Synthetic Approach to 2,3,5-Triamino-2,3,5-trideoxy-D-arabonic Acid Derivatives from 3,4,6-Triazido-3,4,6-trideoxy-1,2-*O*-isopropylidene-α-D-glucopyranose

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3,6-Diazido-3,6-dideoxy-1,2-*O*-isopropylidene-α-D-glucofuranose was converted into the corresponding derivative of α-D-glucopyranose, which was transformed into 3,4,6-triazido-3,4,6-trideoxy-1,2-*O*-isopropylidene-α-D-glucopyranose (**7**) through the sequence of reactions involving displacement of sulfonate ester function with benzoate, followed by debenzoylation, sulfonylation, and nucleophilic substitution. Hydrogenolysis of **7** afforded the corresponding triamino derivative **8**. The tri-*N*-benzyloxycarbonyl derivative of **8** was *O*-deisopropylidenated and oxidized with periodate to afford the piperidinose derivative **11**, deformylation of which yielded 2,3,5-tris(benzyloxycarbonylamino)-2,3,5-trideoxy-D-arabinopyranose (**13**). "Pfitzner-Moffatt" oxidation of **11** failed to give the corresponding lactam **15**. Condensation of the 6-*N*-benzyloxycarbonyl derivative of **8** (**18**) with cyanogen bromide afforded the cyclic guanidine derivative (**20**) hydrobromide. The triazido derivative **7** was converted into 3,4,6-tris(benzyloxycarbonylamino)-3,4,6-trideoxy-D-glucitol (**23**), which was then oxidized successively with periodate and chromium trioxide–acetic acid–pyridine to give 2,3,5-tris(benzyloxycarbonylamino)-2,3,5-trideoxy-D-arabono-1,4-lactone (**25**); this was further transformed into 2,3,5-trianimo-2,3,5-trideoxy-D-arabono-1,5-lactam (**16**).

2,3,5-Triamino-2,3,5-trideoxy-D-arabono-1,5-lactam (**16**) has proved to be a useful intermediate for the synthesis of 2,3,5-triamino-2,3,5-trideoxy-D-arabonic acid derivatives, such as streptolidine[1,2] (**21**) and streptolidine lactam[3] (**27**). Synthesis of the lactam **16** was first accomplished from D-ribose through 2,3,5-triacylamino-2,3,5-trideoxy-D-arabinofuranose.[1,2] Recently **16** has been prepared through a new stereospecific route from 3,4-anhydro-D-iditol derivative.[3]

In view of the preparation of lactam **16**, we were interested in some synthetic approaches to the triamino-D-arabonic acid derivatives from 3,4,6-triazido-3,4,6-trideoxy-1,2-*O*-isopropylidene-α-D-glucopyranose (**7**) which was synthesized from 3,6-diazido-3,6-dideoxy-1,2-*O*-isopropylidene-α-D-glucofuranose[4] (**1**). The following approaches were attempted: (i) transformation of 3,4,6-tris(benzyloxycarbonylamino)-3,4,6-trideoxy-D-glucopyranose derived from **7** to **16** *via* 2,3,5-tris(benzyloxycarbonylamino)-2,3,5-trideoxy-D-arabinopyranose derivative (**11**) (Chart 2), (ii) conversion of triamino glucopyranose derivative **8** into streptolidine **21** (Chart 3), and (iii) transformation of **7** into 2,3,5-tris(benzyloxycarbonylamino)-2,3,5-trideoxy-D-arabono-1,4-lactone (**25**) which can be converted into **16** (Chart 4).

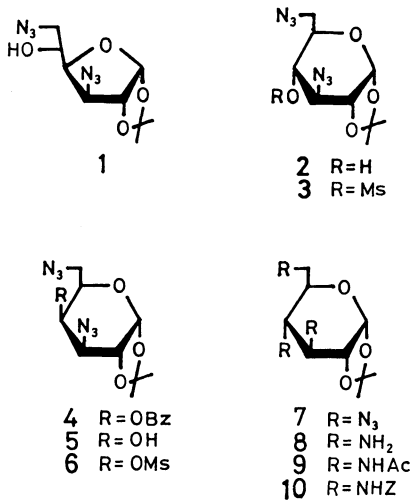

Chart 1.

3,4,6-Triazido-3,4,6-trideoxy-1,2-O-isopropylidene-α-D-glucopyranose (7). 3,6-Diazido-3,6-dideoxy-1,2-*O*-isopropylidene-α-D-glucofuranose[4] (**1**) was converted into 3,6-diazido-3,6-dideoxy-1,2-*O*-isopropylidene-α-D-glucopyranose (**2**) in 55% overall yield by *O*-deisopropylidenation of **1** with warm aqueous acetic acid and the subsequent 1,2-*O*-isopropylidenation with 2,2-dimethoxypropane in hot DMF in the presence of *p*-toluenesulfonic acid.

Kiso and Hasegawa[5a] reported that isopropylidenation of D-glucose with 2,2-dimethoxypropane–DMF–*p*-toleuensulfonic acid gives no 1,2-*O*-isopropylidene-α-D-glucopyranose. The result is not in line with ours. They also reported[5b] that isopropylidenation of D-xylose with the same reagent gives 1,2-*O*-isopropylidene-α-D-xylopyranose as a minor product in 16% yield. Meyer zu Reckendorf and Bischef[6] reported that treatment of 3-(*N*-methylbenzamido)-3-deoxy-D-xylose with the same reagent affords the corresponding 1,2-*O*-isopropylidene-D-xylopyranose derivative in 40% yield. The difference between isopropylidenation of D-glucose and of 3,6-diazido-3,6-dideoxy-D-glucose, in which the hydroxyl groups at C-3 and C-6 position of D-glucose are absent, may thus be explained.

O-Mesylation of **2** afforded the corresponding 4-*O*-mesylate **3** (90% yield), which was allowed to react with sodium benzoate in boiling DMF to give 3,6-diazido-4-*O*-benzoyl-3,6-dideoxy-1,2-*O*-isopropylidene-α-D-galactopyranose (**4**) in 84% yield. Debenzoylation of **4** with sodium methoxide in methanol afforded **5**, the 4-epimer of **2**, in 93% yield. The 4-*O*-mesylate **6** prepared from **5** in 89% yield, was heated with sodium azide in DMSO to give 3,4,6-triazido-3,4,6-trideoxy-1,2-*O*-isopropylidene-α-D-glucopyranose

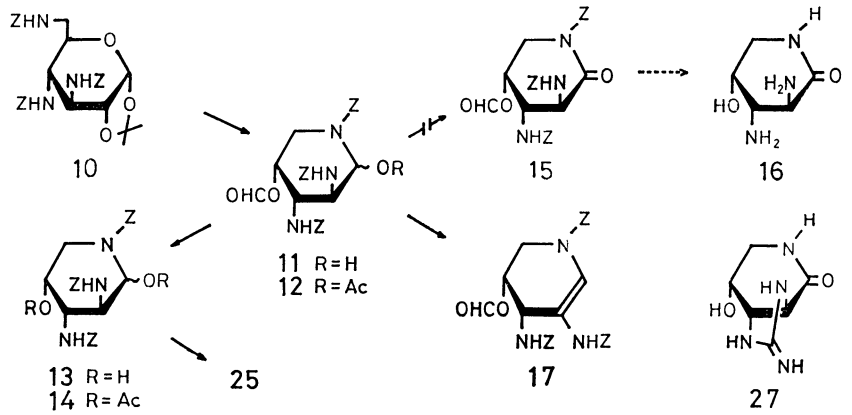

Chart 2.

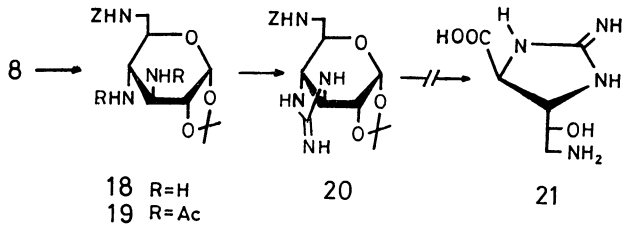

Chart 3.

(**7**) as a syrup in 69% yield after being subjected to chromatography.

*Synthetic Approach to Triamino Arabono-1,4-lactam **16** from Triazido Glucose Derivative **7**.* Hydrogenolysis of **7** over palladium black afforded 3,4,6-triamino-3,4,6-trideoxy-1,2-*O*-isopropylidene-α-D-glucopyranose (**8**) as a colorless syrup, which led to the crystalline tri-*N*-acetyl derivative **9** on treatment with acetic anhydride in methanol. The crystalline tri-*N*-benzyloxycarbonyl derivative **10** was also obtained by the reaction of **8** with benzyl chloroformate in pyridine in 70% yield after being subjected to chromatography. Compounds **8**, **9**, and **10** are the derivatives of the new triamino glucose.

The 1,2-*O*-isopropylidene group of **10** was removed with warm aqueous acetic acid and the resulting free sugar was subjected to periodate oxidation in aqueous acetone to afford a crystalline piperidinose derivative, 4-*O*-formyl-2,3,5-tris(benzyloxycarbonylamino)-2,3,5-trideoxy-D-arabinopyranose (**11**) in 71.5% yield. Compound **11** was converted into the 1-*O*-acetate **12** in good yield. Deformylation of **11** with ammonia in aqueous dioxane gave **13** as crystals (93% yield), which could be converted into the 1,4-di-*O*-acetate **14**.[2b] The PMR spectra of **11**, **12**, **13**, and **14** showed signals in line with piperidinose structure.[7]

Transformation of **11** into **16** was attempted. However, no desired lactam **15** was obtained on treatment with DMSO–DCCI–pyridine–trifluoroacetic acid.[8] Instead, only 2,3,5-tris(benzyloxycarbonylamino)-1,2,3,5-tetradeoxy-4-*O*-formyl-D-*erythro*-pent-1-enopyranose (**17**), the dehydration product, was obtained in 82% yield. The structure of **17** was confirmed by PMR spectroscopy (singlet at δ 7.48 due to the H-1 olefinic proton) and by elemental analysis. When **11** was treated with DMSO–trifluoroacetic anhydride in dichloromethane at −70 °C according to the method of Huang *et al.*[9] no reaction product was detected in TLC, but when the mixture was warmed up to room temperature, the formation of **17** was observed. Oxidation of **11** with chromium trioxide–acetic acid–pyridine,[10] with bromine–water, or with *N*-bromosuccinimide in dioxane afforded only the unchanged material.

*Attempt to Synthesize Streptolidine (**21**) from Triamino Glucose Derivative **8**.* Selective *N*-benzyloxycarbonylation of **8** with *N*-(benzyloxycarbonyloxy)-succinimide[11] in aqueous DMF yielded the 6-*N*-benzyloxy-carbonylated product **18** as a major product in 46% yield after being subjected to chromatography. Acetylation of **18** afforded the di-*N*-acetyl derivative **19**, whose PMR spectrum showed signals at δ 3.03 (H-3) and 2.53(H-4); those of **18** being shifted to downfield by acetylation.

Treatment of **18** with one equivalent of cyanogen bromide in water gave the cyclic guanidine derivative **20** as crystalline hydrobromide in 93% yield after being subjected to chromatography. *O*-Deisopropylidenation of **20** followed by successive oxidation with periodate and with bromide–water afforded no expected product from which streptolidine (**21**) could be derived. Periodate oxidation of the *O*-deisopropylidenation product might have yielded a piperidinose derivative as an intermediary product which resists oxidation with bromine–water as in the case of **11**.

*Transformation of Triazido Glucose Derivative **7** into Triamino Sugar Lactam **16**.* A synthetic approach to triamino sugar lactam **16** involving the conversion of the triazido D-glucose derivative **7** into the glucitol derivative **23** was performed. *O*-Deisopropylidenation of **7** with 20% aqueous acetic acid, followed by sodium borohydride-reduction in aqueous ethanol, afforded 3,4,6-triazido-3,4,6-trideoxy-D-glucitol (**22**) in 60% yield. Hydrogenolysis of **22** over palladium black and subsequent *N*-benzyloxycarbonylation with *N*-(benzyloxycarbonyloxy)succinimide gave the crystalline 3,4,6-tris(benzyloxycarbonylamino)-3,4,6-trideoxy-D-glucitol (**23**) in 98% yield. Periodate-oxidation of **23** afforded the furanose derivative **24**[2b] whose TLC showed a single spot having R_f-value differing from that of piperidinose derivative **13**. With-

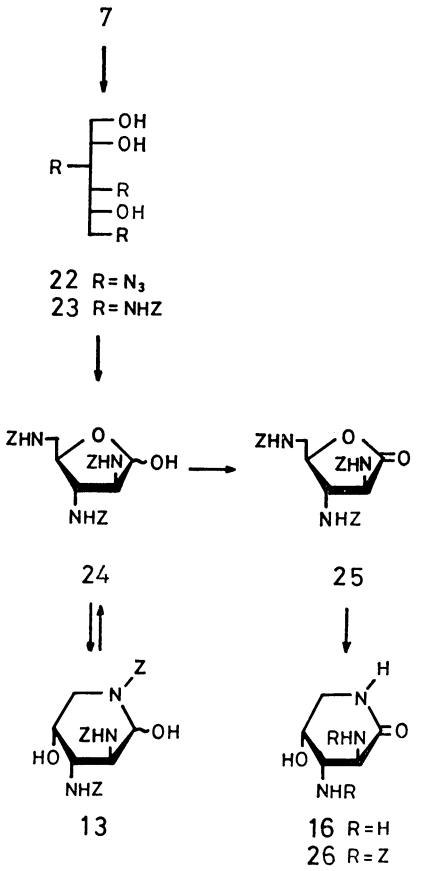

Chart 4.

out purification, **24**, was oxidized with chromium trioxide–acetic acid–pyridine to give the corresponding crystalline 1,4-lactone **25**[2b] as the sole product in 66% yield from **23** after being subjected to chromatography. When the oxidation of **24** was carried out with bromine–water[3] instead of the chromium trioxide reagent, a considerable amount of **13** was isolated together with **25** on column chromatography of the reaction product. During the slow oxidation reaction with bromine–water, **24** might have partially been converted into **13** which resisted bromine-oxidation.

Lactone **25** was also obtained in 42% yield by oxidation of **13** with chromium trioxide reagent. Hydrogenolysis of **25** over palladium black gave **16**, whose structure was confirmed by conversion into 2,3-di-*N*-benzyloxycarbonylated triamino sugar lactam **26**.[3]

Experimental

Melting points were determined on a micro hot-stage and are uncorrected. IR spectra were taken on a Hitachi 225 spectrophotometer, PMR spectra on a Varian A-60D spectrometer using TMS as an internal standard. Specific rotations were determined with a Zeiss Photoelectric polarimeter. TLC was performed on Wakogel B-5 and column chromatography on Wakogel C-200. Hydrogenolysis was conducted under bubbling with hydrogen at room temperature. Concentration was carried out below 40 °C under reduced pressure.

3,6-Diazido-3,6-dideoxy-1,2-O-isopropylidene-α-D-glucopyranose (2). A mixture of 3,6-diazido-3,6-dideoxy-1,2-*O*-isopropylidene-α-D-glucofuranose (**1**)[4] (31.5 g) and 50% aqueous acetic acid (320 ml) was heated at 90—100 °C for 6.5 h, the resulting solution being evaporated to give free sugar as pale yellow crystals (24.6 g, 92%). A mixture of the product (24.6 g), dry DMF (246 ml), 2,2-dimethoxypropane (64 ml), and *p*-toluenesulfonic acid (3.53 g) was kept at 60 °C for 2.5 h, the reaction mixture being poured into cold water (250 ml) and extracted with chloroform (250 ml × 3). The combined extracts were washed with saturated NaCl solution, dried, and evaporated. The residual syrup (31.6 g) was chromatographed on silica gel (1.3 kg) with benzene–ethyl acetate (15:1) to afford a homogeneous sample of **2** (17.2 g, 60%) as a colorless syrup. Chromatography also gave **1** (0.19 g, 0.7%) and a mixture of **1** and **2** (2.0 g, 7%). **2**: $[\alpha]_D^{14}$ +95° (*c* 1.4, $CHCl_3$); δ($CDCl_3$) 1.41 and 1.62 [each s, 6H, $C(CH_3)_2$], 3.6—3.9(m, 5H, H-3,4,5,6,6′), 4.18(dd, H-2 $J_{1,2}$=4.8, $J_{2,3}$=5.9 Hz), and 5.63 (d, H-1).

Found: C, 40.15; H, 5.09; N, 30.77%. Calcd for $C_9H_{14}N_6O_4$: C, 40.00; H, 5.22; N, 31.10%.

3,6-Diazido-3,6-dideoxy-1,2-O-isopropylidene-4-O-mesyl-α-D-glucopyranose (3). A sample of **2** (17.1 g) was mesylated with mesyl chloride (5.36 ml) in pyridine (86 ml) at room temperature for 5 h. Work-up of the reaction mixture in the usual way afforded a practically pure syrup of the 4-*O*-mesylate (**3**) in quantitative yield (22.0 g). Analytical sample of **3** was obtained in 90% yield after being subjected to chromatography on silica gel with benzene–ethyl acetate (12:1); $[\alpha]_D^{17}$ +80° (*c* 1.9, $CHCl_3$); $\nu_{max}^{CCl_4}$ (0.1 M) 2100 (N_3), 1380 and 1185 cm^{-1} (SO_3); δ($CDCl_3$) 1.39 and 1.60 [each s, 6H, $C(CH_3)_2$], 3.12(s, 3H, OMs), *ca.* 3.6(m, 2H, H-6,6′), *ca.* 4.1(m, 1H, H-5), 4.12(dd, 1H, H-3, $J_{2,3}$=4.2, $J_{3,4}$=8.8 Hz), 4.29(dd, 1H, H-2, $J_{1,2}$=4.6 Hz), 4.68(dd, 1H, H-4, $J_{4,5}$=4.3 Hz), and 5.63(d, 1H, H-1).

Found: C, 34.76; H, 4.47; N, 23.83; S, 9.42%. Calcd for $C_{10}H_{16}N_6O_6S$: C, 34.47; H, 4.62; N, 24.12; S, 9.20%.

3,6-Diazido-4-O-benzoyl-3,6-dideoxy-1,2-O-isopropylidene-α-D-galactopyranose (4). A mixture of **3** (669 mg), sodium benzoate (1.39 g), and dry DMF (62 ml) was refluxed for 4 h. The cooled reaction mixture was filtered, and the insoluble matter was washed with ethyl acetate (65 ml). The combined filtrate and washings were evaporated to a syrup, which was dissolved in chloroform, washed with water and saturated NaCl solution, dried and evaporated. The residual yellow syrup was chromatographed on silica gel with benzene–ethyl acetate (12:1) to afford colorless syrup of **4** (604 mg, 84%): $[\alpha]_D^{20}$ +156° (*c* 1.6, $CHCl_3$); ν_{max}^{liq} 2100 (N_3), 1730 cm^{-1} (ester); δ($CDCl_3$), 1.46 and 1.61[each s, 6H, $C(CH_3)_2$], *ca.* 3.5(m, 2H, H-6,6′), 4.01(dd, 1H, H-3, $J_{2,3}$=6.2, $J_{3,4}$=4.0 Hz), *ca.* 4.3(m, 1H, H-5), 4.32(dd, 1H, H-2, $J_{1,2}$=4.6 Hz), 5.58(dd, 1H, H-4, $J_{4,5}$=3.2 Hz), and 5.74(d, 1H, H-1).

Found: C, 51.12; H, 4.56; N, 22.25%. Calcd for $C_{16}H_{18}N_6O_5$: C, 51.33; H, 4.85; N, 22.45%.

3,6-Diazido-3,6-dideoxy-1,2-O-isopropylidene-α-D-galactopyranose (5). A 0.82 M methanolic sodium methoxide solution (2.95 ml) was added to a solution of **4** (604 mg) in methanol (12 ml) and the mixture was kept at room temperature for 3 h. The solution was neutralized with 20% acetic acid and evaporated. The residue was dissolved in ethyl acetate, washed with water and saturated NaCl solution, dried, and evaporated. The residual yellow syrup was chromatographed on silica gel with benzene–ethyl acetate (12:1) to afford **5** as a syrup (406 mg, 93%): $[\alpha]_D^{18}$ +91° (*c* 1.4, $CHCl_3$); δ($CDCl_3$) 1.43 and 1.57[each s, 6H, $C(CH_3)_2$], 2.45(1H, OH), 3.4—4.1(m, 5H, H-3,4,5,6,6′), 4.32(dd, 1H, H-2, $J_{1,2}$=4.6, $J_{2,3}$=7.0 Hz), and 5.71(d, 1H, H-1).

Found: C, 40.22; H, 5.26; N, 31.25%. Calcd for $C_9H_{14}N_6O_4$: C, 40.00; H, 5.22; N, 31.10%.

3,6-Diazido-3,6-dideoxy-1,2-O-isopropylidene-4-O-mesyl-α-D-galactopyranose (6). A sample of **5** (382 mg) was mesylated in the usual way to afford **6** (493 mg) in quantitative yield. Analytical sample was obtained by silica gel column chromatography with benzene–ethyl acetate (12:1) in 89% yield as a pale yellow syrup: $[\alpha]_D^{20}$ +74° (*c* 2.0, $CHCl_3$); $\nu_{max}^{CHCl_3}$ (0.1 M) 2100(N_3), 1360 and 1175 cm^{-1} (SO_3); δ($CDCl_3$) 1.42 and 1.57[each s, 6H, C(CH_3)$_2$], 3.18(s, 3H, OMs), 3.53(m, 2H, H-6,6′), 3.88(dd, 1H, H-3, $J_{2,3}$=6.5, $J_{3,4}$= 2.8 Hz), *ca.* 4.2(m, 1H, H-5), 4.21(dd, 1H, H-2, $J_{1,2}$=4.2 Hz), 4.94(dd, 1H, H-4, $J_{4,5}$=3.8 Hz), and 5.61(d, 1H, H-1).

Found: C, 34.73; H, 4.65; N, 24.10; S, 9.03%. Calcd for $C_{10}H_{16}N_6O_6S$: C, 34.47; H, 4.62; N, 24.12; S, 9.20%.

3,4,6-Triazido-3,4,6-trideoxy-1,2-O-isopropylidene-α-D-glucopyranose (7). A mixture of **6** (375 mg), sodium azide (211 mg) and dry DMSO (7.6 ml) was heated under stirring at 95—100 °C for 1.5 h and then poured into cold water (7.7 ml). The mixture was extracted with chloroform and the combined extracts were washed with saturated NaCl solution, dried, and evaporated. The residual brown syrup was chromatographed on silica gel with benzene–ethyl acetate (30:1) to afford a pale yellow syrup of **7** (218 mg, 69%). A part of this sample was again chromatographed on silica gel with hexane–ethyl acetate (20:1) to give an analytical sample: $[\alpha]_D^{20}$ +239° (*c* 1.47, $CHCl_3$); $\nu_{max}^{CHCl_3}$ 2110 cm^{-1} (N_3); δ($CDCl_3$) 1.42 and 1.59[each s, 6H, C(CH_3)$_2$], 3.5—3.9(m, 5H, H-3, 4,5,6,6′), 4.19(dd, 1H, H-2, $J_{1,2}$=4.8, $J_{2,3}$=5.0 Hz), 5.67(d, 1H, H-1).

Found: C, 36.84; H, 4.49; N, 42.48%. Calcd for $C_9H_{13}N_9O_3$: C, 36.61; H, 4.44; N, 42.70%.

3,4,6-Triamino-3,4,6-trideoxy-1,2-O-isopropylidene-α-D-glucopyranose (8). The triazido compound **7** (114 mg) was hydrogenolized over palladium black in methanol to afford the triamino derivative **8** (77.3 mg, 92%), which was used for the subsequent reaction without purification.

Tri-N-acetyl Derivative (9): Acetylation of **8** (69.1 mg) with acetic anhydride (0.09 ml) in methanol at room temperature for 1 h gave **9** (91.3 mg, 84%) as needles after silica gel chromatography (5:1, chloroform–methanol): mp 253 °C (dec); $[\alpha]_D^{22}$ +59°(*c* 0.59, MeOH); ν_{max}^{KBr} 1645 and 1533 cm^{-1} (amide).

Found: C, 52.24; H, 7.25; N, 12.04%. Calcd for $C_{15}H_{25}N_3O_6$: C, 52.47; H, 7.34; N, 12.24%.

Tri-N-benzyloxycarbonyl Derivative (10): A sample of **8** (244 mg) was *N*-benzyloxycarbonylated with benzyl chloroformate (0.64 ml) in dry pyridine (4 ml) at −40——35 °C for 3 h. The reaction mixture was diluted with water and extracted with chloroform. The extracts were washed with saturated NaCl solution, dried, and evaporated. The residue was chromatographed on silica gel with benzene–acetone (10:1) to afford **10** (490 mg, 71%) as crystals. Recrystallization from ethyl acetate–petroleum ether gave a pure sample: mp 124—125 °C; $[\alpha]_D^{18}$ −28°(*c* 1.21, $CHCl_3$); ν_{max}^{KBr} 3320 (NH), 1690 and 1530 cm^{-1} (amide); δ($CDCl_3$) 1.32 and 1.55[each s, 6H, C(CH_3)$_2$], 3.7—4.3(m, 6H, H-2,3, 4,5,6,6′), 5.20(s, 6H, CH_2Ph), *ca.* 5.5(3H, NH), 5.63(d, 1H, H-1, $J_{1,2}$=4.8 Hz), and 7.48(s, 15H, Ph).

Found: C, 63.83; H, 6.11; N, 6.63%. Calcd for $C_{33}H_{37}N_3O_9$: C, 63.96; H, 6.02; N, 6.78%.

2,3,5-Tris(benzyloxycarbonylamino)-2,3,5-trideoxy-O-formyl-D-arabinopyranose (11). Treatment of **10** (1.78 g) with 67% aqueous acetic acid (26.7 ml) at 55—60 °C for 4.5 h afforded a crystalline free sugar (1.60 g, 96%), which was suspended in acetone (48 ml) to which added a solution of sodium metaperiodate (1.77 g) in water (18 ml). The mixture was stirred at 33°C for 40 h, and the resulting precipitates were collected by filtration and washed with acetone and water to give **11** as a colorless powder (1.14 g, 72%). A part of this product was chromatographed on silica gel with chloroform–ethyl acetate (10:1) to afford an analytical sample: mp 198—199 °C(dec); $[\alpha]_D^{17}$ −20°(constant for 48 h, *c* 0.75, dioxane); ν_{max}^{KBr} 3430 (OH), 3300 (NH), 1718 (OCHO), 1680 and 1540 cm^{-1} (urethane); δ(DMSO-d_6) *ca.* 3.2—4.1(m, 4H, H-2,3,5,5′), 5.10 and 5.18(each s, 6H, OCH_2Ph), *ca.* 5.2(m, 1H, H-4), *ca.* 5.8(m, 1H, H-1), *ca.* 6.5, 7.2, and 7.5(m, 3H, NH and OH), 7.45(s, 15H, Ph), and 8.27(s, OCHO); δ(pyridine-d_5) 3.82(m, 1H, H-5, $J_{5,5}$ = 14.2 Hz), *ca.* 4.4—5.3(m, 5H, H-1,2,3,5′, and OH), 5.18(s, 6H, OCH_2Ph), 5.75(m, 1H, H-4), *ca.* 6.7 and 7.4(m, 2H, NH), and 8.10(s, 1H, OCHO).

Found: C, 62.48; H, 5.52; N, 7.09%. Calcd for $C_{30}H_{31}N_3O_9$: C, 62.38; H, 5.41; N, 7.28%.

1-O-*Acetyl Derivative (12).* A sample of **11** (35.6 mg) was acetylated with acetic anhydride (0.02 ml) in pyridine (0.36 ml) to afford colorless powder of **12** (32.9 mg, 86%): mp 194—198 °C (MeOH); $[\alpha]_D^{19}$ −43° (*c* 1.8, $CHCl_3$); δ($CDCl_3$) 2.10(s, 3H, OAc), *ca.* 3.3 and 4.2—4.5(m, 4H, H-2,3,5,5′), 5.08(s, 4H, OCH_2Ph at 2- and 3-N), 5.21(ABq, OCH_2Ph at 5-N), 5.0—5.4(br, 3H, two NH, H-4), 7.05(m, H-1), 7.37(s, 15H, Ph), and 7.98(s, 1H, OCHO).

Found: C, 62.24; H, 5.51; N, 6.70%. Calcd for $C_{32}H_{33}N_3O_{10}$: C, 62.03; H, 5.37; N, 6.78%.

2,3,5-Tris(benzyloxycarbonylamino)-2,3,5-trideoxy-D-arabinopyranose (13). A mixture of **11** (47.4 mg), dioxane (0.5 ml), and 10% aqueous ammonia (0.1 ml) was kept at room temperature for 2 h. The reaction mixture was evaporated to dryness and the residue was washed with ethanol to afford **13** as a powder (41.9 mg, 93%): R_f 0.64(silica gel, 3:1 benzene–acetone); mp 204—206 °C; δ(DMSO-d_6) *ca.* 3.2(m, 1H, H-5), 3.8—4.0(m, 4H, H-2,3,4,5′), 5.12 and 5.19(each s, 6H, OCH_2Ph), 5.75(m, 1H, H-1), *ca.* 6.6(m, 2H, NH), *ca.* 7.4(m, 1H, NH), and 7.41(s, 15H, Ph); δ(pyridine-d_5) 3.79(m, 1H, H-5, $J_{5,5}$=13.2 Hz), 4.4—5.3(m, 7H, H-1, 2,3,4,5′, OH) 5.18 and 5.21(each s, OCH_2Ph), *ca.* 6.6 and 7.8(2H, NH), and 7.26(s, 15H, CH_2Ph).

Found: C, 63.22; H, 5.85; N, 7.47%. Calcd for $C_{29}H_{31}N_3O_8$: C, 63.38; H, 5.69; N, 7.65%.

1,4-Di-O-Acetyl Derivative (14). A sample of **13** (15 mg) was acetylated with acetic anhydride (0.025 ml) in pyridine (0.15 ml) for 48 h. The crystalline product was recrystallized from chloroform–hexane to afford the pure sample of **14** (12.1 mg, 70%): mp 192.5—194.5 °C (lit,[2b] 186—186.5 °C); $[\alpha]_D^{19}$ −41°(*c* 2.05, $CHCl_3$); δ(DMSO-d_6) 1.92 and 2.11(each s, 6H, CH_3CO), 3.19(dd, 1H, H-5, $J_{5,5'}$= 15 Hz), 4.2—4.4(m, 3H, H-2,3,5′), 5.0—5.2(m, 9H, CH_2Ph, H-4, NH), 6.99(m, 1H, H-1), 7.35—7.40(each s, Ph).

Found: C, 62.52; H, 5.62; N, 6.46%. Calcd for $C_{33}H_{35}O_{10}N_3$: C, 62.55; H, 5.57; N, 6.63%.

2,3,5-Tris(benzyloxycarbonylamino)-1,2,3,5-tetradeoxy-4-O-formyl-D-erythro-pent-1-enopyranose (17). A mixture of dry DMSO, dry pyridine, and trifluoroacetic acid (10:1:0.473 by volume) (3.12 ml) was added to a solution of **11** (1.00 g) in dry DMSO (10 ml). DCCI (1.07 g) was then added to the mixture, and stirred at room temperature for 1 day. The reaction mixture was poured into ice-water (15 ml). The pale yellow precipitates formed were collected by filtration and washed with water. The dried solid was dissolved in dioxane, the insoluble matter was filtered off, and the filtrate was evaporated to afford a colorless solid of **17** (793 mg, 82%). The analytical sample was obtained by silica gel chromatography with benzene–ethyl acetate (6:1): mp 174—177 °C (dec); $[\alpha]_D^{18}$ +90°(*c* 0.5, dioxane); ν_{max}^{KBr} 3320 (NH), 1730(ester), 1695 and 1525 cm^{-1}(amide); δ(DMSO-d_6) 3.4—3.9(m, 3H, H-3,5,5′), *ca.* 4.9(m, 1H, H-4), 5.22 and 5.37(each

s, 6H, CH_2Ph), 7.3—7.8(m, 2H, NH), 7.48(s, 1H, H-1), 7.60(s, 15H, Ph), and 8.42(s, CHO).

Found: C, 64.14; H, 5.30; N, 7.23%. Calcd for $C_{30}H_{29}N_3O_8$: C, 64.39; H, 5.08; N, 7.23%.

3,4-Diamino-6-(benzyloxycarbonylamino)-3,4,6-trideoxy-1,2-O-isopropylidene-α-D-glucopyranose (18). A solution of *N*-(benzyloxycarbonyloxy)succinimide (810 mg) in DMF (7.1 ml) was added dropwise to a solution of **8** (706 mg) in 75% DMF-water (14.1 ml) at −30——20 °C under stirring over a period of 30 min. After being kept at room temperature for 1 h, the reaction mixture was evaporated, the resulting syrup was dissolved in chloroform (20 ml), washed with saturated $NaHCO_3$ and saturated NaCl solution successively, dried, and evaporated. The syrupy residue (1.4 g) was chromatographed on silica gel (140 g) with chloroform–methanol (5:1) to afford a homogeneous sample of the 6-*N*-benzyloxycarbonylated product **18** (527 mg, 40%) as a colorless syrup, which was used for subsequent synthesis without further purification: $\nu_{max}^{CHCl_3}$ (0.1 M) 3400 (NH), 1710 and 1510 cm^{-1}(amide); δ ($CDCl_3$) 1.37 and 1.56 [each s, 6H, $C(CH_3)_2$], 1.66(s, 4H, NH) 2.53(dd, 1H, H-4, $J_{3,4}$=6.0, $J_{4,5}$=8.3 Hz), 3.03(dd, 1H, H-3, $J_{2,3}$=5.0 Hz), 3.6—3.8(m, 3H, H-5,6,6′), 4.07(dd, 1H, H-2, $J_{1,2}$=5.0 Hz), 5.21(s, 2H, CH_2Ph), *ca.* 5.4(m, 1H, NH), 5.63(d, 1H, H-1), and 7.48(s, 5H, Ph).

3,4-Di-N-acetyl Derivative (19). A sample of **18** (33.6 mg) was acetylated with acetic anhydride (0.02 ml) in methanol (0.67 ml) at room temperature for 20 min. Evaporation of the reaction mixture followed by chromatography on silica gel (4 g) with chloroform–methanol (20:1) afforded the pure sample of **19** as a glassy solid (38.5 mg, 93%): $[\alpha]_D^{25}$ +38°(*c* 0.66, $CHCl_3$); ν_{max}^{KBr} 3300 (NH), 1700, 1650 and 1530 cm^{-1}(amide); δ($CDCl_3$) 1.37 and 1.59[each s, 6H, $C(CH_3)_2$], 1.96 and 1.99(each s, 6H, NAc), 3.4—4.5(m, 6H, H-2,3,4,5,6,6′), 5.21(s, 2H, CH_2Ph), 5.65(d, 1H, H-1, $J_{1,2}$=4.8 Hz), *ca.* 5.7 and 6.3(3H, NH), and 7.47(s, 5H, Ph).

Found: C, 57.63; H, 6.58; N, 9.42%. Calcd for $C_{21}H_{29}N_3O_7$: C, 57.92; H, 6.71; N, 9.65%.

3,4-(1,3-Guanidinediyl)-6-benzyloxycarbonylamino-3,4,6-trideoxy-1,2-O-isopropylidene-α-D-glucopyranose (20) Hydrobromide. Cyanogen bromide (138 mg) was added to a solution of **18** (458 mg) in water (4.6 ml) under stirring. After being left to stand at room temperature for 1 h, the reaction mixture was evaporated and the residue was chromatographed on silica gel (60 g) with chloroform–ethanol (5:1) to afford the crystalline hydrobromide of **20** (555 mg, 93%): mp 122—125 °C (dec); ν_{max}^{KBr} 3400—3000 (NH^+), 1700 and 1530(amide), 1675 cm^{-1} (guanidium I); $[\alpha]_D^{20}$ +59°(*c* 0.55, MeOH); δ($CDCl_3$) 1.36 and 1.52[each s, 6H, $C(CH_3)_2$], 3.7—4.4(m, 6H, H-2,3,4,5,6,6′), 5.23(s, 2H, CH_2Ph), *ca.* 5.7(1H, H-1), *ca.* 6.2(br, 1H, NH), 7.2—7.7(br, 4H, guanidinium), and 7.46(s, 5H, Ph).

Found: C, 47.39; H, 5.72; N, 12.41; Br, 17.14%. Calcd for $C_{18}H_{25}N_4O_5Br$: C, 47.27; H, 5.51; N, 12.25; Br, 17.47%.

3,4,6-Tris(benzyloxycarbonylamino)-3,4,6-trideoxy-D-glucitol (23). A mixture of **7** (916 mg) and 20% acetic acid (27.5 ml) was heated at 100—110 °C for 1.5 h and then evaporated. The residual brown syrup was chromatographed on silica gel (43 g) with benzene–ethyl acetate(2:1) to afford 3,4,6-triazido-3,4,6-trideoxy-D-glucose (682 mg, 86.2%) A solution of sodium borohydride (57 mg) in 80% ethanol (1.0 ml) was added to a solution of free sugar (682 mg) in ethanol (5.1 ml) under ice-cooling. The mixture was stirred at the same temperature for 0.5 h, and then warmed up to room temperature, stirring being continued for 3 h, and neutralized with Amberlite IR-120(1.5 ml). The resulting solution was evaporated and the residue was chromatographed on silica gel (65 g) with benzene–ethyl acetate (1:1) to give a colorless syrup of **22** (415 mg, 60%). Triazido compound **22** (632 mg) was hydrogenolized over palladium black in methanol (12 ml) for 4 h to afford the triamino compound as a pale yellow syrup. A solution of *N*-(benzyloxycarbonyloxy)succinimide (2.0 g) in DMF (4 ml) was added to a solution of the triamino compound (450 mg) in DMF (4 ml) and water (0.2 ml). After being kept at room temperature, the reaction mixture was poured into ice-water (150 ml). The precipitates formed were collected by filtration, washed with water, and dried to yield a colorless crystalline solid of **23** (1.43 g, 98% from **22**). Recrystallization from methanol afforded an analytical sample: mp 148.5—149.5 °C; $[\alpha]_D^{20}$ +53°(*c* 0.94, DMF).

Found: C, 62.11; H, 6.04; N, 7.20%. Calcd for $C_{30}H_{35}N_3O_9$: C, 61.95; H, 6.07; N, 7.23%.

2,3,5-Tris(benzyloxycarbonylamino)-2,3,5-trideoxy-D-arabono-1,4-lactone (25). (a) A solution of sodium metaperiodate (273 mg) in water (2 ml) was added to a solution of **23** (430 mg) in acetone (9 ml), and the mixture was stirred at room temperature for 1 h. The mixture was diluted with acetone (9 ml). The precipitates were filtered off, and the filtrate was evaporated to afford 2,3,5-tris(benzyloxycarbonylamino)-2,3,5-trideoxy-D-arabinofuranose (**24**) (404 mg) as a colorless solid: R_f 0.56(silica gel, 3:1 benzene–acetone). Furanose **24** (404 mg) was oxidized with the chromium trioxide–acetic acid–pyridine reagent** (9.2 ml) at room temperature for 1.5 h. The reaction mixture was diluted with water (20 ml), extracted with chloroform, the extracts being washed with saturated NaCl solution, dried, and evaporated. The syrupy residue (300 mg) was chromatographed on silica gel (30 g) with benzene–acetone (6:1) to give **25** (265 mg, 66%) as a colorless solid: mp 89—91 °C (benzene); $[\alpha]_D^{18}$ −26° (*c* 0.97, $CHCl_3$); ν_{max}^{KBr} 3320 (NH), 1785 (1,4-lactone), 1680 and 1510 cm^{-1}(amide); δ($CDCl_3$) *ca.* 3.6, 4.3, and 4.7(m, 5H, H-2,3,-4,5,5′), 5.10(s, 6H, CH_2Ph), *ca.* 5.8(br, 3H, NH), and 7.32(s, 15H, Ph).

Found: C, 63.70; H, 5.47; N, 7.49%. Calcd for $C_{29}H_{29}N_3O_8$: C, 63.61; H, 5.34; N, 7.68%.

(b) A sample of **13** (10.8 mg) was treated with the chromium trioxide–acetic acid–pyridine reagent (0.25 ml) at room temperature for 3 h. The reagent (0.25 ml) was added to the mixture. After being stirred for 30 min, the reaction mixture was worked up as described in (a) to afford a sample of **25** (4.1 mg, 42%) as a semicrystalline solid, whose IR spectrum was identical with that of the sample of **25** prepared from **24**.

5-Amino-2,3-bis(benzyloxycarbonylamino)-2,3,5-trideoxy-D-arabono-1,5-lactam (26). A sample of **25** (209 mg) was hydrogenolized in methanol (6 ml) over palladium black for 5 h. During the course of reaction a fresh catalyst was added every hour. The crude triamino sugar lactam **16** was purified by silica gel chromatography with chloroform–methanol–17% aqueous ammonia (6:6:1) to afford a practically pure sample of **16** (39.7 mg, 72%). Treatment of the sample of triamino sugar lactam **16** with 3 equivalent of *N*-(benzyloxycarbonyloxy)succinimide in aqueous DMF gave a crystalline sample of **26** in 85% yield after being subjected to chromatography with chloroform–methanol (10:1). The sample was identical with the authentic sample[3] of **26**.

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**The reagent[10] is composed of chromium trioxide (1 g), acetic acid (30 ml) and pyridine (1 ml).

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