A New Stereoselective Route to Branched-Chain Nitro and Amino Sugars: Synthesis of Both Enantiomers of Decilonitrose and Avidinosamine

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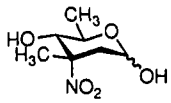
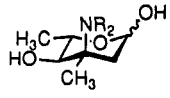
Short, efficient, and highly diastereoselective syntheses of the title carbohydrates (**15**, **21**, and **22**), components of new anthracycline antibiotics, on a gram scale from readily available keto sugar precursors **6** and **17** are described. The syntheses feature the smooth and clean addition of organocerium compounds to benzyloxyimino derivatives **7** and **18**, which provide the branched-chain hydroxyamino sugars (**9**, **20**) bearing an equatorial methyl group with complete regio- and stereocontrol. Treatment of oximino deoxy sugars (**7**, **18**) with methyllithium resulted in β-elimination and afforded pyranoid 1-enol 3-one oximes (**8**, **19**).

Introduction

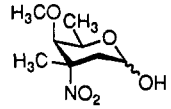
D-Decilonitrose (**1**), its L-enantiomer **2**, and L-avidinosamine (**3**) belong to a family of methyl-branched nitro and amino sugars and have been found as components of antibiotics and antitumor active natural products such as: decilorubicin[1] and arugomycin,[2] viriplanin D,[3] a photooxidation product of viriplanin A, and avidinorubicin.[4] Other members of this group are, e.g., L-evernitrose (from everninomicins),[5] D-rubranitrose (**4**) (from rubradirin),[6] and D-kijanose (**5**) (from kijanimicin and tetrocarcins).[7]



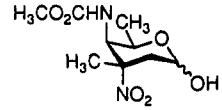
1, D-decilonitrose



2 R = O, L-decilonitrose
3 R = H, L-avidinosamine



4, D-rubranitrose



5, D-kijanose

The novel structural features of these unusual carbohydrates and their significant role in antibiotic activity[8] contribute to the strong interest in the synthesis[9-12] of these nitro and amino sugars. Decilonitrose (**1** and **2**), avidinosamine (**3**), D-rubranitrose (**4**), and D-kijanose (**5**) each contain, as a common structural unit, a tertiary carbon at position 3 bearing an equatorial methyl and an axial nitro or amino group. Introduction of the geminal methyl and nitrogen functionality at C-3 with the proper stereochemistry proved to be the pivotal problem and most critical part in chemical synthesis.

Frequently adopted methods for the synthesis of this class of compounds have relied on spiro-aziridines as intermediates which undergo reductive ring opening to give the desired C-3 functionality.[9-12] Despite its success, the spiroaziridine route suffers from modest diastereoselectivities, most significant in cases where the carbon–nitrogen bond at the branching is required axial, as in decilonitrose (**1** and **2**) and L-avidinosamine (**3**).[13-15] Stereoselective syntheses of these carbohydrates have been developed by Giuliano et al.[16-18] on the basis of the Hg(II)-mediated electrophilic cyclization of allylic isoureas followed by the hydrolysis of the resulting oxazoline. We wished to avoid the use of stoichiometric amounts of toxic mercury compounds and decided to develop another, more convenient and efficient, synthesis of decilonitrose-type sugars. Our approach has been to introduce a methyl branch into O-benzyloximino derivatives of glycosid-3-uloses.

Results and Discussion

The addition of organolithium or Grignard compounds to keto sugars provides a well-established standard method for the synthesis of *C*-methyl-branched sugars.[9,19] The

(1) Ishii, K.; Nishimura, Y.; Naganawa, H.; Kondo, S.; Umezawa, H. *J. Antibiot.* **1984**, *37*, 344.
(2) Kawai, H.; Hayakawa, Y.; Nakagawa, M.; Furihata, K.; Seto, H.; Otake, N. *Tetrahedron Lett.* **1984**, *25*, 1937, 1941.
(3) Kind, R.; Hütter, K.; Zeeck, A.; Schmidt-Bäse, K.; Egert, E. *J. Antibiot.* **1989**, *42*, 7.
(4) Aoki, M.; Shirai, H.; Nakayama, N.; Itezono, Y.; Mori, M.; Satoh, T.; Ohshima, S.; Watanabe, J.; Yokose, K. *J. Antibiot.* **1991**, *44*, 635.
(5) (a) Ganguly, A. K. In *Topics in Antibiotic Chemistry*; Sammes, P. G., Ed.; Ellis Horwood: Chichester, 1978; p 59 (Oligosaccharide Antibiotics). (b) Ganguly, A. K.; Pramanik, B.; Chan, T. M.; Sarre, O.; Liu, Y.-T.; Morton, J.; Girijavallabhan, V. *Heterocycles* **1989**, *28*, 83.
(6) Hoeksema, H.; Mizsak, S. A.; Baczynskyj, L.; Pschigoda, L. M. *J. Am. Chem. Soc.* **1982**, *104*, 5173.
(7) Mallams, A. K.; Puar, M. S.; Rossman, R. R.; McPhail, A. T.; Macfarlane, R. D.; Stephens, R. L. *J. Chem. Soc., Perkin Trans. 1* **1983**, 1497.
(8) Reusser, F. *J. Antibiot.* **1979**, *32*, 1186.
(9) Yoshimura, J. *Adv. Carbohydr. Chem. Biochem.* **1984**, *42*, 69.
(10) Hauser, F. M.; Ellenberger, S. R. *Chem. Rev.* **1986**, *86*, 35.
(11) Pelyvás, I. F.; Monneret, C.; Herczegh, P. *Synthetic Aspects of Aminodeoxy Sugars of Antibiotics*; Springer-Verlag: Berlin, Heidelberg, New York, 1988.
(12) Wade, P. A.; Giuliano, R. M. In *Nitro Compounds: Recent Advances in Synthesis and Chemistry*; Feuer, H., Nielsen, A. T., Eds.; VCH Publishers: New York, 1990; Chapter 2, p 137 (The Role of the Nitro Group in Carbohydrate Chemistry).
(13) Ishii, K.; Nishimura, Y.; Kondo, S.; Umezawa, H. *J. Antibiot.* **1983**, *36*, 454.
(14) Nishimura, Y.; Ishii, K.; Kondo, S. *J. Antibiot.* **1990**, *43*, 54.
(15) Yoshimura, J.; Aqeel, A.; Hong, N.; Sato, K.; Hashimoto, H. *Carbohydr. Res.* **1986**, *155*, 236.
(16) Giuliano, R. M.; Deisenroth, T. W. *Carbohydr. Res.* **1986**, *158*, 249.
(17) Giuliano, R. M.; Deisenroth, T. W.; Frank, W. C. *J. Org. Chem.* **1986**, *51*, 2304.
(18) Giuliano, R. M.; Deisenroth, T. W. *J. Carbohydr. Chem.* **1987**, *6*, 295.
(19) (a) Brimacombe, J. S. *Angew. Chem.* **1971**, *83*, 261; *Angew. Chem., Int. Ed. Engl.* **1971**, *10*, 236. (b) Grisebach, H.; Schmid, R. *Angew. Chem.* **1972**, *84*, 192; *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 159. (c) Williams, N. R.; Wander, J. D. In *The Carbohydrates: Chemistry and Biochemistry*; Pigman, W., Horton, D., Eds.; Academic Press: New York, 1980; Vol. I B, p 761 (Deoxy and Branched-Chain Sugars).

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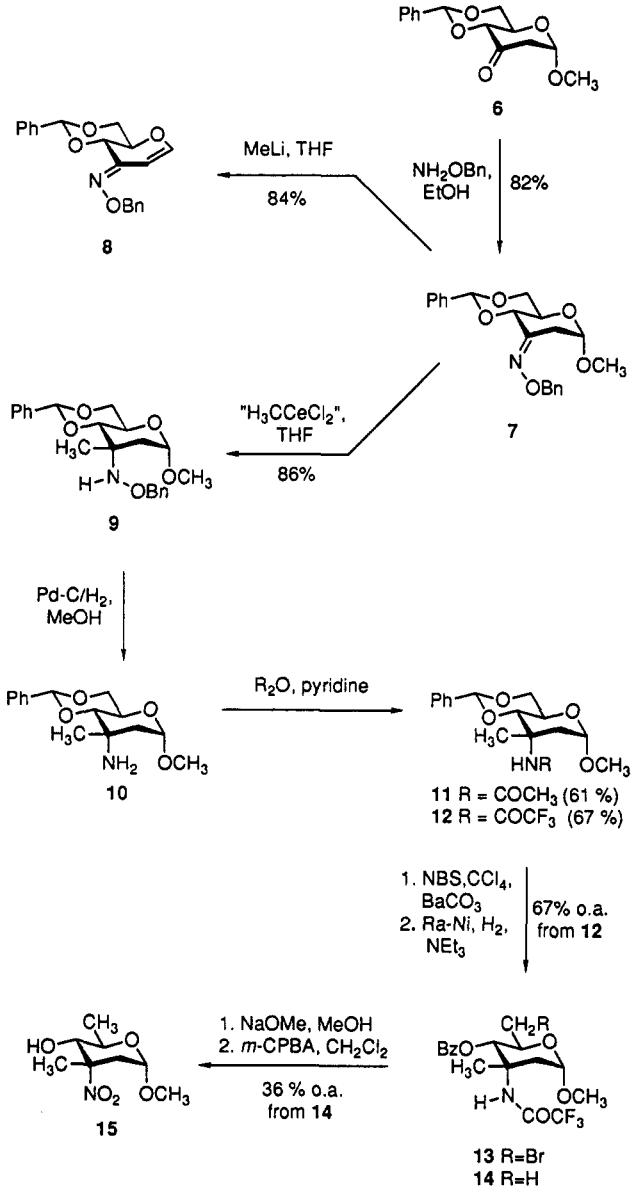
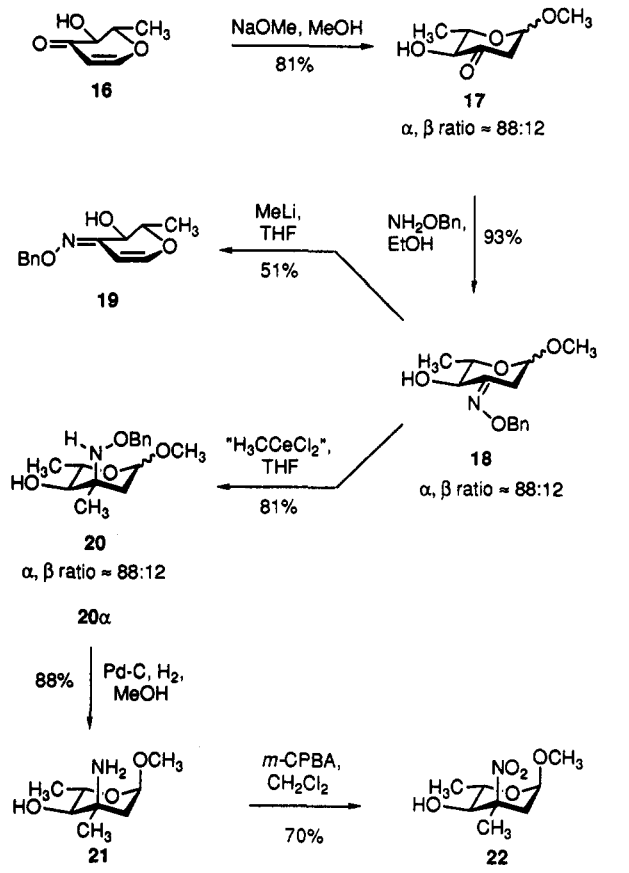
Scheme I



reaction proceeds in excellent yields and, in the vast majority of examples, with high stereoselectivity. As a part of our studies on the synthesis of naturally occurring methyl-branched carbohydrates,[20,21] we were prompted to extend this strategy to the addition of methyl anions to the C=N bond of suitable imine derivatives of glycosiduloses. For this purpose ether derivatives of oximino sugars were considered to be most suitable precursors, as the labile N–O bond of the resulting hydroxylamines can be easily cleaved by reduction under mild conditions.

The 2-deoxyglycosid-3-uloses **6** (Scheme I) and **17** (Scheme II) were chosen as ideally suited intermediates for the syntheses of both enantiomers of decilonitrose. Methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*erythro*-hexopyranosid-3-ulose (**6**) was prepared in four steps starting with methyl α-D-glucoside.[22,23] 1,5-Anhydro-2,6-dideoxy-L-*erythro*-hex-1-en-3-ulose (**16**)[24] was obtained by oxidation

Scheme II



of the readily available L-rhamnal[25] with activated manganese dioxide. The base-catalyzed Michael addition of methanol[26] resulted in a mixture of anomers (**17**, α/β ca. 88:12) according to previous work of Pelyvás et al.[27] Chromatographic separation of the anomeric mixture was difficult to achieve on a preparative scale at this stage and was avoided, especially as a separation turned out to be not essential for the following investigation. Treatment of the ketones **6** and **17** with *O*-benzylhydroxylamine[28] in ethanolic solution at room temperature afforded the oximino ethers **7** and **18**, respectively, in excellent yields.

L-Mycarose, 2,6-dideoxy-3-*C*-methyl-L-*ribo*-hexose, occurs as a sugar component of various therapeutically important macrolide antibiotics, e.g., erythromycin. Syntheses of the D-[29] and L-forms[26,30] of mycarose were achieved by treating the oxoglycosides **6** and **17**, respectively, with methylmagnesium iodide or methyllithium. However, attempts to adapt this procedure to the oximino derivatives **7** and **18** of the ulosides **6** and **17** failed to give the desired hydroxyamino sugar products, instead resulting in rapid β-elimination of methanol and the formation of the pyranoid enolone oximes **8** and **19**, respectively. These compounds constitute new glycal derivatives with potential synthetic significance.

Organocerium compounds have been established as nonbasic and highly nucleophilic reagents for carbonyl

(20) Jütten, P.; Scharf, H.-D. *Carbohydr. Res.* **1991**, *212*, 93.
(21) Žagar, C.; Scharf, H.-D. *Liebigs Ann. Chem.* **1992**, 693.
(22) (a) Rosenfeld, D. A.; Richtmyer, N. K.; Hudson, C. S. *J. Am. Chem. Soc.* **1948**, *70*, 2201. (b) Horton, D.; Cheung, T.-M.; Weckerle, W. *Meth. Carbohydr. Chem.* **1980**, *8*, 195.
(23) Ingle, T. R.; Dhekne, V. V.; Kulkarni, V. R.; Rama Rao, A. V. *Ind. J. Chem. Sect. B* **1983**, *22*, 69.
(24) Paulsen, H.; Bünsch, H. *Chem. Ber.* **1978**, *111*, 3484.
(25) Roth, W.; Pigman, W. *Meth. Carbohydr. Chem.* **1963**, *2*, 407.
(26) Thiem, J.; Elvers, J. *Chem. Ber.* **1978**, *111*, 3514.
(27) Pelyvás, I.; Sztaricskai, F.; Bognár, R. *Carbohydr. Res.* **1979**, *76*, 257.
(28) Plenkiewicz, J.; Szarek, W. A.; Sipos, P. A.; Phibbs, M. K. *Synthesis* **1974**, 56.
(29) Flaherty, B.; Overend, W. G.; Williams, N. R. *J. Chem. Soc. C* **1966**, 398.
(30) Howarth, G. B.; Jones, J. K. N. *Can. J. Chem.* **1967**, *45*, 2253.

additions[31] and have also found use in stereoselective additions to chiral imines and related derivatives,[32] e.g., hydrazones[32a] and aldoxime–ether acetals.[32b] Good yields and high diastereoselectivities have been observed throughout these reactions, which failed when other organometallics were used. To our knowledge, the reaction of carbonyl derivatives with organocerium reagents has not yet been extended to ketoxime ethers, especially not in carbohydrate chemistry.

We generated the methylcerium reagent H_3CCeCl_2 by the reaction of anhydrous $CeCl_3$ with methyllithium at −78 °C in tetrahydrofuran according to the known procedure.[33] During warming, in the temperature range of about −10 to 0 °C, smooth and clean addition to the oximino sugars (**7**, **18**α,β) occurred, and the corresponding hydroxylamines (**9**, **20**α,β) were obtained in excellent yields. For complete conversion 5 equiv of methylcerium chloride was needed. The organocerium reagent reacts in analogy to other C-nucleophiles[26,29,30,34] and attacked the C=N double bond from the equatorial direction to afford, selectively, the 1,2-addition products having the D-*ribo* (**9**) and L-*ribo* configuration (**20**), respectively. The α- and β-anomer of **18** both gave hydroxyamino sugars with an equatorially oriented methyl branch. It is remarkable that the addition reactions proceed quite well even in the presence of unblocked hydroxy groups. The structures of all methylation products were assigned on the basis of extensive ^{1}H-NOE difference spectroscopy.

In addition, the correct configuration of *O*-benzylhydroxyimino sugar compound **9** was independently proved by chemical means. Hydrogenation of **9** over palladium–charcoal furnished, after acetylation, methyl 3-acetamido-4,6-*O*-benzylidene-2,3-dideoxy-3-*C*-methyl-α-D-*ribo*-hexopyranoside (**11**). This compound is a well-developed precursor to both D-rubranitrose (**4**) and D-kijanose (**5**).[35a] The physical constants were in good agreement with those reported in the literature.

With regard to a convenient synthesis of methyl α-D-decilonitroside (**15**, Scheme I), the nitro sugar component of the anthracycline antibiotic viriplanin D,[3] we required a more readily removable N-protecting group. Thus, the methyl-branched amino sugar **10** was conventionally converted into the crystalline *N*-trifluoroacetamide **12**.[35] Reaction of the latter with *N*-bromosuccinimide[36] in gently boiling tetrachloromethane furnished the 6-bromo compound **13**[35] which was converted directly into the trideoxy sugar **14** by hydrogenolysis using Raney nickel catalyst in the presence of triethylamine. Brimacombe et al.,[35a] however, obtained **14** by the more lengthy and less efficient procedure involving the preparation of the intermediate 6-iodo derivative. Treatment of deoxy derivative **14** with 3 equiv of sodium methoxide in methanol resulted in concomitant cleavage of the *O*-benzoyl and *N*-(trifluoroacetyl) group. In the last step, oxidation of the intermediate D-avidinosamine derivative with *m*-chloroperoxybenzoic acid gave methyl α-D-decilonitroside (**15**).

Conversion of *O*-benzylhydroxyamino sugar **20**α into methyl α-L-decilonitroside (**22**, Scheme II), the methyl-branched nitro sugar isolated from antitumor antibiotics decilorubicin[1] and arugomycin,[2] proved to be straightforward. Debenzylation with hydrogen over palladium on charcoal was accompanied by reductive N–O cleavage to afford crystalline methyl α-L-avidinosaminide (**21**) in 88% yield. Avidinosamine is the amino sugar component of the novel anthracycline antibiotic avidinorubicin.[4] Avidinorubicin inhibits the thrombin-induced platelet aggregation and was determined to be strongly related to decilorubicin. On subjecting amino alcohol **21** to peracid oxidation, essentially as described in the D-series, methyl α-L-decilonitroside (**22**) was obtained in 70% yield.

In conclusion, we have demonstrated that the readily accessible oximino ethers of keto sugars serve as key intermediates in the diastereoselective synthesis of branched-chain amino and nitro sugars. Specifically, the described methodology offers a convenient and efficient approach to both enantiomers of decilonitrose (**1**, **2**) and other derivatives that provide good precursors for the synthesis of D-rubranitrose (**4**) and D-kijanose (**5**).

Moreover, expansion of our methodology to other alkylcerium reagents provides access to amino sugars with, e.g., ethyl, butyl, and phenyl branches.

Experimental Section

General Procedures. Melting points were determined on a Büchi 510 melting-point apparatus and are uncorrected. Optical rotations were determined with a Perkin-Elmer 241 polarimeter. Infrared spectra were recorded on a Perkin-Elmer 1750 FT infrared spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian VXR 300 (^{1}H, 300 MHz; ^{13}C, 75 MHz) or Varian unity 500/hrd (^{1}H, 500 MHz; ^{13}C, 125 MHz) spectrometer. ^{1}H-NOE difference spectra were recorded on a Varian unity 500/hrd (^{1}H, 500 MHz). Chemical shifts are given relative to TMS. The anomeric ratio of the products was determined by ^{13}C NMR spectra. Elemental analyses were recorded on a Heraeus CHNO-Rapid apparatus. The progress of reactions was monitored by thin-layer chromatography using aluminum-supported plates of silica gel 60 (0.2 mm, F_{254}; Merck, Darmstadt, Germany). Spots were detected by spraying with EtOH/H_2SO_4/anisaldehyde (18/1/1) and heating or UV activity. For column chromatography, silica gel 60 (0.063–0.1 mm; Merck) was used. All manipulations involving organometallics were carried out under an protective atmosphere of argon. Tetrahydrofuran was distilled from sodium/benzophenone ketyl immediately before use. Cerous chloride heptahydrate was obtained from Fluka and stored under argon. *O*-Benzylhydroxylamine hydrochloride was obtained from Janssen Chimica and stored in an anhydrous atmosphere.

***O*-Benzyl Methyl 4,6-*O*-Benzylidene-2,3-dideoxy-α-D-*erythro*-hexopyranosid-3-ulose Oxime (7).** *O*-Benzylhydroxylamine hydrochloride (5.0 g, 31,3 mmol) was dissolved in anhydrous EtOH (150 mL). To the stirred solution was added finely powdered NaOH (1.28 g, 32 mmol). After 15 min of additional stirring, the precipitated NaCl was filtered off, and to the resulting solution was added methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*erythro*-hexopyranosid-3-ulose (**6**) (5 g, 18.9 mmol)[22,23] with stirring at room temperature. After a few minutes the oxime **7** began to separate as voluminous flakes. The crystallization was complete after 2 h at room temperature. The precipitate was filtered off, washed with cold EtOH, and dried in vacuo to give 5.7 g (82%) of oxime **7**: mp 167–168 °C; $[\alpha]^{25}_D$ 128° (*c* 1.0, $CHCl_3$); IR (KBr) 1650 cm^{-1} (C=N); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25–7.54 (m, 10H, Ph), 5.61 (s, 1H, CHPh), 5.18 (s, 2H, CH_2-Ph), 4.86 (d, 1H, H-1, $J_{1,2ax}$ = 4.3 Hz), 4.30 (dd, 1H, H-6eq, $J_{6eq,5}$

(31) For a review, see: Imamoto, T. *Pure Appl. Chem.* **1990**, *62*, 747.
(32) (a) Denmark, S. E.; Edwards, J. P.; Nicaise, O. *J. Org. Chem.* **1993**, *58*, 569 and references cited therein. (b) Fujioka, H.; Fuji, M.; Okaichi, Y., Yoshida, T.; Annoura, H.; Yasuyuki, K.; Tamura, Y. *Chem. Pharm. Bull.* **1989**, *37*, 602. (c) For a review, see: Molander, G. A. *Chem. Rev.* **1992**, *92*, 29.
(33) Imamoto, T.; Kusumoto, T.; Tawarayama, Y.; Sugiura, Y.; Mita, T.; Hatanaka, Y.; Yokoyama, M. *J. Org. Chem.* **1984**, *49*, 3904.
(34) Kauffmann, T.; Klaffke, W.; Philipp, C.; Thiem, J. *Carbohydr. Res.* **1990**, *207*, 33.
(35) (a) Brimacombe, J. S.; Rahman, K. M. M. *J. Chem. Soc., Perkin Trans. 1* **1985**, 1073. (b) That Thang, T.; Imbach, J. L.; Fizames, C.; Lavelle, F.; Ponsinet, G.; Olesker, A.; Lukacs, G. *Carbohydr. Res.* **1985**, *135*, 241.
(36) Hanessian, S. *Carbohydr. Res.* **1966**, *2*, 86.
(37) Brimacombe, J. S.; Rahman, K. M. M. *Carbohydr. Res.* **1985**, *140*, 163.

= 4.6 Hz, $J_{6eq,6ax}$ = 10.4 Hz), 4.22 (d, 1H, H-4, $J_{4,5}$ = 9.5 Hz), 4.05 (td, 1H, H-5, $J_{5,6eq}$ = 4.8 Hz, $J_{5,4}$ = $J_{5,6ax}$ = 9.9 Hz), 3.82 (t, 1H, H-6ax, $J_{6ax,6eq}$ = $J_{6ax,5}$ = 10.4 Hz), 3.57 (d, 1H, H-2eq, $J_{2eq,2ax}$ = 15.3 Hz), 3.34 (s, 3H, OCH_3), 2.24 (dd, 1H, H-2ax, $J_{2ax,1}$ = 4.6 Hz, $J_{2ax,2eq}$ = 15.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 31.10 (C-2), 54.76 (OCH_3), 64.67 and 78.12 (C-4, 5), 69.49 (C-6), 76.15 (CH_2-Ph), 98.46 and 102.29 (C-1, CHPh), 126.53, 127.70, 128.20, 128.24, 129.12, 137.08, 137.66 (Ph), 149.40 (C-3). Anal. Calcd for $C_{21}H_{23}NO_5$ (369.42): C, 68.28; H, 6.28; N, 3.79. Found: C, 68.44; H, 6.31; N, 3.81.

O-Benzyl 1,5-Anhydro-4,6-O-benzylidene-2-deoxy-D-*erythro*-hex-1-en-3-ulose Oxime (8). To a stirred solution of O-benzyl oxime **7** (1 g, 2.7 mmol) in THF (50 mL) was added MeLi (5.4 mmol, 3.4 mL of 1.6 M ether solution) dropwise at −78 °C. The resulting mixture was stirred for 10 min and then quenched by addition of ice–water (15 mL). The resulting solution was concentrated under reduced pressure and the residue thoroughly extracted with ether. The combined extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Column chromatography of the residue [cyclohexane–EtOAc (4:1)] gave 0.77 g (84%) of **8**: mp 173–174 °C; $[\alpha]^{20}_D$ 207° (*c* 0.89, $CHCl_3$); IR (KBr) 1615 (C=N), 1586 cm^{-1} (C=C); ^1H NMR (300 MHz, $CDCl_3$) δ 7.26–7.55 (m, 10H, Ph), 6.65 (d, 1H, H-1, $J_{1,2}$ = 6.1 Hz), 6.01 (d, 1H, H-2, $J_{2,1}$ = 6.1 Hz), 5.64 (s, 1H, CHPh), 5.22 (d, 1H, CH_2Ph, *J* = 11.8 Hz), 5.15 (d, 1H, CH_2Ph, *J* = 11.8 Hz), 4.55 (d, 1H, H-4, $J_{4,5}$ = 10.8 Hz), 4.43 (dd, 1H, H-6eq, $J_{6eq,5}$ = 5.1 Hz, $J_{6eq,6ax}$ = 10.5 Hz), 4.12 (td, 1H, H-5, $J_{5,6eq}$ = 4.8 Hz, $J_{5,6ax}$ = $J_{5,4}$ = 10.4 Hz), 3.92 (t, 1H, H-6ax, $J_{6ax,6eq}$ = $J_{6ax,5}$ = 10.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 68.27 (C-6), 71.36 and 74.33 (C-4, 5), 76.42 (CH_2Ph), 95.11 (C-2), 102.02 (CHPh), 126.51, 127.82, 128.20, 128.28, 128.29, 129.21, 136.71, 137.43 (Ph), 145.77 (C-3), 150.61 (C-1). Anal. Calcd for $C_{20}H_{19}NO_4$ (337.38): C, 71.20; H, 5.68; N, 4.15. Found: C, 71.42; H, 5.71; N, 4.03.

Methyl 4,6-O-Benzylidene-2,3-dideoxy-3-(O-benzylhydroxyamino)-3-C-methyl-α-D-*ribo*-hexopyranoside (9). Cerium chloride ($CeCl_3 \cdot 7H_2O$) (25.2 g, 67.6 mmol) was dried at 140 °C under vacuum (0.1 mmHg) to constant weight. The resulting powder was cooled under vacuum, and the flask was flushed with argon. Freshly distilled tetrahydrofuran (300 mL) was added and the resulting suspension stirred overnight. The mixture was cooled to −78 °C whereupon MeLi (68.0 mmol, 42.5 mL of 1.6 M ether solution) was added dropwise. The yellow suspension was stirred for 1 h, and then a solution of O-benzyl oxime **7** (5.0 g, 13.5 mmol) in THF (50 mL) was added dropwise. After 2 h at −78 °C the reaction mixture was allowed to warm to 0 °C and then stirred for 1 h. The resulting brown suspension was quenched by addition of saturated aqueous $NaHCO_3$ (135 mL), and the resulting mixture was extracted thoroughly with ether. The combined extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Column chromatography of the residue [cyclohexane–$^iPr_2O$ (2:1)] gave 4.5 g (86%) of syrupy **9**: $[\alpha]^{25}_D$ 72° (*c* 0.9, $CHCl_3$); IR (film) 3281 and 1606 cm^{-1} (NH); ^1H NMR (500 MHz, $CDCl_3$) δ 7.24–7.47 (m, 10H, Ph), 6.00 (bs, 1H, NH), 5.50 (s, 1H, CHPh), 4.86 (d, 1H, CH_2Ph, *J* = 11.0 Hz), 4.79 (d, 1H, CH_2Ph, *J* = 11.3 Hz), 4.71 (d, 1H, H-1, $J_{1,2ax}$ = 4.6 Hz), 4.28 (dd, 1H, H-6eq, $J_{6eq,5}$ = 5.2 Hz, $J_{6eq,6ax}$ = 9.8 Hz), 4.23 (td, 1H, H-5, $J_{5,6eq}$ = 5.2 Hz, $J_{5,6ax}$ = $J_{5,4}$ = 9.8 Hz), 3.66 (t, 1H, H-6ax, $J_{6ax,6eq}$ = $J_{6ax,5}$ = 9.8 Hz), 3.51 (d, 1H, H-4, $J_{4,5}$ = 9.5 Hz), 3.39 (s, 3H, OCH_3), 2.41 (d, 1H, H-2eq, $J_{2eq,2ax}$ = 14.7 Hz), 1.63 (dd, 1H, H-2ax, $J_{2ax,1}$ = 4.7 Hz, $J_{2ax,2eq}$ = 14.8 Hz), 1.32 (s, 3H, CH_3-3); ^1H-NOE measurement (500 MHz, $CDCl_3$) [irradiation in CH_3-3] H-4, 8.95%; ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.35 (CH_3-3), 37.45 (C-2), 55.16 (OCH_3), 56.30 (C-3), 58.84 and 84.24 (C-4, 5), 69.59 (C-6), 76.54 (CH_2Ph), 98.44 and 102.07 (C-1, CHPh), 126.18, 127.42, 128.14, 128.46, 128.89, 137.66, 138.44 (Ph). Anal. Calcd for $C_{22}H_{27}NO_5$ (385.46): C, 68.55; H, 7.06; N, 3.63. Found: C, 68.50; H, 7.01; N, 3.70.

Methyl 3-Amino-4,6-O-benzylidene-2,3-dideoxy-3-C-methyl-α-D-*ribo*-hexopyranoside (10). A solution of **9** (4.3 g, 11.2 mmol) in methanol (200 mL) was hydrogenated in the presence of 10% palladium on charcoal (0.5 g) under a slight overpressure of hydrogen for 20 h at room temperature. Removal of the catalyst and concentration of the filtrate under reduced pressure furnished 3.1 g of **10**[35,38] as a colorless syrup, which was transformed without further purification and characterization into the corresponding 3-acetamido **11** and 3-(trifluoroacetamido) **12** derivatives, respectively.

Methyl 3-Acetamido-4,6-O-benzylidene-2,3-dideoxy-3-C-methyl-α-D-*ribo*-hexopyranoside (11). To a solution of crude amine **10** (3.1 g) in anhydrous dichloromethane (125 mL) and dry pyridine (33.5 mL) was added acetic anhydride (17 mL, 0.180 mol) at 0 °C dropwise. The reaction mixture was stirred for 2 h at room temperature and then poured into ice–water. The aqueous solution was extracted thoroughly with dichloromethane, and the combined extracts were washed successively with dilute HCl, saturated aqueous $NaHCO_3$, and water and dried ($MgSO_4$). Removal of the solvent under reduced pressure and chromatography of the residue on silica gel with cyclohexane–EtOAc (1:1) gave 2.2 g (61% oa) of a colorless syrup, which crystallized on standing: mp 124–125 °C (ether–pentane) (lit.[35a] mp 124–125 °C); $[\alpha]^{20}_D$ 98° (*c* 1.09, $CHCl_3$) (lit.[35a] $[\alpha]^{20}_D$ 107° (*c* 1, $CHCl_3$)); IR (KBr) 3437 (NH), 1690 and 1511 cm^{-1} (NHAc); ^1H NMR (300 MHz, $CDCl_3$) δ 7.35–7.53 (m, 5H, Ph), 5.89 (bs, 1H, NH), 5.61 (s, 1H, CHPh), 4.66 (d, 1H, H-1, $J_{1,2ax}$ = 4.1 Hz), 4.31 (dd, 1H, H-6eq, $J_{6eq,5}$ = 5.1 Hz, $J_{6eq,6ax}$ = 10.1 Hz), 4.02 (td, 1H, H-5, $J_{5,6eq}$ = 4.9 Hz, $J_{5,6ax}$ = 9.9 Hz), 3.74 (t, 1H, H-6ax, $J_{6ax,6eq}$ = $J_{6ax,5}$ = 10.3 Hz), 3.43 (d, 1H, H-4, $J_{4,5}$ = 9.5 Hz), 3.41 (d, 1H, H-2eq, $J_{2eq,2ax}$ = 14.8 Hz), 3.31 (s, 3H, OCH_3), 1.92 (s, 3H, CH_3-Ac), 1.57 (dd, 1H, H-2ax, $J_{2ax,1}$ = 4.1 Hz, $J_{2ax,2eq}$ = 14.9 Hz), 1.50 (s, 3H, CH_3-3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.73 (CH_3-3), 24.63 (CH_3-Ac), 36.39 (C-2), 52.14 (C-3), 55.41 (OCH_3), 59.31 and 83.88 (C-4, 5), 69.36 (C-6), 98.76 (C-1), 101.69 (CHPh), 125.97, 128.27, 129.07, 137.21 (Ph), 170.32 (C=O). Anal. Calcd for $C_{17}H_{23}NO_5$ (321.37): C, 63.54; H, 7.21; N, 4.36. Found: C, 63.44; H, 7.29; N, 4.39.

Methyl 4,6-O-Benzylidene-2,3-dideoxy-3-C-methyl-3-(trifluoroacetamido)-α-D-*ribo*-hexopyranoside (12). To a solution of crude amine **10** (3.0 g) in dichloromethane (125 mL) and dry pyridine (33.5 mL) was added trifluoroacetic anhydride (10 mL, 71 mmol) at 0 °C dropwise. The reaction mixture was stirred for 2 h at room temperature and then poured into ice–water. The aqueous solution was extracted thoroughly with dichloromethane, and the combined extracts were washed successively with dilute HCl, saturated aqueous $NaHCO_3$, and water and dried ($MgSO_4$). Removal of the solvent under reduced pressure and chromatography of the residue on silica gel with cyclohexane–EtOAc (4:1) gave 2.8 g (67% oa) of crystalline **12**: mp 118–120 °C (ether–pentane) (lit.[35a] mp 122–123 °C); $[\alpha]^{25}_D$ 73° (*c* 1.01, $CHCl_3$) (lit.[35a] $[\alpha]_D$ 76° (*c* 0.6, $CHCl_3$)); IR (KBr) 3340 (NH), 1740 and 1560 cm^{-1} ($NHCOCF_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.33–7.50 (m, 5H, Ph), 7.12 (bs, 1H, NH), 5.62 (s, 1H, CHPh), 4.72 (d, 1H, H-1, $J_{1,2ax}$ = 3.4 Hz), 4.30 (dd, 1H, H-6eq, $J_{6eq,5}$ = 4.9 Hz, $J_{6eq,6ax}$ = 10.3 Hz), 3.96 (td, 1H, H-5, $J_{5,6eq}$ = 4.8 Hz, $J_{5,6ax}$ = $J_{5,4}$ = 9.9 Hz), 3.77 (t, 1H, H-6ax, $J_{6ax,6eq}$ = $J_{6ax,5}$ = 10.3 Hz), 3.51 (d, 1H, H-4, $J_{4,5}$ = 9.5 Hz), 3.33 (s, 3H, OCH_3), 3.02 (dd, 1H, H-2eq, $J_{2eq,1}$ = 1.0 Hz, $J_{2eq,2ax}$ = 15.2 Hz), 1.71 (dd, 1H, H-2ax, $J_{2ax,1}$ = 3.9 Hz, $J_{2ax,2eq}$ = 15.0 Hz), 1.58 (s, 3H, CH_3-3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.03 (CH_3-3), 37.27 (C-2), 53.60 (C-3), 55.25 (OCH_3), 59.75 and 83.06 (C-4, 5), 69.16 (C-6), 98.21 and 102.07 (C-1, CHPh), 115.74 (q, 1C, CF_3, *J* = 289 Hz), 126.03, 128.37, 129.23, 136.92 (Ph), 156.53 (q, 1C, C=O, *J* = 36 Hz). Anal. Calcd for $C_{17}H_{20}NO_5F_3$ (375.34): C, 54.40; H, 5.37; N, 3.73. Found: C, 54.45; H, 5.39; N, 3.47.

Methyl 4-O-Benzoyl-6-bromo-2,3,6-trideoxy-3-C-methyl-3-(trifluoroacetamido)-α-D-*ribo*-hexopyranoside (13). A solution of compound **12** (2.8 g, 7.46 mmol) and NBS (1.84 g, 10.3 mmol)[36] in anhydrous tetrachloromethane (120 mL) containing $BaCO_3$ (2.04 g, 10.3 mmol) was boiled to reflux for 1 h at 90 °C. The cooled mixture was filtered and the filtrate successively washed with 5% aqueous $NaHSO_3$ (50 mL), saturated aqueous $NaHCO_3$ (50 mL), and finally with water (20 mL) and dried ($MgSO_4$). Removal of the solvent under reduced pressure and chromatography of the residue on silica gel [cyclohexane-EtOAc (6:1)] gave 2.4 g (71%) of the bromo compound **13**: mp 118–119 °C (lit.[35a] 120–121 °C); $[\alpha]^{20}_D$ −14° (*c* 1.01, $CHCl_3$) (lit.[35a] $[\alpha]_D$ −16° (*c* 0.4, $CHCl_3$)); IR (KBr) 3330 (NH), 1740 (C=O), 1710 and 1550 cm^{-1} ($NHCOCF_3$); ^1H NMR (300 MHz; $CDCl_3$) δ 8.24 (bs, 1H, NH), 7.42–8.04 (m, 5H, Ph), 5.12 (d, 1H, H-4, $J_{4,5}$ = 10.1 Hz),

(38) That Thang, T.; Winternitz, F.; Olesker, A.; Lagrange, A.; Lukacs, G. *J. Chem. Soc., Chem. Commun.* **1979**, 153.

4.93 (d, 1H, H-1, $J_{1,2ax}$ = 3.4 Hz), 4.10 (ddd, 1H, H-5, $J_{5,6eq}$ = 2.7 Hz, $J_{5,6ax}$ = 7 Hz, $J_{5,4}$ = 10 Hz), 3.51 (s, 3H, OCH_3), 3.50 (dd, 1H, H-6eq, $J_{6eq,5}$ = 3 Hz, $J_{6eq,6ax}$ = 10.8 Hz), 3.43 (dd, 1H, H-6ax, $J_{6ax,5}$ = 7 Hz, $J_{6ax,6eq}$ = 11 Hz), 2.28 (dd, 1H, H-2eq, $J_{2eq,1}$ = 1.0 Hz, $J_{2eq,2ax}$ = 14.8 Hz), 1.93 (dd, 1H, H-2ax, $J_{2ax,1}$ = 4.1 Hz, $J_{2ax,2eq}$ = 14.8 Hz), 1.68 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.44 (CH_3-3), 31.96 (C-6), 40.94 (C-2), 55.58 (OCH_3), 56.53 (C-3), 67.22 and 74.90 (C-4, 5), 97.83 (C-1), 128.56, 130.25, 133.70 (Ph), 165.84 (C=O). Anal. Calcd for $C_{17}H_{19}BrF_3NO_5$ (454.24): C, 44.95; H, 4.22; N, 3.08. Found: C, 45.18; H, 4.39; N, 3.08.

Methyl 4-*O*-Benzyl-2,3,6-trideoxy-3-*C*-methyl-3-(trifluoroacetamido)-α-D-*ribo*-hexopyranoside (14). A mixture of the bromide **13** (2.3 g, 5.1 mmol), freshly prepared Raney nickel (≈ 2 g), and triethylamine (2 mL) in isopropyl alcohol (50 mL) was shaken under a slight overpressure of hydrogen for 15 h at room temperature. The suspension was filtered with the aid of Celite and the filtrate concentrated under reduced pressure. The residue was diluted with $CHCl_3$ and washed twice with water. The organic layer was dried ($MgSO_4$) and concentrated to afford 1.8 g (95%) of the trideoxy derivative **14**: mp 118–119 °C (lit.[35a] mp 120–121 °C); $[\alpha]^{20}_D$ 3° (*c* 0.83, $CHCl_3$) (lit.[35a] $[\alpha]_D$ 2° (*c* 1, $CHCl_3$)); IR (KBr) 3355 (NH), 1741 (C=O), 1718 and 1558 cm^{-1} ($NHCOCF_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.26 (bs, 1H, NH), 7.42–8.04 (m, 5H, Ph), 4.98 (d, 1H, H-4, $J_{4,5}$ = 9.8 Hz), 4.82 (d, 1H, H-1, $J_{1,2ax}$ = 3.7 Hz), 4.00 (dq, 1H, H-5, $J_{5,6}$ = 6.4 Hz, $J_{5,4}$ = 9.8 Hz), 3.44 (s, 3H, OCH_3), 2.28 (dd, 1H, H-2eq, $J_{2eq,1}$ = 1.0 Hz, $J_{2eq,2ax}$ = 14.8 Hz), 1.89 (dd, 1H, H-2ax, $J_{2ax,1}$ = 4.0 Hz, $J_{2ax,2eq}$ = 14.8 Hz), 1.65 (s, 3H, CH_3-3), 1.22 (d, 3H, CH_3-5, $J_{6,5}$ = 6.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.52 (C-6), 23.41 (CH_3-3), 40.96 (C-2), 55.21 (OCH_3), 55.33 (C-3), 63.13 and 77.52 (C-4, 5), 97.73 (C-1), 128.46, 129.12, 130.11, 133.39 (Ph), 166.07 (C=O). Anal. Calcd for $C_{17}H_{20}F_3NO_5$ (375.34): C, 54.40; H, 5.37; N, 3.73. Found: C, 54.58; H, 5.38; N, 3.93.

Methyl 2,3,6-Trideoxy-3-*C*-methyl-3-nitro-α-D-*ribo*-hexopyranoside [Methyl α-D-Decilonitroside] (15). A solution of **14** (1.8 g, 4.8 mmol) in anhydrous methanol (100 mL) containing sodium methoxide (0.75 g, 14 mmol) was stirred for 24 h. The mixture was neutralized with Lewatit CNP 80 (H^+) cation-exchange resin and concentrated under reduced pressure, and the residue was placed on silica gel. Elution with cyclohexane–EtOAc (2:1) removed byproduct, and elution with methanol furnished a crude product, which was oxidized with m-CPBA as described for amino alcohol **21** to obtain 350 mg (36% oa) of methyl α-D-decilonitroside **15**: $[\alpha]^{20}_D$ 166° (*c* 1.0, $CHCl_3$) (lit.[17] $[\alpha]^{20}_D$ 183° (*c* 3.68, $CHCl_3$), lit.[3] $[\alpha]^{20}_D$ 141.8 (*c* 0.725, $CHCl_3$)). All physical data and properties were in agreement with those described for its enantiomer **22**.

Methyl 2,6-Dideoxy-α,β-L-*erythro*-hexopyranosid-3-ulose (17). Compound **17** was prepared according to ref 27 and was obtained as an anomeric mixture [α,β ratio ≈ 88:12 (lit.[27] α,β ratio ≈ 15:1)].

***O*-Benzyl Methyl 2,6-Dideoxy-α,β-L-*erythro*-hexopyranosid-3-ulose Oxime (18).** *O*-Benzylhydroxylamine hydrochloride (7.2 g, 45 mmol) was dissolved in anhydrous ethanol (200 mL). To the stirred solution was added finely powdered NaOH (1.84 g, 46 mmol). After 15 min of additional stirring, the precipitated NaCl was filtered off, and to the resulting solution was added the crude 3-ulose **17** [α,β ratio ≈ 88:12] (5.4 g, 34 mmol). The solution was stirred for 2 h at room temperature and then concentrated. Column chromatography of the residue [cyclohexane–EtOAc (6:1)] gave 8.3 g (93%) of syrupy **18** [α,β ratio ≈ 88:12]: $[\alpha]^{25}_D$ −136° (*c* 1.1, $CHCl_3$); IR (film) 3499 (OH), 1653 cm^{-1} (C=N); ^1H NMR (300 MHz, $CDCl_3$) δ, α **anomer**, 7.26–7.36 (m, 5H, Ph), 5.15 (d, 1H, CH_2Ph, *J* = 12.5 Hz), 5.10 (d, 1H, CH_2Ph, *J* = 12.5 Hz), 4.84 (d, 1H, H-1, $J_{1,2ax}$ = 4.4 Hz), 3.78 (dd, 1H, H-4, $J_{4,OH}$ = 3.9 Hz, $J_{4,5}$ = 9.3 Hz), 3.69 (dq, 1H, H-5, $J_{5,6}$ = 6.1 Hz, $J_{5,4}$ = 9.3 Hz), 3.48 (d, 1H, OH, $J_{OH,4}$ = 3.9 Hz), 3.41 (d, 1H, H-2eq, $J_{2eq,2ax}$ = 14.9), 3.32 (s, 3H, OCH_3), 2.18 (dd, 1H, H-2ax, $J_{2ax,1}$ = 4.7 Hz, $J_{2ax,2eq}$ = 14.9 Hz), 1.36 (d, 3H, CH_3-5, $J_{6,5}$ = 5.7 Hz), β **anomer**, 4.33 (dd, 1H, H-1, $J_{1,2eq}$ = 2.7 Hz, $J_{1,2ax}$ = 9.5 Hz), 3.48 (s, 3H, OCH_3), 2.03 (dd, 1H, H-2ax, $J_{2ax,1}$ = 9.1 Hz, $J_{2ax,2eq}$ = 14.9 Hz), 1.41 (d, 3H, CH_3-5, $J_{6,5}$ = 6.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ, α **anomer**, 18.13 (C-6), 30.84 (C-2), 54.60 (OCH_3), 70.18 and 72.28 (C-4, 5), 76.18 (CH_2Ph), 97.77 (C-1), 127.77, 128.01, 128.30, 137.52 (Ph), 153.66 (C=N), β **anomer**, 18.23 (C-6), 31.94 (C-2), 56.43 (OCH_3), 72.15 and 74.72 (C-4, 5), 76.36 (CH_2Ph), 100.65 (C-1), 127.77–137.52 (Ph), 155.05 (C=N). Anal. Calcd for $C_{14}H_{19}NO_4$ (265.31): C, 63.38; H, 7.22; N, 5.28. Found: C, 63.54; H, 7.24; N, 5.30.

***O*-Benzyl 1,5-Anhydro-2,6-dideoxy-L-*erythro*-hex-1-en-3-ulose Oxime (19).** To a stirred solution of oxime **18** (1 g, 3.8 mmol) in absolute THF (20 mL) was added MeLi (19 mmol, 12 mL of 1.6 M ether solution) dropwise at −78 °C. The resulting mixture was stirred for 30 min at −78 °C, allowed to warm to 0 °C, and stirred at this temperature for an additional 15 min. The mixture was quenched by addition of water (57 mL) and extracted thoroughly with ether, and the combined extracts were dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residual oil was purified by column chromatography [cyclohexane–EtOAc (2:1)] to give 0.45 g (51%) of syrupy **19**: $[\alpha]^{20}_D$ −136° (*c* 0.89, $CHCl_3$); IR (film) 3437 (OH), 1620 (C=N), 1595 cm^{-1} (C=C); ^1H NMR (300 MHz, $CDCl_3$) δ 7.26–7.38 (m, 5H, Ph), 6.71 (d, 1H, H-1, $J_{1,2}$ = 5.7 Hz), 5.85 (d, 1H, H-2, $J_{2,1}$ = 6.1 Hz), 5.12 (s, 2H, CH_2Ph), 4.03 (m, 2H, H-4, H-5), 3.16 (s, 1H, OH), 1.41 (d, 3H, CH_3-5, $J_{6,5}$ = 6.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.86 (C-6), 68.79 and 77.73 (C-4, 5), 76.23 (CH_2Ph), 93.09 (C-2), 127.85, 128.07, 128.36, 137.56 (Ph), 149.56 (C-3), 152.38 (C-1). Anal. Calcd for $C_{13}H_{15}NO_3$ (233.27): C, 66.93; H, 6.49; N, 6.01. Found: C, 66.48; H, 6.45; N, 5.99.

Methyl 2,3,6-Trideoxy-3-(*O*-benzylhydroxyamino)-3-*C*-methyl-α,β-L-*ribo*-hexopyranoside (20). Cerium chloride ($CeCl_3 \cdot 7H_2O$) (35.2 g, 94.5 mmol) was dried at 140 °C under vacuum (0.1 mmHg) to constant weight. The resulting powder was cooled under vacuum, and the flask was flushed with argon. Freshly distilled tetrahydrofuran (300 mL) was added and the resulting suspension stirred overnight. The mixture was cooled to −78 °C whereupon MeLi (94.4 mmol, 59 mL of 1.6 M ether solution) was added dropwise. The yellow suspension was stirred for 1 h, and then a solution of *O*-benzyloxime **18** [α,β ratio ≈ 88:12] (5.0 g, 18.9 mmol) in THF (50 mL) was added dropwise. After 2 h at −78 °C the reaction mixture was allowed to warm to 0 °C and then stirred for 1 h. The resulting brown suspension was quenched by addition of saturated aqueous $NaHCO_3$ (190 mL), and the resulting mixture was extracted thoroughly with ether. The combined extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Column chromatography of the residue [cyclohexane–EtOAc (2:1)] gave 3.8 g (72%) of syrupy α anomer and 0.5 g (9%) of syrupy β anomer of **20** [α,β ratio ≈ 88:12]. α **Anomer**: $[\alpha]^{25}_D$ −113° (*c* 1.44, $CHCl_3$); IR (film) 3495 (OH), 3282 cm^{-1} (NH); ^1H NMR (500 MHz, $CDCl_3$) δ 7.27–7.36 (m, 6H, Ph, NH), 4.69 (d, 1H, CH_2Ph, *J* = 11.3 Hz), 4.66 (d, 1H, CH_2Ph, *J* = 11.3 Hz), 4.62 (d, 1H, H-1, $J_{1,2ax}$ = 3.7 Hz), 3.62 (dq, 1H, H-5, $J_{5,6}$ = 6.1 Hz, $J_{5,4}$ = 10.1 Hz), 3.58 (d, 1H, OH, $J_{OH,4}$ ≈ 9 Hz), 3.30 (s, 3H, OCH_3), 3.11 (t, 1H, H-4, $J_{4,5}$ = $J_{4,OH}$ = 9.6 Hz), 2.00 (d, 1H, H-2eq, $J_{2eq,2ax}$ = 14.7 Hz), 1.59 (dd, 1H, H-2ax, $J_{2ax,1}$ = 4.3 Hz, $J_{2ax,2eq}$ = 14.7 Hz), 1.35 (s, 3H, CH_3-3), 1.28 (d, 3H, CH_3-5, $J_{6,5}$ = 6.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.17 (C-6), 23.44 (CH_3-3), 38.27 (C-2), 54.92 (OCH_3), 57.90 (C-3), 65.06 and 78.99 (C-4, 5), 77.94 (CH_2Ph), 98.07 (C-1), 127.98, 128.37, 128.48, 137.13 (Ph); ^1H-NOE measurement (500 MHz, $CDCl_3$) [irradiation in CH_3-3] H-4, 6.1%, H-2ax, 2.7%. Anal. Calcd for $C_{15}H_{23}NO_4$ (281.35): C, 64.04; H, 8.24; N, 4.98. Found: C, 64.08; H, 8.33; N, 5.22. β **Anomer**: $[\alpha]^{25}_D$ 15° (*c* 0.66, $CHCl_3$); IR (film) 3447 (OH), 3280 cm^{-1} (NH); ^1H NMR (500 MHz, toluene-d_8) δ 6.97–7.22 (m, 6H, Ph, NH), 4.64 (dd, 1H, H-1, $J_{1,2eq}$ = 2.1 Hz, $J_{1,2ax}$ = 9.5 Hz), 4.52 (d, 1H, CH_2Ph, *J* = 11.7 Hz), 4.49 (d, 1H, CH_2Ph, *J* = 11.7 Hz), 3.73 (dq, 1H, H-5, $J_{5,6}$ = 6.1 Hz, $J_{5,4}$ = 9.5 Hz), 3.34 (s, 3H, OCH_3), 2.87 (d, 1H, H-4, $J_{4,5}$ = 9.5 Hz), 2.10 (dd, 1H, H-2eq, $J_{2eq,1}$ = 2.1 Hz, $J_{2eq,2ax}$ = 14.5 Hz), 1.41 (dd, 1H, H-2ax, $J_{2ax,1}$ = 9.5 Hz, $J_{2ax,2eq}$ = 13.7 Hz), 1.25 (d, 3H, CH_3-5, $J_{6,5}$ = 6.3 Hz), 1.11 (s, 3H, CH_3-3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.46 (C-6), 23.84 (CH_3-3), 40.47 (C-2), 56.23 (OCH_3), 58.71 (C-3), 70.44 and 78.60 (C-4, 5), 76.67 (CH_2Ph), 99.18 (C-1), 128.04, 128.45, 128.64, 137.34 (Ph); ^1H-NOE measurement (500 MHz, toluene-d_8) [irradiation in CH_3-3] H-4, 4.1%, H-2eq, 2.3%, H-2ax, 2.8%. Anal. Calcd for $C_{15}H_{23}NO_4$ (281.35): C, 64.04; H, 8.24; N, 4.98. Found: C, 63.99; H, 8.31; N, 5.12.

Methyl 3-Amino-2,3,6-trideoxy-3-*C*-methyl-α-L-*ribo*-hexopyranoside [Methyl α-L-Avidinosaminide] (21). A solution of **20** [α anomer] (3.3 g, 11.7 mmol) in methanol (200 mL) was hydrogenated over 10% palladium on charcoal (0.5 g) under a slight overpressure of hydrogen for 2 h at room temperature.

The catalyst was removed and the filtrate concentrated under reduced pressure. The syrupy residue was placed on silica gel. Elution with cyclohexane–EtOAc (1:1) removed benzylic alcohol, and then further elution with methanol furnished 1.8 g (88%) of **21**.[4,16,37] Analytically pure **21** was obtained by crystallization of the crude solid from ether–pentane and subsequent sublimation (60 °C, 0.1 mmHg): mp 99–101 °C (lit.[16] mp 92–94 °C); $[\alpha]^{25}_D$ −181° (*c* 0.97, $CHCl_3$) (lit.[16] $[\alpha]^{25}_D$ −120° (*c* 0.131, $CHCl_3$)); IR (KBr) 3352 and 3283 (primary NH_2), 3117 (OH), 1586 cm^{-1} (NH); ^1H NMR (300 MHz, $CDCl_3$) δ 4.70 (d, 1H, H-1, $J_{1,2ax}$ = 3.7 Hz), 3.50 (dq, 1H, H-5, $J_{5,6}$ = 6.4 Hz, $J_{5,4}$ = 9.8 Hz), 3.32 (s, 3H, OCH_3), 2.87 (d, 1H, H-4, $J_{4,5}$ = 9.8 Hz), 1.90 (dd, 1H, H-2eq, $J_{2eq,1}$ = 1.4 Hz, $J_{2eq,2ax}$ = 14.2 Hz), 1.78 (dd, 1H, H-2ax, $J_{2ax,1}$ = 4.1 Hz, $J_{2ax,2eq}$ = 14.2 Hz), 1.29 (d, 3H, CH_3-5, $J_{6,5}$ = 6.4 Hz), 1.11 (s, 3H, CH_3-3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.09 (C-6), 28.27 (CH_3-3), 42.78 (C-2), 49.97 (C-3), 54.86 (OCH_3), 65.32 (C-5), 75.76 (C-4), 98.69 (C-1). Anal. Calcd for $C_8H_{17}NO_3$ (175.23): C, 54.84; H, 9.78; N, 7.99. Found: C, 54.52; H, 9.81; N, 7.98.

Methyl 2,3,6-Trideoxy-3-*C*-methyl-3-nitro-α-L-*ribo*-hexopyranoside [Methyl α-L-Decilonitroside] (22). A solution of crude methyl α-L-avidinosaminide **21** (1.7 g, 9.7 mmol) in dichloromethane (42 mL) was added dropwise to a stirred boiling solution of m-CPBA (85%) (14.5 g, 71.4 mmol) in dry dichloromethane (170 mL). The mixture was heated to reflux for 20 min. To the cooled solution was added 10% aqueous sodium sulfite solution (100 mL) with stirring, and the mixture was filtered. The organic phase was separated, successively washed with 2 M sodium carbonate (80 mL) and brine (40 mL), dried ($MgSO_4$), and concentrated. Purification of the crude product by chromatography [cyclohexane–EtOAc (4:1)] afforded 1.4 g (70%) of crystalline **22**: mp 98–100 °C (lit.[16] mp 96–98 °C, lit.[37] mp 101.5–103 °C); $[\alpha]^{20}_D$ −172° (*c* 1.0, $CHCl_3$) (lit.[16] $[\alpha]^{20}_D$ −185° (*c* 0.094, $CHCl_3$), lit.[37] $[\alpha]^{20}_D$ −172° (*c* 0.25, $CHCl_3$)); IR (KBr) 3523 (OH), 1545 cm^{-1} (NO_2); ^1H NMR (300 MHz, $CDCl_3$) δ 4.62 (d, 1H, H-1, $J_{1,2ax}$ = 3.4 Hz), 4.13 (dq, 1H, H-5, $J_{5,6}$ = 6.4 Hz, $J_{5,4}$ = 9.3 Hz), 3.30 (s, 1H, OH), 3.27 (d, 1H, H-4, $J_{4,5} \approx 9$ Hz), 3.25 (s, 3H, OCH_3), 2.86 (dd, 1H, H-2eq, $J_{2eq,1}$ = 1.2 Hz, $J_{2eq,2ax}$ = 15.2 Hz), 1.93 (dd, 1H, H-2ax, $J_{2ax,1}$ = 3.7 Hz, $J_{2ax,2eq}$ = 15.1 Hz), 1.70 (s, 3H, CH_3-3), 1.36 (d, 3H, CH_3-5, $J_{6,5}$ = 6.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.18 (C-6), 26.00 (CH_3-3), 40.79 (C-2), 54.66 (OCH_3), 65.35 and 77.04 (C-4, 5), 85.96 (C-3), 96.20 (C-1). Anal. Calcd for $C_8H_{15}NO_5$ (205.21): C, 46.82; H, 7.37; N, 6.83. Found: C, 47.32; H, 7.23; N, 6.96.

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