Highly Functionalized Cyclopentanes by Radical Cyclization of Unsaturated Bromolactones. 2. A Facile Synthesis of the First Carbaaldohexofuranoses and Their Conversion to Carbapentofuranoses

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A novel type of carbasugars, carbaaldohexofuranoses, has been prepared using a 5-exo-trig radical cyclization of C-2 substituted 2,3-unsaturated 7-bromoheptono-1,4-lactones as the key step. During the cyclization step, two stereogenic centers were formed with high stereoselectivity. The lactone moieties of the cyclopentane derivatives were reduced to the alcohols, and the following carbahexofuranoses were synthesized: carba-β-D-mannofuranose, carba-α-L-glucofuranose and 5-amino-5-deoxycarba-α-L-glucofuranose. Side chain degradation of the two former compounds gave the carbapentofuranoses: carba-α-L-xylofuranose and carba-β-D-lyxofuranose.

Introduction

Highly functionalized cyclopentanes as well as cyclohexanes are structural features found in biologically interesting compounds. Polyoxygenated derivatives are often referred to as carbasugars, since they may be viewed as furanose- or pyranose-analogues where the ring oxygen has been replaced by a methylene group. The lack of the acetal moiety preserves them from hydrolysis as compared to the sugar derivatives, thus rendering them biologically resistant, and many glycosidase inhibitors and antiobiotics are found within this class of compounds.[1] The importance of carbafuranoses stems from the interest in having access to carbocyclic analogues of nucleosides[2,3] which have attracted particular interest as antitumor and antiviral agents. (−)-Carbovir has been an attractive synthetic target as exemplified by the recently published synthesis by Trost and co-workers.[4] Oxygenated cyclopentanes, substituted with other functional groups as well, have also been recognized as glycosidase inhibitors, exemplified by the powerful α-mannosidase inhibitor Mannostatin, which has been synthesized in the optically pure form by Ganem and co-workers[5] as well as in the racemic form by the Trost group.[6]

Stereocontrol in the synthesis of such compounds is quite challenging, and the synthons can either be chosen among compounds from the chiral pool or from achiral, easily available compounds, with resolution of either the starting material or some intermediate at an early stage in the synthesis. Thus, using chiral substrates several approaches to the synthesis of polyoxygenated carbocycles from carbohydrates have been reported,[7] and the use of achiral starting materials such as norbornene[8,9] or cyclopentene derivatives[10] has also been described.

An attractive method for the preparation of cyclopentanes is intramolecular radical cyclization, especially when the substrates are carbohydrates, because radical cyclizations can be run under neutral conditions. This means that base-catalyzed epimerization and β-elimination are not competing reactions as in carbanionic carbon−carbon bond-forming reactions.[11] Internal radical cyclization of a suitable carbohydrate derivative possessing both a radical donor as well as a radical acceptor gives rise to cyclic products with preservation of all stereocenters and in the best cases also with stereocontrol at the new C−C bond formed in the ring closing reaction. This strategy to prepare carbocyclic analogues of carbohydrates was first recognized by Wilcox and co-workers who prepared carbafructofuranose from an acyclic unsaturated carbohydrate derivative, where only the *Z*-isomer gave full stereocontrol.[12] Our approach to obtain carbafuranoses was to use 2,3-unsaturated 7-bromo-7-deoxy-heptono-1,4-lactones as synthons. We have shown that a 5-exo-trig-radical cyclization could be initiated, resulting in formation of a cyclopentane ring fused to the five-membered lactone ring,[13] thereby generating one stereocenter with high

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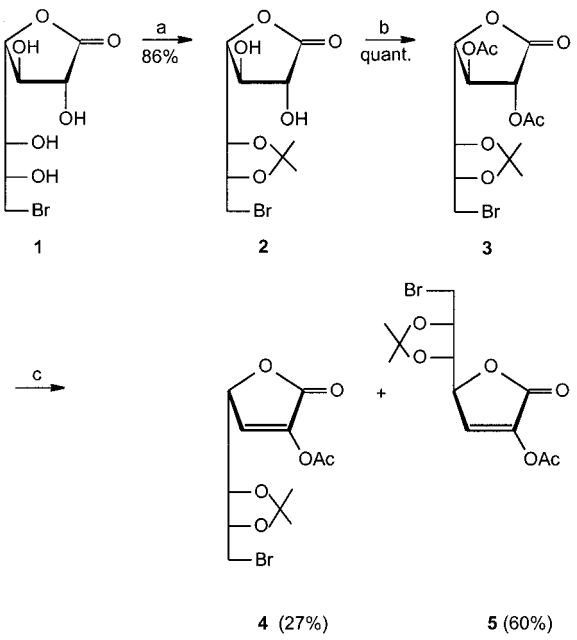
Scheme 1



a: acetone, H^+; b: Ac_2O, pyridine; c. Et_3N, CH_2Cl_2

stereoselectivity. The products obtained were used for preparation of 5-deoxy-carbahexofuranoses.[13] We also showed that the intermediate radical in a tandem reaction could be trapped stereospecifically by unsaturated species giving rise to C-2 alkylated bicyclic systems.[13a]

It was now of interest to investigate the reactivity of the double bond of C-2 substituted 2,3-unsaturated heptono-1,4-lactones in carbocyclization reactions. Using a 2-oxy-substituent, carbaanalogues of aldohexofuranoses might be prepared. While carbahexopyranoses have been prepared and well studied,[14] the corresponding furanoses of aldohexoses have, to our knowledge, not been prepared except for some 5-deoxy analogues.[13,15,16] The already mentioned carba-D-fructofuranose[12] together with the reported racemic *ribo*-carb-2-ulofuranose analogue[9] are the only known carbaanalogues of 2-ketohexofuranoses. Using a nitrogen substituent at C-2 the carbocyclization might give access to biologically important carbaanalogues of aminodeoxy hexofuranoses.

Results

Previously we have prepared 2,3-unsaturated 7-bromo-7-deoxy-heptono-1,4-lactones from the corresponding 2-bromo-2-deoxy-heptono-1,4-lactones, generating the double bond by a reductive *trans*-β-bromo-acetoxy-elimination promoted by $NaHSO_3$.[13] For the preparation of C-2 substituted 2,3-unsaturated lactones, a different approach was needed. Esterified aldono-1,4-lactones readily undergo a β-hydrogen-acyloxy-elimination under alkaline conditions due to the acidic proton α to the carbonyl group. As starting material for this reaction the readily available 7-bromo-7-deoxy-D-*glycero*-D-*galacto*-heptono-1,4-lactone (**1**)[17] was chosen. The exocyclic hydroxyl groups of **1** were protected with an isopropylidene group to give **2** for the purpose of avoiding elimination in the side chain during the subsequent elimination step[18] (Scheme 1). Lactone **2** was acetylated in pyridine to give the esterified heptonolactone **3**. Since no elimination was observed during the acylation procedure[18] a stronger base was required. It was found that triethylamine in dichloromethane caused a fast β-elimination to give a 2,3-unsaturated 1,4-heptonolactone. The β-elimination was, however, always accompanied by an isomerization at C-4 to give the two C-4 epimeric α,β-unsaturated lactones **4** and **5**. The epimers could be separated by crystallization to give **5** in 51% yield, followed by flash chromatographic separation of the remaining mixture. Comparison of the NMR data for **4** and **5** with NMR data for other 2,3-unsaturated aldonolactones[19] did not allow definite assignments of the configurations at C-4, and therefore a chemical proof was performed (Scheme 2).[20] Thus, the unsaturated lactones were assigned as 2-*O*-acetyl-7-bromo-3,7-dideoxy-5,6-*O*-isopropylidene-D-*arabino*-hept-2-enono-1,4-lactone (**4**) and 2-*O*-acetyl-7-bromo-3,7-dideoxy-5,6-*O*-isopropylidene-D-*ribo*-hept-2-enono-1,4-lactone (**5**).

Investigation of the radical cyclization of the two C-2 substituted 2,3-unsaturated lactones was now undertaken (Scheme 3). Thus, **4** was treated with tributyltin hydride to give only one compound as judged by ^1H NMR of the crude product, and the bicyclic lactone **11** was isolated in 90% yield. This indicated that formation of two stereogenic centers during the cyclization reaction occurred stereoselectively. Assignment of the configuration at C-4 of **11** was based on the coupling constant between H-4 and H-5, which was 7.5 Hz and thus indicated cis-oriented protons in the five-membered ring system. The coupling constant between H-1 and H-5, $J_{1,5}$ = 4.5 Hz, did not give a definite proof of cis-oriented protons. It was, however, assumed that the ring closing reaction leading to a cyclopentane ring fused to the five-membered lactone ring should give the thermodynamically more stable cis-fused bicyclic system.[21] The unsaturated lactone **5** was similarly treated with tributyltin hydride to give a bicyclic lactone **17** which was isolated in 90 % yield. ^1H NMR of the crude product revealed no byproducts, again indicating that the formation of two

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(20) The unsaturated lactones were converted into 3,7-dideoxy-heptono-1,4-lactones for comparison with known compounds (Scheme 2). Thus, the double bond of **4** and **5** was catalytically hydrogenated over palladium on charcoal, without the presence of base, to give saturated heptonolactones. It is known that catalytic hydrogenations of C-2 substituted unsaturated aldono-1,4-lactones give saturated lactones with cis-oriented substituents at C-2 and C-4.[31] Further catalytic hydrogenation in the presence of triethylamine caused reduction of the bromine to give the 7-deoxy derivatives **6** and **9**, respectively. Deprotection using acidic methanol yielded the two 3,7-dideoxy-heptono-1,4-lactones, **7** (mp 129−131 °C, $[\alpha]^{20}_D$ −54 (*c* 1.2, H_2O)) and **10** (mp 153 °C, $[\alpha]^{20}_D$ −17 (*c* 1.5, MeOH)), respectively. A comparison of melting points and specific rotations with the data for the known 3,7-dideoxy-D-*gluco*-heptono-1,4-lactone (**7**) (mp 133−134 °C, $[\alpha]^{20}_D$ −59 (*c* 1.5, H_2O))[32] established the configuration at C-4 of **7** and **10**.

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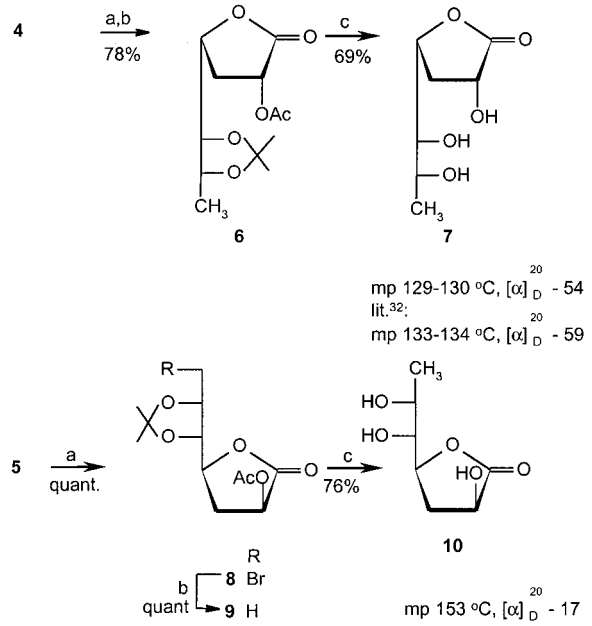
Scheme 2. Structure Proof for 4 and 5



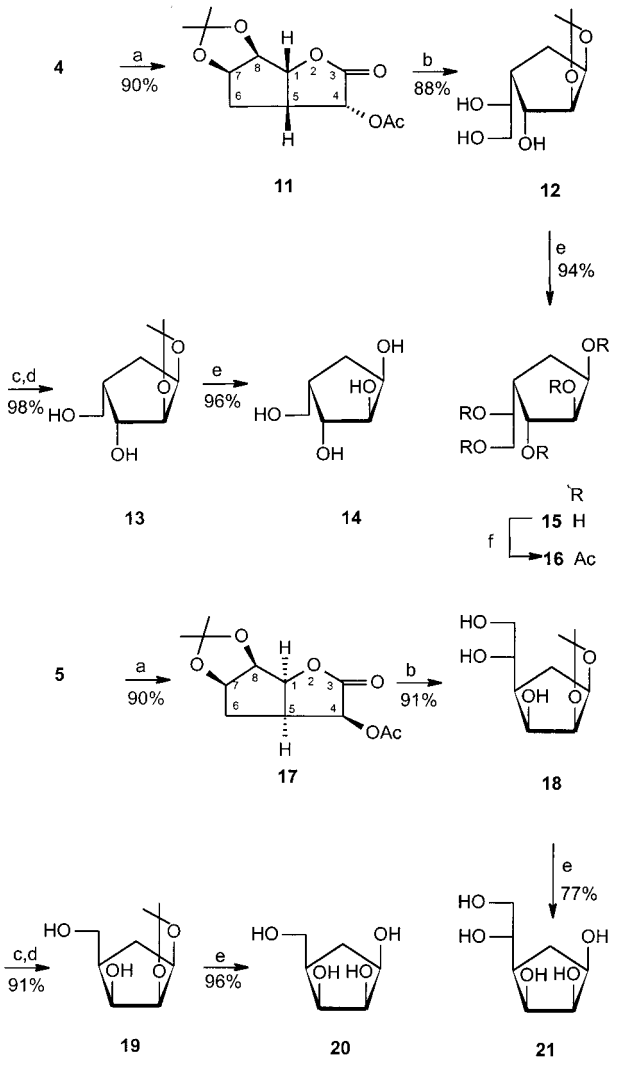
a: Pd/C, H_2, EtOAc; b: Pd/C, H_2, Et_3N, EtOAc; c: HCl,MeOH

stereogenic centers occurred stereoselectively. Assignment of the configuration at C-5 was as above based on the assumption that the thermodynamically more stable cis-fused bicyclic system had been formed, and the coupling constant of 9 Hz between H-4 and H-5 indicated cis-oriented protons. Confirmation of the assignment was obtained by X-ray crystallography of compound **17**.[13a]

The bicyclic lactones **11** and **17** were used for the preparation of carbahexofuranoses and carbapentofuranoses (Scheme 3). Reduction of the lactone moiety to the corresponding alcohol using sodium borohydride in the presence of sodium methoxide allowed the preservation of the isopropylidene group in the carbahexose series. By oxidative cleavage of the exocyclic diol, using sodium periodate, the carbahexoses were degraded to isopropylidene-protected carbapentofuranoses. Thus lactone **11** gave the protected crystalline carbahexofuranose **12**, which was deprotected to give carba-α-L-glucofuranose (**15**). Acetylation gave the crystalline pentaacetate **16**. Likewise, reduction of lactone **17** gave the carbahexose derivative **18**, which after hydrolysis gave crystalline carba-*β*-D-mannofuranose (**21**). Compound **12** was degraded to the isopropylidene-protected carbapentofuranose **13**, which was hydrolyzed to give the new crystalline α-L-xylofuranose (**14**). The enantiomer has previously been reported as a syrup[15] and as a crystalline compound.[22] By the same procedure compound **18** gave the carbapentose derivative **19**, which by deprotection gave crystalline carba-*β*-D-lyxofuranose (**20**), previously reported as a syrup.[15]

To study further the reactivity of the double bond and the stereoselectivity at C-2 in the radical cyclization step, a C-2 nitrogen substituted 2,3-unsaturated 7-bromoheptonolactone was prepared (Scheme 4). Previously we have reported a convenient access to 2-amino-2-deoxyaldonolactones via nucleophilic substitution of 2-bromo-2-deoxy-aldonolactones with azide ions.[23] Hence, treat-

Scheme 3



a: Bu_3SnH, AIBN, EtOAc; b: $NaBH_4$, NaOMe, MeOH; c: $NaIO_4$, H_2O; d: $NaBH_4$, H_2O; e: aq HCl; f: Ac_2O, $HClO_4$

ment of 2,7-dibromo-2,7-dideoxy-D-*glycero*-D-*ido*-heptono-1,4-lactone (**22**)[32] with sodium azide was performed. The crude product, containing a mixture of C-2 epimers of a 2-azido-7-bromo-2,7-dideoxy-heptono-1,4-lactone, was acetylated using pyridine as the solvent to give the 2,3-unsaturated lactone **23**, due to a simultaneous *β*-elimination of acetic acid. Lactone **23** could be isolated by crystallization (24% yield). Flash chromatographic purification of the mother liquor material gave a further amount (13%) of **23** together with a 3,4-unsaturated heptonolactone (32%), which was characterized by NMR alone. The presence of the latter lactone indicates that an isomerization at C-4 of **23** possibly could take place in the presence of pyridine, and thus a proof of structure for compound **23** was performed, as discussed below. Interestingly, the *β*-elimination in this case was induced by pyridine. Pyridine could not induce *β*-elimination of the 2-acetoxylactone **3**, and this indicates a more acidic H-2 proton in the 2-azidolactone. Treatment of the 2-azidolactone **23** with 2 equiv of tributyltin hydride

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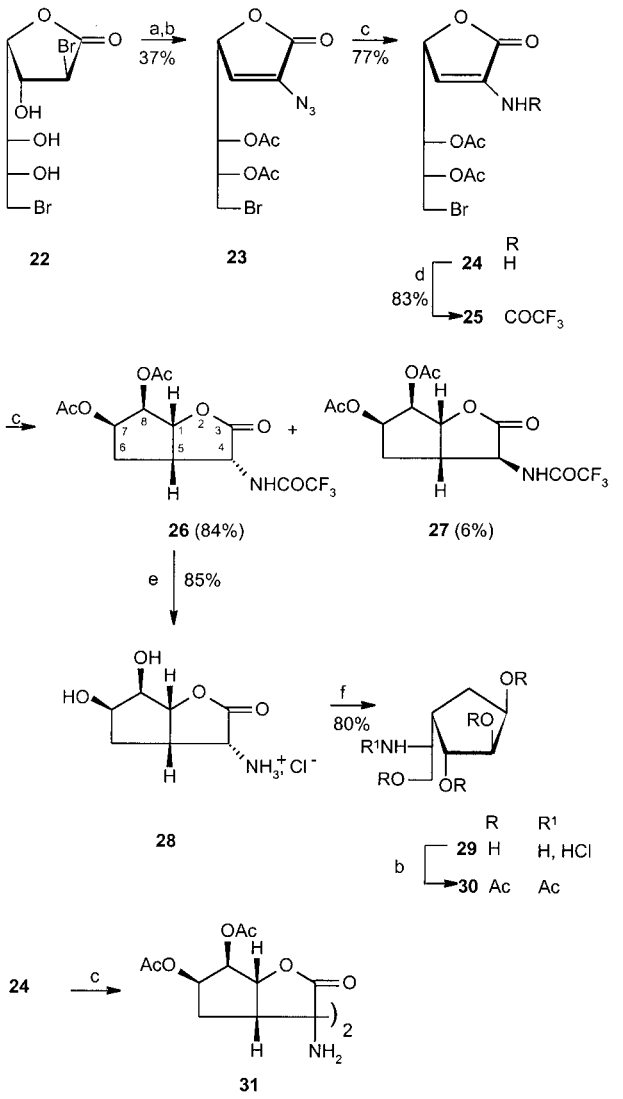
Scheme 4



a: NaN_3, DMF; b: Ac_2O, pyridine; c: Bu_3SnH, AIBN; d: $(CF_3CO)_2O$, EtOAc; e: aq HCl; f: i: $NaBH_4$, H_2O, ii: HCl/H_2O

caused reduction of the azido group to an amino substituent,[24] and the 2,3-unsaturated-2-aminolactone **24** was isolated by crystallization. No traces of a cyclized product were observed in the NMR spectra of the crude product; neither was a product from a debromination at C-7 observed. An alternative attempt to prepare the amine **24** by a Staudinger reduction using PPh_3 to reduce the azide[25] was not successful due to the stability of the intermediate vinylic iminophosphorane. Further treatment of the unsaturated 2-aminolactone **24** with an excess of tributyltin hydride and AIBN in refluxing toluene gave rise to a cyclized compound. The ^1H NMR spectra revealed the absence of a proton on the amino substituted carbon. This showed that the product was not the expected bicyclic compound, but presumably a symmetrical dimer, **31**, of the bicyclic compound. According to earlier studies, amino acid derived radicals often tend to undergo dimerization.[26] The dimerization was avoided by acylation of the amino group prior to cyclization. Thus the amine **24** was treated with trifluoroacetic acid anhydride to give the trifluoroacetamide substituted unsaturated lactone **25**, which by reaction with tributyltin hydride gave a major cyclization product, **26**, together with a minor one, **27**. The major product could be isolated by direct crystallization in 76% yield, and the remaining mixture was separated by flash chromatography. Dimerization in the radical cyclization step could also be avoided by protecting amine **24** with a trimethylsilyl group. This gave a cyclization product with the same configuration as compound **26**, but the workup of the TMS-protected product was troublesome due to cleavage of the protecting group. The configurations at C-4 of the two cis-fused bicyclic lactones **26** and **27** were determined from the coupling constants between H-4 and H-5, which was 9 Hz in the major product and 6 Hz in the minor product. Hence, cis-oriented protons were assigned to **26** and trans-oriented protons were assigned to **27**. The crystalline bicyclic lactone **26**, was deprotected by treatment with aqueous HCl to give the amino acid derivative **28**. This compound was reduced by treatment with sodium borohydride to give an amino substituted cyclopentane **29**, which can be recognized as the carbocyclic analogue of 5-amino-5-deoxy-α-L-glucofuranose. It should be noted that lactone **28** could possibly be used as a synthon for the preparation of a new stereoisomer of carbaanalogues of Nikkomycin.[27] Nikkomycins constitute a class of nucleosides in which the 5′-position is substituted with an amino acid.

Since both a 2,3- and a 3,4-unsaturated heptonolactone had been isolated from the base-catalyzed *β*-elimination leading to compound **23**, a chemical proof of structure was carried out for the purpose of confirming the configuration at C-4 of **23**. The structural proof was done by converting the unsaturated heptonolactone **25** and heptonolactone **7** into the same amino substituted heptonolactone **33** (Scheme 5). Thus the unsaturated lactone **25** was reduced by hydrogenation using palladium on charcoal as the catalyst. By analogy with the reduction of **4** and **5** and with related work[28,31] this was expected to give a saturated lactone with cis-oriented substituents at C-2 and C-4. Further hydrogenation in the presence of triethylamine reduced the primary bromide to a deoxy function to give **32**, which by treatment with acidic methanol gave the aminolactone hydrochloride **33**. The second part of the structure proof started from the known compound 3,7-dideoxy-D-*gluco*-heptono-1,4-lactone (**7**).[32] Protection of the exocyclic hydroxyl groups gave **34**. Upon treatment with an excess of methanesulfonyl chloride the hydroxyl group at C-2 was mesylated, and

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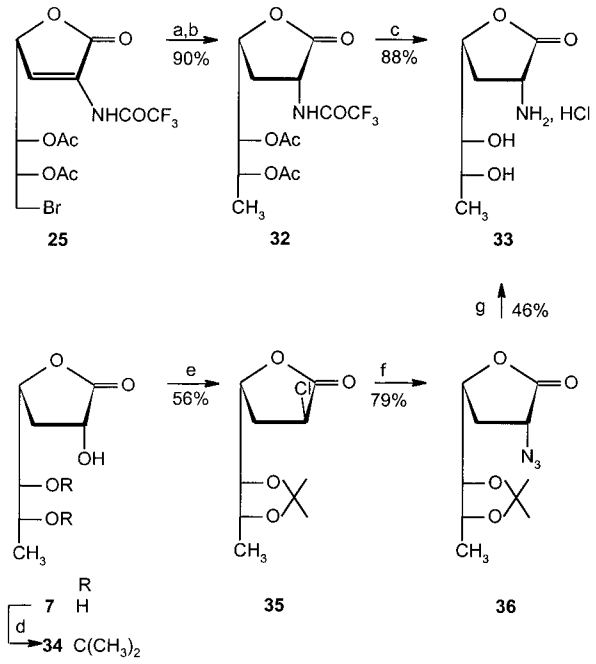
(32) Bock, K.; Lundt, I.; Pedersen, C.; Sonnichsen, R. *Carbohydr. Res.* **1988**, *174*, 331.

Scheme 5. Structure Proof for 25 and Thus 23



a: Pd/C, H_2, EtOAc; b: Pd/C, H_2, Et_3N, EtOAc; c: aq HCl; d: acetone, H^+; e: MsCl, Pyridine; f: NaN_3, CH_3CN; g: Pd/C, H_2, HCl, MeOH

subsequent nucleophilic substitution of the mesylate with chloride gave the chlorolactone **35**. Nucleophilic substitution of the chloride with sodium azide gave the azidolactone **36** which was hydrogenated under acidic conditions to give the aminolactone hydrochloride **33**. Melting points, specific rotations, and NMR spectra showed the aminolactones obtained by the two routes to be identical. The configuration at C-4 could not have been affected in either reaction sequence. Thereby the configuration at C-4 of the unsaturated lactone **25** was established, which meant that the configuration of **23** was also established. Furthermore, the configuration at C-2 in **36** was proven.

The radical cyclizations of compounds **4**, **5**, and **25** showed a high degree of stereoselectivity in the generation of two stereogenic centers. The first stereogenic center which is formed upon the addition of the alkyl radical to the double bond was in all three cases stereospecific in the formation of two cis-annelated five-membered rings. The second stereogenic center, which is formed upon the trapping of tributyltin hydride by the enolate radical,[13] was stereospecific in the case of **4** and **5** as judged by ^{1}H NMR of the crude products, and highly stereoselective in the case of **25**. The stereoselectivity is most likely caused by steric shielding of the enolate radical by the cyclopentane ring. This shielding we also found when the enolate radical was trapped by allyl tributylstannane[13a] and high stereoselectivity has been observed in similar cyclic systems.[29]

Concluding Remarks

In conclusion, we have reported the preparation and radical cyclization of C-2 substituted 2,3-unsaturated 7-bromo-7-deoxy-heptono-1,4-lactones. The 5-exo-trig-radical cyclizations generate two stereogenic centers with high stereoselectivity. The cyclized compounds were used for the preparation of carbaaldohexofuranoses, a novel class of compounds, which by side chain degradation yielded carbapentofuranoses.

Experimental Section

Melting points are uncorrected. Optical rotations were determined on a Perkin-Elmer 241 polarimeter. NMR spectra were recorded at 500, 300, or 250 MHz (^{1}H) and 125.8, 75.5, or 62.9 MHz (^{13}C). Chemical shifts were measured in ppm and coupling constants (J) in Hz. For spectra in D_2O, either dioxane ($\delta = 67.4$), acetone ($\delta = 29.8$), or methanol ($\delta = 49.0$) was used as the internal reference for ^{13}C NMR spectra, and the solvent peak ($\delta = 4.63$) for ^{1}H NMR spectra. For spectra in $CDCl_3$, chloroform-*d* ($\delta = 76.9$) was used as internal reference for ^{13}C NMR spectra while chloroform-H ($\delta = 7.27$) was used for ^{1}H NMR spectra. For spectra in acetone (CD_3, $\delta = 29.8$) was used for ^{13}C spectra and (CD_2H, $\delta = 2.05$) was used for ^{1}H spectra. Assignments of ^{1}H NMR signals were done by homonuclear decoupling experiments, and assignments of ^{13}C NMR signals were, if reported, done by HETCOR experiments. Bu_3SnH was prepared from bis(tributytin) oxide and polymethylhydrosiloxane.[30] Reactions using Bu_3SnH were performed in a nitrogen atmosphere. All concentrations were performed in vacuo. Dry solvents were obtained by storing over molecular sieves. Microanalyses were carried out by Leo Microanalytical Laboratory and Research Institute for Pharmacy and Biochemistry, Prague, Czech Republic.

7-Bromo-7-deoxy-5,6-*O*-isopropylidene-D-*glycero*-D-*galacto*-heptono-1,4-lactone (2). Bromolactone **1**[17] (8.70 g, 32.1 mmol) was suspended in dry acetone, and camphorsulfonic acid (0.74 g, 3.2 mmol) was added to the suspension. The flask was equipped with a Soxhlet apparatus containing 3 Å molecular sieves (20 g), and the reaction mixture was refluxed for 24 h, after which it was neutralized with solid $NaHCO_3$ (20 g), filtered, and concentrated. The residue was suspended in H_2O and extracted with EtOAc. The combined organic phases were dried ($MgSO_4$) and concentrated to give a crystalline residue (9.80 g). Recrystallization from EtOAc:hexane of the residue and of the evaporated mother liquor gave isopropylidene-protected **2** as colorless crystals (8.50 g, 86%), mp 159−160 °C. ^{1}H NMR (500 MHz, CD_3COCD_3): δ 5.28 (d, 1 H, C3-*O*H), 5.15 (d, 1 H, C2-*O*H), 4.65 (ddd, H-6, $J_{6,7} = 5.5$, $J_{6,7'} = 8$), 4.49 (dd, H-5, $J_{5,6} = 6.5$), 4.42 (dd, H-2, $J_{2,3} = 8$), 4.32 (m, H-3, H-4), 3.76 (dd; H-7, $J_{7,7'} = 11$), 3.62 (dd, H-7′), 1.38, 1.35 (2 s, 6 H). ^{13}C NMR (CD_3COCD_3, 62.9 MHz): δ 174, 109.9, 74.6, 74.9, 75.1, 77.8, 77.9, 31.0, 26.9, 25.5. Anal. Calcd for $C_{10}H_{15}BrO_6$ (311.13): C, 38.6; H, 4.86; Br, 25.68. Found: C, 38.74; H, 4.89; Br, 25.82.

2,3-Di-*O*-acetyl-7-bromo-7-deoxy-5,6-*O*-isopropylidene-D-*glycero*-D-*galacto*-heptono-1,4-lactone (3). Lactone **2** (8.76 g, 28.2 mmol) was dissolved in pyridine (40 mL) and Ac_2O (20 mL). The solution was left at room temperature for 1.5 h after which it was concentrated to give a slightly colored crystalline residue (14.58 g). The residue was dissolved in CH_2Cl_2 and washed with H_2O. The organic phase was dried (Na_2SO_4), filtered through activated charcoal, and concentrated to give acetylated **3** (11.27 g, quant) as colorless crystals, mp 109−115 °C. Recrystallization of an aliquot from Et_2O:hexane gave **3**, mp 115 °C, $[\alpha]^{20}_D$ −99 (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.68 (d, H-2, $J_{2,3} = 6.5$), 5.60 (dd, H-3, $J_{3,4} = 6.5$), 4.63 (dd, H-4, $J_{4,5} = 1$), 4.62 (m, H-6, $J_{6,7'} = 5.5$, $J_{6,7} = 9.5$), 4.45 (dd, H-5, $J_{5,6} = 6$), 3.66 (dd, H-7′, $J_{7,7'} = 10.5$), 3.56 (dd, H-7), 2.19, 2.15 (2s, 6 H), 1.47, 1.39 (2 s, 6 H). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ 170, 169.4, 168.5, 110.3, 77.3, 76.2, 74.9, 73.5, 71.3, 28.2, 26.2, 25.0, 20.5, 20.3. Anal. Calcd for $C_{14}H_{19}BrO_8$ (395.20): C, 42.55; H, 4.85; Br, 20.22. Found: C, 42.56; H, 4.88; Br, 20.15.

2-*O*-Acetyl-7-bromo-3,7-dideoxy-5,6-*O*-isopropylidene-D-*arabino*-hept-2-enono-1,4-lactone (4) and 2-*O*-Acetyl-7-bromo-3,7-dideoxy-5,6-*O*-isopropylidene-D-*ribo*-hept-2-enono-1,4-lactone (5). Protected lactone **3** (8.00 g, 20.3 mmol) was dissolved in CH_2Cl_2 (65 mL) and Et_3N (3.34 mL,

24.3 mmol) and left at room temperature for 2.5 h. The solvents were evaporated, the residue was dissolved in CH_2Cl_2 (100 mL), and the organic phase was washed with H_2O, dried (Na_2SO_4), filtered through activated charcoal, and evaporated to give a crystalline crude product (6.89 g, quant). Recrystallization of the residue and of the product from the resulting mother liquor from EtOAc:Et_2O (ca. 1:10) gave **5** (3.51 g, 51%) as colorless crystals, mp 121−124 °C. Flash chromatography of the mother liquor (EtOAc:hexane 1:3) gave crystalline **5** (0.61 g, 9%) and **4** (1.83 g, 27%) as a semicrystalline solid. 2-*O*-Acetyl-7-bromo-3,7-dideoxy-5,6-*O*-isopropylidene-D-*ribo*-hept-2-enono-1,4-lactone (**5**): Repeated crystallizations from EtOAc:Et_2O afforded the product, mp 127−128 °C, $[\alpha]^{20}_D$ −37 (*c* 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.41 (H-3, d, $J_{3,4} = 2$), 5.03 (H-4, dd, $J_{4,5} = 9$), 4.58 (H-6, ddd, $J_{5,6} = 5.5$, $J_{6,7'} = 4.8$, $J_{6,7} = 8.5$), 3.92 (H-5, dd), 3.77 (H-7′, dd, $J_{7,7'} = 11$), 3.58 (H-7, dd), 2.35 (s, 3 H), 1.55, 1.40 (2 s, 6 H). ^{13}C NMR ($CDCl_3$, 62.9 MHz): 166.7, 165.5, 138.2, 132.8, 110.0, 78.2, 77.6, 75.6, 28.8, 27.6, 25.0, 20.8. Anal. Calcd for $C_{12}H_{15}BrO_6$ (335.15): C, 43.01; H, 4.51; Br, 23.84. Found: C, 43.02; H, 4.51; Br, 23.80. 2-*O*-Acetyl-7-bromo-3,7-dideoxy-5,6-*O*-isopropylidene-D-*arabino*-hept-2-enono-1,4-lactone (**4**): Repeated crystallizations from EtOAc:Et_2O gave colorless crystals, mp 91−93 °C, $[\alpha]^{20}_D$ −78 (*c* 0.5, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.21 (H-3, d, $J_{3,4} = 2$), 5.36 (H-4, dd, $J_{4,5} = 1.2$), 4.65 (H-6, ddd, $J_{5,6}$ 6.5, $J_{6,7'} = 6$, $J_{6,7} = 9$), 4.41 (H-5), 3.72 (H-7′, dd, $J_{7,7'} = 10$), 3.69 (H-7, dd), 2.30 (s, 3 H), 1.42, 1.37 (2 s, 6 H). ^{13}C NMR ($CDCl_3$): δ 166.7, 166.6, 138.3, 130.2, 110.3, 76.4, 76.3, 75.3, 28.3, 26.2, 24.9, 20.7. Anal. Calcd for $C_{12}H_{15}BrO_6$ (335.15): C, 43.01; H, 4.51; Br, 23.84. Found: C, 43.13; H, 4.41; Br, 23.90.

2-*O*-Acetyl-3,7-dideoxy-5,6-*O*-isopropylidene-D-*gluco*-heptono-1,4-lactone (6). Compound **4** (0.10 g, 0.3 mmol) was dissolved in EtOAc (4 mL). Palladium on charcoal (5%,15 mg) was added, the suspension was hydrogenated for 5 h at 1 atm, Et_3N (0.08 mL, 0.6 mmol) was added, and the hydrogenation was continued at 1 atm for 40 h. Filtration and concentration gave a crystalline residue which was dissolved in CH_2Cl_2 and washed with H_2O. The organic phase was dried ($MgSO_4$), and evaporation of the solvent gave **6** as slightly colored crystals (60 mg, 78%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 5.48 (dd, H-2, $J_{2,3'} = 9$, $J_{2,3} = 10.5$), 4.45 (m, H-4, H-6), 4.00 (dd, H-5, $J_{4,5} = 2.5$, $J_{5,6} = 6.5$), 2.68 (ddd, H-3′, $J_{3,3'} = 12.5$, $J_{3',4} = 6$), 2.29 (ddd, H-3, $J_{3,4} = 10$), 1.49, 1.38 (2 s, 6 H), 1.39 (d, H.7, $J_{6,7} = 6.5$). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ 171.8, 169.7, 108.8, 77.6, 74.3, 72.2, 67.6, 30.6, 26.7, 25.2, 20.3, 14.8.

3,7-Dideoxy-D-*gluco*-heptono-1,4-lactone (7). Compound **6** (53 mg, 0.2 mmol) was dissolved in 3 mL of HCl/MeOH (0.06 mL AcCl in 3 mL of MeOH), and the solution was left at room temperature for 48 h and then concentrated. The residue was purified by flash chromatography (EtOAc:MeOH 9:1) to give **7** as colorless crystals (25 mg, 69%), mp 125−127 °C, $[\alpha]^{20}_D$ −48 (*c* 1.5, H_2O). The compound was crystallized from EtOH:Et_2O, mp 129−131 °C, $[\alpha]^{20}_D$ −54 (*c* 1.2, H_2O) [lit.[32] mp 133−134 °C, $[\alpha]^{20}_D$ −59 (*c* 1.5, H_2O)]. ^{1}H NMR (D_2O, 500 MHz): δ 4.66 (m, H-2, H-4), 3.77 (dq, H-6, $J_{6,7} = 6.5$), 3.36 (dd, H-5, $J_{4,5} = 3.5$, $J_{5,6} = 7$), 2.56 (ddd, H-3′, $J = 5.5$, 7.5, $J_{3',3} = 12.5$), 2.06 (dd, H-3), 1.15 (d, 3 H, H-7). ^{13}C NMR (D_2O (dioxane), 62.9 MHz): δ 180.5, 77.5, 75.6, 68.7, 67.6, 33.1, 19.1.

2-*O*-Acetyl-7-bromo-3,7-dideoxy-5,6-*O*-isopropylidene-D-*altro*-heptono-1,4-lactone (8). The unsaturated lactone **5** (1.00 g, 3.0 mmol) was dissolved in EtOAc (20 mL), Pd on charcoal (5%, 0.1 g) was added, and the reaction mixture was hydrogenated for 18 h at atmospheric pressure. Filtration and concentration gave 2-*O*-acetyl-7-bromo-3,7-dideoxy-5,6-di-*O*-isopropylidene-D-*altro*-heptono-1,4-lactone (**8**) as colorless crystals (1.04 g, quant), mp 98−112 °C. Recrystallization from Et_2O:hexane afforded compound **8**, mp 119 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 5.46 (dd, H-2, $J_{2,3}$ =10.5, $J_{2,3'} = 8.5$), 4.55 (m, H-4, H-6, $J_{6,7'} = 4$, $J_{6,7} = 8.5$), 4.16 (dd, H-5, $J_{4,5} = 8.5$, $J_{5,6} = 5.5$), 3.65 (dd, H-7′, $J_{7,7'} = 11$), 3.46 (dd, H-7), 2.88 (ddd, H-3′, $J_{3,3'}$ =13.5, $J_{3',4} = 6$), 2.20 (ddd, H-3, $J_{3,4} = 9.5$), 2.17 (s, 3 H), 1.49, 1.40 (2 s, 6 H). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ 172, 169, 109.6, 78.7, 77.4, 72.7, 67.4, 32.4, 29.1, 27.6, 25.0, 20.3. Anal. Calcd for $C_{12}H_{17}BrO_6$ (337.17): C, 42.75; H, 5.08; Br, 23.70. Found: C, 42.96; H, 5.09; Br, 23.74.

2-*O*-Acetyl-3,7-dideoxy-5,6-*O*-isopropylidene-D-*altro*-heptono-1,4-lactone (9). Saturated lactone **8** (0.70 g, 2.1 mmol) was dissolved in EtOAc (25 mL). Palladium on charcoal (5%, 70 mg) and Et_3N (0.56 mL, 4.2 mmol) was added, and the mixture was hydrogenated in a H_2 atmosphere for 20 h at high pressure (ca. 100 Bar). Filtration and concentration gave **9** as a slightly colored syrup (0.55 g, quant). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ 172, 67.4, 72.5, 72.9, 31.8, 78.7, 13.9.

3,7-Dideoxy-D-*altro*-heptono-1,4-lactone (10). Compound **9** (0.55 g, 2.1 mmol, crude product) was dissolved in HCl/MeOH (0.3 M, 30 mL) and left at room temperature for for 72 h. The solution was concentrated to give a crystalline product (0.4 g). Recrystallization from EtOH:Et_2O gave **10** (0.28 g, 76%), mp 149−153 °C, as slightly colored crystals. Flash chromatography of an aliquot (EtOAc) and crystallization from EtOH:Et_2O gave an analytical sample of **10**, mp 153 °C, $[\alpha]^{20}_D$ −17 (*c* 1.5, MeOH). ^{1}H NMR (D_2O, 500 MHz): δ 4.64 (m, H-2, H-4), 3.72 (dd, H-5, $J_{4,5} = 3.5$, $J_{5,6} = 6$), 3.66 (dq, H-6, $J_{6,7} = 6$), 2.56 (ddd, H-3′, $J_{3,3'} = 12$), 2.05 (m, H-3), 1.13 (d, 3 H-7). ^{13}C NMR (D_2O (dioxane), 62.9 MHz): δ 180.1, 78.3, 74.7, 68.0, 68.8, 31.5, 19.2. Anal. Calcd for $C_7H_{12}O_5$ (176.17): C, 47.73; H, 6.87. Found: C, 47.60; H, 6.90.

(1*R*,5*R*)-4(*R*)-*O*-Acetyl-7(*R*),8(*R*)-*O*-isopropylidene-2-oxabicyclo[3.3.0]oct-3-one (11). Compound **4** (0.90 g, 2.7 mmol) was dissolved in dry EtOAc (20 mL) and heated at reflux under a N_2 atmosphere. Via a syringe pump a solution of Bu_3SnH (0.85 mL, 3.2 mmol) and AIBN (44 mg, 0.3 mmol) in EtOAc (9.2 mL) was added over 3 h. The reaction mixture was evaporated, and the residue was suspended in CH_3CN (25 mL) and washed with hexane (4 × 30 mL). The CH_3CN was evaporated to give a colorless crystalline product (0.68 g, 99%), mp 85−95 °C. ^{1}H NMR showed only one product. Flash chromatography (hexane → EtOAc:hexane 2:5) gave the cyclized product **11** (0.62 g, 90%) as colorless crystals, mp 93−100 °C. Repeated crystallizations of an aliquot gave mp 101−104 °C, $[\alpha]^{20}_D$ −106 (*c* 1, $CHCl_3$). The product could also be purified by recrystallization: Starting from **4** (0.41 g, 1.2 mmol) following the procedure described above, the crude product from evaporation of the acetonitrile was recrystallized from Et_2O:hexane to give **11** as slightly colored crystals (0.23 g, 74%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 5.64 (d, H-4, $J_{4,5} = 7.5$), 4.81 (dd, H-7, $J_{6',7} = 4.5$, $J_{7,8} = 5$), 4.71 (d, H-8), 4.66 (d, H-1, $J_{1,5} = 4.5$), 3.49 (m, H-5, $J_{5,6} = 7.5$, $J_{5,6'} = 11{,}5$), 2.18 (s, 3 H), 2.13 (ddd, H-6, $J_{6,6'} = 15$), 1.81 (ddd, H-6′), 1.32, 1.43 (2 s, 6 H). ^{13}C NMR ($CDCl_3$, 62.9 MHz): 172, 169.5 (C-3, OAc), 110.9 (acetal), 85.5 (C-1), 83.7 (C-8), 81.0 (C-8), 70.7 (C-4), 41.2 (C-5), 31.0 (C-6), 26.2, 23.8, 20.3. Anal. Calcd for $C_{12}H_{16}O_6$ (256.25): C, 56.25; H, 6.29. Found: C, 56.27; H, 6.44.

1,2-*O*-Isopropylidenecarba-α-L-glucofuranose (12). Bicyclic lactone **11** (1.53 g, 6.0 mmol) was added to a solution of $NaBH_4$ (0.44 g, 12.0 mmol) and NaOMe (2.4 M in MeOH, 2.5 mL, 6.0 mmol) in dry MeOH (25 mL) at 0 °C. The temperature was raised to room temperature during 1 h, and the solution was left at this temperature for 15 h. The solution was cooled in an ice bath, and HOAc (50%, 6.7 mL, 59 mmol) was added. After 0.5 h the solvent was evaporated. The residue was coevaporated with H_2O (40 mL) and then with MeOH (6 × 30 mL). It was then purified by flash chromatography (EtOAc:acetone 3:1). This gave **12** as colorless crystals (1.15 g, 88%), mp 73−75 °C. The compound could be recrystallized from EtOAc:Et_2O; mp 74−75.5 °C, $[\alpha]^{20}_D$ +17.0 (*c* 0.51, EtOH). ^{1}H NMR (D_2O, 500 MHz): δ 4.76 (m, H-1), 4.40 (d, H-2, $J_{1,2} = 5.5$), 4.06 (d, H-3, $J_{3,4} = 4$), 3.68 (ddd, H-5, $J_{4,5} = 9$, $J_{5,6} = 6.5$, $J_{5,6'} = 3$), 3.58 (dd, H-6′, $J_{6,6'} = 12$), 3.39 (dd, H-6), 2.12 (m, H-4). 1.63 (m, H-4a, H-4a′), 1.34, 1.22 (2 s, 6 H). ^{13}C NMR (D_2O (dioxane), 62.9 MHz): δ 111.2, 86.0, 80.6, 75.6, 71.2, 65.8, 43.6, 32.6, 25.8, 23.7. Anal. Calcd for $C_{10}H_{18}O_5$ (218.25): C, 55.03; H, 8.31. Found: C, 54.81; H, 8.27.

1,2-*O*-Isopropylidenecarba-α-L-xylofuranose (13). Protected carbahexofuranose **12** (0.20 g, 0.92 mmol) was dissolved in H_2O (2.0 mL) and cooled in an ice bath in a flask protected from light. A solution of $NaIO_4$ (0.24 g, 1.1 mmol) in H_2O (2 mL) was added, and stirring was maintained for 1 h at 0 °C,

after which a solution of $NaBH_4$ (0.14 g, 3.7 mmol) in H_2O (2 mL) was added. The reaction mixture was left at room temperature for 18 h and then quenched at 0 °C by addition of HOAc (1.05 mL, 17.8 mmol). The solvents were evaporated and the residue was coconcentrated with MeOH (4 × 30 mL). Flash chromatography (EtOAc:Acetone 7:1) afforded **13** (0.17 g, 98%), as a semicrystalline solid. The crude product could also be purified by extraction. Thus 0.57 g (2.6 mmol) of the starting material **12** was treated as described above with $NaIO_4$ (0.67 g, 3.1 mmol) and $NaBH_4$ (0.38 g, 10.4 mmol) and was quenched with HOAc (2.4 mL), evaporated, and then evaporated from MeOH. The residue was dissolved in H_2O (20 mL) and extracted with EtOAc (12 × 25 mL). The organic phase was dried (Na_2SO_4) and concentrated. This afforded crystalline **13**, (0.42 g, 86%) which was recrystallized from Et_2O:hexane; mp 35−36 °C, $[\alpha]^{20}_D$ +26.5 (*c* 0.56, EtOH) [lit.[15] for enantiomer: oil, $[\alpha]^{20}_D$ −18.8 (*c* 1.6, 90% $CHCl_3$, 10% MeOH)]. CI-MS (NH_3): *m*/*z* 206 ($M + NH_4^+$), 189 ($M + H^+$). ^{1}H NMR (D_2O, 500 MHz): δ 4.76 (dd, H-1, $J_{1,2} = 5.5$, $J_{1,4a} = 5.5$), 4.40 (d, H-2), 4.00 (d, H-3, $J_{3,4} = 4$), 3.64 (dd, H-5′, $J_{4.5'} = 8$, $J_{5',5} = 11$), 3.55 (dd, H-5, $J_{4,5} = 6.5$), 2.26 (m, H-4), 1.74 (dd, H-4a′, $J_{4a',4a} = 14$, $J_{4a',4} = 6.5$), 1.58 (ddd, H-4a, $J_{4a,4} = 14$), 1.35, 1.23 (2 s, 6 H). ^{13}C NMR (D_2O (acetone), 62.9 MHz): δ 109.9; 85.3, 79.1, 74.3, 59.5, 41.8, 31.7, 24.4, 22.3. Anal. Calcd for $C_9H_{16}O_4$ (188.22):C, 57.43; H, 8.57. Found: C, 57.43; H, 8.59.

Carba-α-L-xylofuranose (14). Protected carbafuranose **13** (0.30 g, 1.6 mmol) was suspended in aqueous HCl (1 M, 1.5 mL) and left at room temperature for 18 h. The solvent was evaporated, and the residue was dissolved in H_2O (10 mL) and neutralized with ion-exchange resin (IR 420 OH^-, 3 mL) for 5 min. The ion-exchange resin was filtered off, and the solvent was evaporated. This afforded **14** (0.23 g, 96%), as colorless crystals, mp 82−84 °C. The compound was recrystallized from EtOH:CH_3CN; mp 84−86 °C, $[\alpha]^{20}_D$ −18.6 (*c* 0.7, MeOH) [lit. for the enantiomer: oil, $[\alpha]^{20}_D$ +12.1 (*c* 0.7, MeOH);[15] mp 79.5−80.5 °C, $[\alpha]^{20}_D$ +13.4 (*c* 0.78, MeOH)[22]]. ^{1}H NMR (D_2O, 500 MHz): δ 4.06 (m, H-1, H-3), 3.78 (dd, H-2, $J_{1,2} = 5$, $J_{2,3} = 5$), 3.59 (dd, H-5′, $J_{4,5'} = 7$, $J_{5,5'} = 11$), 3.42 (dd, H-5, $J_{4,5} = 7.5$), 2.36 (m, H-4), 1.67 (m, H-4a, H-4a′). ^{13}C NMR (D_2O (dioxane), 62.9 MHz): δ 79.4, 76.8, 71.6, 62.6, 40.2, 32.9. Anal. Calcd for $C_6H_{12}O_4$ (148.16): C, 48.64; H, 8.16. Found: C, 48.55; H, 8.15.

Carba-α-L-glucofuranose (15). For deprotection, **12** (0.40 g, 1.8 mmol) was dissolved in aqueous HCl (1 M, 2 mL) and left at room-temperature overnight. Evaporation of the solvent gave **15** as a colorless oil which was dried in a desiccator over KOH, 0.31 g (94%). $[\alpha]^{20}_D$ +2.0 (*c* 1.0, MeOH). CI-MS (NH_3): *m*/*z* 196 ($M + NH_4^+$), 178 ($M + H^+$). ^{1}H NMR (D_2O, 500 MHz): δ 4.21 (ddd, H-1, $J_{1.2} = 4.5$), 4.09 (H-3, dd, $J_{3.4} = 6$), 3.85 (dd, H-2, $J_{2,3}$ =3) 3.63 (ddd, H-5, $J_{5,6} = 6.5$, $J_{5,6'} = 2.5$, $J_{4,5} = 9$), 3.59 (dd, H-6′, $J_{6,6'} = 12$), 3.41 (dd, H-6), 2.31 (m, H-4), 1.68 (m, H-4a′, $J_{4a,4a'} = 13.5$), 1.57 (m, H-4a). ^{13}C NMR (D_2O (dioxane), 62.9 MHz): δ 79.0, 77.2, 72.5, 72.2, 65.4, 41.8, 32.4.

Deacetylation of **16** (132 mg, 0.34 mmol) in MeOH (5 mL) using a catalytic amount of NaOMe/MeOH (pH = 12) for 2 h at room temperature followed by neutralization with acidic ion-exchange resin (Amberlite 120, H^+) and concentration gave **15** (57.7 mg, 95%). A ^{1}H NMR spectrum was identical with the one described above. The product was dried in a desiccator (concentrated H_2SO_4, solid KOH) to give a syrup having $[\alpha]^{20}_D$ +1.7 (*c* 1.0, MeOH).

1,2,3,5,6-Penta-*O*-acetylcarba-α-L-glucofuranose (16). Compound **15** (0.060 g, 0.34 mmol) was dissolved in Ac_2O (0.8 mL, 8.5 mmol), and a drop of perchloric acid was added. H_2O was added after stirring at room temperature for 3 h. The water phase was extracted with CH_2Cl_2, and the organic phases were washed with H_2O and aqueous $NaHCO_3$, dried ($MgSO_4$), and concentrated. The crude product was purified by flash chromatography (EtOAc:heptane 2:3) to give **16** (0.111 g, 84%) which crystallized from Et_2O:hexane; mp 66−67 °C , $[\alpha]^{20}_D$ −31.4 (*c* 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.42 (dtr, 1H), 5.35 (dd, 1 H), 5.17 (dd, 1 H), 5.11 (ddd, 1 H), 4.39 (dd, 1 H), 3.97 (dd, 1 H), 2.85 (ddd, 1 H), 2.09, 2.08, 2.04, 2.03, 2.01 (5 s, 15 H), 2.06 (m, 1 H), 1.92 (m, 1 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 170.6, 170.2, 169.9, 169.4, 169.3, 76.1, 74.8, 71.7, 69.4, 63.9, 39.6, 30.5, 20.6, 20.5, 20.45, 20.4, 20.3. Anal. Calcd for $C_{17}H_{24}O_{10}$ (388.38): C, 52.57; H, 6.23. Found: C, 52.50; H, 6.13.

(1*S*,5*S*)-4(*S*)-*O*-Acetyl-7(*R*),8(*R*)-*O*-isopropylidene-2-oxabicyclo[3.3.0]oct-3-one (17). Unsaturated lactone **5** (0.8 g, 2.4 mmol) was cyclized as described for preparation of compound **11**. The crude product contained only one component according to ^{1}H NMR. Flash chromatography (hexane → EtOAc:hexane 1:1) gave **17** (0.55 g, 90%) as colorless crystals, mp 105−113 °C, which was recrystallized from EtOAc:Et_2O (ca.. 1:10); mp 113−114 °C, $[\alpha]^{20}_D$ +87 (*c* 1, $CHCl_3$). X-ray crystallography confirmed the structure of compound **17**.[13a] The product could also be worked up by recrystallization: Starting from **5** (2.01 g, 6.0 mmol) following the procedure described for the preparation of **11**, the crude product from evaporation of the acetonitrile was recrystallized from EtOAc:Et_2O (ca. 1:10) to give **17** as colorless crystals (1.30 g, 85%), mp 110−112 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 5.55 (d, H-4, $J_{4.5} = 9$), 4.74 (ddd, H-7, $J_{7,8} = 5.5$, $J_{6,7} = 3$), 4.72 (dd, H-1, $J_{1,5} = 5.5$, $J_{1,8} = 5.5$), 4.68 (dd, H-8), 3.31 (m, H-5, $J_{5,6} = 7$, $J_{5,6'} = 9.5$), 2.21 (s, 3 H) 2.10 (ddd, H-6, $J_{6,6'} = 15$), 2.05 (ddd, H-6′) 1.52, 1.30 (2 s, 6 H). ^{13}C NMR ($CDCl_3$, 62.9 MHz): 171.5, 169.5 (C-3, OAc), 113.5, 81.8 (C-8), 80.6 (C-7), 79.8 (C-1), 70.0 (C-4), 41.6 (C-5), 27.1 (C6) 25.2, 25.1, 20.3. Anal. Calcd for $C_{12}H_{16}O_6$ (256.25): C, 56.25; H, 6.29. Found: C, 56.16; H, 6.30.

1,2-*O*-Isopropylidenecarba-β-D-mannofuranose (18). Bicyclic lactone **17** (4.0 g, 15.6 mmol) was reduced as described for compound **12** using a solution of $NaBH_4$ (1.16 g, 3.31 mmol) and NaOMe (6.5 mL, 2.4 M in MeOH, 15.6 mmol) in dry MeOH (80 mL). After repeated co-concentrations with MeOH the residue was dissolved in H_2O (20 mL) and extracted with EtOAc (18 × 25 mL). The organic phases were dried ($MgSO_4$) and the solvent was evaporated to give **18** as colorless crystals (3.1 g, 91%), mp 123−127 °C. Recrystallization from EtOAc gave crystals with mp 133−135 °C, $[\alpha]^{20}_D$ −55.5 (*c* 0.49, EtOH). ^{1}H NMR (D_2O, 500 MHz): δ 4.69 (m, H-1, $J_{1,2} = 7$), 4.46 (dd, H-2, $J_{2,3} = 4.5$), 4.02 (dd, H-3), 3.81 (ddd, H-5, $J_{5,6'} = 2.5$, $J_{5,6} = 5.5$), 3.58 (dd, H-6′, $J_{6,6'} = 12$), 3.37 (dd, H-6), 1.99 (m, H-4, $J_{4,5} = 9.5$), 1.94 (m, H-4a′), 1.52 (m, H-4a), 1.43, 1.28 (2 s, 6 H). ^{13}C NMR (D_2O (acetone), 62.9 MHz): 113.3, 80.5, 78.7, 70.3, 69.6, 63.7, 44.6, 29.7, 24.4, 23.4. Anal. Calcd for $C_{10}H_{18}O_5$ (218.25): C, 55.03; H, 8.31. Found: C, 55.22; H, 8.37.

1,2-*O*-Isopropylidenecarba-β-D-lyxofuranose (19). Diol **18** (1.40 g, 6.4 mmol) was oxidized using $NaIO_4$ (1.65 g, 7.7 mmol, in 14 mL H_2O) and subsequently reduced with $NaBH_4$ (0.95 g, 25.7 mmol in 14 mL H_2O) similarly to the preparation of **13**. After repeated evaporations from MeOH the residue was dissolved in H_2O (20 mL) and extracted with EtOAc (12 × 25 mL). The organic phases were dried (Na_2SO_4), filtered, and evaporated to yield a slightly colored oil (1.26 g) which was purified by flash chromatography (EtOAc) to give **19** (1.10 g, 91%) as colorless crystals, mp 57−62 °C. Repeated crystallizations from Et_2O:hexane gave crystals with mp 58−62 °C, $[\alpha]^{20}_D$ −38.6 (*c* 0.51, EtOH). CI-MS (NH_3): *m*/*z* 206 ($M + NH_4^+$), 189 ($M + H^+$). ^{1}H NMR (D_2O, 500 MHz): δ 4.66 (m, H-1), 4.47 (dd, H-2, $J_{1,2} = 5$, $J_{2,3} = 5$), 4.02 (dd, H-3, $J_{3,4} = 5$), 3.74 (dd, H-5′, $J_{5,5'} = 10.5$, $J_{4,5'} = 7$), 3.58 (dd, H-5, $J_{4,5} = 8.5$), 2.16 (m, H-4), 1.86 (ddd, H-4a′, $J_{4a,4a'} = 14.5$), 1.63 (ddd, H-4a), 1.41, 1.25 (2 s, 6 H). ^{13}C NMR (D_2O (methanol), 62.9 MHz): δ 112.7, 80.7, 79.3, 71.6, 60.9, 44.7, 30.3, 25.0, 23.4. Anal. Calcd for $C_9H_{16}O_4$ (188.22): C, 57.43; H, 8.57. Found: C, 57.45; H; 8.62.

Carba-β-D-lyxofuranose (20). Compound **19** (0.73 g, 3.9 mmol) was deprotected as described for the preparation of **14**. This afforded carbafuranose **20** (0.55 g, 96%) as colorless crystals; mp 69−72 °C. The compound was recrystallized from EtOH; mp 74−75.5 °C, $[\alpha]^{20}_D$ −21.3 (*c* 1.0, CH_3OH) [lit.,[15] oil, $[\alpha]^{20}_D$ −12.9° (*c* 1.0, CH_3OH)]. CI-MS (NH_3): *m*/*z* 166 ($M + NH_4^+$), 149 ($M + H^+$). ^{1}H NMR (D_2O, 500 MHz): δ 4.02 (m, H-1, H-3), 3.78 (dd, H-2, ($J_{1,2}$, $J_{2,3}$) = (4.5, 5.5)), 3.67 (dd, H-5′, $J_{4,5'} = 7.5$, $J_{5,5'} = 10.5$), 3.51 (dd, H-5, $J_{4,5} = 6.5$), 2.10 (m, H-4a′), 2.02 (m, H-4), 1.33 (ddd, H-4a, $J_{4a,4a'} = 13.5$). ^{13}C NMR

(D_2O (dioxane), 62.9 MHz): δ 74.7, 73.5, 71.6, 62.3, 41.0, 34.0. Anal. Calcd for $C_6H_{12}O_4$ (148.16): C, 48.64; H, 8.16. Found: C, 48.75; H; 8.08.

Carba-*β*-D-mannofuranose (21). Compound **18** (0.58 g, 2.7 mmol) was dissolved in aqueous HCl (1 M, 6 mL) and left at room temperature for 16 h. The solvent was evaporated, the oil was dissolved in H_2O (10 mL), and ion-exchange resin (IR 420 OH^-, 10 mL) was added and stirred slowly for 0.5 h. The mixture was filtered and the ion-exchange resin was washed thoroughly with H_2O followed by EtOH. The combined solvents were evaporated to give carba-*β*-D-mannofuranose **21** (0.36 g, 77%) as colorless crystals, mp 109−113 °C. Repeated crystallizations from EtOH:acetone gave a sample with mp 113−115 °C, $[\alpha]^{20}_D$ −26 (*c* 1.0, H_2O). ^{1}H NMR (D_2O, 500 MHz): δ 4.04 (m, 2H, H-3, H-5), 3.78 (dd, H-2, $J_{2,3} = 4$), 3.71 (ddd, H-1, $J_{1,2} = 6$, $J_{1,4a'} = 9.5$, $J_{1,4a} = 3$), 3.58 (dd, H-6′, $J_{6,6'} = 12.5$, $J_{5,6'} = 2.5$), 3.38 (dd, H-6, $J_{5,6} = 6.5$), 2.08 (m, H-4), 1.80 (m, H-4a′, $J_{4a,4a'} = 11$), 1.35 (ddd, H-4a). ^{13}C NMR (D_2O (dioxane), 62.9 MHz): δ 74.4, 73.9, 72.6, 71.6, 65.1, 41.4, 34.2. Anal. Calcd for $C_7H_{14}O_5$ (178.18): C, 47.19; H, 7.92. Found: C, 47.38; H, 7.91.

5,6-Di-*O*-acetyl-2-azido-7-bromo-2,3,7-trideoxy-D-*arabino*-hept-2-enono-1,4-lactone (23). Dibromoheptonolactone **22**[32] (14.69 g, 44 mmol) was dissolved in dry DMF (75 mL), and dry NaN_3 (29.0 g, 446 mmol) was added. The suspension was protected from light and stirred vigorously at room temperature for 6.5 h. EtOAc (300 mL) was added to the suspension, which afterward was filtered and concentrated at 25 °C to give a brown oil (20.7 g). The oil was dissolved in dry pyridine (75 mL) and Ac_2O (42 mL), and the solution was kept in a light-protected flask for 3.5 h at room temperature. The reaction mixture was poured into aqueous HCl (2 M, 450 mL) at 0 °C, and stirring was continued at room temperature for 1 h followed by extraction with CH_2Cl_2 (3 × 100 mL). The combined organic phases were washed with H_2O (6 × 100 mL), dried (Na_2SO_4), treated with activated charcoal, filtered, and concentrated (max. 25 °C). The residue was kept at 5 °C for 4 days which resulted in a semicrystalline substance. The residue was suspended in cold Et_2O (3 mL) and filtered to give **23** as slightly colored crystals (3.87 g, 24%), mp 108−112 °C. The mother liquor from the crystallization was purified by flash chromatography (EtOAc:hexane 1:6). This gave a 3,4-unsaturated azidolactone as a syrup (5.10 g, 32%), see below, together with crystalline **23** (2.02 g, 13%). Compound **23** was purified for analysis by flash chromatography (EtOAc:hexane 1:4), followed by solvation in EtOAc at room temperature, treatment with activated charcoal, filtration, and precipitation with hexane. A repeated crystallization from EtOAc:hexane at room temperature gave colorless crystals, mp 111−112 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): 6.48 (d, H-3, $J_{3,4} = 2.5$), 5.40 (dd, H-5, $J_{5,6} = 7.5$), 5.29 (m, H-6, $J_{6,7'} = 3.5$, $J_{6,7} = 4.5$), 5.24 (dd, H-4, $J_{4,5} = 2.5$), 3.82 (dd, H-7′, $J_{7,7'} = 12$), 3.50 (dd, H-7), 2.16, 2.09 (2 OAc). ^{13}C NMR ($CDCl_3$, 62.9 MHz): 169, 126.8, 119.2, 77.4, 69.7, 69.1, 30.8, 20.2, 20.5. Anal. Calcd for $C_{11}H_{12}BrN_3O_6$ (362.14): C, 36.48; H, 3.34; N, 11.60. Found: C, 36.63; H, 3.37; N, 11.32. The 3,4-unsaturated azidolactone was tentatively assigned as 5,6-di-*O*-acetyl-2-azido-7-bromo-2,3,7-trideoxy-hept-3-enono-1,4-lactone based on the following spectra: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 6.35 (d, H-2, $J_{2,3} = 7$), 5.48 (dd, H-3, $J_{3,5} = 2.5$), 5.28 (ddd, H-6), 4.82 (dd, H-5, $J_{5,6} = 9.5$), 3.83 (ddd, H-7′, $J_{6,7'} = 3.3$, $J_{7',7} = 11.5$), 3.78 (dd, H-7, $J_{6,7} = 3$). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ 170, 169 (C-1, 2 OAc), 119.2 (C-3), 76.7, 66.8 (C-5, C-6), 60.8 (C-2), 31.7 (C-7), 20.5, 20.3 (2 × OAc).

5,6-Di-*O*-acetyl-2-amino-7-bromo-2,3,7-trideoxy-D-*arabino*-hept-2-enono-1,4-lactone (24). Azido heptonolactone **23** (3.07 g, 8.48 mmol) was dissolved in dry toluene (60 mL) at 80 °C under a N_2 atmosphere. Bu_3SnH (4.95 mL, 18.7 mmol) and AIBN (0.14 g, 0.85 mmol) dissolved in dry toluene (15 mL) were added during 1 h. Evaporation of the solvent resulted in a solid residue which was dissolved in CH_3CN (600 mL) and washed with hexane (5 × 100 mL). The CH_3CN was evaporated to give a solid (3.01 g) which was triturated with cold EtOAc and filtered to give **24** (2.20 g, 77%) as slightly colored crystals. ^{1}H NMR (CD_3COCD_3, 250 MHz): δ 5.67 (H-3, d, $J_{3,4} = 2.2$), 5.28 (H-6, ddd, $J_{5,6} = 7.0$, $J_{6,7} = 2.7$, $J_{6,7'} = 5.3$), 5.23 (H-5, dd, $J_{4,5} = 2$), 5.20 (H-4, dd), 3.84 (H-7, dd, $J_{7,7'} = 11.5$), 3.65 (H-7′, dd), 4.79 (NH_2), 2.10, 2.0. ^{13}C NMR (CD_3COCD_3, 62.9 MHz): δ 171, 170, 136.5, 108.7, 78.2, 71.3, 71.3, 32.4, 20.7, 20.4.

5,6-Di-*O*-acetyl-7-bromo-2,3,7-trideoxy-2-trifluoroacetamido-D-*arabino*-hept-2-enono-1,4-lactone (25). Aminolactone **24** (1.70 g, 5.05 mmol) was dissolved in dry EtOAc (40 mL) and cooled to 0 °C. $(CF_3CO)_2O$ (1.43 mL, 10.1 mmol) was added slowly, the solution was stirred at 0 °C for 45 min and at room temperature for another 45 min followed by concentration. Recrystallization of the residue from EtOAc:hexane gave trifluoroacetamidolactone **25** as slightly colored crystals (1.80 g, 83%), mp 138 °C. Repeated crystallizations from EtOAc:hexane gave mp 138−141 °C, $[\alpha]^{20}_D$ −14.4 (*c* 0.36, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.25 (bs, NH), 7.51 (H-3, d, $J_{3.4} = 2$), 5.49 (H-5, dd, $J_{4,5} = 2.5$, $J_{5,6} = 7.5$), 5.39 (H-4, dd), 5.31 (H-6, ddd, $J_{6.7} = 3.5$, $J_{6,7'} = 4.5$), 3.78 (H-7′, dd, $J_{7,7'} = 12.0$), 3.49 (H-7, dd), 2.17, 2.04 (2 s, 6 H). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ 169.2, 169.0, 167.3, 155.3 (q, $J_{C,F} = 39.9$ Hz), 129.0, 124.9, 114.8 (q, $J_{C,F} = 287.5$), 79.3, 70.0, 69.3, 30.6, 20.6, 20.2. Anal. Calcd for $C_{13}H_{13}BrF_3NO_7$ (432.15): C, 36.13; H, 3.03; N, 3.24. Found: C, 36.36; H, 3.21; N, 3.47.

(1*R*,5*S*)-7(*R*),8(*R*)-Di-*O*-acetyl-4(*R*)-trifluoroacetamido-2-oxabicyclo[3.3.0]oct-3-one (26) and (1*R*,5*S*)-7(*R*),8(*R*)-di-*O*-acetyl-4(*S*)-trifluoroacetamido-2-oxabicyclo[3.3.0]-oct-3-one (27). Cyclization of trifluoroacetamidolactone **25** (1.98 g, 4.6 mmol) dissolved in EtOAc (20 mL) was done according to the method described for the preparation of **11**, using Bu_3SnH (1.6 mL, 6.0 mmol) and AIBN (0.08 g, 0.5 mmol) dissolved EtOAc (8.5 mL). The crude product was treated with activated charcoal, and the solvents were evaporated to give a crystalline residue (1.58 g, 98%). The main product, **26**, was isolated by crystallization from EtOAc:hexane as colorless crystals (1.23 g, 76%). The residue from concentration of the mother liquor was purified by flash chromatography (EtOAc: hexane 1:2), to give crystalline **26** (0.13 g, 8%), and the C-4-isomer **27** as a colorless syrup (0.09 g, 6%). Title compound **26**: Repeated crystallizations from EtOAc:Et_2O gave an analytically pure sample; mp 134−139 °C, $[\alpha]^{20}_D$ −153 (*c* 0.49, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.15 (bs, 1H, NH), 5.36 (m, H-7, H-8), 4.95 (dd, H-1, $J_{1,5} = 6.5$, $J_{1,8} = 1.5$), 4.78 (m, H-4, $J_{4,5} = 9$), 3.75 (m, H-5), 2.11, 2.07 (2 s, 6 H), 2.01 (ddd, H-6′, $J_{6,6'} = 14$), 1.88 (m, H-6). ^{13}C NMR ($CDCl_3$, 125.8 MHz): δ 171.9, 169.8, 169.3 (C-3, 2 × OAc), 158.3 (q, NHCO, $J_{C,F} = 39.2$), 115.2 (q, CF_3, $J_{C,F} = 287.7$), 84.3 (C-1), 76.9 (C-8), 72.0 (C-7), 52.2 (C-4), 39.2 (C-5), 28.1 (C-6), 20.6, 20.4 (2 × OAc). Anal. Calcd for $C_{13}H_{14}F_3NO_7$ (353.25): C, 44.20; H, 3.99; N, 3.97. Found: C, 44.11; H, 4.02; N, 3.91.

(1*R*,5*S*)-7(*R*),8(*R*)-Di-*O*-acetyl-4(*S*)-trifluoroacetamido-2-oxabicyclo[3.3.0]oct-3-one (27): ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.24 (bd, 1H, NH), 5.42 (ddd, H-7, $J_{7,8} = 4.5$), 5.23 (dd, H-8), 5.09 (dd, H-1, $J_{1,8} = 5.5$, $J_{1,5} = 9.5$), 4.20 (dd, H-4, $J_{4.5} = 6$, $J_{4,NH} = 6$), 3.14 (m, H-5), 2.48 (ddd, H-6′, $J_{6',7} = 4$, $J_{6',5} = 9$, $J_{6,6'} = 15$), 2.26 (ddd, H-6, $J_{6,7} = 5$, $J_{6,5} = 5$), 2.1, 2.07. ^{13}C NMR ($CDCl_3$, 125.8 MHz): 172.7, 169.7, 169.6 (C-3, 2 × OAc), 157.7 (q, NHCO, $J_{C,F} = 38.6$), 115.2 (q, CF_3, $J_{C,F} = 286.1$), 83.9 (C-1), 76.5 (C-8), 72.4 (C-7), 56.9 (C-4), 40.5 (C-5), 34.4 (C-6), 20.6, 20.5 (2 × OAc).

(1*R*,5*S*)-4(*R*)-Amino-7(*R*),8(*R*)-dihydroxy-2-oxabicyclo-[3.3.0]oct-3-one hydrochloride (28). Protected aminolactone **26** (1.0 g, 2.8 mmol) was suspended in aqueous HCl (1 N, 20 mL) and refluxed overnight. Concentration and recrystallization from CH_3CN:MeOH gave **28** as slightly colored crystals, (0.59 g, 85%), $[\alpha]^{20}_D$ −49 (*c* 0.73, MeOH). Treatment with activated charcoal and repeated crystallizations from MeOH:CH_3CN gave colorless crystals; mp 210−215 °C dec, $[\alpha]^{20}_D$ −45.8° (*c* 0.71, MeOH). ^{1}H NMR (D_2O, 500 MHz,): δ 4.84 (dd, H-1, $J_{1,5} = 6.5$, $J_{1,8} = 2.3$), 4.53 (d, H-4, $J_{4,5} = 9.5$), 4.20 (ddd, H-7, $J_{7,8} = 4$), 4.14 (dd, H-8), 3.49 (m, H-5), 1.92 (ddd, H-6′, $J_{6,6'} = 14$, $J_{5,6'} = 9$, $J_{6',7} = 5$), 1.79 (ddd, H-6, $J_{5,6} = 8.5$, $J_{6,7} = 5$). ^{13}C NMR (D_2O (CH_3CN), 62.9 MHz): δ 174, 88.3, 77.4, 72.3, 51.3, 37.7, 29.4. Anal. Calcd for $C_7H_{12}ClNO_4$ (209.63): C, 40.11; H, 5.77; Cl^-, 16.91; N, 6.68. Found: C, 40.01; H, 5.81; Cl^-, 16.35; N, 6.65.

5-Amino-5-deoxycarba-α-L-glucofuranose Hydrochloride (29). Bicyclic aminolactone **28** (0.40 g, 1.9 mmol) was dissolved in H_2O (2 mL) and cooled in an ice bath. A solution of $NaBH_4$ (0.3 g, 8.1 mmol) in H_2O (2 mL) was added at 0 °C, and the solution was kept for 1 h at 0 °C stored at 5 °C for another 40 h. Aqueous HCl (1 N) was added until pH 1, and the solution was concentrated to a residue which was coconcentrated with MeOH (3 × 30 mL). The residue was dissolved in H_2O (25 mL) and stirred slowly for 2.5 h with ion-exchange resin (IR 120 H^+, 40 mL). The ion-exchange resin was filtered off, washed with H_2O and then poured into H_2O (50 mL). The resin was cooled in an ice bath and aqueous ammonia (25%, 30 mL) was added and stirred for 1 h. The resin was filtered off and washed with H_2O, and the filtrate was concentrated. The residue was concentrated with aqueous HCl (1 N, 10 mL) followed by coconcentration with MeOH to give **29** as a slightly colored syrup (0.33 g, 80%). ^{1}H NMR (D_2O, 500 MHz): δ 4.16 (m, H-1), 4.11 (dd, H-3, $J_{2,3} = 4.5$, $J_{3,4} = 7.5$), 3.87 (dd, H-2, $J_{1,2} = 5$), 3.75 (dd, H-6′, $J_{6,6'} = 12.5$, $J_{5,6'} = 3.5$), 3.57 (dd, H-6, $J_{5,6} = 6.5$), 3.27 (m, H-5), 2.51 (m, H-4), 1.74 (m, 2H, H-4, H-4a). ^{13}C NMR (D_2O (methanol), 62.9 MHz): δ 79.1, 75.5, 70.9, 60.3, 53.8, 36.8, 32.4.

***N*-Acetyl-1,2,3,6-tetra-*O*-acetyl-5-amino-5-deoxycarba-α-L-glucofuranose (30).** Compound **29** (0.18 g, 1.0 mmol) was dissolved in pyridine (3 mL), and Ac_2O (2.4 mL, 25 mmol) was added. The solution was stirred for 48 h at room temperature after which time it was evaporated and coconcentrated with toluene (3 × 10 mL). Flash chromatography (EtOAc) gave crystalline **30** (0.25 g, 65%) which was recrystallized from EtOAc; mp 161−162 °C, $[\alpha]^{20}_D$ −11.2 (*c* 1.2, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.69 (bd, 1 H), 5.37 (dtr, 1 H), 5.30 (dd, 1 H), 5.10 (dd, 1 H), 4.27 (m, 1 H), 4.06 (d, 2 H), 2.62 (m, 1 H), 2.04 (s, 3 H), 2.03 (s, 3 H), 2.02 (s, 3 H), 1.98 (s, 3 H), 1.88 (s, 3 H), 2.04−1.80 (m, 2 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 170.7, 169.8, 169.7, 169.5, 169.3, 79.4, 74.9, 71.6, 65.1, 47.1, 39.9, 31.6, 22.9, 20.6, 20.5, 20.4, 20.3. Anal. Calcd for $C_{17}H_{25}NO_9$ (387.38): C, 52.71; H, 6.50; N, 3.61. Found: C, 53.00; H, 6.49; N, 3.58.

Dimeric Compound 31. Unsaturated aminolactone **24** (0.40 g, 1.2 mmol) was suspended in refluxing toluene (150 mL), a solution of Bu_3SnH (2.1 mL, 7.8 mmol) and AIBN (0.12 g) in toluene (40 mL) was added during 7 h, and the solution was refluxed for another 15 h, after which the solvent was evaporated. The crude product was suspended in CH_3CN (50 mL) and washed with hexane (5 × 100 mL), and the CH_3CN was evaporated. Flash chromatography (EtOAc:hexane 3:1) gave as the main product, compound **31**, as an oil (90 mg, 30%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 5.38 (ddd, H-7, $J_{6,7} = J_{6',7} = J_{7,8} = 4$), 5.22 (dd, H-8), 4.87 (dd, H-1, $J_{1,8} = 4.5$, $J_{1,5} = 8$), 3.19 (m, H-5), 2.28 (ddd, H-6, $J_{6,6'} = 14$, $J = 5$, $J = 7$), 2.07 (s, 6 H), 2.01 (ddd, H-6′, $J = 4$, $J = 9$). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ 177, 170, 169, 83.8, 77.2, 72.3, 64.3, 40.7, 29.2, 20.7, 20.4.

5,6-Di-*O*-acetyl-2,3,7-trideoxy-2-trifluoroacetamido-D-*gluco*-heptono-1,4-lactone (32). Unsaturated amidolactone **25** (0.84 g, 1.9 mmol) was dissolved in EtOAc (25 mL), and palladium on charcoal (5%, 0.13 g) was added. The compound was hydrogenated at high pressure (300 psi) for 5 days, after which Et_3N (0.53 mL, 3.8 mmol) was added, and the suspension was hydrogenated at atmospheric pressure for 20 h. Filtration and evaporation gave a solid which was taken up in CH_2Cl_2 and washed with H_2O. The combined water phases were washed with CH_2Cl_2, and the combined organic phases were dried ($MgSO_4$) and evaporated to give an amorphous compound (0.77 g). Flash chromatography (EtOAc:hexane 1:2) afforded **32** as a crystalline compound (0.60 g, 90%), mp 192−194 °C. Repeated crystallizations from EtOAc gave compound **32**, mp 199−201 °C, $[\alpha]^{20}_D$ +10.2 (*c* 1.0, EtOAc). CI-MS (NH_3): *m*/*z* 373 ($M + NH_4^+$), 356 ($M + H^+$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 6.99 (bs, NH), 5.19 (dd, H-5, $J_{4,5} = 5$, $J_{5,6} = 5$), 5.10 (dq, H-6, $J_{6,7} = 6.5$), 4.68 (m, H-2, H-4), 2.89 (ddd, H-3′, $J_{3,3'} = 12.5$), 2.04 (m, H-3), 2.18, 2.06 (2 s, 6 H), 1.30 (d, 3H, H-7). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ 174, 171, 170, 75.6, 72.6, 68.2, 49.9, 31.4, 21.0, 20.6, 15.4. Anal. Calcd for $C_{13}H_{16}F_3NO_7$ (355.26): C, 43.97; H, 4.54; N, 3.94. Found: C, 43.94; H, 4.52; N, 3.70.

2-Amino-2,3,7-trideoxy-D-*gluco*-heptono-1,4-lactone Hydrochloride (33) from 32. Trifluoroacetamidolactone **32** (1.24 g, 3.5 mmol) was dissolved in aqueous HCl (2 N, 8 mL) and refluxed for 2.5 h. Evaporation of the solvent and coconcentration with toluene (3 × 20 mL) gave an oil (1.1 g) which was dissolved in H_2O, treated with activated charcoal, concentrated, and crystallized from MeOH:CH_3CN to give **33** as a colorless crystalline compound (0.65 g, 88%); mp 139−145 °C, $[\alpha]^{20}_D$ −35.2° (*c* 0.56, MeOH). Repeated crystallizations from MeOH:CH_3CN gave mp 160−162 °C, $[\alpha]^{20}_D$ −40 (*c* 0.52, MeOH). CI-MS (NH_3): *m*/*z* 176 ($M - HCl + H^+$). ^{1}H NMR (D_2O, 500 MHz): δ 4.88 (ddd, H-4, $J_{4,5} = 2.5$), 4.43 (dd, H-2, $J_{2,3'} = 9$, $J_{2,3} = 11.5$), 3.77 (dq, H-6, $J_{6,7} = 6.5$), 3.39 (dd, H-5, $J_{5,6} = 7.5$), 2.69 (ddd, H-3′, $J_{3,3'} = 12.5$, $J_{3',4} = 5.5$), 2.31 (ddd, H-3, $J_{3,4} = 10$), 1.18 (d, 3H, H-7). ^{13}C NMR (D_2O (CH_3CN), 62.9 MHz): δ 174.5, 49.6, 28.7, 78.7, 74.5, 67.2, 18.9. Anal. Calcd for $C_7H_{14}ClNO_4$ (211.64): C, 39.73; H, 6.67; N, 6.62. Found: C, 39.80; H, 6.69; N, 6.59.

3,7-Dideoxy-5,6-*O*-isopropylidene-D-*gluco*-heptono-1,4-lactone (34). 3,7-Dideoxy-D-*gluco*-heptono-1,4-lactone (**7**)[32] (1.51 g, 8.6 mmol) was dissolved in dry acetone (250 mL), and camphorsulfonic acid (0.3 g) was added. A Soxhlet extractor was equipped with molecular sieves (3 Å), and the reaction was refluxed overnight. The solution was stirred with $NaHCO_3$ (6 g) until neutral and then filtered and evaporated. The crude product was suspended in H_2O (10 mL) and extracted with EtOAc (4 × 30 mL). The organic phases were dried (Na_2SO_4) and evaporated to give compound **34** as a syrup (2.17 g). The compound was used immediately as it was unstable upon storage. ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ 176, 108.0, 77.6, 74.1, 71.8, 66.7, 32.4, 26.2, 24.6, 14.4.

2-Chloro-2,3,7-trideoxy-5,6-*O*-isopropylidene-D-*manno*-heptono-1,4-lactone (35). Isopropylidene-protected lactone **34** (2.17 g) was dissolved in dry pyridine (20 mL), methanesulfonyl chloride (2.94 g, 25.7 mmol) was added, and the solution was stirred at 40 °C for 3 h. H_2O (10 mL) was added and after stirring for 15 min the suspension was extracted with CH_2Cl_2. The organic phases were washed with H_2O, dried ($MgSO_4$), stirred with activated charcoal, and filtered, and the solvent was evaporated. The crude product was purified by flash chromatography (EtOAc:hexane 1:3) to give compound **35** as a crystalline solid (1.12 g, 56% from 3,7-dideoxy-D-*gluco*-heptono-1,4-lactone), mp 68−70 °C. Repeated crystallizations from Et_2O:hexane gave a sample with mp 70−70.5 °C, $[\alpha]^{20}_D$ −81 (*c* 0.80, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 4.67 (ddd, H-4, $J_{4,5} = 1$), 4.66 (dd, H-2, $J_{2,3'} = 8$, $J_{2,3} = 6.5$), 4.45 (dq, H-6, $J_{6,7} = 6.5$), 4.04 (dd, H-5, $J_{5,6} = 7$), 2.79 (ddd, H-3′, $J_{3,3'} = 13.5$, $J_{3',4} = 4.5$), 2.51 (ddd, H-3, $J_{3,4} = 8$), 1.43 (d, 3H, H-7), 1.41, 1.34 (2 s, 6 H). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ 172.4, 108.6, 78.7, 76.0, 72.4, 50.3, 36.2, 26.2, 24.7, 14.9. Anal. Calcd for $C_{10}H_{15}ClO_4$ (234.68): C, 51.18; H, 6.44. Found: C, 51.24; H, 6.49.

2-Azido-2,3,7-trideoxy-5,6-*O*-isopropylidene-D-*gluco*-heptono-1,4-lactone (36). NaN_3 (2.0 g, 30.8 mmol) was added to a solution of chlorolactone **35** (0.71 g, 3.0 mmol) in CH_3CN (20 mL). The suspension was stirred at reflux overnight. The suspension was filtered and concentrated to a syrup which was dissolved in CH_2Cl_2, washed with H_2O, dried ($MgSO_4$), stirred with activated charcoal, filtered, and concentrated. The crude product was crystallized from Et_2O:hexane to give **36** as slightly colored crystals (0.58 g, 79%), mp 52−58 °C. Repeated crystallizations from Et_2O:hexane at room temperature gave the product as colorless crystals, mp 64−64.5 °C, $[\alpha]^{20}_D$ +46 (*c* 0.80, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 4.43 (dq, H-6, $J_{6,7} = 6.5$), 4.42 (ddd, H-4), 4.29 (dd, H-2, $J_{2,3} = 10.5$, $J_{2,3'} = 9.5$), 3.98 (dd, H-5, $J_{4,5} = 2.5$, $J_{5,6} = 6.5$), 2.53 (ddd, H-3′, $J_{3',4} = 6.5$, $J_{3,3'} = 13$), 2.20 (ddd, H-3, $J_{3,4} = 9.5$), 1.46, 1.36 (2 s, 6 H), 1.38 (d, 3H, H-7). ^{13}C NMR ($CDCl_3$, 125.8 MHz): 172.5, 109.0, 77.7, 75.1, 72.3, 56.7, 30.5, 26.7, 25.2, 14.9. Anal. Calcd for $C_{10}H_{15}N_3O_4$ (241.25): C, 49.79; H, 6.27. Found: C, 49.88; H, 6.27.

2-Amino-2,3,7-trideoxy-D-*gluco*-heptono-1,4-lactone Hydrochloride (33) from 36. Azidolactone **36** (0.75 g, 3.1 mmol) was dissolved in HCl/MeOH (40 mL, 1% AcCl in MeOH), palladium on charcoal (5%, 0.1 g) was added, and the com-

pound was hydrogenated at atmospheric pressure for 17 h. The suspension was refluxed for 1.5 h and filtered through activated charcoal, the solvent was evaporated, and the residue was concentrated with H_2O (4 × 30 mL) and toluene (3 × 30 mL) to give a crude product (0.63 g) which was crystallized from MeOH:CH_3CN to give **33** (0.30 g, 46%), mp 150.5−155.5 °C. Recrystallization from MeOH:CH_3CN gave a sample with mp 159−161 °C, $[\alpha]^{20}_D$ −39.4 (*c* 0.51, MeOH). ^{1}H NMR and ^{13}C NMR data were identical with the values given above for **33**.

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