A Novel and Practical Synthesis of L-Hexoses from D-Glycono-1,5-lactones

Hideyo Takahashi, Yuko Hitomi, Yoshinori Iwai, and Shiro Ikegami*

Contribution from the Faculty of Pharmaceutical Sciences, Teikyo University, Sagamiko, Kanagawa 199-0195, Japan

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Abstract: A novel and efficient conversion of D-glycono-1,5-lactones into the corresponding L-sugars is described. The important intermediate, δ-hydroxyalkoxamates, was provided by a practical alkoxyamination of D-glycono-1,5-lactones mediated by Me_3Al. In contrast to the preparation of β-lactam skeletons from β-hydroxyalkoxamates, the cyclization of δ-hydroxyalkoxamates under Mitsunobu conditions resulted in *O*-alkylation rather than *N*-alkylation. It is noteworthy that δ-hydroxyalkoxamates derived from D-mannono-1,5-lactones afforded the *O*-alkylation product in 91% yield. None of the *N*-alkylation product was detected in this case. These *O*-cyclized oximes, in which the inversion of the configuration at C5 was secured, were efficiently converted into the L-sugars.

Introduction

L-Hexoses, which are known as rare sugars in the natural resources, sometimes play important roles in the microbial world. As notable examples, L-gulose should be key building block on the carbohydrate moiety of antitumor antibiotic bleomycin A_2[1] and L-iduronic acid is a typical component of mammalian dermatan sulfate, heparan sulfate, and heparin.[2] As the need for L-sugars increases in science, it becomes necessary to develop an efficient method that makes rare sugars "common". Herein we describe a novel and practical conversion of glycono-1,5-lactones of D-glucose, D-galactose, and D-mannose into the corresponding rare sugars, L-idose, L-altrose, and L-gulose. A key step in the present process is based on the intramolecular *O*-alkylation of δ-hydroxyalkoxamates.

As a part of our research into the utilization of sugar derivatives as synthetic tools,[3] we were interested in the cyclization of δ-hydroxyalkoxamates derived efficiently from natural D-sugars. Efficient biomimetic β-lactam syntheses have been developed on the basis of the intramolecular *N*-alkylation of β-hydroxyalkoxamates.[4] In contrast, the current studies revealed that a competitive *O*-alkylation took place in several cases with amides and carbamates.[5] We have, therefore, investigated the intramolecular *O*-/*N*-alkylation of such δ-hydroxyalkoxamates under Mitsunobu conditions.[6]

Results and Discussion

Synthesis of δ-Hydroxyalkoxamates from D-Glycono-1,5-lactones. Glycono-1,5-lactones **1** derived from D-glucose, **2** from D-galactose, and **3** from D-mannose were prepared according to the literature procedure.[7] In preliminary studies of the alkoxyamination of glycono-1,5-lactones, we found that Me_3Al accelerated the reaction enormously, even though the preceding formation of a Me_3Al−alkoxyamine complex as an active species was not effective (Scheme 1). $BnONH_2$−Me_3Al complex, which was prepared in situ from alkoxyamine (3.9 equiv) and Me_3Al (3.9 equiv) at room temperature in 0.5 h, provided the δ-hydroxyalkoxamate in 70% yield, and the starting material was recovered in 25% yield. The key to the successful production of δ-hydroxyalkoxamates lay in the preparation of the mixture of glycono-1,5-lactones and alkoxyamine before the

(1) (a) Umezawa, H.; Maeda, K.; Takeuchi, T.; Okami, Y. *J. Antibiot., Ser. A* **1966**, *19*, 200−209. (b) Sugiura, Y.; Takita, T.; Umezawa, H. In *Metal Ions in Biological Systems*; Sigel, H., Ed.; Marcel Dekker: New York, 1985; pp 81−108. (c) Ohno, M.; Otsuka, M. In *Recent Progress in the Chemical Synthesis of Antibiotics*; Lukacs, G., Ohno, M., Eds.; Springer-Verlag: New York, 1990; pp 387−414. (d) Takita, T.; Muraoka, Y.; Nakatani, T.; Fujii, A.; Umezawa, Y.; Naganawa, H.; Umezawa, H. *J. Antibiot*. **1978**, *31*, 801−804. (e) Aoyagi, Y.; Katano, K.; Suguna, H.; Pimeau, J.; Chang, L.-H.; Hecht, S. M. *J. Am. Chem. Soc.* **1982**, *104*, 5537−5538. (f) Boger, D. L.; Honda, T. *J. Am. Chem. Soc.* **1994**, *116*, 5647−5656. (g) Boger, D. L.; Ramsey, T. M.; Cai, H.; Hoehn, S. T.; Stubbe, J. *J. Am. Chem. Soc.* **1998**, *120*, 9139−9148. (h) Katano, K.; An, H.; Aoyagi, Y.; Overhand, M.; Sucheck, S. J.; Stevens, W. C., Jr.; Hess, C. D.; Zhou, X.; Hecht, S. M. *J. Am. Chem. Soc.* **1998**, *120*, 11285−11296.

(2) (a) Sinaÿ, P.; Jacquinet, J.-C. *Carbohydr. Res.* **1984**, *132*, C5−C9. (b) Tollefsen, D. M.; Peacock, M. E.; Monafo, W. J. *J. Biol. Chem.* **1986**, *261*, 8854−8858. (c) Petitou, M.; Lormeau, J.-C.; Choay, J. *Eur. J. Biochem.* **1988**, *176*, 637−640. (d) Maimone, M. M.; Tollefsen, D. M. *J. Biol. Chem.* **1990**, *265*, 18263−18271.

(3) (a) Iimori, T.; Takahashi, H.; Ikegami, S. *Tetrahedron Lett.* **1996**, *37*, 649−652. (b) Takahashi, H.; Iimori, T.; Ikegami, S. *Tetrahedron Lett.* **1998**, *39*, 6939−6942. (c) Takahashi, H.; Kittaka, H.; Ikegami, S. *Tetrahedron Lett.* **1998**, *39*, 9703−9706. (d) Takahashi, H.; Kittaka, H.; Ikegami, S. *Tetrahedron Lett.* **1998**, *39*, 9707−9710.

(4) (a) Mattingly, P. G.; Kerwin, J. F., Jr.; Miller, M. J. *J. Am. Chem. Soc.* **1979**, *101*, 3983−3985. (b) Morrison, M. A.; Miller, M. J. *J. Org. Chem.* **1983**, *48*, 4421−4423. (c) Miller, M. J.; Mattingly, P. G. *Tetrahedron* **1983**, *39*, 2563−2570. (d) Farouz, F.; Miller, M. J. *Tetrahedron Lett.* **1991**, *32*, 3305−3308.

(5) For a discussion of *O*-/*N*-alkylation selectivity in Mitsunobu reaction of various amides and carbamates, see: (a) Miller, M. J.; Mattingly, P. G.; Morrison, M. A.; Kerwin, J. F., Jr. *J. Am. Chem. Soc.* **1980**, *102*, 7026−7032. (b) Bose, A. K.; Sahu, D. P.; Manhas, M. S. *J. Org. Chem.* **1981**, *46*, 1229−1230. (c) Krook, M. A.; Miller, M. J. *J. Org. Chem.* **1985**, *50*, 1126−1128. (d) Galéotti, N.; Montagne, C.; Poncet, J.; Jouin, P. *Tetrahedron Lett.* **1992**, *33*, 2807−2810. (e) Wipf, P.; Miller, C. P. *Tetrahedron Lett.* **1992**, *33*, 6267−6270. (f) Koppel, I.; Koppel, J.; Koppel, I.; Leito, I.; Pihl, V.; Wallin, A.; Grehn, L.; Ragnarsson, U. *J. Chem. Soc., Perkin Trans. 2* **1993**, 655−658.

(6) Review: Mitsunobu, O. *Synthesis* **1981**, 1−28.

(7) (a) Lewis, M. D.; Cha, J. K.; Kishi, Y. *J. Am. Chem. Soc.* **1982**, *104*, 4976−4978. For the efficient glycosylation utilizing carbohydrate lactone, see: (b) Ohtake, H.; Iimori, T.; Ikegami, S. *Tetrahedron Lett.* **1997**, *38*, 3413−3414. (c) Ohtake, H.; Iimori, T.; Ikegami, S. *Heterocycles* **1998**, *47*, 685−688. (d) Ohtake, H.; Iimori, T.; Ikegami, S. *Synlett.* **1998**, 1420−1422.

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Scheme 1

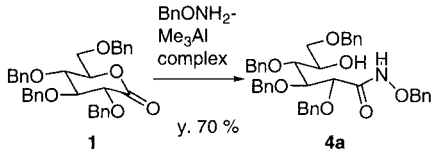
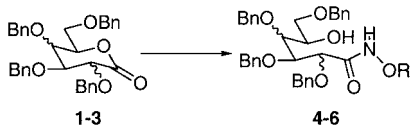


Table 1. Me_3Al-Mediated Amination of Glycono-1,5-lactones[a]



entry			R		yield (%)[b]
1	Glc	**1**	Bn	**4a**	93
2			Me[c]	**4b**	95
3			Et[c]	**4c**	93
4			^{t}Bu[c]	**4d**	96
5	Gal	**2**	Bn	**5**	92
6	Man	**3**	Bn	**6**	quant.

[a] Reactions were conducted using alkoxyamine (3.9 equiv) and Me_3Al (3.9 equiv) in CH_2Cl_2 at room temperature for 1 h. [b] Isolated yield. [c] Hydrochloride salt was used.

addition of Me_3Al. Although it was extremely difficult to identify the structure of an active species, we presume that the true reactive reagent of this reaction is different from the aluminum−amide complex reported by Weinreb et al.[8] Thus, the three kinds of δ-hydroxyalkoxamates were efficiently synthesized from D-glycono-1,5-lactones. The results are summarized in Table 1.

Treatment of **1**−**3** (1 equiv) with *O*-benzylhydroxylamine (3.9 equiv) in CH_2Cl_2 for 30 min, followed by addition of Me_3Al (3.9 equiv) at room temperature, afforded the corresponding δ-hydroxybenzyloxamates **4a**, **5**, and **6** in excellent yields (entries 1, 5, and 6). The conveniently handled, readily available *O*-substituted hydroxyamine hydrochlorides also provided the corresponding δ-hydroxylalkoxamates **4b**, **4c**, and **4d** in excellent yields (entries 2−4).

Intermolecular Alkylation of Alkoxamates. In the preliminary investigation, we examined the intermolecular alkylation of alkoxamate under Mitsunobu conditions (Scheme 2). Treatment of ethyl ester **7** with *O*-benzylhydroxylamine in the presence of Me_3Al afforded the corresponding benzyloxamate **8** in good yield. Its intermolecular alkylation with benzyl alcohol under Mitsunobu conditions provided **9** and **10** in 54% and 24% yields, respectively. The preferred formation of the *O*-alkylated compound over the *N*-alkylated one revealed the promising nucleophilicity of an amide oxygen.

Cyclization of the δ-Hydroxyalkoxamates. We next examined the cyclization of the δ-hydroxyalkoxamates **4**−**6** under Mitsunobu conditions (Table 2). In contrast to the syntheses of β-lactams from β-hydroxyalkoxamates, we found that the cyclization of δ-hydroxyalkoxamates resulted mainly in the *O*-alkylation rather than the *N*-alkylation. With **4a** derived from D-glucose, cyclization with diethylazodicarboxylate (DEAD) (3.0 equiv) and TPP (3.0 equiv) gave **11a** and **14a** in 71% and 13% yields, respectively (entry 1). Similarly, **5** derived from D-galactose provided **12** and **15** in 68% and 30% yields, respectively (entry 5). It is noteworthy that **6** afforded the *O*-alkylation product **13** as the sole product in 91% yield (entry 6). None of the *N*-alkylation product was detected in this case. The significant difference in the ratios of the *O*-/*N*-alkylation dependent on the stereochemistry of sugar derivatives is particularly interesting. Concerning the steric effect of the substitution of a hydroxamate, further studies on the formation of the *O*-/*N*-alkylation products with the different *O*-substituted hydroxamate derivatives (**4b**, **4c**, and **4d**) were carried out. The results indicated that the steric requirement of the hydroxamate moiety did not affect the ratios of the *O*-/*N*-alkylation (entries 1−4). The complete inversion of the stereochemistry at C5 of the *O*-/*N*-alkylation products **11**−**15** was unambiguously determined by a series of NOE experiments after definitive assignments had been established.

Scheme 2

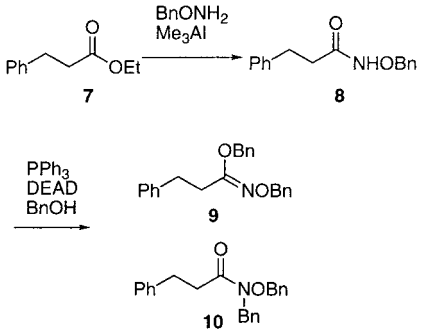
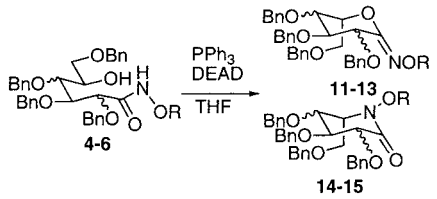


Table 2. Cyclization of δ-Hydroxyalkoxamates under Mistunobu Conditions[a]



				yield (%)[b]			
				O-cyclized		*N*-cyclized	
entry			R				
1	Glc	**4a**	Bn	**11a**	71	**14a**	13
2		**4b**	Me	**11b**	81	**14b**	4
3		**4c**	Et	**11c**	79	**14c**	9
4		**4d**	^{t}Bu	**11d**	79	**14d**	8
5	Gal	**5**	Bn	**12**	68	**15**	30
6	Man	**6**	Bn	**13**	91		−

[a] Reactions were conducted using TPP (3.0 equiv) and DEAD (3.0 equiv) at room temperature for 10−30 min. [b] Isolated yield.

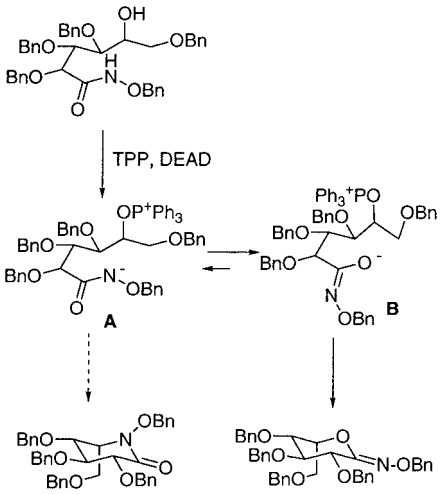
The cyclization of these δ-hydroxyalkoxamates can be rationalized by assuming the formation of the anions **A** and **B** as shown in Scheme 3. Deprotonation of the amide NH by the reduced DEAD anion present in Mitsunobu reaction mixture generates anions **A** and **B**, and with amide anion **A** an intramolecular alkylation is expected to result in the *N*-alkylation. In this δ-hydroxyalkoxamate case, cyclization occurs predominantly via anion **B**, and the corresponding *O*-alkylation products are isolated exclusively. Presumably, the *O*-/*N*-alkylation selectivity is due to the different conformational properties between anions **A** and **B**.[9]

Synthesis of L-Sugars. With these results in hand, we turned our attention to the utilization of the *O*-cyclized oxime compounds **11a**, **12**, and **13** as precursors of L-sugars. Although several routes to L-sugars have already been reported,[1f,10] we

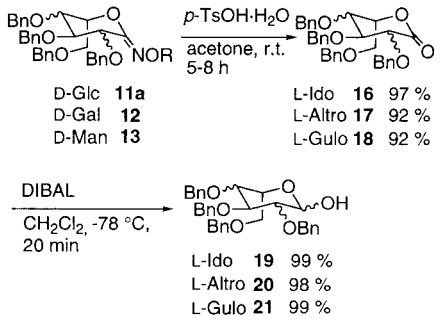
(8) Lewis acid-catalyzed amination of esters: (a) Houghton, R. P.; Williams, C. S. *Tetrahedron Lett.* **1967**, *8*, 3929−3931. (b) Levin, J. I.; Turos, E.; Weinreb, S. M. *Synth. Commun.* **1982**, *12*, 989−993. (c) Lesimple, P.; Bigg, D. C. H. *Synthesis* **1991**, 306−308.

(9) We are now conducting conformational analysis of these anions by employing computer calculations.

Scheme 3



Scheme 4



took advantage of the structural relationships between D-glucose and L-idose, D-galactose and L-altrose, and D-mannose and L-gulose. We envisioned that the inversion of the stereochemistry at C5 of each D-sugar would provide the precursor of the corresponding L-sugar efficiently.

Consequently, the cleavage of the oximes of the *O*-cyclization products **11a**, **12**, and **13** to the parent L-carbohydrate lactones and the subsequent reduction to 2,3,4,6-tetra-*O*-benzyl-L-hexopyranoses were successively investigated (Scheme 4). Of the methods we have examined for the deoximation, acid-catalyzed hydrolysis gave the best results. Treatment of the *O*-cyclized oxime compounds with *p*-TsOH monohydrate (1.0 equiv) in acetone at room temperature gave L-glycono-1,5-lactones in quantitative yields. In the event, we have found that L-idonolactone **16** crystallized, and its stereoconfiguration at C5 was established by X-ray crystallography.[11] The stage was now set for the subsequent reduction of the carbonyl moiety of L-glycono-1,5-lactone. The use of an excess amount of DIBAL completed the reduction of **16** derived from D-glucose to provide 99% of 2,3,4,6-tetra-*O*-benzyl-L-idose **19**.[10f] In contrast, with **17** from D-galactose, the reaction proceeded smoothly to give 2,3,4,6-tetra-*O*-benzyl-L-altrose **20**[12] in 98% yield. Similarly, **18** from D-mannose provided 2,3,4,6-tetra-*O*-benzyl-L-gulose **21**[10i,k] in 99% yield. It should be noted that the conversion of the D-mannono-1,5-lactone to L-gulose was accomplished in 83% overall yield.

We have established a novel and efficient method for the conversion of D-carbohydrate lactones into L-sugars. The key feature of the present method is the *O*-alkylation of *δ*-hydroxyalkoxamates in the inversion of stereochemistry at C5 under Mitsunobu conditions. This is the first application of the Mitsunobu-type cyclization to carbohydrates, and it should also be emphasized that the conversion in three sugar types could be carried out in excellent overall yields. Finally, the *N*-alkylation products obtained simultaneously in the Mitsunobu cyclization could be converted into various analogues of aza sugars, which may represent an appealing entry into potential glycosidase inhibitors.[13] Works concerning the transformation to other L-sugars and aza sugars according to similar concepts are in progress.

Experimental Section

General Experimental. Melting points were determined with a Yanagimoto micro melting point apparatus and were uncorrected. IR spectra were measured with a JASCO FT/IR-8000 spectrometer. HRFAB-MS were taken with a JEOL SX-102A. ^{1}H NMR and ^{13}C NMR spectra were recorded at 400 MHz with a JEOL GSX-400 spectrometer using tetramethylsilane (TMS) as the internal standard. Chemical shifts were reported in ppm downfield from TMS. Optical rotations were measured by a JASCO DIP-370 in a 1-dm cell. Analytical and preparative TLC was conducted on precoated TLC plates (silica gel 60 F_{254}, Merck). Column chromatography was performed using Merck silica gel 60N (100−210 μm). All anhydrous solvents were purified according to standard methods.

General Procedure for Hydroxyamination. A mixture of **1** (50 mg, 0.093 mmol) and benzylhydroxylamine (44.6 mg, 0.36 mmol) in 2 mL of CH_2Cl_2 was stirred at room temperature for 30 min, and a solution of trimethylaluminum (0.34 mL of 1.08 M solution in *n*-hexane, 0.36 mmol) was added. The resulting solution was stirred at room temperature over a period of 1 h. The reaction was quenched with pH.7 phosphate buffer, and the product was extracted with CH_2Cl_2. The combined organic phase was dried over Na_2SO_4 and filtered, and the solvent was removed in vacuo. Purification by silica gel chromatography (hexane/AcOEt = 3:1) gave 57.1 mg (93%) of **4a**.

1*N*-Benzyloxy-2,3,4,6-tetrakis(benzyloxy)-5-hydroxy-(2*R*,3*S*,4*R*,5*R*)-hexanamide (4a): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 (s, 1 H), 7.37−7.20 (m, 25 H), 4.86 (s, 2 H), 4.65 (d, J = 10.6 Hz, 2 H), 4.54 (d, J = 11.9 Hz, 2 H), 4.49 (d, J = 11.6 Hz, 2 H), 4.43 (s, 2 H), 4.28 (d, J = 3.66 Hz, 1 H), 4.04 (dd, J = 3.66 Hz, J = 2.13 Hz, 1 H), 3.87 (m, 1 H), 3.82 (dd, J = 5.50 Hz, J = 2.13 Hz, 1 H), 3.63 (dd, J = 6.41 Hz, J = 3.05 Hz, 1 H), 3.57 (dd, J = 6.41 Hz, J = 3.05 Hz, 1 H), 2.74 (br, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.68, 138.06, 137.97, 137.49, 136.44, 135.32, 128.92, 128.66, 128.59, 128.53, 128.47, 128.39, 128.35, 128.31, 128.22, 128.02, 127.90, 127.85, 127.72, 127.66, 80.39, 79.36, 78.14, 77.47, 75.36, 74.12, 73.79, 73.39, 71.18, 70.98; IR (neat, cm^{-1}) 1697, 1541; HRMS (FAB) exact mass calcd for $C_{41}H_{43}NO_7Na$ (M + Na)$^+$ 684.2937, found 684.2928; $[\alpha]^{24}_D$ +43.4° (*c* 1.07, $CHCl_3$).

1*N*-Methoxy-2,3,4,6-tetrakis(benzyloxy)-5-hydroxy-(2*R*,3*S*,4*R*,5*R*)-hexanamide (4b): ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.02 (s, 1 H), 7.38−7.20 (m, 20 H), 4.70 (d, J = 11.3 Hz, 1 H), 4.69 (d, J = 10.7 Hz, 1 H),

(10) (a) Fisher, E.; Piloty, O. *Chem. Ber.* **1891**, *24*, 521−528. (b) Evans, M. E.; Parrish, F. W. *Carbohydr. Res.* **1973**, *28*, 359−364. (c) B-Muesser, M.; Defaye, J. *Synthesis* **1977**, 568−569. (d) B-Muesser, M.; Defaye, J. *Methods Carbohydr. Chem.* **1980**, *8*, 177−183. (e) Köster, R.; Idelmann, P.; Dahlhoff, W. V. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 547−548. (f) Helleur, R.; Rao, V. S.; Perlin, A. S. *Carbohydr. Res.* **1981**, *89*, 83−90. (g) Katano, K.; Chang, P.-I.; Millar, A.; Pozsgay, V.; Minster, D. K.; Ohgi, T.; Hecht, S. M. *J. Org. Chem.* **1985**, *50*, 5807−5815. (h) González, F. S.; Baer, H. H. *Carbohydr. Res.* **1990**, *202*, 33−47. (i) Oshitari, T.; Tomita, M.; Kobayashi, S. *Tetrahedron Lett.* **1994**, *35*, 6493−6494. (j) Dondoni, A.; Marra, A.; Massi, A. *J. Org. Chem.* **1997**, *62*, 6261−6267. (k) Oshitari, T.; Shibasaki, M.; Yoshizawa, T.; Tomita, M.; Takao, K.; Kobayashi, S. *Tetrahedron* **1997**, *53*, 10993−11006. (l) Adinolfi, M.; Barone, G.; De Lorenzo, F.; Iadonisi, A. *Synlett* **1999**, 336−338. (m) I.-García, J.; C.-Flores, F. G.; H.-Mateo, F.; S.-González, F. *Chem. Eur. J.* **1999**, 1512−1525.

(11) The X-ray crystallographic analysis revealed that **16** exists in a boat form. See Supporting Information.

(12) **20** was converted, after deprotectin, into the acetylated compound, whose structure was spectroscopically identical with that of an authentic sample. Reference: van Dorst, J. A. L. M.; van Heusden, C. J.: Tikkanen, J. M.; Kamerling, J. P.; Vliegenthart, F. G. *Carbohydr. Res.* **1997**, *297*, 209−227.

(13) Reviews: (a) Gijsen, H. J. M.; Qiao, L.; Fitz, W.; Wong, C.-H. *Chem. Rev.* **1996**, *96*, 443−473. (b) Sears, P.; Wong, C.-H. *Angew. Chem., Int. Ed.* **1999**, *38*, 2300−2324.

4.62−4.52 (m, 4 H), 4.51 (d, J = 10.0 Hz, 1 H), 4.48 (d, J = 11.9 Hz, 1 H), 4.33 (d, J = 3.66 Hz, 1 H), 4.07 (dd, J = 3.66 Hz, J = 2.14 Hz, 1 H), 3.94−3.89 (m, 1 H), 3.85 (dd, J = 5.80 Hz, J = 5.49 Hz, 1 H), 3.66−3.62 (m, 1 H), 3.63 (s, 3 H), 3.57 (dd, J = 5.19 Hz, J = 4.58 Hz, 1 H), 2.83 (d, J = 4.27 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.65, 138.03, 137.95, 137.50, 136.59, 128.62, 128.40, 128.36, 128.32, 128.29, 127.99, 127.85, 127.82, 127.69, 127.65, 80.44, 79.45, 77.41, 75.30, 74.11, 73.96, 73.37, 71.25, 70.98, 64.27; IR (neat, cm^{-1}) 1736, 1686; HRMS (EI) exact mass calcd for $C_{35}H_{39}NO_7$ (M^+) 585.2726, found 585.2727; $[\alpha]^{24}_D$ +28.3° (*c* 0.74, $CHCl_3$).

1*N*-Ethoxy-2,3,4,6-tetrakis(benzyloxy)-5-hydroxy-(2*R*,3*S*,4*R*,5*R*)-hexanamide (4c): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 (s, 1 H), 7.35−7.21 (m, 20 H), 4.70 (d, J = 11.30 Hz, 1 H), 4.69 (d, J = 11.00 Hz, 1 H), 4.60−4.48 (m, 6 H), 4.32 (d, J = 3.66 Hz, 1 H), 4.07 (dd, J = 3.66 Hz, J = 1.83 Hz, 1 H), 3.95−3.89 (m, 1 H), 3.87−3.79 (m, 3 H), 3.65 (dd, J = 6.71 Hz, J = 3.05 Hz, 1 H), 3.58 (dd, J = 6.71 Hz, J = 3.05 Hz, 1 H), 2.80 (d, J = 4.27 Hz, 1 H), 1.19 (dd, J = 7.02 Hz, J = 7.01 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.70, 138.06, 137.99, 137.55, 136.64, 128.65, 128.45, 128.39, 128.33, 128.05, 127.99, 127.95, 127.86, 127.80, 127.72, 127.69, 80.45, 79.49, 77.43, 75.33, 74.11, 73.96, 73.42, 72.18, 71.24, 71.02, 13.39; IR (neat, cm^{-1}) 1684; HRMS (EI) exact mass calcd for $C_{36}H_{41}NO_7$ (M^+) 599.2883, found 599.2886; $[\alpha]^{24}_D$ +33.0° (*c* 1.54, $CHCl_3$).

1*N*-*tert*-Butoxy-2,3,4,6-tetrakis(benzyloxy)-5-hydroxy-(2*R*,3*S*,4*R*,5*R*)-hexanamide (4d): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1 H), 7.32−7.23 (m, 20 H), 4.71 (d, J = 10.90 Hz, 1 H), 4.68 (d, J = 10.90 Hz, 1 H), 4.65 (d, J = 11.20 Hz, 1 H), 4.58 (d, J = 11.20 Hz, 1 H), 4.57 (d, J = 11.20 Hz, 1 H), 4.54 (d, J = 11.90 Hz, 1 H), 4.52 (d, J = 11.20 Hz, 1 H), 4.48 (d, J = 11.90 Hz, 1 H), 4.34 (d, J = 3.66 Hz, 1 H), 4.07 (dd, J = 3.66 Hz, J = 2.14 Hz, 1 H), 3.93−3.88 (m, 1 H), 3.86 (dd, J = 5.49 Hz, J = 2.14 Hz, 1 H), 3.64 (dd, J = 6.14 Hz, J = 3.05 Hz, 1 H), 3.58 (dd, J = 6.14 Hz, J = 3.05 Hz, 1 H), 2.82 (d, J = 3.66 Hz, 1 H), 1.24 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.76, 138.03, 137.94, 137.50, 136.57, 128.56, 128.50, 128.29, 128.25, 128.23, 127.95, 127.79, 127.76, 127.61, 127.57, 81.70, 80.59, 79.68, 77.47, 75.39, 74.02, 73.82, 73.29, 71.10, 70.91, 26.23; IR (neat, cm^{-1}) 1699; HRMS (EI) exact mass calcd for $C_{38}H_{45}NO_7$ (M^+) 627.3196, found 627.3194; $[\alpha]^{24}_D$ +30.6° (*c* 1.00, $CHCl_3$).

1*N*-Benzyloxy-2,3,4,6-tetrakis(benzyloxy)-5-hydroxy-(2*R*,3*S*,4*S*,5*R*)-hexanamide (5): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89 (br, 1 H), 7.33−7.20 (m, 21 H), 7.16 (m, 2 H), 7.03 (m, 2 H), 4.90 (m, 2 H), 4.67 (d, J = 10.68 Hz, 1 H), 4.56 (d, J = 10.68 Hz, 1 H), 4.53 (d, J = 12.21 Hz, 1 H), 4.45 (d, J = 12.21 Hz, 1 H), 4.43 (d, J = 11.60 Hz, 1 H), 4.35 (d, J = 10.99 Hz, 1 H), 4.33 (d, J = 11.60 Hz, 1 H), 4.24 (d, J = 2.14 Hz, 1 H), 4.22 (d, J = 10.99 Hz, 1 H), 4.15 (dd, J = 8.24 Hz, J = 2.14 Hz, 1 H), 4.09 (ddd, J = 6.41 Hz, J = 6.41 Hz, J = 1.46 Hz, 1 H), 3.82 (dd, J = 8.24 Hz, J = 1.46 Hz, 1 H), 3.57 (dd, J = 9.46 Hz, J = 6.41 Hz, 1 H), 3.49 (dd, J = 9.46 Hz, J = 6.41 Hz, 1 H), 2.45 (d. J = 8.24 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.91, 137.92, 137.84, 137.49, 136.36, 135.24, 128.85, 128.74, 128.67, 128.52, 128.40, 128.22, 128.18, 127.91, 127.81, 127.72, 127.34, 79.85, 79.19, 78.27, 77.04, 75.24, 73.69, 73.36, 73.28, 71.28, 69.21; IR (neat, cm^{-1}) 1748, 1698; HRMS (FAB) exact mass calcd for $C_{41}H_{43}NO_7Na$ 684.2975 (M + Na)$^+$, found 684.2956; $[\alpha]^{24}_D$ +45.6° (*c* 1.29, $CHCl_3$).

1*N*-Benzyloxy-2,3,4,6-tetrakis(benzyloxy)-5-hydroxy-(2*S*,3*S*,4*R*,5*R*)-hexanamide (6): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89 (s, 1 H), 7.35−7.15 (m, 25 H), 4.85 (d, J = 11.30 Hz, 1 H), 4.79 (d, J = 11.60 Hz, 1 H), 4.66 (s, 2 H), 4.54 (d, J = 11.30 Hz, 1 H), 4.52 (d, J = 11.60 Hz, 1 H), 4.51−4.46 (m, 2 H), 4.45 (d, J = 11.00 Hz, 1 H), 4.36 (d, J = 11.60 Hz, 1 H), 4.25 (d, J = 3.30 Hz, 1 H), 4.10 (dd, J = 4.28 Hz, J = 4.27 Hz, 1 H), 3.97 (m, 1 H), 3.82 (dd, J = 5.18 Hz, J = 2.14 Hz, 1 H), 3.61 (m, 2 H), 2.94 (d, J = 6.10 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.00, 138.03, 137.95, 137.88, 136.85, 135.26, 128.99, 128.59, 128.49, 128.44, 128.38, 128.34, 128.30, 128.26, 128.19, 128.08, 128.02, 127.98, 127.83, 127.79, 127.71, 127.64, 80.85, 79.48, 78.71, 78.18, 74.75, 74.26, 73.40, 72.53, 71.04, 70.72; IR (KBr, cm^{-1}) 1698; HRMS (FAB) exact mass calcd for $C_{41}H_{43}NO_7Na$ (M + Na)$^+$ 684.2937, found 684.2936; mp 79 °C; $[\alpha]^{22}_D$ +5.83° (*c* 1.10, $CHCl_3$). Anal. Calcd for $C_{41}H_{43}NO_7$: C, 74.41; H, 6.55; N, 2.12. Found: C, 74.34; H, 6.58; N, 2.05.

1*N*-Benzyloxy-3-phenylpropanamide (8): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (brs, 1 H), 7.35−7.14 (m, 10 H), 4.79 (brs, 2 H), 2.96 (m, 2 H), 2.34 (brs, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.66, 140.30, 135.24, 129.21, 128.55, 128.38(m), 128.71, 126.34, 78.14, 35.03, 31.23; IR (KBr, cm^{-1}) 1651; HRMS (EI) exact mass calcd for $C_{16}H_{17}NO_2$ (M^+) 255.1259, found 255.1255; mp 81 °C.

General Procedure for Cyclization of δ-Hydroxyalkoxamates. A mixture of **4a** (504 mg, 0.76 mmol), triphenylphosphine (594 mg, 2.27 mmol), and DEAD (0.36 mL, 2.27 mmol) in 7.6 mL of THF was stirred at room temperature for 10 min. The solvent was removed in vacuo. The residue was chromatographed on silica gel (hexane/AcOEt = 7:1) to give 346 mg (71%) of **11a** and 63 mg (13%) of **14a**.

2*N*-Benzyloxy-3,4,5-tris(benzyloxy)-6-benzyloxymethyl-(3*R*,4*S*,5*R*,6*S*)-tetrahydro-2*H*-pyran-2-imine (11a): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (m, 2 H), 7.30−7.20 (m, 23 H), 5.08 (s, 2 H), 4.71 (d, J = 11.60 Hz, 1 H), 4.59 (d, J = 11.60 Hz, 1 H), 4.58 (d, J = 11.60 Hz, 1 H), 4.54 (d, J = 11.90 Hz, 1 H), 4.50−4.45 (m, 3 H), 4.40 (d, J = 11.90 Hz, 1 H), 4.38 (d, J = 11.90 Hz, 1 H), 4.08 (d, J = 5.19 Hz, 1 H), 3.88−3.82 (m, 2 H), 3.76 (dd, J = 5.80 Hz, J = 4.28 Hz, 1 H), 3.72 (dd, J = 3.36 Hz, J = 2.75 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.98, 138.46, 137.94, 137.64, 137.60, 137.53, 128.41, 128.35, 128.33, 128.28, 128.18, 127.99, 127.85, 127.79, 127.71, 127.65, 127.58, 78.16, 76.24, 76.06, 75.20, 74.92, 73.44, 72.48, 71.91, 71.86, 68.11; IR (KBr, cm^{-1}) 1657; HRMS (FAB) exact mass calcd for $C_{41}H_{42}NO_6$ (M + H)$^+$ 644.3012, found 644.3011; mp 65 °C; $[\alpha]^{24}_D$ +30.6° (*c* 1.03, $CHCl_3$). Anal. Calcd for $C_{41}H_{41}NO_6$: C, 76.49; H, 6.42; N, 2.18. Found: C, 76.29; H, 6.54; N, 2.16.

2*N*-Methoxy-3,4,5-tris(benzyloxy)-6-benzyloxymethyl-(3*R*,4*S*,5*R*,6*S*)-tetrahydro-2*H*-pyran-2-imine (11b): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39−7.20 (m, 20 H), 4.92 (d, J = 11.90 Hz, 1 H), 4.57 (m, 2 H), 4.54 (d, J = 11.90 Hz, 1 H), 4.50 (d, J = 11.90 Hz, 1 H), 4.48−4.45 (m, 3 H), 4.40 (d, J = 11.90 Hz, 1 H), 4.16 (d, J = 5.49 Hz, 1 H), 3.89−3.86 (m, 4 H), 3.83 (dd, J = 6.11 Hz, J = 3.66 Hz, 1 H), 3.77−3.72 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.61, 137.86, 137.63, 137.59, 137.48, 128.40, 128.32, 128.30, 127.98, 127.85, 127.81, 127.77, 127.67, 78.29, 75.85, 75.11, 73.44, 72.42, 72.22, 71.74, 67.95, 62.59; IR (neat, cm^{-1}) 1657; HRMS (EI) exact mass calcd for $C_{35}H_{37}NO_6$ (M^+) 567.2621, found 567.2617; $[\alpha]^{24}_D$ +33.8° (*c* 1.11, $CHCl_3$). Anal. Calcd for $C_{35}H_{37}NO_6$: C, 74.05; H, 6.57; N, 2.47. Found: C, 74.30; H, 6.34; N, 2.36.

2*N*-Ethoxy-3,4,5-tris(benzyloxy)-6-benzyloxymethyl-(3*R*,4*S*,5*R*,6*S*)-tetrahydro-2*H*-pyran-2-imine (11c): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.21 (m, 20 H), 4.90 (d, J = 11.60 Hz, 1 H), 4.60 (d, J = 11.90 Hz, 1 H), 4.59 (d, J = 11.60 Hz, 1 H), 4.55 (d, J = 12.21 Hz, 1 H), 4.52−4.46 (m, 4 H), 4.42 (d, J = 11.9 Hz, 1 H), 4.15−4.09 (m, 3 H), 3.89 (dd, J = 5.18 Hz, J = 3.66 Hz, 1 H), 3.85 (dd, J = 5.80 Hz, J = 3.97 Hz, 1 H), 3.78 (dd, J = 5.80 Hz, J = 4.27 Hz, 1 H), 3.74 (dd, J = 3.66 Hz, J = 3.05 Hz, 1 H), 1.31 (dd, J = 7.02 Hz, J = 7.02 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.34, 137.93, 137.70, 137.64, 137.55, 128.37, 128.29, 128.26, 127.91, 127.81, 127.76, 127.73, 127.61, 78.23, 75.87, 75.17, 75.12, 73.39, 72.45, 72.08, 71.82, 69.98, 68.00, 14.64; IR (neat, cm^{-1}) 1657; HRMS (EI) exact mass calcd for $C_{36}H_{39}NO_6$ (M^+) 581.2777, found 581.2775; $[\alpha]^{24}_D$ +35.5° (*c* 1.00, $CHCl_3$).

2*N*-*tert*-Butoxy-3,4,5-tris(benzyloxy)-6-benzyloxymethyl-(3*R*,4*S*,5*R*,6*S*)-tetrahydro-2*H*-pyran-2-imine (11d): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.22 (m, 20 H), 4.90 (d, J = 11.60 Hz, 1 H), 4.65−4.57 (m, 3 H), 4.56−4.46 (m, 5 H), 4.12 (d, J = 5.19 Hz, 1 H), 3.91 (dd, J = 5.19 Hz, J = 4.27 Hz, 1 H), 3.87 (dd, J = 6.10 Hz, J = 3.97 Hz, 1 H), 3.80 (dd, J = 5.49 Hz, J = 5.19 Hz, 1 H), 3.75 (dd, J = 4.27 Hz, J = 3.35 Hz, 1 H), 1.33 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.22, 138.11, 137.93, 137.80, 137.71, 128.33, 128.26, 128.24, 127.78, 127.75, 127.72, 127.68, 127.65, 78.30, 78.27, 75.88, 75.38, 75.23, 73.36, 72.60, 71.95, 71.84, 68.25, 27.44; IR (neat, cm^{-1}) 1665; HRMS (EI) exact mass calcd for $C_{38}H_{43}NO_6$ (M^+) 609.3090, found 609.3092; $[\alpha]^{24}_D$ +28.6° (*c* 0.99, $CHCl_3$).

2*N*-Benzyloxy-3,4,5-tris(benzyloxy)-6-benzyloxymethyl-(3*R*,4*S*,5*S*,6*S*)-tetrahydro-2*H*-pyran-2-imine (12): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.38 (m, 2 H), 7.32−7.19 (m, 21 H), 7.14−7.11 (m, 2 H), 5.12 (d, J = 12.80 Hz, 1 H), 5.07 (d, J = 12.80 Hz, 1 H), 4.68 (d, J = 11.90 Hz, 1 H), 4.63 (d, J = 12.20 Hz, 1 H), 4.56 (d, J = 12.20 Hz, 1 H), 4.54 (d, J = 12.20 Hz, 1 H), 4.52−4.47 (m, 3 H), 4.44

(d, $J = 11.20$ Hz, 1 H), 4.35 (dd, $J = 7.32$ Hz, $J = 2.44$ Hz, 1 H), 4.22 (d, $J = 11.90$ Hz, 1 H), 4.02 (d, $J = 3.97$ Hz, 1 H), 3.94−3.91 (m, 2H), 3.86 (dd, $J = 8.24$ Hz, $J = 3.36$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.09, 138.39, 137.81, 137.63, 128.35, 128.33, 128.27, 128.26, 128.20, 127.98, 127.87, 127.77, 127.75, 127.73, 127.70, 127.54, 127.52, 127.43, 77.10, 75.94, 73.43, 72.75, 72.13, 72.05, 71.33, 70.13, 68.61; IR (neat, cm^{-1}) 1644; HRMS (EI) exact mass calcd for $C_{41}H_{41}NO_6$ (M^+) 643.2933, found 643.2936; $[\alpha]^{24}_D$ −42.0° (*c* 1.00, $CHCl_3$).

2*N*-Benzyloxy-3,4,5-tris(benzyloxy)-6-benzyloxymethyl-(3*S*,4*S*,5*R*,6*S*)-tetrahydro-2*H*-pyran-2-imine (13): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43−7.17 (m, 25 H), 5.10 (d, $J = 12.20$ Hz, 1 H), 5.05 (d, $J = 12.50$ Hz, 1 H), 4.93 (ddd, $J = 6.10$ Hz, $J = 6.10$ Hz, $J = 3.97$ Hz, 1 H), 4.63 (d, $J = 12.50$ Hz, 1 H), 4.60 (d, $J = 12.20$ Hz, 1 H), 4.58 (d, $J = 11.90$ Hz, 1 H), 4.51 (d, $J = 12.20$ Hz, 1 H), 4.46 (d, $J = 11.90$ Hz, 1 H), 4.45 (d, $J = 11.60$ Hz, 1 H), 4.33 (d, $J = 12.20$ Hz, 1 H), 4.28 (d, $J = 11.60$ Hz, 1 H), 4.21 (d, $J = 3.66$ Hz, 1 H), 3.97 (dd, $J = 4.27$ Hz, $J = 3.97$ Hz, 1 H), 3.86−3.80 (m, 2 H). 3.77 (dd, $J = 6.10$ Hz, $J = 4.88$ Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.42, 138.27, 138.08, 137.86, 137.49, 137.09, 128.62, 128.39, 128.34, 128.30, 128.26, 128.17, 127.89, 127.83, 127.77, 127.68, 127.65, 127.56, 78.98, 77.44, 77.08, 76.12, 73.45, 72.66, 70.90, 70.28, 69.82, 68.36; IR (neat, cm^{-1}) 1651; HRMS (EI) exact mass calcd for $C_{41}H_{41}NO_6$ (M^+) 643.2934, found 643.2938; $[\alpha]^{24}_D$ −53.5° (*c* 0.98, $CHCl_3$). Anal. Calcd for $C_{41}H_{41}NO_6$: C, 76.49; H, 6.42; N, 2.18. Found: C, 76.46; H, 6.53; N, 2.03.

1,3,4,5-Tetrakis(benzyloxy)-6-benzyloxymethyl-(3*R*,4*S*,5*R*,6*S*)-tetrahydropyridin-2(1*H*)-one (14a): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.16 (m, 25 H), 5.10 (d, $J = 11.00$ Hz, 1 H), 4.94 (d, $J = 11.00$ Hz, 1 H), 4.89 (d, $J = 11.00$ Hz, 1 H), 4.72 (s, 2 H), 4.70 (d, $J = 11.90$ Hz, 1 H), 4.59 (d, $J = 12.20$ Hz, 1 H), 4.55 (d, $J = 11.00$ Hz, 1 H), 4.44 (d, $J = 12.20$ Hz, 1 H), 4.42 (d, $J = 11.90$ Hz, 1 H), 4.29 (dd, $J = 9.76$ Hz, $J = 7.93$ Hz, 1 H), 4.00 (d, $J = 7.93$ Hz, 1 H), 3.74 (dd, $J = 10.10$ Hz, $J = 10.10$ Hz, 1 H), 3.68 (dd, $J = 10.70$ Hz, $J = 10.70$ Hz, 1H), 3.62 (dd, $J = 9.76$ Hz, $J = 1.83$ Hz, 1H), 3.32 (ddd, $J = 10.70$ Hz, $J = 10.10$ Hz, $J = 1.83$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.99, 138.49, 138.39, 137.81, 137.68, 135.48, 129.58, 128.78, 128.48, 128.45, 128.42, 128.28, 128.22, 128.18, 128.04, 127.85, 127.65, 127.58, 127.54, 127.50, 127.38, 79.97, 79.35, 76.28, 74.94, 73.95, 73.43, 73.24, 64.26, 63.75, 60.83; IR (neat, cm^{-1}) 1701; HRMS (EI) exact mass calcd for $C_{41}H_{41}NO_6$ (M^+) 643.2934, found 643.2954; $[\alpha]^{24}_D$ −33.9° (*c* 0.99, $CHCl_3$).

3,4,5-Tris(benzyloxy)-6-benzyloxymethyl-1-methoxy-(3*R*,4*S*,5*R*,6*S*)-tetrahydropyridin-2(1*H*)-one (14b): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.21 (m, 20 H), 5.07 (d, $J = 10.98$ Hz, 1 H), 4.78 (d, $J = 11.60$ Hz, 1 H), 4.76 (brs, 2 H), 4.69 (d, $J = 10.98$ Hz, 1 H), 4.65 (d, $J = 11.60$ Hz, 1 H), 4.61 (d, $J = 12.21$ Hz, 1 H), 4.45 (d, $J = 12.21$ Hz, 1 H), 4.30 (dd, $J = 10.07$ Hz, $J = 7.93$ Hz, 1 H), 4.01 (d, $J = 7.93$ Hz, 1H), 3.88 (dd, $J = 9.46$ Hz, $J = 5.80$ Hz, 1 H), 3.84 (dd, $J = 10.07$ Hz, $J = 1.22$ Hz, 1 H), 3.78 (ddd, $J = 5.80$ Hz, $J = 3.36$ Hz, $J = 1.22$ Hz, 1 H), 3.73 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.68, 138.48, 138.30, 137.77, 128.44, 128.24, 128.21, 128.14, 128.00, 127.96, 127.88, 127.67, 127.54, 127.48, 127.37, 79.99, 79.20, 76.45, 74.79, 73.91, 73.53, 73.43, 63.89, 61.86, 59.66; IR (neat, cm^{-1}) 1750; HRMS (EI) exact mass calcd for $C_{35}H_{37}NO_6$ (M^+) 567.2621, found 567.2628; $[\alpha]^{24}_D$ +4.72° (*c* 0.45, $CHCl_3$).

3,4,5-Tris(benzyloxy)-6-benzyloxymethyl-1-ethoxy-(3*R*,4*S*,5*R*,6*S*)-tetrahydropyridin-2(*1H*)-one (14c): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39−7.20 (m, 20 H), 5.07 (d, $J = 10.98$ Hz, 1 H), 4.78 (d, $J = 11.60$ Hz, 1 H), 4.76 (brs, 2 H), 4.69 (d, $J = 10.98$ Hz, 1 H), 4.65 (d, $J = 11.60$ Hz, 1 H), 4.61 (d, $J = 12.21$ Hz, 1 H), 4.46 (d, $J = 12.21$ Hz, 1 H), 4.33 (dd, $J = 9.76$ Hz, $J = 7.93$ Hz, 1 H), 4.01 (d, $J = 7.93$ Hz, 1 H), 3.96 (q, $J = 7.02$ Hz, 2 H), 3.89 (dd, $J = 9.46$ Hz, $J = 5.49$ Hz, 1 H), 3.84 (dd, $J = 9.76$ Hz, $J = 1.22$ Hz, 1 H), 3.73 (m, 2 H), 1.22 (t, $J = 7.02$ Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.01, 138.57, 138.40, 137.85, 137.82, 128.46, 128.26, 128.23, 128.21, 128.16, 127.97, 127.89, 127.72, 127.54, 127.52, 127.47, 127.35, 80.07, 79.27, 77.21, 76.44, 74.82, 73.89, 73.57, 73.43, 69.76, 60.41, 13.64; IR (neat, cm^{-1}) 1701; HRMS (EI) exact mass calcd for $C_{36}H_{39}NO_6$ (M^+) 581.2778, found 581.2776; $[\alpha]^{24}_D$ +16.8° (*c* 0.98, $CHCl_3$).

3,4,5-Tris(benzyloxy)-6-benzyloxymethyl-1-*tert*-butoxy-(3*R*,4*S*,5*R*,6*S*)-tetrahydropyridin-2(1*H*)-one (14d): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.37 (m, 2 H), 7.34−7.26 (m, 16 H), 7.20−7.17 (m, 2 H), 5.06 (d, $J = 11.3$ Hz, 1 H), 4.83−4.76 (m, 3 H), 4.68−4.61 (m, 3 H), 4.44 (d, $J = 12.50$ Hz, 1 H), 4.37 (dd, $J = 9.77$ Hz, $J = 8.24$ Hz, 1 H), 4.05 (d, $J = 8.24$ Hz, 1 H), 3.94 (dd, $J = 9.77$ Hz, $J = 5.80$ Hz, 1 H), 3.79 (dd, $J = 10.07$ Hz, $J = 0.91$ Hz, 1 H), 3.74 (dd, $J = 10.07$ Hz, $J = 3.05$ Hz, 1 H), 3.45 (ddd, $J = 5.80$ Hz, $J = 3.05$ Hz, $J = 0.91$ Hz, 1 H), 1.18 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.01, 138.76, 138.54, 137.95, 137.85, 128.47, 128.26, 128.12, 127.96, 127.51, 127.40, 127.21, 82.50, 80.76, 79.41, 76.34, 74.97, 73.72, 73.53, 73.41, 63.37, 63.18, 26.95; IR (neat, cm^{-1}) 1717; HRMS (EI) exact mass calcd for $C_{38}H_{43}NO_6$ (M^+) 609.3090, found 609.3092; $[\alpha]^{24}_D$ +21.4° (*c* 0.43, $CHCl_3$).

1,3,4,5-Tetrakis(benzyloxy)-6-benzyloxymethyl-(3*R*,4*S*,5*S*,6*S*)-tetrahydropyridin-2(1*H*)-one (15): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39−7.36 (m, 4 H), 7.34−7.21 (m, 21 H), 5.05 (d, $J = 11.60$ Hz, 1 H), 4.96 (d, $J = 10.40$ Hz, 1 H), 4.90 (d, $J = 10.40$ Hz, 1 H), 4.72 (d, $J = 11.60$ Hz, 1 H), 4.60 (d, $J = 12.20$ Hz, 1 H), 4.51 (m, 2 H), 4.45 (d, $J = 12.20$ Hz, 1 H), 4.44 (d, $J = 11.90$ Hz, 1 H), 4.38 (d, $J = 11.90$ Hz, 1 H), 4.27 (d, $J = 7.02$ Hz, 1 H), 4.16 (dd, $J = 2.44$ Hz, $J = 2.13$ Hz, 1 H), 3.93 (dd, $J = 7.02$ Hz, $J = 2.13$ Hz, 1 H), 3.78 (ddd, $J = 4.88$ Hz, $J = 2.44$ Hz, $J = 2.44$ Hz, 1 H), 3.68 (dd, $J = 10.38$ Hz, $J = 4.88$ Hz, 1 H), 3.58 (dd, $J = 10.38$ Hz, $J = 2.44$ Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.90, 138.09, 138.00, 137.70, 135.15, 129.50, 128.63, 128.45, 128.40, 128.33, 128.29, 128.08, 128.02, 127.84, 127.76, 127.73, 127.69, 127.64, 77.15, 76.04, 74.87, 73.97, 73.22, 73.18, 72.65, 72.29, 65.83, 61.57; IR (neat, cm^{-1}) 1680; HRMS (EI) exact mass calcd for $C_{41}H_{41}NO_6$ (M^+) 643.2934, found 643.2949; $[\alpha]^{24}_D$ −4.60° (*c* 1.07, $CHCl_3$).

1*N*-Benzyloxy-1-benzyloxy-3-phenylpropanimine (9): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34−7.13 (m, 15 H), 4.95 (s, 2 H), 4.92 (s, 2 H), 2.85 (m, 2 H), 2.74 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.47, 140.77, 138.07, 136.96, 128.54, 128.39, 128.33, 128.26, 128.19, 128.09, 127.64, 127.25, 126.11, 76.02, 71.49, 32.27, 32.20, IR (neat, cm^{-1}) 1638; HRMS (EI) exact mass calcd for $C_{23}H_{23}NO_2$ (M^+) 345.1729, found 345.1728.

1*N*,*N*-Benzylbenzyloxy-3-phenylpropanamide (10): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34−7.16 (m, 15 H), 4.79 (s, 2 H), 4.64 (s, 2 H), 2.95 (m, 2 H), 2.74 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.35, 141.20, 136.50, 134.46, 129.18, 128.88, 128.63, 128.52, 128.46, 128.42 (m), 127.62, 126.06, 77.21, 34.20, 30.62; IR (neat, cm^{-1}) 1665; HRMS (EI) exact mass calcd for $C_{23}H_{23}NO_2$ (M^+) 345.1729, found 345.1727.

General Procedure for Deoximation. A mixture of **11a** (24.3 mg, 0.038 mmol) and *p*-toluenesulfonic acid monohydrate (7.2 mg, 0.038 mmol) in 1 mL of acetone was stirred at room temperature for 4.5 h. The reaction was quenched by pouring it into a saturated $NaHCO_3$ aqueous solution. The aqueous layer was extracted with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4 and filtered, and the solvent was removed in vacuo. Purification by column chromatography on silica gel (hexane/AcOEt = 7:1) afforded 19.7 mg (97%) of **16**.

2,3,4,6-Tetra-*O*-benzyl-L-idono-1,5-lactone (16): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (m, 2 H), 7.30 (m, 16 H), 7.19 (m, 2 H), 5.04 (d, $J = 11.60$ Hz, 1 H), 4.63 (m, 2 H), 4.56 (m, 2 H), 4.56−4.52 (m, 1 H), 4.51 (d, $J = 11.60$ Hz, 1 H), 4.43 (d, $J = 11.90$ Hz, 1 H), 4.31 (d, $J = 11.90$ Hz, 1 H), 4.16 (d, $J = 6.41$ Hz, 1 H), 3.90 (m, 1 H), 3.78−3.74 (m, 2 H), 3.62 (dd, $J = 6.10$ Hz, $J = 3.66$ Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.40, 137.49, 137.37, 137.07, 136.96, 128.47, 128.44, 128.42, 128.40, 128.05, 128.02, 127.95, 127.92, 127.84, 127.82, 79.96, 78.55, 75.89, 75.25, 73.57, 73.30, 72.51, 71.43, 67.91; IR (KBr, cm^{-1}) 1750; HRMS (EI) exact mass calcd for $C_{34}H_{34}O_6$ (M^+) 538.2355, found 538.2362; mp 78 °C; $[\alpha]^{24}_D$ +32.5° (*c* 0.92, $CHCl_3$). Anal. Calcd for $C_{34}H_{34}O_6$: C, 75.82; H, 6.36. Found: C, 75.82; H, 6.46.

2,3,4,6-Tetra-*O*-benzyl-L-altrono-1,5-lactone (17): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34−7.23 (m, 20 H), 4.94 (d, $J = 11.60$ Hz, 1 H), 4.64 (d, $J = 11.60$ Hz, 1 H), 4.63 (d, $J = 11.30$ Hz, 1 H), 4.62 (d, $J = 11.60$ Hz, 1 H), 4.59−4.51 (m, 4 H), 4.46 (d, $J = 11.90$ Hz, 1 H), 4.24 (d, $J = 6.41$ Hz, 1 H), 4.14 (dd, $J = 6.41$ Hz, $J = 3.66$ Hz, 1 H), 4.01 (dd, $J = 3.66$ Hz, $J = 2.44$ Hz, 1 H), 3.70−3.63 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.77, 137.69, 137.65, 137.48, 137.31,

128.44, 128.40, 128.14, 127.99, 127.93, 127.90, 127.84, 127.78, 127.72, 127.65, 78.16, 75.72, 74.59, 73.60, 73.55, 72.83, 72.56, 72.18, 68.82; IR (neat, cm^{-1}) 1744; HRMS (EI) exact mass calcd for $C_{34}H_{34}O_6$ (M^+) 538.2355, found 538.2363; $[\alpha]^{24}_D$ +14.3° (*c* 1.01, $CHCl_3$). Anal. Calcd for $C_{34}H_{34}O_6$: C, 75.82; H, 6.36. Found: C, 75.44; H, 6.49.

2,3,4,6-Tetra-*O*-benzyl-L-gulono-1,5-lactone (18): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36−7.24 (m, 18 H), 7.01 (m, 2 H), 5.07 (d, J = 12.20 Hz, 1 H), 4.87−4.83 (m, 1 H), 4.82 (d, J = 11.90 Hz, 1 H), 4.64 (d, J = 12.20 Hz, 1 H), 4.59−4.54 (m, 2 H), 4.48 (d, J = 11.90 Hz, 1 H), 4.38 (d, J = 11.30 Hz, 1 H), 4.35 (d, J = 3.05 Hz, 1 H), 4.32 (d, J = 11.60 Hz, 1 H), 3.95 (dd, J = 3.05 Hz, J = 1.22 Hz, 1 H), 3.78 (dd, J = 2.44 Hz, J = 1.22 Hz, 1 H), 3.74−3.66 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.41, 137.68, 137.62, 136.99, 128.51, 128.47, 128.44, 128.40, 128.15, 128.11, 127.95, 127.92, 127.88, 127.84, 127.80, 77.58, 75.63, 74.16, 73.80, 73.68, 73.58, 73.42, 72.99, 67.45; IR (neat, cm^{-1}) 1757; HRMS (EI) exact mass calcd for $C_{34}H_{34}O_6$ (M^+) 538.2356, found 538.2354; $[\alpha]^{24}_D$ −75.3° (*c* 1.04, $CHCl_3$). Anal. Calcd for $C_{34}H_{34}O_6$: C, 75.82; H, 6.36. Found: C, 75.68; H, 6.49.

General Procedure for Reduction. To a solution of **16** (132.8 mg, 0.25 mmol) in 2.5 mL of CH_2Cl_2 at −78 °C was added DIBAL-H (1.7 mL of 0.59 M solution in *n*-hexane, 3.0 mmol). The resulting mixture was stirred at that temperature for 20 min. The reaction was quenched with a saturated Rochelle salt aqueous solution and extracted with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4 and evaporated in vacuo. Purification by column chromatography on silica gel (hexane/AcOEt = 3:1) afforded 132.2 mg (99%) of **19**.

2,3,4,6-Tetra-*O*-benzyl-L-idose (19): ^{1}H NMR (400 MHz, $CDCl_3$) δ, α 7.61−7.03 (m, 20 H), 5.18 (dd, J = 9.9 Hz, J = 2.6 Hz, 1 H), 4.68−4.45 (m, 8 H), 4.33 (m, 1 H), 3.92 (d, J = 9.9 Hz, 1 H), 3.75−3.65 (m, 3 H), 3.56 (t, J = 4.7 Hz, 1 H), 3.38 (m, 1 H), β 7.61−7.03 (m, 20 H), 4.92 (dd, J = 12.21 Hz, J = 2.14 Hz, 1 H), 4.68−4.45 (m, 8 H), 4.05 (ddd, J = 6.41 Hz, J = 6.41 Hz, J = 2.14 Hz, 1 H), 3.93 (d, J = 12.21 Hz, 1 H), 3.75−3.65 (m, 3 H), 3.45 (m, 1 H), 3.38 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ, α 138.01, 137.88, 137.58, 137.26, 128.55−127.60 (m), 92.35, 74.99, 73.48, 73.11, 72.90, 72.89, 72.43, 72.40, 68.84, β 138.13, 138.01, 137.93, 137.23, 128.55−127.60 (m), 93.85, 75.58, 74.25, 73.71, 73.44, 73.34, 72.78, 72.68, 68.73, 67.02; HRMS (FAB) exact mass calcd for $C_{34}H_{36}O_6Na$ $(M + Na)^+$ 563.2410, found 563.2403; $[\alpha]^{24}_D$ −3.90° (*c* 2.40, $CHCl_3$).

2,3,4,6-Tetra-*O*-benzyl-L-altrose (20): ^{1}H NMR (400 MHz, $CDCl_3$) δ, major 7.61−7.03 (m, 20 H), 5.05 (m, 1 H), 4.72 (d, J = 11.0 Hz, 1 H), 4.56−4.44 (m, 7 H), 4.25 (ddd, J = 10.07 Hz, J = 4.28 Hz, J = 2.13 Hz, 1 H), 3.99 (dd, J = 10.07 Hz, J = 2.74 Hz, 1 H), 3.90 (m, 1 H), 3.85−3.70 (m, 2 H), 3.60 (m, 2 H), minor 7.61−7.03 (m, 20 H), 5.05 (m, 1 H), 4.69−4.35 (m, 8 H), 4.06 (ddd, J = 9.76 Hz, J = 3.36 Hz, J = 3.36 Hz, 1 H), 3.86−3.72 (m, 4 H), 3.56 (br, 1 H), 3.48 (dd, J = 3.96 Hz, J = 1.83 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ, major 138.45, 138.01, 137.68, 137.10, 128.59−127.42 (m), 93.05, 74.92, 74.65, 74.04, 73.58, 72.31, 72.17, 71.89, 69.34, 67.19, minor 138.37, 138.12, 138.06, 137.52, 128.59−127.42 (m), 91.88, 77.20, 76.82, 73.21, 73.13, 72.68, 72.57, 72.49, 71.99, 69.44; HRMS (FAB) exact mass calcd for $C_{34}H_{36}O_6Na$ $(M + Na)^+$ 563.2409, found 563.2404; $[\alpha]^{24}_D$ −8.64° (*c* 1.10, $CHCl_3$). Anal. Calcd for $C_{34}H_{36}O_6$: C, 75.53; H, 6.71. Found: C, 75.13; H, 6.83.

2,3,4,6-Tetra-*O*-benzyl-L-gulose (21): ^{1}H NMR (400 MHz, $CDCl_3$) δ, major 7.33−7.11 (m, 20 H), 5.23 (m, 1 H), 4.65−4.33 (m, 10 H), 3.84 (br, 1 H), 3.80 (t, J = 3.30 Hz, 1 H), 3.63−3.58 (m, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ, major 138.07, 137.88, 137.72, 137.09, 128.51−127.62 (m), 92.73, 75.09, 74.21, 74.10, 73.38, 73.03, 71.94, 70.75, 68.32, 64.52, minor 138.48, 138.26, 137.98, 137.83, 128.51−127.62 (m), 94.60, 77.64, 74.86, 74.24, 73.46, 73.17, 72.89, 72.67, 72.16, 68.94; HRMS (EI) exact mass calcd for $C_{34}H_{36}O_6$ (M^+) 540.2512, found 540.2498; $[\alpha]^{24}_D$ −8.20° (*c* 1.48, $CHCl_3$). Anal.Calcd for $C_{34}H_{36}O_6$: C, 75.53; H, 6.71. Found: C, 75.39; H, 6.84.

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Supporting Information Available: X-ray structural data for **16** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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