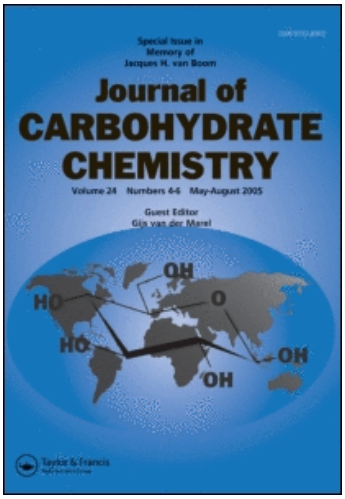

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Syntheses of 6-Guanidino-hexoses and 5-Guanidino-pentoses

Hans Peter Wessel[a]
[a] Pharma Division, Preclinical Research F. Hoffmann-La Roche Ltd., Basel, Switzerland

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SYNTHESES OF 6-GUANIDINO-HEXOSES AND 5-GUANIDINO-PENTOSES[1]

Hans Peter Wessel

Pharma Division, Preclinical Research
F.Hoffmann-La Roche Ltd
CH 4002 Basel, Switzerland

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ABSTRACT

Guanidinations of primary amines were performed with 3,5-dimethylpyrazolylformamidinium nitrate. 6-Deoxy-6-guanidino derivatives of unprotected *N*-acetyl-glucosamine and of glucosamine were prepared, with both products existing as pyranoses. In the pentose series, 5-deoxy-5-guanidinio-**D**-xylose nitrate (**17**) and -**D**-arabinose nitrate (**22**) were synthesized. For both compounds, besides some α-**D**-*xylo*-pyranose and β-**D**-*arabino*-pyranose, mainly the furanoses are found.

INTRODUCTION

In a program directed at the inhibition of serine proteases, guanidino sugars raised our interest as conformationally restricted arginine analogues.[1,2] Carbohydrate derivatives with a guanidino group at the primary carbon atom are poorly described. The guanidines were usually constructed from the corresponding amines. Yoshimura et al.[3] prepared 6-guanidino-derivatives of galactose with cyanamide or with *S*-methylisothiourea; the derivatives include one with the anomeric center unprotected. 6-*N*-Guanyl derivatives of kanamycin and gentamycin were synthesized with pyrazolylformamidine,[4] and amikacin analogues were prepared by reaction with 2-methyl-1-nitro-2-thiopseudourea in dimethyl sulfoxide followed by hydrogenolytic deprotection.[5] Similary, antibacterial 5"-guanidino-analogues of butirosin were obtained.[6] Also in the pentose series, 5'-guanidino-adenosin derivatives were obtained

by reaction with (ethylthio)uronium bromide.[7] Here the syntheses and equilibrium configurations of unprotected terminal guanidino derivatives of glucosamine, xylose, and arabinose are described.

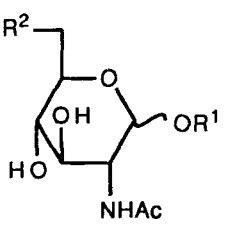
RESULTS AND DISCUSSION

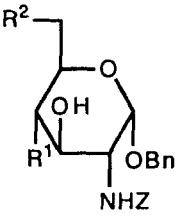
Guanidination reactions were studied with benzyl 2-acetamido-6-amino-2,6-dideoxy-α-D-glucopyranoside (**1**)[8] using 3,5-dimethylpyrazolylformamidinium nitrate (DPFN). This reagent was described to be highly effective[9,10] and has been employed in the guanidination of proteins in the presence of base.[11,12] We obtained best results using DPFN in *N,N*-dimethylformamide at 80 °C without addition of base to afford guanidine **2** in 61% yield. Methanol as a solvent afforded 47% of **2** in the presence of triethylamine; methanol without base added gave only incomplete conversion even after a prolonged reaction time. Guanidinations were followed by TLC detecting with Sakaguchi's reagent, the disappearance of amine could be monitored by spraying with ninhydrin.[13] Due to the DPFN reagent the guanidino derivatives were isolated as guanidinio-pyranose or -furanose nitrates. These salts were conveniently purified by medium pressure liquid chromatography on MCI® gel.

Benzyl glucoside **2** was deprotected by hydrogenolysis to afford virtually quantitatively 2-acetamido-2,6-dideoxy-6-guanidinio-D-glucopyranose nitrate (**3**). The product consists of an α/β-mixture (α/β ≈ 5:1). As expected due to the relative instability of a seven-membered ring, no indication on the presence of a septanose could be detected by ^{1}H NMR. This is in keeping with the results of Yoshimura et al.[3] on the galactose analogue.

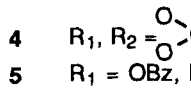
For an alternative approach to guanidination, and to avoid the synthesis of an amino precursor, benzyl 4,6-O-benzylidene-2-benzyloxycarbonylamino-2-deoxy-α-D-glucopyranoside (**4**)[14] was converted by standard *N*-bromosuccinimide opening[15] in carbon tetrachloride[16] to bromide **5** in 71% yield, which on transesterification afforded bromide **6**. However, neither **5** nor **6** could be converted into a guanidino compound by treatment with guanidine, which is in contrast to a report on guanidination of 2,3,4,6,3',4',6'-hepta-O-acetyl-1'-chlorodeoxysucrose.[17]

SCHEME 1

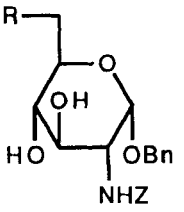




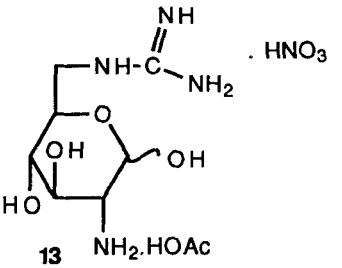
1 R_1 = αBn, R_2 = NH_2
2 R_1 = αBn, R_2 = NH-C(=NH)NH_2 .HNO_3
3 R_1 = H, R_2 = NH-C(=NH)NH_2.HNO_3



4 R_1, R_2 = O, O, CHPh
5 R_1 = OBz, R_2 = Br
6 R_1 = OH, R_2 = Br



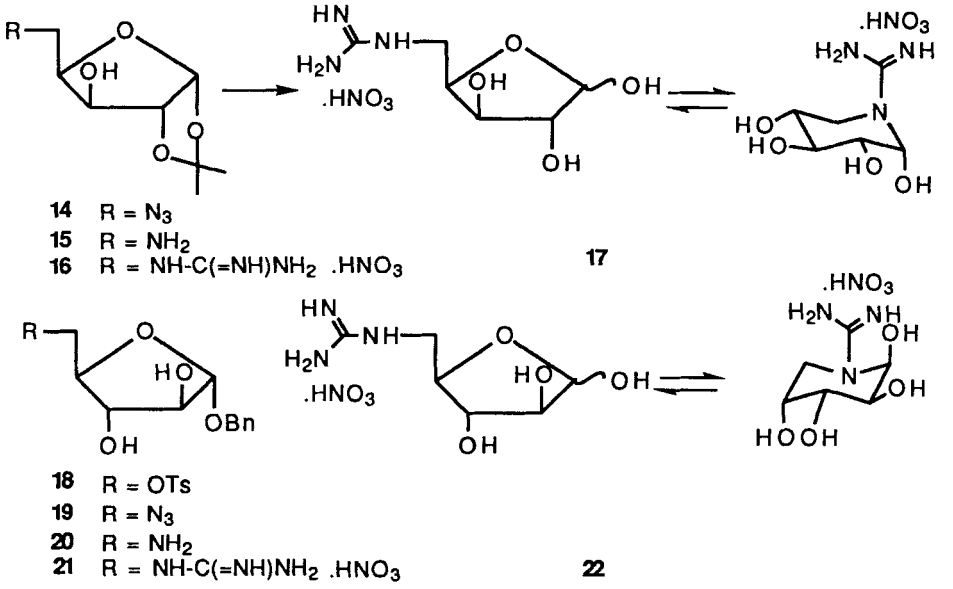
7 R = OH
8 R = OTs
9 R = N_3
10 R = NH_2
11 R = NH-C(=NH)NH_2.HNO_3
12 R = NH-CHO



13 NH_2.HOAc

Thus, benzyl 2-benzyloxycarbonylamino-2-deoxy-α-D-glucopyranoside (**7**)[18,19] was tosylated selectively at the primary hydroxyl group to afford **8** in 73% yield. Treatment of **8** with sodium azide in dimethyl sulfoxide gave the crystalline azide **9** (94%), which was converted to the amine **10** by a Staudinger reaction[20] with triphenylphosphine under hydrolytic reaction conditions. Amine **10** was guanidinated with DPFN in *N,N*-dimethylformamide to furnish **11** (73%). As a by-product, the *N*-formylated, crystalline derivative **12** was isolated. In the ^{1}H NMR spectrum of **12** in dimethyl sulfoxide, *ca.* 15% of a second component not separable by chromatography was observed and attributed to an amide rotamer.[21] Deprotection of the anomeric center of **11** by hydrogenolysis in acetic acid in the presence of palladium-on-charcoal furnished 6-guanidino-glucosamine derivative **13** (98%) as a 1:1 mixture of α- and β-D-pyranose forms; in the poorly resolved ^{1}H NMR spectrum of this substance no further anomeric protons were detected.

SCHEME 2



In the pentose series, 5-azido-5-deoxy-1,2-O-isopropylidene-α-D-xylofuranose (**14**)[23] was transformed quantitatively to the known[24] amine **15** by hydrogenation in ethanol using palladium-on-carbon as a catalyst. Guanidination of **15** with DPFN in *N,N*-dimethylformamide afforded **16** in 78% yield. Liberation of the anomeric center was achieved by treatment of **16** with acidic ion exchange resin in water to give 5-deoxy-5-guanidinio-D-xylose nitrate (**17**) after chromatography. According to the ^{1}H NMR spectrum, three compounds are present in dimethyl sulfoxide solution. The occurrence of two furanoses is evident from two NH-triplets at 7.38 and 7.32 ppm, the assignments of the anomeric protons were made according to the known coupling constants of analogous *xylo*-derivatives.[25] It was found by integration of the anomeric protons that the α- and β-D-furanoses are present in 30% and 43%, respectively, and the α-D-pyranose in 27%. These findings by and large are comparable to data of 5-acetamido-5-deoxy-D-xylose with a pyranose/furanose ratio of 2:1,[27] with the pyranose occurring only in the α-D-form.[28] The amount of pyranose in the guanidino derivative **17** is, however, distinctly lower (27%) than in the analogous acetamido derivative. Regarding the lack of major steric factors in the *xylo* series this should reflect the low basicity of the guanidino-NH group due to mesomeric influence.[29]

The corresponding guanidino derivative with *arabino* configuration was synthesized from the known[18] tosylate **18** which was quantitatively converted first to the azide **19** and then to the amine **20**. Guanidination of **20** with DPFN furnished **21** in 41% yield. The free 5-deoxy-5-guanidinio-**D**-arabinose nitrate (**22**) was obtained by hydrogenolytic removal of the anomeric protecting group of **21**. The equilibrium mixture of **22**, like the xylose analogue, consists of two furanoses and one pyranose. The anomeric proton of the β-pyranose displays, besides a small $^{3}J_{1,2}$ coupling (3.3 Hz), a characteristic long range coupling constant, $^{4}J_{1,5}$ = 1.0 Hz. The same coupling constants are found for the benzyloxycarbonyl protected arabinose analogue which exists in the pyranose form exclusively.[30] For **22**, 24% of the β-**D**-pyranose, 41% of the α-**D**-furanose and 35% of β-**D**-furanose were found in water, similar to the approximately 1:4 pyranose/furanose ratio inferred from optical rotations reported for 5-acetamido-5-deoxy-**L**-arabinose.[31] Thus, for both **17** and **22** only one pyranose form is detected, namely the one with an axial anomeric hydroxyl group which is favoured by the anomeric effect.

EXPERIMENTAL

General Procedures. Solvents and reagents were bought from Fluka. Evaporation: *in vacuo*, conducted with a Büchi rotary evaporator. TLC: precoated silica gel 60F-254 plates (Merck), detection by UV light (254 nm) and spraying with a 10% solution of concentrated sulfuric acid in methanol, Sakaguchi's reagent,[13] or ninhydrin solution[13] followed by heating. MCI® gel refers to CHP20P (75/150 μ) from Mitsubishi Chemical Industries; MCI® gel chromatography was carried out with medium pressure at 2 - 5 bar (Labomatic MD 80 / 100 pump). Melting points were determined with a Büchi Model 510 capillary apparatus and are uncorrected. Specific rotations: Perkin-Elmer Polarimeter 241. IR: Nicolet 7199 FT-IR spectrophotometer. MS: MS 902 (FAB) with data system DS 2050 (VG), VG 7070 F (CI) with data system SS 300, and MS 9 updated with Finnigan ZAB console, data system SS 200. VG Altrichem (EI:70eV). ^{1}H NMR: Bruker AC 250 (250 MHz) with Aspect 3000, chemical shifts in ppm relative to tetramethylsilane or sodium 2,2,3,3-tetradeutero-3-(trimethylsilyl)-propionate as internal standard.

Benzyl 2-Acetamido-2,6-dideoxy-6-guanidinio-α-D-glucopyranoside Nitrate (2). A solution of amine **1**[8] (1.0 g, 3.2 mmol) and 3,5-dimethylpyrazolylformamidinium nitrate (708 mg, 3.5 mmol), in *N,N*-dimethylformamide (DMF, 60 mL) was warmed to 80 °C for 6 h and concentrated. The residue was chromatographed on MCI® gel with water to give 810 mg (61%) of compound **2** as an amorphous solid, $[\alpha]_D^{20}$ + 120.5° (*c* 0.2, water); IR (KBr) 3347 (NH, OH), 1660 (amide), 1620 (C=N), 1544 (nitrate), 1126 (C-O-C), 740, 699 (monosubstituted phenyl); ^{1}H NMR (CD_3OD) δ 4.87 (d, 1H, H-1), 3.89 (dd, 1H, $J_{1,2}$ = 3.5 Hz, $J_{2,3}$ = 11.0 Hz, H-2), 3.71 (dd, 1H, $J_{3,4}$ = 8.8 Hz, H-3), 3.26 (dd, $J_{4,5}$ = 10.0 Hz, H-4), 3.75 (ddd, 1H, $J_{5,6a}$ = 3.5 Hz, $J_{5,6b}$ = 5.5 Hz, H-5), 3.52 (dd, 1H, $J_{6a,6b}$ = 14.0 Hz, H-6a), 3.45 (dd, 1H, H-6b); MS (FAB) 353 (100%, M + H^+).

Anal. Calcd for $C_{16}H_{25}N_5O_8$: C, 46.3; H, 6.1; N, 16.9. Found: C, 45.9; H, 6.2; N, 16.7.

2-Acetamido-2,6-dideoxy-6-guanidinio-D-glucopyranose Nitrate (3). A solution of benzyl glucoside **2** (100 mg, 0.24 mmol) in water (1 mL) and dioxane (5 mL) was hydrogenated in the presence of 10% palladium-on-carbon (100 mg) for 4 days at room temperature. Then the reaction mixture was filtered over filter aid which was washed with water (2 mL). The filtrates were submitted again to hydrogenolysis in the presence of 10% palladium-on-carbon (100 mg). After 1 day the reaction mixture was filtered over filter aid. The filtrate and washings were concentrated and passed through a column of Sephadex® LH 20 using water/acetonitrile 1:1 as eluent to furnish **3** (75 mg, 96%) as a colourless solid; IR (KBr) 3394 (OH, NH), 1657 (C=O), 1547 (amide II), 1384 (nitrate), 1057 (alcohol II); ^{1}H NMR (CD_3SOCD_3, small amount of D_2O added) δ 4.59 (d, ca. 0.83 H, $J_{1,2}$ = 3.2 Hz, H-1α), 4.50 (d, ca. 0.17 H, $J_{1,2}$ = 8 Hz, H-1β); MS (FAB) 263 (100%, M + H^+)

Anal. Calcd for $C_9H_{19}N_5O_8$: C, 33.2; H, 5.9; N, 21.5. Found: C, 33.4; H, 5.8; N, 21.1.

Benzyl 4-O-Benzoyl-2-benzyloxycarbonylamino-6-bromo-2,6-dideoxy-α-D-glucopyranoside (5). To a suspension of benzylidene compound **4**[14] (5.3 g, 10.8 mmol) in carbon tetrachloride (500 mL) were added barium carbonate (*ca.* 1 g), *N*-bromosuccinimide (NBS 1.5 g, 8.4 mmol), and a catalytic amount of benzoyl peroxide. After refluxing for 2 h more NBS (1.0 g, 5.6 mmol) was added and reflux was continued for 4

h. The reaction mixture was cooled, diluted with dichloromethane (150 mL), and washed with aqueous bicarbonate solution and water. The organic solution was dried over sodium sulfate, filtered and concentrated. Chromatography on silica gel (ethyl acetate/hexane 1:4) afforded 3.12 g (71%) of **5** as a solid: mp 171-173 °C (decomp.); $[\alpha]_D^{20}$ + 66.5° (*c* 0.2, dioxane); ^{1}H NMR (CD_3SOCD_3) δ 8.00 (m_c, 2H, Bz), 7.68 (m_c, 1H, Bz), 7.60-7.51 (m, 2H, Bz), 7.46-7.31 (m, 10H, aromat), 5.37 (d, 1H, $J_{3,3\text{-OH}}$ = 6.0 Hz, 3-OH), 5.04 (s, 2H, CH_2Ph), 4.97 (dd ~ t, 1H, H-4), 4.93 (d, 1H, $J_{1,2}$ = 3.3 Hz, H-1), 4.78, 4.54 (2d, 2H, J = 13 Hz, CH_2Ph), 4.04 (br ddd, 1H, J4,5 ≈ 9.5 Hz, H-5), 3.90 (br ddd ~ dt, 1H, H-3), 3.68 (br dd, 1H, H-2), 3.64 (dd, 1H, $J_{5,6a}$ = 2.3 Hz, H-6a), 3.52 (dd, 1H, $J_{5,6b}$ = 6.0 Hz, $J_{6a,6b}$ = 11.3 Hz, H-6b); MS (CI) 572, 570 (10%, M + H^+), 464, 462 (32%, M^+-BnOH).

Anal. Calcd for $C_{28}H_{28}BrNO_7$: C, 59.0; H, 5.0; N, 2.5. Found: C, 58.8; H, 4.9; N, 2.5.

Benzyl 2-Benzyloxycarbonylamino-6-bromo-2,6-dideoxy-α-D-glucopyranoside (6). A solution of **5** (0.9 g, 1.6 mmol) in methanol (5 mL) was treated with a solution of sodium methanolate (36 mg Na in 0.9 mL methanol) for 15 min. The solution was neutralized with acetic acid, concentrated, and chromatographed over silica gel (ethyl acetate/hexane 1:1) to give pure **6** (430 mg, 58%): mp 180-181 °C; $[\alpha]_D^{20}$ + 114.5° (*c* 0.2, dioxane); IR (KBr) 1686 (amide), 1590, 1500 (aromat), 1098 (C-O-C), 1049 (alcohol II), 743, 705 (monosubstituted phenyl); ^{1}H NMR (CD_3SOCD_3) δ 7.40-7.27 (m, 10H, aromat), 5.37 (d, 1H, $J_{3,3\text{-OH}}$ = 6.0 Hz, 3-OH), 5.02 (s, 2H, CH_2Ph), 4.92 (d, 1H, $J_{4,4\text{-OH}}$ = 5.8 Hz, 4-OH), 4.81 (d, 1H, $J_{1,2}$ = 3.7 Hz, H-1), 4.71, 4.46 (2d, 2H, J = 12.5 Hz, CH_2Ph), 3.78-3.71 (m, 1H), 3.66-3.40 (m, 4H), 3.18 (br dt, 1H, H-4); MS (CI) 468, 466 (10%, M + H^+), 360, 358 (20%, M + H^+-BnOH), 278 (100%, 360/358-HBr).

Anal. Calcd for $C_{21}H_{24}BrNO_6$: C, 54.1; H, 5.2; N, 3.0. Found: C, 54.5; H, 5.3; N, 3.0.

Benzyl 2-Benzyloxycarbonylamino-2-deoxy-6-O-tosyl-α-D-glucopyranoside (8). To a solution of compound 7[18] (30.0 g, 74.4 mmol) in pyridine (116 mL) was added dropwise a solution of tosyl chloride (19.85 g, 104.1 mmol) in dichloromethane (30 mL) during 20 min at 0 °C. The reaction was continued for 4.5 h at room temperature. Then the reaction mixture was poured into ice/dilute sulfuric acid.

The product was extracted with dichloromethane. The organic phases were washed with aqueous sodium bicarbonate solution and water, dried (magnesium sulfate), and concentrated. Chromatography on silica gel (ethyl acetate/hexane 2:1) followed by crystallization of the main fraction from ethyl acetate/ether/hexane furnished pure **8** (32.14 g, 77%): mp 127-128 °C, $[\alpha]_D^{20}$ + 101.8° (*c* 0.5, dioxane); IR (KBr) 3370, 3344 (OH), 1701 (amide), 1605, 1500 (aromat), 1532 (amide II), 1359,1175 (SO_2Ar), 1096 (C-O-C), 1040,1002 (alcohol II), 736, 698 (monosubstituted phenyl); ^1H NMR (CD_3SOCD_3) δ 7.77 (d, 2H, Ts), 7.45 (d, 2H, Ts), 7.35-7.27 (m, 10H, aromat), 5.32 (d, J = 6.0 Hz, OH), 5.00 (s, 2H, CH_2Ph), 4.89 (d, J = 6.0 Hz, OH), 4.60, 4.36 (2d, 2H, J = 12.5 Hz, CH_2Ph), 4.25 (dd, 1H, $J_{5,6a}$ = 1.5 Hz, H-6a), 4.13 (dd, 1H, $J_{5,6b}$ = 5.0 Hz, $J_{6a,6b}$ = 10.5 Hz, H-6b), 3.60 (ddd, 1H, $J_{4,5}$ = 10.0 Hz, H-5), 3.49 (ddd, 1H, $J_{3,4}$ = 8.0 Hz, H-3), 3.37 (ddd, 1H, $J_{2,3}$ =10.0 Hz, H-2), 3.11 (ddd, 1H, H-4), 2.41 (s, 3H, Ts); MS (FAB) 580 (10%, M + Na^+), 558 (20%, M + H^+), 450 (70%, M + H^+-BnOH).

Anal. Calcd for $C_{28}H_{31}NO_9S$: C, 60.3; H, 5.6; N, 2.5; S, 5.8. Found: C, 60.2; H, 5.7; N, 2.5; S, 5.7.

Benzyl 6-Azido-2-benzyloxycarbonylamino-2,6-dideoxy-α-D-glucopyranoside (9). A solution of **8** (32.14 g, 57.6 mmol) in dimethyl sulfoxide (75 mL) was stirred in the presence of sodium azide (7.5 g, 115.4 mmol) at 90 °C. After 3 h the yellowish solution was poured onto ice/water (400 mL) to obtain colourless crystals. Recrystallization from ethyl acetate/ether/hexane gave pure **9** (23.14 g, 94%): mp 153-154 °C, $[\alpha]_D^{20}$ + 119.6° (*c* 0.5, dioxane); IR (KBr) 3317 (OH), 2097 (N_3), 1676 (carbamate), 1605, 1497 (aromat), 1542 (amide II), 1044 (alcohol II), 735, 697 (monosubstituted phenyl); ^1H NMR (CD_3SOCD_3) δ 7.36-7.27 (m, 11H, aromat, NH), 5.30 (d, 1H, J = 5.8 Hz, OH), 5.02 (s, 2H, CH_2Ph), 4.90 (d, 1H, J = 5.8 Hz, OH), 4.82 (d, 1H, $J_{1,2}$ = 3.2Hz, H-1), 4.68, 4.48 (2d, 2H, J = 12.2 Hz, CH_2Ph), 3.65 (ddd, 1H, $J_{5,6a}$ = 2.5 Hz, $J_{5,6b}$ = 6.2 Hz, H-5), 3.55 (ddd, 1H, $J_{2,3}$ = 10.2 Hz, H-3), 3.52-3.38 (m, 3H, H-2, H-6), 3.17 (ddd ~ dt, 1H, $J_{3,4}$ = 8.7 Hz, H-4); MS (FAB) 429 (18%, M + H^+)

Anal. Calcd for $C_{21}H_{24}N_4O_6$: C, 58.9; H, 5.7; N, 13.1. Found: C, 58.8; H, 5.6; N, 13.0.

Benzyl 6-Amino-2-benzyloxycarbonylamino-2,6-dideoxy-α-D-glucopyranoside (10). A solution of azide **9** (18.0 g, 42.0 mmol) in

tetrahydrofuran (106 mL) and water (1.1 mL) was stirred in the presence of triphenylphosphine (11.0 g, 42 mmol) at room temperature. After 120 h the solvents were evaporated. The residue was crystallized from methanol to afforded pure **10** (12.28 g, 73%). Chromatography of the mother liquor furnished another 3.7 g (22%) of **10**: mp 163-164 °C; $[\alpha]_D^{20}$ +124.2° (c 0.6, acetone); IR (KBr) 3365, 3342 (OH, NH), 1697 (amide), 1586, 1498 (aromat), 1538 (amide II), 1042 (alcohol II), 735, 697 (monosubstituted phenyl); ^{1}H NMR (CD_3SOCD_3) δ 7.41-7.22 (m, 11H, aromat, NH), 5.01 (s, 2H, CH_2Ph), 4.78 (d, 1H, $J_{1,2}$ = 3.2 Hz, H-1), 4.66, 4.43 (2d, 2H, J = 12.3 Hz, CH_2Ph), 3.53 (dd ~ br t, 1H, H-3), 3.42 (ddd, 1H, $J_{2,NH}$ = 8.0 Hz, H-2), 3.37 (ddd, 1H, $J_{4,5}$ = 9.8 Hz, H-5), 3.12 (dd ~ t, 1H, $J_{3,4}$ ≈ 8.2 Hz, H-4), 2.84 (dd, 1H, $J_{5,6a}$ = 3.0 Hz, $J_{6a,6b}$ = 13.0 Hz, H-6a), 2.62 (dd, 1H, $J_{5,6b}$ = 6.5 Hz, H-6b); MS (FAB) 425 (10%, M + Na^+), 403 (30%, M + H^+).

Anal. Calcd for $C_{21}H_{26}N_2O_6$: C, 62.7; H, 6.5; N, 7.0. Found: C, 62.6; H, 6.5; N, 6.9.

Benzyl 2-Benzyloxycarbonylamino-2,6-dideoxy-6-guanidinio-α-D-glucopyranoside Nitrate (11). A solution of amino compound **10** (5.0 g, 12.4 mmol) in DMF (40 mL) was stirred in the presence of 3,5-dimethylpyrazolylformamidinium nitrate (DPFN, 3.0 g, 14.9 mmol) at 80 °C. After 5 h DPFN (0.3 g, 1.5 mmol) was added, and the reaction was continued for 24 h at 80 °C. Then the solution was concentrated, the residue was chromatographed on MCI® gel using a water/methanol gradient. The fractions obtained with 20-60% aqueous methanol were concentrated, and the residue was crystallized from methanol to yield **11** (4.85 g, 77%). Elution with methanol furnished 460 mg (8.6%) of benzyl 2-(benzyloxycarbonylamino)-2,6-dideoxy-6-formamido-α-D-glucopyranoside (**12**).

11: Colourless solid, mp 182-185 °C (with decomposition); $[\alpha]_D^{20}$ +97.0° (c 0.2, methanol); IR (KBr) 3399 (OH), 1700 (C=O), 1669 (C=N), 1587,1498 (aromat), 1520 (amide II), 1384 (nitrate), 1039 (alcohol II), 739,698 (monosubstituted phenyl); ^{1}H NMR (CD_3SOCD_3) δ 5.38 (d, 1H, OH), 5.02 (s, 2H, CH_2Ph), 4.97 (d, 1H, J = 5.5 Hz, OH), 4.81 (d, 1H, $J_{1,2}$ = 3.2 Hz, H-1), 4.68, 4.46 (2d, 2H, J = 12.8 Hz, CH_2Ph), 3.62-3.36 (m, 5H, H-2, H-3, H-5, H-6), 3.12 (ddd ~ br dt, 1H, H-4); MS (FAB) 445 (100%, M + H^+).

Anal. Calcd for $C_{22}H_{29}N_5O_9$: C, 52.1; H, 5.8; N, 13.8. Found: C, 52.2; H, 6.0; N, 13.7.

12: Two crystallizations from methanol/ethyl acetate gave colourless crystals, mp 180-181 °C; $[\alpha]_D^{20}$ +113.5° (*c* 0.2, dioxane); IR (KBr) 3323 (OH), 1693 (carbamate), 1648 (amide), 1563,1448 (aromat), 1539 (amide II), 732,696 (monosubstituted phenyl); ^{1}H NMR (CD_3SOCD_3) δ 8.05 (s, 1H, CHO), 8.12 (dd ~ t, 1H, CH_2NH), 7.40-7.28 (m, 10H, aromat), 5.18 (d, 1H, J = 5.6 Hz, OH), 5.02 (s, 2H, CH_2Ph), 4.87 (d, 1H, J = 5.2 Hz, OH), 4.77 (d, 1H, $J_{1,2}$ = 3.1 Hz, H-1), 4.67, 4.03 (2d, 2H, J = 12.4 Hz, CH_2Ph), 3.68-3.39 (m, 4H), 3.14-3.00(m, 2H); MS (FAB) 431 (48%, M + H^+), 323 (100%, M + H^+-BnOH).

Anal. Calcd for $C_{22}H_{26}N_2O_7$: C, 61.4; H, 6.1; N, 6.5. Found: C, 61.2; H, 6.1; N, 6.5.

2-Ammonio-2,6-dideoxy-6-guanidinio-α-D-glucopyranose Acetate and Nitrate (13). A solution of glucoside **11** (203 mg, 0.4 mmol) in acetic acid (2 mL) was hydrogenated in the presence of 10% palladium-on-carbon (30 mg) for 6 days. Then the same catalyst (15 mg) and water (1 mL) were added, and the hydrogenolysis was continued for 3 days. The reaction mixture was filtered over a pad of speedex which was washed with water. The filtrates were concentrated and purified over MCI® gel to afford 135 mg (98%) of **13** as a hygroscopic solid; IR (KBr) 3394 (OH), 1668 (C=N), 1620, 1400 (carboxylate), 1549, 1384 (nitrate), 1054 (alcohol II); ^{1}H NMR (CD_3SOCD_3) δ 5.10 (br s, 0.5H, H-1 of α-anomer), 4.41 (d, 0.5H, $J_{1,2}$ = 7.9 Hz, H-1 of β-anomer); MS (FAB) 221 (100%, M + H^+).

Anal. Calcd for $C_9H_{21}N_5O_9$: C, 31.5; H, 6.2; N, 20.4. Found: C, 30.9; H, 6.3; N, 19.7.

5-Deoxy-5-guanidinio-1,2-isopropylidene-α-D-xylofuranose Nitrate (16). A solution of amine **15** (410 mg, 2.2 mmol) and 3,5-dimethylpyrazolylformamidinium nitrate (479 mg, 2.4 mmol) in *N,N*-dimethylformamide was kept at 80 °C for 31 h under argon. Then the reaction mixture was concentrated and chromatographed over MCI® gel. Elution with water afforded 494 mg (78%) of **16** as a syrup: $[\alpha]_D^{20}$ +17.0° (*c* 0.2, water); IR (film) 3349, 3201 (OH, NH), 1666 (C=N), 1555, 1380 (nitrate); ^{1}H NMR (CD_3SOCD_3) δ 7.46 (t, 1H, NH), 5.88 (d, 1H, $J_{1,2}$ = 3.6 Hz, H-1), 4.45 (d, 1H, $J_{2,3}$ < 0.5 Hz, H-2), 4.09 (ddd, 1H, H-4), 4.02 (d, 1H, $J_{3,4}$ ≈ 2.5 Hz, H-3), 3.44-3.24 (m, 2H, H-5), 1.39, 1.24 (2s, 6H, CH_3); MS (FAB) 232 (100%, M + H^+).

Anal. Calcd for $C_9H_{18}N_4O_7$: C, 36.7; H, 6.2; N, 19.0. Found: C, 36.5; H, 6.1; N, 18.9.

5-Deoxy-5-guanidinio-D-xylose Nitrate (17). A solution of compound **16** (330 mg, 1.1 mmol) in water (15 mL) was treated with ion exchange resin Amberlite IR 120 (H^+) for 3.5 h at 60 °C. Filtration was followed by addition of triethylamine (0.5 mL) to the filtrate and concentration. The residue was chromatographed over MCI® gel to afford **17** (73 mg, 25%) as a syrup; IR (film) 3362 (OH), 1550 (NH), 1391, 1339 (nitrate), 1067, 1038 (alcohol II, C-O-C); ^1H NMR (CD_3SOCD_3) δ 7.38, 7.32 (2t, furanoid NH), after addition of D_2O: 5.28 (d, 0.27 H, $J_{1,2}$ ≈ 3.5 Hz, H-1αp), 5.20 (d, 0.30H, $J_{1,2}$ = 4.0 Hz, H-1αf), 4.96 (d, 0.43H, $J_{1,2}$ = 1.8 Hz, H-1βf); MS (FAB) 192 (40%, M + H^+).

Anal. Calcd for $C_6H_{14}N_4O_7$: C, 28.4; H, 5.6; N, 22.0. Found: C, 28.1; H, 5.8; N, 19.8.

Benzyl 5-Azido-5-deoxy-α-D-arabinofuranoside (19). A solution of tosylate **18**[18] (3.18 g, 8.07 mmol) and sodium azide (750 mg, 11.5 mmol) in dimethyl sulfoxide was kept at 90 °C for 1 h, then poured into ice/water and extracted with ethyl acetate. The organic solutions were dried over sodium sulfate and concentrated to afford **19** (2.14 g, 100%) as a syrup. An analytical sample was chromatographed on silica gel using ethyl acetate/hexane 2:1 as a solvent: $[\alpha]_D^{20}$ +132.0° (*c* 0.2, dioxane); IR (film) 3412 (OH), 2103 (N_3), 1602, 1492 (aromat), 1078 (C-O-C), 749, 700 (monosubstituted phenyl); ^1H NMR (CD_3SOCD_3) δ 7.39-7.29 (m, 5H, aromat), 5.08 (s, 1H, $J_{1,2}$ ≈ 0 Hz, H-1), 4.76, 4.53 (2d, 2H, J = 12.0 Hz, CH_2Ph), 4.17 (ddd ~ q, 1H, $J_{3,4}$ = 2.9 Hz, H-4), 4.08 (dd, 1H, $J_{2,3}$ ≈ 1 Hz, $J_{2,2\text{-OH}}$ = 8.1 Hz, H-2), 3.89 (ddd, 1H, H-3), 3.65 (dd, 1H, $J_{4,5a}$ ≈ 3.9 Hz, $J_{5a,5b}$ ≈ 13.5 Hz, H-5a), 3.59 (dd, 1H, $J_{4,5b}$ ≈ 4.1 Hz, H-5b), 2.95 (d, 1H, 2-OH), 2.84 (d, 1H, $J_{3,3\text{-OH}}$ = 10.3 Hz, 3-OH); MS (CI) 283 (30%, M + NH_4^+), 240 (76%, M + NH_4^+-HN_3), 238 (66%, M + H^+-N_2), 220 (60%, 238-H_2O), 91 (100%, Bn).

Anal. Calcd for $C_{12}H_{15}N_3O_4$: C, 54.3; H, 5.7; N, 15.8. Found: C, 54.2; H, 5.7; N, 15.7.

Benzyl 5-Amino-5-deoxy-α-D-arabinofuranoside (20). A solution of azide **19** (2.1 g, 7.9 mmol) and triphenylphosphine (2.1 g, 7.9 mmol) in tetrahydrofuran (10 mL) and water (0.2 mL) was kept at room temperature for 3 days. Triphenylphosphine (0.1 g, 0.4 mmol) was added, and the reaction was continued for another 3 days. The solvents were evaporated, the residue was chromatographed on silica gel using ethyl acetate as eluent to give 1.89 g (100%) of **20** as a syrup; $[\alpha]_D^{20}$

+111.50° (*c* 0.2, dioxane); IR (film) 3361, 3302 (OH, NH), 1592, 1497 (aromat), 1589 (NH_2), 1075, 1008 (C-O-C), 738, 699 (monosubstituted phenyl); ^1H NMR ($CDCl_3$) δ 7.40-7.30 (m, 5H, aromat), 5.07 (s, 1H, $J_{1,2}$ ≈ 0 Hz, H-1), 4.76, 4.53 (2d, 2H, J = 11.7 Hz, CH_2Ph), 3.99 (s, 1H, H-2), 3.88 (br s, 1H, $J_{3,4}$ < 1 Hz, H-3), 4.23 (ddd ~ br d, 1H, H-4), 3.11 (dd, 1H, $J_{4,5a}$ = 3.3 Hz, $J_{5a,5b}$ = 13.7 Hz, H-5a), 2.80 (dd, 1H, $J_{4,5b}$ ≈ 1 Hz, H-5b); MS (EI) 148 (6%, M^+-Bn•), 130 (6%, 148-H_2O); MS (FAB) 240 (100%, M + H^+).

Anal. Calcd for $C_{12}H_{17}NO_4$: C, 60.2; H, 7.2. Found: C, 60.2; H, 7.1.

Benzyl 5-Deoxy-5-guanidinio-α-D-arabinofuranoside Nitrate (21). A solution of amino compound **20** (1.89 g, 7.9 mmol) and 3,5-dimethylpyrazolylformamidinium nitrate (DPFN, 1.81 g, 9.0 mmol) in *N,N*-dimethylformamide (22 mL) was stirred for 9.5 h at 80 °C. More DPFN (1.65 g, 8.2 mmol) was added, and warming to 80 °C was continued for 24 h. The reaction mixture was concentrated and chromatographed on MCI® gel (water → 50% methanol) to afford 1.12 g (41%) of **21** as a syrup; $[\alpha]_D^{20}$ +63.50° (*c* 0.2, water); IR (film) 3352, 3285, 3207 (OH, NH), 1668, 1628 (C=N), 1595, 1497 (aromat), 1538,1388 (nitrate), 1074, 992 (C-O-C, alcohol II), 739, 699 (monosubstituted phenyl); ^1H NMR (CD_3SOCD_3) δ 7.37-7.30 (m, 5H, aromat), 7.07 (very br, ca. 3H, NH_2), 5.50 (very br, 2H, OH), 4.90 (d, 1H, $J_{1,2}$ = 2.0 Hz, H-1), 4.68, 4.48 (2d, 2H, J = 12.5 Hz, CH_2Ph), 3.91 (m, 2H, H-2, H-4), 3.62 (dd, 1H, $J_{2,3}$ = 4.0 Hz, $J_{3,4}$ = 7.5 Hz, H-3), 3.47-3.27 (m, H-5); MS (FAB) 282 (100%, M + H^+).

Anal. Calcd for $C_{13}H_{20}N_4O_7$: C, 45.4; H, 5.9; N, 16.3. Found: C, 44.8; H, 6.1; N, 16.9.

5-Deoxy-5-guanidinio-D-arabinose nitrate (22). A solution of furanoside **21** (822 mg, 2.4 mmol) in water (4 mL) and methanol (4 mL) was hydrogenated in the presence of 5% palladium-on-carbon (100 mg). After 1 day more catalyst (200 mg) was added, and the hydrogenolysis was continued for 2 days. The catalyst was filtered off over speedex and the filtrate was concentrated and dried to give 510 mg (84%) of **22** as a syrup; $[\alpha]_D^{20}$ +5.0° (*c* 0.2, water); IR (film) 3335, 3219 (OH, NH), 1667 (C=N), 1359 (nitrate), 1044 (C-O-C, alcohol II); ^1H NMR (CD_3SOCD_3) δ 7.42 (t, NH), 4.98 (dd, $J_{1,2}$ = 2.8 Hz, $J_{1,1\text{-OH}}$ = 5.8 Hz, H-1αf); ^1H NMR (D_2O): 5.58 (dd, 0.24H, $J_{1,2}$ = 3.3 Hz, $J_{1,5e}$ = 1.0 Hz, H-

1βp), 5.33 (d, 0.35H, $J_{1,2}$ = 4.2 Hz, H-1βf), 5.29 (d, 0.41H, $J_{1,2}$ = 2.4 Hz, H-1αf); MS (FAB) 192 (100%, M + H^+).

Anal. Calcd for $C_6H_{14}N_4O_7$: C, 28.4; H, 5.6; N, 22.0. Found: C, 28.2; H, 5.7; N, 22.3.

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