Pergamon

Tetrahedron 54 (1998) 14065–14080

TETRAHEDRON

[2+2]Cycloaddition of Chlorosulfonyl Isocyanate to (*Z*) 3-*O*-(2'-Silylvinyl) Ethers of 1,2-*O*-Isopropylidene-5-*O*-trityl-α-D-xylofuranose

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Received 14 July 1998; revised 24 August 1998; accepted 10 September 1998

Abstract: The asymmetric [2+2]cycloaddition of chlorosulfonyl isocyanate to 1,2-*O*-isopropylidene-3-*O*-(2'-silylvinyl)-5-*O*-trityl-α-D-xylofuranoses proceeds with high steroselectivity in a good yield to afford the corresponding azetidin-2-ones with (*R*) configuration at the newly formed stereogenic center. The bulky *t*-butyldimethylsilyl substituent causes partial epimerization at C-3' carbon atom of the azetidin-2-one ring. Intramolecular alkylation of the nitrogen atom by the terminal carbon of the sugar chain gives 1-oxacephams; basic conditions of cyclization cause desilylation or partial desilylation of products.

Keywords: azetidinones, cycloadditions, vinyl ethers, isocyanate

The [2+2]cycloaddition of chlorosulfonyl isocyanate (CSI) to 3-*O*- [1-3] and 5-*O*-vinyl [4] ethers of 1,2-*O*-isopropylidene glucofuranoses proceeds with excellent stereoselectivity to afford corresponding azetidin-2-ones with (*R*) configuration at C-4' in the case of the former, but (*S*) configuration at C-4' in the case of the latter.

We have shown that stereoselectivity of [2+2]cycloadditions is sterically controlled. In the case of 3-*O*-vinyl ethers, the bulky R^1 substituent promotes excellent stereoselectivity [1,3], whereas in the case of 5-*O*-vinyl ethers, reducing the size of the substituent at the C-3 carbon atom of the sugar increases stereoselectivity (Scheme 1) [4]. The cycloaddition of CSI to (*E*) and (*Z*) 3-*O*-butyl-1'-enyl-1,2-*O*-isopropylidene-5-*O*-trityl-α-D-xylofuranoses proceeds stereospecifically affording a *trans* substituted azetidin-2'-one from the (*E*) olefin and a *cis* substituted azetidin-2'-one from the (*Z*) olefin [2]; in both cases (*R*) configuration is induced at the C-4' atom of the azetidin-2'-one ring (Scheme 1) [2]. It should be noted that cycloaddition of CSI to but-1'-enyl ethers proceeds in a significantly better yield [2] than the corresponding simple vinyl ethers [1,3,4].

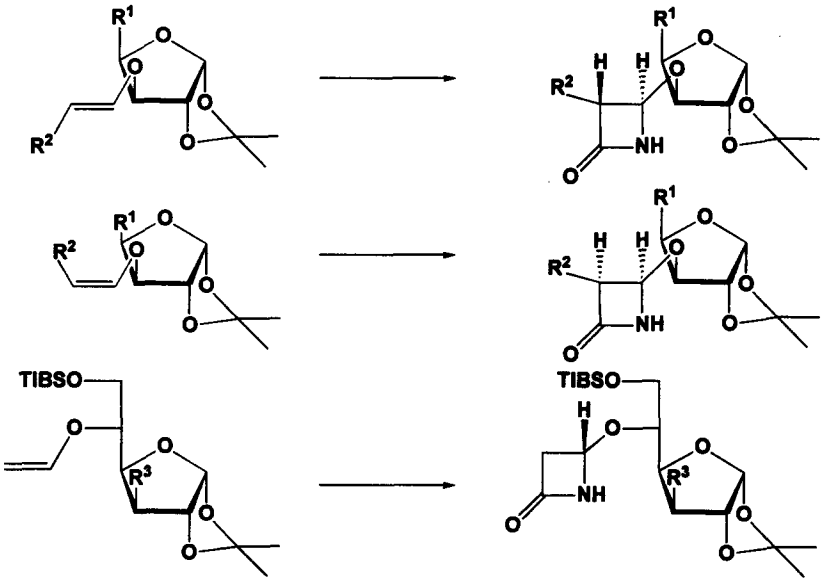
Introduction of the silyl atom to the vinyl ether should open access to "sila-β-lactams" of potential microbiological activity, although, the known [5] compounds have not displayed any

0040-4020/98/$ - see front matter
PII: S0040-4020(98)00857-6

relevant antibiotic activity. 3-Silylated-4-alkoxy-azetidin-2-ones can be subjected to further functionalizations at the C-3 carbon atom *via* stereospecific introduction of a hydroxy function [6-9], or *via* alkylation induced by fluoride anion [10,11]. Moreover, bearing in mind the high yield of [2+2]cycloaddition of CSI to but-1'-enyl ethers [2], we expected even higher yields for silylated vinyl ethers.

For the present work we synthesized three vinyl ethers **6-8** with double bonds of (*Z*) configuration. As starting material, readily available sugar **1** was used. Compound **1** was transformed into acetylene **2** according to the known procedure (Scheme 2) [12]. Acetylene **2** was subjected to silylation with TMS chloride, dimethylphenylsilyl chloride, or *t*-butyldimethylsilyl chloride to afford silylated acetylenes **3-5** which were in turn hydrogenated over Lindlar's catalyst, or reduced with DIBAL-H to give (*Z*) olefins **6-8**, respectively, in excellent yield. Attempts to obtain (*E*) configuration of the double bond *via* reduction of the silylated triple bond using complex hydrides, or sodium in liquid ammonia were unsuccessful. This followed Denmark and Thorarensen's [13] observations.

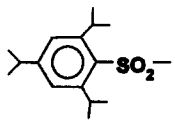
Scheme 1



R^1 = CH—CH_2, CH_2OTs, CH_2OTIBS, CH_2OSiPh_3, CH(OTs)—CH_2(OTs), CH(OTs)—CH_2(OSi*t*-BuMe$_2$), CH_2OTr

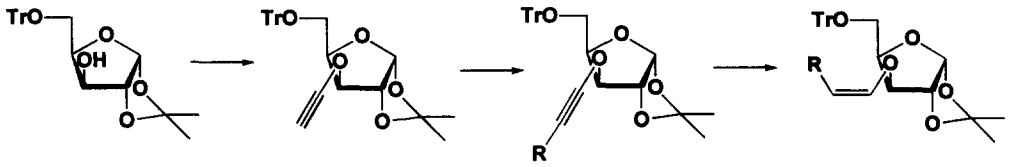
R^2 = H, Et

R^3 = H, OCH_3, OBn, OCH_2SCH_3, $OCHPh_2$

TIBS = 

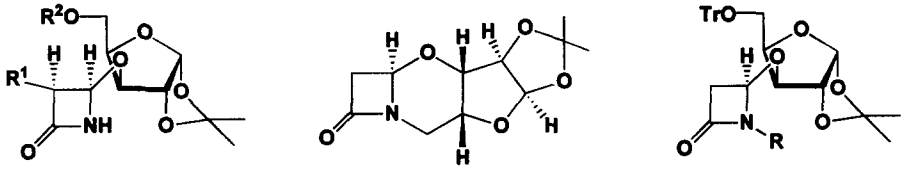
[2+2]Cycloaddition of acid-free CSI [14] to vinyl ethers **6** and **7** performed at -78 °C in anhydrous toluene, followed by the reduction of the *N*-chlorosulfonyl group with Red-Al [15] afforded the β-lactams **9** and **10** as single *cis* diastereomers in 51% and 47% yield, respectively. The trityl substituent in **9** and **10** was removed by hydrolysis, and the free hydroxy groups at C-5 of the sugar portion in **11** and **12** were tosylated under standard conditions to give compounds **13** and **14**, respectively. The intramolecular alkylation of the nitrogen atom in **13** and **14** using a two-phase system (anhydrous potassium carbonate/tetrabutylammonium bromide) in acetonitrile led simultaneously to desilylation and consequently to the formation of the same known [1] 1-oxacepham **15** from both substrates.

Scheme 2



1 **2** **3**: R = Me_3Si; **4**: R = Me_2PhSi; **5**: R = *t*-$BuMe_2Si$ **6**: R = Me_3Si; **7**: R = Me_2PhSi; **8**: R = *t*-$BuMe_2Si$

The formation of compound **15** [1] proved the absolute configuration of the azetidin-2'-one ring (4'R) in β-lactams **9-14** and pointed to the preferred direction of asymmetric induction, which was the same as had been found previously [1,2] for the corresponding simple ethers.



9: $R^1 = Me_3Si$, R^2 = Tr
10: $R^1 = Me_2PhSi$, R^2 = Tr
11: $R^1 = Me_3Si$, R^2 = H
12: $R^1 = Me_2PhSi$, R^2 = H
13: $R^1 = Me_3Si$, R^2 = Ts
14: $R^1 = Me_2PhSi$, R^2 = Ts

15

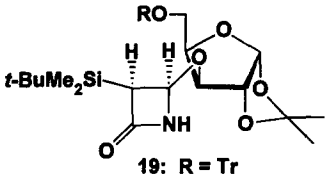
16: R = H
17: R = Bn
18: R = CO_2Et

The 3-trimethylsilyl group can be removed from the β-lactam ring even under mild basic conditions. For example, introduction of a benzyl substituent to the β-lactam nitrogen atom in **9** by benzyl bromide in the presence of sodium hydride, or under PTC conditions gave compound **17** in 77% and 60% yield, respectively. An attempt of *N*-benzylation of **9** using

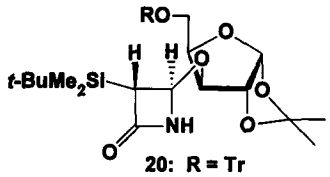
benzyl trichloroacetimidate in the presence of triflic acid [16] led to decomposition of the substrate. Desilylation of **9** took place even when the β-lactam nitrogen atom was acylated with an ethyl chloroformate-triethylamine mixture to afford compound **18**.

Addition of CSI to **8** followed by reduction proceeded in good overall yield (83%) to give four possible diastereomers **19, 20, 21** and **22** in a ratio of 7.2 : 3.5 : 1.0 : 0.3. Compounds **19, 20** and **21** were isolated and characterized. The signals due to the *trans* diastereomer **22** were visible in the ^{1}H NMR spectrum of the crude post-reaction mixture.

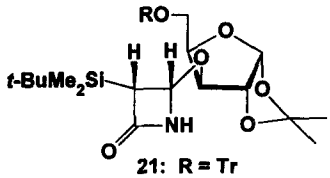
The detritylation of compounds **19** and **20** followed by tosylation of the terminal hydroxy group provided the corresponding tosylates **26** and **27**. Intramolecular alkylation transformed **26** into a mixture of three products **29, 30** and **15** in a ratio of about 1.5 : 1.5 : 2, respectively. Azetidin-2'-one **27**, under the same conditions, gave a mixture of **30** and **15** only (in a ratio of 2.3 : 1).



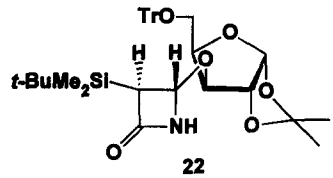
19: R = Tr
23: R = H
26: R = Ts



20: R = Tr
24: R = H
27: R = Ts



21: R = Tr
25: R = H
28: R = Ts



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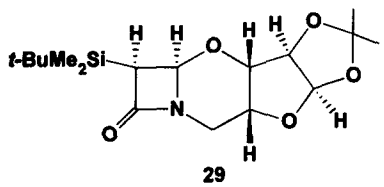
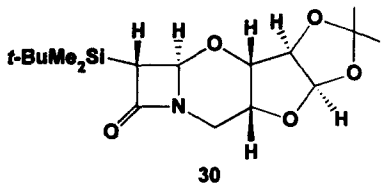
The formation of epimers at the C-3 carbon atom of the azetidin-2-one ring under basic conditions is induced by the steric hindrance of the bulky silyl substituent. The formation of desilylated product **15** proved the absolute configuration at C-4' of compounds **26** and **27**. Compound **21** was transformed into known **31** [1] *via* the same reactions sequence which involved detritylation, tosylation, alkylation and desilylation. The intermediary compounds formed were not characterized. The known (4'*S*) configuration of **31** proved the absolute configuration of **21**.

The outcome of the asymmetric induction of [2+2]cycloaddition of CSI to vinyl ethers **6-8** indicates steric control of the reaction. The large trityl substituent at the C-5 carbon atom of the sugar vinyl ether induced excellent stereoselectivity and the same direction of the asymmetric induction (4'*R*) as was found for the 3-*O*-but-1'-enyl ethers of 5-*O*-trityl-1,2-*O*-isopropylidene-α-D-xylofuranose. Replacement of trimethylsilyl or dimethylphenylsilyl by the

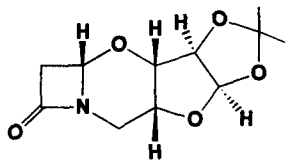
more bulky *t*-butyldimethylsilyl group decreased facial differentiation (4'*R*) *versus* (4'*S*), and caused C-3' epimerization which could occur either at the stage of cycloaddition, or during the reduction of the *N*-chlorosulfonyl group with Red-Al.



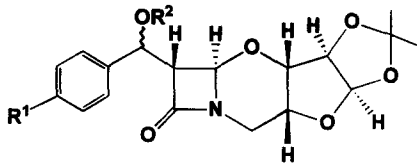
29



30



31



35: R^1 = H, R^2 = H
36: R^1 = Br, R^2 = H
37: R^1 = NO_2, R^2 = H
38: R^1 = Br, R^2 = Ac

The introduction of a silyl substituent to the vinyl ether increased the yield of [2+2]cycloaddition in comparison with that found for unsubstituted vinyl ethers [1,3,4]. The yield is similar to that reported previously for 3-*O*-butyl-1'-enyl-ethers [2]. A simple synthesis of silylated vinyl ethers and easy desilylation of 3-silylated azetidin-2-ones may offer an alternative way to cephams which are exemplified here by compounds **15** and **31**. It is worth noting that the [2+2]cycloaddition of CSI to allylsilanes followed by desilylation at C-4 of the azetidin-2-one ring has been recently used to obtain 4-silylmethyl-azetidin-2-ones in a good yield [17-19].

Attempts at hydroxyalkylation of 3'-trimethylsilyl-azetidin-2'-one **9** with acetaldehyde in the presence of cesium fluoride were unsuccessful. Compound **9** underwent rapid desilylation to give compound **16**. A similar observation has been reported when 3-trimethylsilyl-4-methoxycarbonyl-azetidin-2-one was treated with acetaldehyde and potassium fluoride [20].

Primary alkylation experiments of cepham **29** with benzaldehyde **32** p-bromobenzaldehyde **33**, and p-nitrobenzaldehyde **34** promoted by anhydrous tetrabutylammonium fluoride [21] furnished 3'-(α-hydroxybenzyl) β-lactams **35**, **36** and **37**, respectively, in a relatively good yield. β-Lactams **35-37** had 3',4'-*trans* substituted azetidin-2'-one rings, but were 3:1 epimeric mixtures at the α-hydroxybenzyl fragment. Mixtures **35-37** were not separated into pure components. Stereoisomers **36** after acetylation gave a mixture **38** which was separated by chromatography into pure components. Alkylation of **15** with aldehyde

34, promoted by LDA, proceeded in a lower yield than that involving silylated compound **29** to afford the same mixture of epimers **37**.

EXPERIMENTAL

Melting points are uncorrected. Optical rotations were measured with a JASCO Dip-360 digital polarimeter. ^{1}H NMR spectra were recorded with Bruker AM-500 and Varian Gemini AC-200 spectrometers. Signals for aromatic protons (phenyls) were not characteristic and therefore they were not included in spectral data. IR spectra were taken with a Perkin Elmer FT-IR-1600 spectrophotometer. Mass spectra were obtained with an AMD 604 spectrometer. Column chromatography was performed on Merck Silica gel (230-400 mash).

1,2-*O*-Isopropylidene-5-*O*-trityl-α-D-xylofuranose (**1**) was obtained according to the known procedure [22].

3-*O*-Ethynyl-1,2-*O*-isopropylidene-5-*O*-trityl-α-D-xylofuranose (**2**). To a suspension of oil-free potassium hydride (0.24 g, 6 mmol) in THF (5 mL) was added dropwise with stirring a solution of compound **1** (0.87 g, 2 mmol) in THF (5 mL). The mixture was stirred at room temperature for 3h, then cooled to -50°C and treated with a solution of trichloroethylene (0.31 g, 0.21 mL, 2.4 mmol) in THF (4 mL). The reaction mixture was then allowed to warm to room temperature. After being stirred for 1h, the mixture was cooled to -70°C and treated with n-BuLi (2.5 M solution in hexane, 2.4 mL, 6 mmol) dropwise. The temperature was maintained for 0.5 h. Subsequently, the mixture was warmed to 0°C, poured into a cold saturated aqueous NH_4Cl solution and extracted with toluene (3 x 30 mL). The extract was washed with brine, dried ($MgSO_4$), filtered, and concentrated. The crude product was purified by column chromatography on silica gel using hexane-ethyl acetate 97:3 $^v/_v$ as an eluent to give **2** as a white solid (0.69 g, 75%). Mp. 117.5-118.5°C; $[\alpha]_D$ -34.2° (*c* 1.0, CH_2Cl_2); IR ($CHCl_3$): 2153, 3323 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.33, 1.51 (2s, 6H, isoprop.); 1.59 (s, 1H, ≡CH); 3.36 (dd, 1H, *J* 6.9 and 9.6 Hz, H-5a); 3.46 (dd, 1H, *J* 5.9 and 9.6 Hz, H-5b); 4.31 (ddd, 1H, *J* 2.8, 5.9 and 6.9 Hz, H-4); 4.56 (d, 1H, *J* 2.8 Hz, H-3); 4.87 (d, 1H, *J* 3.8 Hz, H-2); 5.91 (d, 1H, *J* 3.8 Hz, H-1). MS (EI, HR) *m/z*: M^+ calcd for $C_{29}H_{28}O_5$: 456.1937. Found: 456.1937. Anal. Calcd for $C_{29}H_{28}O_5$: C, 76.25; H, 6.18. Found: C, 76.28; H, 6.33.

1,2-*O*-Isopropylidene-3-*O*-(2'-trimethylsilyl-ethynyl)-5-*O*-trityl-α-D-xylofuranose (**3**). To a mixture of n-BuLi (2.5 M in hexane, 0.72 mL, 1.8 mmol) and THF (6 mL) under argon was added **2** (0.68 g, 1.5 mmol) in THF (2 mL) at -50°C with stirring. The mixture was then allowed to warm up slowly to -20°C and treated with TMSCl (0.19 g, 0.23 mL, 1.8 mmol). Stirring was continued for 1h while warming up to room temperature. Subsequently,

hexane (3 x 15 mL) and saturated aqueous NH_4Cl solution (15 mL) were added. The organic layer was separated, washed with water, dried ($MgSO_4$), and concentrated. The residue was purified on a silica gel column using hexane-*t*-butyl methyl ether 97:3 $^v/_v$ as an eluent to afford **3** as a white solid (0.63 g, 80%). Mp. 106.5-108°C; $[\alpha]_D$ -23.2° (*c* 1.0, CH_2Cl_2); IR ($CHCl_3$): 2181 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.12 (s, 9H, Me_3Si); 1.34, 1.51 (2s, 6H, isoprop.); 3.35 (dd, 1H, *J* 6.6 and 9.6 Hz, H-5a); 3.46 (dd, 1H, *J* 6.0 and 9.6, H-5b); 4.29 (ddd, 1H, *J* 2.8, 6.0 and 6.6 Hz, H-4); 4.54 (d, 1H, *J* 2.8 Hz, H-3); 4.84 (d, 1H, *J* 3.8 Hz, H-2); 5.90 (d, 1H, *J* 3.8 Hz, H-1). MS (EI, HR) *m/z*: $(M\text{-}Me_3Si)^+$ calcd for $C_{29}H_{27}O_5$: 455.1858. Found: 455.1858. Anal. Calcd for $C_{32}H_{36}O_5Si$: C, 72.69; H, 6.86. Found: C,72.54; H, 6.92.

3-*O*-(2'-Dimethylphenylsilyl-ethynyl)-1,2-isopropylidene-5-*O*-trityl-α-D-xylofuranose (**4**). Compound **4** was obtained from **2** using dimethylphenylsilyl chloride according to the procedure described above (91%). Oil; $[\alpha]_D$ -18.6° (*c* 0.6, CH_2Cl_2); IR (film): 2182 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.36 (s, 6H, Ph**Me**$_2$Si); 1.33, 1.51 (2s, 6H, isoprop.); 3.35 (dd, 1H, *J* 6.7 and 9.6 Hz, H-5a); 3.47 (dd, 1H, *J* 6.0 and 9.6, H-5b); 4.36 (ddd, 1H, *J* 2.8, 6.0 and 6.7 Hz, H-4); 4.60 (d, 1H, *J* 2.8 Hz, H-3); 4.87 (d, 1H, *J* 3.8 Hz, H-2); 5.90 (d, 1H, *J* 3.8 Hz, H-1). MS (EI, HR) *m/z*: M^+ calcd for $C_{37}H_{38}O_5Si$: 590.2488. Found: 590.2488. Anal. Calcd for $C_{37}H_{38}O_5Si$: C, 75.22; H, 6.48. Found: C, 75.22; H, 6.53.

3-*O*-(2'-*t*-Butyldimethylsilyl-ethynyl)-1,2-isopropylidene-5-*O*-trityl-α-D-xylofuranose (**5**). Compound **5** was obtained from **2** using *t*-butyldimethylsilyl chloride according to the procedure described above (88%). White solid; mp. 93-95°C; $[\alpha]_D$ -23.8° (*c* 1.0, CH_2Cl_2); IR (film): 2180 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.06 (s, 6H, *t*-Bu**Me**$_2$Si); 0.89 (s, 9H, ***t*-Bu**Me$_2$Si); 1.34, 1.55 (2s, 6H, isoprop.); 3.36 (dd, 1H, *J* 6.7 and 9.6 Hz, H-5a); 3.46 (dd, 1H, *J* 6.0 and 9.6 Hz, H-5b); 4.29 (ddd, 1H, *J* 2.8, 6.0 and 6.7 Hz, H-4); 4.54 (d, 1H, *J* 2.8 Hz, H-3); 4.88 (d, 1H, *J* 3.8 Hz, H-2); 5.89 (d, 1H, *J* 3.8 Hz, H-1). MS (EI, HR) *m/z*: M^+ calcd for $C_{35}H_{42}O_5Si$: 570.2801. Found: 570.2801. Anal. Calcd for $C_{35}H_{42}O_5Si$: C, 73.64; H, 7.42. Found: C, 73.65; H, 7.42.

(*Z*) 1,2-*O*-Isopropylidene-3-*O*-(2'-trimethylsilyl-vinyl)-5-*O*-trityl-α-D-xylofuranose (**6**). **Method A:** A stirred solution of **3** (1.85 g, 3.5 mmol) in hexane-ethyl acetate 1:1 $^v/_v$ mixture (25 mL) was hydrogenated over palladium on barium sulfate (5%, 0.075 g) in the presence of quinoline (0.075 g) for 4 h. Subsequently, the solution was passed through Florisil and evaporated. The residue was purified on a silica gel column using hexane-*t*-butyl methyl ether 94:6 $^v/_v$ as an eluent to afford **6** as a white solid (1.83 g, 99%). **Method B:** To a stirred solution of **3** (0.52 g, 1 mmol) in THF (12 mL) under argon, DIBAL-H (1.0 M solution in hexane, 3 mL, 3 mmol) at 0°C was added. The reaction mixture was then allowed to warm to room temperature. After 16 h, 1:1 mixture of THF-methanol (3 mL) was added slowly, with cooling, and was stirred at 0°C for 30 min. Subsequently, the mixture was poured into 30 mL of 10% aqueous tartric acid and extracted with CH_2Cl_2 (3 × 20 mL). The extract was washed with

water, dried (Na_2SO_4), filtered, and concentrated. The crude product was purified by column chromatography on silica gel using hexane-*t*-butyl ether 94:6 $^{v}/_{v}$ as an eluent to afford **6** as a white solid (0.4 g, 76%). Mp. 114.5-116.5°C; $[\alpha]_D$ -41.2° (*c* 1.0, CH_2Cl_2); IR (film): 1609 cm^{-1}; ^1H NMR ($CDCl_3$): δ -0.08 (s, 9H, Me_3Si); 1.31, 1.53 (2s, 6H, isoprop.); 3.27 (dd, 1H, *J* 6.8 and 9.5 Hz, H-5a); 3.47 (dd, 1H, *J* 6.1 and 9.5 Hz, H-5b); 4.22 (d, 1H, *J* 8.2 Hz, =CH-Si); 4.25 (d, 1H, *J* 2.7 Hz, H-3); 4.36 (ddd, 1H, *J* 2.7, 6.1 and 6.8 Hz, H-4); 4.48 (d, 1H, *J* 3.7 Hz, H-2); 5.86 (d, 1H, *J* 3.7 Hz, H-1); 6.52 (d, 1H, *J* 8.2 Hz, O-CH=). MS (LSIMS, HR) *m/z*: $(M+Na)^+$ calcd for $C_{32}H_{38}O_5SiNa$: 553.2386. Found: 553.2385. Anal. Calcd for $C_{32}H_{38}O_5Si$: C, 72.42 ; H, 7.22. Found: C, 72.24; H, 7.42.

(*Z*) 3-*O*-(2'-Dimethylphenylsilyl-vinyl)-1,2-isopropylidene-5-*O*-trityl-α-D-xylofuranose (7) Compound **7** obtained from **4** according to was the procedure described above (97%). White solid; mp. 118-121°C; $[\alpha]_D$ -42.7° (*c* 0.4, CH_2Cl_2); IR (film): 1608 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.18 (s, 6H, Ph**Me**$_2$Si); 1.26, 1.50 (2s, 6H, isoprop.); 3.23 (dd, 1H, *J* 6.9 and 9.4 Hz, H-5a); 3.45 (dd, 1H, *J* 5.9 and 9.4 Hz, H-5b); 4.22 (d, 1H, *J* 2.7 Hz, H-3); 4.24 (d, 1H, *J* 3.6 Hz, H-2); 4.31 (ddd, 1H, *J* 2.7, 5.9 and 6.9 Hz, H-4); 4.42 (d, 1H, *J* 8.1 Hz, =CH-Si); 5.56 (d, 1H, *J* 3.6 Hz, H-1); 6.60 (d, 1H, *J* 8.1 Hz, O-CH=). MS (EI, HR) *m/z*: $(M-Ph)^+$ calcd for $C_{31}H_{35}O_5Si$: 515.2254. Found: 515.2276. Anal. Calcd for $C_{37}H_{40}O_5Si$: C, 74.97; H, 6.81. Found: C, 75.41; H, 6.89.

(*Z*) 3-*O*-(2'-*t*-Butyldimethylsilyl-vinyl)-1,2-isopropylidene-5-*O*-trityl-α-D-xylofuranose (8) Compound **8** was obtained from **5** according to the above procedure (95%). Oil; $[\alpha]_D$ -33.1° (*c* 1.0, CH_2Cl_2); IR ($CHCl_3$): 1610 cm^{-1}; ^1H NMR ($CDCl_3$): δ -0.13 (s, 6H, *t*-Bu**Me**$_2$Si); 0.77 (s, 9H, ***t*-Bu**Me_2Si); 1.31, 1.52 (2s, 6H, isoprop.); 3.25 (dd, 1H, *J* 6.5 and 9.6 Hz, H-5a); 3.49 (dd, 1H, *J* 6.2 and 9.6 Hz, H-5b); 4.21 (d, 1H, *J* 8.4 Hz, =CH-Si); 4.23 (d, 1H, *J* 2.7 Hz, H-3); 4.35 (ddd, 1H, *J* 2.7, 6.2 and 6.5 Hz, H-4); 4.48 (d, 1H, *J* 3.8 Hz, H-2); 5.86 (d, 1H, *J* 3.8 Hz, H-1); 6.58 (d, 1H, *J* 8.4 Hz, O-CH=). MS (LSIMS, HR) *m/z*: $(M+Na)^+$ calcd for $C_{35}H_{44}O_5SiNa$: 595.2856. Found: 595.2856. Anal. Calcd for $C_{35}H_{44}O_5Si$: C, 73.39; H, 7.74. Found: C, 73.15; H, 7.67.

[2+2]Cycloaddition of chlorosulfonyl isocyanate to 2'-silylvinyl ethers 6-8. General procedure. To a suspension of anhydrous sodium carbonate (0.15 g) in anhydrous toluene (2.5 mL) chlorosulfonyl isocyanate (1.6 mmol) was added. The mixture was stirred and upon cooling to -78°C treated dropwise with a solution of a 2'-silylvinyl ether **6, 7** or **8** (1 mmol) in toluene (2 mL). Stirring and cooling was maintained for 2-3.5 h. The mixture was then cooled to -78°C, diluted with toluene (6 mL), treated with Red-Al (1 M solution in toluene, 1.6 mL), and left for 30 min where the temperature of the reaction was maintained. Subsequently, the temperature was allowed to rise to 0°C, water (0.3 mL) was added, and the solution was stirred for 30 min. The mixture was filtered through Celite, evaporated and purified by chromatography on silica gel to give the respective products **9, 10,** and **19-22.**

(3'*S*, 4'*R*) 1,2-*O*-Isopropylidene-3-*O*-(3'-trimethylsilyl-azetidin-2'-on-4'-yl)-5-*O*-trityl-α-D-xylofuranose (9). Compound **9** was obtained from **6** according to the above procedure (51%). White solid; mp. 193-196.5°C; $[\alpha]_D$ -28.3° (*c* 1.0, CH_2Cl_2); IR (KBr): 1762, 3388 cm^{-1}; ^1H NMR ($CDCl_3$): δ -0.05 (s, 9H, Me_3Si); 1.32, 1.55 (2s, 6H, isoprop.); 2.51 (dd, 1H, *J* 3.6 and 4.3 Hz, H-3'); 3.15 (t, 1H, *J* 8.8 Hz, H-5a); 3.60 (dd, 1H, *J* 5.1 and 8.8 Hz, H-5b); 4.02 (d, 1H, *J* 2.7 Hz, H-3); 4.39 (ddd, 1H, *J* 2.7, 5.1 and 8.8 Hz, H-4); 4.55 (d, 1H, *J* 3.7 Hz, H-2); 5.09 (d, 1H, *J* 4.3 Hz, H-4'); 5.80 (d, 1H, *J* 3.7 Hz, H-1); 6.26 (br d, 1H, *J* 3.6 Hz, NH). MS (EI, HR) *m/z*: M^+ calcd for $C_{33}H_{39}O_6SiN$: 573.2547. Found: 573.2546. Anal. Calcd for $C_{33}H_{39}O_6SiN$: C, 69.08; H, 6.85; N, 2.44. Found: C, 68.87; H, 6.70; N, 2.62.

(3'*S*, 4'*R*) 1,2-*O*-Isopropylidene-3-*O*-(3'-dimethylphenylsilyl-azetidin-2'-on-4'-yl)-5-*O*-trityl-α-D-xylofuranose (10). Compound **10** was obtained from **7** according to the above procedure (47%). White solid; mp.87-90°C; $[\alpha]_D$ -23.7° (*c* 0.3, CH_2Cl_2); IR (film): 1752, 3292 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.21, 0.22 (2s, 6H, Ph**Me**$_2$Si); 1.25, 1.51 (2s, 6H, isoprop.); 2.73 (dd, 1H, *J* 3.6 and 4.4 Hz, H-3'); 3.06 (t, 1H, *J* 8.7 Hz, H-5a); 3.57 (dd, 1H, *J* 4.8 and 8.7 Hz, H-5b); 3.89 (d, 1H, *J* 2.8 Hz, H-3); 4.13 (d, 1H, *J* 3.6 Hz, H-2); 4.38 (ddd, 1H, *J* 2.8, 4.8 and 8.7 Hz, H-4); 5.06 (d, 1H, *J* 4.4 Hz, H-4'); 5.66 (d, 1H, *J* 3.6 Hz, H-1); 6.24 (br d, 1H, *J* 3.6 Hz, NH). MS (EI, HR) *m/z*: M^+ calcd for $C_{38}H_{41}O_6SiN$: 635.2702. Found: 635.2703. Anal. Calcd for $C_{38}H_{41}O_6SiN$: C, 71.78; H, 6.50; N, 2.20. Found: C, 71.50; H, 6.70; N, 1.96.

(3'*S*, 4'*R*) 1,2-*O*-Isopropylidene-3-*O*-(3'-trimethylsilyl-azetidin-2'-on-4'-yl)-α-D-xylofuranose (11). A solution of **9** (0.15 g, 0.26 mmol) in formic acid and diethyl ether 3:2 $^v/_v$ (6 mL) was stirred at room temperature until the reaction was complete (15 min; TLC). Subsequently, mixture was diluted with Et_2O, and neutralized with saturated aqueous $NaHCO_3$. The organic layer was separated, dried ($MgSO_4$), and concentrated. The residue was chromatographed with hexane-ethyl acetate 1:9 $^v/_v$ as an eluent to give **11** (0.057 g, 65%). Oil; $[\alpha]_D$ +4.5° (*c* 0.5, CH_2Cl_2); IR ($CHCl_3$): 1757, 3401, 3505 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.17 (s, 6H, Me_3Si); 1.33, 1.50 (2s, 6H, isoprop.); 2.94 (d, 1H, *J* 4.3 Hz, H-3'); 3.76 (dd, 1H, *J* 5.6 and 11.3 Hz, H-5a); 3.91 (dd, 1H, *J* 6.4 and 11.3 Hz, H-5b); 3.99 (d, 1H, *J* 3.2 Hz, H-3); 4.35 (ddd, 1H, *J* 3.2, 5.6 and 6.4 Hz, H-4); 4.63 (d, 1H, *J* 3.8 Hz, H-2); 5.25 (dd, 1H, *J* 0.5 and 4.3 Hz, H-4'); 5.91 (d, 1H, *J* 3.8 Hz, H-1); 6.34 (br s, 1H, NH). MS (EI, HR) *m/z*: $(M+H)^+$ calcd for $C_{14}H_{26}O_6SiN$: 332.1529. Found: 332.1529.

(3'*S*, 4'*R*) 1,2-*O*-Isopropylidene-3-*O*-(3'-dimethylphenylsilyl-azetidin-2'-on-4'-yl)-α-D-xylofuranose (12). Compound **12** was detritylated with 0.5% of p-TsOH in methanol at room temperature (5 h). The crude product was purified on a silica gel column using hexane-ethyl acetate 3:7 $^v/_v$ as an eluent to give **12** (72%). Oil; $[\alpha]_D$ +23.8° (*c* 1.0, CH_2Cl_2); IR ($CHCl_3$): 1747, 3306, 3449 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.43, 0.47 (2s, 6H, Ph**Me**$_2$Si); 1.27, 1.46 (2s, 6H, isoprop.); 3.21 (dd, 1H, *J* 3.4 and 4.3 Hz, H-3'); 3.43 (dd, 1H, *J* 5.8 and 11.3 Hz, H-5a); 3.57

(dd, 1H, *J* 6.3 and 11.3 Hz, H-5b); 3.87 (d, 1H, *J* 3.4 Hz, H-3); 4.28 (ddd, 1H, *J* 3.4, 5.8 and 6.3 Hz, H-4); 4.34 (d, 1H, *J* 3.8, Hz, H-2); 5.24 (d, 1H, *J* 4.3 Hz, H-4'); 5.76 (d, 1H, *J* 3.8 Hz, H-1); 6.48 (br s, 1H, NH). MS (EI, HR) *m/z*: $(M\text{-}Me)^+$ calcd for $C_{18}H_{24}O_6SiN$: 378.1373. Found: 378.1373.

(3'*S*, 4'*R*) 1,2-*O*-Isopropylidene-3-*O*-(3'-trimethylsilyl-azetidin-2'-on-4'-yl)-5-*O*-tosyl-α-D-xylofuranose (13). Compound **13** was obtained from **11** by the standard tosylation procedure (80%). Oil; $[\alpha]_D$ -2.0° (*c* 1.0, CH_2Cl_2); IR (film): 1754, 3320 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.10 (s, 9H, Me_3Si); 1.30, 1.45 (2s, 6H, isoprop.); 2.46 (s, 3H, tosyl); 2.87 (dd, 1H, *J* 3.7 and 4.3 Hz, H-3'); 3.97 (d, 1H, *J* 3.0 Hz , H-3); 4.09 (dd, 1H, *J* 5.7 and 9.6 Hz, H-5a); 4.02 (dd, 1H, *J* 7.4 and 9.6 Hz, H-5b); 4.38 (m, 1H, H-4); 4.60 (d, 1H, *J* 3.6 Hz, H-2); 5.19 (d, 1H, 4.3 Hz, H-4'); 5.83 (d, 1H, *J* 3.6 Hz, H-1); 6.43 (br d, 1H, *J* 3.7 Hz, NH). MS (EI, HR) *m/z*: $(M\text{-}Me)^+$ calcd for $C_{20}H_{28}O_8SiNS$: 470.1305. Found: 470.1322. Anal. Calcd for $C_{21}H_{31}O_8SiNS$: C, 51.94; H, 6.43; N, 2.88. Found: C, 52.04; H, 6.48; N, 2.91.

(3'*S*, 4'*R*) 1,2-*O*-Isopropylidene-3-*O*-(3'-dimethylphenylsilyl-azetidin-2'-on-4'-yl)-5-*O*-tosyl-α-D-xylofuranose (14). Compound **14** was obtained from **12** by the standard tosylation procedure (80%). Oil; $[\alpha]_D$ +2.7° (*c* 0.2, CH_2Cl_2); IR (film): 1757 , 3309 cm^{-1}; ^1H NMR (benzene-d_6): δ 0.34, 0.36 (2s, 6H, Ph**Me**$_2$Si); 1.07, 1.31 (2s, 6H, isoprop.); 1.83 (s, 3H, tosyl); 2.69 (dd, 1H, *J* 3.5 and 4.4 Hz, H-3'); 3.47 (d, 1H, *J* 3.0 Hz, H-3); 4.01 (dd, 1H, *J* 7.0 and 10.0 Hz, H-5a); 4.04 (dd, 1H, *J* 5.9 and 10.0 Hz, H-5b); 4.12 (d, 1H, *J* 3.6 Hz, H-2); 4.37 (m, 1H, H-4); 4.51 (d, 1H, *J* 4.4 Hz, H-4'); 5.54 (br d, 1H, *J* 3.5 Hz, NH); 5.66 (d, 1H, *J* 3.6 Hz, H-1). MS (EI, HR) *m/z*: $(M\text{-}Me)^+$ calcd for $C_{25}H_{30}O_8SSiN$: 532.1478. Found: 532.1461.

(4'*R*) 5-Deoxy-1,2-*O*-isopropylidene-3-*O*:5-*C*-(3'-azetidin-2'-on-1',4'-di-yl)-α-D-xylofuranose (15). Compound **13** or **14** (0.5 mmol) was dissolved in acetonitrile (15 mL) and treated with tetrabutylammonium bromide (0.17 g, 0.5 mmol) and pulverized anhydrous K_2CO_3 (0.7 g). The mixture was stirred and kept under reflux for 1.0-1.5 h. Subsequently, toluene (10 mL) was added, the mixture was filtered, washed with water, dried and evaporated. The crude product was separed on a silica gel using hexane-ethyl acetate 1:1 $^v/_v$ as an eluent to give **15** [0.136g, (73%) and 0.081g (43%), respectively]. White solid. mp. 161.5-164°C. $[\alpha]_D$ +122.3° (*c* 1.0, CH_2Cl_2); IR ($CHCl_3$): 1766 cm^{-1}, (lit.[1], mp. 161-165°C; $[\alpha]_D$ +121.1° (*c* 0.9 ,CH_2Cl_2); IR ($CHCl_3$): 1765 cm^{-1}).

(4'*R*) 3-*O*-(Azetidin-2'-on-4'-yl)-1,2-*O*-isopropylidene-5-*O*-trityl-α-D-xylofuranose (16). To a solution of **9** (0.25 g, 0.435 mmol) and acetaldehyde (0.088 mL, 1.74 mmol) in THF (2 mL) cesium fluoride was added and the mixture was stirred for 3 h. The mixture was filtered and the filtrate was poured into water, and extracted with Et_2O. The crude product was separated, dried ($MgSO_4$), and evaporated. The residue was chromatographed on a silica gel using hexane-ethyl acetate 1:1 $^v/_v$ as an eluent to afford **16** (0.16 g, 75%). Oil; $[\alpha]_D$ -29.5° (*c* 0.17,

CH_2Cl_2); IR (film): 1775, 3296 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.32, 1.55 (2s, 6H, isoprop.); 2.66 (dd, 1H, *J* 1.4 and 15.2 Hz, H-3a'); 2.85 (ddd, 1H, *J* 3.0, 3.9 and 15.2 Hz, H-3'b); 3.14 (t, 1H, *J* 8.8 Hz, H-5a); 3.56 (dd, 1H, *J* 4.9 and 8.8 Hz, H-5b); 4.10 (d, 1H, *J* 3.0 Hz, H-3); 4.42 (ddd, 1H, *J* 3.0, 4.9 and 8.8 Hz, H-4); 4.53 (d, 1H, *J* 3.8 Hz, H-2); 5.05 (dd, 1H, *J* 1.4 and 3.9 Hz, H-4'); 5.86 (d, 1H, *J* 3.8 Hz, H-1); 6.27 (br s, 1H, NH). MS (EI, HR) *m/z*: M^+ calcd for $C_{30}H_{31}O_6N$: 501.2151. Found: 501.2173. Anal. Calcd for $C_{30}H_{31}O_6N$: C, 71.83; H, 6.22; N, 2.79. Found: C, 71.49; H, 6.46; N, 2.87.

(4'*R*) 3-*O*-(*N*-Benzyl-azetidin-2'-on-4'-yl)-1,2-*O*-isopropylidene-5-*O*-trityl-α-D-xylofuranose (17). **Method A.** A suspension of sodium hydride (60% oil dispersion, 0.015 g, 0.38 mmol) in dry DMF (2 mL) was cooled to 0°C and **9** (0.2 g, 0.35 mmol) dissolved in DMF (1 mL) was added slowly. The reaction was stirred for 30 min, and benzyl bromide (0.045 mL, 0.383 mmol) was added. The mixture was stirred for 1.5 h at room temperature, diluted with ether, washed, dried (Na_2SO_4), and evaporated. The residue was purified on a silica gel column using hexane-ethyl acetate 8:2 $^v/_v$ as an eluent to afford **17** (0.158 g, 76.6%). **Method B.** To a cooled at 0°C solution **9** (0.25 g, 0.435 mmol) in THF (5 mL) were added pulverized KOH (0.027 g, 0.48 mmol), benzyl bromide (0.057 mL, 0.48 mmol) and tetrabutylammonium bromide (10% mol), and the mixture was intensively stirred. After 3.5 h, the mixture was poured into water, and extracted with ether. The organic layer was separated, dried (Na_2SO_4), and evaporated. The residue was chromatographed on a silica column using hexane-ethyl acetate 8:2 $^v/_v$ as an eluent afford **17** (0.155 g, 60%). Oil; $[\alpha]_D$ -41.4° (*c* 0.8, CH_2Cl_2); IR ($CHCl_3$): 1757 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.25, 1.51 (2s, 6H, isoprop.); 2.52 (d, 1H, *J* 14.9 Hz, H-3a'); 2.69 (dd, 1H, *J* 3.7 and 14.9 Hz, H-3'b); 3.05 (t, 1H, *J* 8.8 Hz , H-5a); 3.53 (dd, 1H, *J* 5.3 and 8.8 Hz, H-5b); 3.89 (d, 1H, *J* 3.0 Hz, H-3); 4.04 (d, 1H, *J* 3.8 Hz, H-2); 4.14, 4.53 (2d, 2H, *J* 15.2 Hz, Bn); 4.31 (ddd, 1H, *J* 3.0, 5.3 and 8.8 Hz, H-4); 4.82 (dd, 1H, *J* 1.5 and 3.7 Hz, H-4'); 5.70 (d, 1H, *J* 3.8 Hz, H-1); MS (LSIMS, HR) *m/z*: $(M+Na)^+$ calcd for $C_{37}H_{37}O_6NNa$: 614.2462. Found: 614.2518.

(4'*R*) 3-*O*-(*N*-Ethoxycarbonyl-azetidin-2'-on-4'-yl)-1,2-*O*-isopropylidene-5-*O*-trityl-α-D-xylofuranose (18). To a solution of **9** (0.20 g, 0.35 mmol) and Et_3N (0.19 mL, 1.39 mmol) in CH_2Cl_2 (2 mL) was added ethyl chloroformate (0.13 mL, 1.39 mmol) with cooling and stirring. The mixture was stirred at room temperature until disappearance substrate (72 h). Subsequently it was evaporated to dryness and purified on a silica gel using hexane-ethyl acetate 8:2 $^v/_v$ as eluent to afford **18** (0.11 g, 65%). Oil; $[\alpha]_D$ -39.6° (*c* 0.12, CH_2Cl_2); IR (film): 1731, 1822 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.32, 1.55 (2s, 6H, isoprop.); 1.39 (t, 3H, *J* 7.1 Hz, $-CH_3$); 2.46 (dd. 1H, *J* 2.2 and 16.4 Hz, H-3a'); 2.63 (dd, 1H, *J* 4.7 and 16.4 Hz, H-3'b); 3.07 (t, 1H, *J* 8.8 Hz, H-5a); 3.66 (dd, 1H, *J* 4.8 and 8.8 Hz, H-5b); 4.37 (q, 2H, *J* 7.2 and 14.4 Hz, $-CH_2-$); 4.47 (m, 1H, H-4); 4.55 (d, 1H, *J* 3.7 Hz, H-2); 4.48 (d, 1H, *J* 2.6 Hz, H-3); 5.3 (dd, 1H, *J* 2.2 and 4.7 Hz, H-4'); 5.80 (d, 1H, *J* 3.7 Hz, H-1). MS (LSIMS, HR) *m/z*: $(M+Na)^+$ calcd for $C_{33}H_{35}O_8NNa$: 596.2276. Found: 596.2284. Anal. Calcd for $C_{33}H_{35}O_8N$: C, 69.10; H, 6.15; N, 2.44. Found: C, 69.21; H, 6.31; N, 2.30.

(3'*S*, 4'*R*), (3'*R*, 4'*R*), (3'*R*, 4'*S*) and **(3'*S*, 4'*S*) 1,2-*O*-Isopropylidene-3-*O*-(3'-*t*-butyldimethylsilyl-azetidin-2'-on-4'-yl)-5-*O*-trityl-α-D-xylofuranose (19, 20, 21** and **22).** Mixture of **19, 20, 21,** and **22** in a ratio 7.2 : 3.5 : 1.0 : 0.3, respectively, was obtained from **8** according to the general procedure described above (83%).

19: oil; $[\alpha]_D$ -23.1° (*c* 1.0, CH_2Cl_2); IR (film): 1753, 3235 cm^{-1}; ^1H NMR ($CDCl_3$): δ -0.30, 0.006 (2s, 6H, *t*-Bu**Me**$_2$Si); 0.85 (s, 9H, ***t*-Bu**Me$_2$Si); 1.33, 1.56 (2s, 6H, isoprop.); 2.66 (dd, 1H, *J* 3.6 and 4.3 Hz, H-3'); 3.11 (t, 1H, *J* 8.8 Hz , H-5a); 3.63 (dd, 1H, *J* 4.8 and 8.8 Hz, H-5b); 4.02 (d, 1H, *J* 2.8 Hz, H-3); 4.43 (m, 1H, H-4); 4.55 (d, 1H, *J* 3.7 Hz, H-2) 5.07 (d, 1H, *J* 4.3 Hz, H-4'); 5.79 (d, 1H, *J* 3.7 Hz, H-1); 6.31 (br d, 1H, *J* 3.6 Hz, NH). MS (EI, HR) *m/z*: $(M\text{-}t\text{-}Bu)^+$ calcd for $C_{32}H_{36}O_6SiN$: 558.2312. Found: 558.2312. Anal. Calcd for $C_{36}H_{45}O_6SiN$: C, 70.21; H, 7.36; N, 2.27. Found: C, 70.41; H, 7.35; N, 2.20.

20: oil; $[\alpha]_D$ -31.0° (*c* 0.6, CH_2Cl_2); IR (film): 1754, 3288 cm^{-1}; ^1H NMR ($CDCl_3$): δ -0.01, 0.08 (2s, 6H, *t*-Bu**Me**$_2$Si); 0.88 (s, 9H, ***t*-Bu**Me$_2$Si); 1.31, 1.49 (2s, 6H, isoprop.); 2.72 (d, 1H, *J* 1.5 Hz, H-3'); 3.24 (dd, 1H, *J* 6.4 and 10.0 Hz , H-5a); 3.54 (dd, 1H, *J* 6.0 and 10.0 Hz, H-5b); 4.02 (d, 1H, *J* 3.4 Hz, H-3); 4.21 (ddd, 1H, *J* 3.4, 6.0 and 6.4 Hz, H-4); 4.48 (d, 1H, *J* 3.8 Hz, H-2); 4.94 (d, 1H, *J* 1.5 Hz H-4'); 5,89 (d, 1H, *J* 3.8 Hz, H-1); 6.05 (br s, 1H, NH). MS (EI, HR) *m/z*: $(M\text{-}t\text{-}Bu)^+$ calcd for $C_{32}H_{36}O_6SiN$: 558.2312. Found: 558.2312. Anal. Calcd for $C_{36}H_{45}O_6SiN$: C, 70.21; H, 7.36; N, 2.27. Found: C, 70.22; H, 7.48; N, 2.22.

21: oil; $[\alpha]_D$ -43.6° (*c* 0.5, CH_2Cl_2); IR (film): 1759, 3402 cm^{-1}; ^1H NMR ($CDCl_3$): δ -0.14, 0.11 (2s, 6H, *t*-Bu**Me**$_2$Si); 0.87 (s, 9H, ***t*-Bu**Me$_2$Si); 1.32, 1.53 (2s, 6H, isoprop.); 2.91 (dd, 1H, *J* 1.9 and 4.4 Hz, H-3'); 3.19 (dd, 1H, *J* 7.3 and 9.6 Hz , H-5a); 3.60 (dd, 1H, *J* 6.0 and 9.6 Hz, H-5b); 3.96 (d, 1H, *J* 2.7 Hz, H-3); 4.31 (m, 1H, H-4); 4.48 (d, 1H, *J* 3.7 Hz, H-2); 5.17 (d, 1H, *J* 4.4 Hz, H-4'); 5,82 (d, 1H, *J* 3.7 Hz, H-1); 5.96 (br s, 1H, NH). MS(EI, HR) *m/z*: $(M\text{-}t\text{-}Bu)^+$ calcd for $C_{32}H_{36}O_6SiN$: 558.2312. Found: 558.2312. Anal.Calcd for $C_{36}H_{45}O_6SiN$: C, 70.21; H, 7.36; N, 2.27. Found: C, 70.44; H, 7.59; N, 2.16.

22: Signals due to stereoisomer **22** visible in the ^1H NMR spectrum of the crude post reaction mixture. ^1H NMR ($CDCl_3$): δ 4.91 (d, 1H, *J* 1.5 Hz, H-4'); 5.86 (d, 1H, *J* 4.0 Hz, H-1).

(3'*S*, 4'*R*), (3'*R*, 4'*R*) 3-*O*-(3'-*t*-Butyldimethylsilyl-azetidin-2'-on-4'-yl)-1,2-*O*-isopropylidene-α-D-xylofuranose (23 and **24).** Compounds **23** and **24** were obtained from **19** and **20** according to the procedure described for **11.**

23 (76%): oil; $[\alpha]_D$ +16.7° (*c* 0.5, CH_2Cl_2); IR (film): 1749, 3320, 3453 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.08, 0.135 (2s, 6H, *t*-Bu**Me**$_2$Si); 0.93 (s, 9H, ***t*-Bu**Me$_2$Si); 1.38, 1.50 (2s, 6H, isoprop.); 3.03 (dd, 1H, *J* 3.4 and 4.4 Hz, H-3'); 3.77 (dd, 1H, *J* 5.8 and 11.3 Hz, H-5a); 3.92 (dd, 1H, *J* 6.4 and 11.3 Hz, H-5b); 3.98 (d, 1H, *J* 3.4 Hz, H-3); 4.33 (m, 1H, H-4); 4.64 (d, 1H, *J* 3.8 Hz, H-2); 5.29 (dd, 1H, *J* 0.6 and 4.4 Hz, H-4'); 5.90 (d, 1H, *J* 3.8 Hz, H-1); 6.49 (br d, 1H, *J* 3.4 Hz, NH); MS (EI, HR) *m/z*: $(M\text{-}Me)^+$ calcd for $C_{16}H_{28}O_6SiN$: 358.1686. Found: 358.1686. Anal.Calcd for $C_{17}H_{31}O_6SiN$: C, 54.66; H, 8.36; N, 3.75. Found: C,54.71; H, 8.48; N, 3.61

24 (69%): white solid; mp. 121.5-125°C; $[\alpha]_D$ -25.7° (*c* 0.3, CH_2Cl_2); IR (film): 1750, 3306, 3446 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.07, 0.122 (2s, 6H, *t*-BuMe$_2$Si); 0.94 (s, 9H, *t*-BuMe$_2$Si); 1.32, 1.49 (2s, 6H, isoprop.); 2.83 (d, 1H, *J* 1.5 Hz, H-3'); 3.75 (dd, 1H, *J* 5.6 and 11.4 Hz, H-5a); 3.88 (dd, 1H, *J* 5.9 and 11.4 Hz, H-5b); 4.07 (d, 1H, *J* 3.6 Hz, H-3); 4.33 (ddd, 1H, *J* 3.6, 5.6 and 5.9 Hz, H-4); 4.58 (d, 1H, *J* 3.8 Hz, H-2); 5.04 (d, 1H, *J* 1.5 Hz, H-4'); 5.90 (d, 1H, *J* 3.8 Hz, H-1); 6.38 (br s, 1H, NH); MS (EI, HR) *m/z*: $(M\text{-}Me)^+$ calcd for $C_{16}H_{28}O_6SiN$: 358.1686. Found: 358.1686. Anal. Calcd for $C_{17}H_{31}O_6SiN$: C, 54.66; H, 8.36; N, 3.75. Found: C, 54.61; H, 8.54; N, 3.76.

(3'*S*, 4'*R*) 1,2-*O*-Isopropylidene-3-*O*-(3'-*t*-butyldimethylsilyl-azetidin-2'-on-4'-yl)-5-*O*-tosyl-α-D-xylofuranose (26). Compound **26** was obtained from **23** by the standard tosylation procedure (68%). White solid; mp. 134-138°C; $[\alpha]_D$ +0.7° (*c* 0.6 , CH_2Cl_2); IR (film): 1756, 3324 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.03, 0.08 (2s, 6H, *t*-BuMe$_2$Si); 0.91 (s, 9H, *t*-BuMe$_2$Si); 1.29, 1.45 (2s, 6H, isoprop.); 2.45 (s, 3H, tosyl); 2.94 (dd, 1H, *J* 3.6 and 4.4 Hz, H-3'); 3.95 (d, 1H, *J* 3.0 Hz, H-3); 4.12 (dd, 1H, *J* 5.8 and 9.6 Hz, H-5a); 4.20 (dd, 1H, *J* 7.3 and 9.6 Hz, H-5b); 4.37 (m, 1H, H-4); 4.61 (d, 1H, *J* 3.6 Hz, H-2); 5.19 (dd, 1H, *J* 0.7 and 4.4 Hz, H-4'); 5.81 (d, 1H, *J* 3.6 Hz, H-1); 6.41 (br d, 1H, *J* 3.6 Hz, NH). MS (EI, HR) *m/z*: $(M\text{-}Me)^+$ calcd for $C_{23}H_{34}O_8SiNS$: 512.1774. Found: 512.1774. Anal. Calcd for $C_{24}H_{37}O_8SiNS$: C, 54.63; H, 7.07; N, 2.65. Found: C, 54.73; H, 7.23; N, 2.53.

(3'*R*, 4'*R*) 1,2-*O*-Isopropylidene-3-*O*-(3'-*t*-butyldimethylsilyl-azetidin-2'-on-4'-yl)-5-*O*-tosyl-α-D-xylofuranose (27). Compound **27** was obtained from **24** by the standard tosylation procedure (65%). Oil; $[\alpha]_D$ -24.5° (*c* 0.5, CH_2Cl_2); IR ($CHCl_3$): 1758, 3315 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.08, 0.12 (2s, 6H, *t*-BuMe$_2$Si); 0.93 (s, 9H, *t*-BuMe$_2$Si); 1.29, 1.44 (2s, 6H, isoprop.); 2.45 (s, 3H, tosyl); 2.80 (d, 1H, *J* 1.5 Hz, H-3'); 4.09 (dd, 1H, *J* 5.6 and 10.0 Hz, H-5a); 4.11 (d, 1H, *J* 3.3 Hz , H-3); 4.22 (dd, 1H, *J* 7.1 and 10.0 Hz, H-5b); 4.37 (m, 1H, H-4); 4.55 (d, 1H, *J* 3.7 Hz, H-2); 5.05 (d, 1H, *J* 1.5 Hz, H-4'); 5.87 (d, 1H, *J* 3.7 Hz, H-1); 6.47 (br s, 1H, NH). MS (EI, HR) *m/z*: $(M\text{-}t\text{-}Bu)^+$ calcd for $C_{20}H_{28}O_8SiNS$: 470.1305. Found: 470.1305. Anal. Calcd for $C_{24}H_{37}O_8SiNS$: C, 54.63; H, 7.07; N, 2.65. Found: C, 54.62; H, 7.23; N, 2.59.

(3'*S*, 4'*R*) and **(3'*R*, 4'*R*) 5-Deoxy-1,2-*O*-isopropylidene-3-*O*:5-*C*-(3'-*t*-butyldimethylsilyl-azetidin-2'-on-1',4'-di-yl)-α-D-xylofuranose (29, 30)** and **(4'*R*) 5-Deoxy-1,2-*O*-isopropylidene-3-*O*:5-*C*-(3'-azetidin-2'-on-1',4'-di-yl)-α-D-xylofuranose (15).** A mixture of **29, 30** and **15** (31%) was obtained from compound **26** according to the procedure described for **15**. After chromatographical separation pure components were obtained.
29 (25%): white solid; mp. 137-140.5°C; $[\alpha]_D$ +101.7° (*c* 0.4, CH_2Cl_2); IR ($CHCl_3$): 1749 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.09, 0.11 (2s, 6H, *t*-BuMe$_2$Si); 0.92 (s, 9H, *t*-BuMe$_2$Si); 1.33, 1.49 (2s, 6H, isoprop.); 2.67 (ddd, 1H, *J* 1.0, 1.8 and 3.4 Hz, H-3'); 3.57 (ddd, 1H, *J* 1.8, 3.4 and 13.4 Hz, H-5a); 3.67 (ddd, 1H, *J* 1.0, 3.5 and 13.4 Hz, H-5b); 4.31 (d, 1H, *J* 3.4 Hz, H-3); 4.41 (m, 1H, H-4); 4.60 (d, 1H, *J* 3.9 Hz, H-2); 4.98 (d, 1H, *J* 3.4 Hz, H-4'); 5,95 (d, 1H, *J* 3.9 Hz, H-1).

MS (EI, HR) *m/z*: $(M\text{-}Me)^+$ calcd for $C_{16}H_{26}O_5SiN$: 340.1580. Found: 340.1580. Anal. Calcd for $C_{17}H_{29}O_5SiN$: C, 57.43; H, 8.22; N, 3.94. Found: C, 57.60; H, 8.38; N, 3.79.
30 (25%): white solid; mp. 91-94.5°C; $[\alpha]_D$ +90.4° (*c* 0.3, CH_2Cl_2); IR ($CHCl_3$): 1751 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.05, 0.09 (2s, 6H, *t*-Bu**Me**$_2$Si); 0.93 (s, 9H, ***t*-Bu**Me$_2$Si); 1.33, 1.49 (2s, 6H, isoprop.); 2.67 (s, 1H, H-3'); 3.40 (dd, 1H, *J* 2.2 and 13.9 Hz , H-5a); 3.86 (dd, 1H, *J* 5.3 and 13.9 Hz, H-5b); 4.29 (d, 1H, *J* 3.2 Hz, H-3); 4.43 (m, 1H, H-4); 4.59 (d, 1H, *J* 3.8 Hz, H-2); 4.83 (d, 1H, *J* 0.8 Hz, H-4'); 5,95 (d, 1H, *J* 3.8 Hz, H-1). MS (EI, HR) *m/z*: $(M\text{-}Me)^+$ calcd for $C_{16}H_{26}O_5SiN$: 340.1580. Found: 340.1580. Anal.Calcd for $C_{17}H_{29}O_5SiN$: C, 57.43; H, 8.22; N, 3.94. Found: C, 57.22; H, 8.30; N, 4.09.
Intramolecular alkylation of **27** according to the procedure described for **15** afforded a mixture of compounds **30** (54%) and **15** (27%). Chromatographical separation gave pure components.

(4'*S*) 5-Deoxy-1,2-*O*-isopropylidene-3-*O*:5-*C*-(3'-azetidin-2'-on-1',4'-di-yl)-α-D-xylofuranose (31). Compound **21** was subjected to the reaction sequence involving detritylation, tosylation, intramolecular alkylation and desilylation according to procedure described above to afford known **31**. White solid; mp. 153.5-157°C; $[\alpha]_D$ -23.9° (*c* 0.28, CH_2Cl_2); IR ($CHCl_3$): 1771 cm^{-1}, (lit.[1], mp. 156-158°C; $[\alpha]_D$ -29.8° (*c* 0.8, CH_2Cl_2); IR ($CHCl_3$): 1771 cm^{-1}).

Hydroxyalkylation of cepham 29 in the presence of TBAF. General procedure. To a mixture of **29** (0.5 mmol) and aldehyde **32**, **33** or **34** (1.5 mmol) in THF (2 mL) anhydrous tetrabutylammonium fluoride [21] (1 M solution in THF, 0.5 mmol) was added. The resulting yellow solution was stirred at 25°C for 12 h, subsequently poured into 0.5N HCl (10 mL) and extracted with ether (3 × 20 mL). The organic layer was dried ($MgSO_4$), concentrated, and purified on a silica gel to give **35**, **36** or **37**, respectively, as 3:1 mixtures of epimers.

(3'*R*, 4'*R*) 5-Deoxy-1,2-*O*-isopropylidene-3-*O*:5-*C*-[3'-(α-hydroxybenzyl-azetidin-2'-on-1',4'-di-yl]-α-D-xylofuranose (35). A mixture of stereoisomers **35**, in a ratio 3:1 (55%) was obtained from **29** according to the procedure described above. IR (film): 1760, 3346 cm^{-1}. **35a** major isomer: ^1H NMR ($CDCl_3$): δ 1.31, 1.48 (2s, 6H, isoprop.); 3.37 (d, 1H, *J* 4.5 Hz, H-3'); 3.57 (dd, 1H, *J* 1.8 and 13.8 Hz, H-5a); 3.84 (dd, 1H, *J* 4.9 and 13.8 Hz, H-5b); 4.27 (d, 1H, *J* 3.1 Hz, H-3); 4.41 (m, 1H, H-4); 4.56 (d, 1H, *J* 3.8 Hz, H-2); 5.10 (s, 1H, H-4'); 5.12 (d, 1H, *J* 4.5 Hz, CHOH); 5.95 (d, 1H, *J* 3.8 Hz, H-1).
35b minor isomer: ^1H NMR ($CDCl_3$): δ 1.31, 1.48 (2s, 6H, isoprop.); 3.39 (d, 1H, *J* 5.7 Hz, H-3'); 3.53 (dd, 1H, *J* 1.8 and 13.8 Hz, H-5a); 3.83 (dd, 1H, *J* 4.5 and 13.8 Hz, H-5b); 4.28 (d, 1H, *J* 3.2 Hz, H-3); 4.42 (m, 1H, H-4); 4.56 (d,1H, *J* 3.8 Hz, H-2); 4.88 (s, 1H, H-4'); 5.02 (d, 1H, *J* 5.8 Hz, CHOH); 5.93 (d, 1H, *J* 3.8 Hz, H-1). MS (EI, HR), *m/z*: M^+ calcd for $C_{18}H_{21}O_6N$: 347.1369. Found: 347.1369.

(3'*R*, 4'*R*) 5-Deoxy-1,2-*O*-isopropylidene-3-*O*:5-*C*-[3'-(α-hydroxy-p-bromobenzyl-azetidin-2'-on-1',4'-di-yl]-α-D-xylofuranose (36). A mixture of steroisomers **36**, in a ratio 3:1 (76%) was

obtained from **29** according to the procedure described above. IR ($CHCl_3$): 1765, 3452 cm^{-1}. **36a** major isomer: ^1H NMR ($CDCl_3$): δ 1.31, 1.48 (2s, 6H, isoprop.); 3.32 (d, 1H, *J* 4.7 Hz, H-3'); 3.57 (dd, 1H, *J* 1.8 and 13.9 Hz, H-5a); 3.83 (dd, 1H, *J* 4.4 and 13.9 Hz, H-5b); 4.27 (d, 1H, *J* 3.2 Hz, H-3); 4.41 (m, 1H, H-4); 4.56 (d, 1H, *J* 3.8 Hz, H-2); 5.03 (s, 1H, H-4'); 5.08 (d, 1H, *J* 4.8 Hz, CHOH); 5.94 (d, 1H, *J* 3.8 Hz, H-1).
36b minor isomer: ^1H NMR ($CDCl_3$): δ 1.31, 1.48 (2s, 6H, isoprop.); 3.34 (d, 1H, *J* 5.8 Hz, H-3'); 3.54 (dd, 1H, *J* 1.8 and 13.9 Hz, H-5a); 3.82 (dd, 1H, *J* 4.4 and 13.9 Hz, H-5b); 4.28 (d, 1H, *J* 3.0 Hz, H-3); 4.41 (m, 1H, H-4); 4.57 (d, 1H, *J* 3.8 Hz, H-2); 4.86 (s, 1H, H-4'); 4.99 (d, 1H, *J* 5.8 Hz, CHOH); 5.93 (d, 1H, *J* 3.8 Hz, H-1). MS (EI, HR) *m/z*: M^+ calcd for $C_{18}H_{20}O_6NBr$: 425.0474. Found: 425.0474.

(3'*R*, 4'*R*) 5-Deoxy-1,2-*O*-isopropylidene-3-*O*:5-*C*-[3'-(α-hydroxy-p-nitrobenzyl-azetidin-2'-on-1',4'-di-yl]-α-D-xylofuranose (37). A mixture of steroisomers **37**, in a ratio 3:1 (68%) was obtained from **29** according to the procedure described above. IR (CH_2Cl_2): 1768, 3589 cm^{-1}. **37a**: ^1H NMR ($CDCl_3$): δ 1.30, 1.48 (2s, 6H, isoprop.); 3.37 (d, 1H, *J* 4.6 Hz, H-3'); 3.60 (dd, 1H, *J* 1.7 and 13.9 Hz, H-5a); 3.83 (dd, 1H, *J* 4.3 and 13.9 Hz, H-5b); 4.27 (d, 1H, *J* 3.2 Hz, H-3); 4.41 (m, 1H, H-4); 4.53 (d, 1H, *J* 3.8 Hz, H-2); 5.02 (s, 1H, H-4'); 5.24 (d, 1H, *J* 4.6 Hz, CHOH); 5.94 (d, 1H, *J* 3.8 Hz, H-1).
37b: ^1H NMR ($CDCl_3$): δ 1.30, 1.48 (2s, 6H, isoprop.); 3.38 (d, 1H, *J* 5.7 Hz, H-3'); 3.54 (dd, 1H, *J* 1.7 and 13.9 Hz, H-5a); 3.81 (dd, 1H, *J* 4.3 and 13.9 Hz, H-5b); 4.30 (d, 1H, *J* 3.2 Hz, H-3); 4.44 (m, 1H, H-4); 4.59 (d, 1H, *J* 3.8 Hz, H-2); 4.93 (s, 1H, H-4'); 5.17 (d, 1H, *J* 5.2 Hz, CHOH); 5.95 (d, 1H, *J* 3.8 Hz, H-1). MS (EI, HR) *m/z*: M^+ calcd for $C_{18}H_{20}O_8N_2$: 392.1220. Found: 392.1220.

(3'*R*, 4'*R*) 5-Deoxy-1,2-*O*-isopropylidene-3-*O*:5-*C*-[3'-(α-hydroxy-p-nitrobenzyl-azetidin-2'-on-1',4'-di-yl]-α-D-xylofuranose (37). To freshly destilled diisopropylamine (0.098 mL, 0.69 mmol) in dry THF (2 mL) at -15°C under nitrogen, n-BuLi (2.5 M solution in hexane, 0.265 mL, 0.66 mmol) was added dropwise during 5 min, and the mixture was cooled to -75°C. To the LDA solution a mixture of **15** (0.08 g, 0.33 mmol) in THF (1 mL) at -75°C was added. After 20 min, p-nitrobenzaldehyde **34** (0.2 g, 1.32 mmol) in THF (0.5 mL) was added at the same temperature and the mixture was stirred at -75°C for 1.5 h. It was then poured into a cold saturated aqueous NaCl solution, and extracted with Et_2O. The organic layer was dried ($MgSO_4$), concentrated, and the residue was purified by column chromatography on silica gel using hexane-ethyl acetate 6:4 $^v/_v$ as an eluent to give a mixture of stereoisomers **37** in a ratio 3:1; (0.069 g, 53%).

(3'*R*, 4'*R*) 5-Deoxy-1,2-*O*-isopropylidene-3-*O*:5-*C*-[3'-(α-acetoxy-p-bromobenzyl-azetidin-2'-on-1',4'-di-yl]-α-D-xylofuranose (38). A solution **36** (0.03 g, 0.07 mmol) and DMAP (0.01 g) in acetic anhydride and pyridine 1:2 $^v/_v$ (1 mL) was stirred at room temperature until the reaction was complete (TLC). After 45 min, the mixture was poured into water, extracted with

CH_2Cl_2, dried, and evaporated. The residue was separated by column chromatography on silica gel using toluene-*t*-butyl methyl ether-hexane 2:4:4 $^{v}/_{v}$ as an eluent to give **38a** (0.021g, 63%) and **38b** (0.007g, 21%). **38a**: white solid; mp. 150-153°C; $[\alpha]_D$ +30.2° (*c* 0.46, CH_2Cl_2); IR (film): 1747, 1771 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.31, 1.48 (2s, 6H, isoprop.); 2.10 (s, 3H, acetyl); 3.42 (d, 1H, *J* 6.0 Hz, H-3'); 3.53 (dd, 1H, *J* 1.6 and 14.0 Hz, H-5a); 3.81 (dd, 1H, *J* 4.7 and 14.0 Hz, H-5b); 4.26 (d, 1H, *J* 3.0 Hz, H-3); 4.41 (m, 1H, H-4); 4.57 (d, 1H, *J* 3.8 Hz, H-2); 4.98 (s, 1H, H-4'); 5.95 (d, 1H, *J* 3.8 Hz, H-1); 6.02 (d, 1H, *J* 6.0 Hz, CHOAc). MS (EI, HR) *m/z*: $(M\text{-}Me)^+$ calcd for $C_{19}H_{19}O_7NBr$: 425.0345. Found: 425.0345.
38b: white solid; mp. 165-168°C; $[\alpha]_D$ +56.2° (*c* 0.35, CH_2Cl_2); IR (film): 1742, 1770 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.31, 1.48 (2s, 6H, isoprop.); 2.10 (s, 3H, acetyl); 3.41 (d, 1H, *J* 4.7 Hz, H-3'); 3.52 (dd, 1H, *J* 1.7 and 13.9 Hz, H-5a); 3.82 (dd, 1H, *J* 4.7 and 13.9 Hz, H-5b); 4.27 (d, 1H, *J* 3.0 Hz, H-3); 4.41 (m, 1H, H-4); 4.57 (d, 1H, *J* 3.8 Hz, H-2); 4.78 (s, 1H, H-4'); 5.92 (d, 1H, *J* 3.8 Hz, H-1); 6.05 (d, 1H, *J* 4.7 Hz, CHOAc). MS (EI, HR) *m/z*: $(M\text{-}Me)^+$ calcd for $C_{19}H_{19}O_7NBr$: 425.0345. Found: 425.0345.

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