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Ring Opening Reactions of Benzyl 3,4-Anhydro-β-D-Ribopyranoside with Nucleophiles

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Abstract: By the proper choice of metal counterion it is possible to regioselectively cleave with a variety of nucleophiles, the epoxide ring of benzyl 3, 4- anhydro-β-D -ribopyranoside. The resulting 3-deoxy 3-substituted or 4-deoxy 4-substituted glycosides were obtained in good yields. Factors governing the regiochemistry of ring opening are discussed.

INTRODUCTION

The utility of sugar epoxides in the synthesis of deoxy substituted sugars by nucleophilic cleavage of the three membered ring is well established. Some representative nucleophiles which have been used include halides, azide, mercaptides, cyanide, hydride, alkoxides and carbanions.[1]

To fully exploit the synthetic scope of this reaction, a thorough understanding of the factors which govern the regiochemistry of epoxide ring opening is essential. In stereochemically rigid steroidal epoxides, Furst and Plattner predicted trans-diaxial ring opening, as the preferred mode of cleavage.[2] This was extended to conformationally rigid sugar epoxides such as those involving a 4,6 acetal linkage or a 1,6 anhydro

bridge, leading to one principal product,via a trans-diaxial cleavage. 2,3- and 3,4- Anhydrohexopyranosides, which are more flexible, have a dominant half chair conformer in which the C-6 carbon prefers a quasi-equatorial orientation. However the regiochemistry of ring opening is correspondingly less specific than with rigid epoxides mentioned earlier. In 2,3- and 3,4- anhydropentopyranosides, even this factor is absent and the two half chair forms are freely interconvertible. The regiochemistry of ring opening in these substrates is seldom clear cut and any nucleophilic attack is governed by the Curtin-Hammett principle as the activation energy for ring opening of either conformer is much greater than the free energy difference between the conformers.[3]

Relatively few examples of the nucleophilic ring opening reactions of 3,4- anhydroribopyranosides are available in the literature. Reactions of benzyl 2,3- anhydro α-D-ribopyranoside with TMSCN and $Pd(PhCN)_2Cl_2$ to give C-3 substituted xylo derivatives,[4] whereas with LiBr/tetramethylurea, 2-benzyloxy -2,5- dihydrofuran -4- carboxaldehyde is formed exclusively.[5] In the case of alkyl 2,3- anhydro -β-D-ribopyranosides, ring opening studies are well represented.[1] In most cases, the ring opens exclusively at C-3 to give C-3 substituted xylo derivatives. Reaction of benzyl 2,3-anhydro-β-D-ribopyranoside with LiBr/HMPA yields 2-benzyloxy -2,5-dihydrofuran -4-carboxaldehyde and 4-bromo- 4-deoxy- α-L-lyxopyranoside in a ratio of 1.8:1.[6]

In an attempted synthesis of pseudomonic acid C involving nucleophilic ring opening of benzyl 3,4- anhydro -α-D-ribopyranoside as a key step, we observed that reaction occured exclusively at C-3. This result was rationalized as shown in fig.1. Of the two conformers **A** and **B**,

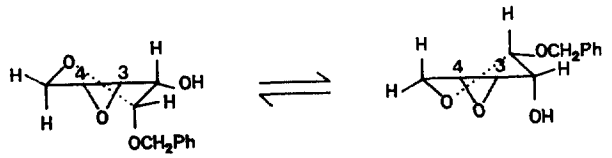


Fig 1

A is the preferred one due to the anomeric effect. It was suggested that nucleophilic attack on **A** occurs at C-3 than at C-4 as the approach of the nucleophile to the latter position involves a repulsive interaction between the incoming nucleophile and pyranose oxygen lone pair.[7] Such an interaction is absent for attack at C-3 and, in the absence of steric factors, ring opening takes place at C-3. In the β-series, it is reported that methyl, ethyl and benzyl 3,4- anhydro-β-ribopyranosides undergo preferential nucleophilic ring opening at C-4, leading to

4-deoxy-4-substituted-lyxose derivatives(Scheme 1). Thus, reaction of methyl 3,4-anhydro-β-L-ribopyranoside with hydrobromic acid and amines gave mainly 4-substituted lyxopyranosides.[8] Similarly, the corresponding ethyl glycoside on treatment with sodium methoxide furnished the C-4 and

Scheme 1

$R=CH_3$: X=Br, NH_2, NHMe, NMe_2, NHPh.
$R=CH_2CH_3$: X=OMe(65:19 ratio, 4:3 subs.) $X=SCH_2Ph$ (at -20°)

C-3 substituted sugars in the ratio of 65:19.[9] The same epoxide reacted with sodium benzyl mercaptide at -20° to give exclusively the 4-lyxo product while at room temperature and above a small amount of C-3 ring opened product was also seen.[10] Magnusson and co-workers observed that benzyl 3,4-anhydro-β-D-ribopyranoside and lithium bromide in HMPA gave 4-bromo-4-deoxy-α-L-lyxopyranoside as a minor product,the major product being the 2(R)-(benzyloxy)-2,5-dihydrofuran-4-carboxaldehyde.[6] Finally, Keck showed that benzyl 3,4-anhydro-D-ribopyranosides and hydriodic acid in acetone gave ring opening at C-4.[11]

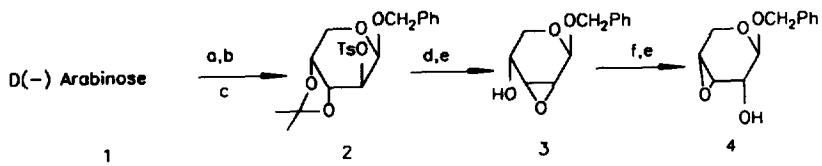
These results indicate that the regiochemistry of ring opening of a 3,4-anhydroribopyranoside is dependent upon the configuration at the anomeric carbon. As only a limited number of examples were available in the β-series, we chose to investigate the ring opening reactions of benzyl 3,4-anhydro-β-D-ribopyranoside. Such a study, we felt, would serve to better understand the factors governing the regiochemistry of ring opening of sugar epoxides. It would also provide a useful comparison to the result of our previous work on the corresponding α- anomer.[7]

RESULTS

Benzyl 3, 4-anhydro-β-D-ribopyranoside (**4**) was prepared as reported[6] from D(-)-arabinose. (Scheme 2). The physical and spectral properties of **4** were in agreement with those reported in the literature.[6]

Sugar epoxides are known to adopt half-chair conformations,with the anomeric substituent prefering the quasi-axial orientation.[12] Thus,of the two possible conformers **4A** and **4B**,(fig.2) **4A**, in which the epoxide has the ^1H conformation, is likely to be the major one in the equilibrium at

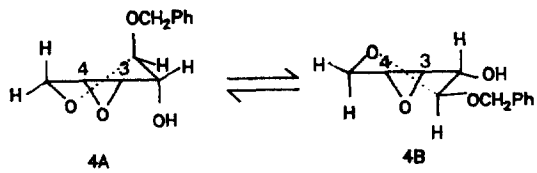
Scheme 2



1 2 3 4

a) $PhCH_2OH$, dry HCl gas b) Acetone, Conc.H_2SO_4, anhydr.$CuSO_4$, rt c) TsCl, pyridine, rt d) 1N H_2SO_4, acetone:H_2O (1:10), reflux e) MeONa, MeOH, rt f)LiBr, 1, 1, 1-trichloroethane, reflux.

room temperature.This is supported by the $J_{1,2}$ coupling constant of 2.2 Hz (in $CDCl_3$),suggesting that the protons H_1 and H_2 are diequatorially disposed in the major conformer. However,the free energy difference between **4A** and **4B** is likely to be small as was shown earlier for the



4A 4B

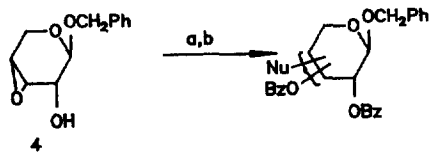
Fig 2

corresponding α-anomer by semi-empirical SCFMO calculations.[7] An approximate value of this free energy difference is about 1 Kcal $mole^{-1}$,estimated using the observed $J_{1,2}$ coupling constant and the values given by Zamojski for $J_{1,2}$ in closely related systems.[13] Therefore, it is reasonable to assume that the product ratios in the nucleophilic ring opening of **4** would be governed by the Curtin-Hammett principle.[3,14]

As shown in the Table 1,nucleophilic ring opening of **4** was carried out with variety of nucleophiles.The counter cation was also varied to examine its influence on the course of the reaction. For the purposes of analysis and identification, the crude product mixture was benzoylated and the isomeric dibenzoates were separated and characterized. The regio- and stereochemistry of the ring opened products were established by ^1H COSY experiments and an incisive analysis of the vicinal proton coupling constants, respectively.

Ring opening at C-3 provided benzyl 3-deoxy -3-substituted β-D-xylopyranoside derivatives while cleavage of the C-4-oxygen bond furnished benzyl 4-deoxy-4-substituted-α-L-lyxopyranoside derivatives. NMR data clearly showed that in the former family of compounds both $^1C_4$ and

Table 1: Ring opening reactions of **4** with different nucleophiles



a) Nucleophile b) PhCOCl, pyridine, rt.

Entry	Nucleophile	Metal Counter cation	Solvent	Yield %	Product (%) C-4	Product (%) C-3
1	H	Li^+	THF	78	6 (07)	7 (93)
2	H	Na^+	EtOH	60[a]	6 (47)	7 (53)
3	Br	Li^+	THF	51[b]	8 (100)	-----
4	Br	Mg^{2+}	THF	74	9 (21)	10 (79)
5	I	Li^+	THF	38	11 (85)	12 (15)
6	I	Na^+	THF	72	11 (96)	12 (04)
7	I	Al^{3+}	CH_3CN	50	11 (60)	12 (40)
8	I	Mg^{2+}	THF	72	11 (19)	12 (81)
9	I	Mg^{2+}	benzene	71	11 (18)	12 (82)
10	I	$(n\text{-}Bu)_4N^+$	THF	no reaction		
11	CN	K^+	DMSO	59[b]	14 (65)[c]	-------
12	C≡CH	Na^+	THF	no reaction		
13	C≡CH	$MgBr^+$	THF	83[d]	9 (11)	10 (89)
14	N_3	Na^+	DMF	70	15 (59)	16 (41)
15	N_3	Na^+	THF	no reaction		
16	SPh	Na^+	THF	80	17 (48)	18 (52)
17	OMe	Na^+	MeOH	73	19 (76)	20 (24)
18	OMe	Mg^{2+}	MeOH	70	19 (07)	20 (93)
19	OMe	Na^+	THF	no reaction		

[a] 26% of epoxy benzoate is recovered. [b] Yield of diol.
[c] 28% of iodo derivative **13** and 7% of complex mixture.
[d] No product corresponding to ring opening by acetylide anion was observed.

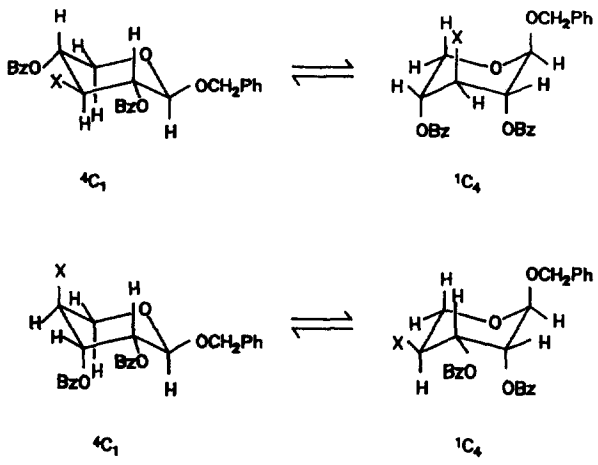


Fig 3

$^4C_1$ confomers(fig.3) are present with no marked preference for either.This is readily derived from the fact that $J_{1,2}$ varied from 4.1 to 6.3Hz (see experimental section for full details). In the α-L-lyxopyranoside series, $J_{1,2}$ varied with one exception from 1.5 to 2.3 Hz and $J_{3,4}$ and $J_{4,5}$, between 10.2 to 11.4 Hz and 10.2 to 11.5 Hz, respectively. These values are indicative of the $^1C_4$ conformer being the major one with the $^4C_1$ conformer being a minor contributor to the conformational equilibrium.

Epoxide **4** reacted with both $NaBH_4$ in ethanol and $LiAlH_4$ in THF, giving the ring opened products 6 and 7 (entries 1 and 2). While the ring opening with $NaBH_4$ was indiscriminate, yielding **6** and **7** in almost equal amounts, $LiAlH_4$ gave predominantly **7**, as a result of hydride attack at C-3.

The ^1H COSY spectrum of 6 showed a ddd signal at δ 5.66 with two cross peaks at δ 5.50 and δ 2.24. The triplet signal at δ 5.50 showed two cross peaks at δ 5.09 and δ 5.66. The doublet signal at δ 5.09 showed a cross peak at δ 5.50. The AB quartet signal at δ 4.72 showed cross peaks with one another. Therefore the doublet signal at δ5.09 was assigned as H-1. The triplet signal at δ 5.50 and ddd signal at δ 5.66 was assigned as H-2 and H-3 respectively. The multiplet signal δ 2.24 showed cross peaks with δ 5.66 and δ 4.00 and was assigned as H-4 and H-4'. Finally, a multiplet signal at δ 4.00 was assigned as H-5 and H-5'. In a similar manner, using the ^1H COSY spectrum of 7 its structure was elucidated as the 3-deoxy derivative, resulting from ring opening at C-3. Thus the

regiochemistries of **6** and **7** were assigned unambiguously.

The stereochemistry of ring opened products was secured by a careful examination of their ^1H NMR specctra, especially the coupling constants between the various protons. Thus, for example, epoxide **4** on reaction with lithium iodide gave two products **11** and **12** in a 85:15 ratio. That **11** and **12** are products of ring opening at C-4 and C-3 respectively, was clearly established from their ^1H COSY spectra, as detailed earlier for compounds **6** and **7**. To determine the stereochemistry of **11**, the coupling constsants $J_{1,2}$, $J_{2,3}$, $J_{3,4}$, $J_{4,5}$ and $J_{4,5'}$ were used. $J_{1,2}$ has a value of 1.8 Hz, suggesting a diequatorial arrangement of H-1 and H-2. Both H-2 and H-3 are double doublets with J values 3.1, 1.8 Hz and 11.1, 3.2 Hz respectively. Thus, therefore, $J_{2,3}$ is 3.1 Hz and $J_{3,4}$, 11.1 Hz. The latter value immediately leads to the conclusion that both H-3 and H-4 are axially positioned and that H-2 and H-3 bear an equatorial-axial relationship. This is further substantiated by the fact that H-5 appears as an apparent triplet (really a double doublet) with $J_{4,5}$=11.5 Hz. All these observation can be accounted for satisfactorily only when **11** is an α-L-lyxopyranoside derivative in the $^1C_4$ conformation.

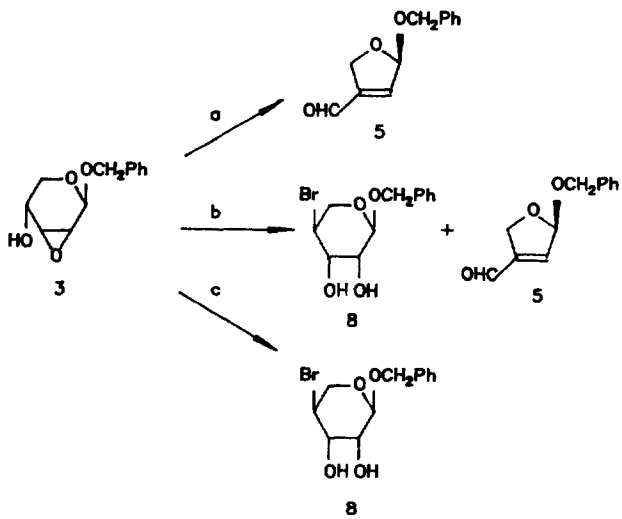
Likewise, in compound **12**, the coupling constants of significance are $J_{1,2}$=5.8Hz, $J_{2,3}$=8.6Hz, $J_{3,4}$=7.6Hz, $J_{4,5}$=4.1Hz and $J_{4,5'}$=7.4Hz. Once again, these values clearly prove that H-2, H-3 and H-4 are all axially oriented, which is possible only if **12** is of the D-xylo configuration. The major conformer of **12**, compatible with the observed coupling constants, is thus $^4C_1$.

It has been reported that lithium bromide reacts with **3** in toluene (Scheme 3) in the presence of N,N,N',N'-tetramethylurea to afford 2(R)-(benzyloxy)-2,5-dihydrofuran -4- carboxaldehyde (**5**) in 34% yield.[6] When HMPA was used instead of tetramethylurea, in addition to aldehyde **5** (25%), benzyl 4-bromo -4- deoxy-α-L-lyxopyranoside (**8**) (13%) was also obtained. Lyxopyranoside **8** was the exclusive isolated product (49%) when the solvent was 1,1,1-trichloroethane. We find that **4** suffers ring cleavage with anhydrous lithium bromide in THF to form **8** (51%)(entry 3). None of the aldehyde **5** could be detected under these conditions, even on careful examination of the crude product mixture. A marked alteration in regiochemistry occured when magnesium bromide in THF was employed. The major product **10** (79%) corresponds to bromide attack at C-3 and the minor product **9** (21%) arises from cleavage of the C-4 oxygen bond (entry 4).

With iodide as nucleophile, the regiochemistry of the ring opening of **4** was very much dependent upon the nature of the counter cation. While lithium iodide in THF gave the C-4 and C-3 ring opened products **11** and **12**, respectively, in a 85:15 ratio(entry 5), sodium iodide furnished the same in a 96:4 ratio (entry 6). Aluminum iodide in acetonitrile afforded **11** and

12 with lesser selectivity (3:2)(entry 7). Magnesium iodide reversed the regioselectivity in both THF and benzene, **11** and **12** were now obtained in a 19:81 ratio (THF)(entry 8) and 18:82 ratio (benzene)(entry 9). Finally, **4** was recovered unchanged on an attempted reaction with tetra-n-butylammonium iodide in THF(entry 10). The chemical yields of the ring opened products are lower when lithium halides are used, perhaps due to competing ring contraction to 2(R)-(benzyloxy)-2,5-dihydrofuran -4-carboxaldehyde (**5**), followed by its decomposition under the reaction conditions.

Scheme 3



a) LiBr, tetramethylurea, toluene. b) LiBr, HMPA, toluene. c)LiBr, 1,1,1 trichloroethane.

When the nucleophile was cyanide, activation of **4** with titanium tetraisopropoxide and tetra-n-butylammonium iodide, as reported by Sharpless, was found necessary.[15] Under these conditions, benzyl 4-deoxy-4-cyano-α-L-lyxopyranoside (**14**) was obtained as the major product, accompanied by benzyl 4-deoxy-4-iodo-α-L-lyxopyranoside (**13**)(entry 11). It is interesting to note that **13** is not formed in the experiments with iodide reported earlier. Potasium cyanide in 1,3- dimethyl-2-imidazolidone was inactive on attempted reaction with **4**, while sodium cyanide in DMF gave a low yield of **14**.

Both sodium acetylide and ethynylmagnesium bromide were unsuccessful in attempts to open up **4** with the acetylide anion. While no reaction was observed with sodium acetylide(entry 12),the Grignard reagent

functioned as a bromide source and the products **9** and **10** were formed in a 11:89 ratio(entry 13). Such halide induced ring openings of epoxides when Grignard reagents are used is well documented.[16] Sodium azide in DMF cleaved **4** to furnish in a 3:2 ratio the C-4 and C-3 opened products **15** and **16**, respectively(entry 14). Epoxide **4** was unreactive towards sodium azide in THF even after prolonged reaction times at reflux(entry 15). Similarly, sodium thiophenoxide in THF gave almost equal amounts of **17**(48%) and **18**(52%)(entry 16).

Finally, when methoxide was employed as a nucleophile, the regiochemistry of the ring opening of **4** again showed a cation dependence. Sodium ethoxide in methanol gave as the major product the C-4 ring opened compound **19**(76%) versus the C-3 isomer **20**(24%)(entry 17). With magnesium methoxide in methanol, the ratio of **19**:**20** was 7:93(entry 18).Epoxide **4** was inert towards sodium methoxide in THF(entry 19).

DISCUSSION

A perusal of the results obtained,as detailed in the previous section, makes it evident that a number of factors have to be considered to understand the regiochemistry of ring opening of **4**. The more important amongst them are conformational and stereoelectronic factors and the nature of the counter cation.

Epoxide **4** can adopt two half chair conformations **4A** and **4B**. NMR studies clearly indicate that both conformations are present(See Results section).Furthermore, the value of the free energy of conformational interconversion is small, especially in comparison with the activation energy for ring opening. This means that the Curtin-Hammett principle should apply to these reactions.[2] The more favourable reaction pathway would then depend upon the difference in the transition state energies leading to the two products, with the provision that the Furst-Plattner rule, involving a trans diaxial ring opening is obeyed in each instance.[17] A prediction of the more favourable transition state can be made based on the premise that many of the non-bonded interactions that exist in the ground state conformers are also present in the corresponding transition states. There is precedent in the literature that the major product in most cases, is derived from a transition state containing the anomeric alkoxyl group in the more stable axial conformation.[1,18]

All these factors, as applied to epoxide **4**,suggest that conformer **4A** with the anomeric substituent in a quasi-axial position, is likely to lead to a transition state with lower energy than that obtained from conformer **4B**, where the anomeric substituent is quasi-equatorial. Attack by the nucleophile at C-4 of conformer **4A** in preference to C-3, leads to

a transition state with fewer 1,3 -diaxial interactions and finally results in a 4- substituted 4-deoxy -α-L-lyxopyranoside. The alternate conformer **4B**, in a similar fashion, would be preferentially cleaved at C-3, as attack at C-4 entails a repulsive 1,3- diaxial interaction between the incoming nucleophile and the lone pair of electrons on the pyranose oxygen.[7] On this basis, it is reasonable to predict that the preferred mode of attack will be at C-4 of the epoxide **4** via conformer **4A**. Attack on conformer **4B**, at best a minor pathway, will be preferentially at C-3. As mentioned in the introduction, this is what is seen with methyl, ethyl and benzyl 3,4- anhydro-β-L-ribopyranosides in the limited number of examples available. The major product results from attack at C-4 and attack, at C-3, if any, minor.

Our results, while largely in agreement with those reported earlier, indicate that ring opening occurs preferentially at C-4 with C-3 as a minor pathway when lithium, sodium, potassium and aluminum are the counter cations. The exact ratio of C-4 and C-3 ring opened products depends on the nature of the nucleophile. However with magnesium salts, the regiochemistry is clear-cut and the major product is now derived from C-3 ring opening.

This could mean that lithium, sodium, potassium and aluminum salts react preferentially through conformer **4A** and magnesium salts react through conformer **4B** as a major pathway. An alternate explanation for the mode of attack observed with magnesium salts could be that conformer **4A** interacts with the magnesium cation and preferentially weakens the C-3 oxygen bond, which is thus easily ruptured by the incoming nucleophile. In order to be an effective regiochemical control element, this weakening and consequent saving in activation energy should be adequate to compensate for a 1,3- diaxial interaction between the anomeric group and the incoming nucleophile. The driving force for this interaction could be a stable magnesium chelate formed from the product containing a cis diaxial 1,3-diol unit.

Recently, Crotti and co-workers, in their study of nucleophilic ring opening of cis- and trans- 2- benzyloxy-4,5- epoxy tetrahydropyran found that the lithium cation exerts a significant effect on the regiochemistry of oxirane cleavage[19]. They have suggested that the role of lithium cation is to chelate and thus stabilize one conformer in preference to another, leading to regioselective ring opening. On the contrary, we find that lithium does not exert any influence, but magnesium does. A possible reason for this could be the fact that Crotti's examples have no free hydroxyl group as is present in our substrate.

Aluminium iodide, sodium borohydride, sodium azide and sodium thiophenoxide also give substantial amounts of C-3 derived products. While

the presence of aluminium and boron, capable of chelation with a cis 1,3-diol unit, is the likely cause for the enhanced formation of C-3 derived products in the first two cases, the results obtained with sodium azide and sodium thiophenoxide cannot be accommodated by this hypothesis. It is worth mentioning that while epoxide **4** does not react with tetra-n-butylammonium iodide alone, the iodo derivative **13** is formed as a minor product when Potasium Cyanide, tetra-n-butylammonium iodide and titanium tetraisopropoxide are all present. A logical conclusion which can be drawn is that **4** is now activated by titanium tetraisopropoxide and hence suffers cleavage by cyanide as well as iodide. The regiochemistry is different from that seen with magnesium iodide and can be accounted for as reported by Sharpless in his observations on the nucleophilic ring opening of 2,3- epoxyalcohols mediated by titanium tetraisopropoxide.[15] Lithium aluminium hydride appears to be an exception for though the cation is lithium, the major product is derived from C-3 ring opening. Here, the strong coordination of the aluminum to the hydroxyl group followed by hydride delivery to the adjacent carbon could account for the regiochemistry observed.[20]

In conclusion, it is clear from our previous work [7] and the present investigation, that the regiochemistry of ring opening of benzyl 3,4- anhydroribopyranosides is critically dependent on the anomeric configuration. When the epoxide ring and the anomeric group are on the same side, the regiochemistry is controlled by a polar repulsive interaction between the incoming nucleophile and the pyranose oxygen lone pair of electrons, directing the attack at C-3. If the epoxide ring and the anomeric substituent are anti to one another, the regiochemistry is now largely controlled by a steric repulsive 1,3- diaxial interaction between the entering nucleophile and the anomeric group, and hence ring opening now occurs at C-4. When a good chelating cation like magnesium is present as the counter cation, the regiochemistry of ring opening is reversed in favour of C-3, probably due to weakening of the C-3 oxygen bond because of chelation with the metal ion.

CONCLUSION

We have shown that the nucleophilic ring opening of benzyl 3,4-anhydro-β-D-ribopyranoside depends upon both the nucleophile used as well as its counter cation. Whilst good C-3 selectivity is obtained with magnesium as counter cation, in other cases the discrimination between C-3 and C-4 ring opening is not so clear-cut.

EXPERIMENTAL

Melting points were determined by using a SUPERFIT melting point apparatus and are uncorrected. Optical rotations were measured with an Autopol II automatic polarimeter at 25°. IR spectra were recorded on Perkin-Elmer Model 1310 spectrophotometer or JASCO FT-IR 5300 instruments. Solid samples were prepared as KBr wafers and liquid samples as a film between NaCl plates. ^{1}H NMR (200 MHz) and ^{13}C NMR (50 MHz) were obtained with a BRUKER AF 200 NMR 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). 2D NMR data were processed using standard software provided with the instrument. Elemental analyses were performed on a Perkin-Elmer 240 C CHN analyser.

Analytical TLC was performed on glass plates coated with 250μm and preparative TLC on glass plates coated with 0.1cm Acme silica gel GF_{254} and visualised by shining UV light and usually eluted with 2-10% ethyl acetate in hexane, unless otherwise mentioned. All moisture sensitive reactions were carried out under dry nitrogen and all solvents distilled from appropriate drying agents prior to use. After appropriate work-up, the organic extract was dried over anhydrous $MgSO_4$.

Benzyl 3,4 anhydro-β-D-ribopyranoside (4) was prepared in 41% overall yield from benzyl 2,3-anhydro-β-D-ribopyranoside (3) according to ref 6. m.p. 66-68°;$[\alpha]_D^{25}$-169.1° (c 0.81,$CHCl_3$) (lit[6]m.p. 66-68°; $[\alpha]_D^{23}$ -166°(c 0.8,$CDCl_3$))

General procedure for benzoylation: Benzoyl chloride (1.1 equiv.) was slowly added to a stirred solution of alcohol (1 equiv.) in dry pyridine (5 ml) at 0°. The reaction mixture was stirred for 15h at room temperature and then poured into chilled aqueous K_2CO_3(15ml). After the mixture was stirred for 1h, the product was extracted with dichloromethane(25ml x 3). The combined organic phase was washed with aqueous $NaHCO_3$, dried and evaporated. To remove the residual pyridine, toluene (5ml x 2) was added and then evaporated from the residue. The crude benzoate was then subjected to chromatographic purification.

General procedure for debenzoylation: To a solution of the benzoate (1

equiv.) in dry methanol (5ml), was added a solution of sodium methoxide (0.1 equiv.) in methanol (0.5ml). The reaction mixture was stirred at room temperature for 30min. The reaction mixture was neutralized by adding ion-exchange resin (Amberlite-120H^+).The resin was filtered off and the methanol removed in vacuo. The residue was then recrystallised from a suitable solvent.

Reaction of **4** *with LAH.* To a stirred solution of LAH (0.009g, 0.225 mmol) in THF (2 ml) was added a solution of epoxy alchohol **4** (0.05g, 0.225 mmol) in THF (2ml). The resulting mixture was stirred at room temperature for 8h and saturated aq. Na_2SO_4 was slowly added . The precipitate formed was filtered and the cake was washed with dichloromethane (2 x5ml). The combined organic phase was dried and concentrated. The residue was benzoylated and chromotographed to give **6** and **7** in an overall yield of 78%. The fast moving spot was benzyl 4-deoxy-2,3-di-O-benzoyl-β-D-ribo -pyranoside (**6**) (0.005g): $[\alpha]_D$ -51.06°(c 0.47, $CHCl_3$). IR: 1724, 1452, 1277, 1115 and 710 cm^{-1}. ^1H NMR: δ 8.14-7.27 (m, 15H, Ar); 5.66 (ddd, 1H, H-3, J=3.2, 4.6 and 11.0); 5.50 (t, 1H, H-2, J=2.7); 5.09 (d, 1H, H-1, J=2.3); 4.84, 4.60 (dd, 2H,OCH_2Ph, J=11.9); 4.00 (m, 2H, H-5, H-5'); 2.24 (m, 2H, H-4, H-4'). ^{13}C NMR: 165.5, 137.1, 133.3, 133.0, 130.0, 129.9, 129.7, 128.5, 128.4, 127.9, 97.6, 69.5, 69.4, 68.1, 58.9,and 27.2 ppm. Anal. Calcd for $C_{26}H_{24}O_6$: C, 72.21; H, 5.59. Found : C, 72.18; H, 5.62. The slow moving spot was benzyl 3-deoxy-2,4-di-O-benzoyl-β-D-ribo -pyronoside (**7**) (0.071g): mp 115-117°(ethanol-water). $[\alpha]_D$ -83.33° (c 0.6, $CHCl_3$). IR(KBr): 1718, 1452, 1282, 1086,and 756 cm^{-1}. ^1H NMR: δ 7.99-7.21 (m, 15H, Ar); 5.09 (m, 2H, H-2, H-4); 4.99 (s, 1H, H-1); 4.81, 4.62 (dd, 2H, OCH_2Ph, J=12.2); 4.17 (dd, 1H, H-5, J=1.96 and 12.94); 3.92 (dt, 1H, H-5', J=1.95 and 12.74); 2.43 (m, 2H, H-3 and H-3'). ^{13}C NMR: 165.7, 165.4, 133.0, 132.9, 129.9, 129.8, 128.5, 128.2, 128.0, 96.1, 69.4, 67.4, 66.3, 61.4 and 26.9 ppm. Anal. Calcd for $C_{26}H_{24}O_6$: C, 72.21; H, 5.59. Found: C, 72.32; H, 5.52.

Reaction of **4** *with Sodium borohydride.* To a stirred solution of $NaBH_4$ (0.009g, 0.225 mmol) in ethanol (2 ml) was added a solution of epoxy alcohol **4** (0.050g, 0.225 mmol) in ethanol (2ml). The resulting mixture was refluxed for 24h. The reaction mixture was cooled and ethanol was removed in vacuum. The residue was partitioned between water (5 ml) and chloroform (15 ml). The chloroform layer was separated and the aqueous layer was extracted with chloroform (2 x 15 ml).The combined chloroform extract was dried and concentrated. The residue was benzoylated and chromatographed to give **6** (0.027g), **7** (0.031g) and epoxy benzoate (0.019g). Epoxy benzoate was debenzoylated to give epoxy alcohol **4** (0.011g).

Reaction of **4** *with Lithium Bromide.* To a stirred solution of LiBr (0.039g, 0.45 mmol) in THF (2 ml) was added a solution of epoxy alcohol **4** (0.050g, 0.225 mmol) in THF (2 ml). The resulting mixture was refluxed for 2h. The reaction mixture was cooled and THF was removed under vacuum. The residue was partitioned between water (10 ml) and chloroform (20 ml). The chloroform layer was separated and the aqueous layer was extracted with chloroform (2 x 20 ml). The combined chloroform layers were dried and concentrated. The residue was crystallised from toluene to give benzyl 4-bromo-4-deoxy-α-L-lyxopyranoside (**8**) (0.035g, 51%): mp 138-140°, $[\alpha]_D$ -63.1°(c 0.95, $CHCl_3$). (lit[6]mp 139-141°, $[\alpha]_D$ +61°(c 0.9, $CHCl_3$)). ^1H NMR: δ 7.35(m, 5H, Ar); 4.95(s,1H, H-1); 4.76, 4.51 (dd, 2H,OCH_2Ph, J=11.9); 4.20 (m, 1H, H-4); 4.06-3.90(m, 4H, H-2, H-3, H-5, H-5′); 2.63, 2.45(d, each 1H, J=3.8 and 2.8). ^{13}C NMR: 136.3, 127.4, 126.8, 98.8, 70.3, 67.9, 62.5, 49.6ppm.

Reaction of **4** *with Magnesium Bromide.* To a stirred mixture of anhydrous magnesium bromide (1.0 mmol) prepared from Magnesium (0.024g, 1.0 mmol) and 1,2-dibromoethane (0.090 ml, 1.0 mmol) in THF (2 ml) was added a solution of epoxy alcohol **4** (0.050g, 0.225 mmol) in THF (2 ml). The resulting mixture was refluxed for 10h. After the mixture was cooled to room temperature, saturated aqueous NH_4Cl was added and the precipitate formed was filtered and cake was washed with dichloromethane (10 ml x 2). The combined organic phase was washed with water, dried and concentrated. The residue was benzoylated and chromotographed to give **9** and **10** in an overall yield of 74%. The fast moving spot was benzyl 4-bromo-4-deoxy-2,3 di-O-benzoyl-α-L-lyxopyranoside (**9**) (0.018g) which was debenzoylated to give **8** (0.009g). The slow moving spot was 3-bromo-3-deoxy-2, 4-di-O-benzoyl-β-D-xylopyronoside (**10**) (0.067g): $[\alpha]_D$ -70.27°(c 0.55, $CHCl_3$). IR: 1720, 1455, 1261, 1100,and 730 cm^{-1}. ^1H NMR: δ 8.04-7.25 (m, 15H, Ar); 5.51 (dd, 1H, H-2, J=6.5 and 8.2); 5.38 (dt, 1H, H-4, J=8.1 and 4.6); 4.90, 4.66 (dd, 2H, OCH_2Ph, J=12.4); 4.71 (d, 1H, H-1, J=5.9); 4.47 (dd, 1H, H-5, J=4.6 and 11.9); 4.35 (t, 1H, H-3, J=8.4); 3.55 (dd, 1H, H-5′, J=7.6 and 11.7). ^{13}C NMR: 165.2, 164.8, 136.8, 133.5,133.3, 129.9, 129.3, 129.2, 128.4, 128.3, 127.8, 127.6, 99.5, 72.6, 71.5, 70.2, 62.8,and 47.1 ppm. Anal. Calcd for $C_{26}H_{23}O_6Br$: C, 61.06; H, 4.53. Found: C, 60.58; H, 4.60.

Reaction of **4** *with Lithium Iodide.* To a stirred solution of LiI (0.060g, 0.45 mmol) in THF (2 ml) was added a solution of epoxy alcohol **4** (0.050g, 0.225 mmol) in THF (2 ml). The resulting mixture was refluxed for 3h. The reaction mixture was cooled and THF was removed in vacuum. The residue was

partitioned between water (10 ml) and chloroform (20 ml). The chloroform layer was separated and the aqueous layer was extracted with chloroform (2 x 20 ml) The organic extracts processed as before. The residue was benzoylated and chromotographed to give **11** and **12** in an overall yield of 38%. The fast moving spot was benzyl 4-iodo-4-deoxy-2,3 di-O-benzoyl-α-L-lyxopyranoside (**11**) (0.042g): $[\alpha]_D$ +134.7°(c 0.23, $CHCl_3$). IR: 1720, 1450, 1260, 1105 and 700 cm^{-1}. ^1H NMR: δ 8.06-7.20 (m, 15H, Ar); 5.74 (dd, 1H, H-3, J=3.2, and 11.1); 5.58 (dd, 1H, H-2, J=1.8 and 3.1); 5.12 (d, 1H, H-1, J=1.8); 4.83, 4.60(dd, 2H,OCH_2Ph, J=11.9); 4.61 (dt, 1H, H-4, J=11.3 and 5.3); 4.27 (t, 1H, H-5, J=11.5); 4.10 (dd, 1H, H-5', J=5.1 and 11.3). ^{13}C NMR: 165.1, 136.5, 132.5, 132.3, 129.9, 129.4, 128.8, 128.6, 128.4, 128.2, 128.1 97.2, 72.3, 70.7, 69.5, 65.5,and 21.8 ppm. Anal. Calcd for $C_{26}H_{23}O_6I$: C, 55.92; H, 4.15. Found : C, 55.85; H, 4.15. The slow moving spot is benzyl 3-iodo-3-deoxy-2,4-di-O-benzoyl-β-D-xylo -pyronoside (**12**) (0.007g): $[\alpha]_D$ -53.69° (c 0.75, $CHCl_3$). IR: 1730, 1452, 1259, 1107,and 709 cm^{-1}. ^1H NMR: δ 8.10-7.27 (m, 15H, Ar); 5.55 (dd, 1H, H-2, J=5.8 and 8.6); 5.41 (dt, 1H, H-4, J=4.1 and 7.6); 4.92, 4.68 (dd, 2H, OCH_2Ph, J=12.5); 4.73 (d, 1H, H-1, J=5.76); 4.45 (m, 2H, H-3, H-5); 3.58 (dd, 1H, H-5', J=7.4 and 11.9). ^{13}C NMR: 165.4, 165.2, 133.7, 133.5, 130.1, 128.5, 127.8, 99.4, 73.2, 72.4, 70.2, 63.3 and 23.7 ppm. Anal. Calcd for $C_{26}H_{23}O_6I$: C, 55.92; H, 4.15. Found: C, 55.85; H, 4.12.

Reaction of **4** *with Sodium Iodide.* To a stirred solution of NaI (0.068g, 0.45 mmol) in THF (2 ml) was added a solution of epoxy alcohol **4** (0.050g, 0.225 mmol) in THF (2 ml). The resulting mixture was refluxed for 40h. Standard work up gave a residue which was benzoylated and chromotographed to give **11** and **12** in an overall yield of 72%. The ratio of **11** (0.087g) and **12** (0.004g) was 96:4.

Reaction of **4** *with Aluminum Iodide.* To a stirred mixture of AlI_3 prepared from aluminium powder (0.012g, 0.44 mmol) and iodine (0.098g, 0.38 mmol) in acetonitrile (2 ml)[21] was added a solution of epoxy alcohol **4** (0.050g, 0.225 mmol) in THF (2 ml). The resulting mixture was refluxed for 30m. The reaction mixture was cooled and a few pieces of ice were added and stirred for 10 minutes. The aqueous layer was extracted with chloroform (3 x 20 ml) and processed as usual to give after benzoylation **11**(0.038g, 60%) and **12**(0.025g, 40%) in an overall chemical yield of 50%.

Reaction of **4** *with Magnesium Iodide.* a) To a solution of epoxy alcohol **4** (0.050g, 0.225 mmol) in benzene (4 ml) was added a solution (1 ml, 0.45 mmol) of MgI_2 in ether[22]. The resulting mixture was refluxed for 2h. The reaction mixture was cooled and diluted with dichloromethane(60 ml). The

dichloromethane layer was washed with sodium thiosulphate solution (2 x 30 ml), followed by cold water (2 x 30 ml) and dried. The solvent was concentrated under vacuum. The residue was benzoylated and chromotographed to give **11**(0.016g, 18%) and **12**(0.073g, 82%) in an overall yield of 71%.
b) A solution of the epoxy alcohol **4** (0.050g, 0.225 mmol) in THF (4 ml) was reacted with a solution of MgI_2 (1 ml, 0.45 mmol) in ether under identical conditions as the previous one. The resulting residue was benzoylated and chromotographed to give **11** and **12** in an overall yield of 72%. The ratios of **11**(0.017g) and **12**(0.074g) was 19:81.

Reaction of **4** *with Potasium Cyanide.* To a stirred solution of epoxy alcohol **4** (0.08g, 0.36 mmol) in dry DMSO (5 ml) was added KCN (0.052g, 0.8 mmol) followed by tetra-n-butylammonium iodide (0.295g, 0.8 mmol). After 5 min, titanium tetraisopropoxide (0.285 ml, 0.96 mmol) was slowly injected and the resulting mixture was stirred at room temperature for 72h. 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 1h). The organic phase was separated, washed with water and aqueous $NaHCO_3$, dried and concentrated. The residue was chromatographed with 30% ethyl acetate-hexane as elutant. The purified product contained benzyl 4-iodo -4- deoxy-α-L-lyxopyranoside(**13**) (0.023g), which on benzoylation gave **11**, a complex mixture (0.005g) and benzyl 4-cyano -4-deoxy-α-L-lyxopyrano -side(**14**) (0.053g), which on benzoylation gave benzyl 4-cyano -4-deoxy-2,3-di-O-benzoyl-α-L-lyxopyranoside(**14A**) (0.074g, 76%): $[\alpha]_D$ -49.62°(c 0.66, $CHCl_3$). IR: 2249, 1732, 1273, 1114 and 709 cm^{-1}. ^1H NMR: δ 8.03-7.26 (m, 15H, Ar); 5.85 (dd, 1H, H-3, J=3.2, and 11.4); 5.63 (t, 1H, H-2, J=2.7); 5.07 (d, 1H, H-1, J=2.1); 4.82, 4.62 (dd, 2H,OCH_2Ph, J=11.7); 4.14 (m, 2H, H-5, H-5'); 3.58 (m, 1H, H-4). ^{13}C NMR: 165.2, 165.0, 136.3, 133.8, 133.7, 130.0, 129.3, 128.8, 128.6, 128.2, 116.5, 97.2, 70.1, 68.0, 67.7, 59.3,and 29.8 ppm. Anal. Calcd for $C_{27}H_{23}O_6N$: C, 70.88; H, 5.06; N, 3.06. Found : 70.75; H, 5.09; N, 3.10.

Reaction of **4** *with Ethynylmagnesium Bromide.* To a solution of ethynylmagnesium bromide (3 ml, 0.15 mmol) in THF[23] was added a solution of epoxy alcohol **4** (0.100g, 0.45 mmol) in THF (2 ml) and the resulting mixture was stirred at room temperature for 48h. The reaction mixture was quenched with saturated ammonium chloride solution (20 ml). The aqueous layer was extracted with chloroform (3 x 40 ml) and worked up as usual. The residue was benzoylated and chromotographed to give **9** and **10** in an overall yield of 83%. The fast moving spot was benzyl 4-bromo-4-deoxy-2,3-di-O-benzoyl-α-L-lyxopyranoside (**9**) (0.017g) which was debenzoylated to give **8** (0.009g) The slow moving spot was benzyl 3-bromo-3-deoxy-2,

4-di-O-benzoyl-β-D-xylopyronoside (10) (0.174g).

Reaction of **4** *with Sodium Azide.* To a stirred solution of epoxy alcohol **4** (0.050g, 0.225 mmol) in DMF (3 ml) was added NaN_3(0.033g, 0.5 mmol). The resulting mixture was stirred at 80°C for 10h. It was cooled to room temperature and diluted with 1:1 acetone-ether (10 ml) and filtered. The filtrate was washed with water, dried and concentrated. The residue was benzoylated and chromatographed to give **15** and **16** in an overall yield of 70%. The fast moving spot was benzyl 4-azido-4-deoxy-2,3-di-O-benzoyl -α-L-lyxopyranoside (**15**) (0.044g): $[\alpha]_D$ +114.6°(c 0.41, $CHCl_3$). IR: 2100, 1720, 1575, 1280, and 700 cm^{-1}. ^1H NMR: δ 8.10-7.26 (m, 15H, Ar); 5.63 (m, 2H, H-2, H-3) 5.02 (d, 1H, H-1, J=1.5); 4.79, 4.59 (dd, 2H,OCH_2Ph, J=11.9); 4.23 (m, 1H, H-4) 3.96 (dd, 1H, H-5, J=5.5 and 11.2); 3.75 (dd appears as triplet, 1H, H-5', J=11.2). ^{13}C NMR: 165.3, 136.5, 133.5, 133.3, 129.8, 129.4, 129.3, 128.6, 128.4, 128.1, 128.0, 96.9, 71.2, 69.7, 69.6, 60.8,and 56.9 ppm. Anal. Calcd for $C_{26}H_{23}N_3O_6$: C, 65.95; H, 4.89; N, 8.87. Found : C, 66.0; H, 4.91; N, 8.86.The slow moving spot was benzyl 3-azido- 3-deoxy-2,4-di-O-benzoyl-β-D-xylopyronoside (**16**) (0.031g): $[\alpha]_D$ -100.0° (c 0.32, $CHCl_3$). IR: 2100, 1720, 1600, 1450 and 1250 cm^{-1}. ^1H NMR: δ 8.07-7.26 (m, 15H, Ar); 5.25 (dd, 1H, H-2, J=6.3 and 8.6); 5.15 (dt, 1H, H-4, J=4.7 and 8.1); 4.88, 4.65 (dd, 2H, OCH_2Ph, J=12.5); 4.72 (d, 1H, H-1, J=6.3); 4.38 (dd, 1H, H-5, J=4.7 and 11.8); 4.04 (t, 1H, H-3, J=8.5); 3.54 (dd, 1H, H-5', J=8.1 and 11.8) ^{13}C NMR: 165.4, 165.0, 136.8, 133.6, 133.5, 130.0, 129.9, 129.3, 129.1, 128.6, 128.5, 127.9, 127.8, 99.1, 71.0, 70.2, 62.6, and 62.4 ppm. Anal. Calcd for $C_{26}H_{23}N_3O_6$: C, 65.95; H, 4.89; N, 8.87. Found : C, 65.80; H, 4.88; N, 8.82.

Reaction of **4** *with sodium thiophenoxide.* To hexane washed NaH (0.010 gm, 0.225 mmol) in three necked RB flask, 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 **4** (0.050 g, 0.225 mmol) in THF (2 ml) was slowly added and the stirring was continued for another 24h at room temperature. The reaction mixture was quenched with water (1 ml) and extracted with dichloromethane (2 X 10 ml). The combined organic extracts were washed with water, sodium bicarbonate, dried and concentrated. The residue was benzoylated and chromatographed to give **17** and **18** in an overall yield of 80%. The fast moving spot was benzyl 4-(phenylthio)-4-deoxy-2,3 -di-O-benzoyl -α-L-lyxopyranoside (**17**) (0.047g): $[\alpha]_D$ +30.76°(c 0.45, $CHCl_3$). IR: 1720, 1455, 1273, 1120 and 710 cm^{-1}. ^1H NMR: δ 8.10-7.20 (m, 20H, Ar); 5.62 (m, 2H, H-2, H-3) 5.02 (s, 1H, H-1); 4.75, 4.53 (dd, 2H, OCH_2Ph, J=11.9); 3.92 (m, 3H, H-4, H-5, H-5'). ^{13}C NMR: 165.4, 136.8, 133.5, 133.4, 133.1, 132.1, 129.8, 129.1,

128.5, 128.3, 128.0, 127.9, 97.2, 70.0, 69.8, 69.3, 62.8,and 44.9 ppm. Anal. Calcd for $C_{32}H_{28}O_6S$: C, 71.09; H, 5.22. Found : C, 70.95; H, 5.19. The slow moving spot was benzyl 3-(phenylthio)-3-deoxy-2,4-di-O-benzoyl -β-D- xylopyronoside (**18**) (0.049g): $[\alpha]_D$ -71.35° (c 0.92, $CHCl_3$). IR: 1722, 1452, 1271, 1111 and 711 cm^{-1}. ^1H NMR: δ 8.00-7.24 (m, 20H, Ar); 5.34 (dd, 1H, H-2, J=4.1 and 5.5); 5.10 (dt, 1H, H-4, J=5.3 and 3.3); 4.86 (d, 1H, H-1, J=2.6); 4.90, 4.64 (dd, 2H, OCH_2Ph, J=12.4); 4.50 (dd, 1H, H-5, J=3.0 and 12.4); 3.71 (m, 2H, H-3, H-5'). ^{13}C NMR: 165.7, 165.3, 137.1, 133.7, 133.2, 133.1, 130.0, 129.9, 129.7, 129.2, 128.4, 128.3, 128.0, 127.7, 98.3, 71.0, 69.8, 61.0, and 49.0 ppm. Anal. Calcd for $C_{32}H_{28}O_6S$: C, 71.09; H, 5.22. Found : C, 71.05; H, 5.25.

Reaction of **4** *with Sodium Methoxide.* To a solution of NaOMe (0.054g, 1.0 mmol) in methanol (2 ml) was added a solution of epoxy alcohol **4** (0.050g, 0.225 mmol) in methanol (2 ml). The resulting mixture was refluxed for 12h. The reaction mixture was cooled and methanol was removed in vacuum. The residue was patitioned between water (10 ml) and chloroform (20 ml). The chloroform layer was separated and the aqueous layer was extracted with chloroform (2 x 20 ml). The combined chloroform extract was dried and concentrated. The residue was benzoylated and chromatographed to give **19** and **20** in an overall yield of 73%. The fast moving spot was benzyl 3-methoxy-3-deoxy-2, 4-di-O-benzoyl-β-D-xylo pyronoside (**20**) (0.018g): $[\alpha]_D$ -73.54° (c 0.77, $CHCl_3$). IR: 1720, 1455, 1260, 1100, and 705 cm^{-1}. ^1H NMR: δ 7.97-7.16 (m, 15H, Ar); 5.19 (dd, 1H, H-2, J=4.0 and 4.8); 5.09 (dt, 1H, H-4, J=5.4 and 3.7); 4.72 (d, 1H, H-1, J=4.2); 4.80, 4.56 (dd, 2H, OCH_2Ph, J=12.5); 4.28 (dd, 1H, H-5, J=3.5 and 12.2); 3.69 (t, 1H, H-3, J=5.6); 3.56 (dd, 1H, H-5', J=5.4 and 12.2) 3.49 (s, 3H, OCH_3). ^{13}C NMR: 165.7, 165.3, 137.1, 133.2, 129.9, 129.8, 128.4, 127.8, 98.0, 77.8, 70.2, 69.6, 60.3 and 59.1 ppm. Anal. Calcd for $C_{27}H_{26}O_7$: C, 70.11; H, 5.66. Found : C, 70.25; H, 5.68.The slow moving spot was benzyl 4-methoxy -4-deoxy-2,3 -di-O-benzoyl-α-L-lyxopyranoside (**19**) (0.058g): $[\alpha]_D$ +16.56°(c 0.84, $CHCl_3$). IR: 1728, 1452, 1275, 1111 and 711 cm^{-1}. ^1H NMR: δ 8.10-7.28 (m, 15H, Ar); 5.69 (m, 2H, H-2, H-3) 5.03 (d, 1H, H-1, J=2.3); 4.85, 4.63 (dd, 2H,OCH_2Ph, J=11.9); 3.94 (m, 3H, H-4, H-5, H-5') 3.47 (s, 3H, OCH_3). ^{13}C NMR: 165.4, 136.8, 133.3, 133.0, 129.8, 129.7, 128.5, 128.3, 127.9, 97.0, 74.8, 71.6, 70.6, 69.4, 61.1,and 58.9 ppm. Anal. Calcd for $C_{27}H_{26}O_7$: C, 70.11; H, 5.66. Found : C, 70.25; H, 5.69.

Reaction of **4** *with Magnesium Methoxide.* To a stirred suspension of $Mg(OMe)_2$ (1.0 mmol) prepared from Mg (0.024g, 1.0 mmol) and methanol (2 ml) was added a solution of epoxy alcohol **4** (0.050g, 0.225 mmol) in methanol (2 ml). The resulting mixture was refluxed for 12h. The reaction

mixture was cooled and concentrated. The residue was partitioned between 5% HCl(20 ml) and chloroform (20 ml) and worked up as usual. The residue was benzoylated and chromatographed to give **19** and **20** in an overall yield of 70%. The ratio of **19:20** was 7:93.

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