A General Synthetic Route to Anomeric α-Azido and α-Amino Acids and Formal Synthesis of (+)-Hidantocidin

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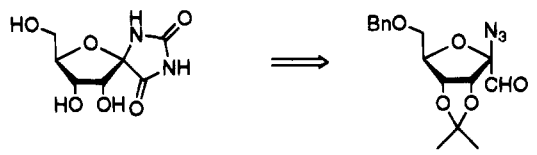
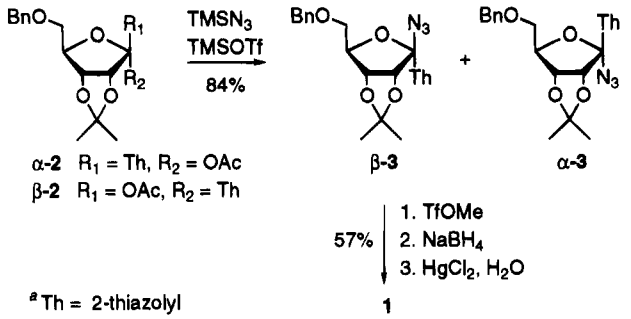
The peculiar α-azido aldehyde **1** sharing its central carbon atom with the D-ribofuranose ring has been reported[1] to be one of the intermediates for the synthesis of (+)-hydantocidin, an interesting herbicide and plant growth regulator isolated[2] recently from the fermentation broth of *Streptomyces Hygroscopicus* SANK 63584. Given the various syntheses of aldehydes based on the equivalence of the thiazole ring to the formyl group reported from this laboratory,[3] we have now investigated an alternative approach to the anomeric azido aldehyde **1** and analogs.



(+)-hydantocidin 1

A route was envisaged via the thiazolyl ketol acetate **2**, a key intermediate in the formylation of D-ribose at the anomeric position.[4] Thus, treatment of either α- or β-anomer **2** (Scheme 1), which were readily available (76–80%) through the addition of 2-lithiothiazole to the corresponding ribonolactone and subsequent acetylation as previously described,[4] with trimethylsilyl triflate (TMSOTf, 0.5 equiv) and trimethylsilyl azide ($TMSN_3$, 1.5 equiv) in CH_2Cl_2 afforded α- and β-azido glycosides[5] α-**3** and β-**3** in a 1:3 ratio[6] and 84% overall yield. The configuration at C-1 of these compounds was tentatively assigned from the ^{13}C resonance of the anomeric carbon.[7] The cleavage of the thiazole ring of the major isomer β-**3** by the standard one-pot protocol[8] using either mercury(II) or copper(II) ion-assisted hydrolysis in the final step afforded the aldehyde **1** in an unusually low yield (~30%).

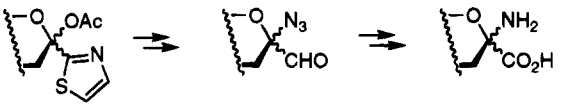
Scheme 1[a]



[a] Th = 2-thiazolyl

The intramolecular cycloaddition[9] of the azido group to the adjacent *N*-methylthiazolium ring, which was formed in the first step of the unmasking sequence, may be responsible for the formation of several byproducts at the expense of the aldehyde.[10] The change of the solvent (THF instead of MeCN) or temperature (0 °C instead of 25 °C) in the first step of the procedure, *i.e.*, the *N*-methylation of the thiazole ring with methyl triflate, did not bring about any improvement. However, a better yield of **1** (57%) was obtained by increasing[11] the concentration of **3** to 0.3 M in this step and using 0.6 equiv of $HgCl_2$ for the hydrolysis of the thiazolidine in the last step.

Stimulated by these results and having ready access to various furanosyl and pyranosyl thiazolyl acetates **A** through the thiazole-based route to formyl glycosides,[4] we decided to explore the scope of the above strategy for the synthesis of anomeric azido aldehydes **B** of both furanoses and pyranoses and convert these products into amino acids[12] **C**.



Hence, we considered the ketol acetate **4** (Scheme 2) that was equally available in both anomeric forms in 76–90% from the corresponding lactone. In fact the anomeric amino esters of type **C** incorporating the D-mannofuranose unit, *i.e.*, α-**8** and β-**8**, have been recently prepared[13] by ring contraction of an amino δ-lactone and converted into anomeric spirohydantoins of D-mannofuranose. It

(1) Mio, S.; Kumagawa, Y.; Sugai, S. *Tetrahedron* **1991**, *47*, 2133.

(2) Nakajima, M.; Itoi, K.; Takamatsu, Y.; Okazaki, H.; Kinoshita, T.; Shindou, M.; Kawakubo, K.; Honma, T.; Toujigamori, M.; Haneishi, T. *J. Antibiot.* **1991**, *44*, 293. Haruyama, H.; Takayama, T.; Kinoshita, T.; Kondo, M.; Nakajima, M.; Haneishi, T. *J. Chem. Soc. Perkin Trans. 1* **1991**, 1637.

(3) For overviews on the "thiazole-aldehyde synthesis" see: Dondoni, A. In *Modern Synthetic Methods*; Scheffold, R., Ed.; Verlag Helvetica Chimica Acta: Basel, 1992; pp 377–437. Dondoni, A. In *New Aspects of Organic Chemistry II*; Yoshida, Z., Ohshiro, Y., Eds.; Kodansha: Tokyo, and VCH: Weinheim, 1992; pp 105–128.

(4) (a) Dondoni, A.; Scherrmann, M.-C. *Tetrahedron Lett.* **1993**, *34*, 731. (b) Dondoni, A.; Scherrmann, M.-C. *J. Org. Chem.* **1994**, *59*, 6404.

(5) For a review on glycosyl azides see: Györgydeák, Z.; Szilágyi, L.; Paulsen, H. *J. Carbohydr. Chem.* **1993**, *12*, 139.

(6) Interestingly enough a similar ratio of anomeric thiazolyl glycosides was obtained in the reduction of **2** by Et_3SiH and TMSOTf (ref 4b).

(7) Downfield chemical shifts have been reported for the anomers having a trans orientation of the C–O bonds at C-1 and C-2 (see: Ohrui, H.; Jones, G. H.; Moffatt, J. G.; Maddox, M. L.; Christensen, A. T.; Byram, S. K. *J. Am. Chem. Soc.* **1975**, *7*, 4602). We observed a similar trend for these *N*-glycosides; α-**2**: $\delta_{C\text{-}1}$ = 104.2, β-**2**: $\delta_{C\text{-}1}$ = 108.4, α-**3**: $\delta_{C\text{-}1}$ = 97.1, β-**3**: $\delta_{C\text{-}1}$ = 102.0.

(8) Dondoni, A.; Marra, A.; Perrone, D. *J. Org. Chem.* **1993**, *58*, 275.

(9) For cycloaddition of azides to benzothiazole derivatives, see: Kadaba, P. K. *Synthesis* **1973**, 71.

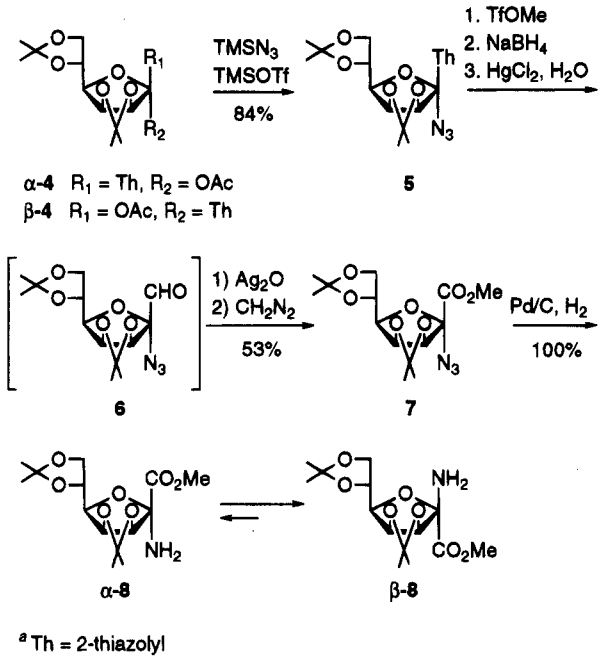
(10) This drawback is not general for the azido group in the thiazole–aldehyde synthesis. The thiazolyl-to-formyl deblocking protocol proved to tolerate quite well the presence of the azido group at C-2 or C-3 of pyranoses leading to aldehydes with the usual high yields. See: ref 4b and Dondoni, A.; Boscarato, A.; Marra, A. *Tetrahedron Asymm.*, in press.

(11) These conditions reduced the workup time, particularly for the evaporation of MeCN from the crude mixture and therefore limited the extent of side reactions to the azido *N*-methylthiazolium intermediate.

(12) The most frequent types of *C*-glycosyl amino acids are those wherein the α-amino acid moiety is linked to the anomeric carbon through at least one bond. See: Bischofberger, K.; Hall, R. H.; Jordaan, A. *J. Chem. Soc. Chem. Commun.* **1975**, 806. Hall, R. H.; Bischofberger, K.; Eitelman, S. J.; Jordaan, A. *J. Chem. Soc. Perkin Trans. 1* **1977**, 743. Simchen, G.; Pürkner, E. *Synthesis* **1990**, 525. Petrus, L.; BeMiller, J. N. *Carbohydr. Res.* **1992**, *230*, 197. Kessler, H.; Wittmann, V.; Köck, M.; Kottenhahn, M. *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 902. Bertozzi, C. R.; Hoeprich, P. D.; Bednarski, M. D. *J. Org. Chem.* **1992**, *57*, 6092. Gurjar, M. K.; Mainkar, A. S.; Syamala, M. *Tetrahedron Asymm.* **1993**, *4*, 2343.

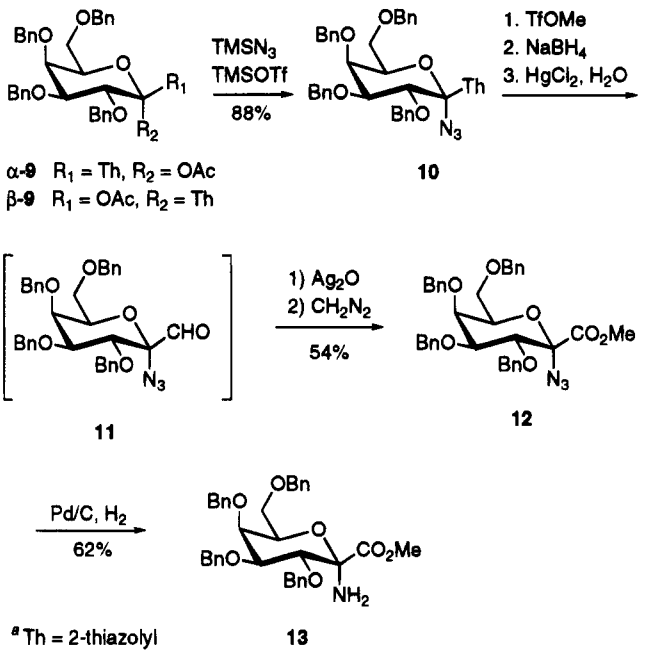
0022-3263/94/1959-7517$04.50/0

Scheme 2[a]



[a] Th = 2-thiazolyl

Scheme 3[a]



[a] Th = 2-thiazolyl

was gratifying to observe that the *N*-glycosidation of either α-**4** or β-**4** under the usual conditions (1.5 equiv of $TMSN_3$ and 0.5 equiv of TMSOTf, CH_2Cl_2, rt) proceeded stereospecifically giving rise, in both cases, to the azido α-mannofuranoside **5** in 84% isolated yield. Since we speculated that under the above conditions the reaction should proceed via an oxycarbenium ion[14] intermediate undergoing nucleophilic addition of the azide ion from the less hindered side, the stereochemistry at the anomeric center of **5** was tentatively assigned as shown. Application of the thiazolyl-to-formyl deblocking procedure to **5**, modified as detailed above, led to the anomeric azido aldehyde **6** which, as a crude material, was converted by oxidation and esterification into the azido ester[15] **7** in 53% isolated yield from **5**. The reduction of the azido group of **7**, carried out by hydrogenation over Pd/C suspended in a 9:1 mixture of *t*BuOH–H_2O, afforded at the early stage of the reaction exclusively the amino ester α-**8** (TLC analysis). As the reaction proceeded, the formation of the anomer β-**8** was also observed such that a 1:5 mixture of α-**8** and β-**8** was isolated in quantitative yield. The existing equilibrium between α-**8** and β-**8**, very likely through an α-imino ester intermediate, was demonstrated by the formation of anomeric mixtures in the same 1:5 ratio from either pure α-**8** or β-**8** in 9:1 *t*BuOH–H_2O. Consistent NMR spectra were obtained for these compounds showing a strong NOE between the NH_2 and C-3 and C-5 protons (ulosonic acid numbering) in the case of α-**8** whereas no enhancement of the same signals was observed in the case of β-**8**. The structure of the kinetic α-amino ester α-**8** confirmed the stereochemical assignments to its precursors **5**–**7** in this series.

Next, it was interesting to examine the D-galactopyranosyl ketol acetate **9** (Scheme 3) since azido aldehydes of type **B** and amino acids of type **C** installed at C-1 of pyranose rings were not previously reported. Also in the case of **9** the *N*-glycosidation of either α- or β-anomer with $TMSN_3$–TMSOTf gave stereospecifically the azido galactopyranoside **10** in 88% isolated yield. The anomeric configuration assigned to **10** is consistent with the axial attack of the nucleophile to the half-chair oxycarbenium ion[14] of the pyranose ring bearing a nonparticipating group at C-2. The crude aldehyde **11** obtained by application of the thiazolyl-to-formyl deblocking procedure was converted into the azido ester **12** (54% yield from **10**) which, by selective reduction of the azido group using Pd-catalyzed hydrogenation in 9:1 *t*BuOH–H_2O, gave the amino ester **13** in 62% yield.[16] The assigned configuration at the anomeric carbon of **12** by NMR spectroscopy relied on a rule established for sialic acids[17] whereas that of **13** was confirmed by NOE experiments showing strong enhancements between the NH_2 and C-4 and C-6 protons (ulosonic acid numbering).

In conclusion, from the above model reactions it appears that a straightforward approach to anomeric α-amino acids of both furanoses and pyranoses has been developed. The biological activity of this new class of sugar-containing α-amino acids and their role as precursors to more complex systems (glycopeptides) are being explored.

Experimental Section

All moisture-sensitive reactions were performed under an argon atmosphere using oven-dried glassware. All solvents were dried over standard drying agents[18] and freshly distilled prior

(13) Burton, J. W.; Son, J. C.; Fairbanks, A. J.; Choi, S. S.; Taylor, H.; Watkin, D. J.; Winchester, B. G.; Fleet, G. W. *Tetrahedron Lett.* **1993**, *34*, 6119.

(14) For reviews on glycosylation reactions see: Paulsen, H. *Angew. Chem. Int. Ed. Engl.* **1982**, *21*, 155. Toshima, K.; Tatsuta, K. *Chem. Rev.* **1993**, *93*, 1503.

(15) The structure of the corresponding β-anomer has been previously assigned by X-ray analysis. Choi, S.; Witty, D. R.; Fleet, G. W. J.; Myers, P. L.; Storer, R.; Wallis, C. J.; Watkin, D.; Pearce, L. *Tetrahedron Lett.* **1991**, *32*, 3569.

(16) Also isolated was 12% of unreacted **12**. The missing material (*ca.* 20%) could not be recovered due to a partial debenzylation leading to a complex mixture of highly polar products. This side reaction was even more substantial when the catalytic hydrogenation was performed in 2:1 MeOH–AcOEt. Finally, the reduction with $NiCl_2 \cdot 6H_2O$ and $NaBH_4$ in EtOH gave **13** in only 50% yield.

(17) Haverkamp, J.; Spoormaker, T.; Dorland, L.; Vliegenthart, J. F. G.; Schauer, R. *J. Am. Chem. Soc.* **1979**, *101*, 4851. Hori, H.; Nakajima, T.; Nishida, Y.; Ohrui, H.; Meguro, H. *Tetrahedron Lett.* **1979**, *19*, 4637.

to use. Flash column chromatography[19] was performed on silica gel 60 (230–400 mesh). Reactions were monitored by TLC on silica gel 60 F_{254} with detection by charring with sulfuric acid. Melting points were determined with a capillary apparatus and are uncorrected. Optical rotations were measured at 20 ± 2 °C in the stated solvent. ^1H (300 MHz) and ^{13}C (75 MHz) NMR were recorded at room temperature for $CDCl_3$ solutions, unless otherwise specified. Assignments were aided by decoupling and/or homo- and heteronuclear two-dimensional experiments (see supplementary material).

Azido 5-*O*-Benzyl-2,3-*O*-isopropylidene-1-(2-thiazolyl)-α,β-D-ribofuranoside (3). A mixture of α- or β-**2** (400 mg, 0.98 mmol), activated 4-Å powdered molecular sieves (400 mg), and $TMSN_3$ (200 μL, 1.47 mmol) in dry CH_2Cl_2 (4 mL) was stirred at room temperature for 10 min and then TMSOTf (90 μL, 0.49 mmol) was added. The mixture was stirred at room temperature for 20 min and then neutralized with Et_3N, diluted with CH_2Cl_2, filtered through Celite, and concentrated. The residue was eluted from a column of silica gel with 8:1 cyclohexane–ethyl acetate to give first α-**3** (79 mg, 21%) as a syrup; $[\alpha]_D = -22.0°$ (*c* 1.1, $CHCl_3$). ^1H NMR: δ 1.42 and 1.74 (2 s, 6 H), 3.62 (d, 2 H, *J* = 4.2 Hz), 4.50 (s, 2 H), 4.61 (dt, 1 H, *J* = 3.0, 4.2 Hz), 4.88 (dd, 1 H, *J* = 3.0, 6.5 Hz), 5.21 (d, 1 H, *J* = 6.5 Hz), 7.19–7.35 (m, 5 H), 7.36 and 7.80 (2 d, 2 H, *J* = 3.2 Hz). Anal. Calcd for $C_{18}H_{20}N_4O_4S$: C, 55.66; H, 5.18; N, 14.42. Found: C, 55.35; H, 5.13; N, 14.19.

Eluted second was oily β-**3** (240 mg, 63%); $[\alpha]_D = -77.8°$ (*c* 1.3, $CHCl_3$). ^1H NMR: δ 1.26 and 1.35 (2 s, 6 H), 3.74 (d, 2 H, *J* = 7.0 Hz), 4.64 (s, 2 H), 4.66 (dt, 1 H, *J* ~ 0.6, 7.0 Hz), 4.74 (d, 1 H, *J* = 6.0 Hz), 4.90 (dd, 1 H, *J* ~ 0.6, 6.0 Hz), 7.23–7.40 (m, 5 H), 7.45 and 7.92 (2 d, 2 H, *J* = 3.2 Hz). Anal. Found: C, 55.75; H, 5.25; N, 14.40.

Azido 6-*O*-Benzyl-3,4-*O*-isopropylidene-β-D-*ribo*-2-hexosulofuranoside (1). A mixture of β-**3** (210 mg, 0.54 mmol) and activated 4-Å powdered molecular sieves (500 mg) in dry CH_3CN (1.8 mL) was stirred at room temperature for 10 min, and then methyl triflate (79 μL, 0.70 mmol) was added. The suspension was stirred for 15 min and then concentrated to dryness (bath temperature not exceeding 40 °C). To the crude *N*-methylthiazolium salt was added cold (0 °C) MeOH (1.5 mL) and then $NaBH_4$ (44 mg, 1.17 mmol). The mixture was stirred at room temperature for an additional 10 min, diluted with acetone (4 mL), filtered through Celite, and concentrated. To a solution of the crude thiazolidine in 10:1 CH_3CN–H_2O (4 mL) was added $HgCl_2$ (88 mg, 0.32 mmol). The mixture was stirred for 15 min and then filtered through Celite. Acetonitrile was evaporated (bath temperature not exceeding 40 °C) to afford a residue that was suspended in CH_2Cl_2 (5 mL) and washed with 20% aqueous KI (3 × 5 mL) and water (5 mL); the organic layer was dried (Na_2SO_4) and concentrated. Flash chromatography of the residue gave 103 mg (57%) of oily **1**; $[\alpha]_D = -80.0°$ (*c* 0.5, $CHCl_3$), lit.[1] $[\alpha]_D = -83.5°$ (*c* 1.08, $CHCl_3$). The ^1H NMR spectrum of this product in $CDCl_3$ at room temperature was very complex due to the presence of the hydrate form of the aldehyde. A ^1H NMR spectrum corresponding to the one described[1] was obtained from **1** after several coevaporations with benzene.

Azido 2,3:5,6-Di-*O*-isopropylidene-1-(2-thiazolyl)-α-D-mannofuranoside (5). α- or β-**4** (620 mg, 1.60 mmol) was glycosidated as described for the preparation of **3**. Flash chromatography (cyclohexane–ethyl acetate 6:1) afforded 496 mg (84%) of **5** as a white solid; mp 86–87 °C (from hexane); $[\alpha]_D = +101.4°$ (*c* 1.1, $CHCl_3$). ^1H NMR: δ 1.26, 1.35, 1.41, and 1.49 (4 s, 12 H), 4.15 (dd, 1 H, *J* = 4.5, 8.6 Hz), 4.20 (dd, 1 H, *J* = 5.9, 8.6 Hz), 4.27 (dd, 1 H, *J* = 3.8, 7.1 Hz), 4.54 (ddd, 1 H, *J* = 4.5, 5.9, 7.1 Hz), 4.73 (d, 1 H, *J* = 5.9 Hz), 4.95 (dd, 1 H, *J* = 3.8, 5.9 Hz), 7.44 and 7.92 (2 d, 2 H, *J* = 3.3 Hz). Anal. Calcd for $C_{15}H_{20}N_4O_5S$: C, 48.90; H, 5.47; N, 15.20. Found: C, 48.63; H, 5.38; N, 15.09.

Methyl (Azido 3,4:6,7-di-*O*-isopropylidene-α-D-*manno*-2-heptulofuranosid)onate (7). **5** (200 mg, 0.54 mmol) was treated as described for the preparation of **1** to give 134 mg of crude aldehyde **6** which was used directly in the next step. ^1H NMR (DMSO-d_6, 140 °C): δ 1.30, 1.33, 1.39, 1.43 (4 s, 12 H), 3.99 (dd, 1 H, *J* = 5.6, 8.6 Hz), 4.09 (dd, 1 H, *J* = 6.1, 8.6 Hz), 4.25 (dd, *J* = 3.5, 6.1 Hz), 4.44 (dt, 1 H, *J* = 5.6, 6.1 Hz), 4.77 (d, 1 H, *J* = 5.8 Hz), 5.00 (dd, 1 H *J* = 3.5, 5.8 Hz), 9.5 (s, 1 H). To a vigorously stirred mixture of silver nitrate (184 mg, 1.08 mmol), NaOH (87 mg, 2.17 mmol), and water (5 mL) was added a solution of the crude aldehyde **6** in freshly distilled THF (10 mL). Stirring was continued for 36 h at room temperature, then acetic acid was added up to pH = 5, and the mixture was filtered through Celite. The solution was concentrated and the residue was dissolved in 1:1 MeOH–Et_2O (10 mL), treated with an ethereal solution of diazomethane at 0 °C for 20 min, and then concentrated. Flash chromatography (cyclohexane–ethyl acetate 5:2) of the residue afforded pure **7** (100 mg, 53% from **5**) as a white solid; mp 112–113 °C (from cyclohexane); $[\alpha]_D = +119.2°$ (*c* 0.6, $CHCl_3$). ^1H NMR: δ 1.31, 1.38, 1.44, and 1.47 (4 s, 12 H), 3.87 (s, 3 H), 4.03 (dd, 1 H, *J* = 3.5, 8.5 Hz), 4.11 (dd, 1 H, *J* = 4.0, 9.0 Hz), 4.17 (dd, 1 H, *J* = 6.0, 9.0 Hz), 4.52 (ddd, 1 H, *J* = 4.0, 6.0, 8.5 Hz), 4.63 (d, 1 H, *J* = 5.9 Hz), 4.87 (dd, 1 H, *J* = 3.5, 5.9 Hz). Anal. Calcd for $C_{14}H_{21}N_3O_7$: C, 48.97; H, 6.17; N, 12.23. Found: C, 48.75; H, 6.08; N, 12.02.

Methyl (Amino 3,4:6,7-di-*O*-isopropylidene-α,β-D-*manno*-2-heptulofuranosid)onate (8). A vigorously stirred mixture of **7** (90 mg, 0.26 mmol) and 10% palladium on activated carbon (23 mg) in 9:1 *t*BuOH–H_2O (4 mL) was degassed under vacuum and saturated with hydrogen (by a H_2-filled balloon) three times. The suspension was stirred for an additional 1 h at room temperature under a slightly positive pressure of H_2 (balloon), filtered through a plug of cotton, and concentrated to afford in quantitative yield α- and β-**8** in a 1:5 ratio. Flash chromatography (cyclohexane–ethyl acetate 5:2) afforded first β-**8** as a syrup (66 mg, 80%); $[\alpha]_D = -3.0°$ (*c* 0.4, $CHCl_3$), lit.[13] $[\alpha]_D = -4.0°$ (*c* 0.5, $CHCl_3$). ^1H NMR: δ 1.36, 1.37, 1.43, and 1.53 (4 s, 12 H), 2.50 (s, 2 H), 3.66–3.73 (m, 1 H), 3.79 (s, 3 H), 3.98 (dd, 1 H, *J* = 4.3, 8.9 Hz), 4.07 (dd, 1 H, *J* = 6.3, 8.9 Hz), 4.35 (ddd, 1 H, *J* = 4.3, 6.3, 8.0 Hz), 4.83–4.88 (m, 2 H). Anal. Calcd for $C_{14}H_{23}NO_7$: C, 52.98; H, 7.30; N, 4.41. Found: C, 52.76; H, 7.43; N, 4.30.

Eluted second was α-**8** (13 mg, 16%); $[\alpha]_D = +67.8°$ (*c* 0.4, CH_3CN), lit.[13] $[\alpha]_D = +70.1°$ (*c* 0.5, CH_3CN).^1H NMR: δ 1.32, 1.38, 1.44, and 1.46 (4 s, 12 H), 1.85 (s, 2 H), 3.80 (s, 3 H), 4.10 (dd, 1 H, *J* = 4.0, 9.0 Hz), 4.15 (dd, 1 H, *J* = 6.0, 9.0 Hz), 4.19 (dd, 1 H, *J* = 3.5, 8.2 Hz), 4.50 (ddd, 1 H, *J* = 4.0, 6.0, 8.2 Hz), 4.51 (d, 1 H, *J* = 6.0 Hz), 4.87 (dd, 1 H, *J* = 3.5, 6.0 Hz). Anal. Found: C, 52.69; H, 7.48; N, 4.28.

Azido 2,3,4,6-Tetra-*O*-benzyl-1-(2-thiazolyl)-α-D-galactopyranoside (10). α- or β-**9** (1.00 g, 1.50 mmol) was glycosidated as described for the preparation of **3**. Flash chromatography (cyclohexane–ethyl acetate 6:1) of the residue gave oily **10** (856 mg, 88%); $[\alpha]_D = +33.7°$ (*c* 0.7, $CHCl_3$). ^1H NMR: δ 3.65 (dd, 1 H, *J* = 5.7, 9.2 Hz), 3.71 (dd, 1 H, *J* = 7.5, 9.2 Hz), 4.02 (dd, 1 H, *J* = 2.9, 9.8 Hz), 4.08 (dd, 1 H, *J* ~ 0.8, 2.9 Hz), 4.23 (ddd, 1 H, *J* ~ 0.8, 5.7, 7.5 Hz), 4.40 (d, 1 H, *J* = 9.8 Hz), 4.45 and 4.52 (2 d, 2 H, *J* = 11.6 Hz), 4.46 and 4.64 (2 d, 2 H, *J* = 10.4 Hz), 4.65 and 5.00 (2 d, 2 H, *J* = 11.6 Hz), 4.73 and 4.78 (2 d, 2 H, *J* = 10.9 Hz), 7.15–7.40 (m, 20 H), 7.42 and 7.85 (2 d, 2 H, *J* = 3.2 Hz). Anal. Calcd for $C_{37}H_{36}N_4O_5S$: C, 68.49; H, 5.59; N, 8.63. Found: C, 68.54; H, 5.56; N, 8.62.

Methyl (Azido 3,4,5,7-tetra-*O*-benzyl-α-D-*galacto*-2-heptulopyranosid)onate (12). **10** (700 mg, 1.07 mmol) was treated as described for the preparation of **1** to afford 467 mg of crude **11** which was used directly in the next step. ^1H NMR (DMSO-d_6, 140 °C): δ 3.63 (dd, 1 H, *J* = 6.3, 10.3 Hz), 3.70 (dd, 1 H, *J* = 5.1, 10.3, Hz), 4.03 (dd, 1 H, *J* = 2.8, 9.7 Hz), 4.15–4.21 (m, 2 H), 4.35 (d, 1 H, *J* = 9.7 Hz), 4.49 and 4.54 (2 d, 2 H, *J* = 11.5 Hz), 4.60 and 4.86 (2 d, 2 H, *J* = 11.6 Hz), 4.62 and 4.78 (2 d, 2 H, *J* = 11.5 Hz), 4.71 and 4.81 (2 d, 2 H, *J* = 12.0 Hz), 7.15–7.40 (m, 20 H), 9.48 (s, 1 H). Aldehyde **11** was treated with Ag_2O and then CH_2N_2 as described for the preparation of **7** to afford, after flash chromatography (cyclohexane–ethyl acetate 5:2), 360 mg of **12** as an oil (54% from **10**); $[\alpha]_D = +34.9°$ (*c* 1.6, $CHCl_3$). ^1H NMR: δ 3.58 (dd, 1 H, *J* = 5.8, 9.2 Hz), 3.64 (dd, 1 H, *J* = 7.5, 9.2 Hz), 3.71 (s, 3 H), 3.91 (dd, 1 H, *J* = 2.9, 9.8 Hz), 4.03 (dd, 1 H, *J* ~ 0.8, 2.9 Hz), 4.08 (ddd, 1 H, *J* ~ 0.8, 5.8, 7.5 Hz), 4.42 and 4.50 (2 d, 2 H, *J* = 11.6 Hz), 4.51 (d, 1 H, *J* = 9.8 Hz), 4.63 and 4.88 (2 d, 2 H, *J* = 11.6 Hz), 4.69 and 4.96 (2 d, 2 H, *J* = 11.4 Hz), 4.73 (s, 2 H), 7.20–7.40 (m, 20 H). Anal.

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Calcd for $C_{36}H_{37}N_3O_7$: C, 69.32; H, 5.97; N, 6.73. Found: C, 69.54; H, 5.94; N, 6.78.

Methyl (Amino 3,4,5,7-tetra-*O*-benzyl-α-D-*galacto*-2-heptulopyranosid)onate (13). **12** (300 mg, 0.48 mmol) was hydrogenated as described for the preparation of **8**. Flash chromatography (cyclohexane–ethyl acetate 5:2) of the residue gave first unreacted **12** (36 mg, 12%). Eluted second was **13** as a syrup (178 mg, 62%); $[\alpha]_D = +26.0°$ (*c* 0.6, $CHCl_3$). ^1H NMR: δ 2.21 (s, 2 H), 3.52 (dd, 1 H, J = 5.5, 9.3 Hz), 3.62 (dd, 1 H, J = 7.5, 9.3 Hz), 3.69 (s, 3 H), 3.91 (dd, 1 H, J = 3.0, 9.8 Hz), 4.01 (dd, 1 H, $J \sim 0.8$, 3.0 Hz), 4.38 (ddd, 1 H, $J \sim 0.8$, 5.5, 7.5 Hz), 4.42 and 4.48 (2 d, 2 H, J = 12.0 Hz), 4.50 (d, 1 H, J = 9.8 Hz), 4.66 and 4.89 (2 d, 2 H, J = 11.0 Hz), 4.66 and 4.96 (2 d, 2 H, J = 11.5 Hz), 4.68 and 4.74 (2 d, 2 H, J = 11.7 Hz), 7.20–7.40 (m, 20 H). Anal. Calcd for $C_{36}H_{39}NO_7$: C, 72.34; H, 6.77; N, 2.34. Found: C, 72.10; H, 6.88; N, 2.21.

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Supplementary Material Available: A listing of ^1H and ^{13}C NMR data with peak assignements for compounds **3**, **5–8**, and **10–13** (2 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.