleum ether, 62 mg (78%) of the aldehyde **61**: evaporative distillation 130-140 °C (0.005 mmHg); $[\alpha]^{22}_D$ -2.5° (*c* 1.1, $CHCl_3$); IR ($CHCl_3$) 3600, 3450, 2750, 1720, 1460, 1390, 1230, 1130, 1100, 1060, 960 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.97 (d, 3 H, J = 6 Hz, CH_3CHCC), 1.18 (d, 3 H, J = 6 Hz, CH_3CHOC), 9.64 (d, 1 H, J = 3 Hz, CHO). Anal. Calcd for $C_{19}H_{34}O_4$: C, 69.90; H, 10.50. Found: C, 69.77; H, 10.44.

4(*S*)-[5(*S*)-Ethyl-3(*S*)-methyl-5-(5(*R*)-ethyl-5-hydroxy-6(*S*)-methyl-2(*R*)-tetrahydropyranyl)-2(*S*)-tetrahydrofuryl]hexan-3-ol. To a stirred solution of 62 mg (0.19 mmol) of the aldehyde **61** in 4 mL of dry THF at -78 °C under argon was added 0.72 mL (0.58 mmol) of an 0.8 M solution of ethylmagnesium bromide in THF. The resulting solution was stirred at 0 °C for 30 min, treated with 5 mL of saturated aqueous NH_4Cl, and then diluted with 25 mL of ether. The organic phase was separated, washed with 10 mL of saturated aqueous NH_4Cl and 10 mL of saturated aqueous NaCl, and then dried ($MgSO_4$). After removal of the solvents at reduced pressure and chromatography of the residue on 10 g of silica gel with 50% ether in petroleum ether, there was obtained 60 mg (89%) of a diastereoisomeric mixture of the corresponding alcohols: evaporative distillation 120-130 °C (0.005 mmHg); IR ($CHCl_3$) 3600, 3500, 1460, 1380, 1130, 1100, 1060, 960 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.20 (d, 3 H, J = 6 Hz, CH_3CHOC).

4(*R*)-[5(*S*)-Ethyl-3(*S*)-methyl-5-(5(*R*)-ethyl-5-hydroxy-6(*S*)-methyl-2(*R*)-tetrahydropyranyl)-2(*S*)-tetrahydrofuryl]hexan-3-one (3). By the procedure described for the preparation of the aldehyde **61**, 35 mg (0.10 mmol) of the above alcohols in 1 mL of dry dichloromethane with 50 mg (0.23 mmol) of pyridinium chlorochromate afforded, after chromatography on 10 g of silica gel with 35% ether in petroleum ether, 31.4 mg (90%) of the ketone **3**. The spectral and physical data obtained on this ketone were identical with those of the same ketone obtained from the reverse aldol of lasalocid A (X537A).

Silacyclobutene Synthesis via Intramolecular Cyclization of Unsaturated Silylenes

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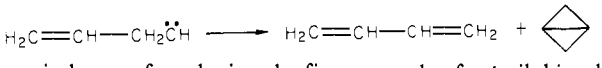
Abstract: Flash vacuum pyrolysis of methoxydisilanes is used to generate 1-, 2-, and 3-propenylsilylenes. Each of these silylenes affords siletene (silacyclobutene) products although the mechanistic origins are probably different in each case. Isobutenylmethylsilylene produces the first example of a methylenesilacyclobutane, and this ring is shown to undergo a remarkable rearrangement to 1,3-dimethylsiletene.

In view of the rich harvest of novel cyclic hydrocarbons which have been generated from intramolecular additions of alkenylcarbenes,[1] it is surprising that the chemistry of only vinylsilylene has been investigated to date.[2] As part of a systematic study of intramolecular reactions of silylenes, we have studied the chemistry of 1-, 2-, and 3-propenylsilylenes and report here that all afford the silacyclobutene ring.

It has been known since 1963 that allylcarbenes undergo intramolecular π addition to produce bicyclo[1.1.0]butanes.[1,3]



thus, in hopes of producing the first example of a 1-silabicyclo[1.1.0]butane, we generated allylsilylene **2** by the thermally induced α elimination of Me_3SiOMe from disilane **1** (680 °c, horizontal quartz chip packed tube (10^{-4} torr). An 87% mass recovery was realized in the flash vacuum pyrolysis (FVP) and Me_3SiOMe was formed in 68% yield. The only other major product was 1-methylsiletene (**3**) (25%, 37% based on Me_3SiOMe). By analogy with carbene chemistry, **3** could have arisen via π addition to form silabicyclo[1.1.0]butane **4**, followed by homolysis of the internal ring bond[4] and hydrogen migration, or by cyclization of 1-sila-1,3-butadiene **5**, as 1-sila-1,3-butadienes are known to close to siletenes.[6] Formation of **5** could arise from 1,2-hydrogen migration to silicon in **2**. However, the thermal rearrangement of a silylene to a silene by hydrogen migration has never been observed.[7] Alternatively, **3** might arise directly from

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(2) Barton, T. J.; Burns, G. T.; Wulff, W. D.; Goure, W. F. *J. Am. Chem. Soc.* **1982**, *104*, 1149.
(3) Lemal, D. M.; Menger, F.; Clark, G. W. *J. Am. Chem. Soc.* **1963**, *85*, 2529.
(4) This is not the path of bicyclo[1.1.0]butane which thermally isomerizes to 1,3-butadiene through cleavage of two external ring bonds.[5]
(5) Doering, W. von E.; Coburn, J. F., Jr. *Tetrahedron Lett.* **1965**, 991.
(6) Burns, G. T.; Barton, T. J. *J. Organomet. Chem.* **1981**, *216*, C5.

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