Regiospecific Ring-Opening Reactions of Benzyl 3,4-Anhydro-α-D-ribopyranoside with Nucleophiles: A Systematic Study[1]

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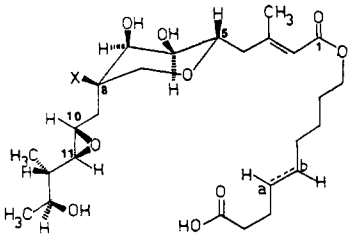
Nucleophilic ring-opening reactions of the title compound **6** and its (benzyloxy)methyl ether **27** with different nucleophiles resulted in exclusive formation of 3-substituted 3-deoxyxylose derivatives. On the basis of these experiments, it is postulated that the regioselectivity of the ring-opening reaction is controlled by a polar repulsive interaction between the entering nucleophile and the pyranose oxygen lone pair of electrons.

Sugar epoxides are useful intermediates in the preparation of a variety of deoxy substituted sugars through a nucleophilic attack and opening of the epoxide ring. A wide range of nucleophiles have been used and to mention a few are halides, azide, amines, hydride, alkoxides, mercaptides, and carbanions.

The regiochemistry of ring opening of sugar epoxides held in a rigid conformation, either by a 4,6-acetal group or by a 1,6-anhydro bridge, is governed by the Furst–Plattner rule of diaxial opening leading to one principal product.[2] In conformationally flexible epoxides, such a clear-cut application of the Furst–Plattner rule is often not possible, as the two conformers of the epoxides are in dynamic equilibrium and any nucleophilic attack on such a system is governed by the Curtin–Hammett principle.[3] In 2,3- and 3,4-anhydrohexopyranosides, the alkyl substitution at C-5 controls the conformational equilibrium by preferring an equatorial orientation.[4] In 2,3- and 3,4-anhydropentopyranosides, such a preference is not seen. This makes both carbons of the anhydro ring in pentopyranosides equally susceptible to attack by the nucleophile and hence both the ring-opened regiomers are possible, provided the difference in the transition state energies for the two pathways is small.

It is cited in the literature that methyl, ethyl, and benzyl 3,4-anhydro-β-ribopyranosides undergo preferential nucleophilic ring opening at C-4, leading to 4-deoxylyxose derivatives.[5] However, no examples of ring-opening reactions of 3,4-anhydro-α-ribopyranosides are available. In connection with our program on the total synthesis of pseudomonic acid C (**1c**),[6] an antibiotic isolated from a strain of *Pseudomonas fluorescens*, we envisaged the ring

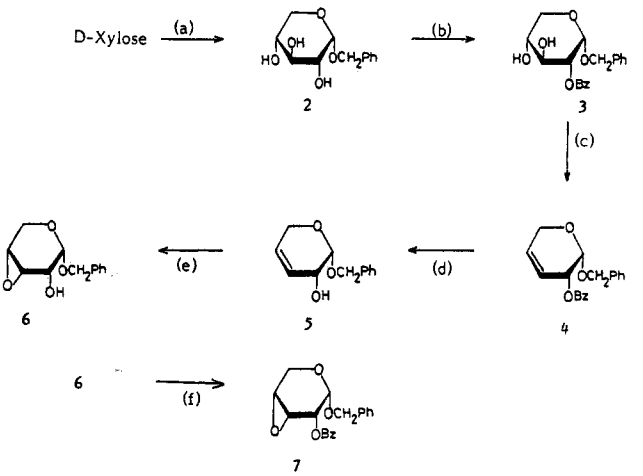


(1a): X=H; C_a-C_b=C_2H_4
(1b): X=OH; C_a-C_b=C_2H_4
(1c): X=H; C_{10}-C_{11}-no epoxide; double bond; C_a-C_b=C_2H_4
(1d): X=H; Ca-Cb=(E)-CH=CH

Pseudomonic acids A-D (1a)-(1d)

opening of a 3,4-anhydroribopyranoside with a carbon nucleophile to incorporate the side chain at C-8 (pseudomonic acid numbering) as a viable strategy. To this end, we synthesized benzyl 3,4-anhydro-α-D-ribopyranoside (**6**) from D-xylose. Preliminary experiments in this direction using lithium acetylide as nucleophile showed that the ring opening took place at C-3 of **6**.

Scheme I[a]



[a] (a) $PhCH_2OH$, H^+; (b) PhCOCl, Py, −40 °C; (c) TPP, CHI_3, imidazole, toluene, reflux; (d) MeOH–H_2O–TEA (5:2:1) room temperature; (e) MCPBA, DCM, 5–8 °C; (f) PhCOCl, Py, room temperature.

As the factors controlling the regiochemistry in the nucleophilic ring-opening reactions of 3,4-anhydroribopyranosides are not yet well established, a systematic study of ring-opening reactions of **6** and its derivatives was undertaken in order to have a better insight into these reactions and also to understand the change in regiochemistry, i.e., from substitution at C-4 to C-3 when the configuration at C-1 is changed from β to α. The results of these investigations are presented below.

Results

D-xylose was converted to benzyl 3,4-anhydro-α-D-ribopyranoside **6**, as shown in Scheme I. Dehydroxylation of the monobenzoate **3**[7] was achieved by a combination of triphenylphosphine, iodoform, and imidazole to give **4**,[8] which was hydrolyzed to the allylic alcohol **5** using a mixture of methanol, water, and triethylamine. Hydroxyl-assisted epoxidation[9] of allylic alcohol **5** with MCPBA in dichloromethane at 5 °C gave **6**. The assignment of the structure of **6** as benzyl 3,4-anhydro-α-D-ribopyranoside followed from its spectral data.

(1) Taken in part from the Ph.D. thesis of M.V.R., University of Hyderabad, 1987.
(2) Mills, J. A. [cited by: Newth, F. H.; Homer, R. F. *J. Chem. Soc.* **1953**, 989].
(3) Curtin, D. Y. *Rec. Chem. Prog.* **1954**, *15*, 111.
(4) Eliel, E. L.; Allinger, N. L.; Angyal, S. J.; Morrison, G. A. In *Conformational Analysis*; Interscience: New York, 1965; Vol. 42, pp 356, 371.
(5) (a) Overend, W. G.; White, A. C.; Williams, N. R. *Chem. Ind. (London)* **1963**, 1840. (b) Kent, P. W.; Ward, P. F. V. *J. Chem. Soc.* **1953**, 416. (c) Lung Fu, Y.; Miroslav, B. *J. Org. Chem.* **1980**, *45*, 3836. (d) Sundin, A.; Frejd, T.; Magnusson, G. *J. Org. Chem.* **1986**, *51*, 3927.
(6) (a) Crimmin, M. J.; O'Hanlon, P. J.; Rogers, N. H. *J. Chem. Soc., Perkin Trans. 1* **1985**, 541, 549 and references cited therein. (b) Williams, D. R.; Moore, I. L.; Yamada, M. *J. Org. Chem.* **1986**, *51*, 3916 and references cited therein.
(7) (a) Friedman, N.; Cohen, S.; Bergmann, E. D. *Isr. J. Chem.* **1970**, *8*, 663. (b) Jones, J. K. N.; Sivakumaran, T. *Can. J. Chem.* **1967**, *45*, 2493.
(8) Bessodes, M.; Abushanab, E.; Panzica, R. P. *J. Chem. Soc., Chem. Commun.* **1981**, 26.
(9) Henbest, H. B. *Proc. Chem. Soc.* **1963**, 159.

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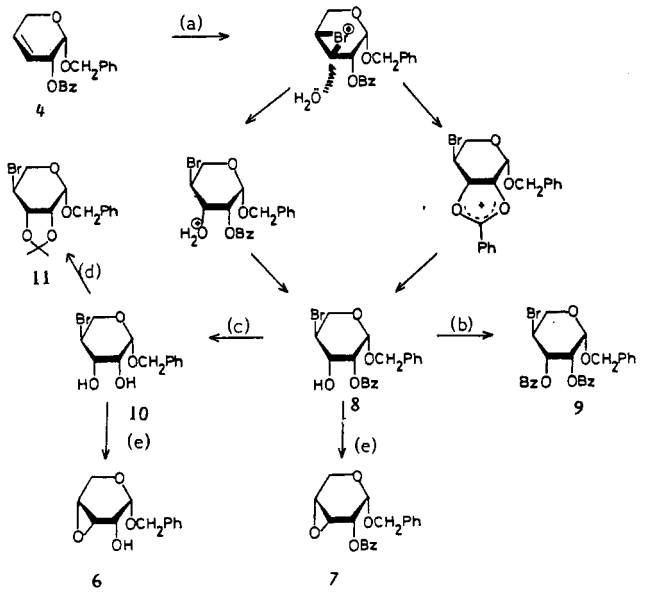
Scheme II[a]



[a] (a) NBS, aqueous DMSO, room temperature; (b) PhCOCl, Py, room temperature; (c) MeOH–H_2O–TEA (5:2:1); (d) Me_2CO, H^+, $CuSO_4$; (e) NaH, THF, room temperature.

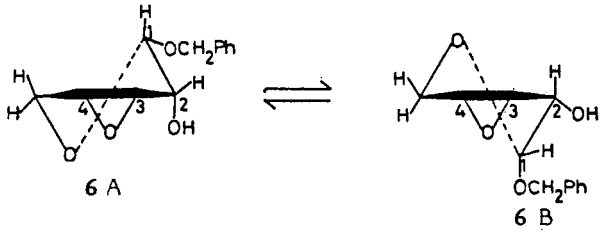


Figure 1.

The characteristic IR bands due to the epoxy system are in agreement with the reported values, which lie in the range of 840–855 ± 5 and 890–895 ± 5 cm^{-1} for methyl 3,4-anhydroribopyranoside having the α-configuration.[10]

As the relationship between the epoxy protons and the proton at C-2 was not evident from the 100-MHz ^1H NMR spectrum of **6**, **6** was benzoylated to give **7** in order to determine the configuration of the epoxide **6**. The observed $J_{2,3}$ for the epoxy benzoate **7** is about 3 Hz which is in agreement with the reported J values for the syn relationship between H-2 and H-3.[11]

So as to confirm the configuration of the epoxide **6** unambiguously, the same epoxide was synthesized from bromohydrin **8**, as depicted in Scheme II. Treatment of allylic benzoate **4** with NBS in aqueous DMSO gave the bromohydrin **8**. The spectral data support the structure of benzyl 4-bromo-4-deoxy-2-*O*-benzoyl-β-L-lyxopyranoside (**8**). The confirmation of the regio- and stereochemical relationship between the two hydroxyl groups in **8** was based on decoupling experiments on both **8** and the dibenzoate **9**, in addition to the formation of the isopropylidene derivative **11**. The bromohydrin **8** being a single product as shown in Scheme II, can cyclize only to **7**. Both **8** and **10** on cyclization using sodium hydride in THF or DMF gave **7** and **6**, respectively. Both epoxy alcohol **6** and the epoxy benzoate **7** prepared by two different routes showed identical physical and spectral properties. These experiments unambiguously proved the stereochemistry of the epoxide **6**.

(10) Chmielewski, M.; Zamejksi, A. *Rocz. Chem.* **1972**, *46*, 2039.
(11) Sweet, F.; Brown, R. K. *Can. J. Chem.* **1968**, *46*, 1481.

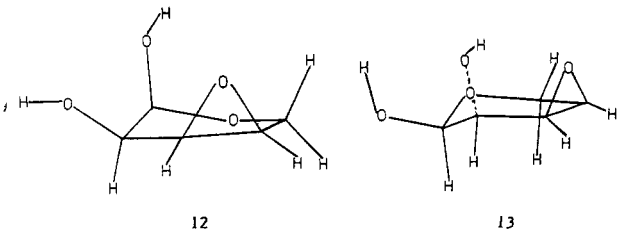
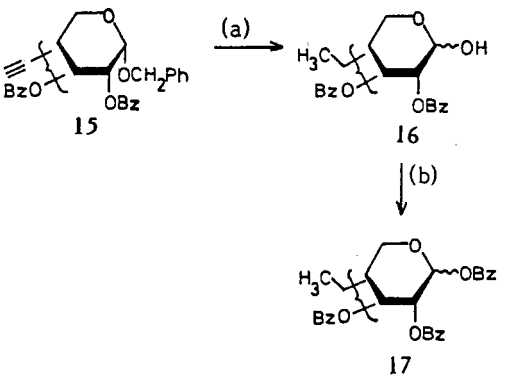


Figure 2.

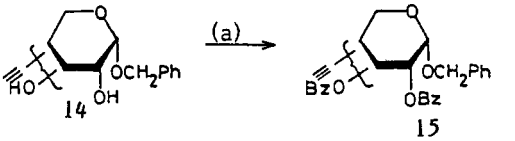
Scheme III[a]



[a] (a) H_2, 60 psi, Pd/C, MeOH; (b) PhCOCl, Py, DMAP, room temperature.

Of the two possible conformers for the epoxide **6** (**6A** and **6B**) (Figure 1) it was not possible to predict a priori which conformer, **6A** or **6B**, is the predominant one on the basis of the anomeric and other polar and steric effects. Experimentally, the position of conformational equilibrium (**6A** ⇌ **6B**) could not be determined by the method of Buchanan[12] as the requisite vicinal proton coupling constants could not be obtained from the 100-MHz ^1H NMR spectrum of **6**. A variable temperature ^1H NMR study of the epoxide **6** in acetone-d_6 showed no change in the spectral pattern from 25 to −80 °C. Semiempirical SCFMO calculations, using the MNDO program,[13] of ground-state energies of two conformers in a model 3,4-anhydroribopyranose (Figure 2) resulted in a small energy difference of 1.304 kcal mol^{-1} between **12** and **13**.[14] Although it was not possible to deduce the free energy difference between **6A** and **6B** either from vicinal proton coupling constants or from the low-temperature ^1H NMR experiments, it can be concluded that the free energy difference between the two conformers is relatively small.

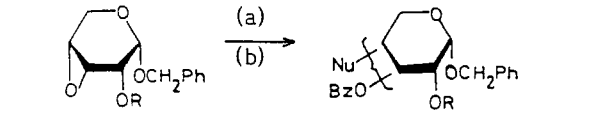
Reaction of **6** with lithium acetylide gave a ring-opened product **14** as evidenced by spectral data. However, the regiochemistry of ring opening could not be determined unambiguously. Several attempts at the preparation of the isopropylidene derivative of **14** were futile, but the dibenzoate **15** could be obtained by a standard procedure.



(a) PhCOCl, Py, DMAP, room temperature.

(12) Buchanan, J. G.; Fletcher, R.; Parry, K.; Thomas, W. A. *J. Chem. Soc. B* **1969**, 377.
(13) (a) Dewar, M. J. S.; Thiel, W. *J. Am. Chem. Soc.* **1977**, *99*, 4899. (b) Thiel, W. Program No. 353, Quantum Chemistry Program Exchange, Indiana University, Bloomington, Indiana. (c) Jemmis, E. D.; Reddy, A. C., personal communication.
(14) The heat of formation of **12** is −148.403 kcal mol^{-1}, and that of **13** is −147.099 kcal mol^{-1}.

Table I. Ring-Opening Reactions of 6 and 27 with Different Nucleophiles



R = -H, 6 R = -Bz

- CH_2OCH_2Ph 27 $-CH_2OCH_2Ph$

(a) Nucleophile; (b) PhCOCl, Py, DMAP, room temperature.

run	nucleophile	metal counterion	substrate	yield, %	site of subst	product
1	C≡CH	Li^+	6	95	C-3	15
			27			
2	CN	K^+	6	82	C-3	18
			27	78	C-3	28
3	Br	Mg^{2+}	6	90	C-3	19
			27	88	C-3	29
4	N_3	Na^+	6	80	C-3	20
			27	76	C-3 (60)[a]	30A
					C-4 (40)[a]	30B
5	SPh	Na^+	6	75	C-3	22
			27	73	C-3	32
6	H	Li^+	6	90	C-3	23
			27	75	C-3	33
7	OMe	Na^+	6	81	C-3	24
			27	70	C-3	34

While this indicated that the ring opening had occured at C-3, more definitive evidence was sought to prove this point. As decoupling experiments on **15** were ambiguous, it was converted to a suitable derivative **17** as shown in Scheme III. Hydrogenolysis of **15** at 60 psi using 10% Pd on carbon afforded **16**, which was benzoylated to give **17**. The ^1H NMR spectrum of **17** was suitable for decoupling experiments as the signals of significance were distinct and well separated. ^1H NMR: δ 6.21 (d, 1 H, H-1), 5.20 (dd, 1 H, H-2), 5.10 (dq, 1 H, H-4), 3.70–4.30 (m, 2 H, H-5, H-5′), 2.10–2.50 (m, 1 H, H-3). These assignments are based on decoupling experiments.

Irradiation of the anomeric doublet at δ 6.21 simplifies the doublet of doublet at δ 5.20, proving that it is due to H-2. Irradiation of the H-2 signal affects the multiplet at δ 2.10–2.50 and leaves the doublet of quartet at δ 5.10 due to the second benzoate methine proton unchanged. Irradiation of H-5 and H-5′ signals causes collapse of the doublet of quartet at δ 5.10 and vice versa. Finally, irradiation of the multiplet at δ 2.10–2.50 alters both the signals due to the two benzoate methine protons. These decoupling experiments unambiguously prove that the acetylide substitution in **14** is at C-3 instead of at C-4 as required for the construction of pseudomonic acid C.

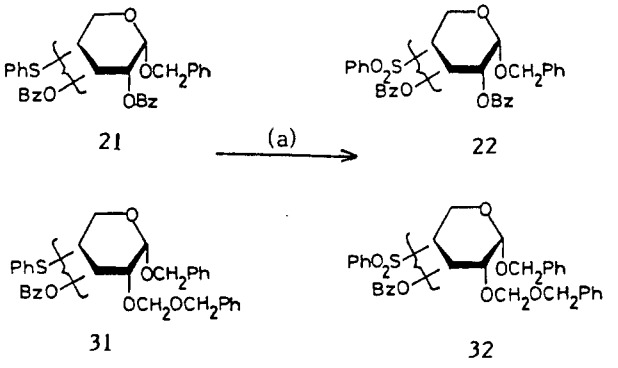
The result obtained in the nucleophilic ring-opening reaction of **6** with lithium acetylide is different from that obtained in the nucleophilic ring opening of 3,4-anhydroribopyranoside with β-configuration. This led us to systematically investigate the reaction of **6** with different nucleophiles.

For this purpose, the epoxide **6** was reacted with a variety of nucleophiles as listed in Table I. The use of different reagents was to provide a wide nucleophilicity range and also to obtain an insight into the effect of the metal counterion on the ring-opening reactions. For the purposes of analysis, the crude ring opened product, after appropriate workup, was benzoylated by a standard procedure and then subjected to chromatographic purification. The yields reported are of pure dibenzoates. Assignment of structures of the product derivatives followed from their respective spectral data, and the regiochemistry was determined from decoupling experiments.

Of the various attempts made for effecting the ring opening of **6** with cyanide as a nucleophile, only with the specific conditions of Sharpless[15] was the reaction successful. Thus, the treatment of **6** with dry potassium cyanide in DMSO in the presence of titanium(IV) isopropoxide and tetrabutylammonium iodide gave after benzoylation **18**. While the gross structure of **18** corresponded to ring opening of **6** by cyanide, its regiochemistry was established by decoupling experiments which proved that the nitrile group is at C-3.

Reaction of **6** with magnesium bromide in refluxing THF, after benzoylation, gave **19**. Decoupling experiments proved that the bromine is present at C-3. Epoxide **6** when treated with sodium azide in DMF at 80 °C gave a primary product which was benzoylated to the dibenzoate **20**. The spectral data of **20** showed that the azido group is at C-3. The reaction of **6** with sodium phenyl sulfide in THF yielded **21**, after benzoylation. Although the ^1H NMR spectrum of **21** resembled those of the 3-substituted 3-deoxyxylose derivatives obtained earlier, suggesting that the phenylthio group is at C-3, decoupling experiments did not establish the regiochemistry unequivocally as the signals of significance were merged. In order to determine the position of phenylthio substitution unambiguously in **21**, it was oxidized to the corresponding sulfone **22**, using

Scheme IV[a]



[a] (a) MCPBA, DCM, 5–8 °C.

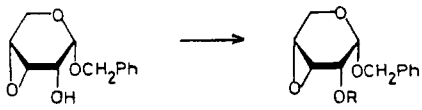
(15) Sharpless, K. B.; Caron, M. *J. Org. Chem.* **1985**, *50*, 1557.

MCPBA (Scheme IV). The ^1H NMR spectrum of **22** was suitable for decoupling experiments, which proved that the phenylthio substitution in **21** is at C-3. In reaction 6, **6** was treated with LAH in THF to give **23**, after benzoylation. The spectral data was again in favor of the 3-deoxy 3-substituted structure for **23**. The ring opening of **6** with sodium methoxide in THF at room temperature gave, on benzoylation, **24** with C-3 substitution.

Thus, all the nucleophiles under different conditions opened **6** regioselectively at C-3.

It is possible that the free 2-hydroxyl group of **6** could be associated with the metal counterion of the nucleophile, thereby directing the incoming nucleophile to attack at C-3 instead of at C-4. It is cited in the literature that there are specific directing effects in the opening of vicinal hydroxy epoxides.[16] When the hydroxyl group was free, the nearer bond (C-3) of the epoxide was displaced, and when this was a trimethylsilyl ether, the remote bond (C-4) was preferentially severed.

Therefore, in an attempt to change the regiochemistry in the nucleophilic ring opening of the epoxide **6**, the 2-hydroxy group was sought to be protected as ethers and an ester. The derivatives of the epoxy alcohol **6**, compounds **25–27** were prepared by using standard procedures. The structures of these compounds were in agreement with their respective spectral data.



6 R = -Bz **7**; -TBDMS, **25**; -TBDPS, **26**; - CH_2OCH_2Ph, **27**.

The choice of (benzyloxy)methyl ether **27** for the systematic investigation was dictated by its relative stability under different conditions in comparison to other derivatives of **6**, namely, **7**, **25**, and **26**.

Compound **27** was reacted with all the nucleophiles, as listed in Table I, under indentical reaction conditions corresponding to **6**. For the purpose of analysis, the crude ring-opened product, after appropriate workup, was benzoylated by a standard procedure and then purified. The yields reported are of pure monobenzoates.

In all the reactions of **27**, except in the case of azide, the nucleophiles opened regioselectively at C-3. The reaction of **27** with sodium azide gave, after benzoylation, the two components **30A** and **30B** in a ratio of 60:40, which were separable by chromatography. Decoupling experiments proved that **30A** corresponded to the 3-deoxy-3-azidoxylose derivative and **30B** to the 4-deoxy-4-azidolyxose derivative. Lithium acetylide did not react with **27**.

Thus, in all the runs, except in the reaction of **27** with sodium azide and lithium acetylide, all the nucleophiles opened regioselectively at C-3 on both substrates.

Discussion

The various factors which determine the regioselectivity in epoxide ring opening of anhydro sugars have been reviewed.[17] The more important among these are steric, polar, and conformational effects. In most of the examples reported, the observed regioselectivity was rationalized by using these three criteria. In the case 2,3- and 3,4-anhydropentopyranosides, where a dynamic conformational equilibrium is possible, it is difficult to assess the factors affecting the regioselectivity of epoxide ring opening.

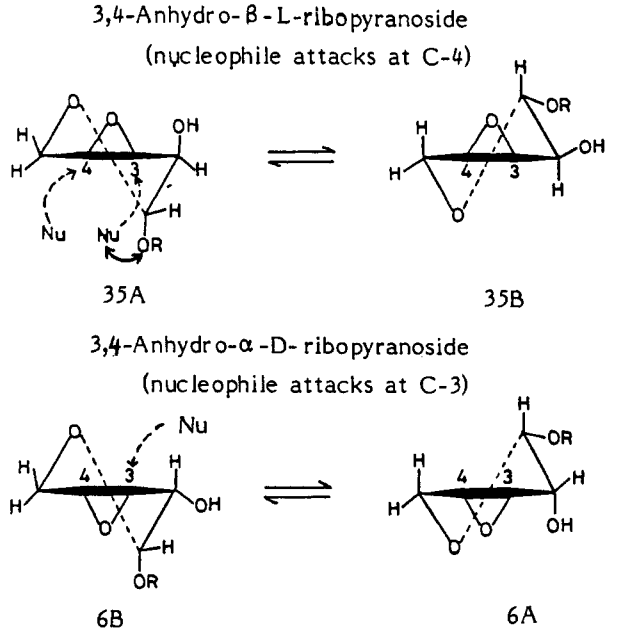


Figure 3.

In examples where the conformational free energy difference is very small, it has been emphasized that it is the relative transition-state energies which determine the regioselectivity of the epoxide ring opening and not the relative proportions of conformers in the ground state; i.e., the Curtin–Hammett principle operates. However, effects of conformational factors on the regioselectivity may be predicted to some extent since many of the nonbonded interactions that exist in the ground-state conformers are also present in the corresponding transition states. In such cases, the regioselectivity is determined by simple steric and electronic factors in the regioisomeric transition states. It is also cited that the major product in most of the cases is derived from a transition state containing the anomeric alkoxyl group in the more stable axial conformation.[17]

The regioselectivity observed in the case of 3,4-anhydro-β-ribopyranosides is rationalised by considering the steric and polar interactions that arise in the transition state.[5] Of the two possible conformers shown in Figure 3, conformer **35A** is the one most likely to be attacked by the nucleophile, as the anomeric substituent can be then axially oriented in the transition state with minimum perturbation. Ring opening at C-4 in preference to C-3, by diaxial opening, occurs as the latter transition state involves a 1,3-interaction between the entering nucleophile and the alkoxy substituent and one 1,3-diaxial interaction (all axial substituents).

In the case of 3,4-anhydro-α-ribopyranoside **6** and its derivatives, in conformation **6B**, the diaxial opening at C-3 or at C-4 does not involve any 1,3-interaction between the entering nucleophile and the anomeric alkoxyl group. The results in the ring-opening reactions of these epoxides show an almost exclusive attack at C-3. This means that while 1,3-diaxial interactions are absent in the transition state of these epoxides, the regioselectivity is governed by yet another factor.

It is cited in the literature that the polar interactions between the oxygen atom of the oxirane ring and either the anomeric oxygen or the oxygen atom of the pyranose ring are possible.[18]

(16) Danishefsky, S.; Tsai, M. Y.; Kitahara, T. *J. Org. Chem.* **1977**, *42*, 394.

(17) (a) Buchanan, J. G.; Stable H. Z. In *Selective Organic Transformations*; Thyagarajan, B. S., Ed.; Wiley Interscience: New York, 1972; Vol. 2, p 1. (b) Williams, N. R. In *Advances in Carbohydrate Chemistry and Biochemistry*; Tipson, R. S., Ed.; Academic: New York, 1970; Vol. 25, p 109 and references cited therein.

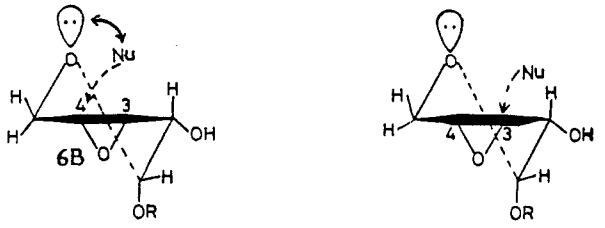


Figure 4.

Based on these observations, it is likely that polar interactions between the entering nucleophile and the oxygen atom of the pyranose ring control the regioselectivity in the ring-opening reactions of 3,4-anhydropentopyranosides when the steric factors are not playing a role. In the case of 3,4-anhydro-β-ribopyranosides, where the anomeric oxygen and the oxirane oxygen are anti to one another, it is the 1,3-interaction between the entering nucleophile and the anomeric alkoxy substituent which controls the regioselectivity. In the case of 3,4-anhydro-α-ribopyranosides the anomeric oxygen and the oxirane oxygen are syn to each other, and there is no 1,3-interaction between the entering nucleophile and the anomeric alkoxy substituent. In such cases, there seems to be a marked 1,3-polar repulsive interaction between the entering nucleophile at C-4 and the electron lone pair on the pyranose oxygen, and this factor controls the regioselectivity, directing the attack to C-3 where the interaction, if any, is less.

The preference for the anomeric substituent to be axial in benzyl 3,4-anhydro-α-ribopyranoside (**6**) as in conformer **6B** imparts a strong directionality to the pyranose oxygen lone pair, which is oriented in nearly the same direction as that of the incoming nucleophile (Figure 4). As a consequence, a polar repulsive interaction can be envisaged, and the magnitude of such an interaction is likely to be greater for attack at C-4 than for that at C-3.

On the basis of this hypothesis, the observed regioselectivity, i.e., preferential attack at C-3 in **6** and its derivatives can be rationalized. Thus, in all the runs of Table I, except in run 4 with the substrate **27**, the results of ring-opening reactions of both the substrates **6** and **27** with various nucleophiles can be satisfactorily explained.

The ring-opening reaction of **27** with sodium azide gives a mixture of regioisomers, viz., 3-deoxy-3-azidoxylose derivative and 4-deoxy-4-azidolyxose derivative in the ratio of about 60:40, respectively. The reasons for this are not clear.

It is interesting to note that the regiochemistry of ring opening of 3,4-anhydroribopyranosides is dependent upon the configuration of the anomeric oxygen. In the β-series, the governing factor seems to be the diaxial interaction between the alkoxy group and the incoming nucleophile, directing the attack to C-4. When the configuration is α, this interaction is absent and a polar repulsive interaction between the incoming nucleophile and the pyranose oxygen lone pair electrons is dominant, and this directs the attack at C-3. This explanation receives support from the result obtained in the ring-opening reactions of methyl 3,4-anhydro-α-D-arabinopyranoside (**36**)[19] (Figure 5) and benzyl 3,4-anhydro-β-L-ribopyranoside (**35**)[5d] (Figure 3). Thus, there seems to be an important role for the pyranose

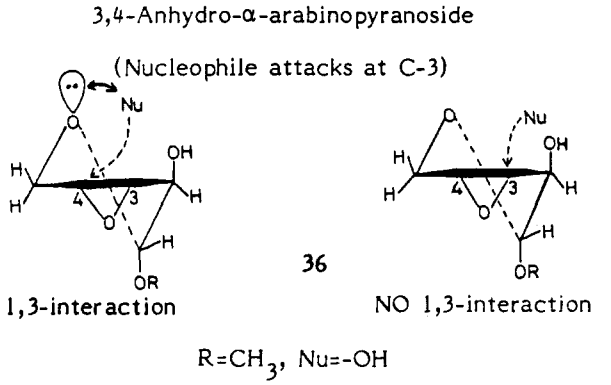


Figure 5.

oxygen lone pair of electrons in governing the regiochemistry of epoxide ring-opening reactions when other factors are not of overriding significance. Further experiments are under way to test the validity and generality of this hypothesis.

Experimental Section

Melting points were determined by using a Buchi 510 capillary point apparatus and are uncorrected. Optical rotations were measured with an Autopol II automatic polarimeter at 25 °C. IR spectra were recorded on Perkin-Elmer Model 1310 or 297 spectrophotometer. Solid samples were prepared as KBr wafers and liquid samples as a film between NaCl plates. ^{1}H NMR (100 MHz) and ^{13}C NMR (25 MHz) were obtained with a Jeol-FX-100 spectrometer. All spectra were measured in chloroform-*d* solution with tetramethylsilane as internal standard unless otherwise stated. Spectral assignments are as follows: (1) chemical shift on the δ scale (TMS = δ 0.00), (2) multiplicity, (3) number of hydrogens integrated for by the signal, (4) assignment of the signal, and (5) coupling constant in hertz (Hz). Decoupling experiments were carried out by irradiating the frequency of the signal concerned with high power (6–8 W) and observing the affected signals. Mass measurements were carried out on AEI-MS 5076 mass spectrometer in the electron impact or chemical ionization (CI) mode. Elemental analyses were performed on a Perkin-Elmer 240 C CHN analyser.

HPLC analysis was done with an LKB instrument fitted with a Merk m-Porasil column and UV detector. Analytical TLC was performed on (10 × 5 cm) glass plates coated with (250 μm) with Acmes' silic gel G or GF254 containing 13% calcium sulfate as binder. Column chromatography was performed with Acmes' silica gel (100–200 mesh) and usually eluted with 20–30% ethyl acetate–hexane, unless otherwise mentioned. All moisture-sensitive reactions were carried out under dry nitrogen, and all solvents were distilled from appropriate drying agents just before use. Petroleum ether refers to the fraction boiling between 60–80 °C. Hydrogenations were carried out on Parr hydrogenation apparatus in 250-mL pressure bottles.

Benzyl 2-*O*-Benzoyl-α-D-*erythro*-pent-3-enopyranoside (4). To a stirred solution of **3**[6] (5g, 14.5 mmol) in dry toluene (100 mL) was added triphenylphosphine (15.2 g, 58.0 mmol), iodoform (11.3 g, 29.0 mmol), and imidazole (1.97 g, 29.0 mmol) and refluxed for 21 h. The reaction mixture after attaining room temperature was washed with aqueous $NaHCO_3$ (100 mL). The aqueous layer was extracted with toluene (2 × 25 mL). The combined organic phase was washed with aqueous $Na_2S_2O_3$ and water and dried. The solvent was evaporated and the crude material chromatographed on a column of silica gel (200g) to give a syrupy **4** (3.8 g, 85%): $[\alpha]_D$ +37.5° (*c* 1.3, $CHCl_3$). IR (neat): 1720, 875, 845, and 820 cm^{-1}. ^{1}H NMR δ 7.28–7.81 (m, 10 H, Ar); 5.84 (dq, 2 H, *HC*=C*H*); 5.50 (br t, 1 H, H-2); 5.16 (d, 1 H, H-1, J = 4); 4.68 (center of AB q, 2 H, OCH_2Ph, J = 12); 3.80–4.40 (m, 2 H, H-5, H-5′).

Benzyl α-D-*erythro*-Pent-3-enopyranoside (5). To **4** (3.10 g, 10.0 mmol) was added a mixture of methanol–water–triethylamine in a ratio of 5:2:1 (250 mL) and stirred at room temperature for 30 h. The reaction mixture was concentrated to a

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thick syrup at room temperature under vacuum. The resulting syrup was extracted with hot petroleum ether (200 mL), concentrated to about (50 mL), and cooled in the refrigerator. The needle-like crystals formed were filtered and recrystallized from hexane to give pure **5** (2.0 g, quantitative): mp 68 °C; $[\alpha]_D$ +68° (*c* 0.46, $CHCl_3$). IR 3350, 3270, 880, 875, and 825 cm^{-1}. ^1H NMR: δ 7.26 (s, 5 H, Ar); 5.80–5.84 (m, 2 H, C*H*=C*H*); 4.96 (d, 1 H, H-1, *J* = 4); 4.70 (center of AB q, 2 H, OCH_2Ph, *J* = 12); 3.80–4.25 (m, 3 H, H-2, H-5, H-5′); 2.10 (br s, 1 H, O*H*). ^{13}C NMR: 137.1, 128.4, 127.9, 127.8, 126.2, 125.5, 95.9, 70.0, 64.2, and 60.3 ppm. Mass spectrum: 206.237 (M^+ = 206). Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84. Found: C, 69.68; H, 6.48.

Benzyl 3,4-Anhydro-α-D-ribopyranoside (6). To a stirred solution of **5** (2.06 g, 10.0 mmol) in dry DCM (50 mL) at 0 °C was added slowly a solution of MCPBA (2.0 g, 12.0 mmol) in DCM (25 mL). After the addition was over the reaction mixture was stirred at 8–9 °C for 24 h. After 20% aqueous Na_2SO_3 (25 mL) was added, the reaction mixture was stirred for 2 h. The organic layer was separated and washed successively with aqueous $NaHCO_3$ and water and dried. Evaporation of the solvent and recrystallization of the resulting solid from hexane gave **6** (2.13 g, 96%): mp 99–100 °C; $[\alpha]_D$ +114° (*c* 0.42, $CHCl_3$). IR: 3460, 890, and 850 cm^{-1}. ^1H NMR: δ 7.28 (s, 5 H); 4.56 (d, 1 H, H-1, *J* = 4); 4.55 (center of AB q, 2 H, OCH_2Ph, *J* = 12); 3.64–4.15 (m, 3 H, H-2, H-5, H-5′); 3.88 (d, 2 H, H-3, H-4); 2.62 (br d, 1 H, OH). ^{13}C NMR: 136.8, 128.5, 127.97, 127.92, 96.2, 69.8, 64.8, 59.5, 52.9, and 51.5 ppm. Mass spectrum: 222.236 (M^+ = 222). Anal. Calcd for $C_{12}H_{14}O_4$: C, 64.854; H, 6.34. Found: C, 64.66; H, 6.37.

General Procedures for Benzoylation on a 1-mmol Scale. Procedure A. Benzoyl chloride (1.1 equiv was slowly added to a stirred solution of alcohol (1 equiv) in dry pyridine (5 mL) at 0 °C. The reaction mixture was stirred for 15 h at room temperature and then poured into chilled aqueous K_2CO_3 (15 mL). After the mixture was stirred for 1 h, the product was extracted with DCM (3 × 25 mL). The combined organic phase was washed with aqueous $NaHCO_3$, dried, and evaporated. To remove the residual pyridine, toluene (2 × 5 mL) was added to and then evaporated from the residue. The crude benzoate was then subjected to chromatographic purification.

Procedure B. To a stirred solution of alcohol (1 equiv) in dry pyridine (5 mL) at 0 °C was added DMAP (5 mg) followed by benzoyl chloride (1.1 equiv). The reaction mixture was stirred for 12 h at room temperature and then poured into chilled aqueous K_2CO_3 (15 mL). After the mixture was stirred for 1 h, the product was extracted with DCM (3 × 25 mL). The combined organic phase was successively washed with dilute HCl, water, and aqueous $NaHCO_3$, dried, and evaporated to give the crude benzoate, which was then subjected to chromatographic purification.

Benzyl 2-*O*-Benzoyl-3,4-anhydro-α-D-ribopyranoside (7). Benzoylation of **6** (0.445 g, 2.0 mmol) was achieved by using the standard procedure B to give, after column chromatography, pure **7** (0.53 g, 81%): mp 115–116 °C; $[\alpha]_D$ +92° (*c* 0.62, $CHCl_3$). IR: 1720, 890, and 850 cm^{-1}. ^1H NMR: δ 7.28–7.81 (m, 10 H, Ar); 5.27 (dd, 1 H, H-2, *J* = 2, 6); 4.85 (d, 1 H, H-1, *J* = 3); 4.70 (center of AB q, 2 H, OCH_2Ph, *J* = 12); 3.87–4.30 (m, 2 H, H-5, H-5′); 3.41–3.70 (m, 2 H, H-3, H-4). ^{13}C NMR: 165.90, 137.1, 133.0, 129.9, 128.2, 94.8, 69.9, 67.7, 59.4, 52.3, and 49.1 ppm. Anal. Calcd for $C_{19}H_{18}O_5$: C, 69.92; H, 5.55. Found: C, 69.59; H, 5.36.

Benzyl 4-Bromo-4-deoxy-2-*O*-benzoyl-β-L-lyxopyranoside (8). To a stirred solution of **4** (1.2 g, 3.87 mmol) in 8:2 DMSO–water (10 mL) was added NBS (0.90 g, 5.0 mmol) in small portions. After the reaction mixture was stirred at room temperature for 10 h, another lot of NBS (0.45 g, 2.50 mmol) in small portions was added and the stirring continued for 20 h. The reaction mixture was diluted with water (20 mL) and extracted with ether (3 × 25 mL). The combined organic phase was repeatedly washed with water, dried, and concentrated, and the residue was subjected to column chromatography, to give syrupy **8** (1.25 g, 80%): $[\alpha]_D$ +103° (*c* 0.68, $CHCl_3$). IR (film): 3500 and 1720 cm^{-1}. ^1H NMR: δ 7.28–8.18 (m, 10 H, Ar); 5.68 (t, 1 H, H-2); 5.20 (d, 1 H, H-1, *J* = 4); 4.72 (center of AB q, OCH_2Ph, *J* = 12); 3.60–4.50 (m, 4 H, H-3, H-4, H-5, H-5′); 2.46 (br s, 1 H, OH).

Benzyl 4-Bromo-4-deoxy-2,3-di-*O*-benzoyl-β-L-lyxopyranoside (9). The bromohydrin **8** (0.814 g, 2.0 mmol) was benzoylated by using the standard procedure A to give, after column chromatography, syrupy **9** (0.93, 91%), which solidified on long standing: $[\alpha]_D$ +118° (*c* 0.935, $CHCl_3$). IR (film): 1720 cm^{-1}; ^1H NMR: δ 7.28–8.20 (m, 15 H, Ar); 5.88 (t, 1 H, H-2, *J* = 4); 5.40 (dd, 1 H, H-3, *J* = 4, 11); 5.10 (d, 1 H, H-1, *J* = 4); 4.70 (center of AB q, 2 H, OCH_2Ph, *J* = 12); 3.60–4.50 (m, 3 H, H-4, H-5, H-5′). Anal. Calcd for $C_{26}H_{23}O_6Br$: C, 61.06; H, 4.53. Found: C, 61.10; H, 4.46.

Benzyl 4-Bromo-4-deoxy-β-L-lyxopyranoside (10). The bromohydrin **8** (1.35 g, 3.30 mmol) was added to a mixture of methanol–water–triethylamine in the ratio of 5:2:1 (110 mL) and stirred at room temperature for 24 h. The reaction mixture was concentrated at room temperature under vacuum to a thick syrup and was extracted with ether (3 × 40 mL). The combined organic phase was washed with water and concentrated, and the residue was filtered through a column of silica gel to give **10** (0.96 g, 96%): mp 55–56 °C; $[\alpha]_D$ +72° (*c* 0.47, $CHCl_3$). IR 3450 cm^{-1}. ^1H NMR: δ 7.28 (s, 5 H, Ar); 4.62 (center of AB q, 2 H, OCH_2Ph); 4.60 (d, 1 H, H-1, *J* = 4); 3.80–4.20 (m, 2 H, H-5, H-5′); 2.90–3.50 (m, 5 H, H-2, H-3, H-4, 2 O*H*). ^{13}C NMR: 137.3, 128.2, 127.9, 127.8, 96.7, 70.0, 65.0, 59.7, 53.2, and 51.79 ppm.

Benzyl 4-Bromo-4-deoxy-2,3-isopropylidene-β-L-lyxopyranoside (11). To a stirred solution of **10** (0.030 g, 0.10 mmol) in dry acetone (5 mL) was added anhydrous $CuSO_4$ (0.050 g) followed by a catalytic amount of sulfuric acid. The resulting mixture was stirred for 10 h at room temperature, neutralized with $NaHCO_3$, and filtered. The residue was washed with DCM (2 × 10 mL), and the combined organic phase was evaporated. The resulting material was chromatographed over silica gel to yield syrupy **11** (0.028 g, 85%). IR (film): 1110, 1099, and 820 cm^{-1}. ^1H NMR: δ 4.80 (d, 1 H, H-1, *J* = 3); 4.72 (center of AB q, 2 H, OCH_2Ph, *J* = 12); 3.50–4.30 (m, 5 H, H-2, H-3, H-4, H-5, H-5′); 1.40 (s, 3 H); 1.29 (s, 3 H).

Benzyl 3,4-Anhydro-α-D-ribopyranoside (6) and Benzyl 2-*O*-Benzoyl-3,4-anhydro-α-D-ribopyranoside (7). A 50% suspension of NaH (0.048 g, 1.0 mmol) was placed in a three-necked flask, and the mineral oil was washed with dry hexane. THF (3 mL) was injected, and then a solution of the bromohydrin **10** (0.2 g, 0.66 mmol) in THF (3 mL) was slowly added. The resulting mixture was stirred at room temperature for 6 h, quenched with water (2 mL), and extracted with DCM (3 × 20 mL). The combined organic phase was washed with water, dried, and evaporated to a solid residue to give **6** (0.092 g, 63%), identical by spectral data and other parameters with **6** obtained from the epoxidation of **5** with MCPBA.

Compound **8** (0.081 g, 0.20 mmol) was transformed to **7** (0.039 g, 61%), following the same procedure as described above.

Benzyl 3-Ethynyl-3-deoxy-α-D-xylopyranoside (14). Acetylene was purified by passing it through a −78 °C trap, concentrated sulfuric acid trap, and a sodium hydroxide trap. Acetylene, purified as mentioned, was allowed to pass through THF (5 mL) at −78 °C for 10 min. *n*-BuLi (1 mL, 1.2 M in hexane, 1.20 mmol) was slowly introduced. After 10 min, a solution of **6** (0.222 g, 1.0 mmol) in THF (5 mL) was slowly added at −78 °C and the stirring continued for 15 min. The reaction mixture was allowed to reach room temperature, and water (2 mL) was added followed by anhydrous K_2CO_3 to salt out the organic layer, which was then decanted. The pasty residue was washed with DCM (2 × 25 mL), and the combined organic phase was washed with water, dried, and concentrated to a solid residue. It was recrystallized from benzene–hexane to give **14** (0.240 g, 95%); mp 95.5–96 °C; $[\alpha]_D$ +144° (*c* 0.38, $CHCl_3$). IR: 3460, 3350, 3310 (s), and 2120 (w) cm^{-1}. ^1H NMr: δ 7.28 (s, 5 H, Ar); 4.88 (d, 1 H, H-1, *J* = 4); 4.68 (center of AB q, 2 H, OCH_2Ph, *J* = 12); 2.95–4.0 (m, 5 H, H-2, H-3, H-4, H-5, H-5′); 2.60 (br d, 2 H, 2 O*H*); 2.20 (d, 1 H, *H*C≡C). ^{13}C NMR: 137.1, 128.1, 127.9, 127.8, 96.45, 81.78, 72.50, 70.51, 70.04, 68.75, 63.87, and 40.09 ppm. Anal. Calcd for $C_{14}H_{16}O_4$: C, 67.72; H, 6.49. Found: C, 67.53; H, 6.41.

Benzoylation of 14. Compound **14** (0.248 g, 1.0 mmol) was benzoylated by the standard procedure B, to give, after chromatography, the dibenzoate **15**, which was recrystallized from benzene–hexane (0.41 g, 90%): mp 105 °C; $[\alpha]_D$ +87.3° (*c* 0.4, $CHCl_3$). IR: 3310, 2120, and 1720 cm^{-1}. ^1H NMR: δ 7.28–8.20 (m, 15 H, Ar); 5.10–5.40 (m, 2 H, H-2, *H*COBz); 4.90 (d, 1 H, H-1, *J* = 3.5); 4.74 (center of AB q, 2 H, OCH_2Ph); 3.50–4.20 (m, 3 H, H-5, H-5′, *H*CC≡CH); 2.05 (d, 1 H, *H*C≡C). Mass spectrum: 456.494 (M^+ = 456). Anal. Calcd for $C_{28}H_{24}O_6$: C, 73.67; H, 5.29. Found: C, 73.49; H, 5.40.

3-Ethyl-3-deoxy-2,4-di-*O*-benzoyl-D-xylopyranose (16). Hydrogenation of **15** (0.114 g, 0.25 mmol) was achieved in methanol (5 mL) over 10% Pd on carbon catalyst (20 mg) at 60 psi. After 6 h, no more hydrogen was absorbed. The catalyst was filtered, and the solvent was evaporated to give the syrupy hemiacetal **16** (0.069 g, 75%). IR (film): 3450 and 1720 cm^{-1}. ^1H NMR: δ 7.28–8.20 (m, 10 H, Ar); 4.86–5.18 (m, 3 H, H-1, H-2, *HCOBz*); 3.56–4.24 (m, 2 H, H-5, H-5′); 2.08–2.48 (m, 1 H, *H*CEt); 1.50–2.0 (m, 5 H, CH_2CH_3).

3-Ethyl-3-deoxy-1,2,4-tri-*O*-benzoyl-D-xylopyranoside (17). Benzoylation of **16** (0.036 g, 0.10 mmol) by the standard procedure B followed by purification of the crude material on a column of silica gel gave syrupy **17** (0.040 g, 86%). IR (film): 1720 cm^{-1}. ^1H NMR: δ 7.28–8.20 (m, 15 H, Ar); 6.21 (d, 1 H, H-1, J = 5); 5.20 (dd, 1 H, H-2, J = 5, 8); 5.10 (dq, 1 H, H-4); 3.70–4.30 (m, 2 H, H-5, H-5′); 2.10–2.50 (m, 1 H, H-3); 1.50–2.0 (m, 5 H, CH_2CH_3).

Reaction of 6 with Potassium Cyanide. To a stirred solution of epoxy alcohol **6** (0.10 g, 0.45 mmol) in dry DMSO (5 mL) was added potassium cyanide (0.065 g, 1.0 mmol) followed by tetrabutylammonium iodide (0.369 g, 1.0 mmol). After 5 min, titanium(IV) isopropoxide (0.357 mL, 1.20 mmol) was slowly injected, and the resulting mixture was stirred at room temperature for 72 h. Ether (20 mL) followed by 5% H_2SO_4 (5 mL) was added, and the two-phase mixture was stirred till two clear layers were formed (about 1 h). The organic phase was separated, washed with water and aqueous $NaHCO_3$, dried, and concentrated. The residue was benzoylated by following the standard procedure B, and the resulting material was chromatographed to give benzyl 3-cyano-3-deoxy-2,4-di-*O*-benzoyl-α-D-xylopyranoside (**18**) (0.168 g, 82%): mp 144–146 °C; $[\alpha]_D$ +106° (*c* 0.38, $CHCl_3$). IR: 2250 and 1720 cm^{-1}; ^1H NMR: δ 7.28–8.20 (m, 15 H, Ar); 5.54 (dd, 1 H, H-2, J = 5, 12); 5.44 (d, 1 H, H-1, J = 4); 5.20–5.40 (m, 1 H, H-4); 4.76 (center of AB q, 2 H, OCH_2Ph); 4.14 (dd, 1 H, H-3, J = 5, 11); 3.68–3.90 (m, 2 H, H-5, H-5′). Anal. Calcd for $C_{27}H_{23}O_6N$: C, 70.88; H, 5.06; N, 3.06. Found: C, 70.62; H, 4.88; N, 3.0.

Reaction of 6 with Magnesium Bromide. To a stirred mixture of anhydrous magnesium bromide (1.0 mmol) prepared from Mg (0.024 g, 1.0 mmol) and 1,2-dibromoethane (0.90 mL, 1.0 mmol) in THF (5 mL) was added a solution of epoxy alcohol **6** (0.050 g, 0.225 mmol) in THF (2 mL). The resulting mixture was refluxed for 5 h. After the mixture was allowed to reach room temperature, saturated aqueous NH_4Cl was added, and the precipitate formed was filtered. The cake was washed with DCM (2 × 10 mL), and the combined organic phase was washed with water, dried, and concentrated. The residue was benzoylated by following the standard procedure A, and the resulting crude material was chromatographed to give benzyl 3-bromo-3-deoxy-2,4-di-*O*-benzoyl-α-D-xylopyranoside (**19**) (0.103 g, 90%): mp 148–150 °C; $[\alpha]_D$ +118.3° (*c* 0.34, $CHCl_3$). IR: 1720, 1160, and 1020 cm^{-1}. ^1H NMR: δ 7.28–8.24 (m, 15 H, Ar); 5.20–5.64 (m, 2 H, H-2, H-4); 4.86 (d, 1 H, H-1, J = 4); 4.72 (center of AB q, OCH_2Ph); 3.64–4.24 (m, 3 H, H-5, H-5′, *H*CBr). Anal. Calcd for $C_{26}H_{23}O_6Br$: C, 61.06; H, 4.53. Found: C, 61.0; H, 4.47.

Reaction of 6 with Sodium Azide. To a stirred solution of **6** (0.50 g, 0.225 mmol) in dry DMF (3 mL) was added sodium azide (0.033 g, 0.50 mmol). The resulting mixture was stirred at 80 °C for 10 h. After it was allowed to reach room temperature, it was diluted with 1:1 acetone–ether (10 mL) and filtered at the pump. The filtrate was washed with water, dried, and concentrated. The residue was benzoylated following the standard procedure B, and the resulting material was chromatographed to give benzyl 3-azido-3-deoxy-2,4-di-*O*-benzoyl-α-D-xylopyranoside (**20**) (0.085 g, 80%); mp 104–106 °C; $[\alpha]_D$ +138.6° (*c* 0.36, $CHCl_3$). IR: 2100 and 1720 cm^{-1}. ^1H NMR: δ 7.28–8.24 (m, 15 H, Ar); 5.04–5.44 (m, 2 H, H-2, H-4); 5.0 (d, 1 H, H-1, J = 4); 4.72 (center of AB q, 2 H, OCH_2Ph); 4.48 (t, 1 H, HCN_3, J = 11); 3.64–4.20 (m, 2 H, H-5, H-5′). Anal. Calcd for $C_{26}H_{23}N_3O_6$: C, 65.95; H, 4.89; N, 8.87. Found: C, 65.87; H, 4.90; N, 8.79.

Reaction of 6 with Sodium Phenyl Sulfide. A 50% suspension of NaH (0.010 g, 0.225 mmol) was placed in a three-necked flask, and the mineral oil was removed by washing with dry hexane. THF (2 mL) was added, and a solution of thiophenol (0.023 mL, 0.225 mmol) in THF (1 mL) was added slowly. The resulting mixture was stirred for 30 min, and then a solution of **6** (0.050 g, 0.225 mmol) in THF (2 mL) was slowly added and was stirred for 6 h at room temperature. Water (1 mL) was injected and the mixture extracted with DCM (2 × 10 mL). The combined organic phase was washed with water and aqueous $NaHCO_3$, dried, and concentrated. The residue was benzoylated by the standard procedure B, and the resulting material was chromatographed to give benzyl 3-(phenylthio)-3-deoxy-2,4-di-*O*-benzoyl-α-D-xylopyranoside (**21**) (0.091 g, 75%). IR: 1720, 1610, and 1600 cm^{-1}. ^1H NMR: δ 7.28–8.24 (m, 20 H, Ar); 5.28 (dd, 1 H, H-2, J = 4, 11); 5.12 (d, 1 H, H-1, J = 4); 4.86–5.08 (m, 1 H, *H*COBz); 4.76 (center of AB q, 2 H, OCH_2Ph); 3.76–4.24 (m, 3 H, *H*CSPh, H-5, H-5′).

Oxidation of 21 with MCPBA. To a stirred solution of **21** (0.054 g, 0.10 mmol) in DCM (5 mL) at 0 °C was added a solution of MCPBA (0.049 g, 0.30 mmol) in DCM (3 mL). The resulting mixture was stirred overnight at 8–9 °C. The reaction mixture was stirred at room temperature for 2 h after adding 20% aqueous Na_2SO_3 (5 mL), and the separated organic phase was successively washed with aqueous $NaHCO_3$ and water, dried, and concentrated. The residue was chromatographed to give benzyl 3-(phenylsulfonyl)-3-deoxy-2,4-di-*O*-benzoyl-α-D-xylopyranoside (**22**) (0.036 g, 63%): mp 148–152 °C; $[\alpha]_D$ +116° (*c* 0.38, $CHCl_3$). IR: 1720, 1610, 1600, 1300, and 1140 cm^{-1}. ^1H NMR: δ 7.28–8.20 (m, 20 H, Ar); 5.48–5.76 (m, 1 H, H-4); 5.40 (dd, 1 H, H-2, J = 5, 12); 5.12 (d, 1 H, H-1, J = 4); 4.56 (center of AB q, 2 H, OCH_2Ph); 4.26 (t, 1 H, H-3); 3.64–4.12 (m, 2 H, H-5, H-5′). Anal. Calcd for $C_{32}H_{28}O_8S$: C, 67.12; H, 4.92. Found: C, 67.0; H, 5.16.

Reaction of 6 with LAH. To a stirred solution of LAH (0.009 g, 0.225 mmol) in THF (2 mL) was added a solution of epoxy alcohol **6** (0.050 g, 0.225 mmol) in THF (2 mL). The resulting mixture was stirred at room temperature for 5 h and saturated aqueous Na_2SO_4 was slowly added. The precipitate formed was filtered and the cake washed with DCM (2 × 5 mL). The combined organic phase was dried and concentrated, and the residue was benzoylated by the standard procedure B to give, after chromatography, benzyl 3-deoxy-2,4-di-*O*-benzoyl-α-D-xylopyranoside (**23**) (0.087 g, 90%): $[\alpha]_D$ +110.6° (*c* 0.33, $CHCl_3$). IR (film): 1720 cm^{-1}. ^1H NMR: δ 7.28–8.20 (m, 15 H, Ar); 5.24–5.60 (m, 2 H, H-2, H-4); 5.20 (d, 1 H, H-1, J = 4); 4.80 (center of AB q, OCH_2Ph); 3.80–4.20 (m, 2 H, H-5, H-5′); 2.30–2.72 (m, 2 H, CH_2). Anal. Calcd for $C_{26}H_{24}O_6$: C, 72.21; H, 5.59. Found: C, 72.40; H, 5.70.

Reaction of 6 with Sodium Methoxide. To a stirred suspension of sodium methoxide (0.054 g, 1.0 mmol) in THF (2 mL) was added a solution of **6** (0.050 g, 0.225 mmol) in THF (3 mL), and the resulting mixture was stirred at room temperature for 48 h. Water (2 mL) was added and the mixture extracted with DCM (2 × 10 mL). The combined organic phase was washed repeatedly, dried, and concentrated. The residue was benzoylated by the standard procedure B and chromatographed to give benzyl 3-methoxy-3-deoxy-2,4-di-*O*-benzoyl-α-D-xylopyranoside (**24**) (0.084 g, 81%): mp 114–117 °C; $[\alpha]_D$ +108° (*c* 0.31, $CHCl_3$). IR: 1720, 1020, and 1010 cm^{-1}. ^1H NMR: δ 7.28–8.20 (m, 15 H, Ar); 5.08–5.44 (m, 2 H, H-2, *H*COBz); 5.04 (d, 1 H, H-1, J = 4); 4.64 (center of AB q, 2 H, OCH_2Ph); 3.64–4.14 (m, 3 H, $HCOCH_3$, H-5, H-5′); 3.60 (s, 3 H, OCH_3). Anal. Calcd for $C_{27}H_{26}O_7$: C, 70.11; H, 5.66. Found: C, 69.61; H, 5.80.

Benzyl 2-*O*-(*tert*-Butyldimethylsilyl)-3,4-anhydro-α-D-ribopyranoside (25). To a stirred solution of **6** (1.10 g, 5.0 mmol) in DMF (10 mL) was added imidazole (0.71 g, 11.0 mmol) followed by *tert*-butyldimethylchlorosilane (0.83 g, 5.50 mmol). The resulting mixture, after being stirred at room temperature for 14 h, was diluted with water (5 mL) and then extracted with ether (2 × 50 mL). The combined organic phase was repeatedly washed with water, dried, and concentrated. The residue was chromatographed on a column of silica gel to give syrupy **25** (1.38 g, 86%): $[\alpha]_D$ +89° (*c* 0.271, $CHCl_3$). IR (film) 1000, 890, and 850 cm^{-1}. ^1H NMR: δ 7.29 (m, 5 H, Ar); 4.52 (center of AB q, 2 H, OCH_2Ph); 4.44 (d, 1 H, H-1); 3.44–4.18 (m, 3 H, H-2, H-5, H-5′); 3.2 (m, 2 H, H-3, H-4); 0.84 (s, 9 H); 0.05 (s, 6 H).

Benzyl 2-*O*-(*tert*-Butyldiphenylsilyl)-3,4-anhydro-α-D-ribopyranoside (26). To a stirred solution of **6** (0.222 g, 1.0 mmol) in DMF (5 mL) was added imidazole (0.142 g, 2.10 mmol) followed by *tert*-butyldiphenylchlorosilane (0.302 g, 1.10 mmol). The resulting mixture was stirred at room temperature for 20 h and diluted with water (5 mL). It was extracted with ether (3

× 20 mL), and the combined organic layers were washed with water, dried, and concentrated. The residue was purified over silica gel to give syrupy **26** (0.36 g, 78%): $[\alpha]_D$ +106° (*c* 0.48, $CHCl_3$). IR (film): 1610, 1000, 890, and 850 cm^{-1}; ^1H NMR δ 7.28–8.10 (m, 15 H, Ar); 4.50 (center of AB q, 2 H, OCH_2Ph); 4.39 (d, 1 H, H-1); 3.40–4.08 (m, 3 H, H-2, H-5, H-5′); 2.84–3.20 (m, 2 H, H-3, H-4); 0.94 (d, 9 H).

Benzyl 2-*O*-[(Benzyloxy)methyl]-3,4-anhydro-α-D-ribopyranoside (27). To a stirred solution of **6** (1.20 g, 5.40 mmol) in THF (10 mL) was added diisopropylethylamine (2.2 mL, 16.20 mmol). After 5 min, benzyl chloromethyl ether (1.12 mL, 6.48 mmol) was slowly added, and the resulting mixture was stirred at room temperature for 20 h. Water (5 mL) was added and extracted with ether (3 × 50 mL). The combined organic phase was successively washed with dilute HCl, water, aqueous $NaHCO_3$, and water, dried, and evaporated. The residue was chromatographed to give syrupy **27** (1.38 g, 76%), which solidified on long standing in the refrigerator: $[\alpha]_D$ +73.5° (*c* 0.72, $CHCl_3$). IR (film): 1610, 1010, 890, and 850 cm^{-1}. ^1H NMR: δ 7.28–7.40 (m, 10 H, Ar); 4.86 (d, 1 H, H-1); 4.40–4.80 (m, 6 H, OCH_2Ph, OCH_2OCH_2Ph); 3.60–4.50 (m, 2 H, H-5, H-5′); 3.12–3.40 (m, 2 H, H-3, H-4). Anal. Calcd for $C_{20}H_{22}O_5$: C, 70.158, H, 6.47. Found: C, 69.84; H, 6.60.

Reaction of 27 with Potassium Cyanide. To a stirred solution of **27** (0.076 g, 0.225 mmol) in dry DMSO (2 mL) was added potassium cyanide (0.033 g, 0.50 mmol) followed by tetrabutylammonium iodide (0.184 g, 0.50 mmol). After 5 min, titanium(IV) isopropoxide (0.178 mL, 0.60 mmol) was slowly injected. Under identical reaction and workup conditions as reported for **18**, the reaction mixture after benzoylation and purification gave benzyl 3-cyano-3-deoxy-2-*O*-[(benzyloxy)methyl]-4-*O*-benzoyl-α-D-xylopyranoside (**28**) as a syrup (0.081 g, 78%): $[\alpha]_D$ +93.4° (*c* 0.36, $CHCl_3$). IR: 2250 and 1720 cm^{-1}. ^1H NMR: δ 7.28–8.20 (m, 15 H, Ar); 5.20–5.40 (m, 1 H, H-4); 5.06 (d, 1 H, H-1, *J* = 4); 4.40–4.96 (m, 6 H, OCH_2Ph, OCH_2OCH_2Ph); 3.96–4.20 (m, 2 H, H-2, H-5); 3.44–3.90 (m, 2 H, H-3, H-5′). Anal. Calcd for $C_{28}H_{27}O_6N$: C, 71.02; H, 5.74; N, 2.95. Found: C, 70.61; H, 5.46; N, 2.81.

Reaction of 27 with Magnesium Bromide. (Benzyloxy)methyl ether **27** (0.076 g, 0.225 mmol) was reacted with magnesium bromide under identical conditions as reported for the reaction of **6**. The resulting material, after benzoylation, was chromatographed to give benzyl 3-bromo-3-deoxy-2-*O*-[(benzyloxy)methyl]-4-*O*-benzoyl-α-D-xylopyranoside (**29**) (0.108 g, 88%): $[\alpha]_D$ +112° (*c* 0.42, $CHCl_3$). IR: 1720, 1160, and 1010 cm^{-1}. ^1H NMR: δ 7.28–8.24 (m, 15 H, Ar); 5.24–5.60 (m, 1 H, *H*COBz); 5.06 (d, 1 H, H-1); 4.48–5.04 (m, 6 H, OCH_2Ph, OCH_2OCH_2Ph); 3.64–4.28 (m, 3 H, H-5, H-5′, *H*CBr). Anal. Calcd for $C_{27}H_{27}O_6Br$: C, 61.48; H, 5.16. Found: C, 61.0; H, 4.90.

Reaction of 27 with Sodium Azide. Compound **27** (0.076 g, 0.225 mmol) was reacted with sodium azide under identical conditions as reported for **20**. The resulting residue was benzoylated by procedure B and chromatographed to give **30** (0.083 g, 76%), which contains two components. The slow moving spot is benzyl 3-azido-3-deoxy-2-*O*-[(benzyloxy)methyl]-4-*O*-benzoyl-α-D-xylopyranoside (**30A**) (0.050 g): $[\alpha]_D$ +117.8° (*c* 0.34, $CHCl_3$). IR (film): 2100, 1720, and 1020 cm^{-1}. ^1H NMR: δ 7.28–8.20 (m, 15 H, Ar); 4.40–4.94 (m, 1 H, *H*COBz); 4.92 (d, 1 H, H-1); 4.32–4.84 (m, 6 H, OCH_2Ph, OCH_2OCH_2Ph); 4.24 (t, *H*CN_3, *J* = 11); 4.12–4.56 (m, 3 H, H-2, H-5, H-5′). Anal. Calcd for $C_{27}H_{27}O_6N_3$: C, 66.24; H, 5.56; N, 8.58. Found: C, 65.67; H, 5.38; N, 8.0. The fast moving spot is benzyl 4-azido-4-deoxy-2-*O*-[(benzyloxy)methyl]-3-*O*-benzoyl-β-L-lyxopyranoside (**30B**) (0.030 g). IR (film): 2100, 1720, and 1020 cm^{-1}. ^1H NMR: δ 7.28–8.20 (m, 15 H, Ar); 5.36 (dd, 1 H, *H*COBz, *J* = 4, 10); 5.08 (d, 1 H, H-1, *J* = 4); 4.64–5.12 (m, 6 H, OCH_2Ph, OCH_2OCH_2Ph); 4.16–4.60 (m, 2 H, *H*CN_3, H-5); 3.48–3.76 (m, 1 H, H-5′).

Reaction of 27 with Sodium Phenyl Sulfide. Under identical conditions as reported for **21**, **27** (0.076 g, 0.225 mmol) gave, after reaction with sodium phenyl sulfide, benzoylation, and purification, benzyl 3-(phenylthio)-3-deoxy-2-*O*-[(benzyloxy)methyl]-4-*O*-benzoyl-α-D-xylopyranoside (**31**) (0.091 g, 73%). IR: 1720, 1610, 1600, and 1010 cm^{-1}. ^1H NMR: δ 7.28–8.24 (m, 20 H, Ar); 5.04–5.28 (m, 1 H, *H*COBz); 4.96 (d, 1 H, H-1, *J* = 4); 4.28–4.84 (m, 6 H, OCH_2Ph, OCH_2OCH_2Ph); 3.40–4.0 (m, 4 H, H-2, *H*CSPh, H-5, H-5′).

Oxidation of 31 with MCPBA. Under identical conditions as reported for **22**, **31** (0.055 g, 0.10 mmol) was oxidized to give the corresponding sulfone, benzyl 3-(phenylsulfonyl)-3-deoxy-2-*O*-[(benzyloxy)methyl]-4-*O*-benzoyl-α-D-xylopyranoside (**32**) (0.035 g, 60%), after chromatography: $[\alpha]_D$ +106° (*c* 0.41, $CHCl_3$). IR (film): 1720, 1610, 1600, 1300, 1140, and 1010 cm^{-1}; ^1H NMR: δ 7.28–8.20 (20 H, Ar); 5.20–5.64 (m, 1 H, H-4); 5.08 (d, 1 H, H-1, *J* = 4); 4.32–4.96 (m, 6 H, OCH_2Ph, OCH_2OCH_2Ph); 4.22 (dd, 1 H, H-2, *J* = 4, 10); 4.0 (t, 1 H, H-3); 3.40–4.04 (m, 2 H, H-5, H-5′). Anal. Calcd for $C_{33}H_{32}O_8S$: C, 67.33; H, 5.48. Found: C, 67.0; H, 5.60.

Reaction of 27 with LAH. Under identical conditions as reported for **23** the (benzyloxy)methyl ether **27** (0.076 g, 0.225 mmol) was reduced with LAH. The residue, after benzoylation and chromatography gave benzyl 3-deoxy-2-*O*-[(benzyloxy)methyl]-4-*O*-benzoyl-α-D-xylopyranoside (**33**) (0.077 g, 76%). IR (film): 1720, 1610, 1600, 1140, and 1010 cm^{-1}. ^1H NMR: δ 7.28–8.20 (m, 15 H, Ar); 5.24–5.40 (m, 1 H, *H*COBz); 5.04 (d, 1 H, H-1, *J* = 4); 4.40–4.94 (m, 6 H, OCH_2Ph, OCH_2OCH_2Ph); 3.86–4.20 (m, 2 H, H-5, H-5′); 2.26–2.76 (m, CH_2).

Reaction of 27 with Sodium Methoxide. Under identical conditions as reported for **24**, the (benzyloxy)methyl ether **27** (0.076 g, 0.225 mmol) was reacted with sodium methoxide (0.054 g, 1.0 mmol) in THF (5 mL) except that the resulting mixture was stirred at room temperature for 4 days. The residue was benzoylated and chromatographed to give benzyl 3-methoxy-3-deoxy-2-*O*-[(benzyloxy)methyl]-4-*O*-benzoyl-α-D-xylopyranoside (**34**) (0.075 g, 76%): $[\alpha]_D$ +102° (*c* 0.42, $CHCl_3$). IR (film): 1720, 1610, 1600, 1020, and 1010 cm^{-1}. ^1H NMR: δ 7.28–8.20 (m, 15 H, Ar); 4.92–5.36 (m, 1 H, *H*COBz); 4.88 (d, 1 H, H-1, *J* = 4); 4.24–4.80 (m, 6 H, OCH_2Ph, OCH_2OCH_2Ph); 3.28–4.08 (m, 3 H, $HCOCH_3$, H-5, H-5′); 3.60 (s, 3 H, OCH_3).

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