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Carbohydrate Research 307 (1998) 33–43

CARBOHYDRATE RESEARCH

Formation of β-lactams fused to the pyranoid ring via the Mitsunobu reaction

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Received 4 August 1997; accepted 10 December 1997

Abstract

N-Tosyl-2-*C*-carbamoyl glycosides having the α-L-*arabino*- and β-D-*xylo*- configuration form under Mitsunobu conditions 2-*C*:3-*N*-carbonyl-2,3-dideoxy-3-*N*-tosylamino-α-L-lyxo- and β-D-arabinopyranosides, respectively, having the β-lactam ring fused to the pyranoid one; neither the formation of the γ-lactam ring nor that of the 3,4-epoxide were observed. The γ-lactam 2-*C*:4-*N*-carbonyl-2,4-dideoxy-4-*N*-tosylamino-β-D-xylopyranoside can be obtained after protection of the 3-hydroxy group in the starting glycoside of α-L-*arabino*-configuration. The structure and configuration of methyl 2-*C*:3-*N*-carbonyl-2,3-dideoxy-3-*N*-tosylamino-β-D-ribopyranoside and methyl 2-*C*:3-*N*-carbonyl-2,3-dideoxy-3-*N*-tosylamino-β-D-*erythro*-pyranosid-4-ulose were proved by X-ray crystallography.

Keywords: *N*-Tosyl-2-*C*-carbamoyl glycosides; 2-*C*:3-*N*-Carbonyl-2,3-dideoxy-3-*N*-tosylamino-α-L-lyxo- and β-D-ribopyranosides; Intramolecular Mitsunobu reaction; β-Lactams

1. Introduction

Compounds having a four-membered β-lactam ring fused to the sugar ring have been reported to be intermediates in the synthesis of aminodeoxy sugars [1], carbapenems [2], clavams [3], 1-oxacephems [4], and uracyl derivatives [5]. While in case of aminodeoxy sugars bicyclic skeletons were formed from non-carbohydrate precursors [1], the other syntheses [2–5] involved the transformation of readily available carbohydrate substrates. The synthesis of 6-epithienamycin led to the introduction of the β-lactam ring by an intramolecular *N*-alkylation of the 4-*C*-carbamoyl glycoside by the neighbor C-3 atom bearing a leaving group; application of a direct Mitsunobu [diethyl azodicarboxylate (DEAD)–triphenylphosphine (TPP)] procedure for that purpose has failed due to the low activity of the N-unsubstituted carbamoyl group [2]. Syntheses carried out in our laboratory [3–5] have employed the direct formation of sugar β-lactams by a [2 + 2]cycloaddition of isocyanates to glycals [6,7]. An attempt to perform [2 + 2]cycloaddition of chlorosulfonyl isocyanate to 2,3-unsaturated glycosides has failed due to the low stability of the sugar substrate in the presence of the acid-contaminated isocyanate [8].

Cycloadducts of trichloroacetyl isocyanate or tosyl isocyanate with glycals in the presence of alcohol undergo a rapid opening of a four-membered ring to afford 2-*C*-carbamoyl glycosides having a trans-located aglycone with respect to the

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0008-6215/98/$19.00
PII S0008-6215(98)00017-2

carbamoyl function [9,10]. Owing to the high stereoselectivity of the [2 + 2]cycloaddition, the configuration of glycosides obtained by alcoholysis of the cycloadduct is defined and the carbamoyl group is always *anti* to the C-3 substituent. Deprotection at O-3 forms the β-hydroxy amide fragment suitable for the β-lactam ring construction via the Appel (carbon tetrachloride-TPP) or Mitsunobu procedure.

For the present studies we selected readily available L-arabinal and D-xylal which should provide, after the cycloaddition-alcoholysis procedure, α-L-*arabino*- and β-D-*xylo*-carbamoyl glycosides, respectively. Both glycosides differ only by the configuration at C-4. Our choice of glycals resulted from the expectation that cyclization of α-L-*arabino*- and β-D-*xylo*-carbamoyl glycosides to form a β-lactam ring fused to the pyranoid one, should provide in both cases the (S) configuration at C-3 (C-4 of the azetidin-2-one ring). This would allow to use bicyclic β-lactams as precursors in the synthesis of carbapenem antibiotics (Scheme 1).

2. Results and discussion

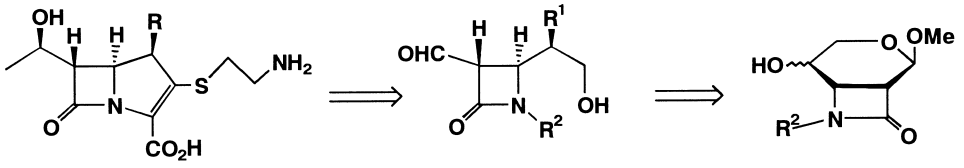
For the first cyclizations we used 4-*O*-protected α-L-*arabino* glycoside **5**. The 4-*O*-protected *arabino* glycoside **5** was prepared from L-arabinal **1** by a four-step reaction sequence, which involved silylation, followed by [2 + 2]cycloaddition of tosyl isocyanate to the glycal double bond, methanolysis of the cycloadduct **3**, and regioselective protection of the HO-4 group in **4** by the *tert*-butyldiphenylsilyl function (Scheme 2).

Preliminary experiments using the Appel procedure allowed to obtain β-lactam **6** from glycoside **5** in 54% yield. We failed, however, to remove the *O*-silyl and *N*-tosyl groups from **6**. All experiments using standard procedures gave decomposition products.

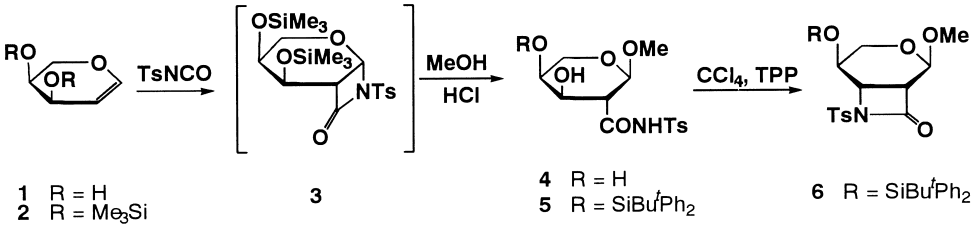
We noticed that the HO-4 group in L-arabinal **1** could be selectively benzylated to give **7** in 48% yield. Subsequent standard silylation of the HO-3 group with trimethylsilylchloride followed by a [2 + 2]cycloaddition of tosyl isocyanate and subsequent methanolysis of the resulting cycloadduct provided glycoside **10**.

The Mitsunobu procedure allowed to transform glycoside **10** into **11** in 46% yield. Reduction of the tosyl substituent in **11** with sodium naphthalene deprotected the nitrogen atom to afford **12**. Subsequent hydrogenolysis of the benzyl group at O–4 over 10% Pd-C gave β-lactam **13** (Scheme 3).

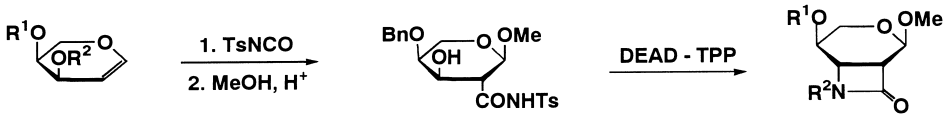
Cyclization of the glycosides **4**, **14**, **15**, and **16** in boiling tetrahydrofuran in the presence of DEAD and TPP afforded the respective β-lactams **17**, **18**, **20**, and **21** in 42–52% yield (Scheme 4). We did not notice epoxide or γ-lactam formation. The last observation is particularly interesting in the case of the α-L-*arabino* glycosides **4** and **14** because from the former we expected the formation of at least some amount of the less strained γ-lactam ring. It should be noted that compound **26** (Scheme 5) obtained from the known glycoside **24** [9] by a standard reaction sequence involving introduction of a *tert*-butoxycarbonyl function to the amide nitrogen atom and subsequent de-*O*-benzylation, unexpectedly did not undergo cyclization either under Appel or Mitsunobu conditions.



Scheme 1.



Scheme 2.

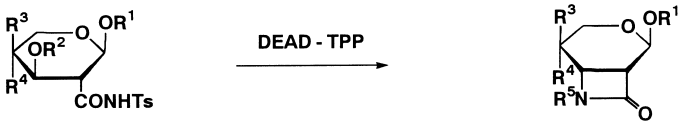


7 R^1 = Bn, R^2 = H
8 R^1 = Bn, R^2 = Me_3Si
9 R^1 = Bn, R^2 = $SiBu^tMe_2$

10

11 R^1 = Bn, R^2 = Ts
12 R^1 = Bn, R^2 = H
13 R^1 = R^2 = H

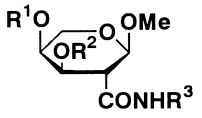
Scheme 3.



14 R^1 = Bn, R^2 = R^4 = H, R^3 = OH
15 R^1 = Me, R^2 = R^3 = H, R^4 = OH
16 R^1 = Bn, R^2 = R^3 = H, R^4 = OH

17 R^1 = Me, R^3 = OH, R^4 = H, R^5 = Ts
18 R^1 = Bn, R^3 = OH, R^4 = H, R^5 = Ts
Na / $C_{10}H_8$ → **19** R^1 = Bn, R^3 = OH, R^4 = R^5 = H
20 R^1 = Me, R^3 = H, R^4 = OH, R^5 = Ts
Na / $C_{10}H_8$ → **21** R^1 = Bn, R^3 = H, R^4 = OH, R^5 = Ts
22 R^1 = Me, R^3 = R^5 = H, R^4 = OH
23 R^1 = Bn, R^3 = R^5 = H, R^4 = OH
Na / $C_{10}H_8$

Scheme 4.



24 R^1 = R^2 = Bn, R^3 = H
25 R^1 = R^2 = Bn, R^3 = CO_2Bu^t
26 R^1 = R^2 = H, R^3 = CO_2Bu^t

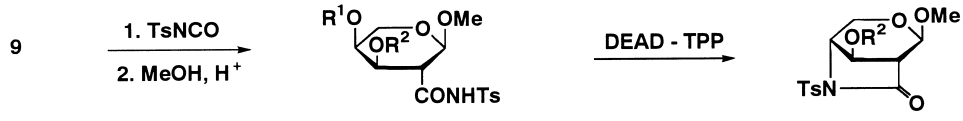
Scheme 5.

The Mitsunobu reaction involving *vic*-diols have been investigated in the past [11–13]. In the case of acyclic *vic*-diols, the AcylOH-DEAD-TPP-reagent provided respective monoesters, whereas in the case of cyclic trans-diols, the respective epoxides were formed [12,13]. We did not find any information on cyclization to the *vic*-diol fragment using a Mitsunobu procedure.

Formation of the bicyclic compound having a γ-lactam ring required the selective protection of the hydroxy group at C-3. The suitably protected 2-carbamoyl glycoside **28** was obtained from glycal **9** (Scheme 6) using standard transformations consisting of the [2+2]cycloaddition of tosyl isocyanate, methanolysis of the cycloadduct, and hydrogenolytic removal of the benzyl group at O-4. Compound **28** was subjected to a Mitsunobu reaction at 55°C to afford **29** in 45% yield.

Oxidation of the HO-4 group in the methyl glycosides **13**, **17**, **20**, and **22** with the ruthenium tetroxide-sodium periodate reagent [14] gave the same N-unsubstituted compound **30** (Scheme 7) from both **13** and **22**, and the same *N*-tosyl compound **31** from both **17** and **20**. The benzyl glycosides **18**, **19**, **21**, and **23** under the same conditions underwent decomposition. The tosyl-free benzyl-glycosides **19** and **23** can be oxidized by the methyl sulfoxide–acetic anhydride reagent to afford the same ketone **32** from both compounds.

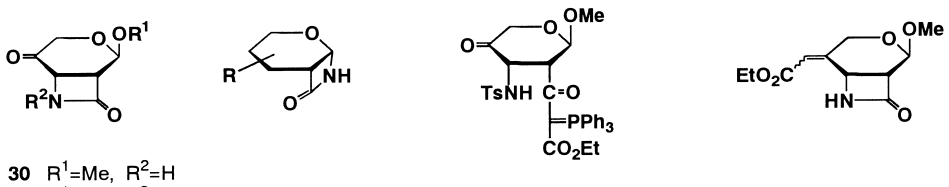
Structures and configurations of all β-lactam compounds were easily proved by their spectral



H_2, Pd-C → **27** R^1 = Bn, R^2 = $SiBu^tMe_2$
H_2, Pd-C → **28** R^1 = H, R^2 = $SiBu^tMe_2$

29

Scheme 6.



Scheme 7.

and analytical data. The additional proof of the geometry of the bicyclic β-lactams came from a X-ray crystallographic analysis of the glycosides **20** and **31** (Tables 1 and 2, Figs. 1 and 2).

Our X-ray investigations performed for the representative group of 2-*C*:1-*N*-carbonyl-2-deoxy-glycosylamines **33** have shown that the conformation of the pyranoid ring in such a fused bicyclic system strongly depends on substitution and configuration [15–17]; the boat-like conformation ^{O,3}B dominates, however. In the case of compound **20** a similar geometry ^{1,4}B of the pyranoid ring was observed (Tables 1 and 2, Fig. 1). Introduction of a carbonyl function at C-4 (**31**) caused a flattening towards a twist-boat conformation (Tables 1 and 2, Fig. 2). This new molecular skeleton has a slightly different geometry compared to the molecules having the 2-*C*-1-*N*-carbonyl-2-deoxy-glycopyranosylamine skeletons **33** investigated previously [15–17]. In particular, the new topology of the β-lactam and sugar rings introduces less strain in the latter. That might be seen by the valence angles close to the tetrahedral values for hydrogen atoms located at the rings fusion (Tables 1 and 2). Due to the electron withdrawing effect of the tosyl group located at the β-lactam nitrogen atom, the C=O bond length in both compounds is very short [1.186(4) and 1.190(4)Å].

Electrophilic properties of the β-lactam carbonyl group versus the ketone one in such a strained

Table 1
Crystal data and structure refinement for compounds **20** and **31**

Identification code	**20**	**31**
Empirical formula	$C_{14}H_{17}NO_6S$	$C_{14}H_{17}NO_6S$
Formula weight	327.35	325.34
Temperature (K)	293(2)	293(2)
Wavelength (Å)	1.54178	1.54178
Crystal system	Orthorhombic	Orthorhombic
Space Group	$P2_12_12_1$	$P2_12_12_1$
Unit cell dimensions (Å):		
a	7.3070(10).	8.6150(10)
b	8.7200(10).	12.342(2)
c	25.223(4)	13.902(2)
Volume (Å^3)	1607.1(4)	1478.1(4)
Z	4	4
Density (calculated) (Mg m^{-3})	1.353	1.466
Absorption coefficient (mm^{-1})	2.050	2.229
F(000)	688	680
Crystal size (mm)	0.17×0.20×0.30	0.20×0.20×0.35
θ-range for data collection (°)	3.50 to 74.69	4.79 to 74.69
Index ranges	0≤h≤9, 0≤k≤10, 0≤l≤31	0≤h≤10, 0≤k≤15, 0≤l≤17
Reflections collected	1831	1564
Independent reflections	1831 [R(int) = 0.0000]	1564 [R(int) = 0.0000]
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	1830/0/204	1564/0/200
Goodness-of-fit on F^2	1.045	0.931
Final R indices [I > 2σ (I)]	R_1 = 0.0456, wR_2 = 0.1317	R_1 = 0.0361, wR_2 = 0.1032
R indices (all data)	R_1 = 0.0460, wR_2 = 0.1346	R_1 = 0.0363, wR_2 = 0.1039
Absolute structure parameter	0.02(3)	0.13(3)
Extinction coefficient	0.0008(4)	0.0066(7)
Largest diff. peak and hole $\Delta\rho$(eÅ^{-3})	0.190 and −0.249	0.175 and −0.213

Table 2
Selected bond lengths [Å], angles [°] and torsion angles [°] for compounds **20** and **31**

	20	**31**
O(1)-C(1)	1.406(4)	1.419(3)
O(1)-C(5)	1.442(4)	1.416(4)
C(1)-O(2)	1.411(4)	1.388(4)
C(1)-C(2)	1.502(4)	1.510(5)
C(2)-C(7)	1.532(4)	1.525(5)
C(2)-C(3)	1.541(4)	1.554(4)
C(3)-N(8)	1.502(4)	1.488(4)
C(3)-C(4)	1.511(4)	1.202(3)
C(4)-C(5)	1.530(4)	1.497(4)
C(6)-O(2)	1.428(5)	1.441(4)
O(3)-C(7)	1.186(4)	1.190(4)
C(7)-N(8)	1.403(4)	1.409(4)
C(1)-O(1)-C(5)	117.5(2)	117.5(2)
O(1)-C(1)-O(2)	112.9(3)	112.6(2)
O(1)-C(1)-C(2)	112.3(2)	109.8(2)
O(2)-C(1)-C(2)	105.6(2)	105.8(2)
C(1)-C(2)-C(7)	115.1(2)	113.0(3)
C(1)-C(2)-C(3)	113.8(3)	113.0(2)
C(7)-C(2)-C(3)	87.6(2)	87.2(2)
N(8)-C(3)-C(4)	114.4(2)	113.3(3)
N(8)-C(3)-C(2)	87.2(2)	87.2(2)
C(4)-C(3)-C(2)	113.8(3)	115.2(2)
O(4)-C(4)-C(3)	108.3(3)	120.9(3)
O(4)-C(4)-C(5)	109.0(3)	121.5(3)
C(3)-C(4)-C(5)	111.1(3)	117.7(2)
O(1)-C(5)-C(4)	115.6(2)	115.1(2)
C(1)-O(2)-C(6)	114.8(3)	113.0(3)
O(3)-C(7)-N(8)	132.2(3)	131.3(3)
O(3)-C(7)-C(2)	136.6(3)	137.4(3)
N(8)-C(7)-C(2)	91.2(2)	91.3(2)
C(7)-N(8)-C(3)	94.1(2)	94.3(2)
C(7)-N(8)-S(1)	132.3(2)	134.4(2)
C(3)-N(8)-S(1)	131.6(2)	129.6(2)
C(5)-O(1)-C(1)-O(2)	−69.1(3)	−48.0(3)
C(5)-O(1)-C(1)-C(2)	50.1(4)	69.6(3)
O(1)-C(1)-C(2)-C(7)	50.7(4)	51.9(3)
O(2)-C(1)-C(2)-C(7)	174.1(2)	173.7(2)
O(1)-C(1)-C(2)-C(3)	−48.2(3)	−45.2(3)
O(2)-C(1)-C(2)-C(3)	75.1(3)	76.6(3)
C(1)-C(2)-C(3)-N(8)	116.5(3)	114.3(3)
C(7)-C(2)-C(3)-N(8)	0.0(2)	0.4(2)
C(1)-C(2)-C(3)-C(4)	1.0(3)	−0.2(4)
C(7)-C(2)-C(3)-C(4)	−115.5(2)	−114.1(3)
N(8)-C(3)-C(4)-O(4)	64.2(3)	107.7(4)
C(2)-C(3)-C(4)-O(4)	162.4(3)	−154.0(3)
N(8)-C(3)-C(4)-C(5)	−55.4(4)	−71.9(3)
C(2)-C(3)-C(4)-C(5)	42.7(4)	26.3(4)
C(1)-O(1)-C(5)-C(4)	−3.4(4)	−42.1(4)
O(4)-C(4)-C(5)-O(1)	−162.9(3)	173.8(3)
C(3)-C(4)-C(5)-O(1)	−43.6(4)	−6.5(4)
O(1)-C(1)-O(2)-C(6)	−59.0(4)	−64.3(4)
C(2)-C(1)-O(2)-C(6)	178.0(3)	175.7(3)
C(1)-C(2)-C(7)-O(3)	63.1(4)	64.8(5)
C(3)-C(2)-C(7)-O(3)	178.3(3)	178.6(5)
C(1)-C(2)-C(7)-N(8)	−115.2(3)	−114.3(3)
C(3)-C(2)-C(7)-N(8)	0.0(2)	−0.5(2)
O(3)-C(7)-N(8)-C(3)	−178.5(3)	−178.7(4)
C(2)-C(7)-N(8)-C(3)	0.0(2)	0.5(2)

bicyclic system are noteworthy. Compound **31** treated with ethyl (triphenylphosphoranylidene) acetate (**34**) underwent an unexpected reaction at the β-lactam carbonyl group leaving the ketone function untouched. The addition of the reagent was followed by the opening of the four-membered β-lactam ring to afford the stable ylide **35**. Reaction of β-lactams having an electron withdrawing group at the nitrogen atom with Wittig reagents are known [18] but they lead to a C=C double bond formation without opening of the four-membered ring. The nucleophilic ring opening of activated monocyclic β-lactams by trimethylsulphoxonium ylide, lithiated sulphones and cuprates, however, has been reported [19]. Removal of the tosyl substituent from the nitrogen atom in **31** decreased the reactivity of the β-lactam carbonyl group. Ylide **34** reacted with ketone **30** to give the expected mixture of olefins **36**.

In summary, we demonstrated that intramolecular amide formation between functional groups located within the pyranoid ring can be performed by the Mitsunobu procedure, even in the presence of a *trans-vic*-diol fragment. The preference of β-lactam formation over γ-lactam should be noted.

3. Experimental

General.—All melting points were uncorrected. Optical rotations were measured using a Jasco

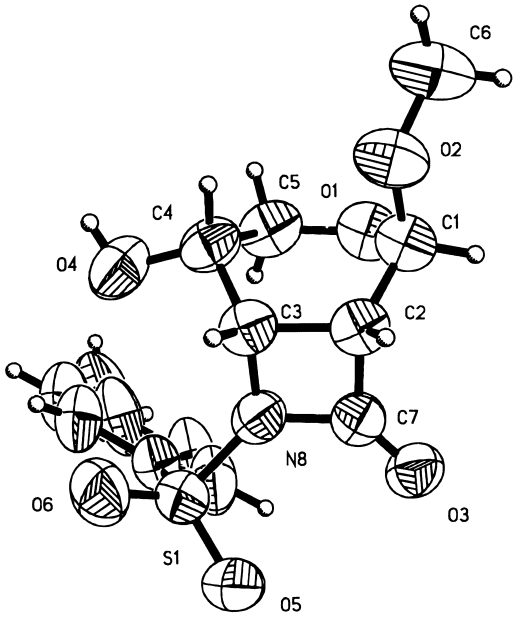


Fig. 1. ORTEP drawing of compound **20**. Thermal ellipsoids shown at 50% probability level.

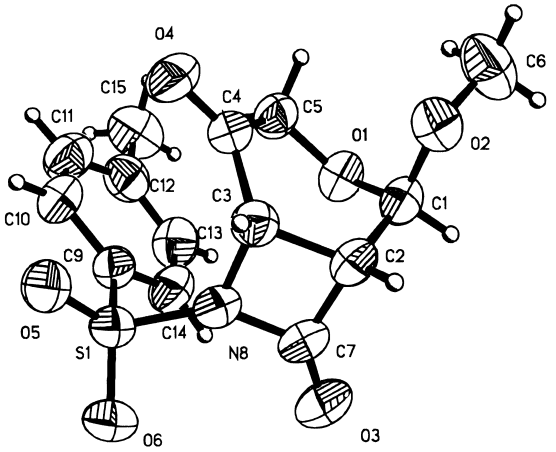


Fig. 2. ORTEP drawing of compound **31**. Thermal ellipsoids shown at 50% probability level.

DIP-360 digital polarimeter. IR spectra were obtained on a FT-IR-1600 Perkin-Elmer spectrophotometer. The ^{1}H NMR spectra were recorded with a Bruker AM-500 spectrometer. Mass spectra were obtained with an AMD-604 spectrometer. Column chromatography was performed on Merck Kieselgel 60 (230-400 mesh).

Methyl 2-deoxy-2-C-*(*N-*tosylcarbamoyl)*-α-L-*arabinopyranoside* (**4**).—3,4-Di-*O*-trimethylsilyl-L-arabinal **2** (4.0 g, 16.0 mmol) in MeCN (30 mL) was treated with *p*-toluenesulfonyl isocyanate (3.6 mL, 24.0 mmol) and left for 4 h. Subsequently, the mixture was cooled to 0°C, treated with MeOH (8 mL) and conc HCl (0.01 mL), and left for 15 min. The solution was concentrated and purified by chromatography using 1:2:0.1 hexane–EtOAc–MeOH as eluent to afford **4** (3.4 g, 61%); $[\alpha]_D$ +35° (*c* 0.8, CH_2Cl_2); IR (film): *ν* 3385 (OH), 3224 (NH), 1717 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$): *δ* 4.25 (d, 1 H, $J_{1,2}$ 8.4 Hz, H-1), 4.13 (d, 1 H, $J_{5a,5b}$ 12.8 Hz, H-5a), 3.95 (m, 2 H, H-3,4), 3.51 (d, 1 H, H-5b), 3.30 (s, 3 H, OCH_3), 2.89 (dd, 1 H, $J_{2,3}$ 10.1 Hz, H-2), 2.41 (s, 3 H, Ts); HRMS (LSIMS): *m/z* 346.09554 $[M+H]^+$; Calcd for $C_{14}H_{20}NO_7S$: 346.09605.

Methyl 4-O-tert-*butyldiphenylsilyl-2-deoxy-2*-C-*(*N-*tosylcarbamoyl)*-α-L-*arabinopyranoside* (**5**).—Compound **4** (0.25 g, 0.72 mmol) in DMF (10 mL) was treated with 4-dimethylaminopyridine (0.3 g) and *tert*-butyldiphenylsilyl chloride (0.3 g) for 6 days. Subsequently, the mixture was poured into water, and extracted with CH_2Cl_2. The extract was washed, dried, and concentrated. The crude product was purified on a silica gel column to afford **5** (0.27 g, 62%); $[\alpha]_D$ +45.0° (*c* 0.8, CH_2Cl_2); IR (film): *ν* 3460 (OH), 1715 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$): *δ* 4.18 (d, 1 H, $J_{1,2}$ 8.2 Hz, H-1), 3.73–3.86 (m, 2 H, H-3,4), 3.64 (dd, 1 H, $J_{4,5a}$ 2.2, $J_{5a,5b}$ 13.0 Hz, H- 5), 3.39 (s, 3 H, OCH_3), 3.09 (bd, 1 H, H-5b), 2.73 (dd, 1 H, $J_{2,3}$ 9.8 Hz, H-2), 2.44 (s, 3 H, Ts), 1.08 (s, 9 H, *t*-Bu); MS (LSIMS): *m/z* 584 $[M+H]^+$. Anal. Calcd for $C_{30}H_{37}NO_7S$: C, 61.72; H, 6.39; N, 2.40. Found: C, 61.7; H, 6.8; N, 2.4.

Methyl 4-O-tert-*butyldiphenylsilyl-2*-C*:3*-N-*carbonyl-2,3-dideoxy-3*-N-*tosylamino*-α-L-*lyxopyranoside* (**6**).—Compound **5** (0.4 g, 0.68 mmol) in MeCN (3 mL) was treated with TPP (0.38 g, 1.37 mmol) and cooled to 0°C. Subsequently, CCl_4 (0.13 mL, 1.37 mmol) and Et_3N (0.19 mL, 1.37 mmol) were added. The solution was kept at room temperature for 2.5 h, then concentrated, and purified by chromatography using 5:1 hexane–EtOAc as eluent to give **6** as a syrup (0.21 g, 54%); $[\alpha]_D$ −46.0° (*c* 0.6, CH_2Cl_2); IR (film): *ν* 1820 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$): *δ* 4.85 (d, 1 H, $J_{1,2}$ 1.3 Hz, H-1), 4.24 (m, 2 H, H-3,4), 3.52 (dd, 1 H, $J_{4,5a}$ 6.4, $J_{5a,5b}$ 12.1 Hz, H-5a), 3.39 (dd, 1 H, $J_{2,3}$ 6.6 Hz, H-2), 3.35 (dd, 1 H, $J_{4,5b}$ 5.8 Hz, H-5b), 3.33 (s, 3 H, OCH_3), 2.43 (s, 3 H, Ts), 1.09 (s, 9 H, t-BuPh_2Si). Anal. Calcd for $C_{32}H_{39}NO_6SSi$: C, 63.69; H, 6.23; N, 2.47. Found: C, 63.8; H, 6.3; N, 2.4.

1,5-Anhydro-4-O-*benzyl-2-deoxy*-L-erythro-*pent-1-enitol* (**7**).—Crude L-arabinal **1** (2.0 g, 17.2 mmol) in DMF (16 mL) was cooled to 0°C and treated with NaH (0.48 g, 20.6 mmol), then upon stirring benzyl bromide (2.4 mL, 20.6 mmol) was slowly added. The mixture was cooled and stirred for an additional 4 h. Subsequently, the solution was diluted with EtOAc, filtered through Celite and concentrated. Chromatographic purification using 4:1 hexane–EtOAc as eluent gave **7** (1.7 g, 48%), mp 56–57°C; $[\alpha]_D$ −102.3° (*c* 0.4, CH_2Cl_2); IR (film): *ν* 3218 (OH), 1640 (C=C) cm^{-1}; ^{1}H NMR ($CDCl_3$): *δ* 6.43 (dd, 1 H, $J_{1,2}$ 6.0, $J_{1,3}$ 0.8 Hz, H-1), 4.90 (dd, 1 H, $J_{2,3}$ 4.9 Hz, H-2), 4.66 and 4.69 (2 d, each 1 H, *J* 11.8 Hz, Bn), 4.23 (t, 1 H, $J_{3,4}$ 4.1 Hz, H-3), 3.95 (d, 2 H, H-5a,5b), 3.75 (dt, 1 H, $J_{4,5a}$ 6.3, $J_{4,5b}$ 6.8 Hz, H-4). Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.80; H, 6.84. Found: C, 70.0; H, 7.1.

1,5-Anhydro-4-O-*benzyl-2-deoxy-3*-O-*trimethylsilyl*-L-erythro-*pent-1-enitol* (**8**).—Compound **7** (1.0 g, 4.84 mmol) in pyridine was cooled to 0°C and treated with Me_3SiCl (1.4 mL, 11.6 mmol). The mixture was kept for 2 h at room temperature, subsequently the solution was poured into ice-water and extracted with hexane. The extract was washed, dried, concentrated, and distilled from an

air bath to give **8** (1.1 g, 81%), bp 70–73°C / 0.1 Torr; $[\alpha]_D$ −296° (*c* 1, CH_2Cl_2); IR (film): *ν* 1640 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$): *δ* 6.34 (d, 1 H, $J_{1,2}$ 6.0 Hz, H-1), 4.78 (dd, 1 H, $J_{2,3}$ 5.3 Hz, H-2), 4.59 and 4.69 (2 d, each 1 H, *J* 12.1 Hz, Bn), 4.31 (m, 1 H, H-3), 3.95 (t, 1 H, $J_{4,5a}$ 10.0, $J_{5a,5b}$ 10.2 Hz, H-5a), 3.90 (dq, 1 H, $J_{3,5b}$ 1.2, $J_{4,5b}$ 3.7 Hz, H-5b), 3.65 (dt, 1 H, $J_{3,4}$ 3.7 Hz, H-4); HRMS (LSIMS): *m/z* 301.1237 $[M+Na]^+$; Calcd for $C_{15}H_{22}NaO_3Si$: 301.1236.

*1,5-Anhydro-4-*O*-benzyl-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-*L*-erythro-pent-1-enitol* (**9**).—Compound **7** (1.40 g, 6.78 mmol) in DMF (10 mL) was treated with *tert*-butyldimethylsilyl chloride (1.38 g, 8.48 mmol). The mixture was kept for 8 h at room temperature, then poured into ice-water, and the solution was extracted with toluene. The extract was washed, dried, concentrated, and purified by chromatography to afford **9** as a syrup (1.88 g, 86.5%); $[\alpha]_D$ −185° (*c* 0.9, CH_2Cl_2); IR (film): *ν* 1640 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$): *δ* 6.32 (d, 1 h, $J_{1,2}$ 6.0 Hz, H-1), 4.76 (dd, 1 H, $J_{2,3}$ 5.3 Hz, H-2), 4.72 and 4.57 (2 d, each 1 H, *J* 12.0 Hz, Bn), 3.32 (m, 1 H, H-3), 3.97 (t, 1 H, $J_{4,5a}$ 10.0, $J_{5a,5b}$ 10.2 Hz, H-5a), 3.90 (m, 1 H, $J_{3,5b}$ 1.4, $J_{4,5b}$ 3.6 Hz, H-5b), 3.63 (dt, 1 H, $J_{3,4}$ 3.6 Hz, H-4), 0.09, 0.10, and 0.91 (3 s, 3,3,9 H, *t*-BuMe_2Si); HRMS (LSIMS): *m/z* 343.17056 $[M+Na]^+$; Calcd for $C_{12}H_{28}NaO_3Si$: 343.17054.

*Methyl 4-*O*-benzyl-2-deoxy-2-*C*-(*N*-tosylcarbamoyl)-α-L-arabinopyranoside* (**10**).—Compound **10** was obtained from **8** according to the procedure described for **4**; yield 64% as a syrup; $[\alpha]_D$ +53.7° (*c* 1.3, CH_2Cl_2); IR (film): *ν* 3516 (OH), 3226 (NH), 1715 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$): *δ* 4.25 (d, 1 H, $J_{1,2}$ 8.3 Hz, H-1), 4.10 (m, 1 H, H-5a), 3.90 (bdd, 1 H, $J_{2,3}$ 10.4, $J_{3,4}$ 3.6 Hz, H-3), 3.58 (m, 1 H, H-4), 3.40 (s, 3 H, OCH_3), 3.29 (dd, 1 H, $J_{3,5b}$ 1.1, $J_{5a,5b}$ 13.3 Hz, H-5b), 2.66 (dd, 1 H, H-2), 2.42 (s, 3 H, Ts); HRMS (LSIMS): *m/z* 436.14244 $[M+H]^+$; Calcd for $C_{12}H_{25}NO_7S$: 436.14300.

*Methyl 4-*O*-benzyl-2-*C*:3-*N*-carbonyl-2,3-dideoxy-3-*N*-tosylamino-α-L-lyxopyranoside* (**11**).—To a solution of compound **10** (0.80 g, 1.83 mmol) in THF (8 mL) was added TPP (0.76 g, 2.75 mmol) and DEAD (0.36 mL, 2.75 mmol). The mixture was boiled under reflux for 4 h, then cooled and concentrated. The crude product was purified by chromatography (4:1 hexane–EtOAc) to afford **11** as syrup (0.35 g, 45.8%); $[\alpha]_D$ −58.6° (*c* 2, CH_2Cl_2); IR (film): *ν* 1798 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$): *δ* 4.89 (d, 1 H, $J_{1,2}$ 1.0 Hz, H-1), 4.67 and 4.80 (2 d, each 1 H, *J* 11.8 Hz, Bn), 4.26 (dd, 1 H, $J_{2,3}$ 6.9, $J_{3,4}$ 2.4 Hz, H-3), 3.99 (ddd, 1 H, $J_{4,5a}$ 6.6, $J_{4,5b}$ 8.9 Hz, H-4), 3.67 (dd, 1 H, $J_{5a,5b}$ 11.9 Hz, H-5a), 3.53 (dd, 1 H, H-5b), 3.40 (dd, 1 H, H-2), 3.32 (s, 3 H, OCH_3), 2.45 (s, 3 H, Ts); HRMS (LSIMS): *m/z* 440.11416 $[M+Na]^+$; Calcd for $C_{12}H_{23}NO_6SNa$: 440.11437. Anal. Calcd for $C_{21}H_{23}NO_6S$: C, 60.41; H, 5.55; N, 3.35. Found: C, 61.0; H, 5.8; N, 3.3.

*Methyl 3-amino-4-*O*-benzyl-2-*C*:3-*N*-carbonyl-2,3-dideoxy-α-L-lyxopyranoside* (**12**).—A solution of naphthalene (0.55 g, 4.32 mmol) in dry 1,2-dimethoxyethane (DME, 5 mL) was stirred with sodium (0.1 g, 4.32 mmol) under N_2 for 30 min. Subsequently, a solution of compound **11** (0.30 g, 0.72 mmol) in DME (0.5 mL) was added slowly. Stirring and cooling were continued for 10 min, then a saturated solution of NH_4Cl was added dropwise until the blue color disappeared. The mixture was diluted with water and extracted with EtOAc (3×5 mL). The combined extracts were dried and concentrated, and the residue was purified by chromatography using 3:1 hexane–EtOAc as eluent to give **12** as a syrup (0.13 g, 68.6%); $[\alpha]_D$ −45.1° (*c* 0.3, CH_2Cl_2); IR (film): *ν* 3298 (NH), 1759 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$): *δ* 4.93 (s, 1 H, H-1), 3.53 and 4.69 (2 d, each 1 H, *J* 12.1 Hz, Bn), 3.58–3.82 (m, 3 H, H-3,4,5a), 3.51 (t, 1 H, $J_{4,5b}$ 8.9, $J_{5a,5b}$ 9.3 Hz, H-5b), 3.42 (dd, 1 H, $J_{1,2}$ 0.7, $J_{2,3}$ 5.7 Hz, H-2); HRMS (LSIMS): *m/z* 286.13436 $[M+H]^+$; Calcd for $C_{14}H_{17}NNaO_4$: 286.13437.

*Methyl 3-amino-2-*C*:3-*N*-carbonyl-2,3-dideoxy-α-D-lyxopyranoside* (**13**).—Compound **12** (0.10 g, 0.30 mmol) was hydrogenated in MeOH (1.5 mL) over 10% Pd-C (wet, Degussa type) for 3 h. Subsequently, the mixture was filtered through Celite and the solution was concentrated. The crude product was purified by chromatography using 1:1.5:0.1 hexane–EtOAc–MeOH as eluent to afford **13** (0.046 g, 89%); mp 117–118°C; $[\alpha]_D$ −86.8° (*c* 0.3, CH_2Cl_2); IR (film): *ν* 3450 (OH), 3204 (NH), 1760 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$): *δ* 5.01 (d, 1 H, $J_{1,2}$ 1.6 Hz, H-1), 4.29 (m, 1 H, H-3), 3.89–3.97 (m, 3 H, H-4,5a,5b), 3.50 (s, 3 H, OCH_3), 3.49 (dd, 1 H, $J_{2,3}$ 5.5 Hz, H-2); HRMS (LSIMS): *m/z* 174.0766 $[M+H]^+$; Calcd for $C_7H_{12}NO_4$: 174.0766.

*Benzyl 2-deoxy-2-*C*-(N-tosylcarbamoyl)-α-L-arabinopyranoside* (**14**).—Compound **14** was obtained from 3,4-di-*O*-trimethylsilyl-L-arabinal **2** according to the procedure described for **4** using benzyl alcohol

instead of MeOH; yield 65%; $[\alpha]_D$ +7.0° (*c* 0.2, CH_2Cl_2); IR (film): *ν* 3276 (OH), 1704 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$): *δ* 4.36 (d, 1 H, $J_{1,2}$ 8.3 Hz, H-1), 4.04 (dd, 1 H, $J_{4,5a}$ 1.8, $J_{5a,5b}$ 12.3 Hz, H-5a), 3.84 (dd, 1 H, $J_{2,3}$ 10.5, $J_{3,4}$ 3.2 Hz, H-3), 3.78 (bs, 1 H, H-4), 3.25 (d, 1 H, H-5b), 2.85 (dd, 1 H, H-2), 2.35 (s, 3 H, Ts). Anal. Calcd for $C_{20}H_{23}NO_7S$: C, 56.99; H, 5.50; N, 3.32. Found: C, 57.3; H, 5.6; N, 3.3.

Methyl 2-deoxy-2-C-*(*N-*tosylcarbamoyl)*-β-D-*xylo-pyranoside* (**15**).—Compound **15** was obtained from 3,4-di-*O*-trimethylsilyl-D-xylal according to the procedure described for **4**; yield 58%; mp 180–182°C; $[\alpha]_D$ +15.3° (*c* 0.4, MeOH); IR (KBr): *ν* 1720 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$): *δ* 4.30 (d, 1 H, $J_{1,2}$ 8.3 Hz, H-1), 4.03 (dd, 1 H, $J_{4,5a}$ 5.3, $J_{5a,5b}$ 11.5 Hz, H-5a), 3.82 (dd, 1 H, $J_{2,3}$ 10.1, $J_{3,4}$ 8.7 Hz, H-3), 3.67 (m, 1 H, H-4), 3.45 (s, 3 H, OCH_3), 3.25 (dd, 1 H, $J_{4,5b}$ 9.9 Hz, H-5b), 2.46 (dd, 1 H, H-2), 2.35 (s, 3 H, Ts). Anal. Calcd for $C_{14}H_{19}NO_7S$: C, 48.69; H, 5.54; N, 4.05. Found: C, 48.3; H, 5.6; N, 4.0.

Benzyl 2-deoxy-2-C-*(*N-*tosylcarbamoyl)*-β-D-*xylo-pyranoside* (**16**).—Compound **16** was obtained from 3,4-di-*O*-trimethylsilyl-D-xylal according to the procedure described for **4** using benzyl alcohol instead of MeOH; yield 59% isolated as a syrup, $[\alpha]_D$ −10.0° (*c* 0.95, CH_2Cl_2); IR (film): *ν* 3270 (OH), 1714 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$): *δ* 4.44 (d, 1 H, $J_{1,2}$ 8.3 Hz, H-1), 4.32 and 4.69 (2 d, each 1 H, *J* 11.8 Hz, Bn), 3.98 (dd, 1 H, $J_{4,5a}$ 5.2, $J_{5a,5b}$ 11.3 Hz, H-5a), 3.80 (dd, 1 H, $J_{2,3}$ 10.3, $J_{3,4}$ 9.0 Hz, H-3), 3.66 (m, 1 H, H-4), 3.38 (bt, 1 H, $J_{4,5b}$ 10.5 Hz, H-5b), 2.64 (dd, 1 H, H-2), 2.37 (s, 3 H, Ts). Anal. Calcd for $C_{14}H_{19}NO_7S$: C, 56.99; H, 5.50; N, 3.32. Found: C, 56.7; H, 5.5; N, 3.3.

Methyl 2-C*:3*-N-*carbonyl-2,3-dideoxy-3*-N-*tosyl-amino*-α-L-*lyxopyranoside* (**17**).—Compound **17** was obtained from **4** according to the procedure described for **11**; yield 52% isolated as a syrup; $[\alpha]_D$ −24.3° (*c* 0.9, CH_2Cl_2); IR (film): *ν* 3453 (OH), 1798 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$): *δ* 4.96 (d, 1 H, $J_{1,2}$ 1.3 Hz, H-1), 4.26 (bm, 1 H, H-4), 4.22 (ddd, 1 H, $J_{2,3}$ 6.3, $J_{3,4}$ 3.1, $J_{3,5b}$ 1.4 Hz, H-3), 4.02 (dd, 1 H, $J_{4,5a}$ 4.7, $J_{5a,5b}$ 12.5 Hz, H-5a), 3.86 (m, 1 H, $J_{4,5b}$ 2.2 Hz, H-5b), 3.45 (s, 1 H, OCH_3), 3.44 (dd, 1 H, H-2), 2.46 (s, 3 H, Ts); HRMS (LSIMS): *m/z* 350.06698 $[M+Na]^+$; Calcd for $C_{14}H_{17}NNaO_6S$: 350.06742.

Benzyl 2-C*:3*-N-*carbonyl-2,3-dideoxy-3*-N-*tosyl-amino*-α-L-*lyxopyranoside* (**18**).—Compound **18** was obtained from **14** according to the procedure described for **11** (46.2%); mp 122–123°C $[\alpha]_D$ −64.6° (*c* 1.1, CH_2Cl_2); IR (film): *ν* 3455 (OH), 1797 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$): *δ* 5.18 (d, 1 H, $J_{1,2}$ 1.3 Hz, H-1), 4.56 and 4.78 (2 d, each 1 H, *J* 11.5 Hz, Bn), 4.16–4.36 (m, 2 H, H-3,4), 4.04 (dd, 1 H, $J_{4,5a}$ 4.3, $J_{5a,5b}$ 12.9 Hz, H-5a), 3.90 (bd, 1 H, H-5b), 3.46 (dd, 1 H, $J_{2,3}$ 6.3 Hz, H-2), 2.45 (s, 3 H, Ts); HRMS (LSIMS): *m/z* 404.11664 $[M+H]^+$; Calcd for $C_{20}H_{22}NO_6S$: 404.11678.

Benzyl 3-amino-2-C*:3*-N-*carbonyl-2,3-dideoxy*-α-D-*lyxopyranoside* (**19**).—Compound **19** was obtained from **18** according to the procedure described for **12**; yield 58.0% isolated as a syrup; $[\alpha]_D$ −12.2° (*c* 1.1, CH_2Cl_2); IR (film): *ν* 3410 (OH, NH), 1772 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$): *δ* 5.20 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1), 4.61 and 4.84 (2 d, each 1 H, *J* 11.5 Hz, Bn), 4.34 (dd, 1 H, $J_{4,5a}$ 4.0, $J_{5a,5b}$ 12.1 Hz, H-5a), 3.90–4.06 (m, 3 H, H-3,4,5), 3.51 (bm, 1 H, H-2). Anal. Calcd for $C_{13}H_{15}NO_4$: C, 62.63; H, 6.06; N, 5.62. Found: C, 62.8; H, 6.2; N, 5.5.

Methyl 3-amino-2-C*:3*-N-*carbonyl-2,3-dideoxy*-α-L-*lyxopyranoside* (**13**).—Compound **13** was obtained from **17** according to the procedure described for **12** (60.0%). Spectral and analytical data of **13** are described above.

Methyl 2-C*:3*-N-*carbonyl-2,3-dideoxy-3*-N-*tosyl-amino*-β-D-*ribopyranoside* (**20**).—Compound **20** was obtained from **15** according to the procedure described for **11** (47.0%); mp 152–154°C; $[\alpha]_D$ +7.7° (*c* 0.5, CH_2Cl_2); IR (film): *ν* 3280 (OH), 1795 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$): *δ* 4.87 (d, 1 H, $J_{1,2}$ 1.4 Hz, H-1), 4.50 (ddd, 1 H, $J_{3,4}$ 2.9, $J_{4,5a}$ 6.7, $J_{4,5b}$ 9.9 Hz, H-4), 4.36 (ddd, 1 H, $J_{3,5a}$ 1.0, $J_{2,3}$ 6.7 Hz, H-3), 3.98 (ddd, 1 H, $J_{5a,5b}$ 10.7 Hz, H-5a), 3.73 (t, 1 H, H-5b), 3.38 (dd, 1 H, H-2), 3.40 (s, 3 H, OCH_3), 2.47 (s, 3 H, Ts); HRMS (EI): *m/z* 327.0775 ($M^{+\bullet}$); Calcd for $C_{14}H_{17}NO_6S$: 327.0776. Anal. Calcd for $C_{14}H_{17}NO_6S$: C, 51.36; H, 5.23; N, 4.28. Found: C, 51.4; H, 5.2; N, 4.3

Benzyl 2-C*:3*-N-*carbonyl-2,3-dideoxy-3*-N-*tosyl-amino*-β-D-*ribopyranoside* (**21**).—Compound **21** was obtained from **16** according to the procedure described for **11** (42.0%); mp 101–103°C; $[\alpha]_D$ −25.2° (*c* 1, CH_2Cl_2); IR (film): *ν* 3383 (OH), 1796 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$): *δ* 5.08 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1), 4.58 (m, 1 H, H-4), 4.50 and 4.73 (2 d, each 1 H, *J* 11.6 Hz, Bn), 4.38 (ddd, 1 H, $J_{2,3}$ 6.6, $J_{3,5a}$ 1.1, $J_{3,4}$ 2.7 Hz, H-3), 3.98 (bdd, 1 H, $J_{4,5a}$ 6.6, $J_{5a,5b}$ 10.5 Hz, H-5a), 3.74 (t, 1 H, $J_{4,5b}$ 10.1 Hz, H-5b), 3.49 (dd, 1 H, H-2), 2.46 (s, 3 H, Ts); HRMS (EI): *m/z* 403.1085 ($M^{+\bullet}$); Calcd for $C_{20}H_{21}NO_6S$: 403.10895. Anal. Calcd for $C_{20}H_{21}NO_6S$: C, 59.53; H, 5.25; N, 3.47. Found: C, 59.0; H, 5.3; N, 3.3.

*Methyl 3-amino-2-*C*:3-*N*-carbonyl-2,3-dideoxy-*β*-*D*-ribopyranoside* (**22**).—Compound **22** was obtained from **20** according to the procedure described for **12**; yield 63.2% isolated as a syrup; $[\alpha]_D$ −43.2° (*c* 0.4, CH_2Cl_2); IR (film): *ν* 3319 (NH, OH), 1745 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$): *δ* 4.85 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1), 4.33 (bm, 1 H, H-4), 3.97 (t, 1 H, $J_{2,3}$ 5.7, $J_{3,4}$ 4.1 Hz, H-3), 3.82 (dd, 1 H, $J_{4,5a}$ 5.9, $J_{5a,5b}$ 10.8 Hz, H-5a), 3.67 (dd, 1 H, $J_{4,5b}$ 8.5 Hz, H-5b), 3.37 (dt, 1 H, $J_{2,NH}$ 1.6 Hz, H-2), 3.32 (s, 3 H, OCH_3); HRMS (LSIMS): *m/z* 174.0766 $[M+H]^+$; Calcd for $C_7H_{12}NO_4$: 174.0766.

*Benzyl 3-amino-2-*C*:3-*N*-carbonyl-2,3-dideoxy-*β*-*D*-ribopyranoside* (**23**).—Compound **23** was obtained from **21** according to the procedure described for **12**; yield 67% isolated as a syrup; $[\alpha]_D$ −77.9° (*c* 0.7, CH_2Cl_2); IR (film): *ν* 3298 (NH, OH), 1746 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$): *δ* 5.13 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1), 4.45 (m, 1 H, H-4), 4.04 (m, 1 H, H-3), 3.90 (dd, 1 H, $J_{4,5a}$ 5.9, $J_{5a,5b}$ 10.7 Hz, H-5a), 3.76 (dd, 1 H, $J_{4,5b}$ 8.7 Hz, H-5b), 3.49 (m, 1 H, $J_{2,NH}$ 1.1, $J_{2,3}$ 5.6 Hz, H-2); Anal. Calcd for $C_{13}H_{15}NO_4$: C, 62.63; H, 6.06; N, 5.62. Found: C, 62.6; H, 6.3; N, 5.5.

*Methyl 3,4-di-*O*-benzyl-2-*C*-(*N*-tert-butoxycarbonyl)carbamoyl-2-deoxy-α-L-arabinopyranoside* (**25**).—To a solution of **24** (0.18 g, 0.5 mmol) in THF (5 mL) was added KH (0.15 g, 20% dispersion in mineral oil), and the resulting suspension was stirred for 10 min. Subsequently, 2-(*tert*-butoxycarbonyloxyi mino)-2-phenylacetonitrile (BOC-ON; 0.15 g, 0.6 mmol) was added and the stirring was continued for an additional 5 min. The mixture was then treated with *t*-BuOH (2 mL) and diluted with toluene (25 mL). The resulting solution was washed with water, dried, and concentrated. The crude product was purified by chromatography using 6:1:3:2 $CHCl_3$–EtOAc–toluene–hexane as eluent to afford **25** (0.22 g, 94%); mp 95–96°C; $[\alpha]_D$ +54.6° (*c* 1, CH_2Cl_2); IR (film): *ν* 3320 (NH), 1775 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$): *δ* 7.56 (bs, 1 H, NH), 4.61 and 4.75 (2 d, each 1 H, *J* 12.4 Hz, Bn), 4.47 (dd,1 H, $J_{1,2}$ 8.3 Hz, H-1), 4.43 and 4.48 (2 d, each 1 H, *J* 11.3 Hz, Bn), 4.14 (dd, 1 H, $J_{4,5a}$ 2.2, $J_{5a,5b}$ 13.0 Hz, H-5a), 3.87 (dd, 1 H, $J_{2,3}$ 11.0, $J_{3,4}$ 3.1 Hz, H-3), 3.63 (bt, 1 H, H-4), 3.49 (s, 3 H, OCH_3), 3.31 (dd, 1 H, $J_{4,5b}$ 0.9 Hz, H-5b), 2.90 (bs, 1 H, H-2), 1.49 (s, 9 H, t-Bu). Anal. Calcd for $C_{26}H_{33}NO_7$: C, 66.22; H, 7.05; N, 2.96. Found: C, 66.3; H, 7.1; N, 3.1.

*Methyl 2-*C*-(*N*-tert-butoxycarbonyl-carbamoyl)-2-deoxy-α-L-arabinopyranoside* (**26**).—Compound **25** (0.83 g, 1.8 mmol) was hydrogenated in MeOH (10 mL) in the presence of 10% Pd-C under standard conditions to afford **26** as a syrup (0.51 g, 99%); $[\alpha]_D$ +15.4° (*c* 1, H_2O); ^1H NMR (D_2O) (5:4 mixture of amide isomers): *δ* 4.50 (d, 0.6 H, $J_{1,2}$ 8.6 Hz, H-1 major), 4.47 (d, 0.4 H, $J_{1,2}$ 8.6 Hz, H-1 minor), 4.07 (dd, 0.6 H, $J_{3,4}$ 3.3, $J_{2,3}$ 11.0 Hz, H-3 major), 4.00 (dd, 1 H, $J_{4,5a}$ 2.1, $J_{5a,5b}$ 13.2 Hz, H-5a major and minor), 3.99 (dd, 0.4 H, $J_{2,3}$ 11.0, $J_{3,4}$ 3.3 Hz, H-3 minor), 3.89 (m, 1 H, H-4), 3.69 (dd, 0.6 H, $J_{4,5b}$ 3.3 Hz, H-5b major), 3.68 (dd, 0.4 H, $J_{4,5b}$ 3.3 Hz, H-5b minor), 3.49 and 3.50 (2 s, 3 H, OCH_3 major and minor), 2.72 (bs, 0.6 H, H-2a major), 2.66 (dd, 0.4 H, $J_{2,3}$ 11.0 Hz, H-2a minor), 1.25 and 1.50 (2 s, 9 H, t-Bu major and minor); HRMS (EI): *m/z* 259.1062 $[M\text{-}CH_3OH]^+$; Calcd for $C_{11}H_{17}NO_6$: 259.1056.

*Methyl 4-*O*-benzyl-3-*O*-tert-butyldimethylsilyl-2-deoxy-2-*C*-(*N*-tosylcarbamoyl)-α-L-arabinopyranoside* (**27**).—Compound **27** was obtained from **9** according to the procedure described for **4**; yield 48% isolated as a syrup; $[\alpha]_D$ +65.6° (*c* 1, CH_2Cl_2); IR (film): *ν* 1717 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$): *δ* 4.25 (d, 1 H, $J_{1,2}$ 8.3 Hz, H-1), 4.16 (dd, 1 H, $J_{4,5a}$ 2.3, $J_{5a,5b}$ 12.9 Hz, H-5a), 4.07 (dd, 1 H, $J_{3,4}$ 3.1 Hz, H-3), 3.54 (bt, 1 H, H-4), 3.36 (dd, 1 H, $J_{4,5b}$ 1.1 Hz, H-5b), 3.35 (s, 3 H, OCH_3), 2.83 (dd, 1 H, $J_{2,3}$ 10.4 Hz, H-2), 2.51 (s, 3 H, Ts), 0.90, 0.10, and 0.09 (3 s, 3,3,9 H, *t*-BuMe_2Si); HRMS (LSIMS): *m/z* 518.20312 $[M\text{-}OCH_3]^+$; Calcd for $C_{26}H_{36}NO_6SSi$: 518.20326.

*Methyl 3-*O*-tert-butyldimethylsilyl-2-deoxy-2-*C*-(*N*-tosylcarbamoyl)-α-L-arabinopyranoside* (**28**).—Catalytic hydrogenolysis of **27** in MeOH in the presence of 10% Pd-C under conditions described for **26** afforded **28**; yield 92.6% isolated as a syrup; $[\alpha]_D$ +48.7° (*c* 1.2, CH_2Cl_2); IR (film): *ν* 3657 (OH), 3211 (NH), 1717 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$): *δ* 4.13 (dd, 1 H, $J_{4,5a}$ 1.9, $J_{5a,5b}$ 13.0 Hz, H-5a), 4.11 (d, 1 H, $J_{1,2}$ 8.3 Hz, H-1), 4.05 (dd, 1 H, $J_{2,3}$ 10.3, $J_{3,4}$ 3.4 Hz, H-3), 3.67 (bs, 1 H, H-4), 3.43 (d, 1 H, $J_{4,5b}$ 1.2 Hz, H-5b), 3.30 (s, 3 H, OCH_3), 2.62 (dd, 1 H, H-2), 2.42 (s, 3 H, Ts), −0.08, 0.05, and 0.80 (3 s, 3,3,9 H, *t*-BuMe_2Si); HRMS (LSIMS): *m/z* 460.18211 $[M+H]^+$; Calcd for $C_{20}H_{34}NO_7SSi$: 460.18253.

*Methyl 3-*O*-tert-butyldimethylsilyl-2-*C*:4-*N*-carbonyl-2,4-dideoxy-4-*N*-tosylamino-β-D-xylopyranoside* (**29**).—Compound **29** was obtained according to the procedure described for **11**; yield 45.3% isolated as a syrup; $[\alpha]_D$ −7.4° (*c* 1, CH_2Cl_2); IR (film): *ν* 1801 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$): *δ* 4.88 (d, 1 H, $J_{1,2}$ 1.0 Hz, H-1), 4.26 (ddd, 1 H, $J_{3,4}$

2.3, $J_{4,5a}$ 6.2, $J_{4,5b}$ 8.6 Hz, H-4), 4.07 (dd, 1 H, $J_{2,3}$ 6.7 Hz, H-3), 3.64 (dd, 1 H, $J_{5a,5b}$ 11.8 Hz, H-5a), 3.44 (m, 1 H, H-5), 3.35 (dd, 1 H, H-2), 3.33 (s, 3 H, OCH_3), 2.45 (s, 3 H, Ts), 0.10, 0.20, and 0.90 (3 s, 3,3,9 H, t-BuMe_2Si). Anal. Calcd for $C_{20}H_{31}NO_6SSi$: C, 54.39; H, 6.60; N, 2.96. Found: C, 54.3; H, 6.7; N, 2.8.

*Methyl 3-amino-2-*C*:3-*N*-carbonyl-2,3-dideoxy-*β-D-erythro-*pyranosid-4-ulose* (**30**).—Compound **30** was obtained from **13** or **22** according to the procedure described for **31**; yield 93% isolated as a syrup; $[\alpha]_D$ +36.4° (*c* 0.25, CH_2Cl_2); IR (film): *ν* 3313 (NH), 1769 (C=O, *β*-lactam), 1731 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$): *δ* 6.20 (bm, 1 H, NH), 5.10 (d, 1 H, $J_{1,2}$ 1.1 Hz, H-1), 4.17 and 4.44 (2 d, each 1 H, $J_{5a,5b}$ 18.2 Hz, H-5a,5b), 4.01 (bd, 1 H, $J_{2,3}$ 5.2 Hz, H-3), 3.77 (m, 1 H, $J_{2,NH}$ 1.8 Hz, H-2), 3.45 (s, 3 H, OCH_3); HRMS (EI): *m/z* 171.05388 ($M^{+\bullet}$); Calcd for $C_7H_9NO_4$: 171.05316.

*Methyl 2-*C*:3-*N*-carbonyl-2,3-dideoxy-3-*N*-tosyl-amino-*β-D-erythro-*pyranosid-4-ulose* (**31**).—Compound **17** or **20** (0.30 g, 0.91 mmol) dissolved in a mixture of CCl_4 (1.8 mL), MeCN (0.6 mL), and water (0.5 mL), was oxidized with RuO_2–$NaIO_4$ in the presence of benzyltriethylammonium chloride according to [14] to afford **31** (0.27 g, 91%); mp 131–132 °C; $[\alpha]_D$ −13.1° (*c* 1, CH_2Cl_2); IR (film): *ν* 1810 (C=O, *β*-lactam), 1740 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$): *δ* 5.06 (d, 1 H, $J_{1,2}$ 1.2 Hz, H-1), 4.25 (bd, 1 H, $J_{2,3}$ 5.8 Hz, H-3), 3.99 and 4.05 (2 d, each 1 H, *J* 18.2 Hz, H-5a,5b), 3.75 (dd, 1 H, H-2), 3.40 (s, 3 H, OCH_3), 2.47 (s, 3 H, Ts); HRMS (LSIMS): *m/z* 325.0615 ($M^{+\bullet}$); Calcd for $C_{14}H_{15}NO_6S$: 325.0620.

*Benzyl 3-amino-2-*C*:3-*N*-carbonyl-2,3-dideoxy-β-D-erythro-pyranosid-4-ulose* (**32**).—Compound **19** or **23** (0.11 g, 0.44 mmol) was dissolved in Me_2SO (0.9 mL) and Ac_2O (0.26 mL) and kept at 0°C for 48 h. Subsequently, EtOH (0.5 mL) and H_2O (1 mL) were added and the temperature was allowed to rise to room temperature. After 30 min, 30% NH_4OH (1.5 mL) was added and the mixture was extracted with CH_2Cl_2. The extract was washed, dried, and concentrated. The product was purified by chromatography to give **32** as a syrup (0.035 g, 35%); $[\alpha]_D$ −16.2° (*c* 0.45, CH_2Cl_2); IR (film): *ν* 3396 (NH), 1780 (C=O, *β*-lactam), 1743 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$): *δ* 5.32 (d, 1 H, $J_{1,2}$ 1.2 Hz, H-1), 4.23 and 4.46 (2 d, each 1 H, $J_{5a,5b}$ 18.2 Hz, H-5a,5b), 4.02 (d, H, $J_{2,3}$ 5.3 Hz, H-3), 3.79 (m, 1 H, H-2). Anal. Calcd for $C_{13}H_{13}NO_4$: C, 63.15; H, 5.39; N, 5.66. Found: 63.1; H, 5.5; N, 5.4.

*Methyl 2-*C*-[carbethoxymethylene (triphenylphosphorane)]carbonyl-2,3-dideoxy-3-*N*-tosylamino-4-ulo-β-D-erythro-pyranoside* (**35**).—Compound **31** (0.3 g, 0.092 mmol) in toluene (2 mL) was treated with ethyl (triphenylphosphoranylidene)acetate (**34**; 0.038 g, 0.11 mmol) and kept at room temperature for 8 h. Subsequently, the solvent was evaporated and the residue was purified by chromatography to give **35** as a foam (0.032 g, 58%); $[\alpha]_D$ +51.7° (*c* 1, CH_2Cl_2); IR (film): *ν* 3366 (NH), 1734 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$): *δ* 5.47 (d, 1 H, $J_{1,2}$ 2.1 Hz, H-1), 5.03 (d, 1 H, $J_{3,NH}$ 7.8 Hz, NH), 4.68 (dd, 1 H, $J_{2,3}$ 4.9 Hz, H-2), 4.27 (m, 1 H, H-3), 3.85 and 3.93 (2 d, each ^1H, $J_{5a,5b}$ 16.2 Hz, H-5a,5b), 3.65 and 3.81 (2 dq, each 1 H, Et), 3.51 (s, 3 H, OCH_3), 2.36 (s, 3 H, Ts), 0.69 (t, 3 H, Et); MS (EI): *m/z* 673 ($M^{+\bullet}$). Anal. Calcd for $C_{36}H_{36}NO_8PS$: C, 64.17; H, 5.38; N, 2.07. Found: C, 64.6; H, 6.0; N, 1.8.

*Methyl 3-amino-2-*C*:3-*N*-carbonyl-4-*C*-ethoxy-carbonylmethylene-2,3,4-trideoxy-*β-D-erythro *pyranoside* (**36**).—Compound **30** (0.021 g, 0.12 mmol) in toluene (0.8 mL) was treated with ethyl (triph-enylphosphoranylidene)acetate (**34**; 0.063 g, 0.18 mmol) and kept for 18 h at room temperature. Subsequently, the mixture was concentrated and purified by chromatography to give **36** as a syrup (0.014 g, 48%); $[\alpha]_D$ −7.4° (*c* 0.9, CH_2Cl_2); IR (film): *ν* 3316 (NH), 1768 (C=O, *β*-lactam), 1711 (C=O), 1650 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$): *δ* 6.86 (m, 1 H, CH), 6.33 (bd, 1 H, NH), 5.09 (d, 1 H, $J_{1,2}$ 1.3 Hz, H-1), 4.90 (m, 1 H, $J_{3,4}$ 4.7 Hz, H-3), 4.44 (m, 1 H, H-5a), 4.18 (dq, 2 H, Et), 4.13 (dt, 1 H, $J_{3,5}$ 1.0, $J_{4,5b}$ 1.0, $J_{5a,5b}$ 15.3 Hz, H-5b), 3.40 (s, 3 H, OCH_3), 3.38–3.41 (m, 1 H, H-2), 1.29 (t, 3 H, Et); HRMS (LSIMS): *m/z* 242.10272 $[M+H]^+$; Calcd $C_{11}H_{16}NO_5$: 242.10283.

*X-ray structure determination of compounds **20** and **31**.*—The crystals suitable for X-ray structure analysis were obtained by slow evaporation of a hexane–Et_2O solution. Data were collected on an Enraf–Nonius Mach3 diffractometer with graphite monochromatized CuK_α radiation in the *θ*-range 3.73 to 74.93°. Lorentz and polarization corrections were applied to the independent reflections. The structures were solved by direct methods [20]

[1] Tables of atomic coordinates, bond lengths, and bond angles have been deposited with the Cambridge Crystallographic Data Centre. These tables may be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 IEZ, UK.

and refined against F^2 using SHELXL93 [21].[1] All but hydroxy H-atoms were placed in ideal positions and refined with the riding model and fixed isotropic displacement parameters. Crystallographic parameters, data collection and structure refinement details are shown in Tables 1 and 2.[2]

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