Total Synthesis of Carbohydrates. 2. Regiochemical Control of Nucleophilic Ring Opening of Acylated 2,3-Epoxy Alcohols

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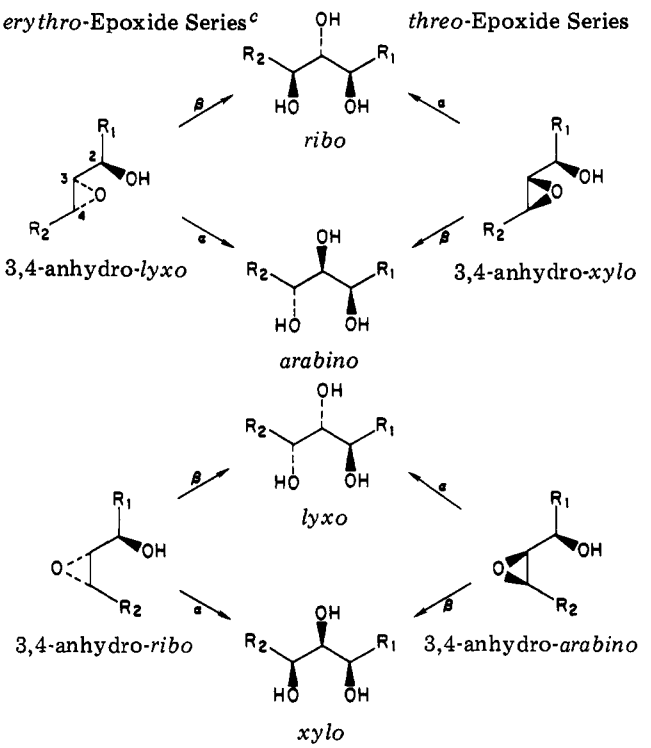
Neighboring-group-assisted α-ring-opening reactions of a series of acylated 2,3-epoxy alcohols are described. The phenylurethane functional group proved to be ideal for this purpose. This group is more reactive than acetate or methyl carbonate neighboring groups, and the resulting triol functionality is liberated in a protected, differentiated form. Problems of competitive attack by nucleophiles at the β position or acyl transfer isomerization of the carbonate after the ring opening were encountered with a number of substrates but could be suppressed or eliminated entirely by judicious choice of reaction conditions. The urethane functional group is also useful for delivery of nitrogen nucleophiles to the epoxide α position under basic reaction conditions.

A renaissance of interest in the chemical synthesis of carbohydrates and polyhydroxylated natural products has occurred in recent years.[3,4] The approaches initiated independently in our laboratory[3a,b] and in the Masamune–Sharpless[3d–f] and Kishi[3g,h] groups depend heavily on the stereo- and regiochemically controlled nucleophilic additions to 2,3-epoxy alcohol derivatives. Scheme I illustrates one strategy by which the four diastereomeric relationships of a 2,3,4-triol system, which occur in natural products with complexity ranging from that of simple carbohydrates to molecules as complex as palytoxin,[5] can be obtained from epoxy alcohol precursors.[6] Thus, it is apparent that each triol diastereomer can be prepared, at least in principle, by either of two nucleophilic ring-opening reactions.

Scheme I[a,b]



[a] Nucleophilic attack at C(3) and C(4) of the oxirane is depicted here as "α" and "β" opening reactions, respectively. [b] The descriptors *ribo*, *arabino*, *lyxo*, and *xylo* are used according to the rules of carbohydrate nomenclature.[7] For the generalized structures shown here, R_1 takes priority over R_2. Note that when the priorities of R_1 and R_2 are reversed, the *arabino* and *lyxo* descriptors also switch. [c] The terms threo and erythro refer to the stereochemical relationships between C(2) and C(3) of the epoxy alcohol substrates.

The success and generality of this approach will be highly dependent on the regiochemical control of the two modes of substitution reactions. In the absence of overriding steric or stereoelectronic factors, the preferred mode of ring opening of epoxyallylic alcohols or their ether derivatives is nucleophilic attack at the β-position, the carbon atom furthest removed from the hydroxyl or alkoxyl functionality.[8] In cases, however, where the epoxy alcohol substrate contains a branched alkyl group or an alkoxyl substituent at the γ-position (i.e., C(5) of the Scheme I epoxides), as would be the case in many problems in

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(3) For recent papers on this subject, see: (a) Roush, W. R.; Brown, R. J. *J. Org. Chem.* **1982**, *47*, 1371. (b) Roush, W. R.; Brown, R. J. *J. Org. Chem.*, following paper in this issue. (c) Roush, W. R.; Harris, D. J.; Lesur, B. M. *Tetrahedron Lett.* **1983**, *24*, 2227. (d) Katsuki, T.; Lee, A. W. M.; Ma, P.; Martin, V. S.; Masamune, S.; Sharpless, K. B.; Tuddenham, D.; Walker, F. J. *J. Org. Chem.* **1982**, *47*, 1373. (e) Ma, P.; Martin, V. S.; Masamune, S.; Sharpless, K. B.; Viti, S. M. *Ibid.* **1982**, *47*, 1378. (f) Lee, A. W. M.; Martin, V. S.; Masamune, S.; Sharpless, K. B.; Walker, F. J. *J. Am. Chem. Soc.* **1982**, *104*, 3515. (g) Minami, N.; Ko, S. S.; Kishi, Y. *Ibid.* **1982**, *104*, 1109. (h) Finan, J. M.; Kishi, Y. *Tetrahedron Lett.* **1982**, *23*, 2719. (i) Danishefsky, S.; Kerwin, J. F., Jr. *J. Org. Chem.* **1982**, *47*, 1597. (j) Danishefsky, S.; Kobayashi, S.; Kerwin, J. F., Jr. *Ibid.* **1982**, *47*, 1981. (k) Danishefsky, S.; Kerwin, J. F., Jr.; Kobayashi, S. *J. Am. Chem. Soc.* **1982**, *104*, 358. (l) Yamaguchi, M.; Mukaiyama, T. *Chem. Lett.* **1981**, 1005. (m) Mukaiyama, T.; Yuki, Y.; Suzuki, K. *Ibid.* **1982**, 1169. (n) Mukaiyama, T.; Yamada, T.; Suzuki, K. *Ibid.* **1983**, 5. (o) Fronza, G.; Fuganti, C.; Grasselli, P.; Pedrocchi-Fantoni, G.; Zirotti, C. *Tetrahedron Lett.* **1982**, *23*, 4143. (p) Kozikowski, A. P.; Ghosh, A. K. *J. Am. Chem. Soc.* **1982**, *104*, 5788. (q) Müller, I.; Jäger, V. *Tetrahedron Lett.* **1982**, *23*, 4777. (r) See also ref 5b.

(4) Reviews of chemical syntheses of carbohydrates: (a) Jones, J. K. N.; Szarek, W. A. In "The Total Synthesis of Natural Products"; ApSimon, J., Ed.; Wiley Interscience: New York, 1973; Vol. I, p 1. (b) Hough, L.; Richardson, A. C. "The Carbohydrates"; Academic Press: New York, 1972; Vol. IA, p 113. (c) Zamojski, A.; Banaszek, A.; Grynkiewicz, G. *Adv. Carbohydr. Chem. Biochem.* **1982**, *40*, 1.

(5) (a) Moore, R. E.; Bartolini, G.; Barchi, J.; Bothner-By, A. A.; Dadok, J.; Ford, J. *J. Am. Chem. Soc.* **1982**, *104*, 3776 and references cited therein. (b) Cha, J. K.; Christ, W. J.; Finan, J. M.; Fujioka, H.; Kishi, Y.; Klein, L. L.; Ko, S. S.; Leder, J.; McWhorter, W. W., Jr.; Pfaff, K.-P.; Yonaga, M.; Uemura, D.; Hirata, Y. *Ibid.* **1982**, *104*, 7369 and references cited therein.

(6) A second set of epoxy alcohols, formally generated by switching R_1 and R_2, can also be used as precursors of the Scheme I triols. (It should be noted, however, that the stereochemical consequences of substitution reactions on this new set is not identical with that depicted in Scheme I.) The selection of one particular substrate over the other alternatives for use in a particular synthesis may be based on the ease of preparation of the substrates and/or on the requirement that an α- or β-ring-opening reaction be performed.

(7) "The Carbohydrates", 2nd ed.; Pigman, W., Horton, D., Herp, A., Eds.; Academic Press: New York, 1970; Vol. IIB, p 809.

(8) Buchanan, J. G.; Sable, H. Z. *Sel. Org. Transform.* **1972**, *2*, 1 and references cited therein.

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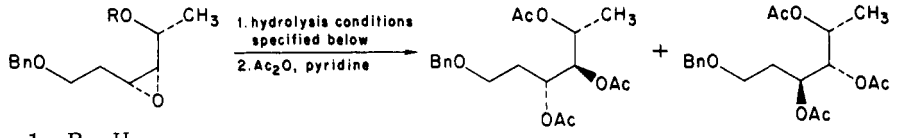
Scheme II



1a, R = H
b, R = Ac
c, R = CO_2CH_3

2 3

entry	compd	hydrolysis conditions	combined yield, %	ratio[a] of 2/3
1	1a	75% Me_2SO, H_2O, H^+, 23 °C	51	2 only
2	1b	4:1 HOAc, H_2O, 100 °C	>95	67:33
3	1c[b,c]	4:1 HOAc, H_2O, 100 °C	71	21:79[d]
4	1c[e,c]	5% $HClO_4$, CH_3CN, 23 °C	95	2 only
5	1c[f,c]	$BF_3 \cdot Et_2O$, Et_2O, 0 °C	60	3 only

[a] Product ratios determined by ^1H NMR spectroscopy. [b] A mixture of 5a, 11, and a third, unidentified compound was obtained from this solvolysis reactions. The presence of 11 in the mixture indicated that acyl transfer occurs under these reaction conditions. The dihydroxy methyl carbonate, which would be produced by attack of H_2O on C(β) of 1c, was not detected. [c] The unseparated crude product mixture was transformed to the corresponding triols (NaOMe, MeOH, 23 °C) prior to acetylation. [d] Ratio determined by product isolation. [e] The crude product contained 11 and the aforementioned unidentified compound. [f] The crude product consisted of a mixture of 5a and 6a.

carbohydrate chemistry, poor selectivity with increased amounts of attack at the α-position would be anticipated.[8,9] Thus, use of β-ring-opening reactions may well be restricted to special cases in which R_2 is a simple alkyl chain.

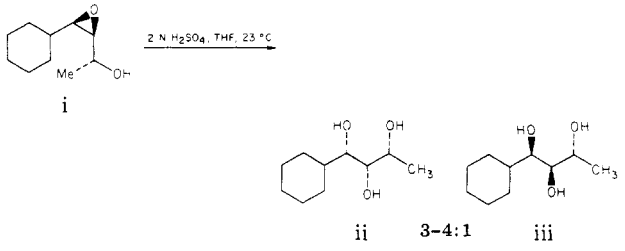
In contrast, we imagined that neighboring-group-assisted α-ring-opening reactions of acylated 2,3-epoxy alcohols might be generally applicable to a wide variety of substrates.[8,10] An examination of the literature revealed that acetates,[11] carbonates,[12] and urethanes[13] were known to participate in the opening of carbohydrate, cyclitol, and steroidal epoxides. Relatively few cases in the acyclic series had been reported, however.[14] In connection with our work[3a,b] on the synthesis of certain 2,6-dideoxyhexoses[15] we have examined the neighboring-group-assisted solvolysis reactions of representative members of the four classes of diastereomeric epoxy alcohols listed in Scheme I. We report herein the results of this study.

Results and Discussion

The first series of substrates examined were the acetate (1b) and methyl carbonate (1c) derivatives of epoxy alcohol 1a. Solvolysis of these compounds under a variety of conditions (Scheme II) led in most cases to a mixture of products which were conveniently analyzed and separated after conversion into the acetates 2 and 3. The structures of these compounds were assigned initially on the basis of the smooth conversion of 1a to 3 (entry 1) by a sequence involving a well-precedented β-ring-opening reaction;[8] these structures were later confirmed by correlation with compounds subsequently described. It was striking, however, that mixtures of α and β ring-opened products were obtained when acetate 1b and carbonate 1c were treated with protic acids. Indeed, β attack was the sole mode of reaction when carbonate 1c was solvolyzed in a mixture of 5% aqueous $HClO_4$ and CH_3CN (1:19) at room temperature. Thus, it was clear that under these conditions the acetate and carbonate neighboring groups were incapable of effectively directing the desired α-opening process, at least in this stereochemical series. Complete control of the neighboring-group-assisted reaction mode was realized only when carbonate 1c was treated with $BF_3 \cdot Et_2O$ under aprotic, nonnucleophilic solvent conditions (entry 5). The sluggishness and poor yield of this reaction, however, prompted us to search for a more nucleophilic neighboring group.[16]

We thus turned to an examination of phenylurethanes 4a and 4b (Scheme III).[17] Here, too, competitive nucleophilic attack at the epoxide β position proved to be a serious problem under strongly acidic and/or nucleophilic conditions. For example, treatment of 4a or 4b with 48% aqueous HBr in acetone effected clean conversion to bromides 7a and 7b, respectively, in very high yield.

(9) (a) Thus, for example, we have observed that solvolysis of the cyclohexyl-substituted epoxy alcohol i afforded a 3–4:1 mixture of β-opened (ii) and α-opened (iii) products: Roush, W. R.; DiMare, M., unpublished results. (b) In cases where alkoxy or hydroxyl substituents occur at C(2) and C(5), the inductive effects which favor β attack in simple 2,3-epoxy alcohols will be cancelled, and the product distribution will be governed largely by steric effects.



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(10) (a) Capon, B. *Q. Rev., Chem. Soc.* **1964**, *18*, 45. (b) Goodman, L. *Adv. Carbohydr. Chem.* **1967**, *22*, 109.

(11) (a) Buchanan, J. G. *J. Chem. Soc.* **1958**, 995. (b) Buchanan, J. G.; Fletcher, R. *Ibid.* **1965**, 6316. (c) Buchanan, J. C.; Fletcher, R. *J. Chem. Soc. C* **1966**, 1926. (d) Hasegawa, A.; Sable, H. Z. *J. Org. Chem.* **1966**, *31*, 4149, 4154, 4161. (e) Coxon, J. M.; Hartshorn, M. P.; Kirk, D. N. *Tetrahedron* **1964**, *20*, 2547. (f) Buchanan, J. G.; Edgar, A. R. *J. Chem. Soc., Chem. Commun.* **1967**, 29. (g) Rastetter, W. H.; Adams, J.; Bordner, J. *Tetrahedron Lett.* **1982**, *23*, 1319. (h) Mubarak, A.; Fraser-Reid, B. *J. Org. Chem.* **1982**, *47*, 4265.

(12) Julia, S.; Fürer, B. *C. R. Hebd. Seances Acad. Sci.* **1963**, *257*, 710.

(13) (a) Gross, P. H.; Brendel, K.; Zimmerman, H. K. *Justus Liebigs Ann. Chem.* **1964**, *680*, 159. (b) Noorzad, H. M.; Gross, P. H. *Carbohydr. Res.* **1973**, *31*, 229. (c) Kusumoto, S.; Imaoka, S.; Kambayashi, Y.; Shiba, T. *Tetrahedron Lett.* **1982**, *23*, 2961.

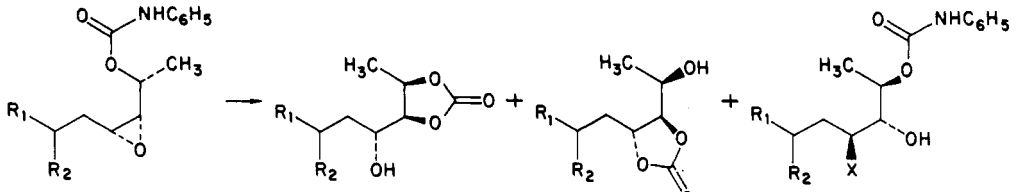
(14) (a) Buchanan, J. G.; Edgar, A. R. *Carbohydr. Res.* **1969**, *10*, 295. (b) Additional cases were reported after our work was initiated: Corey, E. J.; Hopkins, P. B.; Munroe, J. E.; Marfat, A.; Hashimoto, S. *J. Am. Chem. Soc.* **1980**, *102*, 7986. See also ref 3d,g.

(15) (a) Williams, N. R.; Wander, J. D. In "The Carbohydrates"; Pigman, W., Horton, D., Eds.; Academic Press: New York, 1980; Vol. IB, p 761. (b) Hanessian, S.; Haskell, T. H. *Ibid.*, Vol. IIA, p 139. (c) Chmielewski, M. *Tetrahedron* **1979**, *35*, 2067.

(16) Kishi[3g] has also noted that methyl carbonates react sluggishly under acidic conditions. Whereas our solution to this problem involved use of phenylurethanes, Kishi achieved satisfactory results by using benzyl carbonates as the neighboring group.

(17) Urethanes are well-known to be outstanding neighboring groups. See ref 10 and the following recent papers: (a) Georges, M.; Fraser-Reid, B. *Tetrahedron Lett.* **1981**, *22*, 4635. (b) Pauls, H. W.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1980**, *102*, 3956. (c) For recent examples of urethane-assisted epoxide solvolyses, see ref 14b.

Scheme III



4a, R_1 = H; R_2 = $OCH_2C_6H_5$
b, R_1,R_2 = CH_2

5a,b

6a,b

7a,b

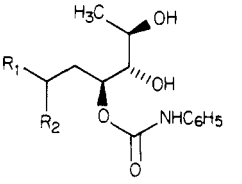
entry	compd	conditions	yield,[a] % 5/6[b,c]	yield,[a] % 7[d]
1	4a	HBr, acetone, 23 °C		98 (X = Br)
2	4b	HBr, acetone, 23 °C		94 (X = Br)
3	4a	5% $HClO_4$, CH_3CN, 23 °C	61 (5:1)	29 (X = OH)
4	4b	5% $HClO_4$, CH_3CN, 23 °C	86 (6:1)	9 (X = OH)
5	4a	4:1 HOAc, H_2O, 100 °C	90 (1:6)	trace (X = OH)
6	4b	4:1 HOAc, H_2O, 100 °C	98 (3:7)	
7[e]	4a	BF_3·Et_2O, CH_2Cl_2, 23 °C	71 (1:4)	
8[e]	4b	BF_3·Et_2O, CH_2Cl_2, 23 °C	95 (1:5)	
9[e]	4a	BF_3·Et_2O, Et_2O, 0 °C	80 (10:1)	
10[e]	4b	BF_3·Et_2O, Et_2O, −20 °C	89 (>20:1)	

[a] The yields of product isolated by chromatography; the yields listed under the 5/6 heading are the combined yields of acyl transfer isomers 5 and **6**. [b] The values in parentheses refer to the ratio of carbonates 5 and **6**, respectively. [c] Carbonates 5a and **6a** were correlated with triacetate 2 by transesterification (NaOMe, MeOH) and acylation (Ac_2O, pyridine). The correlation of **5b** and **6b** with 2 is outlined in Scheme VIII. [d] Diol **7a** was correlated with triacetate 3 by reduction ($LiAlH_4$, THF, reflux, 63%) and peracetylation (Ac_2O, pyridine, >95% yield) and with triol 28 as outlined in Scheme IX. [e] All Lewis acid incued epoxide openings were worked up with a mild acid treatment (two-phase hydrolysis using 0.5 N H_2SO_4) to hydrolyze the intermediate iminocarbonate.

Carbonates **5** and **6** were not detected under these conditions (entries 1, 2). Moreover, significant quantities (9–29%) of diols **7a,b**, which probably resulted from β attack by water, were observed when **4a** and **4b** were treated with aqueous $HClO_4$ in CH_3CN (entries 3, 4). This pathway was, however, essentially eliminated when the solvolysis was conducted in aqueous acetic acid at reflux (entries 5, 6).

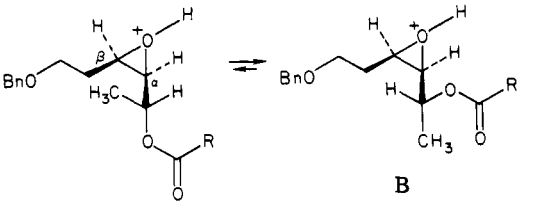
Although a workable solution to the problem of α vs. β attack had been found, we were concerned about the substantial amount of acyl transfer, **5** → **6**, which occurred when urethanes **4** were subjected to the conditions specified in entries 5 and 6 of Scheme III. One can envisage many reaction sequences wherein a neighboring-group-assisted α-ring-opening reaction might be performed not only to control the regioselectivity of an epoxide hydrolysis but also to differentiate the resulting hydroxyl functionalities. It was therefore desirable to find conditions which suppressed this potentially deleterious side reaction. Although significant acyl transfer also occurred when **4a** and **4b** were treated with BF_3·Et_2O in CH_2Cl_2 (entries 7, 8), this process was effectively suppressed by performing the epoxide ring-opening reaction with BF_3·Et_2O *in diethyl ether* (entries 9, 10).

The data summarized in Schemes II and III confirmed our expectation that phenylurethanes would be more reactive than acetate or carbonate groups in neighboring-group-assisted reactions. We were most surprised, however, that the phenylurethane failed to compete effectively with external nucleophiles under strongly acidic, protic conditions (see Scheme III, entries 1–5). That **7a,b** (X = OH) probably arise by external attack by water on **4a,b** and not by a neighboring-group-assisted pathway (a process that is discussed in more detail subsequently) follows from consideration of the fate of the six-membered iminium carbonate species that would be produced if the urethane group added intramolecularly to the epoxide β position. First of all, it would be expected that this intermediate should hydrolyze to a more stable carbonate structure (**11** or one of its acyl-transfer isomers in the case of **4a**; see Scheme IV) under the conditions specified in entries 3–5 of Scheme III. Such species, however, were not detected in the reaction mixtures. Second, if the iminium carbonate intermediate were to follow a less likely pathway and hydrolyze to a dihydroxy urethane product, a mixture of **7** (X = OH) and the acyl-transfer isomer **7′** should have been produced. The latter compound, however, was not observed among the reaction products.



7′

It seems most probable, therefore, that **7a,b** are produced by attack by water at C(β) of **4a,b**. By analogy, we believe that triacetate **3** (Scheme II) is also produced from epoxides **1b** and **1c** by external β attack by water and not by neighboring-group-assisted pathways. Examination of molecular models of these systems reveals that unfavorable steric interactions develop between the γ-methylene and the methyl group as the acyloxy carbonyl adopts the necessary orientation (A) for backside displacement at

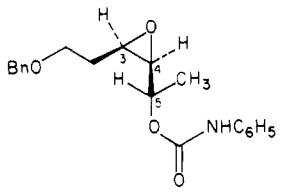


A B

1b, R = CH_3
c, R = OCH_3
4a, R = NHC_6H_5

C(α). Thus, consideration of nonbonded interactions leads one to conclude that protonated or hydrogen bond activated forms of **1b,c** and **4a,b** will exist predominantly in conformation B wherein the neighboring group occupies an unreactive orientation.[18] Both conformations, however, are susceptible to external nucleophilic attack at the β-position. To the extent that the two modes of reaction (α internal and β external) may have different pH rate profiles, it is not surprising that the product distribution data display a pH dependence, with greater amounts of β-opened products being obtained at lower pH.[19]

We suspected that these problems might be most pronounced in the epoxy alcohol series represented by **1** and **4**. Examination of molecular models of urethanes **8–10**,



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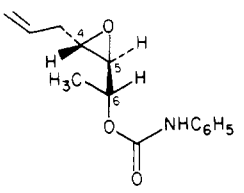

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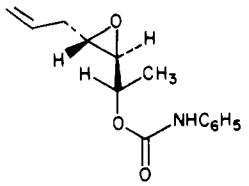


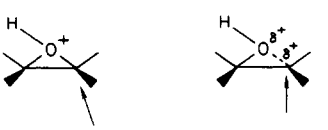
(−)-**10**

representatives of the three remaining diastereomeric epoxy alcohol series, leads one to conclude that each system can easily adopt a conformation in which the acyloxy group is properly positioned for attack at C(α).[18] Indeed, this reactive conformation corresponds to the most stable one for erythro epoxide derivatives **8** and **10**. For **9** on the other hand, the reactive conformation is destabilized by an interaction between the methyl group and C(4)–H; this interaction, however, is clearly less severe than that present in conformation A of urethanes **4**. Thus, we suspected that the solvolytic ring-opening reactions of each of these compounds would proceed with greater regioselectivity than the problematic cases summarized in Schemes II and III. This hypothesis indeed proved to be correct (see Scheme IV).

Significant levels of β-ring-opening products were obtained from **8–10** only when the solvolysis reactions were performed with aqueous HBr in acetone (entries 1, 5, and 9). It is interesting to note the ratio of products resulting from the two modes of attack (intramolecular α vs. external β) parallels the trend which one would predict on the basis of the conformational preferences of the epoxy alcohol substrates discussed above (**4** > **9** > **8** ≈ **10**).[18] All other sets of reaction conditions, with one important qualification, effected smooth conversion of the substrate to the expected α-ring-opened carbonate derivatives (**11**, **13**, and **15**, respectively), without detectable quantities (<2%) of β-opened diols **12**, **14**, or **17** (X = OH) being observed.

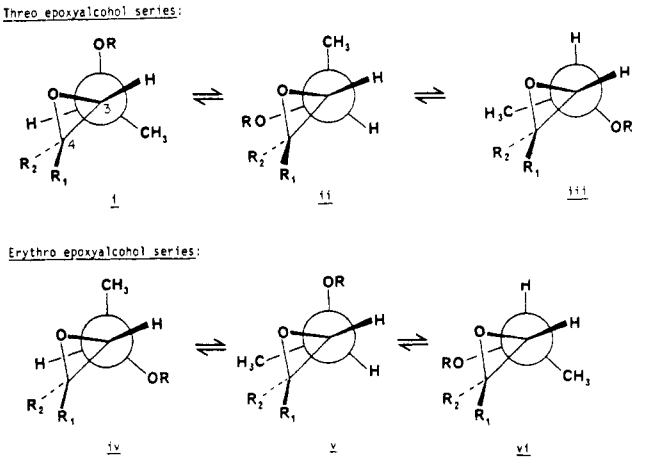
With erythro epoxide derivative **10**, however, small quantities of δ-carbonate **16** were isolated under a variety of conditions; similar results were obtained with the isomeric *erythro*-urethane **18** (Scheme V). In both cases we believe that the minor carbonate **16** derives *not* from β attack by water followed by transesterification but rather from intramolecular attack by the neighboring group at the β-position. This interpretation is necessitated by the observations that **16** is obtained under anhydrous conditions (BF_3·Et_2O, CH_2Cl_2 or Et_2O) as well as conditions under which protic impurities such as water would be rapidly consumed (Et_2AlCl, Scheme V). Moreover, δ-carbonate **16** was not observed under reaction conditions where the γ-carbonate isomer **13** might have, at least in principle, isomerized to **16**.[20] Thus, it seems unlikely that **16** derives from transesterification of the unobserved **17** (X = OH) under the reaction conditions specified in Schemes IV and V.

The alternative explanation that **16** derives from a kinetically controlled attack of the acyloxy group at the β-position is precedented by an example in the steroid literature.[11e,21] It is probable that these solvolysis reactions proceed with substantial carbonium ion character at the carbon atom undergoing substitution.[8] Under these circumstances the preferred angle of nucleophile approach need not be coincident with the C–O bond axis of the epoxide substrate (see below), a trajectory that appears to be strained for **10** and **18**. Rather, nucleophilic attack



might occur along an approach vector which is nearly

(18) The lowest energy conformation of a secondary epoxy allylic alcohol system should be the one in which the smallest substituent (i.e., H) on the carbinol carbon atom bisects or eclipses the plane occupied by the epoxide ring system. In this manner, nonbonded interactions between the substituents on C(2) and C(4) are minimized (refer to numbering system of Scheme I). Although conformation i is the most stable one for



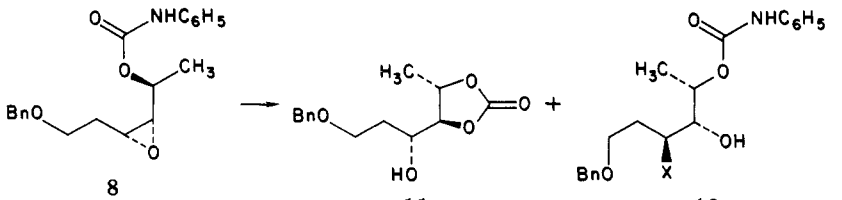
threo epoxy alcohols, neighboring-group-assisted solvolysis reactions must proceed via conformation iii, the least stable conformation. For erythro epoxy alcohols, however, neighboring-group-assisted solvolysis reactions will proceed via conformation iv, the lowest energy conformation in this series. These equilibria will favor i and iv to a greater extent when the epoxy alcohol derives from a *Z* olefin ($R_2 \neq H$) than when the original olefin had an *E* configuration. This argument is supported by our observation that $J_{2,3}$ values for **1**, **4**, and **8** (*Z* olefin derived epoxides) fall in the range of 8.3–8.8 Hz, whereas $J_{2,3}$ values for **9**, **10**, and **18** (*E* olefin derived epoxides) fall in the range of 4.6–5.3 Hz.

(19) One expects carbonium ion character to develop more easily at the β-carbon atom as a consequence of the alkoxyl's inductive effect which destabilizes carbonium ion character at the α-position (see ref 8). Thus, acid catalysis should accelerate substitution reactions at the β-position more than at the α-position.

(20) In fact, all attempts to purify **16** by silica gel chromatography resulted in the equilibration of **16** with **13** and the second γ-carbonate acyl transfer isomer.

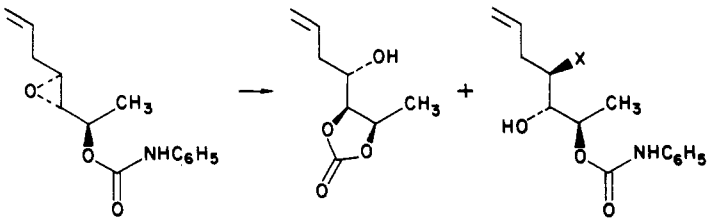
(21) Formation of six-membered rings is also observed in the cyclizations of epoxy nitrile anions as long as closure to a five-membered ring is precluded on steric grounds: Stork, G.; Cohen, J. F. *J. Am. Chem. Soc.* **1974**, *96*, 5270. Stork, G.; Cama, L. D.; Coulson, D. R. *Ibid.* **1974**, *96*, 5268.

Scheme IV



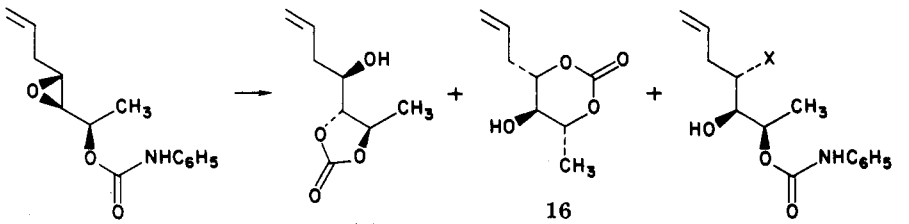
8 11 12

entry	conditions	yield, % 11[a]	12
1	HBr, acetone, 23 °C	48	36 (X = Br)
2	5% $HClO_4$, CH_3CN, 23 °C	87	
3	HOAc, H_2O, 4:1, 100 °C	94 (1.6:1)[b]	
4	$BF_3 \cdot Et_2O$, Et_2O, −20 °C	73	



9 13 14

entry	conditions	yield, % 13	14
5	HBr, acetone, 23 °C	11	67 (X = Br)
6	5% $HClO_4$, CH_3CN, 23 °C	74	
7	HOAc, H_2O, 4:1, 100 °C	74	
8	$BF_3 \cdot Et_2O$, Et_2O, −20 °C	82	



(+)-10 15 16 17

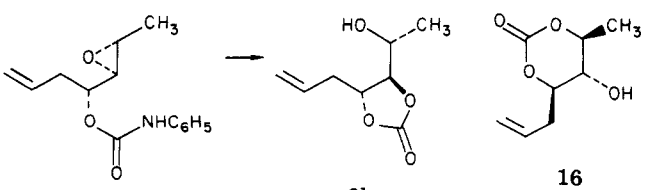
entry	conditions	yield, % 15	17
9	HBr, acetone, 23 °C	41	41 (X = Br)
10	5% $HClO_4$, CH_3CN, 23 °C	85[c]	
11	HOAc, H_2O, 4:1, 100 °C	95[c]	
12	$BF_3 \cdot Et_2O$, Et_2O, 0 °C	>95[d]	
13	Et_2AlCl, Et_2O, 0 °C	95	
14	$SnCl_4$, Et_2O, 0 °C	only	

[a] Carbonate 11 was correlated with triacetate 3 by transesterification (NaOMe, MeOH) and acetylation (Ac_2O, pyridine). [b] A 1.6:1 mixture of 11 and its 3,4-acyl transfer isomer was obtained. [c] A 30:1 mixture of 15 and 16 was obtained from this experiment (NMR analysis). [d] A 16:1 ratio of 15 and 16 was obtained (NMR analysis).

perpendicular to the oxirane C–C bond axis, coincident with the developing p orbital at the electrophilic carbon atom. Examination of molecular models of **10** or **18** reveals that the carbonyl oxygen atom is not precluded from approaching the epoxide β-carbon atom in this manner.

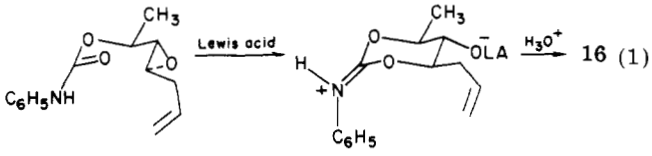
One can reasonably ask, however, why such intramolecular β-ring-opening processes were not observed in the cases of **4**, **8**, or **9**. For **10** it is readily apparent that as the β-ring-opening reaction proceeds the methyl, allyl, and Lewis acid coordinated alkoxyl groups move into equatorial positions about the intermediate iminium carbonate ring system (eq 1). For **4**, **8**, and **9**, on the other hand, one (**8**, **9**) or both (**4**) of the alkyl groups must adopt axial positions

Scheme V



18 6b 16

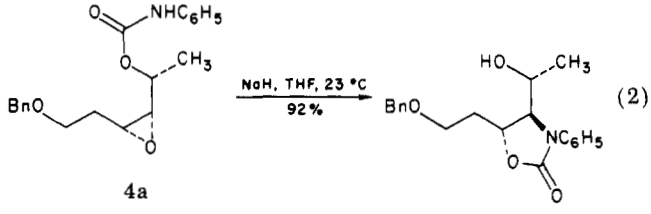
entry	conditions	% yield	6b/16 ratio
1	$BF_3 \cdot Et_2O$, CH_2Cl_2, 23 °C	>95	4:1
2	$BF_3 \cdot Et_2O$, Et_2O, 0 °C	88	10:1
3	Et_2AlCl, Et_2O, −20 °C	95	60:1



10

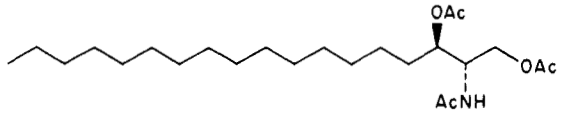
in the initially formed iminium carbonate product. The transition states must reflect the nonbonded interactions which these axial substitution experience along the reaction coordinant. Evidently these processes are sufficiently energetic that they are not observed in direct competition with the dominant α-ring-opening pathway.[22]

In summary, the neighboring-group-assisted α-ring-opening reactions of acylated 2,3-epoxy alcohol derivatives are applicable to a range of secondary epoxy alcohols which are of interest for use in syntheses of polyhydroxylated natural products (Scheme I). The phenylurethane functional group is ideal for these purposes not only because of its reactivity but also because the resulting triol functionality is liberated in a protected, differentiated form. The problems of competitive attack by a nucleophile at the β-position or acyl transfer after the ring opening can be suppressed or eliminated entirely by judicious choice of reaction conditions. It is also of interest that the urethane functional group is useful for delivery of nitrogen nucleophiles to the epoxide α-position.[23] For example, treatment of **4a** with NaH in THF at room temperature[24] afforded urethane **19** in 92% yield (eq 2). We have ap-



4a

19

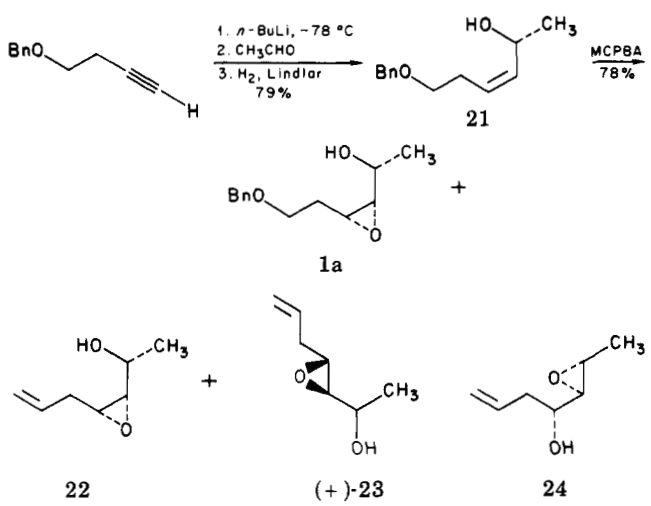


20

plied this reaction to the synthesis of dihydrosphingosine triacetate (**20**).[25] This and other applications of this process will be reported in due course.[26]

Synthesis of Epoxy Alcohol Substrates. All urethanes, acetates, and carbonates were prepared from the corresponding epoxy alcohols by using standard acylation procedures (see Experimental Section). Epoxy alcohol **1a** was synthesized as outlined in Scheme VI. Epoxy alcohols **22** (precursor of **4b**), (+)-**23** (precursor of **10**), and **24** (precursor of **18**) were synthesized as described in our preliminary report[3a] or in the accompanying paper.[3b] Epoxy alcohols **25** (precursor of **8**) and **26** (precursor of **9**) were prepared from **1a** and (−)-**23**, respectively, by application of the Mitsunobu inversion reaction (Scheme VII).[27] It is also pertinent to note that epoxide rearrangement[28] of **25** or **26** was not observed during the

Scheme VI

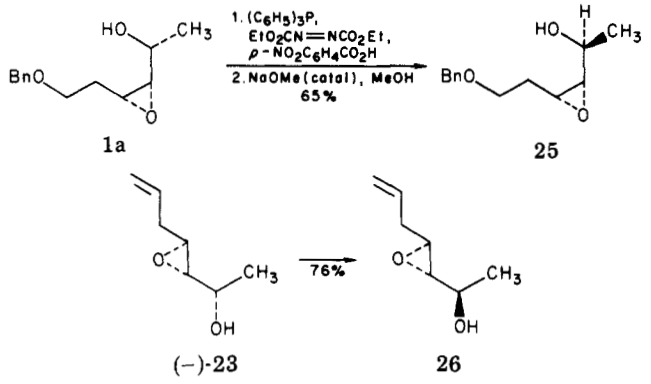


21

1a

22 (+)-23 24

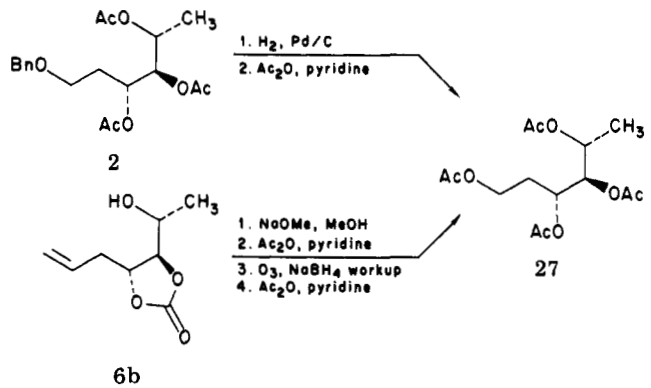
Scheme VII



1a 25

(−)-23 26

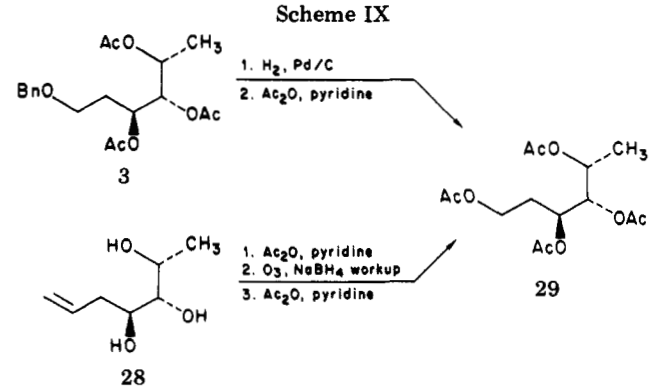
Scheme VIII



2 27

6b

Scheme IX



3 29

28

(22) We thank Dr. D. Kerkman of Abbott Laboratories for helpful discussions regarding the formation of **16**.

(23) Farrissey, W. J., Jr.; Nashu, A. M. *J. Heterocycl. Chem.* **1970**, *7*, 331.

(24) We mistakenly reported in our original paper[3a] that this reaction was performed in THF at reflux.

(25) Roush, W. R.; Adam, M. A., unpublished research.

(26) Kishi[3g] has recently reported additional examples of the intramolecular α addition of nitrogen nucleophiles to epoxides in 2,3-epoxyurethane systems.

conditions used to transesterify the intermediate *p*-nitrobenzoyl esters.

Stereochemical Correlations. Triacetate **2** was correlated with carbonates **5b** and **6b** as outlined in Scheme VIII. The stereochemistry of **5b**/**6b** is known unambiguously by virtue of the conversion of these compounds to 2,6-dideoxy-*arabino*-hexose.[3a] A similar sequence (Scheme IX) was used to correlate triacetate **3** with triol **28**, which was prepared by solvolysis of **22** with 20% aqueous $HClO_4$ in THF (65% yield); triol **28** has been transformed into 2,6-dideoxy-*xylo*-hexose, as described in the accompanying paper.[3b] Methanolysis (NaOMe, MeOH) of **13** afforded the corresponding *ribo* triol which is an intermediate in the synthesis of 2,6-dideoxy-*ribo*-hexose (digitoxose).[3a] Carbonate **15** has also been correlated with a sugar, 2,6-dideoxy-*lyxo*-hexose, as described in the following paper.[3b]

Experimental Section

^1H NMR spectra were measured at 250 and 270 MHz on Bruker 250 and 270 instruments. Chemical shifts are reported in δ units relative to internal Me_4Si. ^{13}C NMR spectra were measured at 62.8 MHz on a Bruker 250 instrument; carbon resonances are reported in δ_c units calibrated against the 77.0-ppm line of $CDCl_3$. Infrared spectra were measured on a Perkin-Elmer Model 283B infrared spectrophotometer and were calibrated with the 1601-cm^{-1} absorption of polystyrene. Mass spectra were measured at 70 eV on a Varian MAT 44 instrument. High-resolution mass spectra were provided by the Facility supported by NIH Grant RR00317 (principal investigator, Professor K. Biemann) from the Biotechnology Resources Branch, Division of Research Resources, and were obtained on a CEC 21-110B high-resolution mass spectrometer equipped with a PDP-1145-based computer system to process data recorded on photographic plates. Melting points were recorded on a Fisher-Johns hot-state melting point apparatus and are uncorrected. Optical rotations were measured on a Perkin-Elmer 144 polarimeter by using a 1-cm^3 capacity quartz cell (10-cm path length). Elemental analyses were performed by Robertson Laboratories, Florham Park, NJ.

All reactions were conducted in oven-dried (120 °C) or flame-dried glassware under atmospheres of dry argon or nitrogen. All solvents were purified before use: ether, THF, and DME were distilled from sodium benzophenone ketyl; CH_2Cl_2 and Me_2SO were distilled from CaH_2; toluene was distilled from sodium metal. Preparative thin-layer chromatography (TLC) was performed by using 20 × 20 cm plates coated with 0.5- and 2-mm thicknesses of silica gel containing PF 254 indicator (Analtech). Unless indicated otherwise, compounds were eluted from the adsorbents with ether or ethyl acetate. Column chromatography was performed by using activity I Woelm silica gel. Flash chromatography was performed as described by Still.[29] All chromatography solvents were distilled prior to use.

(*Z*)-1-(Benzyloxy)hex-3-en-5-ol (21). To a solution of 5.0 g (30 mmol) of 1-(benzyloxy)but-3-yne[30] in 200 mL of THF at −78 °C (dry ice/acetone) was added 22 mL (35 mmol) of 1.6 M *n*-BuLi in hexane. The mixture was stirred for 30 min, and then 4 mL (71 mmol) of acetaldehyde was added via syringe. The reaction mixture was stirred at −78 °C for 1 h and then quenched with 10 mL of methanol. The mixture was warmed to room temperature, 30 mL of 2 N HCl was added, and the mixture was stirred for 10 min. The layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (3×). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated in vacuo to give the crude product. This material was flash chromatographed on a 50 mm × 150 mm column of silica gel with 3:1 hexane–ether as the eluent to afford 352 mg (7%) of recovered acetylene and 5.24 g (82%, R_f 0.44, 1:1 hexane–ether) of the product. A portion was further purified by Kugelrohr distillation (150 °C, 2.5 mm): ^1H NMR ($CDCl_3$) δ 7.3 (s, 5 H, aromatic), 4.53 (s, 2 H, benzylic CH_2), 4.49 (br quintet, 1 H, H_5), 3.55 (t, J = 7 Hz, 2 H, H_1), 2.51 (td, J = 2.2, 6.8 Hz, 2 H, H_2), 2.0 (br, 1 H, OH), 1.40 (d, J = 6.6 Hz, 3 H, H_6); ^{13}C NMR ($CDCl_3$) δ 134.0, 124.4, 123.7, 79.6, 76.9, 74.6, 64.3, 44.2, 20.5, 16.1; IR (neat) 3100–3700 (br OH), 2240, 1080, 690 cm^{-1}; mass spectrum, m/e 204 (parent ion). Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44: H, 7.90. Found: C, 76.65; H, 8.15.

A suspension of 2.20 g (10.8 mmol) of the above propargylic alcohol and 260 mg of Lindlar catalyst in 30 mL of reagent grade CH_3OH was stirred under an atmosphere of H_2 for 19 h at room temperature. The reaction mixture was then filtered through Celite and concentrated in vacuo to give 2.20 g of crude **21**. This material was purified by bulb-to-bulb distillation (110 °C, 0.8 mm) to give 2.12 g (96%) of pure **21**: ^1H NMR ($CDCl_3$) δ 7.3 (s, 5 H, aromatic), 5.35–5.6 (m, 2 H, olefin), 4.54 (br quintet, 1 H, H_5), 4.46 (s, 2 H, benzylic), 3.35–3.5 (m, 2 H, H_1), 3.2 (br, 1 H, OH), 2.15–2.6 (m, 2 H, H_2), 1.19 (d, J = 6.4 Hz, 3 H, H_6); ^{13}C NMR ($CDCl_3$) δ_c 138.2, 136.7, 128.3, 127.6, 126.7, 73.0, 69.4, 63.1, 28.3, 23.3; IR (neat) 3100–3700 (br, OH), 3020, 1100, 690 cm^{-1}; mass spectrum, m/e 188 ($M^+ - H_2O$). Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.83; H, 9.00.

***lyxo*-1-(Benzyloxy)-3,4-epoxyhexan-5-ol (1a).** A solution of 821 mg (3.99 mmol) of **21** in 30 mL of CH_2Cl_2 was cooled to 0 °C and treated with 1.1 g of commercial 85% *m*-chloroperbenzoic acid. After 3 h a white precipitate had formed, and all starting material had been consumed. The precipitate was removed by filtration, and the filtrate was washed with saturated $NaHSO_3$, saturated $NaHCO_3$ (2×), and then saturated NaCl. The combined aqueous layers were extracted with CH_2Cl_2 (2×). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated in vacuo to afford 1.04 g of crude product. This material was flash chromatographed over 160 g of silica gel with 3:1 hexane–ether as the eluant to yield 47 mg (5%) of *erythro*-epoxide **25** (R_f 0.27 1:1 hexane–ether; identical in all respects with the sample subsequently described) and 694 mg (78%) of *threo*-epoxide **1a**: R_f 0.22; ^1H NMR ($CDCl_3$) δ 7.3 (s, 5 H, aromatic), 4.52, 4.50 (AB, J_{AB} = 12.3 Hz, benzylic), 3.55–3.7 (m, 3 H, H_1 and H_5), 3.17 (dt, J = 4.4, 6.8 Hz, 1 H, H_3), 2.9 (dd, J = 4.4, 7.9 Hz, 1 H, H_4), 2.5 (br, 1 H, OH), 1.7–2.0 (m, 2 H, H_2), 1.21 (d, J = 6.4 Hz, 3 H, H_6); ^{13}C NMR ($CDCl_3$) δ_c 138.3, 128.4, 127.6, 73.1, 67.4, 66.3, 61.4, 55.3, 28.9, 19.2; IR (neat) 3100–3700 (br, OH), 1260, 1100, 690 cm^{-1}; mass spectrum, m/e 159 ($M^+ - C_2H_7O_2$). Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.25, H, 8.16. Found: C, 70.45; H, 7.91.

***lyxo*-1-(Benzyloxy)-3,4-epoxyhex-5-yl Acetate (1b).** A solution of 36 mg (0.16 mmol) of **1a** in 0.1 mL of pyridine was treated with 1 mL of acetic anhydride and allowed to stand overnight at room temperature. The reaction was quenched by the addition of 2 mL of H_2O and 15 mL of ether. The layers were separated, and the organic phase was washed with 5 mL of 3 N HCl and then saturated $NaHCO_3$ (2×). The ethereal extracts were dried (Na_2SO_4), filtered, and concentrated to afford 45 mg of crude product. This material was combined with 71 mg of additional product obtained in a separate experiment and chromatographed on a 0.5-mm preparative silica gel plate with 1:1 hexane–ether as the eluent to yield a total of 95 mg of the acetate: R_f 0.52; ^1H NMR ($CDCl_3$) δ 7.25 (s, 5 H, aromatic), 4.66 (qd, J = 6.6, 8.8 Hz, 1 H, H_5), 4.44 (s, 2 H, benzylic), 3.56 (dd, J = 5, 7 Hz, 2 H, H_1), 3.11 (dt, J = 4.5, 7.2 Hz, 1 H, H_3), 2.96 (dd, J = 4.5, 8.8 Hz, 1 H, H_4), 1.99 (s, 3 H, acetate), 1.65–1.96 (m, 2 H, H_2), 1.19 (d, J = 6.6 Hz, 3 H, H_6); IR (neat) 2980, 2860, 1735, 1450, 1370, 1240, 805, 735, 690 cm^{-1}; mass spectrum, m/e 264 (parent ion).

Methyl *lyxo*-1-(Benzyloxy)-3,4-epoxyhex-5-yl Carbonate (1c). A 0 °C solution of 222 mg (1 mmol) of **1a** in 7 mL of CH_2Cl_2 and 1 mL of pyridine was treated with 0.2 mL of methyl chloroformate. The cooling bath was removed after 2.5 h, and the reaction was continued at 23 °C for 1 h. The reaction was quenched by the addition of 20 mL of H_2O. The layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (3×). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated in vacuo to afford 298 mg of yellow oil. This material was bulb-to-bulb distilled (183 °C, 3.4 mm) to yield pure **1c**: 261

(27) (a) Kurihara, T.; Nakajima, Y.; Mitsunobu, O. *Tetrahedron Lett.* **1976**, 2455. (b) Mitsunobu, O.; Kimura, J.; Iiizumi, K.; Yanagida, N. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 510. (c) Mitsunobu, O.; Eguchi, M. *Ibid.* **1971**, *44*, 3427. (d) For an application of this procedure to an epoxy allylic alcohol, see: Hungerbühler, E.; Seebach, D.; Wasmuth, D. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 958.

(28) (a) Payne, G. B. *J. Org. Chem.* **1962**, *27*, 3819. (b) Angyal, S. J.; Gilham, P. T. *J. Chem. Soc.* **1957**, 3691. (c) See also ref 8.

(29) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

(30) Johnson, W. S.; Wiedhaup, K.; Brady, S. F.; Olsen, G. L. *J. Am. Chem. Soc.* **1974**, *96*, 3979.

mg (93%); ^{1}H NMR ($CDCl_3$) δ 7.3 (s, 5 H, aromatic), 4.60 (m, J = 6.5, 8.5 Hz, 1 H, H_5), 4.5 (s, 2 H, benzylic), 3.76 (s, 3 H, OCH_3), 3.63 (dd, J = 5.1, 7.1 Hz, 2 H, H_1), 3.18 (dt, J = 4.4, 7.2 Hz, 1 H, H_3), 3.04 (dd, J = 4.4, 8.6 Hz, 1 H, H_4), 1.7–2.0 (m, 2 H, H_2), 1.31 (d, J = 6.5 Hz, 3 H, H_6); ^{13}C NMR ($CDCl_3$) δ_c 155.2, 138.4, 128.4, 127.7, 74.3, 73.2, 67.3, 58.1, 54.6, 54.3, 29.0, 16.8; IR (neat) 3030, 2860, 1745, 1435, 1250, 1100 cm^{-1}; mass spectrum, m/e 280 (parent ion).

***ribo*-1-(Benzyloxy)-3,4-epoxyhexan-5-ol (25).** To a solution of 582 mg (2.62 mmol) of **1a** and 816 mg (3.11 mmol) of triphenylphosphine in 15 mL of toluene was added 525 mg (3.14 mmol) of *p*-nitrobenzoic acid (PNBA). Diethyl azodicarboxylate (0.5 mL, 550 mg, 3.1 mmol) was then added by syringe. As the PNBA dissolved, a new precipitate separated from the yellow solution. The reaction mixture was stirred at room temperature for 45 min, and then all volatile components were removed in vacuo to give 2.87 g of a yellow oil. This material was dissolved in 1:1 ether–hexane and filtered through 13 g of silica gel. The resulting crude *p*-nitrobenzoate (1.37 g) was chromatographed by using the flash procedure[29] (180 g of silica gel, 4:1 hexane–ether) to afford pure ester: 763 mg (78%); R_f 0.73 (1:1 hexane–ether); ^{1}H NMR ($CDCl_3$) δ 8.1–8.3 (m, 4 H, *p*-nitrobenzoate), 7.3 (s, 5 H, aromatic), 4.99 (qd, J = 6.4, 8.2 Hz, 1 H, H_5), 4.47, 4.44 (AB, J_{AB} = 12 Hz, 2 H, benzylic), 3.62 (t, J = 6 Hz, 2 H, H_1), 3.24 (dt, J = 4, 8.7 Hz, 1 H, H_3), 3.12 (dd, J = 3.9, 8.2 Hz, 1 H, H_4), 1.8–2.1 (m, 2 H, H_2), 1.56 (d, J = 6.4 Hz, 3 H, H_6); IR (neat) 2860, 1728, 1610, 1525, 1350, 1270, 1100 cm^{-1}; mass spectrum, m/e 371 (parent ion).

The *p*-nitrobenzoate (757 mg, 2.04 mmol) prepared above was dissolved in 5 mL of 0.2 N NaOMe in MeOH. A precipitate formed after a few minutes, and the reaction mixture was worked up after a total of 25 min. The suspension was diluted with methanol until a clear solution was obtained. This was then passed through 10 cm^3 of Dowex 50W-X8 H^+ ion-exchange resin which was pretreated with methanol. The solvent was removed in vacuo to afford 910 mg of crude product, which was purified by flash chromatography (180 g of silica gel, 2:1 hexane–ether). In this manner 349 mg (95%) of methyl *p*-nitrobenzoate (R_f 0.72) and 377 mg (83%) of **25** (R_f 0.27, 1:1 hexane–ether) were obtained. A 562-mg sample was distilled (Kugelrohr, 180 °C, 6 mm) to yield pure **25**: 499 mg (88%); ^{1}H NMR ($CDCl_3$) δ 7.3 (s, 5 H, aromatic), 4.53 (s, 2 H, benzylic), 3.78 (br, 1 H, OH), 3.4–3.7 (m, 3 H, H_1 and H_5), 2.97 (dt, J = 3.8, 10.2 Hz, 1 H, H_3), 2.79 (dd, J = 4, 8.7 Hz, 1 H, H_4), 2.10 (dq, J = 14.7, 3.3 Hz, 1 H, H_{2a}), 1.72 (m, 1 H, H_{2b}), 1.31 (d, J = 6.2 Hz, 3 H, H_6); ^{13}C NMR ($CDCl_3$) δ_c 137.0, 128.6, 128.1, 73.6, 66.6, 64.7, 60.1, 55.5, 28.3, 20.1; IR (neat) 3100–3700 (broad OH), 3040, 2980, 1100, 950, 815 cm^{-1}; mass spectrum, m/e 177 (parent – C_2H_5O). Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.25; H, 8.16. Found: C, 70.07; H, 7.89.

***xylo*-4,5-Epoxyhept-1-en-6-ol (26).** Epoxy alcohol **23**[3b] ($[\alpha]^{30}_D$ – 2.4° (*c* 12.6, CH_2Cl_2); 92% ee) was converted via the inverted *p*-nitrobenzoate ester [90% yield from **23**; ^{1}H NMR ($CDCl_3$) δ 8.25 (m, 4 H, aromatic), 5.77 (m, 1 H, H_2), 5.15 (m, 2 H, H_1), 5.0 (quintet, J = 6.4 Hz, 1 H, H_6), 3.0 (m, 2 H, H_5 and H_4), 2.37 (m, 2 H, H_3), 1.44 (d, J = 6.5 Hz, 3 H, H_7); IR (neat) 3120, 3080, 2990, 1735, 1640, 1610, 1530, 1350, 1270, 1100 cm^{-1}; mass spectrum, m/e 236 (M^+ – C_3H_5); $[\alpha]^{29}_D$ –40.1° (*c* 4.06, CH_2Cl_2)] into **26** in 76% overall yield by using the procedure described above for the synthesis of **25**. Data for **26**: bp (Kuglerohr) 100–105 °C (20 mm); ^{1}H NMR ($CDCl_3$) δ 5.76 (m, 1 H, H_2), 5.10 (m, 2 H, H_1), 3.55 (br quintet, J = 6 Hz, H_6), 2.95 (dt, J = 2.2, 5.5 Hz, 1 H, H_4), 2.73 (dd, J = 2.2, 5.2 Hz, 1 H, H_5), 2.2–2.5 (m, 3 H, OH and H_3), 1.23 (d, J = 6.5 Hz, 3 H, H_7); ^{13}C NMR ($CDCl_3$) δ 132.9, 117.4, 67.5, 62.3, 55.3, 35.7, 19.4; IR (neat) 3100–3700, 3080, 2980, 1640, 925 cm^{-1}; mass spectrum, m/e 128 (parent ion); $[\alpha]^{28}_D$ –23.2° (*c* 4.35, CH_2Cl_2).

***lyxo*-1-(Benzyloxy)-3,4-epoxy-5-[(*N*-phenylcarbamoyl)oxy]hexane (4a).** A solution of 2.45 g (11.0 mmol) of **1a** in 80 mL of CH_2Cl_2 and 20 mL of pyridine was treated with 3.0 mL (3.3 g, 27 mmol) of phenyl isocyanate.[31] The reaction mixture was stirred at room temperature for 15 h, and then all volatile components were removed in vacuo. The residue was dissolved in acetone, and 10 mL of water was added. The mixture was stirred vigorously, leading to the formation of a white precipitate. The solvents were removed in vacuo, the residue was taken up in $CHCl_3$, and the insoluble portion was removed by filtration. The solvent was evaporated to give 4.3 g of crude product. This material was purified by flash chromatography (185 g silica gel, 2:1 hexane–ether) to give chromatographically homogeneous **4a** which was crystallized from acetone–hexane to give pure **4a**: 3.24 g (84%); mp 77.5–78 °C; ^{1}H NMR ($CDCl_3$) δ 7.2–7.4 (m, 9 H, aromatic), 7.04 (tt, J = 1.5, 7.3 Hz, 1 H, *p*-H of urethane), 6.64 (br, 1 H, NH), 4.74 (qd, J = 6.3, 8.8 Hz, 1 H, H_5), 4.52 (s, 2 H, benzylic), 3.65 (dd, J = 5.3, 7.0 Hz, 2 H, H_1), 3.22 (dt, J = 4.4, 7.4 Hz, 1 H, H_3), 3.05 (dd, J = 4.4, 8.8 Hz, 1 H, H_4), 1.77–2.0 (m, 2 H, H_2), 1.33 (d, J = 6.3 Hz, 3 H, H_6); IR (CH_2Cl_2) 3440, 1740, 1600, 1515, 1440, 1200, 690 cm^{-1}; mass spectrum, m/e 341 (parent ion). Anal. Calcd for $C_{20}H_{21}NO_4$: C, 70.36; H, 6.79; N, 4.10. Found: C, 70.43; H, 6.91; N, 4.18.

***lyxo*-4,5-Epoxy-6-[(*N*-phenylcarbamoyl)oxy]hept-1-ene (4b)** was prepared from **22**[3b] in 89% yield by using the procedure described above for preparation of **4a**. Data for **4b**: mp 55.5–56 °C; ^{1}H NMR ($CDCl_3$) δ 7.2–7.4 (m, 4 H, aromatic), 7.0 (br t, J = 7 Hz, 1 H, *p*-H), 6.67 (br, 1 H, NH), 5.85 (m, 1 H, H_2), 5.2 (m, 2 H, H_1), 4.8 (m, J = 6.3, 8.5, 1 H, H_6), 3.16 (dt, J = 4.4, 6.6 Hz, 1 H, H_4), 3.08 (dd, J = 4.4, 8.5 Hz, 1 H, H_5), 2.35 (m, 2 H, H_3), 1.39 (d, J = 6.3 Hz, 3 H, H_7); ^{13}C NMR ($CDCl_3$) δ 153.1, 138.3, 133.0, 128.8, 123.1, 118.8, 117.5, 70.7, 58.4, 55.6, 32.4, 17.4; IR (CH_2Cl_2) 3440, 2980, 1730, 1640, 1600, 1525, 1440, 905 cm^{-1}; mass spectrum, m/e 247 (parent ion). Anal. Calcd for $C_{14}H_{17}NO_3$: C, 68.00; H, 6.93; N, 5.66. Found: C, 68.10; H, 6.96; N, 5.35.

***ribo*-1-(Benzyloxy)-3,4-epoxy-5-[(*N*-phenylcarbamoyl)oxy]hexane (8)** was prepared in 93% yield from **25** by using the procedure described for **4a**. Data for **8**: ^{1}H NMR ($CDCl_3$) δ 7.2–7.4 (m, 9 H, aromatic), 7.03 (br t, J = 6.8 Hz, 1 H, *p*-H of urethane), 6.65 (br, 1 H, NH), 4.66 (m, 1 H, H_5), 4.48, 4.45 (AB, J_{AB} = 12 Hz, 2 H, benzylic), 3.59 (t, J = 6 Hz, 2 H, H_1), 3.18 (dt, J = 4, 8 Hz, 1 H, H_3), 2.94 (dd, J = 4, 8.3 Hz, 1 H, H_4), 1.7–2.1 (m, 2 H, H_2), 1.41 (d, J = 6.4 Hz, 3 H, H_6); IR (CH_2Cl_2) 3420, 2920, 1740, 1600, 1525, 1400, 1210 cm^{-1}; mass spectrum, m/e 341 (parent ion). Anal. Calcd for $C_{20}H_{23}NO_4$: C, 70.36; H, 6.79; N, 4.10. Found: C, 70.43; H, 6.81; N, 3.87.

***xylo*-4,5-Epoxy-6-[(*N*-phenylcarbamoyl)oxy]hept-1-ene (9)** was prepared in 95% yield from **26** by using the procedure described for **4a**: mp <23 °C (waxy solid); ^{1}H NMR ($CDCl_3$) δ 7.2–7.4 (m, 4 H, aromatic), 7.04 (br t, J = 7.1 Hz, 1 H, *p*-H), 6.72 (br, 1 H, NH), 5.78 (m, 1 H, H_2), 5.15 (m, 2 H, H_1), 4.84 (m, 1 H, H_6), 2.98 (dt, J = 2.1, 5.4 Hz, 1 H, H_4), 2.90 (dd, J = 2.1, 5.3 Hz, 1 H, H_5), 2.34 (m, 2 H, H_3), 1.35 (d, J = 6.6 Hz, 3 H, H_7); IR (CH_2Cl_2) 3420, 2985, 1730, 1640, 1590, 1520, 1440, 1210 cm^{-1}; mass spectrum, m/e 247 (parent ion); $[\alpha]^{22}_D$ +5.3° (*c* 3.9, CH_2Cl_2). Anal. Calcd for $C_{14}H_{17}NO_3$: C, 68.00; H, 6.93; N, 5.66. Found: C, 68.06; H, 7.30; N, 5.57.

***arabino*-4,5-Epoxy-6-[(*N*-phenylcarbamoyl)oxy]hept-1-ene (10)** was prepared in 78% yield from (+)-**23** ($[\alpha]^{30}_D$ +2.8° (*c* 12.5, CH_2Cl_2); 90% ee) by using the procedure described for **4a**: mp 55.5–56 °C; ^{1}H NMR ($CDCl_3$) δ 7.2–7.4 (m, 4 H, aromatic), 7.05 (br t, J = 7.1 Hz, 1 H, *p*-H), 6.59 (br, 1 H, NH), 5.79 (m, 1 H, H_2), 5.15 (m, 2 H, H_1), 4.87 (dq, J = 4.6, 6.5 Hz, 1 H, H_6), 3.03 (dt, J = 2.1, 5.4 Hz, 1 H, H_4), 2.86 (dd, J = 2.1, 4.6 Hz, 1 H, H_5), 2.32 (br t, J = 6 Hz, 2 H, H_3), 1.29 (d, J = 6.5 Hz, 3 H, H_7); IR (CH_2Cl_2) 3420, 2980, 1735, 1640, 1590, 1520, 1440, 1210 cm^{-1}; mass spectrum, m/e 247 (parent ion); $[\alpha]^{22}_D$ +27° (*c* 4.25, CH_2Cl_2). Anal. Calcd for $C_{14}H_{17}NO_3$: C, 68.00; H, 6.93; N, 5.66. Found: C, 68.14; H, 7.13; N, 5.72.

***lyxo*-5,6-Epoxy-4-[(*N*-phenylcarbamoyl)oxy]hept-1-ene (18)** was prepared from *lyxo*-5,6-epoxyhept-1-en-4-ol[3b] ($[\alpha]^{23}_D$ +3.0° (*c* 7.2, CH_2Cl_2); 95% ee) in 71% yield by using the procedure described for **4a**: mp 57–57.5 °C; ^{1}H NMR ($CDCl_3$) δ 7.2–7.4 (m, 4 H, aromatic), 7.05 (br t, J = 7.2 Hz, 1 H, *p*-H), 6.59 (br, 1 H, NH), 5.82 (m, 1 H, H_2), 5.15 (m, 2 H, H_1), 4.74 (br q, J = 5 Hz, 1 H, H_4), 3.08 (dq, J = 2.0, 5.4 Hz, 1 H, H_6), 2.76 (dd, J = 2.0, 5.5 Hz, 1 H, H_5), 1.96 (m, 2 H, H_3), 1.30 (d, J = 5.4 Hz, 3 H, H_7); IR (CH_2Cl_2) 3420, 3040, 2985, 1740, 1640, 1600, 1540, 1210 cm^{-1}; mass spectrum, m/e 247 (parent ion); $[\alpha]^{23}_D$ +24° (*c* 1.08, CH_2Cl_2). Anal. Calcd for $C_{14}H_{17}NO_3$: C, 68.00; H, 6.93; N, 5.66. Found: C, 67.85; H, 6.89; N, 5.44.

***arabino*-1-(Benzyloxy)hexane-3,4,5-triol Triacetate (2).** A solution of 37 mg (0.13 mmol) of carbonate **1c** in 4 mL of ether

(31) Agarwal, K. L.; Khorana, H. G. *J. Am. Chem. Soc.* **1972**, *94*, 3578.

was cooled in an ice bath and was treated with 20 μL of BF_3·Et_2O. The solution was kept at 0 °C for 2 h and then was warmed to 23 °C for another hour. TLC analysis of the reaction mixture revealed that **1c** was still present, so a second 30-μL portion of BF_3·Et_2O was added. Two hours later the reaction was quenched by the addition of 3 mL of water; the resulting two-phase system was stirred for 2 h. The solution was diluted with CH_2Cl_2 (20 mL), and the aqueous layer was extracted with additional portions of CH_2Cl_2 (2×). The combined extracts were dried (Na_2SO_4) and filtered, and the solvents were evaporated to yield 39 mg of crude product (a mixture of carbonates **5a** and **6a**). This material was dissolved in 5 mL of 0.2 N NaOMe in MeOH, and the solution was kept at 23 °C for 48 h. The solution was then passed through 6 cm^3 of Dowex 50W-X8 H^+ ion-exchange resin, and the solvent was removed in vacuo to give 31 mg of crude *arabino* triol. This material was dissolved in 5 mL of ether and was treated with 0.5 mL of pyridine and 2 mL of acetic anhydride. The reaction mixture was worked up after 18 h by dilution with 15 mL of ether and extraction with 3 N HCl and then saturated $NaHCO_3$ (3×). The organic extracts were dried (Na_2SO_4), filtered, and concentrated to give 44 mg of crude **2**. This material was purified by preparative TLC on a 0.25-mm silica gel plate with 1:1 hexane–ether as the eluent to yield pure **2**: 29 mg (60% overall yield); R_f 0.45 (1:1 hexane–ether); bp 180 °C (3 mm; Kuglerohr); ^1H NMR ($CDCl_3$) δ 7.3 (s, 5 H, aromatic), 5.37 (m, 1 H, H_3), 5.08 (dd, J = 3.5, 7.8 Hz, 1 H, H_4), 4.95 (m, 1 H, H_5), 4.45, 4.43 (AB, J_{AB} = 12 Hz, 2 H, benzylic), 3.45 (m, 2 H, H_1), 2.10 (s, 3 H, acetate), 2.00 (s, 3 H, acetate), 1.99 (s, 3 H, acetate), 1.80 (m, 2 H, H_2), 1.16 (d, J = 6.4 Hz, 3 H, H_6); ^{13}C NMR ($CDCl_3$) δ_c 169.9, 138.4, 128.4, 127.9, 74.7, 73.3, 68.5, 67.5, 66.3, 31.6, 20.6, 16.2; IR (neat) 3020, 2860, 1740, 1370, 1220, 840 cm^{-1}; mass spectrum, m/e 366 (parent ion). Anal. Calcd for $C_{19}H_{26}O_7$: C, 62.28; H, 7.15. Found: C, 62.40; H, 7.23.

***xylo*-1-(Benzyloxy)hexane-3,4,5-triol Triacetate (3).** A solution of 102 mg (0.46 mmol) of **1a** in 3 mL of Me_2SO and 1 mL of 2 N H_2SO_4 was stirred at 23 °C for 3 h. The solution was diluted with 20 mL of methanol and passed through 9 cm^3 of Dowex 1X-8 ion-exchange resin (pretreated with 5 N NaOH and then methanol). The solvents were concentrated in vacuo, and the slightly colored residue was purified by flash chromatography on 55 g of silica gel with 2:1 ethyl acetate–hexane as the eluent. In this manner 56 mg (51%) of the *xylo* triol was obtained: ^1H NMR ($CDCl_3$, D_2O exchange) δ 7.3 (s, 5 H, aromatic), 4.49 (s, 2 H, benzylic), 3.88 (m, 2 H, H_5 and H_3), 3.67 (m, 2 H, H_1), 3.14 (t, J = 3 Hz, 1 H, H_4), 1.9–2.05 (m, 1 H, H_{2a}), 1.7–1.8 (m, 1 H, H_{2b}), 1.19 (d, J = 6.3 Hz, 3 H, H_6); IR (CH_2Cl_2) 3100–3700 (br, OH), 3040, 2920, 1600, 1250, 1090 cm^{-1}; mass spectrum, m/e 240 (parent ion).

The triol prepared above was converted by the standard acylation procedure (Ac_2O, pyridine, Et_2O) to afford, in quantitative yield, *xylo* triacetate **3**: R_f 0.4 (1:1 hexane–ether); bp 185 °C (3 mm; Kuglerohr); ^1H NMR ($CDCl_3$) δ 7.3 (s, 5 H, aromatic), 5.28 (m, 1 H, H_3), 5.05 (m, 2 H, H_5 and H_4), 4.40 (s, 2 H, benzylic), 3.40 (m, 2 H, H_1), 2.04 (s, 3 H, acetate), 1.97 (s, 3 H, acetate), 1.94 (s, 3 H, acetate), 1.78 (q, J = 6 Hz, 2 H, H_2), 1.13 (d, J = 6.1 Hz, 3 H, H_6); IR (neat) 3020, 2860, 1740, 1370, 1240 cm^{-1}; mass spectrum, m/e 366 (parent ion). Anal. Calcd for $C_{19}H_{26}O_7$: C, 62.28; H, 7.15. Found: C, 62.35; H, 7.40.

Representative Procedures for Urethane Solvolysis Reactions. The physical, analytical, and spectroscopic data for the products of the solvolysis reactions of **4a,b**, **8–10**, and **18** are tabulated in the section immediately following these representative procedures. The product distributions and yields of isolated (chromatographed) products obtained from individual experiments are summarized in Schemes III–V.

(1) HBr in Acetone. A solution of 54 mg (0.22 mmol) of **9** in 4 mL of acetone was treated with 0.2 mL of 48% HBr at 23 °C for 2 h. The reaction mixture was diluted with 8 mL of H_2O and was extracted with CH_2Cl_2 (4 × 8 mL). The combined extracts were dried (Na_2SO_4), filtered, and concentrated in vacuo. The crude product was chromatographed on a 0.5-mm silica gel plate with 1:1 hexane–ether as the eluent (two developments) to give bromohydrin **14** (48 mg, 67%; R_f 0.59) and carbonate **13** (4 mg, 11%; R_f 0.28) from the well-resolved bands.

(2) Aqueous Perchloric Acid. To a solution of 63 mg (0.19 mmol) of urethane **4a** in 3 mL of acetonitrile was added 1 mL of 5% aqueous $HClO_4$. The cloudy solution was stirred for 19 h at room temperature and then was diluted with 15 mL each of CH_2Cl_2 and water. The aqueous phase was extracted with two additional portions of CH_2Cl_2. The combined organic extracts were dried (Na_2SO_4), filtered, and concentrated in vacuo to give 72 mg of crude product. A portion which was insoluble in $CHCl_3$ was removed by filtration, and the remainder (60 mg) was chromatographed on a 0.5-mm silica gel plate with 95:5 toluene–*t*-BuOH as the eluent. Although carbonates **5a** and **6a** are separable by TLC (R_f 0.44 for **5a**; R_f 0.33 for **6a**), in this experiment the mixture of **5a** and **6a** (5:1, respectively, as determined by ^1H NMR analysis) was isolated as a single band (30 mg, 61% yield). The slower moving band (R_f 0.26) afforded 19 mg (29%) of dihydroxyurethane **7a** (X = OH). A sample of 63 mg of **7a** (combined from several experiments) was recrystallized from ethyl acetate–hexane to give 50 mg (79%) of amorphous, white crystals; mp 128–129 °C. A pure sample of **5a** was obtained by chromatography of mixtures of **5a** and **6a**. Attempted Kugelrohr distillation of **5a** (213 °C, 2 mm) resulted in nearly complete isomerization to the more stable isomer **6a**.

(3) Aqueous Acetic Acid. A solution of 61 mg (0.18 mmol) of **8** in 2 mL of 4:1 HOAc/H_2O was heated at 100 °C for 45 min, at which time the reaction was judged complete by analytical TLC. The volatile components of the mixture were removed in vacuo, and the crude product (89 mg) was purified by flash chromatography (20 g silica gel, 95:5 toluene–*t*-BuOH). In this manner 27.5 mg (58%) of *xylo* carbonate **11** (R_f 0.44) and 17 mg (36%) of its 3,4-carbonate acyl transfer isomer **11′** (R_f 0.39) were obtained.

(4) BF_3·Et_2O in Et_2O. To a solution of 500 mg (2.02 mmol) of **18** in 40 mL of dry Et_2O at 0 °C was added 0.27 mL (2.2 mmol) of BF_3·Et_2O. A precipitate formed immediately. The mixture was stirred at 0 °C for 75 min, and then 40 mL of 1 N H_2SO_4 was added (precipitate redissolved). The ice bath was removed, and the two-phase system was stirred at room temperature for 5 h. The aqueous layer was separated and extracted with CH_2Cl_2 (4 × 20 mL). The combined extracts were dried (Na_2SO_4) and concentrated in vacuo. The crude product[32] was purified by flash chromatography (50 mm × 6 in. silica gel pad; 2% MeOH–CH_2Cl_2) to give 306 mg (88%) of **6b** (R_f 0.33; 4% MeOH–CH_2Cl_2); slower moving fractions containing **16** (R_f 0.24, 4% MeOH–CH_2Cl_2) were not recovered from this experiment.[32] *Ribo* carbonate **16** was, however, isolated from several experiments by using BF_3·Et_2O in CH_2Cl_2 (see Scheme V and footnote 20).

(5) Et_2AlCl in Et_2O. A solution of 281 mg (1.14 mmol) of **10** in 40 mL of Et_2O was cooled to 0 °C and treated with 0.75 mL of 25% Et_2AlCl in hexane. The reaction was judged complete by TLC analysis after 30 min. The solution was removed from the ice bath, and 20 mL of 1 N H_2SO_4 was added. The two-phase system was stirred for 1.5 h, and then the aqueous phase was extracted with CH_2Cl_2 (5×). The combined extracts were dried (Na_2SO_4), filtered, and concentrated to afford 215 mg of crude product which was purified by flash chromatography (55 g silica gel, 1:1 EtOAc–hexane; 25-mL fractions). Fractions 5–9 were combined and concentrated to give 185 mg (94%) of *lyxo* carbonate **15**.

***arabino*-1-(Benzyloxy)hexane-3,4,5-triol 4,5-carbonate (5a)**: ^1H NMR ($CDCl_3$) δ 7.3 (s, 5 H, aromatic), 4.84 (br quintet, 1 H, H_5), 4.50 (s, 2 H, benzylic), 4.39 (dd, J = 2.0, 7.8 Hz, H_4), 4.02 (br d, J = 9.3 Hz, 1 H, H_3), 3.6–3.8 (m, 2 H, H_1), 3.25 (br, 1 H, OH), 2.0 (br m, 1 H, H_{2a}), 1.7 (d of quintets, J = 14.7, 3 Hz, 1 H, H_{2b}), 1.56 (d, J = 6.4 Hz, 3 H, H_6); ^{13}C NMR ($CDCl_3$) δ 155.3, 137.8, 128.5, 127.9, 81.2, 76.2, 73.3, 68.4, 68.0, 33.1, 14.1; IR (neat) 3100–3600 (-OH), 2920, 2860, 1790, 1190, 1090, 695 cm^{-1}.

Carbonates **5a** and **6a** were correlated with *arabino* triacetate **2** by transesterification (NaOMe, MeOH) and acetylation (Ac_2O, pyridine, Et_2O); see the procedure for preparation of **2**.

***arabino*-1-(Benzyloxy)hexane-3,4,5-triol 3,4-carbonate (6a)**: ^1H NMR ($CDCl_3$) δ 7.3 (s, 5 H, aromatic), 4.82 (br q, 1 H, H_3), 4.48 (s, 2 H, benzylic), 4.20 (dd, J = 4.8, 5.8 Hz, 1 H, H_4), 3.94 (br m, J = 4.8, 6.4 Hz, 1 H, H_5), 3.62 (t, J = 5.9 Hz, 2 H, H_1), 2.68 (br d, J = 4.8 Hz, 1 H, OH), 2.01 (q, J = 6.0 Hz, 2 H, H_2), 1.20 (d, J = 6.4 Hz, 3 H, H_6); ^{13}C NMR ($CDCl_3$) δ 155.0, 138.1, 128.6,

(32) Analysis of the crude product obtained from smaller scale experiments revealed that the product consisted of a 10:1 mixture of **6b** and **16**.

127.9, 84.5, 75.9, 73.5, 66.9, 65.7, 35.0, 18.1; IR (CH_2Cl_2) 3200–3700 (OH), 1800, 1190, 1080 cm^{-1}; mass spectrum, *m/e* 266 (parent ion). Anal. Calcd for $C_{14}H_{18}O_5$: C, 63.15; H, 6.81. Found: C, 63.21; H, 7.02.

***arabino*-Hept-1-ene-4,5,6-triol 5,6-carbonate (5b)**: ^1H NMR ($CDCl_3$) δ 5.73 (m, 1 H, H_2), 5.18 (m, 2 H, H_1), 4.87 (m, 1 H, H_6), 4.47 (dd, J = 1.6, 7.7 Hz, 1 H, H_5), 3.81 (br t, H_4), 2.52 (br, 1 H, OH), 2.38 (m, 2 H, H_3), 1.54 (d, J = 6.6 Hz, 3 H, H_7); ^{13}C NMR ($CDCl_3$) δ 155.2, 133.1, 119.4, 80.0, 76.1, 68.3, 38.4, 14.3; IR (CH_2Cl_2) 3200–3700 (OH), 3060, 2940, 1800, 1640, 995 cm^{-1}; mass spectrum, *m/e* 131 (parent – C_3H_5).

Transesterification of **5b** or **6b** (NaOMe, MeOH) afforded *arabino*-hept-1-ene-4,5,6-triol[3b] in 95% yield. The correlation of this compound with **2** (via **27**) is outlined in Scheme VIII and is described in detail in a subsequent procedure.

***arabino*-Hept-1-ene-4,5,6-triol 4,5-carbonate (6b)**: ^1H NMR ($CDCl_3$) δ 5.73 (m, 1 H, H_2), 5.2 (m, 2 H, H_1), 4.70 (q, J = 5.4 Hz, 1 H, H_4), 4.12 (dd, J = 3.9, 5.4 Hz, 1 H, H_5), 4.0 (br m, 1 H, H_6), 3.1 (br, 1 H, OH), 2.49 (m, 2 H, H_3), 1.15 (d, J = 6.8 Hz, 3 H, H_7); ^{13}C NMR ($CDCl_3$) δ 154.8, 130.3, 120.5, 83.2, 76.7, 66.7, 38.6, 18.1; IR (CH_2Cl_2) 3300–3700 (-OH), 3060, 2975, 1800, 1640, 1375, 1180, 1060 cm^{-1}; mass spectrum, *m/e* 131 (parent – C_3H_5); $[\alpha]^{23}_D$ +59.4° (*c* 8.8, CH_2Cl_2). Anal. Calcd for $C_8H_{12}O_4$: C, 55.81; H, 7.03. Found: C, 55.54; H, 7.35.

***xylo*-1-(Benzyloxy)-3-bromo-5-[(*N*-phenylcarbamoyl)oxy]hexan-4-ol (7a, X = Br)**: ^1H NMR ($CDCl_3$) δ 7.2–7.4 (m, 9 H, aromatic), 7.10 (tt, J = 1.5, 7.0 Hz, 1 H, *p*-H of urethane), 6.70 (br, 1 H, NH), 5.15 (m, 1 H, H_5), 4.54, 4.53 (AB, J_{AB} = 11.5 Hz, 2 H, benzylic), 4.38 (dt, J = 3, 7 Hz, 1 H, H_3), 3.7 (m, 2 H, H_1), 3.50 (dt, J = 2.9, 7 Hz, 1 H, H_4), 2.74 (d, J = 7.7 Hz, 1 H, OH), 2.25 (m, 2 H, H_2), 1.33 (d, J = 6.3 Hz, 3 H, H_6); IR (CH_2Cl_2) 3100–3700 (OH), 3420, 3020, 1720, 1595, 1520, 1440 cm^{-1}; mass spectrum, *m/e* 421, 423 (parent ions). Anal. Calcd for $C_{20}H_{22}BrNO_4$: C, 56.88; H, 5.73; N, 3.32. Found: C, 57.09; H, 5.88; N, 3.05.

***xylo*-4-Bromo-6-[(*N*-phenylcarbamoyl)oxy]hept-1-en-5-ol (7b, X = Br)**: ^1H NMR ($CDCl_3$) δ 7.2–7.4 (m, 4 H, aromatic), 7.04 (br t, J = 7.2 Hz, 1 H, *p*-H of urethane), 6.90 (br, 1 H, NH), 5.80 (m, 1 H, H_2), 5.0–5.2 (m, 3 H, H_1 and H_6), 4.06 (dt, J = 3.4, 6.9 Hz, 1 H, H_4), 3.51 (dd, J = 3.4, 6.4 Hz, 1 H, H_5), 2.65–2.9 (m, 3 H, OH and H_3), 1.30 (d, J = 6.4 Hz, 3 H, H_7); IR (CH_2Cl_2) 3500–3700 (OH), 3420, 3040, 2980, 1730, 1640, 1600, 1520, 1440, 1210 cm^{-1}; mass spectrum, *m/e* 327, 329 (parent ions).

***xylo*-1-(Benzyloxy)-5-[(*N*-phenylcarbamoyl)oxy]hexane-3,4-diol (7a, X = OH)**: mp 128–129 °C; ^1H NMR ($CDCl_3$) δ 7.2–7.4 (m, 9 H, aromatic), 7.03 (br t, J = 7.3 Hz, 1 H, *p*-H of urethane), 6.9 (br, 1 H, NH), 5.05 (dq, J = 4.9, 6.4 Hz, 1 H, H_5), 4.49 (s, 2 H, benzylic), 3.87 (br m, J = 3.9 Hz, 1 H, H_3), 3.68 (m, 2 H, H_1), 3.41 (br t, 1 H, H_4), 3.31 (br, 1 H, OH), 3.13 (br, 1 H, OH), 1.8 (m, 2 H, H_2), 1.34 (d, J = 6.4 Hz, 3 H, H_6); IR (CH_2Cl_2) 3100–3700 (OH), 3040, 2920, 1730, 1600, 1520, 1440, 1210, 1090 cm^{-1}; mass spectrum, *m/e* 359 (parent ion). Anal. Calcd for $C_{20}H_{25}NO_5$: C, 66.84; H, 7.01; N, 3.90. Found: C, 66.94; H, 6.97; N, 4.03.

***xylo*-6-[(*N*-Phenylcarbamoyl)oxy]hept-1-ene-4,5-diol (7b, X = OH)**: mp 105–107 °C; ^1H NMR ($CDCl_3$) δ 7.2–7.4 (m, 4 H, aromatic), 7.04 (m, 2 H, NH and *p*-H of phenyl), 5.80 (m, 1 H, H_2), 5.0–5.2 (m, 3 H, H_1 and H_6), 3.70 (m, 1 H, H_4), 3.44 (t, J = 4.5 Hz, 1 H, H_5), 2.35–2.65 (m, 2 H, H_3), 1.34 (d, J = 6.5 Hz, 3 H, H_7); IR (CH_2Cl_2) 3200–3700 (OH), 3420, 2930, 1730, 1640, 1600, 1520, 1440, 1210 cm^{-1}; mass spectrum, *m/e* 265 (parent ion).

***xylo*-1-(Benzyloxy)hexane-3,4,5-triol 4,5-carbonate (11)**: ^1H NMR ($CDCl_3$) δ 7.3 (m, 5 H, aromatic), 4.75 (quintet, J = 6.3 Hz, 1 H, H_5), 4.50, 4.49 (AB, J_{AB} = 10 Hz, 2 H, benzylic), 4.10 (dd, J = 2.8, 6.3 Hz, 1 H, H_4), 3.86 (m, 1 H, H_3), 3.7 (m, 2 H, H_1), 3.42 (d, J = 4.7 Hz, 1 H, OH), 1.7–2.0 (m, 2 H, H_2), 1.41 (d, J = 6.4 Hz, 3 H, H_6); ^{13}C NMR ($CDCl_3$) δ 154.7, 137.5, 128.3, 127.7, 84.8, 74.8, 73.1, 68.8, 67.4, 32.0, 19.5; IR (CH_2Cl_2) 3200–3700 (OH), 3040, 2935, 1800, 1380, 1365, 1180, 1080 cm^{-1}; mass spectrum, *m/e* 266 (parent ion). Anal. Calcd for $C_{14}H_{18}O_5$: C, 63.15; H, 6.81. Found: C, 62.92; H, 6.79.

***xylo*-1-(Benzyloxy)hexane-3,4,5-triol 3,4-carbonate (11′)**: ^1H NMR ($CDCl_3$) δ 7.3 (s, 5 H, aromatic), 4.74 (q, J = 6.3 Hz, 1 H, H_3), 4.47 (s, 2 H, benzylic), 4.24 (dd, J = 3.4, 6.3 Hz, 1 H, H_4), 3.78 (br dq, J = 3.4, 6.6 Hz, 1 H, H_5), 3.63 (t, J = 5 Hz, 2 H, H_1), 2.32 (br, 1 H, OH), 2.03 (m, 2 H, H_2), 1.21 (d, J = 6.6 Hz, 3 H, H_6); ^{13}C NMR ($CDCl_3$) δ 154.5, 137.7, 128.5, 127.8, 84.5, 73.5, 66.9, 65.5, 34.3, 18.5; IR (CH_2Cl_2) 3300–3700 (-OH), 3040, 2945, 1800, 1600, 1540, 1175, 1090 cm^{-1}; mass spectrum, *m/e* 266 (parent ion).

Carbonates **11** and **11′** were correlated with *xylo* triacetate **3** by using the procedure described above for the correlation of **5a** and **6a** with **2**.

***arabino*-1-(Benzyloxy)-4-bromo-5-[(*N*-phenylcarbamoyl)oxy]hexan-4-ol (12)**: ^1H NMR ($CDCl_3$) δ 7.2–7.4 (m, 9 H, aromatic), 7.05 (br t, J = 7.1 Hz, 1 H, *p*-H of urethane), 6.78 (br, 1 H, NH), 4.93 (m, 1 H, H_5), 4.49–4.60 (m, 3 H, benzylic and H_3), 3.59–3.73 (m, 3 H, H_1 and H_4), 3.47 (br d, J = 7.4 Hz, 1 H, OH), 2.16–2.22 (m, 2 H, H_2), 1.40 (d, J = 6.2 Hz, 3 H, H_6); IR (CH_2Cl_2) 3100–3700 (OH), 3420, 3040, 1735, 1600, 1520, 1440, 1210 cm^{-1}; mass spectrum, *m/e* 421, 423 (parent ions).

***ribo*-Hept-1-ene-4,5,6-triol 5,6-carbonate (13)**: ^1H NMR ($CDCl_3$) δ 5.79 (m, 1 H, H_2), 5.16 (m, 2 H, H_1), 4.90 (m, 1 H, H_6), 4.38 (dd, J = 7.2, 9.3 Hz, 1 H, H_5), 3.84 (br m, 1 H, H_4), 2.58 (d of m, J = 14.3 Hz, 1 H, H_{3a}), 2.36 (d, J = 4.5 Hz, 1 H, OH), 2.21 (td, J = 8.2, 14.3 Hz, 1 H, H_{3b}), 1.46 (d, J = 6.7 Hz, 3 H, H_7); ^{13}C NMR ($CDCl_3$) δ_c 154.4, 132.5, 120.0, 79.9, 76.5, 67.4, 38.8, 14.8; IR (CH_2Cl_2) 3580, 3040, 2920, 1802, 1640, 1180, 1085, 1015 cm^{-1}; mass spectrum, *m/e* 131 (parent – C_3H_5); $[\alpha]^{29}_D$ +19° (*c* 4.1, CH_2Cl_2). Anal. Calcd for $C_8H_{12}O_4$: C, 55.81; H, 7.02. Found: C, 55.67; H, 7.22.

Trans-esterification of **13** by using the usual procedure (NaOMe, MeOH, 95% yield) afforded *ribo*-hept-1-ene-4,5,6-triol.[3b]

***lyxo*-4-Bromo-6-[(*N*-phenylcarbamoyl)oxy]hept-1-en-5-ol (14, X = Br)**: ^1H NMR ($CDCl_3$) δ 7.35 (m, 4 H, aromatic), 7.07 (br t, J = 7 Hz, 1 H, *p*-H), 6.92 (br, 1 H, NH), 5.91 (m, 1 H, H_2), 5.37 (dq, J = 2.8, 6.5 Hz, 1 H, H_6), 5.2 (m, 2 H, H_1), 4.05 (td, J = 3.7, 8 Hz, 1 H, H_4), 3.72 (dd, J = 2.8, 7.9 Hz, 1 H, H_5), 2.4–2.95 (m, 3 H, OH and H_3), 1.37 (d, J = 6.5 Hz, 3 H, H_7); IR (CH_2Cl_2) 3200–3700 (OH), 3040, 2980, 1730, 1640, 1595, 1520, 1440, 1210 cm^{-1}; mass spectrum, *m/e* 327, 329 (parent ions).

***lyxo*-Hept-1-ene-4,5,6-triol 5,6-carbonate (15)**: ^1H NMR ($CDCl_3$) δ 5.78 (m, 1 H, H_2), 5.2 (m, 2 H, H_1), 4.80 (quintet, J = 6.3 Hz, 1 H, H_6), 4.06 (t, J = 6 Hz, 1 H, H_5), 3.87 (m, 1 H, H_4), 2.14–2.4 (m, 3 H, H_3 and OH), 1.47 (d, J = 6.3 Hz, 3 H, H_7); ^{13}C NMR ($CDCl_3$) δ_c 155.0, 132.8, 119.0, 84.3, 75.1, 69.9, 37.0, 20.3; IR (CH_2Cl_2) 3300–3700 (OH), 3040, 1800, 1640, 1180, 920 cm^{-1}; mass spectrum, *m/e* 131 (parent – C_3H_5); $[\alpha]^{26}_D$ +37.9° (*c* 3.6, CH_2Cl_2). Anal. Calcd for $C_8H_{12}O_4$: C, 55.81; H, 7.02. Found: C, 56.09; H, 7.05.

***ribo*-Hept-1-ene-4,5,6-triol 4,6-carbonate (16)**: ^1H NMR ($CDCl_3$) δ 5.8 (m, 1 H, H_2), 5.2 (m, 2 H, H_1), 4.25 (m, H_6 and H_4), 3.48 (dt, J = 5.4, 9.3 Hz, 1 H, H_5), 2.94 (br d, J = 5 Hz, 1 H, OH), 2.4–2.7 (m, 2 H, H_3), 1.43 (d, J = 6.3 Hz, 3 H, H_7); IR (CH_2Cl_2) 3100–3700 (OH), 3040, 2920, 1750, 1640, 1245, 1200, 1080 cm^{-1}. Transesterification (NaOMe, MeOH) of **16** afforded a triol which was identical with that prepared by transesterification of *ribo* carbonate **13**. Carbonates **10** prepared from (+)-**10** and (+)-**18** are enantiomeric.

***ribo*-4-Bromo-6-[(*N*-phenylcarbamoyl)oxy]hept-1-en-5-ol (17)**: ^1H NMR ($CDCl_3$) δ 7.2–7.4 (m, 4 H, aromatic), 7.06 (br t, J = 7.1 Hz, 1 H, *p*-H), 6.70 (br, 1 H, NH), 5.86 (m, 1 H, H_2), 5.1–5.27 (m, 3 H, H_1 and H_6), 4.0 (m, 2 H, H_5 and H_4), 2.4–2.9 (m, 3 H, OH and H_3), 1.34 (d, J = 6.2 Hz, 3 H, H_7); IR (CH_2Cl_2) 3500–3700 (OH), 3420, 3040, 2980, 1733, 1640, 1600, 1520, 1440, 1210; mass spectrum, *m/e* 327, 329 (parent ions); $[\alpha]^{28}_D$ +13.7° (*c* 1.15, CH_2Cl_2).

***ribo*-6-Bromo-4-[(*N*-phenylcarbamoyl)oxy]hept-1-en-5-ol** was prepared in 45% yield by treatment of **18** with HBr in acetone (35% of carbonate **6b** was also obtained): mp 77–77.5 °C; ^1H NMR ($CDCl_3$) δ 7.2–7.4 (m, 4 H, aromatic), 7.06 (br t, J = 7.1 Hz, 1 H, *p*-H), 6.73 (br, 1 H, NH), 5.82 (m, 1 H, H_2), 5.1–5.2 (m, 2 H, H_1), 5.00 (td, J = 3.8, 7.5 Hz, 1 H, H_4), 4.32 (dq, J = 3.7, 6.7 Hz, 1 H, H_6), 3.97 (dd, J = 3.7, 7.5 Hz, 1 H, H_5), 2.39–2.70 (m, 3 H, OH and H_3), 1.70 (d, J = 6.7 Hz, 3 H, H_7); IR (CH_2Cl_2) 3500–3700 (-OH), 3420, 3040, 2980, 1735, 1640, 1595, 1520, 1440, 1205 cm^{-1}; mass spectrum, *m/e* 327, 329 (parent ions); $[\alpha]^{28}_D$ +18.8° (*c* 2.4, CH_2Cl_2). Anal. Calcd for $C_{14}H_{18}BrNO_3$: C, 51.23; H, 5.53; Br, 24.35. Found: C, 51.36; H, 5.85; Br, 24.35.

***arabino*-1-(Benzyloxy)-3,5-dihydroxy-4-(*N*-phenylamino)hexane 3,4-Carbamate (19)**. A solution of 26 mg (0.076 mmol) of **4a** in 5 mL of THF was treated with 9 mg of 50%

NaH–oil dispersion. The resulting suspension was stirred at 23 °C for 2 h, at which point 8 mL of CH_2Cl_2 and 3 mL of 15% NH_4Cl solution were added. The aqueous layer was separated and extracted with CH_2Cl_2 (2×). The combined extracts were dried (Na_2SO_4), filtered, and concentrated to afford 33 mg of a pale yellow solid. This crude material was crystallized from CCl_4 to yield white crystals: 24 mg (95%); mp 128–129.5 °C; ^1H NMR ($CDCl_3$) δ 7.3 (m, 10 H, aromatic), 4.84 (m, 1 H, H_3), 4.53, 4.52 (AB, J_{AB} = 12 Hz, 2 H, benzylic), 4.13 (dd, J = 2.2, 4.4 Hz, 1 H, H_4), 4.05 (br m, 1 H, H_5), 3.73 (t, J = 5.9 Hz, 2 H, H_1), 2.1 (m, 2 H, H_2), 1.70 (d, J = 4 Hz, 1 H, OH), 1.15 (d, J = 6.6 Hz, 3 H, H_6); IR (CH_2Cl_2) 3200–3700 (OH), 3020, 2920, 1745, 1595, 1495 cm^{-1}; high-resolution mass spectrum, calcd for $C_{20}H_{23}NO_4$ m/e 341.162 71, found m/e 341.163 89.

Correlation of Urethane 7a (X = OH) with *xylo*-Triacetate 3. A solution of 19 mg (0.053 mmol) of **7a** (X = OH) in 5 mL of THF was treated with 6 mg (0.16 mmol) of $LiAlH_4$, and the resulting suspension was heated to reflux for 5 h. The reaction was quenched by the addition of 2 mL of H_2O which was followed by 2 mL of 1 N NaOH. The resulting precipitate was removed by filtration through a Celite pad and was washed with several portions of ether. The aqueous phase was separated from the filtrate and was extracted with CH_2Cl_2 (5×). The combined organic phases were concentrated in vacuo to afford 30 mg of crude material which was purified by flash chromatography (15 g of silica gel; EtOAc as the eluent) to yield 8 mg (63%) of the *xylo* triol. This material was acylated by the usual procedure (see preparation of **2**) to afford **3** in quantitative yield.

Correlation of 2 with 6b via *arabino*-Hexane-1,3,4,5-tetraol Tetraacetate (27). A solution of 20.3 mg (0.055 mmol) of **2** in 7 mL of reagent grade MeOH was hydrogenated over 10.1 mg of 5% Pd/C under an atmosphere of H_2. The reaction mixture was stirred for 4 h, filtered, and concentrated in vacuo. The crude product (8.8 mg, 65%) was purified by chromatography on a 0.5-mm silica gel plate with 3:1 ether–hexane as the eluent, giving 7.7 mg (55%) of the desired primary alcohol. This material was then acylated according to the conditions described previously (Ac_2O, pyridine, Et_2O) to give 7.5 mg (78%) of **27** following chromatographic purification (0.25-mm silica gel preparative plate, 2:1 ether–hexane).

Tetraacetate **27** prepared in this manner was identical with a sample prepared from carbonate **6b**. Thus, 37 mg (0.21 mmol) of **6b** was treated with NaOMe in MeOH, and the crude triol was acylated with acetic anhydride and pyridine in Et_2O according to the procedure described previously for the synthesis of **2** from **5a** and **6a**. The triacetate (35 mg) was isolated in 60% overall yield by chromatography (0.5-mm silica gel plate, 3:1 ether–hexane). A portion of this product (26 mg, 0.096 mmol) was dissolved in 20 mL of MeOH and cooled to −78 °C. A stream of dry O_3/O_2 was passed through the solution until it developed a deep blue color. The solution was then purged with O_2 to remove excess O_3 and was quenched with 3 mL of Me_2S. The reaction mixture was then allowed to warm to room temperature and was stirred for 19 h. To this mixture was then added 10.8 mg (3 equiv) of $NaBH_4$. The solution was stirred for 1 h and then was diluted with 11 mL of 0.1 N HCl. The mixture was extracted with CH_2Cl_2 (4×), and the extracts were dried (Na_2SO_4), filtered, and concentrated in vacuo. The crude product was chromatographed (0.5-mm silica gel plate, 3:1 ether–hexane) to give 19.8 mg of crude primary alcohol. This intermediate was acylated as described above to give **27**: 14.5 mg (45%); ^1H NMR ($CDCl_3$) δ 5.3 (dt, J = 3.4, 6.4 Hz, 1 H, H_3), 5.1 (dd, J = 7.5, 3.4 Hz, 1 H, H_4), 4.95 (dt, J = 7.5, 6.4 Hz, 1 H, H_5), 4.05 (t, J = 6.4 Hz, 2 H, H_1), 2.11 (s, 3 H, acetate), 2.03 (s, 3 H, acetate), 2.02 (s, 3 H, acetate), 2.00 (s, 3 H, acetate), 1.84 (m, 2 H, H_2), 1.17 (d, J = 6.4 Hz, 3 H, H_6); IR (CH_2Cl_2) 2960, 1740, 1368, 1228, 1042, 677 cm^{-1}; mass spectrum, m/e 303 ($M^+ - CH_3$).

Correlation of 3 with 28 via *xylo*-Hexane-1,3,4,5-tetraol Tetraacetate (29). *Xylo* triacetate **3** and *xylo* triol **28**[3b] were transformed into *xylo* tetraacetate **29** by using procedures exactly analogous to those described above for the synthesis of *arabino* tetraacetate **27**. Data for **29**: ^1H NMR ($CDCl_3$) δ 5.24 (td, J = 8.0, 4.6 Hz, 1 H, H_3), 5.10 (m, 2 H, H_5 and H_4), 4.07 (t, J = 6.3 Hz, 2 H, H_1), 2.12 (s, 3 H, acetate), 2.09 (s, 3 H, acetate), 2.06 (s, 3 H, acetate), 2.05 (s, 3 H, acetate), 1.88 (td, J = 6.3, 8.0 Hz, 2 H, H_2), 1.24 (d, J = 6.0 Hz, 3 H, H_6); IR (CH_2Cl_2) 2920, 1732, 1424, 1327, 1230 cm^{-1}; mass spectrum, m/e 303 ($M^+ - CH_3$).

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Total Synthesis of Carbohydrates. 3. Efficient, Enantioselective Syntheses of 2,6-Dideoxyhexoses

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Highly diastereoselective syntheses of five 2,6-dideoxyhexoses are described. The syntheses of (+)-olivose (**1**), (+)-digitoxose (**3**), (+)-oliose (**4**) and (+)-cymarose (**5**) are short (four to seven steps), relatively efficient (14–22%), and enantioselective. These syntheses feature the kinetic resolution–enantioselective epoxidation of racemic allylic alcohols **13** and **17** and the highly regioselective ring-opening reactions of erythro epoxy alcohols (+)-**14**, (−)-**14**, and (+)-**18**. Syntheses of racemic **1** and boivinose (**2**) are also described.

Considerable effort has been devoted to the synthesis of carbohydrates from noncarbohydrate precursors in recent years.[3] Rare monosaccharides are important structural components of numerous antibiotics,[4] and functionalized monosaccharides continue to be of interest as intermediates in natural products synthesis.[5] In the preceding paper[6a] we outlined a general strategy for the syn-

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