# Enolate Claisen Rearrangement of Esters from Furanoid and Pyranoid Glycals[1a]

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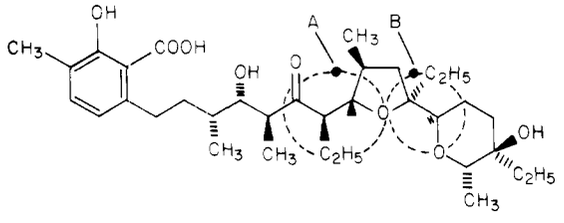
A general method is described for the formation of furanoid and pyranoid glycals. Thus, lithium–ammonia reduction of the corresponding 1-chloro-2,3-*O*-isopropylidene furanoid and pyranoid carbohydrate derivatives affords the desired glycals in 87–92% yields. Several examples that reveal the scope of this process are described. The formation of *C*-glycosides from the glycal esters through application of the ester enolate Claisen rearrangement is explored. The characteristics and stereochemistry of this process in both the acyclic and cyclic series of glycal derivatives are described.

The total synthesis of polyether antibiotics constitutes a provocative challenge to the ingenuity of the organic chemist. These antibiotics are important representatives of a relatively new and rapidly expanding class of molecules known as ionophores.[2] The importance of these molecules is derived from their unique capacity to facilitate the transfer of cations across biological membranes. Among the more interesting examples of the polyether antibiotics is lasalocid A (I),[3] which has been shown[3] to form lipid

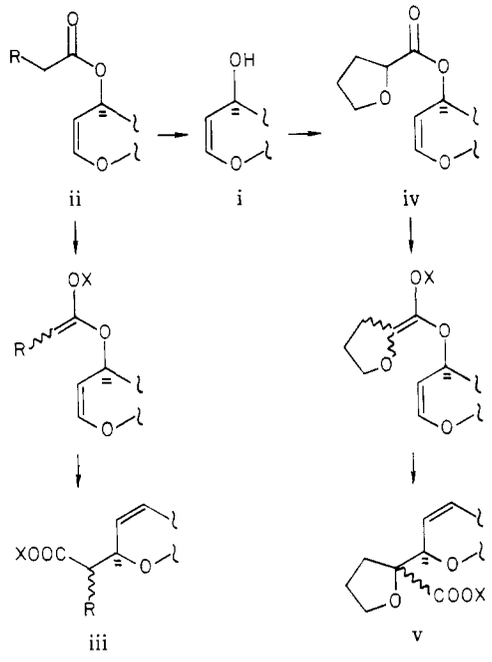


lasalocid A (I)

soluble complexes with divalent calcium cations and with metabolically essential amines (e.g., catecholamines). In addition, lasalocid A, as well as several other polyether antibiotics, exerts a profound positive effect upon the contractility of heart muscle[3a] and, in in vivo experiments, causes dramatic increases in coronary flow and cardiac output.[4] These observations have resulted in considerable interest in the potential application of these molecules as cardiovascular drugs, and the development of efficient, versatile syntheses of analogues of the polyethers could expedite the discovery of more efficacious cardiotonic agents. This investigation was undertaken to evaluate one synthetic approach to the polyether molecules.[5]

The two structural units encircled in structure I are characteristic features which are present in nearly all of the polyether antibiotics. They are similar in that both are created (in effect, but not in the accepted biogenetic scheme) by the stereospecific attachment of a chiral carbon residue to the C-1 position of a saturated oxygen heterocycle. They are dissimilar in regard to the nature of the attached carbon residue. In one case (A), the attachment results in an aldol-type structure and a 1,3 relationship of carbon–oxygen bonds. In the second case (B), the attachment results in a 1,2 relationship of carbon–oxygen bonds and provides a glycol diether. The prevalence of these structural units in all polyether antibiotics suggests that a practical preliminary goal in a program directed toward the preparation of synthetic analogues of these ionophores would be the development of efficient methods for generating these systems.

Scheme I



One means of potential general utility for the attainment of this goal is a scheme which incorporates the ester enolate Claisen rearrangement as a key carbon–carbon bond-forming reaction. In such an approach (outlined in Scheme I, where the partial structures are meant to denote both furanoid and pyranoid rings), a heterocyclic allylic alcohol (i) is used to provide either the aliphatic ester ii or the $\alpha$-alkoxy ester iv, and these esters, in turn, by [3,3] sigmatropic rearrangement, generate, respectively, the desired aldol-type structural unit iii and the glycol diether congener v. Since the clinically and biologically interesting molecule lasalocid A contains both of these structural units and is one of the least complex of the polyether antibiotics, the total synthesis of this system is an attractive and

(1) (a) Grateful acknowledgment is made for the support of this investigation through Public Health Service Research Grant No. HL 21367 from the National Heart and Lung Institute and the Hoffmann-LaRoche Foundation. (b) Upjohn Company Predoctoral Research Fellow, 1979–80.

(2) Excellent reviews of the physical properties and physiological activities of the ionophores have been published: (a) Pressman, B. C. *Annu. Rev. Biochem.* **1976**, *45*, 501–530. (b) Westley, J. W. *Adv. Appl. Microbiol.* **1977**, *22*, 177–223. (c) Westley, J. W. *Annu. Rep. Med. Chem.* **1975**, *10*, 246.

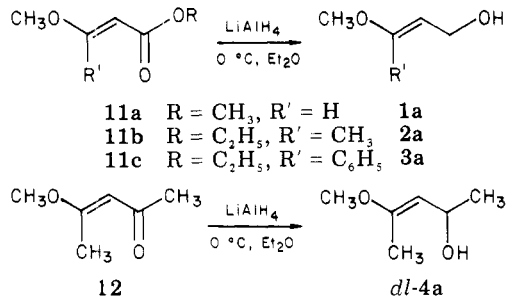
(3) (a) Pressman, B. C. In "The Role of Membranes in Metabolic Regulation"; Mehlman, M. A., Hanson, R. W., Eds.; Academic Press: New York; p 149. (b) Schadt, H.; Haeusler, G. *J. Membr. Biol.* **1974**, *18*, 277–294. (c) Johnson, R. G.; Scarpa, A. *FEBS Lett.* **1974**, *47*, 117–121.

(4) Pressman, B. C.; de Guzman, N. T. *Ann. N.Y. Acad. Sci.* **1975**, *264*, 373–386. de Guzman, N. T.; Pressman, B. C.; Lasseter, K.; Palmer, R. *Clin. Res.* **1973**, *21*, 413.

(5) For another approach to this problem, an approach which has resulted in the first total synthesis of an ionophoric antibiotic, see: Kishi, Y.; Schmid, G.; Vranesic, B.; Okigawa, M.; Smith Palmer, T. *J. Am. Chem. Soc.* **1978**, *100*, 2933–2935.

0022-3263/80/1945-0048$01.00/0 

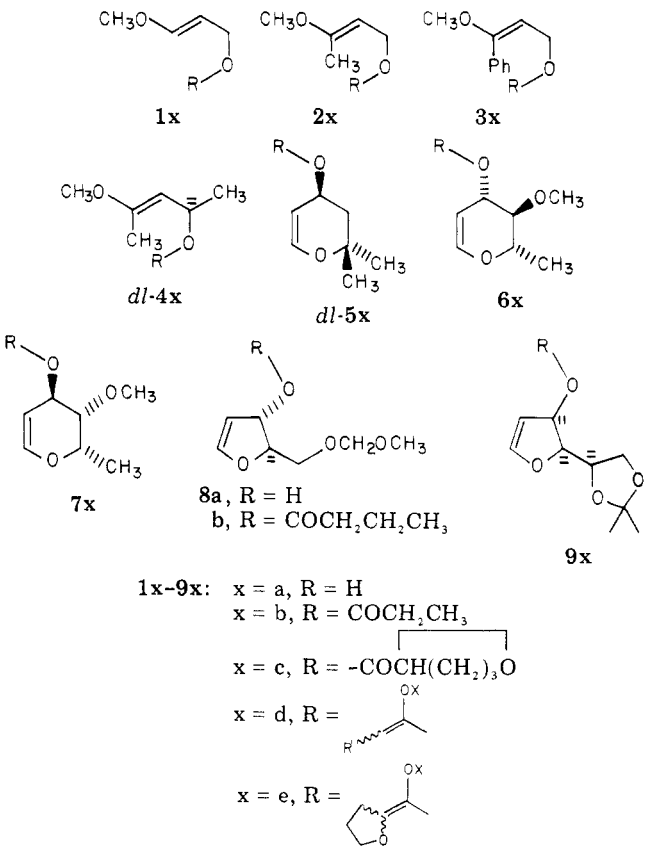
Scheme II




practical goal that would serve to evaluate this proposed approach. To begin this project and to test the applicability of the enolate Claisen rearrangement in as convenient a manner as possible, it was necessary first to develop a convenient method for the preparation of furanoid and pyranoid alcohols of type i and then to establish that models of the required structural units can be constructed by sigmatropic rearrangements of ester enolates derived from those alcohols.[6]

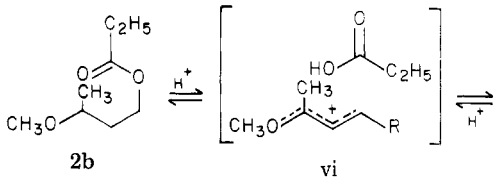
In the initial phase of this investigation the γ-methoxy allylic alcohols **1a**–*dl*-**4a** were prepared, and the Claisen rearrangements of ester enolates derived from these alcohols were examined. These alcohols are the most readily available and least sterically hindered analogues of the more complex heterocyclic alcohols which would be required for the total synthesis of lasalocid A. Previous experience established that the ester enolate Claisen rearrangement could be successfully applied to derivatives of β-methoxy allylic alcohols[7] and thereby demonstrated the compatibility of the reaction conditions with enol ether functional groups. Alcohols **1a**–*dl*-**4a** were convenient models for evaluating any special characteristics associated with the reactions of γ-alkoxy allylic alcohols and their esters.

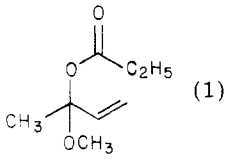
The desired alcohols were prepared by hydride reduction of the corresponding carbonyl compounds (Scheme II). Reduction of ester **11a**, which can be conveniently prepared by the addition of methyl alcohol to methyl propiolate,[8] afforded the sensitive alcohol **1a** in 36% yield. Distillation of this alcohol was accomplished only with low recovery and was accompanied by the formation of nonvolatile, apparently polymeric material. Attempts to prepare ester **1b** by acylation of alcohol **1a** using propionic anhydride and pyridine in dichloromethane also resulted in polymer formation and provided only low yields of impure ester. Ester **1b** was prepared, however, in 70% yield under aprotic conditions by treatment of a solution of the alcohol in tetrahydrofuran with 1 equiv of *n*-butyllithium, followed by reaction of the resulting lithium alkoxide with propionic anhydride. The alcohols **2a** and **3a** were obtained in 60–70% yield by reduction of the esters **11b** and **11c**[10,11] with lithium aluminum hydride. In contrast to




alcohol **1a**, the more substituted alcohols **2a** and **3a** could be distilled without significant decomposition. Furthermore, alcohol **2a** did provide up to 66% yields of ester **2b** by acylation with propionic anhydride in pyridine. However, esters **2b** and **3b** were obtained in higher and more consistent yields by the reaction of the corresponding alkoxides with propionic anhydride.

Initial attempts at acylation of the alcohol **2a** were complicated by the production of a byproduct believed to be isomeric ester **13** on the basis of nuclear magnetic




(1)

13

resonance and infrared spectral data. The production of this compound could be suppressed by thorough washing of the crude ester with base prior to distillation. The nuclear magnetic resonance spectrum of a sample of the ester **2b** showed no change after heating the sample for 60 min at 110 °C. The formation of the isomeric ester **13**, as inferred by the appearance of typical terminal olefin spectral characteristics and corresponding shifts in the methyl and ethyl group resonances, was observed immediately following the addition of a catalytic amount of acid to this sample. This type of allylic rearrangement has been well documented in the carbohydrate literature for the

(6) Portions of this work were published earlier in preliminary form. See: Ireland, R. E.; Wilcox, C. S. *Tetrahedron Lett.* **1977**, 2839–2842. Ireland, R. E.; Wilcox, C. S.; Thaisrivongs, S. *J. Org. Chem.* **1978**, *43*, 786–787.

(7) (a) Ireland, R. E.; Mueller, R. H. *J. Am. Chem. Soc.* **1972**, *94*, 5897–5898. (b) Ireland, R. E.; Mueller, R. H.; Willard, A. K. *Ibid.* **1976**, *98*, 2868–2877.

(8) Winterfeldt, E.; Preuss, H. *Ber. Dtsch. Chem. Ges.* **1966**, *99*, 450–458.

(9) Compounds containing one or more asymmetric centers and obtained as racemic mixtures will be designated by the prefix *dl* placed before the identifying numeral. Products without chirality and products obtained as single enantiomers from chiral starting materials will have no prefix.

(10) Smissman, E. E.; Voldeng, A. N. *J. Org. Chem.* **1964**, *29*, 3161–3165.

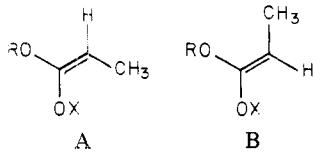
(11) Blaise, E. E.; Maire, M. *Ann. Chim. Phys.* **1908**, *15*, 567–574.

acetate derivatives of the pyranoid glycals.[17] Acid catalysis of this process has been demonstrated previously.[18] The appearance of this byproduct illustrates the sensitivity of these esters toward heterolytic cleavage of the carbon–oxygen bond adjacent to the enol ether. The singular stability of the oxygen substituted allylic cation vi (R = H) undoubtedly contributes to the facility of this bond scission.

The secondary alcohol *dl*-**4a** was prepared in 89% yield from the β-methoxypentenone **12**[12,13] by reduction with lithium aluminum hydride. Attempts to isolate ester *dl*-**4b** were uniformly unsuccessful. However, treatment of a solution of alcohol *dl*-**4a** in tetrahydrofuran at −78 °C first with a small excess of *n*-butyllithium to form the lithium alcoholate and then with propanoyl chloride generated an equimolar solution of the ester, *dl*-**4b**, and lithium chloride. The high-yield formation of the ester by this process is inferred by the successful utilization of this solution in the ester enolate Claisen rearrangement (vide infra). The decreased stability of ester **4b** relative to ester **2b** can be attributed to the increased stability of the allylic cation vi (R = $CH_3$) and the concomitant ease of carbon–oxygen bond cleavage in the secondary vs. the primary alkyl ester.

With the preparation of these acyclic models thus completed, attention was turned toward the investigation of the [3,3] sigmatropic rearrangements of the silylketene acetals derived from these esters. In each case the ester was first deprotonated at −78 °C by lithium diisopropylamide (LDA); *tert*-butylmethylchlorosilane (TBSCl) was then added, and after cooling was discontinued the mixture warmed to room temperature. In this manner the ketene acetals **1d**–*dl*-**4d** (X = *t*-Bu$(CH_3)_2$Si) were produced.

Previously obtained results from this laboratory[7] demonstrate that under these conditions, and dependent upon the solvent employed during the deprotonation, variable proportions of the two geometrically isomeric ketene acetals will be obtained. Specifically, it was shown that when the deprotonation is effected by LDA in a 23 vol % mixture of hexamethylphosphoric triamide (HMPA) in tetrahydrofuran (THF), the *E*-type enolate anion A is

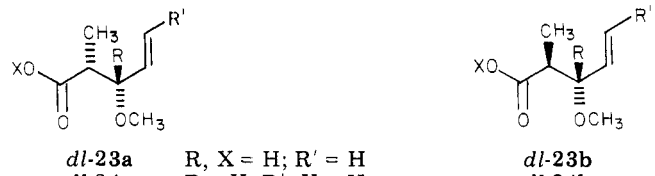


A B

X = Li, *t*-Bu$(CH_3)_2$Si

preferentially formed and silylated. When LDA is used with THF in the absence of HMPA the predominant product was shown to be derived by silylation of the *Z*-type enolate anion, B.

Subsequent sigmatropic rearrangement of these ketene acetals generated a mixture of diastereomeric γ,δ-unsaturated silyl esters. These esters provided the products *dl*-**23a,b**–*dl*-**26a,b**. The relative quantities of the diastereomers were determined by NMR analysis of the product mixtures. Ester **1b** afforded, after hydrolysis of the resultant silyl ester with dilute aqueous acid, the acids *dl*-**23a** and *dl*-**23b** (X = H). In the same manner ester **2b** yielded *dl*-**24a** and *dl*-**24b** (X = H). In the case of ester **3b** the derived silyl esters were cleaved with potassium fluoride in HMPA,[31] and the resultant carboxylate salts were alkylated with methyl iodide[31] to yield esters *dl*-**25a** and *dl*-**25b** (X = $CH_3$). A mixture of ester *dl*-**4b** and lithium chloride in THF was prepared (vide supra) and added to a solution of LDA in the desired solvent. Completion of the experiment in the usual manner yielded acids *dl*-**26a** and *dl*-**26b** (X = H). The yields and ratios obtained in these experiments are collected in Table I.



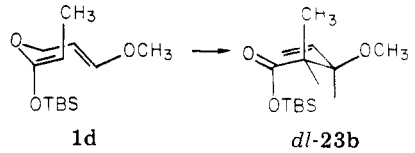
| | | | | | |
|---|---|---|---|---|---|
| *dl*-**23a** | R, X = H; R′ = H | | *dl*-**23b** | | |
| *dl*-**24a** | R = H; R′, X = H | | *dl*-**24b** | | |
| *dl*-**25a** | R = $C_6H_5$; R′ = H, X = $CH_3$ | | *dl*-**25b** | | |
| *dl*-**26a** | R, R′ = $CH_3$; X = H | | *dl*-**26b** | | |

Table I. Products Obtained from Esters 1b-*dl*-4b

| react-ant | solvent[a] | prod-ucts[b] | yield, % | a/b[d] | $\tau_{1/2}$,[e] |
|---|---|---|---|---|---|
| **1b** | THF | **23a,b** | 80 | 1/5 | <5 |
| **1b** | HMPA-THF | **23a,b** | 75 | 4/1 | <5 |
| **2b** | THF | **24a,b** | 76 | 1/4 | 9 ± 2 |
| **2b** | HMPA-THF | **24a,b** | 80 | 3/1 | 9 ± 2 |
| **3b** | THF | **25a,b**[c] | 67 | 1/1 | 42 ± 8 |
| **3b** | HMPA-THF | **25a,b**[c] | 72 | 1/1 | 42 ± 8 |
| **4a**[f] | THF | **26a,b** | 60 | 3/7 | 10 ± 2 |
| **4a**[f] | HMPA-THF | **26a,b** | 59 | 4/1 | 10 ± 2 |

[a] Solvent employed during deprotonation of allylic ester. THF = 100% THF, HMPA-THF = 23% (v/v) HMPA/THF. [b] Isolated as the carboxylic acids (X = H), except in *c*. [c] Isolated as the methyl esters (X = $CH_3$). [d] Ratio of diastereomers (XXa/XXb) as determined by NMR. [e] Half-life at 35 °C for the sigmatropic rearrangement as determined by NMR (see ref 7b). [f] The required ester was prepared from this alcohol just prior to deprotonation and was not isolated.

The stereochemistry indicated for the products is based upon the following reasoning. In the absence of any unusual steric constraints and in accordance with prior experimental observations[7,14] these rearrangements are assumed to occur via a chairlike transition state. In this event, and on the basis of the preferential formation and silylation of isomeric enolate anions as described above, the configurational assignments indicated may be readily predicted. As an example of this, deprotonation and silylation of ester **1b** are expected, on the basis of previous results with propanoate esters,[7] to yield a mixture of silyl ketene acetals **1d** wherein the predominant geometrical isomer is of type B. Rearrangement of these isomeric acetals through a chairlike transition state will produce a mixture of diastereomeric silyl esters in which *dl*-**23b** is the major component. This transformation is illustrated for the major isomer in eq 2. On the basis of analogous reasoning, the products in the remaining examples were assigned the given relative configurations.

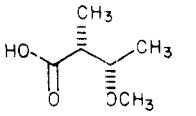


1d *dl*-23b (2)

Tentative support for the proposed assignments was obtained from the nuclear magnetic resonance spectral data. It was observed that the doublet assigned to the α-methyl group of products *dl*-**23**–**26a** was consistently at lower field than was the corresponding doublet in the

(12) Eistert, B.; Arndt, F.; Loewe, L.; Ayca, E. *Ber. Dtsch. Chem. Ges.* **1951**, *84*, 156–169.
(13) Awang, D. *Can. J. Chem.* **1971**, *49*, 2672–2675.
(14) Doering, W. von E.; Roth, W. R. *Tetrahedron* **1962**, *18*, 67–74. Also: Johnson, W. S.; Werthermann, L.; Bartlett, W. R.; Brockson, T. J.; Li, T.-t.; Faulkner, J.; Petersen, M. R. *J. Am. Chem. Soc.* **1970**, *92*, 741–742.

isomeric compounds, *dl*-**23**–**26b**. This is consistent with the work of Maskens and Polgar, who found that the α-methyl group in *erythro*-3-methoxy-2-methylbutyric acid (vii) resonates at lower field than the corresponding methyl



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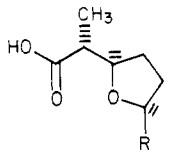


viii

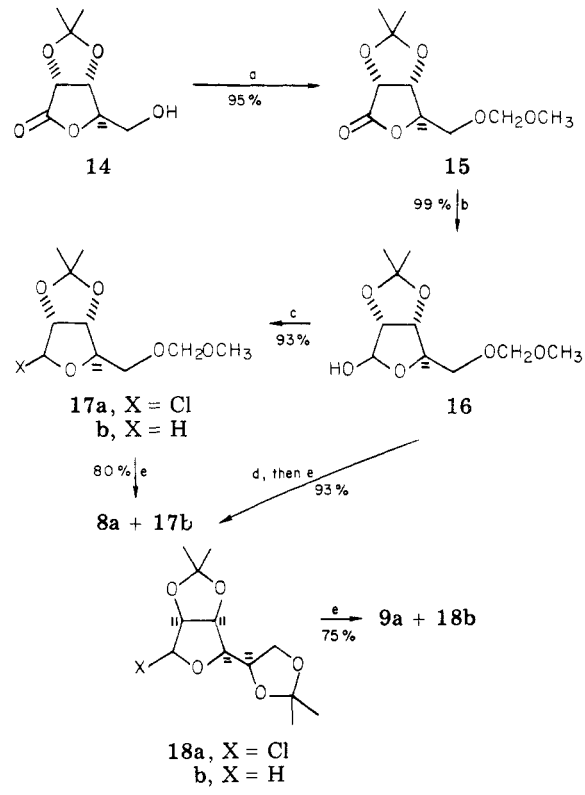
group in the threo isomer.[15] In addition, it is known from the work of Gerlach and Prelog that the α-methyl group of nonactic acid [(viii), R = $CH_2CH(OH)CH_3$] resonates at higher field than does the α-methyl group of 2-*epi*-nonactic acid.[16] While these observations cannot be considered as proof of the proposed relative stereochemistries, a reassuring consistency is nevertheless recognized.

Results from this preliminary investigation indicated that the ester enolate Claisen rearrangement could be successfully applied to esters of γ-methoxy allylic alcohols. The reactions proceed in good overall yield, and the experimental evidence indicates that diastereomeric β-methoxy carboxylic acids or esters are obtained in proportions dependent upon the solvent employed during deprotonation. Furthermore, experimental procedures were developed which allow the enolate Claisen rearrangement to be applied to esters which are too unstable to be isolated under aqueous conditions.

With these encouraging results in hand, attention was turned toward a search for efficient methods for the preparation of heterocyclic alcohols of the type required for the synthesis of lasalocid A. Alcohol *dl*-**5a** was readily available by reduction of the corresponding enone[17] and therefore constituted a practical starting point for these investigations. However, for the efficient use of alcohols of this type in a convergent plan of synthesis such as the scheme proposed for lasalocid A, a convenient preparation of optically active congeners of *dl*-**5a** was required. For this purpose, the carbohydrates appeared to be ideal starting materials.

The alcohols **6a**–**9a** are representative of the class of carbohydrate derivatives known as pyranoid and furanoid glycals.[18] The pyranoid representatives of this group have long been recognized as valuable intermediates for carbohydrate synthesis. However, because of the logical emphasis of carbohydrate synthesis upon functional group manipulation, scant use has been made of these substrates in carbon–carbon bond forming reactions.[19] In the past, the preparation of these pyranoid glycals has been accomplished most often by some modification of the method of Fischer and Zach.[20,21] This method involves the reduction of peracetylated pyranosyl bromides by elemental zinc in acetic acid and invariably yields the acetylated allylic alcohol derivative. Acylated glycals are known to undergo acid-catalyzed rearrangements analogous to the reaction observed with ester **2b**.[18] The furanoid glycals are particularly susceptible to this undesirable reaction, and therefore the classical technique, incorporating acidic reduction media, is inapplicable for the preparation of all but the most stable of furanoid glycal derivatives.[22] Results from the single previous successful preparation of furanoid glycal esters suggest that the lability of glycal derivatives is related, not unexpectedly, to the nature of the leaving group on C-3.[23,24]

Scheme III. Preparation of Furanoid Glycals 8a and 9a[a]

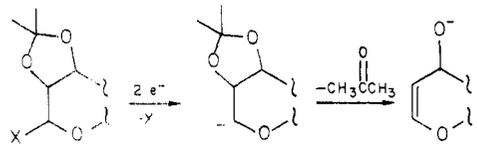



[a] (a) $ClCH_2OCH_3$, $C_2H_5N(i\text{-}C_3H_7)_2$, $H_2CCl_2$; (b) DIBAL, $Et_2O$, −78 °C; (c) $Ph_3P$-$CCl_4$, THF, 67 °C; (d) $P(NMe_2)_3$-$CCl_4$, −78 → 0 °C; (e) excess Li-$NH_3$, 2 h, then $NH_4Cl$.

For the purposes at hand, a synthesis of glycals with an unsubstituted C-3 hydroxyl group, suitable for acylation with any one of several reagents, was desired. In addition to being a requisite of efficiency and convenience, this specification was a practical necessity for the successful isolation of the furanoid substrates. By analogy with ester *dl*-**4b**, and in consideration of prior reports upon furanoid glycal esters, these alcohols were expected to be more stable than their corresponding esters and therefore more easily isolated, purified, and stored. No known general technique met this requirement.

The fragmentation of β-alkoxyethyl halides on treatment with metals in inert solvent suggested that the reaction generalized in eq 3 could provide a solution to this problem. While the technique is essentially equivalent to the successful classical method, the use of an inert or basic reduction medium offered the advantage that the acid-catalyzed destruction of these sensitive products could be

(15) Maskens, K.; Polgar, N. *J. Chem. Soc., Perkin Trans. 1* **1973**, 109–115.
(16) Gerlach, H.; Prelog, V. *Justus Liebigs Ann. Chem.* **1963**, *669*, 121–135.
(17) Kosower, E. M.; Sorensen, T. S. *J. Org. Chem.* **1963**, *28*, 692–695.
(18) (a) Helferich, B. *Adv. Carbohydr. Chem.* **1952**, *7*, 209–245. (b) Ferrier, R. J. *Ibid.* **1969**, *24*, 199–266.
(19) Exceptions may be found in the reports of Matsuura, K.; Nishiyama, K.; Yamada, K.; Araki, Y.; Ishido, Y. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 2538–2542. Also: Fraser-Reid, B.; Walker, D. L.; Saunders, J. K. *Chem. Commun.* **1974**, 319–320. See A. Rosenthal [*Adv. Carbohydr. Chem.* **1968**, *23*, 59–114] for a review of the "oxo reaction" as applied to glycals.
(20) Fischer, E.; Zach, F. *Sitzungsber. K. Preuss. Akad. Wiss.* **1913**, *16*, 311.
(21) The reduction of 2-iodo-2-deoxypyranosides with methyllithium constitutes a notable alternative. See: Sharma, M.; Brown, R. K. *Can. J. Chem.* **1966**, *44*, 2825–2835.
(22) Bischofberger, K.; Hall, R. H. *Carbohydr. Res.* **1972**, *52*, 223–227.
(23) Ness, R. K.; Fletcher, Jr., H. G. *J. Org. Chem.* **1963**, *28*, 435–437.
(24) Haga, M.; Ness, R. K. *J. Org. Chem.* **1965**, *30*, 158–162.



ix (3)

avoided. Furthermore, the use of a ketal or acetal for protection of both the C-2 and C-3 hydroxyl groups provides for the direct generation of the desired, unprotected allylic alcohol, in efficient fulfillment of our requirements.

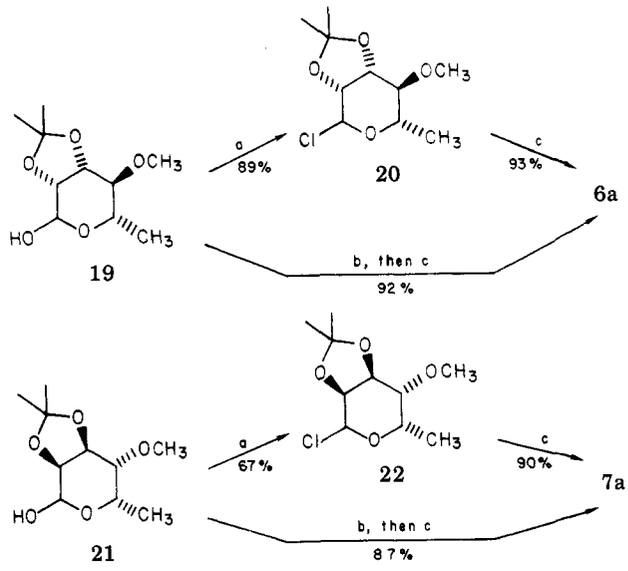
To evaluate these possibilities, the furanosyl chloride **17a** was prepared for an investigation of reductive fragmentation methods (Scheme III). Lactone **14**, prepared from ribonic acid γ-lactone in 95% yield,[25] afforded the protected lactone **15** by alkylation with chloromethyl methyl ether in the presence of diisopropylethylamine. Reduction of the protected lactone **15** with diisobutylaluminum hydride at −78 °C provided the lactol **16**, which was converted to chloride **17a** with triphenylphosphine and carbon tetrachloride in tetrahydrofuran.

After trying several unsuccessful methods for the reduction of this chloride (including metal–halogen exchange using zinc or magnesium and transmetalation with organolithium reagents), we developed a satisfactory technique. Addition of a solution of the chloride to an excess of lithium in liquid ammonia at −78 °C and isolation of the reduction products under anhydrous conditions following acidification of the reaction mixture with solid ammonium chloride afforded a 93% yield of a 6:1 mixture of glycal **8a** and tetrahydrofuran **17b**. Byproduct **17b** is most likely produced by protonation of the intermediate carbanion (ix, eq 3) prior to fragmentation. Reduction of furanosyl chloride **18a**[26] afforded the alcohol **9a** in 75% yield, together with a 9% yield of the tetrahydrofuran derivative **18b**. Glycals **8a** and **9a** could be purified by chromatography on silica gel with 90 and 95% recoveries, respectively. Despite the lability of these products which results in only moderate recovery after purification, pure furanoid glycals are available by this procedure, and given the relatively inert nature of the byproduct, for preparative purposes the mixture of products could be used without adverse effect in subsequent synthetic transformations.

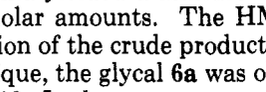
The utilization of this methodology for preparation of pyranoid glycals was even more rewarding. Reaction of lactol **19**[27a] with triphenylphosphine and carbon tetrachloride afforded the pyranosyl chloride **20**. Reduction of this chloride with lithium in ammonia produced the glycal **6a** in 90% yield. Lactol **21**[27b] provided the chloride **22**, an unstable liquid, in 67% yield. This chloride was converted in 90% yield to glycal **7a**. In the reductions of **20** and **22** the glycals **6a** and **7a** were the only detectable products. No byproduct analogous to **17b** or **18b** was observed.

In light of the instability of the intermediate chlorides formed in this process, an alternative method for the transformation of these lactols to glycals was examined. It is known that hexamethylphosphorus triamide (tris(dimethylamino)phosphine, TDAP) reacts at very low temperatures with carbon tetrachloride in the presence of alcohols to form adducts of type xi.[27] Warming of these adducts leads to the formation of alkyl chlorides and HMPA at temperatures and rates determined by the nature of the alkyl portion. Adding TDAP to a solution of lactol **18** and carbon tetrachloride in tetrahydrofuran at −78 °C, then warming this mixture to 0 °C and immediately adding it to a solution of excess lithium in liquid ammonia yielded a mixture of glycal **6a** and HMPA in equimolar amounts. The HMPA is easily removed by filtration of the crude product through silica gel. By this technique, the glycal **6a** was obtained in 92% yield from lactol **19**. In the same manner lactol **21** afforded glycal **7a** in 87% yield, and lactol **16** was converted in 93% yield to a 6:1 mixture of **8a** and **17b**. Apparently, the high reactivity of TDAP relative to triphenylphosphine obviates the need for destructively high temperatures during the preparation of the sensitive chlorides. Alternatively, in analogy with the dissolving metal reductions of tetramethylphosphorodiamidates developed in this laboratory,[28] reduction of adduct xi may lead directly to carbanion formation.

**Scheme IV. Preparation of Pyranoid Glycals 6a and 7a**[a]



[a] (a) $Ph_3P$-$CCl_4$, THF, 67 °C; (b) $P(NMe_2)_3$-$CCl_4$, THF, −78 °C; (c) Li-$NH_3$, 2 h, then $NH_4Cl$.



xi

These experiments resulted in the ready availability of optically active heterocyclic alcohols of the type required for the successful realization of the proposed approach to lasalocid A and analogues of the polyether antibiotics. The next phase of this work required the acylation of these alcohols and the [3,3] sigmatropic rearrangements of the silyl ketene acetals obtained from the resulting esters. The preparations and reactions of the simple aliphatic esters were examined first.

With some minor modifications, the experimental techniques applied to these reactions were the same as those used for their acyclic counterparts, as described above. Esters *dl*-**5b** and **6b** were obtained from their corresponding alcohols by acylation with propanoyl chloride and pyridine in dichloromethane. In contrast to the acyclic ester *dl*-**4b**, these conformationally more restricted esters could be isolated in high yield. These esters were

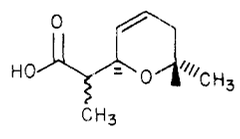
(25) Hough, L.; Jones, J. K. N.; Mitchell, D. L. *Can. J. Chem.* **1958**, *36*, 1720–1728.
(26) Freudenberg, K.; Wolf, A. *Ber. Dtsch. Chem. Ges.* **1927**, *60*, 232–238.
(27) (a) Angyal, S. J.; Pickles, V. A.; Ahluwalia, R. *Carbohydr. Res.* **1967**, *3*, 300–307. (b) Ireland, R. E.; Wilcox, C. S. *J. Org. Chem.*, in press.
(28) Downie, J. M.; Lee, J. B.; Matough, M. F. S. *Chem. Commun.* **1968**, 1350–1351.
(29) Ireland, R. E; Muchmore, D. C.; Hengartner, U. *J. Am. Chem. Soc.* **1972**, *94*, 5098–5100.

Table II. Products Obtained from Furanoid and Pyranoid Glycals

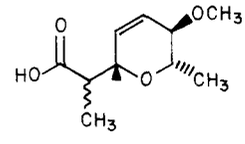
| reactant | solvent[a] | product | yield, % | a/b[b] |
|---|---|---|---|---|
| *dl*-5b | HMPA-THF | *dl*-27a,b | 79 | 1/11 |
| 6b | THF | 28a,b | 73 | 4/1 |
| 6c | HMPA-THF | 28a,b | 71 | 1/4 |
| 6a[c] | THF | 28a,b | 79 | 4/1 |
| 7a | THF | 29a,b | 69 | 4/1 |
| 7a | HMPA-THF | 29a,b | 74 | 1/4 |
| 8a | THF | 30a,b | 73 | 4/1[d] |
| 8a | HMPA-THF | 30a,b | 60 | 1/4[d] |
| 9a | THF | 31a,b | 52 | 4/1 |
| 9a | HMPA-THF | 31a,b | 54 | 1/1 |

[a] Solvent employed during deprotonation of allylic ester. THF = 100% THF, HMPA-THF = 23% (v/v) HMPA/THF. [b] Ratio of diastereomers (XXa/XXb) determined by NMR. See discussion in text. [c] In this case, and in those listed below, the required ester was prepared just prior to use and was not isolated. [d] Ratio determined by GC analysis of hydrogenated methyl esters (see Experimental Section).

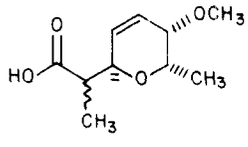
converted to silyl ketene acetals *dl*-**5d** and **6d** by the action of LDA and TBSCl as described for ester **2b**. Hydrolysis of the silyl esters obtained by rearrangement of these acetals afforded the acids *dl*-**27a,b** and **28a,b**. Change of



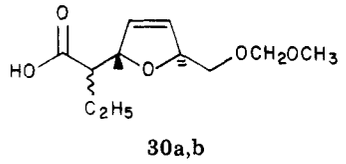
*dl*-27a,b



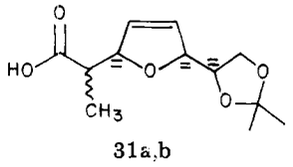
28a,b



29a,b



30a,b

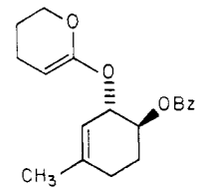


31a,b

the solvent employed during deprotonation resulted in the expected variation of side chain stereochemistry (Table II). The rates of rearrangement of the silyl ketene acetals *dl*-**5d** and **6d** (X = *t*-Bu$(CH_3)_2$Si) at 35 °C were determined by NMR analysis to be 100 ± 15 min and 30 ± 5 min, respectively. For preparative purposes, these reactions were expedited by heating of the acetals at 67 °C.

While esters could be obtained in good yield from *dl*-**5a** and **6a**, the esters derived from **7a**, and especially the esters of furanoid glycals **8a** and **9a**, were too unstable to allow isolation in acceptable yields. Therefore each of these esters was prepared by the reaction of a lithium alcoholate with the appropriate acyl chloride, and the resulting solution of ester was used immediately for the Claisen rearrangement. Ketene acetals derived from the furanoid glycal esters rearranged very quickly at 35 °C ($\tau_{1/2} \leq 5$ min). The products obtained from the furanoid glycal esters were produced in higher yield by silylation of the enolate anions with trimethylchlorosilane rather than with *tert*-butyldimethylchlorosilane. The results of these reactions are collected in Table II.

The prediction of the stereochemical outcome in these reactions, or assignment of relative stereochemistry to the major product in each reaction, is more complicated here than in the acyclic examples discussed above. Of course, the orientation of the new carbon–carbon bond at C-1 in these heterocycles is specified with certainty by the disposition of the allylic carbon–oxygen bond prior to rearrangement. However, although enolization and silylation of these esters are expected to exhibit the same selectivity found earlier, and solvent variation does provide the expected control of stereoisomer ratios, ill-defined nonbonded interactions between the substituents on the heterocyclic ring and the silyl ketene acetal must cast doubt upon the favorable nature of a chairlike transition state for these rearrangements. This doubt is further amplified by a report from Lythgoe[30] that the intermediate cyclohexenyl ketene acetal *dl*-**32** rearranges exclusively through a



*dl*-32

boatlike transition state. In the light of this uncertainty the configuration of the carbon $\alpha$ to the carbonyl in products *dl*-**27–31** is not specified. In lieu of this assignment the ratio of diastereomers (Table II) is based solely upon the NMR spectra of the products. Of the two diastereomers, XXa and XXb, the isomer in which the doublet attributed to the $\alpha$-methyl group appears at higher field is defined as XXa. The isomer having the lower field methyl group resonance is designated XXb. It is interesting to note that enolization and silylation in 100% THF consistently afforded a mixture of final products in which the isomer with the higher field doublet predominates.

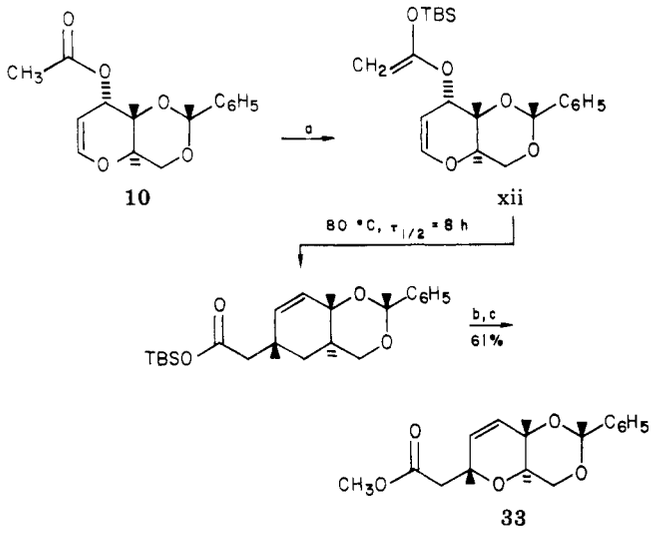
The last glycal we investigated was the acetate **10**, generously provided to us for this purpose by Professor B. Fraser-Reid, Waterloo, Ontario. The ketene acetal xii was prepared by deprotonation of the acetate with potassium hexamethyldisilazide in tetrahydrofuran at −78 °C followed by silylation of the enolate anion with TBSCl. The ketene acetal xii rearranges very slowly relative to the monocyclic intermediates described above. The restricted conformational mobility inherent to the bicyclic framework no doubt contributes to this difference. The rearrangement is completed by heating the silyl ketene acetal for 23 h at 100 °C, and the resultant silyl ester is converted to methyl ester **33** by treatment with potassium fluoride followed by methyl iodide in HMPA.[31] The overall yield of ester **33** is 61%.

The successful preparation of the carboxylic acids *dl*-**27a,b** through **31** and ester **33** demonstrated that the ester enolate Claisen rearrangement could be usefully applied to esters of both furanoid and pyranoid glycals. The technique allows for the stereospecific attachment of side chains to the C-1 position of saturated furanoid and pyranoid rings. The final stage of this developmental project called for the production of the tetrahydro-2-furoyl esters of pyranoid alcohols of type i and the utilization of these products in the Claisen rearrangement.

The ester **6c** was prepared and isolated in 90% yield by the reaction of tetrahydro-2-furoyl chloride with glycal **6a** and pyridine in diethyl ether. A solution of this ester in tetrahydrofuran was treated first with LDA, and then with

(30) Lythgoe, B.; Cave, R. J.; Metcalfe, D. A.; Waterhouse, I. *J. Chem. Soc., Perkin Trans. 1* **1977**, 1218–1228.

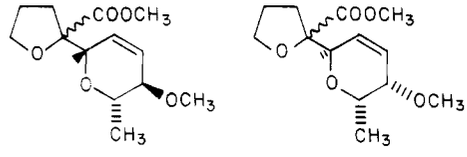
(31) Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190–6191. Shaw, K.; Kunerth, D.; Sherry, J. *Tetrahedron Lett.* **1973**, 689–692.




TBS = $t$-Bu($CH_3$)$_2$Si

(a) KH, TBSCl; (b) KF, HMPA; (c) MeI, HMPA

trimethylchlorosilane, to yield the silyl ketene acetal, **6e**. Subsequent rearrangement of this acetal afforded, after esterification of the resultant carboxylic acid with diazomethane, the isomeric methyl esters **34a** and **34b** in a




**34a,b** **35a,b**

combined yield of 62%. The ester **7c**, prepared immediately prior to use and not isolated, afforded, by the same process, the isomeric esters **35a** and **35b** in 67% yield. These isomers, and those obtained from glycal **6c**, could be separated by chromatography on silica gel.

The effects of a few variations of solvent and base upon the ratios of products obtained have been investigated (Table III). These effects are not so dramatic as those found with the simple aliphatic esters. Nevertheless, a synthetically useful preponderance of one diastereomer of the interesting products **34** and **35** is readily obtained. The successful preparation of these products is suggestive of the practical value of this reaction for the preparation of polyether antibiotics.

In summary, this investigation demonstrates that the ester enolate Claisen rearrangement, as applied in Scheme I, is a useful and stereoselective method for the attachment of chiral side chains to the C-1 position of oxygen heterocycles. An efficient new method for the preparation of optically active furanoid and pyranoid glycals was developed, and chiral oxygen heterocycles of interest as models or intermediates for the synthesis of lasalocid A were derived from those alcohols. This method has potential application in the field of $C$-glycoside synthesis. The ubiquitous occurrence of furanoid and pyranoid rings among the abundant acetogenous fungal metabolites and the unique properties of heterocyclic ethers as chelating ligands in ionophores in general further emphasize the value of the synthetic methods described in this report.

## Experimental Section[32]

Boiling points are uncorrected. Melting points were determined by using a Hoover capillary melting point apparatus and are uncorrected. Infrared (IR) spectra were determined on a Perkin-Elmer 237B or 737B or a Beckman 4210 infrared spectrometer. Proton nuclear magnetic resonance ($^1$H NMR) spectra were recorded on Varian T-60 or EM-390 spectrometers. Chemical shifts are reported as $\delta$ values in parts per million relative to tetramethylsilane ($\delta$ 0.0) as an internal standard. Optical rotations were measured in 1-dm cells of 1-mL capacity using a Perkin-Elmer Model 141 polarimeter. Chloroform, when used as a solvent for optical rotation determinations or for IR spectra, was filtered through neutral alumina immediately prior to use.

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 60 mL/min. The indicated liquid phase was absorbed on 60–80 mesh Chromosorb W AW 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. 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 $\mu$m) manufactured by E. Merck and Co., Darmstadt.

Silica gel columns for chromatography utilized E. Merck Silica Gel 60, 70–230 mesh ASTM. Acidic silica gel refers to Silicar CC-4 Special "for column chromatography", sold by Mallinckrodt Chemical Works, St. Louis, MO.

"Dry" solvents were distilled shortly before use from an appropriate drying agent. Ether, tetrahydrofuran (THF), and dimethoxyethane were distilled under dry argon from sodium metal in the presence of benzophenone. Benzene and toluene were distilled from calcium hydride. Hexane and dichloromethane were distilled from phosphorus pentoxide. Methanol was distilled from magnesium methoxide. Hexamethylphosphoramide (HMPA) was distilled at ~1.0 mmHg from pulverized calcium hydride.

Triethylamine was distilled under argon from sodium benzophenone immediately prior to use. Diisopropylamine, pyridine, hexamethyldisilazane, and dimethylhydrazine 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; butanoyl chloride and propanoyl chloride were 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

Table III. Preparation of Glycol Ethers 34a,b and 35a,b

| reactant | solvent[a] | products | yield,[b] % | a/b[c] |
|---|---|---|---|---|
| **6c** | THF | **34a,b** | 76 | 5/1 |
| **6c** | THF-HMPA | **34a,b** | 56 | 1/1 |
| **6c** | THF[d] | **34a,b** | 67 | 7/1 |
| **6a**[e] | THF | **34a,b** | 80 | 5/1 |
| **7a**[e] | THF | **35a,b** | 73 | 5/1 |
| **7a**[e] | THF-HMPA | **35a,b** | 67 | 1/1 |

[a] Solvent employed during deprotonation of allylic ester. THF = 100% THF, HMPA-THF = 23% (v/v) HMPA/THF. [b] Yield of carboxylic acid obtained upon hydrolysis of silyl ester. [c] Ratio of diastereomers obtained by NMR analysis of unfractionated product. [d] Potassium hexamethyldisilazide used as base. [e] The required ester was generated just prior to deprotonation and was not isolated.

(32) In cases where reaction intermediates or products were isolated "by solvent extraction ($Na_2SO_4$)", the procedure followed was to dilute the reaction mixture with the indicated solvent or to extract the aqueous solution with several portions of the indicated solvent; the combined organic extracts were washed first with several portions of water and then with saturated sodium chloride and dried over anhydrous sodium sulfate. Drying over anhydrous magnesium sulfate ($MgSO_4$) or anhydrous potassium carbonate ($K_2CO_3$) is indicated by the appropriate parenthetical substitution. After drying, the solution was filtered and the solvent was evaporated from the filtrate under reduced pressure (water aspirator) using a rotary evaporator. The use of the terms "base wash" or "acid wash" indicates washing of the organic solution with saturated aqueous sodium bicarbonate solution or with 10% aqueous hydrochloric acid, respectively, prior to the aforementioned washing with water.

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, 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.

Mass spectral analyses were performed by Dr. Kai Feng, UCLA. Elemental combustion analyses were performed by Spang Microanalytical Laboratory, Eagle Harbor, MI.

**(*E*)-3-Methoxy-2-propen-1-ol (1a).** A solution of 1.16 g (0.01 mol) of ester **11a** in 5 mL of dry ether was added dropwise, over a period of 15 min, to a stirred, argon-protected, ice-cooled solution of 0.38 g (0.01 mol) of lithium aluminum hydride in 40 mL of dry ether. After 5 min at 0 °C, this mixture was hydrolyzed,[33] and the resulting white precipitate was removed by filtration and washed with 50 mL of ether. The combined filtrates were dried ($K_2CO_3$), and removal of solvent under reduced pressure afforded 915 mg of a colorless liquid. Distillation [kugelrohr, 100 °C (30 mmHg)] of this liquid provided 0.32 g (36%) of alcohol **1a**: IR ($CCl_4$) 3600 (OH), 1665 $cm^{-1}$ (C=C); $^1H$ NMR ($CCl_4$) $\delta$ 3.1 (br s, 1 H, OH), 3.48 (s, 3 H, $OCH_3$), 3.93 (d, 2 H, $J$ = 7 Hz, $CH_2O$), 4.83 (m, 1 H, C=CHC), 6.42 (d, 1 H, $J$ = 12.5 Hz, OCH=C).

Anal. Calcd for $C_4H_8O_2$: C, 54.52; H, 9.15. Found: C, 54.50; H, 9.08.

**(*E*)-3-Methoxy-2-buten-1-ol (2a).** In the manner described for the preparation of alcohol **1a**, 4.32 g (0.03 mol) of ester **11b**,[10] in 10 mL of ether, with 1.14 g (0.03 mol) of lithium aluminum hydride in 100 mL of ether, afforded, after distillation [kugelrohr, 100 °C (10 mmHg)], 2.52 g (82%) of alcohol **2a**, a colorless, clear liquid: IR (neat) 3500–3200 (OH), 1660 $cm^{-1}$ (C=C); $^1H$ NMR ($CCl_4$) 1.70 (s, 3 H, C=$CH_3$), 3.40 (s, 3 H, $OCH_3$), 4.47 (t, 1 H, C=CH).

Anal. Calcd for $C_5H_{10}O_2$: C, 58.79; H, 9.87. Found: C, 58.75; H, 9.81.

**(*E*)-3-Methoxy-3-phenyl-2-buten-1-ol (3a).** A mixture of 19.2 g (0.10 mol) of ethyl benzoylacetate, 10.6 g (0.10 mol) of trimethyl orthoformate, and 6 drops of concentrated sulfuric acid was stirred at room temperature for 36 h. After the addition of 0.5 mL of quinoline, distillation of the dark red reaction mixture, first at atmospheric pressure (removal of methyl formate and methanol) and then under reduced pressure, provided 16.4 g (80%) of a colorless liquid, bp 122–124 °C (1.3 mmHg). Analysis of this product by $^1H$ NMR indicated the presence of two geometrical isomers of the $\beta$-methoxy ester **11c**. Integration of the vinylic protons indicated that the major isomer ($\delta$ 5.1) and the minor isomer ($\delta$ 5.5) were present in a 4:1 ratio.[34]

A solution of 10.3 g of the above mixture in 10 mL of dry ether was added to a stirred solution of 1.9 g (0.05 mmol) of lithium aluminum hydride in 220 mL of dry ether. The ester was added at such a rate as to cause the ether to boil mildly. After 1 h at room temperature, workup of this mixture as described for the isolation of alcohol **1a** provided the crude product, distillation of which provided three fractions: A, 2.5 g, bp 82–85 °C (0.6 mmHg); B, 2.0 g, bp 85–92 °C (0.6 mmHg); and C, 2.7 g, bp 92–94 °C (0.6 mmHg). Fractions A and B were mixtures of the desired alcohol (~50%) with several byproducts, and were discarded. Fraction C was the alcohol **3a** (26% yield, based on ethyl benzoylacetate): bp 92–94 °C (0.6 mmHg); IR ($CCl_4$) 3600 (OH), 1640 $cm^{-1}$ (C=C); $^1H$ NMR ($CCl_4$) $\delta$ 3.57 (s, 3 H, $OCH_3$), 4.00 (d, 2 H, $J$ = 8 Hz, $CH_2O$), 4.87 (t, 1 H, $J$ = 8 Hz, C=CH), 7.3 (br s, 5 H, Ar H).

Anal. Calcd for $C_{10}H_{12}O_2$: C, 73.14; H, 7.37. Found: C, 73.09; H, 7.32.

**(*E*)-2-Methoxy-2-penten-4-ol (4a).** In the manner described for the preparation of alcohol **1a** from ester **11a**, 3.68 g (0.03 mol) of enone **12**,[12] in 15 mL of dry ether, with 1.22 g (0.03 mol) of lithium aluminum hydride in 100 mL of dry ether, afforded, after distillation, 3.3 g of the alcohol **4a**: bp 51–53 °C (3.1 mmHg); IR (neat) 3600–3200 (OH), 1665 $cm^{-1}$ (C=C); $^1H$ NMR ($CCl_4$) $\delta$ 1.20 (d, 3 H, $J$ = 6 Hz, $CCH_3$), 1.77 (s, 3 H, C=$CCH_3$), 3.43 (s, 3 H, $OCH_3$), 4.45 (m, 2 H, C=CH and OCH); mass spectrum, $m/e$ (calcd for $C_6H_{10}O$ ($M^+$ – 18) 98.073, found 98.074.

**(*E*)-3-Methoxy-2-propen-1-yl Propanoate (1b).** To a stirred, argon-protected solution of 0.32 g (3.6 mmol) of alcohol **1a** in 25 mL of dry THF at −78 °C was added 1.42 mL (3.6 mmol) of a 2.52 M solution of $n$-butyllithium in hexane. After 3 min, 0.46 mL (3.6 mmol) of propionic anhydride was added rapidly, and the mixture was allowed to warm to room temperature. After 40 min, $n$-pentane extraction ($Na_2SO_4$),[32] followed by distillation [kugelrohr, 80 °C (1.5 mmHg)], afforded 0.36 g (70%) of ester **1b**, a colorless liquid: IR ($CCl_4$) 1735 $cm^{-1}$ (C=O), 1655 $cm^{-1}$ (C=C); $^1H$ NMR ($CCl_4$) $\delta$ 1.10 (t, 3 H, $J$ = 7 Hz, $CCH_3$), 2.23 (q, 2 H, $J$ = 7 Hz, $CH_2C$), 3.52 (s, 3 H, $OCH_3$), 6.52 (d, 1 H, $J$ = 12 Hz, OCH=C).

Anal. Calcd for $C_7H_{12}O_3$: C, 58.31; H, 8.39. Found: C, 58.42; H, 8.36.

**(*E*)-3-Methoxy-2-buten-1-yl Propanoate (2b).** In the manner described for the preparation of ester **1b**, 1.20 g (0.012 mol) of alcohol **2a**, in 40 mL of dry THF, with 4.7 mL (0.012 mol) of 2.52 M $n$-butyllithium in hexane and 1.51 mL (0.012 mol) of propionic anhydride provided, after distillation [kugelrohr, 95–100 °C (2.0 mmHg)], 1.55 g (84%) of the ester **2b**: IR ($CCl_4$) 1735 (C=O), 1660 $cm^{-1}$ (C=C); $^1H$ NMR ($CCl_4$) $\delta$ 1.10 (t, 3 H, $J$ = 7 Hz, $CH_3$) 1.83 (s, 3 H, C=$CH_3$), 3.48 (s, 3 H, $OCH_3$), 4.50 (s, 3 H, $OCH_2$ and C=CH).

Anal. Calcd for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 60.79; H, 8.80.

**(*E*)-3-Methoxy-3-phenyl-2-buten-1-yl Propanoate (3b).** In the manner described for the preparation of ester **1b**, 0.33 g (2.0 mmol) of alcohol **3a**, in 10 mL of dry THF, with 0.79 mL (2.0 mmol) of 2.52 M $n$-butyllithium in hexane and 1.51 mL (2.0 mmol) of propionic anhydride, provided, after distillation [kugelrohr, 120 °C (0.6 mmHg)], 320 mg (73%) of the ester **3b**: IR ($CCl_4$) 1735 (C=O), 1648 $cm^{-1}$ (C=C); $^1H$ NMR ($CCl_4$) $\delta$ 1.10 (t, 3 H, $J$ = 7 Hz, $CCH_3$), 2.28 (q, 2 H, $J$ = 7 Hz, $CCH_2$), 3.67 (s, 3 H, $OCH_3$), 4.90 (dd, 1 H, $J$ = 6.5 Hz, $J$ = 9.8 Hz, C=CH), 7.27 (s, 5 H, Ar H).

Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.88; H, 7.32. Found: C, 70.80; H, 7.36.

**(±)-3,4-Dihydro-2,2-dimethyl-2*H*-pyran-4-yl Propanoate (*dl*-5b).** To a stirred solution of 1.02 g (8.0 mmol) of alcohol **5a**[17] in 30 mL of dry tetrahydrofuran under argon at 0 °C was added 3.17 mL (8.0 mmol) of a 2.52 M solution of $n$-butyllithium in hexane. After 3 min, cooling was discontinued, and 1.04 mL (8.0 mmol) of propionic anhydride was added. After 20 min at room temperature, during which time a flocculent white precipitate appeared, the product was isolated by ether extraction ($K_2CO_3$),[32] and distillation [kugelrohr, 100 °C (4.2 mmHg)] afforded 1.19 g (85%) of the ester, **5b**, a colorless liquid: $R_f$ 0.35 (silica gel, 10% ether–petroleum ether); IR ($CCl_4$) 1730 (C=O), 1640 (C=C), 1185 $cm^{-1}$ (C–O); $^1H$ NMR ($CCl_4$) $\delta$ 1.10 (t, 3 H, $J$ = 7 Hz, $CH_3$), 1.31 (s, 6 H, 2 × $CH_3$), 4.70 (dd, 1 H $J$ = 4 Hz, $J$ = 6 Hz, C=CHC), 5.08 (m, 1 H, OCH), 6.27 (dd, 1 H, $J$ = 1 Hz, $J$ = 6 Hz, OCH=C).

Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 65.22; H, 8.82.

**1,5-Anhydro-2,6-dideoxy-4-*O*-methyl-L-*arabino*-hex-1-enitol (6a). A. From Reduction of Chloride 20.** To a stirred solution of 38 mg (5.4 mmol) of lithium wire in 15 mL of anhydrous liquid ammonia under an argon atmosphere at −78 °C was added a solution of 210 mg (0.89 mmol) of the pyranosyl chloride **20** in 1 mL of dry THF. Cooling was then discontinued (ammonia refluxed), and after 120 min, 380 mg (7.0 mmol) of anhydrous ammonium chloride was cautiously added to the blue reaction mixture. The resulting colorless mixture was diluted with 15 mL

(33) Reaction mixtures obtained in reductions with lithium aluminum hydride were hydrolyzed by the method of Fieser and Fieser: Fieser, L. F.; Fieser, M. "Reagents for Organic Synthesis"; Wiley-Interscience: New York, 1967; p 584.

(34) The assignment of olefin geometry to these products is based upon the $^1H$-NMR spectra in comparison with the expected olefinic proton resonances calculated using the method of: Pascual, C.; Meier, J.; Simon, W. *Helv. Chim. Acta* **1966**, *49*, 164–168.

of ether, the ammonia was allowed to evaporate, and ~0.5 g of anhydrous magnesium sulfate was added. The ethereal suspension was filtered, and the solid was washed by trituration with five 3-mL portions of ether. Removal of solvent from these filtrates and drying of the residue under vacuum (1 mmHg) afforded 122 mg (95%) of a crystalline product, mp 76–77 °C. This product was homogeneous by TLC (silica gel, 40% ethyl acetate—benzene). The analytical sample was obtained by recrystallization from *n*-hexane and melted at 76–77 °C: $R_f$ 0.27 (40% ethyl acetate–benzene); IR ($CCl_4$) 3600 (OH), 1640 $cm^{-1}$ (C=C); $^1H$ NMR ($CCl_4$) $\delta$ 1.35 (d, 3 H, $J$ = 7 Hz, $CHCH_3$), 2.20 (br s, 1 H, OH), 3.01 (dd, 1 H, $J$ = 9 Hz, $J'$ = 6 Hz, OCH), 3.57 (s, 3 H, $OCH_3$), 4.62 (dd, 1 H, $J$ 6 Hz, $J'$ = 2 Hz, C=CHC), 6.23 (d, 1 H, $J$ = 6 Hz, OCH=C); $[\alpha]^{24}_D$ -0.2° (*c* 1.2, $HCCl_3$).

Anal. Calcd for $C_7H_{12}O_3$: C, 58.31; H, 8.39. Found: C, 58.32; H, 8.30.

**B. From Lactol 19, via Phosphonium Chloride Adduct.** To a stirred solution of 300 mg (1.36 mmol) of lactol **19** and 0.20 mL (2.0 mmol) of carbon tetrachloride in 3 mL of dry THF at −78 °C under an argon atmosphere was added 0.27 mL (1.5 mmol) of tris(dimethylamino)phosphine. After 30 min, the mixture was warmed in an ice–water bath, and after 3 min at 0 °C, the entire reaction mixture was taken up in an argon flushed syringe and added rapidly to a cold (−78 °C) stirred solution of 116 mg (16.7 mmol) of lithium wire in 40 mL of anhydrous liquid ammonia. Two 1-mL rinses with dry THF sufficed to complete the transfer. Cooling was discontinued (ammonia reflux), and after 120 min, 1.2 g (22 mmol) of anhydrous ammonium chloride was added to the blue reaction mixture. The resulting colorless mixture was diluted with a total of 40 mL of ether as the ammonia was allowed to evaporate, and ~1 g of anhydrous magnesium sulfate was added. The ethereal suspension was filtered, and the solids were washed with ether. The combined filtrates were concentrated under reduced pressure to ~4 mL in volume. This concentrate was transferred to a column of silica gel (3 cm high and 2 cm in diameter) and eluted with 100 mL of 40% ethyl acetate–benzene. Removal of solvents from the eluate and drying of the residue under vacuum (1 mmHg) afforded 187 mg (95%) of fine white crystals, mp 76–77 °C. This product was spectrally identical with the product obtained in A, above.

**1,5-Anhydro-2,6-dideoxy-4-*O*-methyl-3-*O*-propionyl-L-*arabino*-hex-1-enitol (6b).** To a stirred solution of 149 mg (1.03 mmol) of glycal **6a** and 97 μL (1.20 mmol) of dry pyridine in 2.0 mL of dry dichloromethane at 0 °C under an argon atmosphere was added 104 μL (1.20 mmol) of propanoyl chloride. Cooling was then discontinued, and after 90 min at room temperature the product was isolated by pentane extraction ($MgSO_4$).[33] Distillation [kugelrohr, 90 °C (0.7 mmHg)] afforded 190 mg (92%) of the ester **6b**: $R_f$ 0.58 (silica gel, 40% ethyl acetate–benzene); IR ($CHCl_3$) 1720 (C=O), 1640 $cm^{-1}$ (C=C); $^1H$ NMR ($CDCl_3$) $\delta$ 1.14 (t, 3 H, $J$ = 7 Hz, $CH_2CH_3$), 1.35 (d, 3 H, $J$ = 7 Hz, $CHCH_3$), 2.32 (q, 2 H, $J$ = 7 Hz, $CH_2CH_3$), 3.25 (dd, 1 H, $J$ = 8.0 Hz, $J'$ = 5.5 Hz, $HCOCH_3$), 3.50 (s, 3 H, $OCH_3$), 3.98 (dq, 1 H, $J$ = 7 Hz, $J'$ = 8 Hz, $CHCH_3$), 4.69 (dd, 1 H, $J$ = 6 Hz, $J'$ = 3 Hz, C=CHC), 5.27 (m, 1 H, C=CCH), 6.32 (dd, 1 H, $J$ = 6 Hz, $J'$ = 1.2 Hz, OCH=C); $[\alpha]^{23}_D$ +125° (*c* 1.1, $CHCl_3$).

Anal. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05. Found: C, 60.00; H, 8.06.

**(±)-Tetrahydro-2-furancarboxylic Acid.** Adam's catalyst, freshly prepared from 500 mg of platinum oxide, was added to a stirred solution of 4.0 g (39 mmol) of tetrahydrofurfuryl alcohol and 3.2 g (39 mmol) of sodium bicarbonate in 200 mL of water at 60 °C, and dry air was bubbled through this mixture. After 48 h, analytical TLC (silica gel, 40% ethyl acetate—benzene) indicated no starting material ($R_f$ 0.12) remained. The catalyst was removed from the cooled reaction mixture by filtration and washed with 20 mL of water. The combined filtrates were acidified (pH ~2.5) with concentrated HCl, saturated with sodium chloride (80 g), and extracted with 15 100-mL portions of ether. The combined extracts were dried ($MgSO_4$) and the ether was removed under reduced pressure. Distillation of the residue [kugelrohr, 80 °C (13 mmHg)] afforded 3.92 g (87%) of the carboxylic acid; lit.[35] bp 131–132 °C (14 mmHg).

(35) Kaufmann W. E.; Adams, R. *J. Am. Chem. Soc.* **1923**, *45*, 3029–3044.

**(±)-Tetrahydro-2-furancarbonyl Chloride.** A mixture of 232 mg (2.0 mmol) of tetrahydro-2-furancarboxylic acid and 0.45 mL (5.0 mmol) of oxalyl chloride was stirred under argon for 14 h. Excess oxalyl chloride was then removed under reduced pressure (50–100 mmHg) and distillation of the residue [kugelrohr, 95–100 °C (33 mmHg)] afforded 233 mg (87%) of tetrahydro-2-furancarbonyl chloride, a colorless liquid: IR ($CHCl_3$) 1780 (C=O), 1080 $cm^{-1}$ (C–O); *m/e* calcd for $C_4H_7O$ ($M^+$ − COCl) 71.050, found 71.047.

This product effervesces very slowly at room temperature and was stored under an argon atmosphere at −20 °C for up to 3 weeks.

**1,5-Anhydro-2,6-dideoxy-4-*O*-methyl-3-*O*-[(±)-tetrahydro-2-furoxyl]-L-*arabino*-hex-1-enitol (6c).** A stirred solution of 200 mg (1.4 mmol) of glycal **6a** and 0.27 mL (3.3 mmol) of dry pyridine in 3 mL of dry ether under an argon atmosphere at −5 ± 2 °C was treated with 0.19 mL (0.22 g, 1.54 mmol) of (±)-tetrahydro-2-furancarbonyl chloride. After 30 min, pentane extraction ($MgSO_4$)[32] followed by distillation [kugelrohr, 110 °C (0.7 mmHg)] afforded 300 mg (89%) of the ester **6c**: $R_f$ 0.31 (50% ether–petroleum ether); IR ($CCl_4$) 1740, 1760 (C=O), 1655 $cm^{-1}$ (C=C); $^1H$ NMR ($CCl_4$) $\delta$ 1.33 (d, 3 H, $J$ = 6 Hz, $CHCH_3$), 3.17, 3.20 (2 × dd, 1 H, $J$ = 6 Hz, $J'$ = 8 Hz), 3.42 (s, 3 H, $OCH_3$), 4.17–4.35 (m, 1 H, α-OCH), 5.17 (br d, 1 H, $J$ = 6 Hz), 6.26 (d, 1 H, $J$ = 6 Hz, OCH=C).

Anal. Calcd for $C_{12}H_{18}O_5$: C, 59.49; H, 7.49. Found: C, 59.52; H, 7.34.

**1,5-Anhydro-2,6-dideoxy-4-*O*-methyl-L-*xylo*-hex-1-enitol (7a). A. From Reduction of Chloride 22.** By procedure A described for the preparation of glycal **6a**, 73 mg (0.31 mmol) of freshly prepared chloride **22** in 2 mL of dry THF with 21 mg (3.0 mmol) of lithium metal in 10 mL of anhydrous liquid ammonia and 240 mg (4.5 mmol) of anhydrous ammonium chloride provided, after distillation [kugelrohr, 95 °C (1.0 mmHg)], 41 mg (92%) of the pyranoid glycal **7a**, a colorless liquid: $R_f$ 0.17 (silica gel, 40% ethyl acetate–benzene); IR ($CCl_4$) 3600 (OH), 1632 $cm^{-1}$ (C=C); $^1H$ NMR ($CDCl_3$) $\delta$ 1.38 (d, 3 H, $J$ = 6 Hz, $HCCH_3$), 3.49 (s, 3 H, $OCH_3$), 4.92 (dd, 1 H, $J$ = 6 Hz, $J'$ = 1.5 Hz, C=CHC), 6.50 (d, 1 H, $J$ = 6 Hz, OCH=C); $[\alpha]^{23}_D$ -121.5° (*c* 1.4, $CHCl_3$).

Anal. Calcd for $C_7H_{12}O_3$: C, 58.31; H, 8.39. Found: C, 58.37; H, 8.35.

**B. From Lactol 21, via Phosphonium Chloride Adduct.** By a procedure identical with process B described for the preparation of glycal **6a**, 220 mg (1.0 mmol) of lactol **21**, with 0.14 mL (1.5 mmol) of carbon tetrachloride and 0.20 mL (1.1 mmol) of tris(dimethylamino)phosphine in 2 mL of dry THF, and 83 mg (12 mmol) of lithium metal in 30 mL of anhydrous liquid ammonia, with 870 mg (16 mmol) of anhydrous ammonium chloride, provided, after distillation, 125 mg (87%) of a colorless, clear oil. This product was identical (IR, NMR, $[\alpha]_D$) with the material obtained in part A, above.

**1,5-Anhydro-2,6-dideoxy-4-*O*-methyl-3-*O*-propionyl-L-*xylo*-hex-1-entiol (7b).** To a stirred solution of 63 mg (0.44 mmol) of glycal **7a** and 42 μL (0.52 mmol) of dry pyridine in 2 mL of dry dichloromethane at 0 °C under an argon atmosphere was added 46 μL (0.52 mmol) of propanoyl chloride. The mixture was stirred at room temperature for 90 min, after which the product was isolated by pentane extraction ($MgSO_4$).[33] Distillation [kugelrohr, 90 °C (0.8 mmHg)] afforded 67 mg (76%) of the ester **7b**: $R_f$ 0.52 (silica gel, 40% ethyl acetate–benzene); IR ($CHCl_3$) 1720 (C=O), 1640 $cm^{-1}$ (C=C); $^1H$ NMR ($CCl_4$) $\delta$ 1.12 (t, 3 H, $J$ = 7 Hz, $CH_2CH_3$), 1.30 (d, 3 H, $J$ = 6 Hz, $CHCH_3$), 2.22 (q, 2 H, $J$ = 7 Hz, $CH_2CH_3$), 3.00 (dd, 1 H, $J$ = 1.5 Hz, $J'$ = 1 Hz, $CHOCH_3$), 3.43 (s, 3 H, $OCH_3$), 3.83 (q, 1 H, $J$ = 6 Hz, $J'$ = 1.5 Hz, $CHCH_3$), 5.00 (dd, $J$ = 5 Hz, $J'$ = 2 Hz), 6.41 (d, 1 H, $J$ = 6 Hz, OCH=C); $[\alpha]^{22}_D$ -200° (*c* 0.7, $CHCl_3$).

Anal. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05. Found: C, 59.85; H, 8.13.

**1,4-Anhydro-2-deoxy-5-*O*-methoxymethyl-D-*erythro*-pent-1-enitol (8a). A. From Reduction of Chloride 17a.** By procedure A described for the preparation of glycal **6a**, 178 mg (0.70 mmol) of freshly prepared chloride **17a** in 2 mL of dry THF with 22 mg (3 mmol) of lithium wire in 25 mL of anhydrous liquid ammonia and 240 mg of anhydrous ammonium chloride provided, after distillation [kugelrohr, 70–80 °C (0.005 mmHg)], 105 mg of a mixture of glycal **8a** and the simple reduction product **17b**. Analysis of this mixture by NMR revealed these products were

obtained in a 6:1 (**8a**:**17b**) ratio. Chromatography of this mixture on Florisil with 75% ether–petroleum ether provided pure products for analysis.

Fraction I, **17b**: $R_f$ 0.52 (silica gel, 75% ether—petroleum ether); IR ($CHCl_3$) 1030 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.35 (s, 3 H, $CH_3$), 1.52 (s, 3 H, $CH_3$), 3.37 (s, 3 H, $OCH_3$), 3.58 (d, 2 H, $J$ = 5 Hz, $CHCH_2OCH_2OCH_3$), 3.95 (s, 1 H, OCH, H), 4.00 (s, 1 H, OCH, H), 4.60 (s, 2 H, $OCH_2O$); $[\alpha]^{22}_D$ 36°($c$ 0.94, $CHCl_3$).

Anal. Calcd for $C_{10}H_{18}O_5$: C, 55.03; H, 8.31. Found: C, 55.16; H, 8.23.

Fraction II, **8a**: $R_f$ 0.25 (silica gel, 75% ether–petroleum ether); IR ($CHCl_3$) 3570 (OH), 1610 $cm^{-1}$ (C=C); $^1H$ NMR ($CDCl_3$) 2.57 (d, 1 H, $J$ = 6 Hz, OH), 3.37 (s, 3 H, $OCH_3$), 4.63 (s, 2 H, $OCH_2O$), 5.13 (dd, 1 H, $J = J'$ = 3 Hz, C=CHC), 6.52 (d, 1 H, $J$ = 3 Hz, OCH=C); $[\alpha]^{24}_D$ +259° ($c$ 0.91, $CHCl_3$).

Anal. Calcd for $C_7H_{12}O_4$: C, 52.49; H, 7.55. Found: C, 52.41; H, 7.65.

**B. From Lactol 16, via Phosphonium Chloride Adduct.** To a stirred solution of 15 g (64 mmol) of lactol **16** and 7.5 mL (78 mmol) of carbon tetrachloride in 200 mL of dry THF at −78 °C under argon was added 12.2 mL (67 mmol) of tris(dimethylamino)phosphine. After 45 min the mixture was warmed to 0 °C (ice–water bath), then taken up in an argon-flushed syringe, and added rapidly to a cold (−78 °C), stirred solution of 5.5 g (0.78 mol) of lithium metal in 800 mL of anhydrous liquid ammonia. Cooling was then discontinued (ammonia reflux), and after 150 min 42 g (0.79 mol) of anhydrous ammonium chloride was added to the blue reaction mixture. The resulting colorless mixture was diluted slowly with ether (750 mL) as the ammonia was allowed to evaporate, and ~10 g of anhydrous magnesium sulfate was added. The resulting ethereal suspension was filtered, and concentration of the filtrates under reduced pressure afforded a crude mixture of glycal **8a**, byproduct **17b**, and HMPA. This mixture was placed on a 100-g column of silica gel and eluted with 700 mL of 75% ether–petroleum ether. Concentration of the eluate afforded, after distillation [kugelrohr, 110 °C (0.01 mmHg)], 10.1 g of a colorless mixture of glycal **8a** and byproduct **17b**. This mixture is identical with the mixture obtained in part A above, and the ratio of components is 6:1 (**8a**:**17b**). On the basis of this ratio, the yield of glycal **8a** is 80%. This mixture was used without further purification for the enolate Claisen rearrangements described below.

**1,4-Anhydro-2-deoxy-5,6-*O*-isopropylidene-D-*arabino*-hex-1-enitol (9a).** To a mechanically stirred solution of 3.48 g (0.48 mol) of lithium wire in 800 mL of anhydrous liquid ammonia under an argon atmosphere at −78 °C was added a solution of 22.5 g (0.081 mol) of the furanosyl chloride **18a**[26] in 225 mL of dry THF. Cooling was then discontinued (ammonia reflux), and after 135 min 39 g (0.73 mol) of anhydrous ammonium chloride was cautiously added. The colorless, heterogeneous mixture was diluted with 800 mL of ether, and the ammonia was allowed to evaporate. The resulting ethereal suspension was filtered, and the filter cake was washed with ether. Concentration of the combined filtrates under reduced pressure and distillation [kugelrohr, 70–110 °C (0.06 mmHg)] provided 13.0 g (86%) of a colorless oil, a mixture of glycal **9a** and byproduct **18b**.

A portion of this oil (421 mg) was chromatographed on 42 g of silica gel. Elution with 60% ether–petroleum ether provided 37 mg of the byproduct **18b**, which was characterized by IR and NMR spectra and was not further purified. Continued elution provided 69 mg of glycal **9a** contaminated with a small amount of byproduct, followed by 300 mg of pure glycal **9a**. On the basis of this result the yield of **9a** from the furanosyl chloride is calculated to be 75%. For the pure glycal **9a**: $R_f$ 0.40 (silica gel, 60% ether–petroleum ether); IR (neat) 3600–3000 (OH), 1605 $cm^{-1}$ (C=C); $^1H$ NMR ($CDCl_3$) $\delta$ 1.37 (s, 3 H, $CH_3$), 1.45 (s, 3 H, $CH_3$), 2.07 (br s, 1 H, OH), 4.77–5.07 (m, 1 H, C=CCH), 5.24 (dd, 1 H, $J \approx J'$ = 3 Hz, C=CHC), 6.57 (d, 1 H, $J$ = 3 Hz, OCH=C); $[\alpha]^{23}_D$ −100° ($c$ 1.0, $CHCl_3$).

Anal. Calcd for $C_9H_{14}O_4$: C, 58.05; H, 7.58. Found: C, 57.97; H, 7.48.

**Methyl (*E*)-3-Methoxy-2-propenoate (11a).** The ester **11a** was prepared according to Winterfeldt and Preuss,[8] except that heating of the reaction mixture under argon at atmospheric pressure at 120 °C for 5 min prior to distillation of the product was followed by isolation of only the *E* isomer, **11a**: bp 64–65 °C (12 mmHg) [lit.[8] bp 80 °C (16 mmHg)]; IR ($CCl_4$) 1720 (C=O), 1630 $cm^{-1}$ (C=C); $^1H$ NMR ($CCl_4$) $\delta$ 3.62 (s, 3 H, $OCH_3$), 3.68 (s, 3 H, $OCH_3$), 5.10 (d, 1 H, $J$ = 12.5 Hz, C=CHC), 7.52 (d, 1 H, $J$ = 12.5 Hz, C=CHO).

**2,3-*O*-(1-Methylethylidene)-5-*O*-methoxymethyl-D-ribonic Acid γ-Lactone (15).** To a stirred, ice-cooled solution of 18.5 g (98 mmol) of hydroxy lactone **14**[25] in 200 mL of dry dichloromethane was added 68.5 mL (0.39 mol) of diisopropylethylamine and 29.9 mL (0.39 mol) of chloromethyl methyl ether. Cooling was then discontinued, and after 5 h at room temperature an additional 17 mL (98 mmol) of diisopropylethylamine was added, followed by 7.5 mL (98 mmol) of chloromethyl methyl ether. After 4 h at room temperature the reaction mixture was diluted with 2 L of ether and washed with five 400-mL portions of saturated aqueous $NaHCO_3$ and 400 mL of saturated aqueous NaCl. The combined aqueous extracts were washed with three 400-mL portions of ether, and the combined organic extracts were dried ($MgSO_4$) and concentrated to afford 21.7 g (95%) of the methoxymethyl ether **15**. Chromatography of a portion of this product on silica gel with 40% ethyl acetate–benzene afforded the analytical sample: $R_f$ = 0.40 (40% ethyl acetate–benzene); IR ($CHCl_3$) 1780 $cm^{-1}$ (C=O); $^1H$ NMR ($CDCl_3$) $\delta$ 1.38 (s, 3 H, $CH_3$) 1.47 (s, 3 H, $CH_3$), 3.33 (s, 3 H, $OCH_3$), 3.78 (d, 2 H, $J$ = 2 Hz, $CCH_2O$), 4.77 (s, 2 H, $OCH_2O$); $[\alpha]^{25}_D$ −55° ($c$ 0.90, $CHCl_3$).

Anal. Calcd for $C_{10}H_{10}O_6$: C, 51.72; H, 6.94. Found: C, 51.76; H, 6.94.

**2,3-*O*-(1-Methylethylidene)-5-*O*-methoxymethyl-D-ribose (16).** To a stirred solution of 21.7 g (93 mmol) of lactone **15** in 600 mL of dry ether under argon at −78 °C was added, dropwise, over 1 h, a solution of 24 mL (130 mmol) of diisobutylaluminum hydride in 75 mL of dry ether. After 1.5 h the reaction mixture was cautiously treated with 26 mL of methanol, warmed to room temperature, and diluted with 1.5 L of ether. This solution was washed with three 400-mL portions of 0.5 M aqueous sodium potassium tartrate and 300 mL of saturated NaCl and dried ($MgSO_4$). After removal of solvent under reduced pressure, chromatography of the residue on 250 g of silica gel with 60% ether–petroleum ether provided 21.9 g (95%) of the lactol **16**, as a mixture of anomers: $R_f$ 0.20 (60% ether–petroleum ether); IR ($CHCl_3$) 3400 $cm^{-1}$ (OH); $^1H$ NMR ($CDCl_3$) $\delta$ (major anomer, minor anomer) 1.32, 1.38 (s, 3 H, $CH_3$), 1.47, 1.55 (s, 3 H, $CH_3$), 3.38 (s, 3 H, $OCH_3$), 3.63, 3.60 (d, 2 H, $J$ = 5 Hz, $CCH_2O$), 4.65 (s, 2 H, $OCH_2O$), 5.32, 5.37 (d, 1 H, $J_{major}$ = 9 Hz, $J_{minor}$ = 7 Hz, OCHO); $[\alpha]^{25}_D$ +0.90°($c$ 0.89, $CHCl_3$).

Anal. Calcd for $C_{10}H_{18}O_6$: C, 51.27; H, 7.75. Found: C, 51.15; H, 7.64.

**2,3-*O*-(1-Methylethylidene)-5-*O*-methoxymethyl-β-D-ribofuranosyl Chloride (17a).** By the procedure described for the preparation of pyranosyl chloride **20**, 169 mg (0.72 mmol) of lactol **16** in 3.6 mL of dry THF with 350 μL of carbon tetrachloride and 380 mg of triphenylphosphine afforded, after distillation [kugelrohr, 70–80 °C (0.005 mmHg)], 170 mg (93%) of the chloride **17a** as a mixture of anomers (ratio ~1:10): IR ($CHCl_3$) 690 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ (major isomer, minor isomer) 1.33, 1.37 (s, 3 H, $CH_3$), 1.47, 1.65 (s, 3 H, $CH_3$), 3.38 (s, 3 H, $OCH_3$), 4.63 (s, 2 H, $OCH_2O$), 6.13, 6.18 (s, 1 H, OCHCl); $[\alpha]^{25}_D$ −45° ($c$ 1.14, $CHCl_3$).

Anal. Calcd for $C_{10}H_{17}ClO_5$: C, 47.53; H, 6.78. Found: C, 47.46; H, 6.75.

**6-Deoxy-2,3-*O*-(1-methylethylidene)-4-*O*-methyl-α,β-L-mannopyranosyl Chloride (20).** To a stirred solution of 220 mg (1.0 mmol) of lactol **19**[27] and 0.48 mL (5.0 mmol) of carbon tetrachloride in 5 mL of dry THF under an argon atmosphere was added 525 mg (2.0 mmol) of triphenylphosphine. The mixture was heated at reflux for 3 h, then cooled to room temperature, and concentrated under reduced pressure (~20 mmHg) to a thick paste. This residue was extracted by trituration with six 2-mL portions of dry ether and discarded. Removal of solvents from the ethereal extract and distillation [kugelrohr, 60 °C (0.005 mmHg)] afforded 210 mg (89%) of the chloride **20**, a colorless oil: IR (neat) 1375, 1112, 860, 700 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.31 (d, 3 H, $J$ = 6 Hz, $CHCH_3$), 1.36 (s, 3 H, $CH_3$), 1.54 (s, 3 H, $CH_3$), 3.53 (s, 3 H, $OCH_3$), 6.19 (s, 1 H, OCHCl); $[\alpha]^{25}_D$ −114° ($c$ 1.61, $CHCl_3$).

Anal. Calcd for $C_{10}H_{17}O_4Cl$: C, 50.74; H, 7.24. Found: C, 50.55; H, 7.28.

**6-Deoxy-2,3-*O*-(1-methylethylidene)-4-*O*-methyl-α,β-L-gulopyranosyl Chloride (22).** By the procedure described above for the preparation of pyranosyl chloride **20**, 190 mg (0.88 mmol) of the lactol **21** with 458 mg (1.76 mmol) of triphenylphosphine and 0.42 mL (4.4 mmol) of carbon tetrachloride in 6 mL of dry THF provided, after distillation [kugelrohr, 85 °C (0.05 mmHg)], 146 mg (70%) of the pyranosyl chloride **22**. This chloride was quite labile and was stored under argon at −20 °C for brief periods only: IR (neat) 1380, 910, 850 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.35 (d, 3 H, $J$ = 6 Hz, $CHCH_3$), 1.37 (s, 3 H, $CCH_3$), 1.52 (s, 3 H, $CCH_3$), 3.50 (s, 3 H, $OCH_3$), 5.32 (d, 1 H, $J$ = 6 Hz, OCHCl).

**(*R**,*S**)- and (*S**,*S**)-(±)-3-Methoxy-2-methyl-4-pentenoic Acids (*dl*-23a and *dl*-23b). A. Deprotonation in THF.** To a stirred solution of 1.1 mmol of LDA in 3.4 mL of dry THF,[7b] prepared under argon and cooled to −78 °C, was added, over a 2-min period, 144 mg (1.0 mmol) of ester **1b**. After 3 min at −78 °C, 0.66 mL (1.1 mmol) of a 1.66 M solution of *tert*-butyldimethylchlorosilane in dry HMPA was added; the mixture was allowed to warm to 0° C, and after 30 min, worked up by pentane extraction ($Na_2SO_4$).[33] The resulting crude silyl ester was hydrolyzed in 30 mL of THF with 2 mL of 10% aqueous hydrochloric acid. After being stirred at room temperature for 80 min, the mixture was diluted with 80 mL of ether, washed with four 30-mL portions of water, and then extracted with three 15-mL portions of 1 N aqueous sodium hydroxide. The combined basic extract was washed with two 15-mL partions of ether, cooled in ice, and acidified (pH ≈2.5) with 6 N hydrochloric acid. The product which separated was isolated by dichloromethane extraction ($Na_2SO_4$).[33] Drying of the resulting residue for several hours under vacuum (1 mmHg) afforded 115 mg (80%) of a mixture of the acids *dl*-**23a** and *dl*-**23b**. The $^1H$ NMR spectrum of a solution of this mixture in carbon tetrachloride revealed two doublets of unequal intensity, assigned to the α-methyl groups of the diastereomeric products. The major doublet (δ 0.97, $J$ = 7 Hz) and the minor (δ 1.17, $J$ = 7 Hz) appeared in a ratio of 5:1. This mixture, without further purification, provided the following analytical data: IR ($CCl_4$) 3600–2400 ($CO_2H$), 1710 (C=O), 930 $cm^{-1}$ (C=C); $^1H$ NMR ($CCl_4$) 0.97, 1.17 (two doublets, 5:1 ratio, 3 H, $J$ = 7 Hz, α-$CH_3$), 3.23 (s, 3 H, $OCH_3$), 4.95–5.7 (m, 3 H, $CCH{=}CH_2$).

Anal. Calcd for $C_7H_{12}O_3$: C, 58.31; H, 8.39. Found: C, 58.10; H, 8.47.

**B. Deprotonation in 23% HMPA–THF.** To a solution of 1.1 mmol of LDA in 2.6 mL of dry THF at −78 °C[7b] was added 0.8 mL of dry HMPA. The heterogeneous mixture was stirred for 5 min, and then 144 mg (1.0 mmol) of ester **1b** was added, followed after 3 min by 0.37 mL (1.1 mmol) of a 2.99 M solution of *tert*-butyldimethylchlorosilane in dry hexane. The mixture was allowed to warm to 0 °C and stirred for 30 min. Completion of this experiment as described in A, above, gave 108 mg (75%) of a mixture of *dl*-**23a** and *dl*-**23b**. The $^1H$ NMR spectrum of a solution of this mixture in carbon tetrachloride revealed two doublets of unequal intensity. The major doublet (δ 1.17, $J$ = 7 Hz) and the minor doublet (δ 0.97, $J$ = 7 Hz) appeared in a ratio of 4:1. Except for the change in relative magnitudes for these doublets, the spectral data for this mixture were exactly as described in A.

Anal. Calcd for $C_7H_{12}O_3$: C, 58.31; H, 8.39. Found: C, 58.17; H, 8.49.

**(*R**,*S**)- and [*S**,*S**)-[±]-2,3-Dimethyl-3-methoxy-4-pentenoic Acids (*dl*-24a and *dl*-24b). A. Deprotonation in THF.** In the manner described for the preparation of *dl*-**23a** and *dl*-**23b** from ester **1b**, 158 mg (1 mmol) of ester **2b** in 0.5 mL of dry THF was added to 1.1 mmol of LDA in 3.6 mL of dry THF at −78 °C under argon, and this mixture was treated with 0.77 mL of 1.42 M *tert*-butyldimethylchlorosilane in dry hexamethylphosphoramide, warmed, and stirred at 0 °C for 1.0 h and then at 67 °C for 0.5 h. The mixture was then cooled. Completion of this experiment as described for the isolation of *dl*-**23a,b**, above, provided 119 mg (76%) of a mixture of acids *dl*-**24a** and *dl*-**24b**. The $^1H$ NMR spectrum of a solution of this mixture in carbon tetrachloride revealed two doublets of unequal intensity, assigned to the α-methyl groups of the diastereomeric products. The major doublet (δ 1.07, $J$ = 7 Hz) and the minor one (δ 1.14, $J$ = 7 Hz) appeared in a ratio of 4:1. This mixture, after distillation [kugelrohr, 90 °C (0.5 mmHg)], provided 115 mg (73%) of material which was spectrally identical to the undistilled product: IR ($CCl_4$) 3600–2500 ($CO_2H$), 1710 $cm^{-1}$ (C=O); $^1H$ NMR ($CCl_4$) δ 1.07, 1.14 (two doublets, 4:1 ratio, 3 H, $J$ = 7 Hz, α-$CH_3$), 1.32 (s, 3 H, β-$CH_3$), 3.12 (s, 3 H, $OCH_3$), 5.0–5.4 (m, 2 H, $CH{=}CH_2$), 5.93 (dd, 1 H, $J$ = 11 Hz, $J'$ = 16 Hz, $CH{=}CH_2$).

Anal. Calcd for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 60.71; H, 9.02.

**B. Deprotonation in 23% HMPA–THF.** In the manner described for the preparation of *dl*-**23a** and *dl*-**23b**, 158 mg (1.0 mmol) of the ester **2b**, dissolved in 0.4 mL of dry THF, added to 1.1 mmol of LDA in a mixture of 2.8 mL of dry THF and 0.8 mL of dry HMPA, and treated with 0.37 mL (1.1 mmol) of a 2.99 M solution of *tert*-butyldimethylchlorosilane in hexane, provided, after completion of the experiment as described in part A, 127 mg (80%) of a mixture of acids *dl*-**24a** and *dl*-**24b**. The $^1H$ NMR spectrum of a solution of this mixture in carbon tetrachloride revealed two doublets of unequal intensity. The major (δ 1.14, $J$ = 7 Hz) and the minor doublet (δ 1.07, $J$ = 7 Hz) appeared in a ratio of 1:3. Without further purification, this mixture provided the following spectral data: IR ($CCl_4$) 3500–2700 ($CO_2H$), 1710 $cm^{-1}$ (C=O); $^1H$ NMR ($CCl_4$) δ 1.07, 1.14 (two doublets, 3:1 ratio, 3 H, $J$ = 7 Hz, α-$CH_3$), 1.32 (s, 3 H, β-$CH_3$), 3.12 (s, 3 H, $OCH_3$), 5.0–5.4 (m, 2 H, $CH{=}CH_2$), 5.93 (dd, 1 H, $J$ = 11 Hz, $J'$ = 16 Hz, $CH{=}CH_2$).

Anal. Calcd for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 60.86; H, 8.96.

**Methyl (*R***S**)- and (*S**,*S**)-(±)-3-Methoxy-2-methyl-3-phenyl-4-pentenoate (*dl*-25a and 25b). A. Deprotonation in THF.** To a stirred solution of 1.1 mmol of LDA in 3.4 mL of dry THF prepared under argon and cooled to −78 °C was added, over a 2 min period, a solution of 220 mg (1.0 mmol) of ester **3b** in 0.4 mL of dry THF. After 3 min at −78 °C, 0.66 mL (1.1 mmol) of a 1.66 M solution of *tert*-butyldimethylchlorosilane in dry HMPA was added; the mixture was allowed to warm to 0 °C and, after 30 min, worked up by ether extraction ($Na_2SO_4$).[33] The residue was dissolved in 5 mL of dry THF and heated at 67 °C for 3 h. After cooling and removal of THF under reduced pressure, the residue was dissolved in 4 mL of dry HMPA and stirred for 18 h at room temperature with 188 mg (2 mmol) of $KF{\cdot}2H_2O$ and 250 mg (2.5 mmol) of $KHCO_3$. Then 0.19 mL (3 mmol) of methyl iodide was added, and after 3 h at room temperature, the products were isolated by ether extraction ($Na_2SO_4$), including a base wash.[33] Spectral analysis ($^1H$ NMR) of the resiude indicated the presence of two diastereomeric products in a 47:53 ratio. Chromatography on silica gel with 5% ethyl ether–petroleum ether provided, in addition to 10 mg of mixed fractions, the following pure products:

Fraction I: 76 mg, $R_f$ 0.24 (silica gel, 10% ether–petroleum ether); IR ($CCl_4$) 1740 (C=O), 1080, 940 $cm^{-1}$; $^1H$ NMR ($CCl_4$) δ 1.11 (d, 3 H, $J$ = 7 Hz, α-$CH_3$), 2.90 (s, 3 H, $OCH_3$), 3.32 (s, 3 H, $OCH_3$), 5.23 (dd, 1 H, $J$ = 11.1 Hz, $J'$ = 2.6 Hz, HC=CHH), 5.40 (dd, 1 H, $J$ = 18.2 Hz, $J'$ = 2.6 Hz, HC=CHH), 6.23 (dd, 1 H, $J$ = 11.1 Hz, $J'$ = 18.2 Hz, $HC{=}CH_2$), 7.23 (br s, 5 H, Ar H).

Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.63; H, 7.73.

Fraction II: 70 mg, $R_f$ 0.20 (silica gel, 10% ether–petroleum ether); IR ($CCl_4$) 1732 (C=O), 1080, 930 $cm^{-1}$; $^1H$ NMR ($CCl_4$) δ 0.97 (d, 3 H, $J$ = 7 Hz, α-$CH_3$), 2.97 (s, 3 H, $OCH_3$), 3.55 (s, 3 H, $OCH_3$), 5.08 (dd, 1 H, $J$ = 11.1 Hz, $J'$ = 2.1 Hz, HC=CH, H), 5.35 (dd, 1 H, $J$ = 18.2 Hz, $J'$ = 2.1 Hz, HC=CH, H), 6.18 (dd, 1 H, $J$ = 11.1 Hz, $J'$ = 18.2 Hz, $HC{=}CH_2$), 7.23 (br s, Ar H).

Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.74; H, 7.79.

Comparison of these data with spectra obtained before chromatography indicated that the product obtained as fraction II predominated prior to separation. The total yield of *dl*-**25a** and *dl*-**25b** was 156 mg (67%).

**B. Deprotonation in 23% HMPA–THF.** This experiment was performed exactly as in A, above, except 1.1 mmol of LDA was dissolved in 2.6 mL of dry THF, and after cooling to −78 °C, before ester **3b** (1.0 mmol) was added, 0.8 mL of dry HMPA was added. After 10 min, completion of the experiment as in A provided 86 mg of fraction I, 80 mg of fraction II, and 5 mg of mixed fractions. Spectral analysis ($^1H$ NMR) of the crude methyl esters prior to chromatography indicated that the product obtained as fraction I predominated (48:52) prior to separation. The

total yield of *dl*-**25a** and *dl*-**25b** was 171 mg (72%).

**(*R**,*S**)- and (*S**,*S**)-(±)-(*E*)-2,3-Dimethyl-3-methoxy-4-hexenoic Acids (*dl*-26a and *dl*-26b). A. Deprotonation in THF.** To a stirred solution of 174 mg (1.5 mmol) of alcohol *dl*-**4a** in 3 mL of dry THF at −78 °C under an argon atmosphere was added 0.48 mL (1.65 mmol) of a 3.4 M solution of *n*-butyllithium in hexane and, after 3 min, 0.14 mL (1.65 mmol) of propanoyl chloride. The mixture was warmed, stirred at 0 °C for 5 min, and then cooled again to −78 °C, and 3 mL (1.5 mmol) of a 0.5 M solution of LDA in dry THF at 0 °C was rapidly added. After 3 min, 1.61 mL (1.8 mmol) of a 1.13 M solution of *tert*-butyldimethylchlorosilane in HMPA was added, cooling was discontinued, and the mixture was stirred for 1 h at room temperature. Completion of this experiment in the manner described for the isolation of *dl*-**23a** and *dl*-**23b** provided 155 mg (60%) of a colorless oil, a mixture of *dl*-**26a** and *dl*-**26b**. The $^1$H NMR spectrum of a solution of this mixture in carbon tetrachloride revealed two doublets of unequal intensity, assigned to the α-methyl groups of the diastereomeric products. The major doublet (δ 1.08, $J$ = 7 Hz) and the minor (δ 1.13, $J$ = 7 Hz) one appeared in a ratio of 7:3. Chromatography of this mixture on acidic silica gel with 20% ether–petroleum ether afforded a pure sample of each diastereomer. The minor isomer was eluted first: IR ($CCl_4$) 3600–2500 cm$^{-1}$ ($CO_2H$), 1710 cm$^{-1}$ (C=O); $^1$H NMR ($CCl_4$) δ 1.13 (d, 3 H, $J$ = 7 Hz, α-$CH_3$), 1.34 (s, 3 H, $CCH_3$), 1.76 (d, 3 H, $J$ = 5 Hz, C=CH**C**$H_3$), 3.22 (s, 3 H, $OCH_3$), 10.1 (s, 1 H, $CO_2H$).

Anal. Calcd for $C_9H_{16}O_3$: C, 62.76; H, 9.36. Found: C, 62.73; H, 9.35.

Continued elution provided the more polar isomer: IR ($CCl_4$) 3500–2600 ($CO_2H$), 1710 cm$^{-1}$ (C=O); $^1$H NMR ($CCl_4$) δ 1.08 (d, 3 H, $J$ = 7 Hz, α-$CH_3$), 1.30 (s, 3 H, $CCH_3$), 1.76 (d, 3 H, $J$ = 5 Hz, C=CH**C**$H_3$), 3.21 (s, 3 H, $OCH_3$), 10.4 (s, 1 H, $CO_2H$).

Anal. Calcd for $C_9H_{12}O_3$: C, 62.76; H, 9.36. Found: C, 62.73; H, 9.35.

**B. Deprotonation in 23% HMPA–THF.** This experiment was performed exactly as in A, above, except 1.65 mmol of LDA was dissolved in 3.9 mL of a 23% (v/v) solution of HMPA in THF, and to this solution was added the solution of ester in THF described in A. Completion of this experiment as described above afforded a 4:1 mixture of the diastereomers, *dl*-**26a** and *dl*-**26b**. The isomer having the lower field doublet (δ = 1.13, α-$CH_3$) was the major product.

**(αR*,2R*)- and (αS*,2R*)-(±)-5,6-Dihydro-α,6,6-trimethyl-2*H*-pyran-2-acetic Acids (*dl*-27a and *dl*-27b).** To a stirred solution of 1.19 mmol of LDA in 5.6 mL of dry THF under an argon atmosphere at −78 °C was added 1.7 mL of dry HMPA. After 5 min, a solution of 200 mg (1.08 mmol) of ester *dl*-**5b** in 0.4 mL of dry THF was added dropwise over a 2 min period, and after 3 additional min, 0.40 mL (1.19 mmol) of a 2.44 M solution of *tert*-butyldimethylchlorosilane in hexane was added. This mixture was stirred for 30 min at 0 °C, diluted with 100 mL of ice-cold *n*-pentane, and washed with 3 × 33 mL of ice-cold water. The organic phase was dried ($MgSO_4$), and pentane was removed at 15–20 °C under reduced pressure. Spectral analysis of this residue indicated the product at hand was the silyl ketene acetal **5d**: IR ($CCl_4$) 1675 (C=C, acetal), 1640 cm$^{-1}$ (C=C, enol ether); $^1$H NMR ($CCl_4$) δ 0.24 [s, 6 H, $Si(CH_3)_2$], 6.42 (d, 1 H, $J$ = 6 Hz, OCH=CH). The rearrangement of this acetal at 35 °C to afford the *tert*-butyldimethylsilyl ester was evidenced by a gradual and synchronous disappearance of the singlet at δ 0.24 and the doublet at δ 6.42 and the simultaneous appearance and growth of a singlet at δ 0.33 (attributed to the $Si(CH_3)_2$ of the silyl ester) and a multiplet at δ ≈ 5.8. The half-life at 35 °C was 100 ± 10 min. When no acetal remained the silyl ester was hydrolyzed in 10 mL of THF with 1.8 mL of 10% aqueous hydrochloric acid. The hydrolysis mixture was diluted with 100 mL of ether, washed with 4 × 30 mL of water, and extracted with 4 × 8 mL of 1 N aqueous NaOH. The combined extracts were washed with 4 × 10 mL of *n*-pentane and acidified (pH ≈ 2) with 10% aqueous hydrochloric acid. The product was isolated by dichloromethane extraction ($Na_2SO_4$).[33] Drying of the residue for several hours under vacuum afforded 158 mg (76%) of a mixture of *dl*-**27a** and *dl*-**27b**. The $^1$H NMR spectrum of a solution of this mixture in carbon tetrachloride revealed two doublets of unequal intensity. The major doublet (δ 1.16, $J$ = 7 Hz) and the minor one (δ 1.12, $J$ = 7 Hz) appeared in a ratio of (11:1) and represent the two diastereomeric products. The analytical sample was prepared by distillation [kugelrohr, 100 °C (0.7 mmHg)]: IR ($CCl_4$) 3500–2400 ($CO_2H$), 1710 (C=O), 1200 cm$^{-1}$ (C–O); $^1$H NMR ($CCl_4$) δ 1.12, 1.16 (overlapping doublets, 11:1 ratio, 3 H, $J$ = 7 Hz, α-$CH_3$), 1.20 (s, 6 H, 2 × $CH_3$), 4.2–4.45 (m, 1 H, β-CH), 5.5–5.9 (m, 2 H, CH=CH).

Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 65.16; H, 8.78.

**[2*S*-[2α(*S**- and -*R**),5β,6α]]-5,6-Dihydro-α,6-dimethyl-5-methoxy-2*H*-pyran-2-acetic Acids (28a and 28b). A. From Ester 6b by Deprotonation in THF.** By the procedure described for the preparation of **27a,b**, 100 mg (0.50 mmol) of ester **6b** in 0.5 mL of dry THF, added to 0.55 mmol of LDA dissolved in 1.5 mL of dry THF and treated with 0.38 mL of a 1.45 M solution of *tert*-butyldimethylchlorosilane in HMPA, provided the silyl ketene acetal **6d**: $^1$H NMR ($CCl_4$) δ 0.19 (s, 6 H, 2 × $SiCH_3$), 1.45 (d, 3 H, $J$ = 6 Hz, C=CHC**H**$_3$), 3.50 (s, 3 H, $OCH_3$). Rearrangement at 35 °C ($\tau_{1/2}$ = 30 ± 5 min) afforded the silyl ester: $^1$H NMR ($CCl_4$) δ 0.25 (s, 6 H, 2 × $SiCH_3$), 3.33 (s, 3 H, $OCH_3$). After hydrolysis there was obtained 73 mg (73%) of a mixture of the diastereomeric acids, **28a** and **28b**. The $^1$H NMR spectrum of a solution of this mixture in carbon tetrachloride revealed two overlapping doublets. The major doublet (δ 1.07, $J$ = 7 Hz) and the minor one (δ 1.12, $J$ = 7 Hz) appeared in a ratio of 4:1. Distillation [kugelrohr, 120 °C (0.5 mmHg)] of this mixture afforded the analytical sample: IR ($HCCl_3$) 3600–2500 ($CO_2H$), 1700 cm$^{-1}$ (C=O); $^1$H NMR ($CCl_4$) δ 1.07, 1.12 (two doublets, 4:1 ratio, 3 H, $J$ = 7 Hz, α-$CH_3$), 1.21 (d, 3 H, $J$ = 6 Hz, CHC**H**$_3$), 3.32 (s, 3 H, $OCH_3$), 5.5–6.0 (m, 2 H, CH=CH).

Anal. Calcd for $C_{10}H_{12}O_4$: C, 59.98; H, 8.05. Found: C, 59.99; H, 8.03.

**B. From Ester 6b by Deprotonation in 23% HMPA–THF.** A solution of 0.55 mmol of LDA in 1.7 mL of 23% (by volume) HMPA–THF, with 100 mg (0.5 mmol) of ester **6b** dissolved in 0.2 mL of dry THF, and 0.24 mL (0.55 mmol) of a 2.3 M solution of *tert*-butyldimethylchlorosilane in dry hexane provided the ketene acetal **6d**. Rearrangement at 35 °C ($\tau_{1/2}$ = 30 ± 5 min) afforded the silyl ester, from which there was obtained 71 mg (71%) of a mixture of the diastereomeric acids **28a** and **28b**. Analysis of this mixture by NMR spectroscopy as described in A indicated that the ratio of diastereomers was 1:4 and that the isomer having the lower field doublet (δ 1.12) was the major product. Distillation [kugelrohr, 120 °C (0.5 mmHg)] afforded an analytical sample, spectrally identical (except as noted) with the product obtained in A.

**C. From Glycal 6a by Deprotonation in THF.** To a stirred solution of 51 mg (0.35 mmol) of glycal **6a** in 0.7 mL of dry THF under an atmosphere of argon at −78 °C was added 0.16 mL (0.38 mmol) of a 3.45 M solution of *n*-butyllithium in hexane followed by 34 μL (0.38 mmol) of propanoyl chloride. After 30 min at −78 °C and 10 min at 0 °C, the entire reaction mixture was added to a cold (−78 °C), stirred, argon-protected solution of 0.77 mmol of LDA in 2.2 mL of dry THF. After 5 min, this mixture was treated with 0.53 mL (0.77 mmol) of a solution of *tert*-butyldimethylchlorosilane in dry HMPA. Completion of this experiment exactly as described in A (except the rearrangement was completed by heating a solution of the silyl ketene acetal in carbon tetrachloride at 75 °C for 40 min) afforded 56 mg (79%) of a product identical (NMR, IR) with the product obtained in A.

**[2*R*-[2α(*S**- and -*R**],5β,6β]]-5,6-Dihydro-α,6-dimethyl-5-methoxy-2*H*-pyran-2-acetic Acids (29a and 29b). A. From Glycal 7a by Deprotonation in THF.** By the procedure described for the preparation of **28a,b** from glycal **6a**, a solution of 62 mg (0.43 mmol) of glycal **7a** in 0.7 mL of dry THF with 0.19 mL (0.46 mmol) of a 2.45 M solution of *n*-butyllithium in hexane, treated with 41 μL (0.47 mmol) of propanoyl chloride, added to 0.95 mmol of LDA dissolved in 2.7 mL of dry THF, and treated with 0.65 mL (0.96 mmol) of a 1.45 M solution of *tert*-butyldimethylchlorosilane in dry HMPA, provided 59 mg (69%) of a mixture of the acids **29a** and **29b**. Analysis of this mixture ($^1$H NMR), as described in previous examples, indicated the two products were present in a ratio of 4:1. Distillation [kugelrohr, 120 °C (0.5 mmHg)] of this mixture provided the analytical sample: IR ($CHCl_3$) 3600–2400 ($CO_2H$), 1705 cm$^{-1}$ (C=O); $^1$H NMR ($CCl_4$) δ 1.14, 1.18 (2 d, 4:1 ratio, 3 H, $J$ = 7 Hz, α-$CH_3$), 1.14 (d, 3 H, $J$ = 6 Hz, CHC**H**$_3$), 3.30 (s, 3 H, $OCH_3$), 5.81 (s, 2 H, CH=CH).

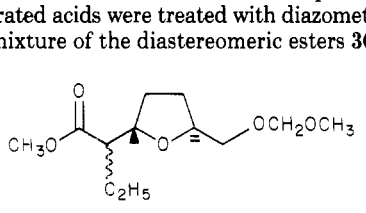
Anal. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05. Found: C, 59.96; H, 8.05.

**B. From Glycal 7a by Deprotonation in 23% HMPA–THF.** By the procedure described in A, 62 mg (0.43 mmol) of glycal **7a** in 0.8 mL of dry THF with 0.19 mL (0.46 mmol) of a 2.45 M solution of *n*-butyllithium in hexane, treated with 41 μL (0.47 mmol) of propanoyl chloride, added to 0.95 mmol of LDA dissolved in 3.0 mL of 23% (by volume) HMPA–THF and treated with a solution of 143 mg (0.95 mmol) of *tert*-butyldimethylchlorosilane in 0.7 mL of dry hexane, afforded 64 mg (74%) of a mixture of acids **29a** and **29b**. The $^1$H NMR spectrum of a solution of this mixture in carbon tetrachloride revealed two doublets (major, δ 1.18; minor, δ 1.14) in a ratio of 4:1. Except for the inversion of relative magnitude for these doublets, the product was the same as described in A.

**[2*R*-[2α(*S**- and -*R**),5β]]-2,5-Dihydro-α-ethyl-5-methoxymethylenoxymethylfuran-2-acetic Acids (30a and 30b). A. From Glycal 8a by Deprotonation in THF.** To a stirred solution of 138 mg (0.70 mmol of **8a**) of the 6:1 mixture of **8a** and **17b** (described above) in 2.8 mL of dry THF at −78 °C under argon was added 0.35 mL (0.84 mmol) of a 2.41 M solution of *n*-butyllithium in hexane, followed after 5 min by 87 μL (0.84 mmol) of butanoyl chloride. After 5 min at 0 °C the entire reaction mixture was taken up in an argon flushed syringe and added, dropwise, to a stirred solution of 0.94 mmol of LDA in 3 mL of dry THF at −78 °C under argon. After 10 min, the reaction mixture was treated with 0.24 mL (1.4 mmol of TMSCl) of the supernatant centrifugate from a mixture of 0.36 mL of trimethylchlorosilane and 0.12 mL of dry triethylamine. After 10 min at −78 °C and 1 h at room temperature, the reaction mixture was diluted with 10 mL of 0.5 N aqueous NaOH and washed with 2 mL of ether. The organic phase was extracted with three 10-mL portions of 0.5 N NaOH, and the combined aqueous extracts were washed with 20 mL of ether and acidified (pH ~2). Ether extraction ($MgSO_4$)[32] afforded 118 mg (73%) of a mixture of the diastereomeric acids, **30a** and **30b**. A portion of this material was treated with diazomethane in ether, and chromatography of the resulting methyl esters on silica gel with 40% ether–petroleum ether provided the analytical sample as a mixture of isomers: $R_f$ 0.29 (40% ether–petroleum ether); IR ($CHCl_3$) 1720 (C=O), 740 cm$^{-1}$ (C=C); $^1$H NMR ($CDCl_3$) δ 6.90 (t, 3 H, $J$ = 6 Hz, $CH_3CH_2$), 1.52 (m, 2 H, $CH_3CH_2$), 3.33 (s, 3 H, $OCH_3$), 3.53 (d, 2 H, $J$ = 5 Hz, $CCH_2O$), 3.72 (s, 3 H, $OCH_3$), 4.62 (s, 2 H, $OCH_2O$), 5.92 (m, 2 H, CH=CH).

Anal. Calcd for $C_{12}H_{20}O_5$: C, 59.00; H, 8.25. Found: C, 58.92; H, 8.21.

A separate portion of the mixture of isomeric acids was hydrogenated over 5% rhodium on carbon at 50 psi for 2 h, and the resulting saturated acids were treated with diazomethane in ether to provide a mixture of the diastereomeric esters **36a** and **36b** in




**36a,b**

a ratio of 4:1, as determined by VPC analysis (4% SE-30, 110 °C). Chromatography of this mixture on silica gel with 50% ether–petroleum ether provided analytical samples of each isomer.

Fraction I (minor isomer): $R_f$ = 0.40 (50% ether—petroleum ether); IR ($CHCl_3$) 1720 cm$^{-1}$ (C=O); $^1$H NMR ($CDCl_3$) δ 0.88 (t, 3 H, $J$ = 7 Hz, $CH_3CH_2$), 3.33 (s, 3 H, $OCH_3$), 3.46 (d, 2 H, $J$ = 6 Hz, $CCH_2O$), 3.65 (s, 3 H, $OCH_3$), 4.60 (s, 2 H, $OCH_2O$); $[\alpha]^{25}_D$ −17° (*c* 0.90, $CHCl_3$).

Anal. Calcd for $C_{12}H_{22}O_5$: C, 58.52; H, 9.00. Found: C, 58.47; H, 8.97.

Fraction II (major isomer): $R_f$ 0.25 (50% ether—petroleum ether); IR ($CHCl_3$) 1720 cm$^{-1}$ (C=O); $^1$H NMR ($CDCl_3$) δ 0.89 (t, 3 H, $J$ = 7 Hz, $CH_3CH_2$), 3.33 (s, 3 H, $OCH_3$), 3.46 (d, 2 H, $J$ = 6 Hz, $CCH_2O$), 3.69 (s, 3 H, $OCH_3$), 4.60 (s, 2 H, $OCH_2O$); $[\alpha]^{27}_D$ +3.4° (*c* 1.15, $CHCl_3$).

Anal. Calcd for $C_{12}H_{22}O_5$: C, 58.52; H, 9.00. Found: C, 58.58; H, 9.05.

**B. From Glycal 8b by Deprotonation in 23% HMPA–THF.** By the same procedure and with the same quantities of reactants as described in A, above, with the exception that 0.64 mL of dry HMPA was added to the solution of ester in THF at 0 °C and 0.69 mL of dry HMPA was added to the solution of LDA in THF at −78 °C, there was obtained 97 mg (60%) of a mixture of the isomeric acids **30a** and **30b**. The ratio of diastereomers (determined, as described above, by VPC analysis of the hydrogenated methyl esters) was found to be 1:1, with the major isomer having the higher $R_f$ [$R_f$ 0.40 (50% ether—petroleum ether)].

**[2*S*-[2α(*S**- and -*R**),5α,5α*R*]-2,5-Dihydro-5-(2,2-dimethyl-1,3-dioxolan-4-yl)-α-methylfuran-2-acetic Acids (31a and 31b). A. From Glycal 9a by Deprotonation in THF.** By the procedure described for the preparation of acids **30a,b** from glycal **8a**, 194 mg (1.04 mmol) of glycal **9a** with 0.45 mL (1.09 mmol) of *n*-butyllithium and 95 μL (1.09 mmol) of propanoyl chloride in 3 mL of dry THF, added to 2.18 mmol of LDA in 5 mL of dry THF, afforded, following workup and distillation [kugelrohr, 110–140 °C (0.01 mmHg)], 132 mg (52%) of a mixture of diastereomeric acids, **31a** and **31b**. The $^1$H NMR spectrum of a solution of this mixture in carbon tetrachloride revealed two doublets of unequal intensity, attributed to the α-methyl groups of the diastereomeric acids. The major doublet (δ 1.18, $J$ = 7 Hz) and the minor one (δ 1.13, $J$ = 7 Hz) appeared in a ratio of 4:1: IR ($CDCl_3$) 3600–2400 ($CO_2H$), 1705 cm$^{-1}$ (C=O); $^1$H NMR ($CDCl_3$) δ 1.13, 1.18 (overlapping doublets, 4:1 ratio, 3 H, $J$ = 7 Hz, α-$CH_3$), 1.33 (s, 3 H, $CCH_3$), 1.40 (s, 3 H, $CCH_3$), 5.8–6.1 (m, 2 H, CH=CH). A portion of this material was hydrogenated at 50 psi over 5% rhodium on carbon in THF for 5 h. After removal of solvent under reduced pressure, chromatography of the residue on silica gel with 1% acetic acid in 50% ether–*n*-hexane afforded a saturated derivative of a single isomer of the title compound in 56% yield; for the saturated acid: IR ($CDCl_3$) 1705 cm$^{-1}$ (C=O); $^1$H NMR ($CDCl_3$) δ 1.22 (d, 3 H, $J$ = 7 Hz, α-$CH_3$), 1.35 (s, 3 H, $CCH_3$), 1.41 (s, 3 H, $CCH_3$), 9.8 (s, 1 H, OH); $[\alpha]^{23}_D$ +33° (*c* 1.2, $CHCl_3$).

Anal. Calcd for $C_{12}H_{20}O_5$: C, 59.00; H, 8.25. Found: C, 59.10; H, 8.24.

**B. From Glycal 9a by Deprotonation in 23% HMPA–THF.** By the procedure described for the preparation of acids **30a** and **30b** (part B), 342 mg (1.84 mmol) of glycal **9a** with 0.79 mL (2.05 mmol) of 2.45 M *n*-butyllithium in hexane and 0.18 mL of propanoyl chloride in 3.5 mL of dry THF, added to 3.86 mmol of LDA in 13 mL of 23% HMPA–THF and treated with 5.79 mmol of trimethylchlorosilane, afforded, after distillation [kugelrohr, 110–135 °C (0.08 mmHg)], 242 mg (54%) of a mixture of diastereomeric acids, **31a** and **31b**. The $^1$H NMR spectrum of a solution of this mixture in carbon tetrachloride revealed two doublets, as described in part A, and the ratio of isomers was 1:1.

**[2*R*,5α,6β]-Methyl 5,6-Dihydro-5-hydroxy-6-hydroxymethyl-2*H*-pyran-2-acetate Benzylidene Acetal (33).** To a stirred suspension of 80 mg (2.0 mmol) of potassium hydride (oil free) in 7 mL of dry THF at 23 °C under argon was added 0.48 mL (2.2 mmol) of dry hexamethyldisilazane. After 1 h at room temperature the resulting solution was cooled to −78 °C and treated dropwise with a solution of 276 mg (1.0 mmol) of acetate **10** in 1 mL of dry THF. After 10 min at −78 °C this mixture was treated with 1.38 mL (2.0 mmol) of 1.45 M *tert*-butyldimethylchlorosilane in HMPA. Cooling was then discontinued, and after standing 30 min at room temperature the solution afforded, following *n*-pentane extraction,[32] 532 mg of a colorless oil, the ketene acetal xii: $^1$H NMR ($CCl_4$) δ 0.17 (s, 3 H, $SiCH_3$), 0.23 (s, 3 H, $SiCH_3$), 3.15 (d, 1 H, $J$ = 2 Hz, C=C**H**, H), 3.32 (d, 1 H, $J$ = 2 Hz, C=CH, **H**), 6.43 (d, 1 H, $J$ = 6 Hz, OCH=C). This oil was taken up in 20 mL of pentane, dried ($MgSO_4$), and filtered through a fine frit. The filtrate was concentrated and the residue was dissolved in 7 mL of dry toluene and heated at 100 °C for 22 h. After the solution was cooled, toluene was removed under reduced pressure, and the residue was dissolved in 3 mL of dry HMPA and treated with 282 mg (3 mmol) of $KF{\cdot}2H_2O$ and 300 mg (3 mmol) of $KHCO_3$. The resulting mixture was stirred for 12 h, and then 0.25 mL (4.0 mmol) of dry MeI was added. After 2 h, *n*-pentane extraction ($MgSO_4$)[32] afforded 265 mg (91%) of a crystalline solid, crude ester **33**. Recrystallization from hexane, followed by chromatography of the mother liquor on silica gel with 10% ethyl acetate–benzene, provided 32 mg of a 1:1 mixture

of starting material and product, and 151 mg of ester **33**, mp 95–95.5 °C. The yield based on unrecovered starting material is therefore 61%. The analytical sample was obtained by recrystallization from *n*-hexane: mp 95–95.5 °C; $R_f$ 0.30 (10% ethyl acetate–benzene); IR ($CHCl_3$) 1730 (C=O), 690 $cm^{-1}$ (C=C); $^1H$ NMR ($CDCl_3$) $\delta$ 2.50 (dd, 1 H, $J$ = 16 Hz, $J'$ = 6 Hz, $\alpha$-$CH_2$), 2.74 (dd, 1 H, $J$ = 16 Hz, $J'$ = 9 Hz, $\alpha$-$CH_2$), 3.71 (s, 3 H, $OCH_3$), 5.55 (s, 1 H, ArCH), 6.04 (br d, 1 H, $J$ = 10 Hz, C=CH), 7.2–7.6 (m, 5 H, ArH); $[\alpha]^{23}_D$ +67° (*c* 1.2, $CHCl_3$).

Anal. Calcd for $C_{16}H_{18}O_5$: C, 66.19; H, 6.25. Found: C, 66.23; H, 6.28.

**Methyl (2*S*- and -2*R*,2′*S*,5*R*,6*S*)-2-(5,6-Dihydro-5-methoxy-6-methyl-2′*H*-pyran-2′-yl)tetrahydro-2-furancarboxylates (34a and 34b). A. From Ester 6c by Deprotonation in THF.** To a stirred solution of 2.7 mmol of LDA in 3 mL of dry THF at −78 °C under an argon atmosphere was added a solution of 300 mg (1.24 mmol) of ester **6c** in 1 mL of dry THF and, after 6 min, 0.62 mL (3.7 mmol of TMSCl) of the supernatant centrifugate from a mixture of 0.94 mL of trimethylchlorosilane (TMSCl) with 0.30 mL of dry triethylamine. After 20 min at 0 °C and 2.5 h at room temperature, the reaction mixture was diluted with 30 mL of ice-cold 0.5 N aqueous NaOH and washed with four 20-mL portions of ether. The aqueous solution was acidified (pH ~2), and after the addition of 18 g of sodium chloride, dichloromethane extraction ($MgSO_4$)[32] provided 247 mg (82%) of a mixture of diastereomeric carboxylic acids. This mixture was methylated with diazomethane in ether, and chromatography of the product on 28 g of silica gel with 50% ether–petroleum ether afforded pure samples of each diastereomeric methyl ester, **34a** and **34b**.

Fraction I: 25 mg; $R_f$ 0.30 (50% ether–petroleum ether); IR ($HCCl_3$) 1735 $cm^{-1}$ (C=O); $^1H$ NMR ($CCl_4$) $\delta$ 1.24 (d, 3 H, $J$ = 6 Hz, $CHCH_3$), 3.33 (s, 3 H, $OCH_3$), 3.69 (s, 3 H, $OCH_3$), 4.43 (br s, 1 H, H-2′), 5.6–6.0 (m, 2 H, CH=CH); $[\alpha]^{24}_D$ −110° (*c* 0.84, $HCCl_3$).

Anal. Calcd for $C_{13}H_{20}O_5$: C, 60.92; H, 7.87. Found: C, 60.76; H, 7.89.

Fraction II: 150 mg, $R_f$ 0.28 (50% ether–petroleum ether); IR ($HCCl_3$) 1735 $cm^{-1}$ (C=O); $^1H$ NMR ($CCl_4$) $\delta$ 1.24 (d, 3 H, $J$ = 6 Hz, $CHCH_3$), 3.33 (s, 3 H, $OCH_3$), 3.64 (s, 3 H, $OCH_3$), 4.21 (br s, 1 H, H-2′), 5.6–6.0 (m, 2 H, CH=CH); $[\alpha]^{24}_D$ −134° (*c* 0.96, $HCCl_3$).

Anal. Calcd for $C_{13}H_{20}O_5$: C, 60.92; H, 7.87. Found: C, 60.97; H, 7.77.

The overall yield, including 22 mg of mixed fractions, was 62%. Comparison of the above spectral data with $^1H$ NMR data obtained for the unfractionated acids and esters indicated the two isomers were produced in a ratio of 5:1.

**B. From Ester 6c by Deprotonation 23% HMPA–THF.** In the manner described in A, a solution of 0.77 mmol of LDA in 2.0 mL of 23% (by volume) HMPA–THF with 85 mg (0.35 mmol) of ester **6c** in 0.5 mL of dry THF and 1.05 mmol of TMSCl (treated with triethylamine as in A) provided, after rearrangement and hydrolysis, 48 mg (56%) of a colorless oil which contained (by $^1H$ NMR) a mixture of the two diastereomeric carboxylic acids in a ratio of 1:1.

**C. From Ester 6c by Deprotonation in THF with Lithium Hexamethyldisilazide.** By the procedure described in B, 0.77 mmol of hexamethyldisilazide in 2 mL of dry THF with 85 mg of ester **6c** provided 57 mg (67%) of a clear, colorless oil which contained (by $^1H$ NMR analysis) a mixture of the two diastereomeric acids in a ratio of 7:1. The predominant isomer in this case was the same as the major isomer obtained in part A.

**D. From Glycal 6a by Deprotonation in THF.** To a stirred solution of 100 mg (0.69 mmol) of glycal **6a** in 1.4 mL of dry THF at −78 °C under an argon atmosphere was added 0.45 mL (0.73 mmol) of a 1.64 M solution of *n*-butyllithium in hexane, followed, after 5 min, by 85 μL (0.76 mmol) of (±)-tetrahydro-2-furancarbonyl chloride. This mixture was stirred for 10 min at 0 °C and then taken up in a dry syringe and added dropwise to a solution of 1.52 mmol of LDA in 4 mL of dry THF. After 12 min, 4.56 mmol of TMSCl (pretreated with dry triethylamine) was added. After 20 min at −78 °C and 2.5 h at room temperature, hydrolysis of this reaction mixture and isolation of the product as described in A provided 133 mg (80%) of a mixture of the diastereomeric carboxylic acids. The isomer ratio, as determined by $^1H$ NMR, was 5:1. The mixture was identical with the mixture of acids obtained in A.

**Methyl (2*S*- and -2*R*,2α*R*,5*S*,6*S*)-2-(5,6-Dihydro-5-methoxy-6-methyl-2′*H*-pyran-2′-yl)tetrahydro-2-furancarboxylate (35a and 35b). A. From Glycal 7a by Deprotonation in THF.** A solution of 110 mg (0.76 mmol) of glycal **7a** in 1.5 mL of dry THF at −78 °C under an argon atmosphere was treated with 0.46 mL (0.80 mmol) of a 1.64 M solution of *n*-butyllithium in hexane and, after 5 min, with 94 μL (0.83 mmol) of (±)-tetrahydro-2-furancarbonyl chloride. The resulting mixture, after 10 min at 0 °C, was added to a solution of 1.67 mmol of LDA in 4.3 mL of dry THF at −78 °C under an argon atmosphere, and after 10 minutes at −78 °C, the reaction was quenched with 2.5 mmol of TMSCl (pretreated with dry triethylamine). After 2.5 h at room temperature, treatment of this reaction mixture as described above (A) for the preparation of **34a** and **34b** afforded 135 mg (75%) of a mixture of diastereomeric acids, **35a** and **35b**. This mixture was methylated with diazomethane in ether, and chromatography of the products on silica gel with 50% ether–petroleum ether afforded pure samples of each of the diastereomeric methyl esters.

Fraction I: 25 mg; $R_f$ 0.20 (50% ether–petroleum ether); IR ($CCl_4$) 1740 $cm^{-1}$ (C=O); $^1H$ NMR ($CCl_4$) $\delta$ 1.10 (d, 3 H, $J$ = 6 Hz, $CHCH_3$), 3.26 (s, 3 H, $OCH_3$), 3.65 (s, 3 H, $OCH_3$), 4.35–4.43 (m, 1 H, 2′-H), 5.6–6.0 (m, 2 H, HC=CH); $[\alpha]^{22}_D$ +188° (*c* 0.9, $HCCl_3$).

Anal. Calcd for $C_{12}H_{20}O_5$: C, 60.90; H, 7.87. Found: C, 60.87; H, 7.82.

Fraction II: 101 mg; $R_f$ 0.15 (50% ether–petroleum ether); IR ($CCl_4$) 1760, 1740 $cm^{-1}$ (C=O); $^1H$ NMR ($CCl_4$) $\delta$ 1.06 (d, 3 H, $J$ = 6 Hz, $CHCH_3$), 3.27 (s, 3 H, $OCH_3$), 3.64 (s, 3 H, $OCH_3$), 4.16–4.29 (m, 1 H, 2′-H), 5.79–5.89 (m, 2 H, CH=CH); $[\alpha]^{22}_D$ +199° (*c* 1.1, $HCCl_3$).

Anal. Calcd for $C_{12}H_{20}O_5$: C, 60.90; H, 7.87. Found: C, 61.01; H, 7.83.

The combined yield of the pure methyl esters was 65%. Comparison of the above spectral data with $^1H$ NMR data obtained for the unfractionated acids and esters indicated the two isomers were produced in a ratio of (5:1).

**B. From Glycal 7a by Deprotonation in 23% HMPA–THF.** By the procedure described in A, 65 mg (0.45 mmol) of glycal **7a** with 0.20 mL (0.47 mmol) of 2.38 M *n*-butyllithium in hexane and 55 μL (0.49 mmol) of (±)-tetrahydro-2-furancarbonyl chloride with 0.99 mmol of LDA in 2.6 mL of 23% (by volume) HMPA–THF and 1.45 mmol of TMSCl (pretreated with dry triethylamine) afforded 75 mg (67%) of a mixture of the acids **35a** and **35b** and 69 mg (60%) of the purified methyl esters. The two isomers, which were identical (NMR, IR, TLC) with the products obtained in A, were produced in approximately equimolar quantities.

**Registry No. 1a**, 66737-00-6; **1b**, 65500-01-8; **2a**, 67935-23-3; **2b**, 65500-02-9; **3a**, 72050-09-0; **3b**, 65500-03-0; *dl*-**4a**, 72050-10-3; *dl*-**5a**, 72065-28-2; *dl*-**5b**, 72050-11-4; *dl*-**5d**, 72050-12-5; **6a**, 65904-41-8; **6b**, 72050-13-6; **6c**, 72050-14-7; **6d**, 72059-85-9; **7a**, 65981-48-8; **7b**, 72074-90-9; **8a**, 72050-15-8; **8b**, 72050-16-9; **9a**, 68144-11-6; **10**, 72074-91-0; **11a**, 5788-17-0; **11b**, 22157-27-3; **11c**, *E* isomer, 72050-17-0; **11c**, *Z* isomer, 72050-18-1; **12**, 10556-94-2; **14**, 30725-00-9; **15**, 72050-19-2; **16**, isomer 1, 72050-20-5; **16**, isomer 2, 72050-21-6; **17a**, isomer 1, 72050-22-7; **17a**, isomer 2, 72050-23-8; **17b**, 72050-24-9; **18a**, 6160-67-4; **18b**, 24807-77-0; **19**, 56644-86-1; **20**, 72120-44-6; **21**, 72050-25-0; **22**, 72120-45-7; *dl*-**23a**, 72050-26-1; *dl*-**23b**, 72050-27-2; *dl*-**24a**, 72065-29-3; *dl*-**24b**, 72050-28-3; *dl*-**25a**, 72050-29-4; *dl*-**25b**, 72050-30-7; *dl*-**26a**, 72074-92-1; *dl*-**26b**, 72050-31-8; *dl*-**27a**, 72050-32-9; *dl*-**27b**, 72050-33-0; **28a**, 72050-34-1; **28b**, 72050-35-2; **29a**, 72050-36-3; **29b**, 72050-37-4; **30a**, 72050-38-5; **30a**, methyl ester, 72059-86-0; **30b**, 72050-39-6; **30b**, methyl ester, 72050-40-9; **31**, saturated derivative, 72050-41-0; **31a**, 72050-42-1; **31b**, 72075-47-9; **33**, 72050-43-2; **34a**, 72050-44-3; **34a** acid, 72050-45-4; **34b**, 72050-46-5; **34b** acid, 72050-47-6; **35a**, 72050-48-7; **35a** acid, 72065-30-6; **35b**, 72050-49-8; **35b** acid, 72059-87-1; **36a**, 72050-50-1; **36b**, 72074-93-2; xii, 72050-51-2; propionic anhydride, 123-62-6; propanoyl chloride, 79-03-8; (±)-tetrahydro-2-furancarboxylic acid, 72050-52-3; (±)-tetrahydro-2-furancarbonyl chloride, 72074-94-3; tetrahydrofurfuryl alcohol, 97-99-4; oxalyl chloride, 79-37-8; chloromethyl methyl ether, 107-30-2; *tert*-butyldimethylchlorosilane, 18162-48-6; ethyl benzoylacetate, 94-02-0.