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Synthesis of γ-aminobutyric acid analogs based on carbohydrate scaffolds

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ABSTRACT

γ-Aminobutyric acid analogs based on sugar scaffolds were prepared in six to nine steps starting from D-glucal and D-galactal. The key step in the synthesis is the Vilsmeier–Haack reaction that affords the corresponding 2-*C*-formyl glycal on treatment with DMF and $POCl_3$. Oxidation of the aldehyde and reduction of the 4-azido group provided the corresponding GABA analog. Acylamide and tetrazole analogs were also prepared as the bioisosteres of the carboxylic acid.

1. Introduction

γ-Aminobutyric acid (GABA), the primary neurotransmitter in the mammalian central nervous system, is essential for maintaining the balance between neuronal excitation and inhibition. Low GABA levels are related to a series of neurological disorders such as Parkinson's disease, Huntington's chorea, Alzheimer's disease, and epilepsy.[1] As reported, one of the most effective ways to prevent central nervous system disorders is to use GABA analogs to deactivate γ-aminobutyric acid aminotransferase that degrades GABA so as to increase the concentration of GABA in the brain.[2] Several synthetic GABA analogs have been used as anticonvulsant drugs such as vigabatrin, gabapentin, and pregabalin[3] (Fig. 1). Since compounds with a restricted conformation can provide substantial information on drug discovery, the design and synthesis of new structurally rigid GABA analogs are very important for locking the active conformations.

The relatively rigid skeletons found in carbohydrates make them ideal platforms for the presentation of pharmacophores.[4] Furthermore, acylation or alkylation of the additional hydroxyl or amino groups on the carbohydrate scaffolds may improve the drugable properties. Hindsgaul and co-workers pioneered the field of sugar-fused GABA analogs in 2001.[5] From then on, more effort has been devoted to the design and synthesis of GABA analogs on carbohydrate backbones.[6] The above-mentioned hybrid molecules are carbohydrate derivatives bearing both amino and carboxylic acid functionalities and are termed sugar amino acids.[7] Herein we report the synthesis of the sugar amino acid analogs of GABA, **10a**, **10b**, **11a**, and **11b**, in which the amino and carboxylic acid groups are engineered into carbohydrate scaffolds. In addition, the acylamide and tetrazole groups are well-known bioisosteres of carboxylic acids, and their higher lipophilicities may potentially improve their in vivo bioavailability.[8] Previous studies also indicate that tetrazole may be a good replacement for carboxylic acid group in GABA analogs.[9] Four acylamide analogs, **14a**, **14b**, **15a**, and **15b,** and two tetrazole analogs, **20** and **21,** were also prepared (Scheme 1).

2. Results and discussion

The D-glucal (**1a**) and D-galactal (**1b**) were prepared from D-glucose and D-galactose via classical methods, respectively.[10] Mesylation after regioselective 3,6-di-O-benzoylation of **1a** and **1b** were carried out in a one-pot procedure to furnish **2a** and **2b**, which were subsequently treated with sodium azide and tetrabutylammonium chloride in toluene to give the corresponding azides **3a** and **3b**.[11] Compounds **3a** and **3b** were quantitatively debenzoylated with sodium methoxide in methanol, and the intermediates were benzylated or methylated without further purification to provide 3,6-di-O-benzylated products **4a** and **4b**, or 3,6-di-O-methylated products **5a** and **5b** in 72–92% yields. A Vilsmeier–Haack reaction[12] was carried out smoothly to give the 4-azido-4-deoxy-2-*C*-formyl-D-galactal **6a** or **7a** in good yield from **4a** or **5a**, respectively. However, the gluco-type substrate **4b** or **5b** could not be consumed completely even by extending the reaction time or increasing the equivalent of $POCl_3$, which led to the lower yielding of **6b** or **7b** (Scheme 2). When a 1:1 mixture of **4a** and **4b** was treated under the same conditions, and the reaction was quenched after 4 h, the ratio of **6a** and **6b** was determined as 5:1 by ^1H

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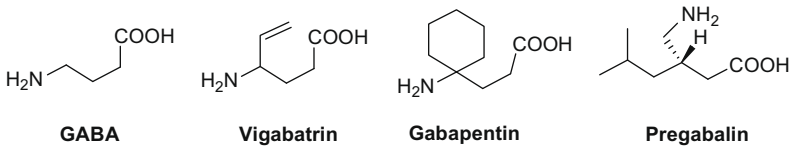
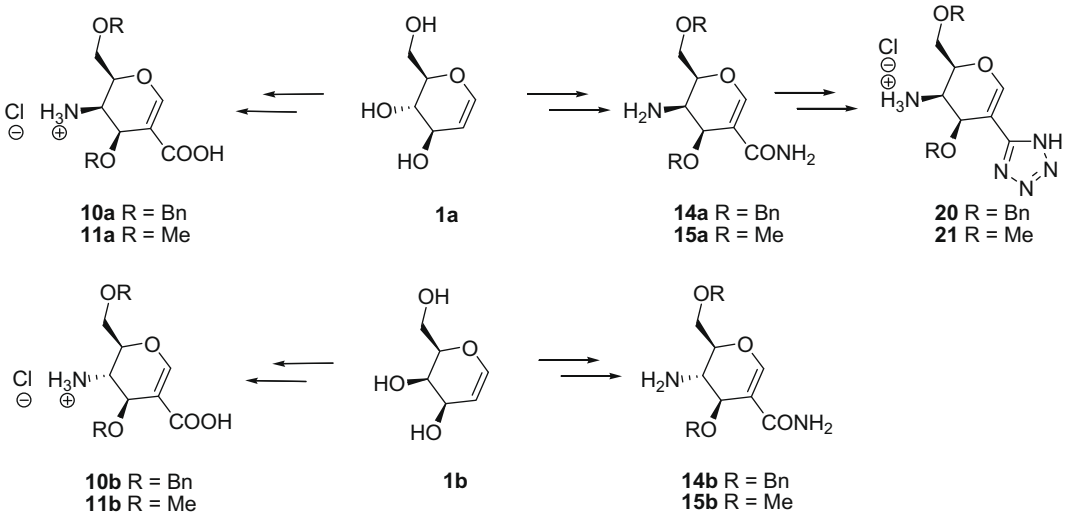


Figure 1. Chemical structures of GABA and some analogs.

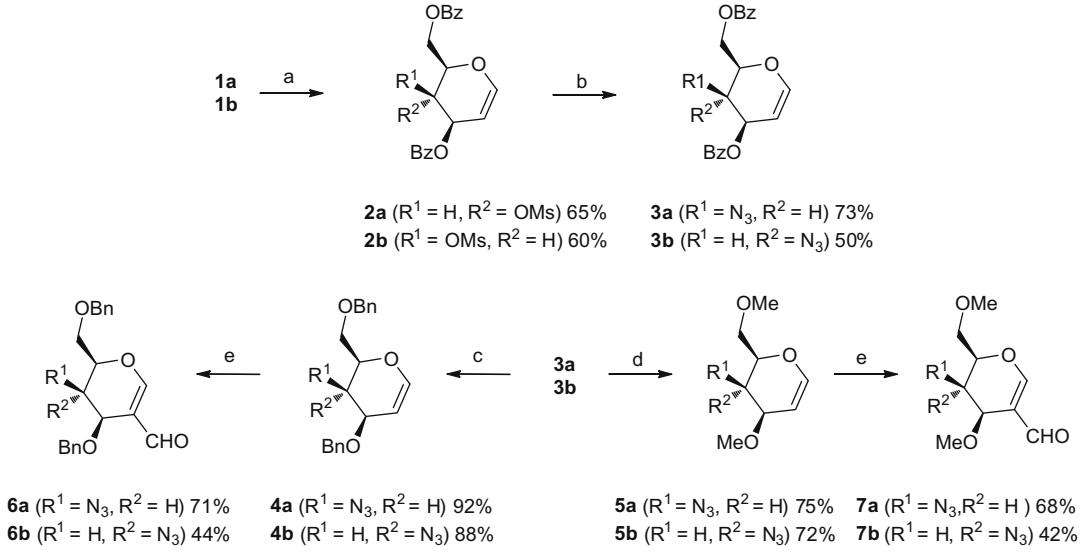
NMR spectroscopy. Here we provide a possible mechanism for the different reaction rates derived from the 4-azido group. The pseudo-equatorial 4-azido group in the gluco-type substrate is closer to the incoming Vilsmeier reagent[13] (**D**), or the pseudo-equatorial azido group plays a stronger role than the pseudo-axial one in decreasing the electron density of the double bond by means of its parallel relationships to the double bond (**C**). In the case of the 4-axial azido counterpart, the electrophilic species reacts readily with the electron-rich double bond from the less sterically hindered side (**A** or **B**) (Fig. 2).

With the intermediates **6a, 6b, 7a**, and **7b** in hand, we continued to carry out the functional group manipulations outlined in Scheme 3. Oxidation of the aldehydes using $NaClO_2$ and H_2O_2[14] led to the corresponding carboxylic acids **8a, 8b, 9a, 9b** in excellent yields (>90%). Reduction of the azides using PPh_3 gave the corresponding amines in good yields, which were then converted into their hydrochloride salts **10a, 10b, 11a, 11b** by treatment of 1 M HCl.

The carboxylic acids **8a, 8b, 9a,** and **9b** were converted into acylamides **12a, 12b, 13a,** and **13b** on treatment with di-*tert*-butyl



Scheme 1. General scheme of target sugar amino acid analogs.



Scheme 2. Reagents and conditions: (a) 2.3 equiv BzCl, pyridine, 0 °C, 1.5 h, then 2 equiv MsCl, 0 °C to rt, 0.5 h; (b) 5 equiv NaN_3, 3 equiv Bu_4NCl, toluene, reflux, 24 h; (c) NaOMe, MeOH, rt, 0.5 h, then 2.4 equiv NaH, 2.4 equiv BnBr, DMF, 0 °C to rt, 12 h; (d) NaOMe, MeOH, rt, 0.5 h, then 2.4 equiv NaH, 2.4 equiv MeI, THF, 0 °C to rt, 12 h; (e) 5 equiv $POCl_3$, DMF, 0 °C to rt, 10 h.

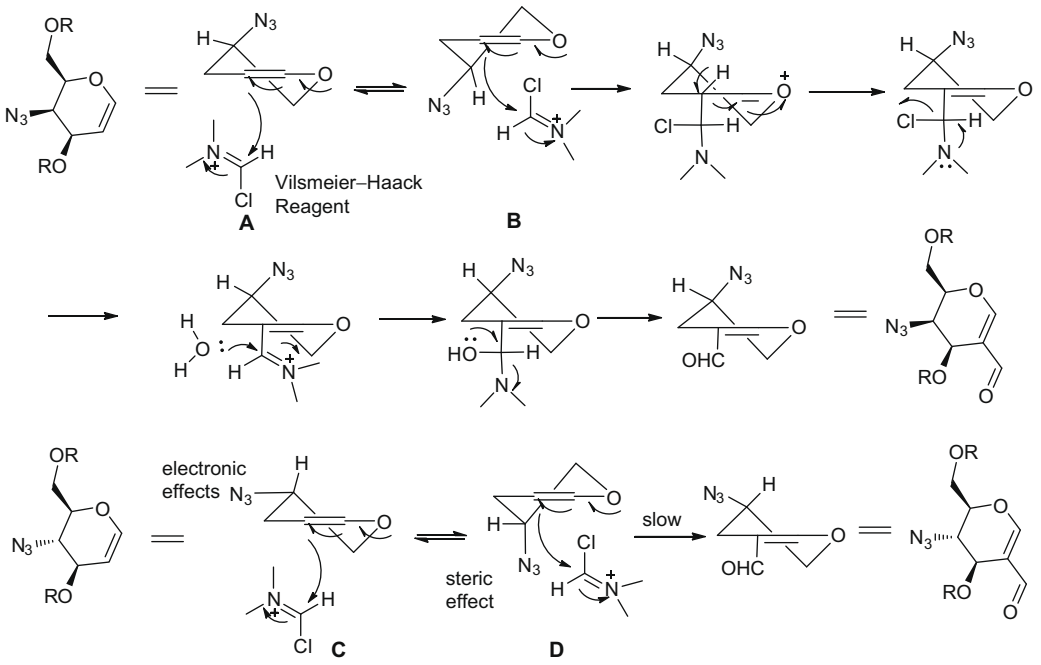
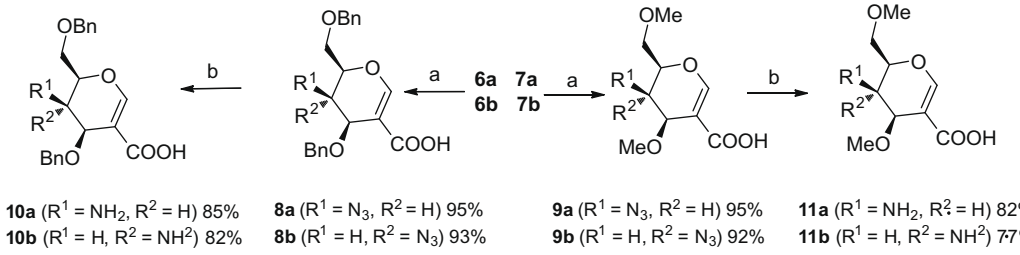
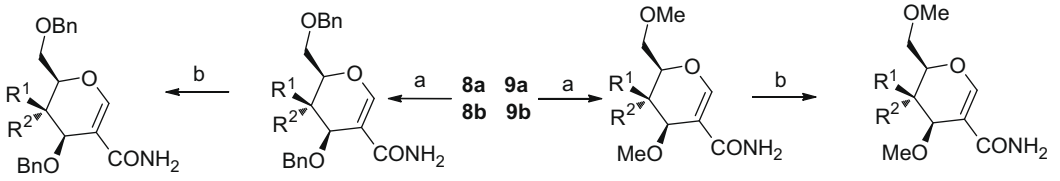


Figure 2. A plausible explanation for the different results of 4-azide$_{eq}$ and 4-azide$_{ax}$ (3-OR and 5-CH_2OR were omitted for clarity).



10a (R^1 = NH_2, R^2 = H) 85% **8a** (R^1 = N_3, R^2 = H) 95% **9a** (R^1 = N_3, R^2 = H) 95% **11a** (R^1 = NH_2, R^2 = H) 82%
10b (R^1 = H, R^2 = NH^2) 82% **8b** (R^1 = H, R^2 = N_3) 93% **9b** (R^1 = H, R^2 = N_3) 92% **11b** (R^1 = H, R^2 = NH^2) 77%

Scheme 3. Reagents and conditions: (a) 3 equiv NaH_2PO_4, 6 equiv $NaClO_2$, 5 equiv H_2O_2, 2:2:1 MeCN–^{t}BuOH–H_2O, rt, 2 h; (b) 3 equiv PPh_3, 10:1 THF–H_2O, 60 °C, 3 h then HCl.



14a (R^1 = NH_2, R^2 = H) 80% **12a** (R^1 = N_3, R^2 = H) 92% **13a** (R^1 = N_3, R^2 = H) 88% **15a** (R^1 = NH_2, R^2 = H) 77%
14b (R^1 = H, R^2 = NH^2) 76% **12b** (R^1 = H, R^2 = N_3) 89% **13b** (R^1 = H, R^2 = N_3) 84% **15b** (R^1 = H, R^2 = NH^2) 71%

Scheme 4. Reagents and conditions: (a) 1.6 equiv Boc_2O, 3 equiv NH_4HCO_3, 2 equiv Py, MeCN, rt, 16 h; (b) 3 equiv PPh_3, 10:1 THF–H_2O, 60 °C, 3 h.

dicarbonate, ammonium bicarbonate, and pyridine in good yields.[15] Reduction using PPh_3 was again employed to convert the azides into amines, which provided the acylamide bearing GABA derivatives **14a, 14b, 15a, 15b** in 71–80% yields (Scheme 4).

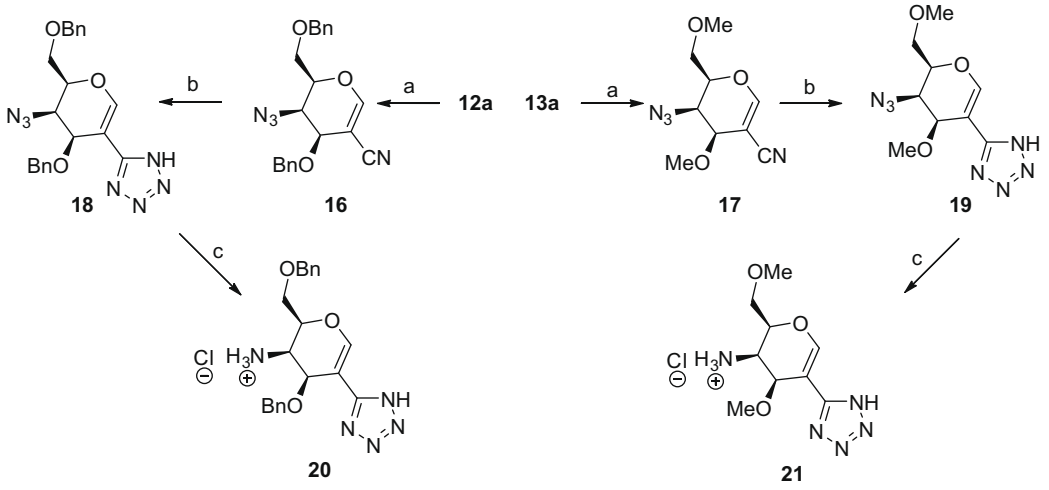
Nitriles **16** and **17** were prepared in high yield ($\geqslant$95%) by treatment of acylamide **12a** and **13a** with trifluoroacetic anhydride in dry pyridine.[16] Treatment of nitriles with trimethylsilylazide in the presence of catalytic amounts of Bu_2SnO produced the desired tetrazoles **18** and **19** in 92% and 88% yield, respectively.[17] Finally, reduction of the azides was carried out, and the tetrazole GABA analogs **20** and **21** were obtained as their hydrochloride salts in good yield (Scheme 5).

In summary, we have successfully synthesized a series of novel GABA analogs based on glycal scaffolds. Preparations of the corresponding acylamide and tetrazole derivatives extend the general class of known GABA analogs. These compounds have rigid skeletons with a restricted conformation about the amino and carboxylic functional groups, which may provide information on the active conformation of the neurotransmitter GABA.

3. Experimental

3.1. Synthesis, general procedures

All chemicals, reagents, and solvents were purchased from commercial sources where available. THF was distilled over sodium metal, and MeCN was distilled over P_2O_5 under a nitrogen atmosphere. When dry conditions were required, the reactions were



Scheme 5. Reagents and conditions: (a) 2 equiv TFAA, 4 equiv Py, THF, rt, 0.5 h; **16**: 96%, **17**: 95%; (b) 5 equiv $TMSN_3$, 0.2 equiv Bu_2SnO, toluene, reflux, 24 h; **18**: 92%, **19**: 88%; (c) 3 equiv PPh_3,10:1 THF–H_2O, 60 °C, 3 h, then HCl; **20**: 78%, **21**: 75%.

performed under an argon atmosphere. Thin-layer chromatography (TLC) plates were purchased from Liangchen Chemical Engineering Co. Ltd (Anhui Province). All compounds were visualized with 5% H_2SO_4 in EtOH, followed by heating. Detection with UV light was employed when possible. Flash column chromatography was performed on silica gel 200–300 mesh. The boiling range of the petroleum ether used as an eluent in column chromatography was 60–90 °C. NMR spectra were recorded on a JEOL-300 (300 MHz) or a Bruker AMX-400 (400 MHz) instrument. Chemical shift values (δ) were reported in parts per million (ppm) downfield from TMS as an internal standard; *J* values were given in hertz. Mass spectra were recorded on a Bruker Apex IV FTMS instrument. Optical rotations were measured at 25 °C using an Optical Activity AA-10R automatic polarimeter.

3.2. 2,6-Anhydro-3-azido-1,4-di-*O*-benzyl-3,5-dideoxy-D-*arabino*-hex-5-enitol (4a) and 1,5-anhydro-4-azido-3,6-di-*O*-benzyl-2,4-dideoxy-D-*arabino*-hex-1-enitol (4b)

Compound **3a** or **3b** (5.0 g, 13.2 mmol) was dissolved in dry MeOH (50 mL), and then 75 mg of Na was added. The reaction mixture was stirred at room temperature for 1 h, and then the solution was acidified with Dowex 50WX4-100 (H^+) ion-exchange resin (Sigma–Aldrich) to pH 7.0. After filtration, the filtrate was evaporated under reduced pressure to obtain a white solid. Without further treatment, the white solid was dissolved in dry DMF (60 mL), and then NaH (759 mg, 31.6 mmol) was added slowly at 0 °C. The mixture was stirred at 0 °C until hydrogen evolution had ceased, and it was then stirred for 30 min at room temperature. BnBr (3.78 mL, 31.6 mmol) was added dropwise with stirring, and the mixture was allowed to stir overnight. Then the mixture was cooled to 0 °C, and the reaction was quenched by the addition of MeOH (10 mL). The mixture was concentrated and then partitioned between water and CH_2Cl_2. The combined organic layer was dried over $MgSO_4$, filtered, concentrated to dryness, and then purified by silica gel column chromatography (40:1 petroleum ether–EtOAC) to give **4a** (4.26 g, 92% yield) or **4b** (4.08 g, 88% yield) as a colorless syrup. Compound **4a**: $[\alpha]_D$ −32 (*c* 1.5, $CHCl_3$).^{1}H NMR (300 MHz, $CDCl_3$): δ 7.36–7.28 (m, 10H, Ph), 6.34 (d, 1H, *J* 6.3 Hz, H-1), 4.81 (d, 1H, H-2), 4.68–4.50 (m, 4H, 2 × PhCH_2), 4.38 (d, 1H, *J* 4.5 Hz, H-3), 4.06 (t, 1H, *J* 6.3 Hz, H-5), 3.94 (d, 1H, H-4), 3.68 (d, 2H, H-6); ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.40 (C-1), 137.52–127.47 (Ph), 100.74 (C-2), 74.40, 73.55, 71.35, 70.64, 68.61, 55.13. HRMS: *m/z* Calcd for $C_{20}H_{21}N_3O_3Na$ $[M+Na]^+$, 374.1475. Found 374.1477. Compound **4b:** $[\alpha]_D$ +35 (*c* 1.5 $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.36–7.30 (m, 10H, Ph), 6.39 (d, 1H, *J* 6.3 Hz, H-1), 4.87 (dd, 1H, H-2), 4.69–4.54 (m, 4H, 2 × PhCH_2), 4.15 (d, 1H, *J* 7.5 Hz, H-3), 3.93 (t, 1H, H-4), 3.84 (dd, 1H, *J* 9.9, 2.4 Hz, H-5), 3.75 (d, 2H, H-6)**;** ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.87 (C-1), 137.72–127.74 (Ph), 100.04 (C-2), 76.14, 74.83, 73.53, 70.70, 68.60, 59.22. HRMS: *m/z* Calcd for $C_{20}H_{21}N_3O_3Na$ $[M+Na]^+$: 374.1475. Found 374.1470.

3.3. 2,6-Anhydro-3-azido-3,5-dideoxy-1,4-di-*O*-methyl-D-*arabino*-hex-5-enitol (5a) and 1,5-anhydro-4-azido-2,4-dideoxy-3,6-di-*O*-methyl-D-*arabino*-hex-1-enitol (5b)

Compound **3a** or **3b** (5.0 g, 13.2 mmol) was dissolved in dry MeOH (50 mL), and then 75 mg Na was added. The reaction mixture was stirred at room temperature for 1 h, and the solution was acidified with Dowex 50WX4-100 (H^+) ion-exchange resin (Sigma–Aldrich) to pH 7.0. After filtration, the filtrate was evaporated under reduced pressure to obtain a white solid. Without further treatment, the white solid was dissolved in dry THF (10 mL) and added dropwise with stirring into a 0 °C suspension of NaH (759 mg, 31.6 mmol) in THF (50 mL). The mixture was stirred at 0 °C until hydrogen evolution had ceased, and then it was stirred for 1 h at room temperature. MeI (1.97 mL, 31.6 mmol) was then added dropwise with stirring, and the mixture was allowed to stir overnight. Then the mixture was cooled to 0 °C and the reaction was quenched by the addition of MeOH (10 mL). The mixture was concentrated, then partitioned between water and CH_2Cl_2. The combined organic layer was dried over $MgSO_4$, filtered, concentrated to dryness, and then purified by silica gel column chromatography (20:1 petroleum ether–EtOAC) to give **5a** (1.97 g, 75% yield) or **5b** (1.89 g, 72% yield) as a colorless syrup. Compound **5a:** $[\alpha]_D$ −84 (*c* 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.37 (d, 1H, *J* 6.3 Hz, H-1), 4.81 (d, 1H, H-2), 4.24 (t, 1H, *J* 4.8 Hz, H-3), 4.08 (t, 1H, *J* 6.6 Hz, H-5), 3.96 (d, 1H, H-4), 3.67–3.57 (m, 2H, H-6), 3.44 (d, 6H, 2 × CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.30 (C-1), 100.50 (C-2), 74.24, 73.63, 71.17, 59.17, 56.39, 54.43. HRMS: *m/z* Calcd for $C_8H_{13}N_3O_3Na$ $[M+Na]^+$, 222.0849. Found 222.0849. Compound **5b:** $[\alpha]_D$ +29 (*c* 0.7 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.42 (d, 1H, *J* 6.0 Hz, H-1), 4.88 (dd, 1H, H-2), 3.97 (d, 1H, *J* 5.1 Hz, H-3), 3.86–3.83 (m, 1H, H-5), 3.82–3.80 (m, 1H, H-4), 3.70–3.68 (m, 2H, H-6), 3.45 (s, 6H, 2 × CH_3); ^{13}C NMR (100 MHz,

$CDCl_3$): δ 144.87 (C-1), 99.83 (C-2), 76.48, 76.06, 71.03, 59.26, 58.76, 55.81. HRMS: *m/z* Calcd for $C_8H_{13}N_3O_3Na$ $[M+Na]^+$, 222.0849. Found 222.0841.

3.4. 2,6-Anhydro-3-azido-1,4-di-*O*-benzyl-3,5-dideoxy-5-*C*-formyl-D-*arabino*-hex-5-enitol (6a) and 1,5-anhydro-4-azido-3,6-di-*O*-benzyl-2,4-dideoxy-2-*C*-formyl-D-*arabino*-hex-1-enitol (6b)

To a solution of **4a** or **4b** (1.0 g, 2.85 mmol) in DMF (10 mL) was added $POCl_3$ (1.49 mL, 14.2 mmol) slowly at 0 °C. The mixture was stirred at room temperature for 10 h then poured into satd aq $NaHCO_3$ (50 mL). The mixture was stirred for 10 h and then extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layer was dried ($MgSO_4$), filtered, concentrated to dryness, and then purified by silica gel column chromatography (6:1 petroleum ether–EtOAc) to give **6a** (767 mg, 71% yield) or **6b** (475 mg, 44% yield) as a colorless syrup. Compound **6a:** $[\alpha]_D$ +51 (*c* 1.1, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 9.34 (s, 1H, C*H*O), 7.35–7.28 (m, 10H, Ph), 7.24 (s, 1H, H-1), 4.85–4.73 (m, 2H, PhCH_2), 4.61 (d, 1H, *J* 4.2 Hz, H-3), 4.58–4.48 (m, 2H, PhCH_2), 4.36–4.34 (m, 1H, H-5), 3.89 (t, 1H, H-4), 3.85–3.73 (m, 2H, H-6); ^{13}C NMR (75 MHz, $CDCl_3$): δ 189.09 (*C*HO), 163.54, 163.50 (C-1), 137.77–127.85 (Ph), 119.04 (C-2), 77.45, 73.53, 73.49, 67.95, 67.69, 56.54. HRMS: *m/z* Calcd for $C_{21}H_{21}N_3O_4Na$ $[M+Na]^+$, 402.1424. Found 402.1431. Compound **6b:** $[\alpha]_D$ +23 (*c* 1.6 $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 9.39 (s, 1H, C*H*O), 7.35–7.25 (m, 10H, Ph), 7.22 (s, 1H, H-1), 4.81–4.66 (m, 2H, PhCH_2), 4.55–4.51 (m, 3H, PhCH_2 and H-3), 4.37–4.36 (m, 1H, H-5), 4.40–3.99 (m, 1H, H-4), 3.83–3.69 (m, 2H, H-6); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.70 (*C*HO), 163.82 (C-1), 137.78–127.94 (Ph), 117.98 (C-2), 78.29, 73.53, 73.32, 68.10, 67.53, 56.61. HRMS: *m/z* Calcd for $C_{21}H_{21}N_3O_4Na$ $[M+Na]^+$, 402.1424. Found 402.1416.

The other compounds (**7a and 7b**) were also prepared by the same procedure as described above, and their spectral and analytical data are given below.

3.5. 2,6-Anhydro-3-azido-3,5-dideoxy-5-*C*-formyl-1,4-di-*O*-methyl-D-*arabino*-hex-5-enitol (7a) and 1,5-anhydro-4-azido-2,4-dideoxy-2-*C*-formyl-3,6-di-*O*-methyl-D-*arabino*-hex-1-enitol (7b)

Compound **7a** (68% yield) or **7b** (42% yield) was obtained as a colorless syrup. Compound **7a:** $[\alpha]_D$ +75 (*c* 1.5, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 9.37 (s, 1H, C*H*O), 7.30 (s, 1H, H-1), 4.45–4.38 (m, 2H, H-5, H-3), 4.01 (t, 1H, *J* 4.2, 3.6 Hz, H-4), 3.79–3.66 (m, 2H, H-6), 3.57 (s, 3H, CH_3), 3.42 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 188.92 (*C*HO), 163.42 (C-1), 118.74 (C-2), 77.62, 70.34, 69.09, 59.26, 59.15, 56.26. HRMS: *m/z* Calcd for $C_9H_{13}N_3O_4Na$ $[M+Na]^+$, 250.0798. Found 250.0801. Compound **7b:** $[\alpha]_D$ +32 (*c* 1.5, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 9.38 (s, 1H, C*H*O), 7.36 (s, 1H, H-1), 4.51–4.47 (m, 1H, H-5), 4.12 (dd, 1H, *J* 1.2, 3.6 Hz, H-3), 3.40 (t, 1H, H-4), 3.72 (dd, 1H, *J* 6.8, 10.8 Hz, H-6a), 3.61 (dd, 1H, *J* 4.4 Hz, H-6b), 3.51 (s, 3H, CH_3), 3.40 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.29 (*C*HO), 163.51 (C-1), 117.57 (C-2), 78.15, 70.41, 69.05, 59.05, 58.14, 55.75. HRMS: *m/z* Calcd for $C_9H_{13}N_3O_4Na$ $[M+Na]^+$, 250.0798. Found 250.0794.

3.6. 2,6-Anhydro-3-azido-1,4-di-*O*-benzyl-5-carboxy-3,5-dideoxy-D-*arabino*-hex-5-enitol (8a) and 1,5-anhydro-4-azido-3,6-di-*O*-benzyl-2-carboxy-2,4-dideoxy-D-*arabino*-hex-1-enitol (8b)

To a solution of **6a** or **6b** (400 mg, 1.05 mmol) in 5 mL of a mixed solution of 2:2:1 MeCN–^{t}BuOH–H_2O were cautiously added $NaH_2PO_4{\cdot}2H_2O$ (0.493 g, 3.16 mmol) and 35% aq H_2O_2 (161 μL, 5.27 mmol). The resulting mixture was stirred for a few minutes in a water bath, and then $NaClO_2$ (569 mg, 6.33 mmol) was added. O_2 evolved from the solution, and a deep-yellow mixture was obtained. The mixture was stirred for 2 h, and then complete consumption of the starting product was observed by TLC. On completion of the reaction, the mixture was diluted with water (50 mL), acidified with 10% aq HCl, and extracted with CH_2Cl_2 (5 × 50 mL). The combined organic layer was washed with water and dried ($MgSO_4$). The pure compound, **8a** (396 mg, 95% yield) or **8b** (388 mg, 93% yield), was isolated as a colorless syrup by removal of solvent. Compound **8a:** $[\alpha]_D$ +14 (*c* 1.4, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 7.63 (s, 1H, H-1), 7.35–7.29 (m, 10H, Ph), 4.83–4.73 (m, 2H, PhCH_2), 4.59 (d, 1H, *J* 3.9 Hz, H-3), 4.58–4.48 (m, 2H, PhCH_2), 4.38–4.36 (m, 1H, H-5), 3.95 (t, 1H, H-4), 3.86–3.73 (m, 2H, H-6); ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.50 (*C*OOH), 157.36 (C-1), 137.65–127.88 (Ph), 106.47 (C-2), 76.58, 73.72, 73.61, 69.09, 67.98, 57.02. HRMS: *m/z* Calcd for $C_{21}H_{21}N_3O_5Na$ $[M+Na]^+$, 418.1373. Found 418.1376. Compound **8b:** $[\alpha]_D$ −8.0 (*c* 1.0 $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 7.74 (s, 1H, H-1), 7.36–7.28 (m, 10H, Ph), 4.79–4.67 (m, 2H, PhCH_2), 4.51–4.50 (m, 3H, H-3 and PhCH_2), 4.33–4.30 (m, 1H, H-5), 3.98 (d, 1H, *J* 2.8 Hz, H-4), 3.79–3.73 (m, 2H, H-6); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.20 (*C*OOH), 158.04 (C-1), 138.30–128.51 (Ph), 107.07 (C-2), 77.13, 74.26, 74.15, 68.92, 68.51, 57.53. HRMS: *m/z* Calcd for $C_{21}H_{21}N_3O_5Na$ $[M+Na]^+$, 418.1373. Found 418.1370.

Compounds **9a** and **9b** were also prepared by the same procedure as described above and their spectral and analytical data are given below.

3.7. 2,6-Anhydro-3-azido-5-carboxy-3,5-dideoxy-1,4-di-*O*-methyl-D-*arabino*-hex-5-enitol (9a) and 1,5-anhydro-4-azido-2-carboxy-2,4-dideoxy-3,6-di-*O*-methyl-D-*arabino*-hex-1-enitol (9b)

Compound **9a** (95% yield) or **9b** (92% yield) was obtained as a colorless syrup. Compound **9a:** $[\alpha]_D$ +32 (*c* 1.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 7.59 (s, 1H, H-1), 4.35–4.32 (m, 2H, H-5, H-3), 3.98 (t, 1H, *J* 4.0, 4.0 Hz, H-4), 3.71 (dd, 1H, *J* 7.6, 11.2 Hz, H-6a), 3.65 (dd, 1H, *J* 3.6 Hz, H-6b), 3.55 (s, 3H, CH_3), 3.39 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.36 (*C*OOH), 157.07 (C-1), 106.24 (C-2), 76.38, 70.53, 70.18, 59.15, 59.00, 56.54. HRMS: *m/z* Calcd for $C_9H_{13}N_3O_5Na$ $[M+Na]^+$, 266.0747. Found 266.0746. Compound **9b:** $[\alpha]_D$ +29 (*c* 1.5, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 7.71 (s, 1H, H-1), 4.49–4.46 (m, 1H, H-5), 4.06 (s, 1H, H-3), 4.00 (t, 1H, *J* 3.2 Hz, H-4), 3.72 (dd, 1H, *J* 6.8, 10.4 Hz, H-6a), 3.62 (dd, 1H, *J* 4.8 Hz, H-6b), 3.51 (s, 3H, CH_3), 3.41 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.96 (*C*OOH), 157.13 (C-1), 104.89 (C-2), 76.70, 70.65, 70.33, 59.12, 57.78, 55.49. HRMS: *m/z* Calcd for $C_9H_{13}N_3O_5Na$ $[M+Na]^+$, 266.0747. Found 266.0746.

3.8. 3-Amino-2,6-anhydro-1,4-di-*O*-benzyl-5-carboxy-3,5-dideoxy-D-*arabino*-hex-5-enitol hydrochloride (10a) and 4-amino-1,5-anhydro-3,6-di-*O*-benzyl-2-carboxy-2,4-dideoxy-D-*arabino*-hex-1-enitol hydrochloride (10b)

To a stirred solution of **8a** or **8b** (50 mg, 0.126 mmol) in 10:1 THF–H_2O (3 mL) at 60 °C was added Ph_3P (100 mg, 0.379 mmol). After 3 h, the reaction mixture was cooled to room temperature, and 1 M HCl (0.126 mL) was added. The mixture was concentrated to dryness, diluted with water (20 mL), and washed with EtOAc (3 × 20 mL). The water layer was evaporated under reduced pressure to give **10a** (44 mg, 85% yield) or **10b** (42 mg, 82% yield) as a pale-yellow syrup. Compound **10a:** $[\alpha]_D$ −51 (*c* 1.5, MeOH). ^1H NMR (300 MHz, DMSO-d_6): δ 7.49 (s, 1H, H-1), 7.37–7.26 (m, 10H, Ph), 4.73–4.48 (m, 4H, 2 × PhCH_2), 4.37–4.35 (m, 1H, H-5), 4.22 (d, 1H, *J* 4.4 Hz, H-3), 3.47–3.40 (m, 2H, H-6), 3.20–3.19 (m, 1H, H-4); ^{13}C NMR (75 MHz, MeOH-d_4): δ 167.91 (*C*OOH), 154.63 (C-1), 139.08–127.05 (Ph), 108.03 (C-2), 78.19, 72.82,

72.25, 70.01, 67.43, 48.67. HRMS: *m/z* Calcd for $C_{21}H_{24}NO_5$ $[M+H]^+$, 370.1649. Found 370.1651. Compound **10b:** $[\alpha]_D$ −7.0 (*c* 1.7 MeOH). ^1H NMR (400 MHz, MeOH-d_4): δ 7.70 (s, 1H, H-1), 7.31–7.22 (m, 10H, Ph), 4.73–4.70 (m, 2H, $PhCH_2$), 4.67 (s, 1H, H-3), 4.48–4.44 (m, 2H, $PhCH_2$), 4.40 (s, 1H, H-5), 4.03 (s, 1H, H-4), 3.83–3.78 (dd, 1H, *J* 7.2, 10.8 Hz, H-6a), 3.75–3.71 (dd, 1H, *J* 6.0 Hz, H-6b); ^{13}C NMR (100 MHz, MeOH-d_4): δ 167.84 (*C*OOH), 156.12 (C-1), 137.66–127.50 (Ph), 104.47 (C-2), 74.54, 72.90, 72.06, 67.24, 48.24, 46.10. HRMS: *m/z* Calcd for $C_{21}H_{23}NO_5Na$ $[M+Na]^+$, 392.1468. Found 392.1467.

Compounds **11a, 11b, 20**, and **21** were also prepared by the same procedure as described above, and their spectral and analytical data are given below.

3.9. 3-Amino-2,6-anhydro-5-carboxy-3,5-dideoxy-1,4-di-*O*-methyl-D-*arabino*-hex-5-enitol hydrochloride (11a) and 4-amino-1,5-anhydro-2-carboxy-2,4-dideoxy-3,6-di-*O*-methyl-D-*arabino*-hex-1-enitol hydrochloride (11b)

Compound **11a** (82% yield) or **11b** (77% yield) was obtained as a pale-yellow syrup. Compound **11a:** $[\alpha]_D$ +74 (*c* 1.3, MeOH). ^1H NMR (400 MHz, MeOH-d_4): 7.60 (s, 1H, H-1), 4.51 (d, 1H, *J* 5.6 Hz, H-3), 4.46 (d, 1H, *J* 1.6 Hz, H-5), 4.15 (dd, 1H, H-4), 3.77 (d, 2H, H-6), 3.45, 3.35 (s, 6H, 2 × CH_3); ^{13}C NMR (100 MHz, D_2O): δ 168.06 (*C*OOH), 156.39 (C-1), 105.62 (C-2), 72.96, 69.79, 68.54, 57.98, 57.42, 45.75. HRMS: *m/z* Calcd for $C_9H_{16}NO_5$ $[M+H]^+$, 218.1023. Found 218.1019; *m/z* Calcd for $C_9H_{15}NO_5Na$ $[M+Na]^+$: 240.0842. Found 240.0839. Compound **11b:** $[\alpha]_D$ +61 (*c* 1.5, MeOH). ^1H NMR (400 MHz, MeOH-d_4): 7.58 (s, 1H, H-1), 4.46 (dd, 1H, *J* 2.8, 4.4 Hz, H-5), 4.10 (t, 1H, H-4), 3.99 (s, 1H, H-3), 3.69 (dd, 1H, *J* 3.6, 10.8 Hz, H-6a), 3.56 (dd, 1H, *J* 4.0 Hz, H-6b), 3.36, 3.30 (s, 6H, 2 × CH_3); ^{13}C NMR (100 MHz, MeOH-d_4): δ 168.42 (*C*OOH), 155.03 (C-1), 105.61 (C-2), 76.31, 70.82, 70.28, 57.88, 56.51, 55.09. HRMS: *m/z* Calcd for $C_9H_{16}NO_5$ $[M+H]^+$, 218.1023. Found 218.1019.

3.10. 3-Amino-2,6-anhydro-1,4-di-*O*-benzyl-3,5-dideoxy-5-(1*H*-tetrazol-5-yl)-D-*arabino*-hex-5-enitol hydrochloride (20)

Compound **20** (78% yield) was obtained as a pale-yellow syrup. **20:** $[\alpha]_D$ +38 (*c* 1.6, MeOH). ^1H NMR (400 MHz, MeOH-d_4): δ 7.44 (s, 1H, H-1), 5.56 (d, 1H, *J* 2.8 Hz, H-3), 4.84–4.62 (m, 4H, 2 × PhCH_2), 4.61 (s, 1H, H-5), 4.19 (s, 1H, H-4), 3.92 (d, 2H, H-6); ^{13}C NMR (100 MHz, MeOH-d_4): δ 152.80 (*C*HN_4), 149.84 (C-1), 137.21–127.73 (Ph), 100.74 (C-2), 73.79, 73.42, 72.63, 69.10, 68.68, 46.76. HRMS: *m/z* Calcd for $C_{21}H_{24}N_5O_3$ $[M+H]^+$, 394.1874. Found 394.1876.

3.11. 3-Amino-2,6-anhydro-3,5-dideoxy-1,4-di-*O*-methyl-5-(1*H*-tetrazol-5-yl)-D-*arabino*-hex-5-enitol hydrochloride (21)

Compound **21** (75% yield) was obtained as a pale-yellow syrup. **21:** $[\alpha]_D$ +74 (*c* 0.7, MeOH). ^1H NMR (400 MHz, MeOH-d_4): δ 7.57 (s, 1H, H-1), 4.78 (d, 1H, *J* 4.0 Hz, H-3), 4.53 (s, 1H, H-5), 4.33–4.32 (m, 1H, H-4), 3.85 (d, 2H, H-6); ^{13}C NMR (100 MHz, MeOH-d_4): δ 151.91 (*C*HN_4), 150.22 (C-1), 99.95 (C-2),73.93, 71.38, 70.98, 58.50, 56.88, 45.39. HRMS: *m/z* Calcd for $C_9H_{16}N_5O_3$ $[M+H]^+$, 242.1248. Found 242.1242; *m/z* Calcd for $C_9H_{15}N_5O_3Na$ $[M+Na]^+$: 264.1067. Found 264.1061.

3.12. 2,6-Anhydro-3-azido-1,4-di-*O*-benzyl-5-carbamoyl-3,5-dideoxy-D-*arabino*-hex-5-enitol (12a) and 1,5-anhydro-4-azido-3,6-di-*O*-benzyl-2-carbamoyl-2,4-dideoxy-D-*arabino*-hex-1-enitol (12b)

To a solution of compound **8a** or **8b** (200 mg, 0.506 mmol) in MeCN (10 mL) were added successively Boc_2O (0.177 g, 0.810 mmol), NH_4HCO_3 (0.120 g, 1.52 mmol), and pyridine (0.082 mL, 1.01 mmol), and the mixture was stirred for 16 h at room temperature. Water (50 mL) was added, and then the mixture was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layer was dried ($MgSO_4$), filtered, concentrated to dryness, and then purified by silica gel column chromatography (30:1 CH_2Cl_2–EtOAc) to give **12a** (183 mg, 92% yield) or **12b** (177 mg, 89% yield) as a pale-yellow syrup. Compound **12a:** $[\alpha]_D$ +4.0 (*c* 1.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 7.49 (s, 1H, H-1), 7.49–7.32 (m, 10H, Ph), 4.89 (d, 1H, $PhCH_2$), 4.71 (d, 1H, *J* 4.0 Hz, H-3), 4.62–4.55 (m, 3H, PhCH_2), 4.20–4.15 (m, 2H, H-5, H-4), 3.75 (d, 2H, H-6); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.92 (*C*ONH_2), 154.44 (C-1), 137.24–127.95 (Ph), 107.60 (C-2), 75.73, 73.76, 72.38, 71.85, 67.85, 53.84. HRMS: *m/z* Calcd for $C_{21}H_{23}N_4O_4$ $[M+H]^+$, 395.1714. Found 395.1720; *m/z* Calcd for $C_{21}H_{22}N_4O_4Na$ $[M+Na]^+$: 417.1533. Found 417.1542. Compound **12b:** $[\alpha]_D$ +75 (*c* 1.7 $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 7.59 (s, 1H, H-1), 7.39–7.33 (m, 10H, Ph), 4.71–4.59 (m, 4H, 2 × PhCH_2), 4.46 (t, 1H, *J* 2.8 Hz, H-3), 4.21 (m, 2H, H-5, H-4), 3.82 (d, 2H, H-6); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.54 (*C*ONH_2), 155.07 (C-1), 137.87–128.57 (Ph), 108.22 (C-2), 76.34, 74.38, 72.99, 72.47, 68.46, 54.45. HRMS: *m/z* Calcd for $C_{21}H_{22}N_4O_4Na$ $[M+Na]^+$, 417.1533. Found 417.1526.

Compounds **13a** and **13b** were also prepared by the same procedure as described above and their spectral and analytical data are given below.

3.13. 2,6-Anhydro-3-azido-5-carbamoyl-3,5-dideoxy-1,4-di-*O*-methyl-D-*arabino*-hex-5-enitol (13a) and 1,5-anhydro-4-azido-2-carbamoyl-2,4-dideoxy-3,6-di-*O*-methyl-D-*arabino*-hex-1-enitol (13b)

Compound **13a** (88% yield) or **13b** (84% yield) was obtained as a pale-yellow syrup. Compound **13a:** $[\alpha]_D$ +24 (*c* 1.0 $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 7.49 (s, 1H, H-1), 4.47 (d, 1H, *J* 4.0 Hz, H-3), 4.14–4.11 (m, 2H, H-5, H-4), 3.64 (d, 2H, H-6), 3.58 (s, 3H, CH_3), 3.41 (s, 3H, CH_3), 3.45, 3.38 (s, 2H, $CONH_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.10 (*C*ONH_2), 154.53 (C-1), 107.41 (C-2), 75.64, 74.25, 70.36, 59.34, 56.74, 53.01. HRMS: *m/z* Calcd for $C_9H_{15}N_4O_4$ $[M+H]^+$, 243.1088. Found 243.1084; *m/z* Calcd for $C_9H_{14}N_4O_4Na$ $[M+Na]^+$: 265.0907. Found 265.0906. Compound **13b:** $[\alpha]_D$ +87 (*c* 1.8 $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 7.56 (s, 1H, H-1), 7.31 (d, 1H, *J* 6.0 Hz, H-3), 4.10–4.02 (m, 2H, H-5, H-4), 3.69 (d, 2H, H-6), 3.41 (d, 6H, 2 × CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.93 (*C*ONH_2), 155.42 (C-1), 107.15 (C-2), 77.01, 74.04, 70.09, 59.24, 54.90, 53.90. HRMS: *m/z* Calcd for $C_9H_{14}N_4O_4Na$ $[M+Na]^+$, 265.0907. Found 265.0903.

3.14. 3-Amino-2,6-anhydro-1,4-di-*O*-benzyl-5-carbamoyl-3,5-dideoxy-D-*arabino*-hex-5-enitol (14a) and 4-amino-1,5-anhydro-3,6-di-*O*-benzyl-2-carbamoyl-2,4-dideoxy-D-*arabino*-hex-1-enitol (14b)

To a stirred solution of **12a** or **12b** (50 mg, 0.127 mmol) in 10:1 THF–H_2O (3 mL) at 60 °C was added Ph_3P (100 mg, 0.380 mmol). After 3 h, the reaction mixture was cooled to room temperature and then concentrated to dryness. The residue was purified by silica gel column chromatography (10:1 CH_2Cl_2–MeOH) to give **14a** (37 mg, 80% yield) or **14b** (35 mg, 76% yield) as a pale-yellow syrup. Compound **14a:** $[\alpha]_D$ +76 (*c* 1.7 $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 7.58 (s, 1H, H-1), 7.37–7.26 (m, 10H, Ph), 4.75 (d, 1H, PhCH_2), 4.60 (d, 1H, *J* 4.5 Hz, H-3), 4.64–4.59 (m, 3H, PhCH_2), 4.19 (t, 1H, *J* 6.0 Hz, H-5), 3.82 (d, 2H, H-6), 3.46 (d, 1H, H-4); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.74 (*C*ONH_2), 155.95 (C-1), 138.55–128.87 (Ph), 108.11 (C-2), 78.79, 74.53, 73.98, 71.68, 69.74, 45.66. HRMS: *m/z* Calcd for $C_{21}H_{25}N_2O_4$ $[M+H]^+$, 369.1809. Found 369.1807; *m/z* Calcd for $C_{21}H_{24}N_2O_4Na$ $[M+Na]^+$: 391.1628.

Found 391.1630. Compound **14b:** $[\alpha]_D$ +77 (*c* 1.2 $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 7.62 (s, 1H, H-1), 7.36–7.25 (m, 10H, Ph), 4.59–4.48 (m, 4H, 2 × PhCH_2), 4.20 (d, 1H, *J* 5.2 Hz, H-3), 4.16 (dd, 1H, *J* 5.2 Hz, H-5), 3.81 (dd, 1H, *J* 5.6, 10.8 Hz, H-6a), 3.73 (dd, 1H, *J* 4.0 Hz, H-6b), 3.57 (t, 1H, H-4); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.68 (*C*ONH_2), 154.94 (C-1), 37.67–127.81 (Ph), 106.72 (C-2), 80.12, 74.15, 73.51, 68.16, 68.10, 45.91. HRMS: *m/z* Calcd for $C_{21}H_{24}N_2O_4Na$ $[M+Na]^+$, 391.1628. Found 391.1619.

Compounds **15a** and **15b** were also prepared by the same procedure as described above, and their spectral and analytical data are given below.

3.15. 3-Amino-2,6-anhydro-5-carbamoyl-3,5-dideoxy-1,4-di-*O*-methyl-D-*arabino*-hex-5-enitol (15a) and 4-amino-1,5-anhydro-2-carbamoyl-2,4-dideoxy-3,6-di-*O*-methyl-D-*arabino*-hex-1-enitol (15b)

Compound **15a** (77% yield) or **15b** (71% yield) was obtained as a pale-yellow syrup. Compound **15a:** $[\alpha]_D$ +83 (*c* 1.2, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 7.57 (s, 1H, H-1), 4.30–4.22 (m, 2H, H-3, H-5), 4.13 (t, 1H, *J* 5.6 Hz, H-4), 3.71 (d, 2H, H-6), 3.47, 3.41 (s, 6H, 2 × CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.84 (*C*ONH_2), 155.00 (C-1), 107.02 (C-2), 77.79, 74.82, 71.45, 59.36, 55.87, 44.20. HRMS: *m/z* Calcd for $C_9H_{17}N_2O_4$ $[M+H]^+$, 217.1183. Found 217.1175; *m/z* Calcd for $C_9H_{16}N_2O_4Na$ $[M+Na]^+$: 239.1002. Found 239.0995. Compound **15b:** $[\alpha]_D$ +67 (*c* 1.3 $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 7.62 (s, 1H, H-1), 4.11–4.05 (m, 2H, H-3, H-5), 3.76 (dd, 1H, *J* 6.0 Hz, H-4), 3.64–3.60 (m, 2H, H-6), 3.41, 3.33 (s, 6H, 2 × CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.72 (*C*ONH_2), 155.35 (C-1), 106.57 (C-2), 80.03, 75.42, 70.73, 59.31, 52.45, 44.96. HRMS: *m/z* Calcd for $C_9H_{16}N_2O_4Na$ $[M+Na]^+$, 239.1002. Found 239.0997.

3.16. 2,6-Anhydro-3-azido-1,4-di-*O*-benzyl-5-*C*-cyano-3,5-dideoxy-D-*arabino*-hex-5-enitol (16)

To a solution of **12a** (100 mg, 0.254 mmol) in dry THF at room temperature was added pyridine (82 μL, 1.02 mmol) and TFAA (71 μL, 0.508 mmol). The mixture was allowed to stir for 30 min at room temperature. It was then concentrated to dryness, and the residue was partitioned between water and CH_2Cl_2. The combined organic layer was dried ($MgSO_4$), and filtered, and the pure compound **16** (92 mg, 96% yield) was isolated by removal of solvent to give a pale-yellow syrup. Compound **16:** $[\alpha]_D$ +57 (*c* 1.2, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 7.44–7.30 (m, 10H, Ph), 7.02 (s, 1H, H-1), 4.78–4.50 (m, 4H, 2 × PhCH_2), 4.40 (t, 1H, H-3), 4.12–4.01 (m, 2H, H-5, H-4), 3.69–3.67 (m, 2H, H-6); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.77 (C-1), 137.04–127.89 (Ph), 116.40 (*C*N), 90.33 (C-2), 75.82, 73.59, 72.24, 70.05, 67.51, 53.71. HRMS: *m/z* Calcd for $C_{21}H_{21}N_4O_3$ $[M+H]^+$, 377.1608. Found 377.1612; *m/z* Calcd for $C_{21}H_{20}N_4O_3Na$ $[M+Na]^+$, 399.1428. Found 399.1434.

3.17. 2,6-Anhydro-3-azido-5-*C*-cyano-3,5-dideoxy-1,4-di-*O*-methyl-D-*arabino*-hex-5-enitol (17)

Compound **17** was also prepared by the same procedure as described above. Compound **17** (95% yield) as a pale-yellow syrup. $[\alpha]_D$ +40 (*c* 1.3, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 7.06 (s, 1H, H-1), 4.26 (d, 1H, *J* 3.6 Hz, H-3), 4.15–4.13 (m, 2H, H-5, H-4), 3.63 (d, 2H, H-6), 3.60, 3.41 (s, 6H, 2 × CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.90 (C-1), 116.48 (*C*N), 90.38 (C-2), 75.94, 73.14, 70.29, 59.42, 58.21, 53.09. HRMS: *m/z* Calcd for $C_9H_{12}N_4O_3Na$ $[M+Na]^+$, 247.0802. Found 247.0799.

3.18. 2,6-Anhydro-3-azido-1,4-di-*O*-benzyl-3,5-dideoxy-5-(1*H*-tetrazol-5-yl)-D-*arabino*-hex-5-enitol (18)

Compound **16** (90 mg, 0.239 mmol) was dissolved in dry toluene (5 mL). To the solution were added $TMSN_3$ (157 μL, 1.20 mmol) and *n*-Bu_2SnO (12 mg, 0.048 mmol). After stirring at 110 °C for 24 h, the mixture was evaporated in vacuo. The residue was purified by silica gel column chromatography (40:1 CH_2Cl_2–MeOH) to give **18** (92 mg, 92% yield) as a pale-yellow syrup. Compound **18:** $[\alpha]_D$ +46 (*c* 1.4, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 7.58 (d, 1H, *J* 1.2 Hz, H-1), 7.42–7.34 (m, 10H, Ph), 4.95 (d, 1H, PhCH_2), 4.85 (d, 1H, *J* 3.6 Hz, H-3), 4.65–4.61 (m, 3H, PhCH_2), 4.33–4.31 (m, 2H, H-5, H-4), 3.79 (d, 2H, H-6); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.81 (*C*HN_4), 151.17 (C-1), 137.83–128.68 (Ph), 99.11 (C-2), 75.99, 74.39, 73.24, 72.68, 68.29, 53.94. HRMS: *m/z* Calcd for $C_{21}H_{22}N_7O_3$ $[M+H]^+$, 420.1779. Found 420.1784; *m/z* Calcd for $C_{21}H_{21}N_7O_3Na$ $[M+Na]^+$, 442.1591. Found 442.1598.

3.19. 2,6-Anhydro-3-azido-3,5-dideoxy-1,4-di-*O*-methyl-5-(1*H*-tetrazol-5-yl)-D-*arabino*-hex-5-enitol (19)

Compound **19** was prepared by the same procedure as described above. Compound **19**: (88% yield) as a pale-yellow syrup. $[\alpha]_D$ +87 (*c* 1.8, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 7.61 (s, 1H, H-1), 4.66 (t, 1H, H-3), 4.34–4.28 (m, 2H, H-5, H-4), 3.70 (d, 2H, H-6), 3.67, 3.45 (s, 6H, 2 × CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.30 (*C*HN_4), 150.57 (C-1), 98.54 (C-2), 75.32, 74.41, 70.28, 59.43, 57.05, 52.46. HRMS: *m/z* Calcd for $C_9H_{14}N_7O_3$ $[M+H]^+$, 268.1153. Found 268.1157.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.carres.2010.03.033.

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