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Divergent Synthesis of L-Sugars and L-Iminosugars from D-Sugars

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Abstract: An efficient divergent synthesis of L-sugars and L-iminosugars from D-sugars is described. The important intermediate, δ-hydroxyalkoxamate, prepared from D-glucono-/galactono-1,5-lactone, was cyclized under Mitsunobu conditions to give the O-cyclized oxime compound and the N-cyclized lactam compound as mixtures. A more detailed investigation revealed that the appropriate protecting groups and solvents controlled the specificity for the O-/N-cyclization of the δ-hydroxyalkoxamate. Suitable protection at the 6-position of δ-hydroxyalkoxamate, derived from D-glucono-1,5-lactone, afforded the corresponding O-alkylation product alone. Thus we succeeded in applying this to the total synthesis of L-iduronic acid. In contrast, with both TBDMS as the protecting group and RCN as the solvent the efficient conversion of D-glucono/galactono-1,5-lactone into the corresponding L-iminosugars (L-idonolactam and L-altronolactam) was achieved.

Keywords: azasugars · carbohydrates · lactams · lactones · Mitsunobu reaction

Introduction

While D-sugars are abundant in nature and frequently used as chiral resources in the synthesis of complex natural products, L-sugars are rare and have been overlooked in synthetic organic chemistry. L-Sugars, however, play important roles in the microbial world. They are key constituents of antibiotics,[1] oligosaccharides,[2–3] and clinically useful nucleosides.[4–6] To take notable examples, L-gulose is a key building block of the carbohydrate moiety of the antitumor antibiotic bleomycin A_2[7–14] and L-iduronic acid is also a typical component of mammalian dermatan sulfate, heparan sulfate, and heparin.[15–18] As the requirement for L-sugars increases in scientific fields, it becomes necessary to develop an efficient method that makes them readily available and thus numerous synthetic routes for L-sugars have been reported recently.[19–36]

As a part of our program for the utilization of sugar derivatives as synthetic tools,[37–41] we became interested in the cyclization of hydroxyalkoxamates derived from natural D-sugars. In fundamental research, efficient biomimetic methods for β-lactam syntheses were developed based on the intramolecular N-alkylation of β-hydroxyalkoxamates derived from amino acids.[42–45] In contrast, recent studies have revealed that competitive O-alkylation occurs in several cases with amides and carbamates.[46–52] We have therefore investigated the intramolecular cyclization of δ-hydroxyalkoxamates derived from D-glycono-1,5-lactone under Mitsunobu conditions.[53] It was found that the cyclization of δ-hydroxyalkoxamates derived from D-glycono-1,5-lactone resulted mainly in O-alkylation rather than N-alkylation. Taking advantage of the structural relationships between D-glucose and L-idose, D-galactose and L-altrose, and D-mannose and L-gulose, we utilized the O-alkylated products, which had inverted stereochemistry at C5, as precursors for the corresponding L-sugars (Scheme 1).[54]

While these results were successfully applied to the novel and practical synthesis of rare L-sugars, we continued to investigate methods by which N-cyclized products could be converted into precursors for the corresponding L-iminosugars. Here we describe the divergent synthesis of L-sugars and L-iminosugars based on the specifically controlled O-/N-alkylation of δ-hydroxyalkoxamate.

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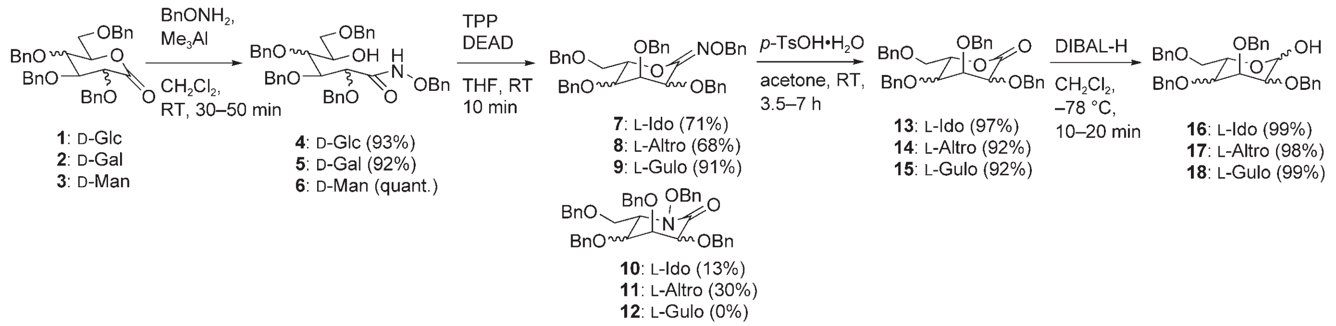
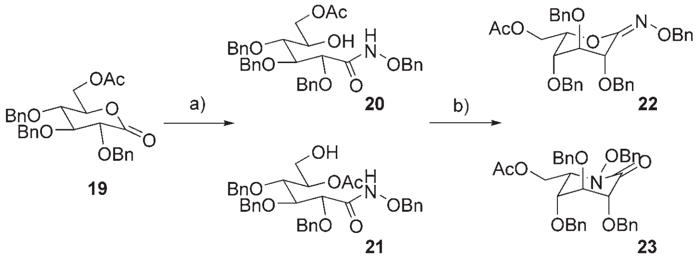


Scheme 1. Synthesis of L-pyranose from D-glycono-1,5-lactone.

Results and Discussion

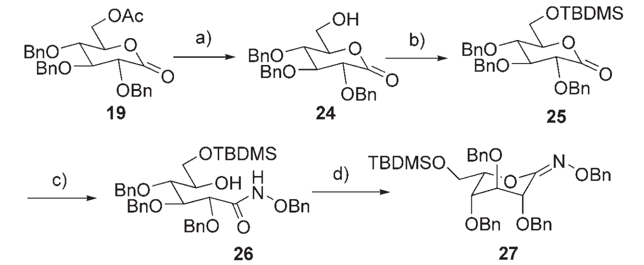
An approach to L-iduronic acid: As an extension of the previous work, we first reconsidered O-cyclization from a synthetic point of view. In this case, we focused on the synthesis of L-iduronic acid. Thus it was necessary to protect O6 of D-glucono-1,5-lactone, so that subsequent oxidation of C6 could take place to provide uronic acid. Initially, the 6-acetylated lactone **19**[55] was examined (Scheme 2).



Scheme 2. Cyclization of 6-acetyloxy-δ-hydroxyalkoxamate. a) BnONH$_2$, Me$_3$Al, CH$_2$Cl$_2$, −40 °C, 1 h, 52 % (**20**/**21** 30:1); b) DEAD, TPP, THF, RT, 10 min, 96 % (**22**/**23** 2.5:1); DEAD = diethylazodicarboxylate; TPP = triphenylphosphine.

Treatment of **19** with BnONH$_2$ and Me$_3$Al at 0 °C preferentially afforded δ-hydroxyalkoxamate **21** with the expected product **20** (**20**/**21** 1:3.9). To control the migration reaction, several conditions were examined. It was found that a lower temperature (−40 °C) decreased the migration of the acetyl group and gave **20** selectively (**20**/**21** 30:1). Although **20** easily cyclized under Mitsunobu conditions, moderate selectivity for O-cyclization was observed (96 % yield, **22**/**23** 2.5:1). Variations in the reaction conditions did not significantly change the O-/N-alkylation ratio. As satisfactory results were not obtained with the 6-acetylated lactone, the protecting group at O6 was changed to TBDMS (Scheme 3).

The 6-acetylated lactone **19** was hydrolyzed under basic conditions to give **24**,[56] which was successively protected at O6 with TBDMS. Alkoxyamidation of **25** proceeded smoothly and the expected δ-hydroxyalkoxamate **26** was obtained in 92 % yield. Exceeding our expectations, **26** cyclized easily under Mitsunobu conditions to give **27** as the sole

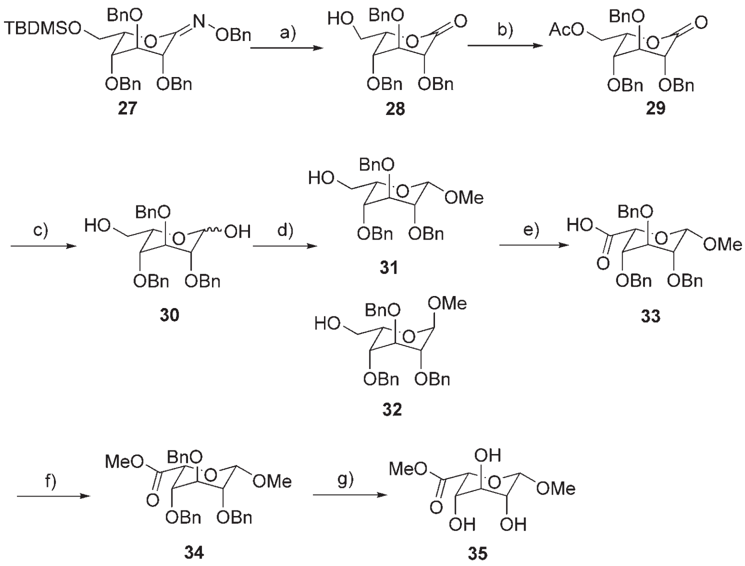


Scheme 3. Cyclization of 6-siloxy-δ-hydroxyalkoxamate. a) K$_2$CO$_3$, MeOH, 0 °C, 2 h, 87 %; b) TBDMSCl, imidazole, DMF, RT, 2 h, 85 %; c) BnONH$_2$, Me$_3$Al, CH$_2$Cl$_2$, RT, 1.5 h, 92 %; d) TPP, DEAD, THF, RT, 10 min, 95 %; TBDMS = *tert*-butyldimethylsilyl.

product in 95 % yield. No N-cyclized product was detected in this case. The modification at the 6-position might affect the stability of the intermediate, which leads to O-cyclization. So far we have only limited information on this specificity for O-cyclization, although it should be investigated in detail in future. After we had confirmed that O-cyclized **27** was obtained in good yield, the next step was to complete the synthesis of L-iduronic acid (Scheme 4).

The O-cyclized compound **27** was hydrolyzed under acidic conditions to give L-idonolactone **28**. Acetylation of **28** and the successive reduction of **29** with DIBAL-H gave L-idose **30** as an anomeric mixture. L-Idose **30**[57] was treated with MeOH under acidic conditions to give methyl L-idosides **31** and **32** (**31**/**32** 2.2:1). Oxidation of the β-anomer **31**[58] with chromium trioxide/H$_2$SO$_4$ (Jones reagent), followed by esterification of the intermediate acid provided methyl uronate **34**[59,60] in 72 % yield. Finally, **34** was hydrogenolyzed with Pd(OH)$_2$/C to give unprotected methyl uronate **35**.[60] Thus the synthesis of L-iduronic acid from D-glucono-1,5-lactone was achieved.

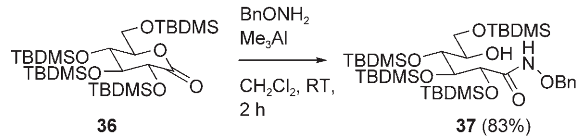
N-Cyclization of D-glucono/galactono-1,5-lactones: Since D-iminosugars (for example, Nojirimycin) were discovered to be potent glycosidase inhibitors in nature, numerous studies have been performed to develop effective procedures for the synthesis of various D-iminosugars and analogues.[61–71] What appears lacking, however, is the synthesis of L-iminosugars,[72] which are enantiomers of D-iminosugars. To apply



Scheme 4. Synthesis of L-iduronic acid. a) TsOH, acetone, RT, 6 h, 79 %; b) Ac_2O, pyridine, RT, 0.5 h, 99 %; c) DIBAL-H, CH_2Cl_2, RT, 14 min, 88 %; d) sat. HCl/MeOH, 50 °C, 5 h, 97 % (**31**/**32** 2.2:1); e) CrO_3/H_2SO_4 RT, 1.5 h; f) CH_2N_2, Et_2O, 0 °C, 3 h, 72 % (from **31**); g) $Pd(OH)_2$/C, H_2, MeOH, RT, 22 h, quant; Ts = *p*-toluenesulfonyl; DIBAL-H = diisobutylaluminium hydride.

divergent cyclization to the synthesis of L-iminosugars, it is necessary to increase the ratio of the N-cyclized product, which is a precursor of L-iminosugars. In the beginning, we focused on the effects of the solvent on the cyclization of the benzyl-protecting δ-hydroxyalkoxamate **4**,[73] derived from D-glucono-1,5-lactone (Table 1). The reaction was carried out with DEAD (3.0 equiv) and TPP (3.0 equiv) in a suitable solvent at room temperature. Although the reactions proceeded efficiently, contrary to our expectations the O-cyclized compound **7** rather than the N-cyclized compound **10** was obtained in all cases. In particular, toluene gave the optimum ratio of O-alkylation (Table 1, entry 1). CH_2Cl_2, DMSO, and cyclohexane gave similar results (entries 3–5), although C_6F_6, EtCN, and MeCN gave the best ratios of N-alkylation among the various solvents examined (entries 6–8).

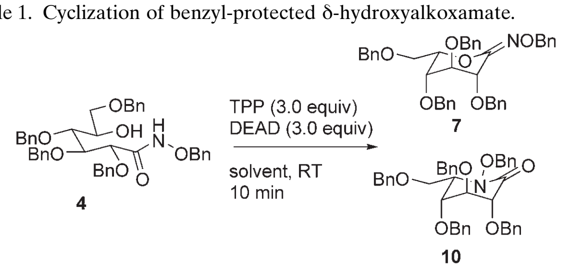
In expectation of the steric effect of the bulky protecting group, we next examined the replacement of the benzyl-protecting group in **4** with TBDMS. The δ-hydroxyalkoxamate **37**, derived from silyl-protecting D-glucono-1,5-lactone **36**,[74] was prepared according to the previous procedure (Scheme 5). Treatment of **36** with *O*-benzylhydroxyamine in CH_2Cl_2 for 30 minutes, followed by the addition of Me_3Al at room temperature afforded the corresponding δ-hydroxybenzyloxamate **37** in 83 % yield. A summary of solvent effects in the cyclization of **37** under Mitsunobu conditions is shown in Table 2.[75]



Scheme 5. Me_3Al-mediated amidation of silyl-protected D-glucono-1,5-lactone.

With bulky TBDMS-protecting groups, the effects of solvent were seen more clearly than with other protectors. While a higher ratio of O-cyclization was observed with C_6F_6 and toluene (Table 2, entries 1 and 2), N-cyclization preferentially occurred with CH_2Cl_2, DMSO, MeCN, and EtCN (entries 5–8). In particular, an excellent ratio of **39** was obtained with RCN as the solvent (entries 7 and 8). It is noteworthy that the effects of RCN on N-cyclization were

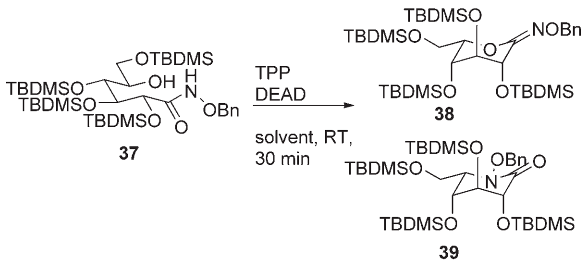
Table 1. Cyclization of benzyl-protected δ-hydroxyalkoxamate.



Entry	Solvent	Yield of **7** [%][a]	Yield of **10** [%][a]	Ratio of **7**/**10**[b]
1	toluene	78	10	7.8:1
2	THF	71	13	5.5:1
3	CH_2Cl_2	67	28	2.4:1
4	DMSO	64	28	2.3:1
5	cyclohexane	64	28	2.3:1
6	C_6F_6	55	31	1.8:1
7	EtCN	54	30	1.8:1
8	MeCN	40	23	1.7:1

[a] Isolated yield. [b] The ratio was based on isolated yields.

Table 2. Cyclization of TBDMS-protected δ-hydroxybenzyloxamate **37**.



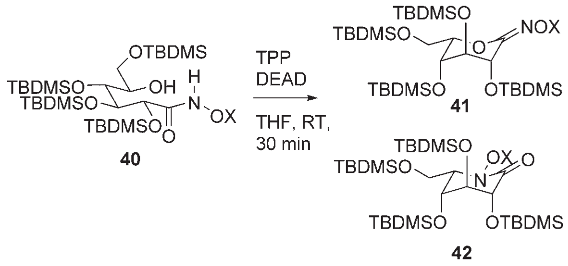
Entry	Solvent	Yield [%][a]	Ratio of **38**/**39**[b]
1	C_6F_6	78	27:1.0
2	toluene	71	22:1.0
3	cyclohexane	50	5.7:1.0
4	THF	79	1.6:1.0
5	CH_2Cl_2	62	1.0:1.6
6	DMSO	63	1.0:1.7
7	MeCN	61	1.0:4.1
8	EtCN	73	1.0:6.6

[a] Isolated yield. [b] The ratio was determined by using NMR spectroscopic analysis.

seen in several cases (Table 1, entries 7 and 8; Table 2, entries 7 and 8). One explanation for these results may be that both bulky TBDMS-protecting groups and coordination of the cyano group of RCN affect the conformation of the intermediate that is suitable for N-cyclization.

We further extended this to alkoxamate. To determine the steric effect of the substitution of a hydroxamate, studies on the formation of O-/N-alkylation products with various O-substituted hydroxamate derivatives (**40a–d**) were carried out (Table 3).[76]

Table 3. Effects of the alkoxy moiety of hydroxamate on the cyclization.



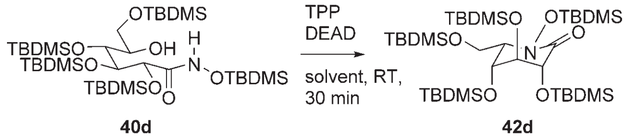
Entry	X[a]	Yield [%][b]	Ratio of **41**/**42**[c]
1	Me **40a**	99	1.3:1.0
2	Et **40b**	76	1.0:1.2
3	*t*Bu **40c**	56	1.0:1.3
4	TBDMS **40d**	69	1.0:1.8

[a] X denotes the alkoxamate-protective group. [b] Isolated yield. [c] The ratio was determined by using NMR spectroscopic analysis.

Whilst the cyclization of **40a** provided the O-alkylated product **41a** rather than the N-alkylated **42a** (Table 3, entry 1), cyclization of **40b–d** resulted mainly in N-alkylated **42b–d**[77] (entries 2–4). The results indicate that the steric requirement of the hydroxamate moiety partly affected the ratios of O-/N-alkylation: better selectivity for N-alkylation was observed with the bulky TBDMS group (entry 4).

Considering the results obtained, we finally determined the best approach to the N-cyclized product (Table 4). In the optimized run, DEAD (8.0 equiv) and TPP (8.0 equiv) were added at room temperature to a solution of the δ-hydroxyalkoxamate **40d** in EtCN, which provided the N-cyclized product **42d** in 81% yield with complete selectivity (Table 4, entry 4).

Table 4. Cyclization of the fully TBDMS-protected δ-hydroxyalkoxamate.



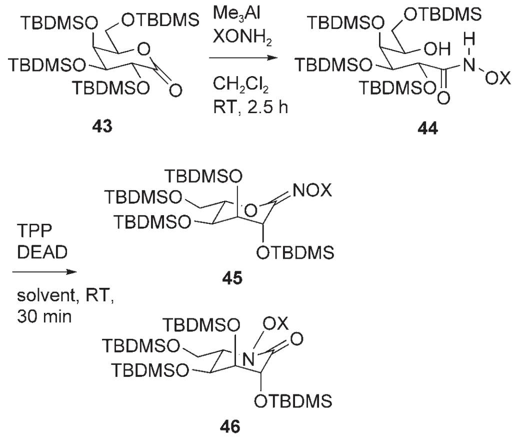
Entry	Solvent	TPP [equiv]	DEAD [equiv]	Yield [%][a]
1	MeCN	6.0	6.0	61
2		8.0	8.0	78
3	EtCN	6.0	6.0	78
4		8.0	8.0	81

[a] Isolated yield.

After we had established efficient conditions for the N-cyclization of δ-hydroxyalkoxamate derived from D-glucono-1,5-lactone, we examined the cyclization of D-galactono-1,5-lactone. The TBDMS-protected δ-hydroxyalkoxamate **44** derived from D-galactono-1,5-lactone **43**[61] was employed in this cyclization.

As observed in the case of D-glucose, the TBDMS-protecting group along with RCN as solvent increased the ratio of N-cyclization (Table 5). Better selectivity for N-cyclization was observed for the reaction of **44b** in RCN (Table 5, entries 5, and 6).

Table 5. Cyclization of TBDMS-protected δ-hydroxyalkoxamate derived from D-galactono-1,5-lactone **43**.



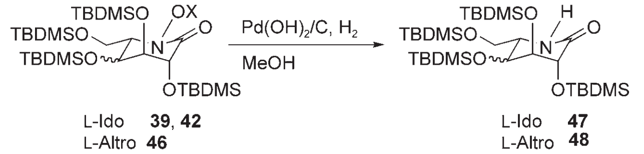
Entry	X[a]	Solvent	Yield [%][b]	**45**/**46**[c]
1	Bn **44a**	THF	80	1.6:1.0
2		MeCN	73	1.0:1.7
3		EtCN	82	1.0:3.3
4	TBDMS **44b**	THF	69	1.0:1.2
5		MeCN	80	1.0:7.1
6		EtCN	75	1.0:7.8

[a] X denotes the alkoxamate-protective group. [b] Isolated yield. [c] The ratio was determined by using NMR spectroscopic analysis.

As previously reported, the δ-hydroxyalkoxamate **6** derived from D-mannono-1,5-lactone **3** afforded the O-alkylated product as the sole product in excellent yield (Scheme 1). We further investigated the cyclization of γ-hydroxyalkoxamates derived from readily available D-mannono-1,4-lactone, but only the O-alkylation product was obtained. It is noteworthy that no effect from the solvent and protecting group was observed and hence no N-alkylation product was detected in any case. It appears characteristic of D-mannose derivatives to show this strange specificity for O-alkylation. While this unique feature of mannose was successfully applied to the synthesis of L-ribose from D-mannono-1,4-lactone,[78] we reluctantly abandoned attempts to obtain N-alkylated products from D-mannose derivatives.

Synthesis of L-iminosugars: To synthesize L-iminosugars, we next examined the reduction of the N-alkylated products. Of the methods examined, hydrogenolysis by using $Pd(OH)_2/C$ as a catalyst gave the best results. Thus L-idonolactam **47**[79,80] and L-altronolactam **48**[80] were obtained in good yields (Table 6).

Table 6. Reduction of N-cyclization products.



Entry	X[a]	Yield [%][b]
1	Bn **39**	**47** 83
2	Me **42a**	84
3	Et **42b**	86
4	*t*Bu **42c**	78
5	TBDMS **42d**	76
6	Bn **46a**	**48** 86
7	TBDMS **46b**	79

[a] X denotes the alkoxamate-protective group. [b] Isolated yield.

Conclusions

We have established a divergent synthesis of L-sugars and L-iminosugars based on the O/N-alkylation of δ-hydroxyalkoxamates derived from D-sugars. It was found that the TBDMS protection at position 6 of δ-hydroxyalkoxamates derived from D-glucono-1,5-lactones leads to complete O-cyclization, which is the key step in the synthesis of L-iduronic acid. In the synthesis of L-iminosugars, both the use of bulkier TBDMS as the protecting group and RCN as the solvent are the key to the N-cyclization of D-glucose/galactose derivatives. The N-alkylation products obtained could be converted into various analogues of L-iminosugars, which may represent an appealing route to potential glycosidase inhibitors.[55] Unfortunately, we have not yet developed any means to achieve N-cyclization in the case of D-mannose. However, such complete selectivity for O-cyclization allows us to synthesize L-gulose and L-ribose derivatives efficiently. It should be emphasized that the divergent conversion of commercially available D-sugars into valuable L-sugars and L-iminosugars could benefit various studies in the field of medicinal chemistry.

Experimental Section

General experimental: Melting points were determined with a Yanagimoto micro melting point apparatus and are uncorrected. IR spectra were measured with a JASCO FTIR-8000 spectrometer. HRFABMS were taken with a JEOL SX-102A spectrometer. ^{1}H and ^{13}C NMR spectra were recorded with 400 and 600 MHz pulse Fourier transform NMR spectrometers (JEOL AL-400, JEOL ECP-600) in $CDCl_3$ solution with TMS as an 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 by using Merck silica gel 60N (100–210 μm). All anhydrous solvents were purified according to standard methods.

General procedure for the cyclization of δ-hydroxyalkoxamates: A mixture of **4** (504 mg, 0.76 mmol), triphenylphosphine (594 mg, 2.27 mmol), and DEAD (0.36 mL, 2.27 mmol) in THF (7.6 mL) was stirred at room temperature for 30 min. After this time, the solvent was removed in vacuo. The residue was chromatographed on silica gel (hexane/AcOEt 7:1) to give **7** (346 mg, 71 %) and **10** (63 mg, 13 %).

General procedure for hydroxyamination: A mixture of **1** (50 mg, 0.093 mmol) and benzylhydroxyamine (44.6 mg, 0.36 mmol) in CH_2Cl_2 (2 mL) was stirred at room temperature for 30 min and then a solution of trimethylaluminum (0.34 mL of a 1.08 M solution in *n*-hexane, 0.36 mmol) was added. The resulting solution was stirred at room temperature for a period of 1 h. After this time, 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, filtered, and the solvemt was removed in vacuo. Purification by silica-gel chromatography (hexane/AcOEt 3:1) gave **4** (57.1 mg, 93 %).

6-*O*-Acetyl-1*N*-benzyloxy-2,3,4-tribenzyloxy-5-hydroxy-(2*R*,3*R*,4*R*,5*R*)-hexanamide (20) and 5-*O*-acetyl-1*N*-benzyloxy-2,3,4-tribenzyloxy-6-hydroxy-(2*R*,3*R*,4*R*,5*R*)-hexanamide (21): A mixture of **19** (51.9 mg, 0.106 mmol) and benzylhydroxyamine (26.3 mg, 0.212 mmol) in CH_2Cl_2 (2 mL) was stirred at room temperature for 30 min and then a solution of trimethylaluminum (0.196 mL of 1.08 M solution in *n*-hexane, 0.212 mmol) was added at −40 °C. The resulting solution was stirred at −40 °C for a period of 1 h. After this time, 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, filtered, and the solvent was removed in vacuo. Purification by silica-gel chromatography (hexane/AcOEt 3:1) gave products **20**/**21** 30:1 (33.7 mg, 52 %).

*Compound (**20**)*: $[\alpha]_D^{24} = +58.5$ (c = 1.10 in $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.92 (s, 1H), 7.38–7.25 (m, 20H), 4.89 (s, 2H), 4.66 (d, J = 11.0 Hz, 1H), 4.61 (d, J = 11.0 Hz, 1H), 4.56 (d, J = 11.0 Hz, 1H), 4.46 (d, J = 11.0 Hz, 1H), 4.44 (d, J = 11.0 Hz, 1H), 4.41 (d, J = 11.0 Hz, 1H), 4.30 (d, J = 2.8 Hz, 1H), 4.28 (dd, J = 2.8, 11.5 Hz, 1H), 4.09 (dd, J = 2.8, 5.5 Hz, 1H), 4.08 (dd, J = 5.5, 11.5 Hz, 1H), 3.91 (ddd, J = 2.5, 5.5, 7.7 Hz, 1H), 3.70 (dd, J = 5.5, 7.7 Hz, 1H), 2.98 (s, 1H), 2.04 ppm (s, 3H); ^{13}C NMR (150 MHz, CD_3OD): δ = 171.1, 169.4, 137.4, 136.0, 135.2, 128.9, 128.8, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 128.0, 79.6, 77.0, 76.8, 76.4, 75.1, 73.8, 74.0, 70.4, 65.6, 20.9 ppm; IR (neat): $\tilde{\nu}$ = 3387, 1738, 1684 cm^{-1}; HRMS (FAB-Gly+NaI): calcd for $C_9H_{17}O_6$: 617.2754; found: 617.2749.

*Compound (**21**)*: $[\alpha]_D^{28} = +44.2$ (c = 1.10 in $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.89 (s, 1H), 7.23–7.41 (m, 20H), 4.95 (ddd, J = 2.8, 3.9, 6.1 Hz, 1H), 4.88 (s, 2H), 4.76 (d, J = 11.5 Hz, 1H), 4.70 (d, J = 10.4 Hz, 1H), 4.66 (d, J = 11.5 Hz, 1H), 4.58 (d, J = 10.4 Hz, 1H), 4.50 (d, J = 11.0 Hz, 1H), 4.43 (d, J = 11.0 Hz, 1H), 4.17 (d, J = 3.3, 1H), 4.02 (dd, J = 2.8, 7.7 Hz, 1H), 4.00 (dd, J = 3.3, 7.7 Hz, 1H), 3.93 (dd, J = 3.9, 12.1 Hz, 1H), 3.88 (dd, J = 6.1, 12.1 Hz, 1H), 1.99 ppm (s, 3H); ^{13}C NMR (150 MHz, CD_3OD): δ = 170.5, 138.0, 137.9, 137.1, 135.2, 129.2, 129.0, 128.9, 128.8, 128.7, 128.6, 128.5, 128.3, 128.2, 128.0, 80.8, 78.2, 79.2, 74.2, 74.0, 73.3, 70.4, 65.7, 62.3, 20.1 ppm; IR (neat): $\tilde{\nu}$ = 3393, 1736, 1680 cm^{-1}; HRMS (FAB-Gly+NaI): calcd for $C_9H_{16}O_6Na$: 636.2574; found: 636.2581.

2*N*-Benzyloxy-3,4,5-tris(benzyloxy)-6-acetoxymethyl-(3*R*,4*S*,5*R*,6*S*)-tetrahydo-2*H*-pyran-2-imine (22) and 1,3,4,5-tetrakis(benzyloxy)-6-acetoxymethyl-(3*R*,4*S*,5*R*,6*S*)-tetrahydropyridine-2(1*H*)-one (23): Compound **20** (271 mg, 0.442 mmol) was converted into products **22**/**23** 2.5:1 (251 mg, 0.422 mmol, 96 %).

*Compound (**22**)*: M.p. 108 °C (hexane/AcOEt); $[\alpha]_D^{24} = +2.30$ (c = 1.00 in $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.42–7.22 (m, 20H), 5.09 (s, 2H), 4.72 (d, J = 11.5 Hz, 1H), 4.64 (d, J = 12.1 Hz, 1H), 4.59 (d, J = 12.1 Hz, 1H), 4.49 (d, J = 11.5 Hz, 1H), 4.48 (m, 1H), 4.43 (dd, J = 7.2, 11.6 Hz, 1H), 4.42 (d, J = 12.1 Hz, 1H), 4.38 (dd, J = 4.4, 11.6 Hz, 1H), 4.37 (d, J = 12.1, 1H), 4.07 (d, J = 5.0, 1H), 3.88 (dd, J = 4.4, 5.0 Hz, 1H), 3.67 (dd, J = 2.8, 4.4 Hz, 1H), 1.99 ppm (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.6, 149.4, 138.3, 137.4, 137.2, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 77.9, 76.8, 75.1, 71.6, 77.0, 74.9, 74.6, 71.7, 62.8, 20.8 ppm; IR (KBr): $\tilde{\nu}$ = 1744, 1645 cm^{-1}; HRMS (EI): calcd for $C_{36}H_{37}NO_7$: 595.2570; found: 595.2582.

*Compound (**23**)*: $[\alpha]_D^{24}$ = +26.4 (*c* = 1.00 in $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.42–7.19 (m, 20H), 5.27 (d, *J* = 11.0 Hz, 1H), 4.92 (d, *J* = 11.0 Hz, 1H), 4.86 (d, *J* = 11.0 Hz, 1H), 4.79 (d, *J* = 11.0 Hz, 1H), 4.75 (s, 2H); 4.54 (d, *J* = 11.5 Hz, 1H), 4.49 (d, *J* = 3.3, 11.5 Hz, 1H), 4.42 (d, *J* = 11.5 Hz, 1H), 4.12 (dd, *J* = 2.2, 11.5 Hz, 1H), 3.98–3.94 (m, 2H), 3.62 (m, 1H), 3.39 (ddd, *J* = 2.2, 3.3, 5.5 Hz, 1H), 1.97 ppm (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.1, 169.0, 138.1, 137.2, 135.2, 129.6, 128.9, 128.6, 128.5, 128.3, 128.1, 128.0, 84.5, 79.2, 77.2, 75.7, 75.0, 74.9, 73.3, 64.2, 58.1, 20.8 ppm; IR (neat): $\tilde{\nu}$ = 1748, 1703 cm^{-1}; HRMS (EI): calcd for $C_{36}H_{37}NO_7$: 595.2570; found: 595.2566.

2,3,4-Tri-*O*-benzyl-6-*O*-[*tert*-butyl(dimethyl)silyl]-D-glucono-1,5-lactone (25): Imidazole (31.8 mg, 0.467 mmol) and TBDMSCl (70.42 mg, 0.467 mmol) were added to a solution of **24** (69.8 mg, 0.156 mmol) in DMF (1.5 mL) at 0 °C. The solution was stirred at RT for 2 h and was then poured into water. The aqueous layer was extracted with CH_2Cl_2 and the combined organic extracts were dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by chromatography on silica gel with (hexane/AcOEt 3:1) to give the lactone compound **25** (74.8 mg, 0.133 mmol, 85.4 %). $[\alpha]_D^{24}$ = +76.0 (*c* = 1.00 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.27–7.11 (m, 15H); 4.87 (s, 2H); 4.89 (d, *J* = 11.2 Hz, 1H); 4.64 (d, *J* = 10.8 Hz, 1H); 4.28 (d, *J* = 11.2 Hz, 1H); 4.54–4.47 (m, 3H); 4.16 (m, 1H); 3.94 (d, *J* = 7.2 Hz, 1H); 3.83 (dd, *J* = 7.2, 7.2 Hz, 1H); 3.78 (dd, *J* = 7.2, 7.2 Hz, 1H); 3.73 (dd, *J* = 2.4, 11.6 Hz, 1H); 3.65 (dd, *J* = 2.4, 11.6 Hz, 1H); 0.74 (s, 9H); −0.08 ppm (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 169.6, 137.7, 137.6, 137.1, 128.5, 128.5, 128.4, 128.3, 128.1, 128.1, 128.0, 127.9, 81.0, 79.4, 77.8, 75.7, 74.2, 74.05, 73.92, 61.62, 25.83, 18.24, −5.48, −5.28 ppm. IR (neat): $\tilde{\nu}$ = 1757 cm^{-1}; HRMS (EI): calcd for $C_{33}H_{42}O_6Si$: 562.2751; found: 562.2775.

1*N*-Benzyloxy-2,3,4-tribenzyloxy-6-*tert*-butyldimethylsilyloxy-5-hydroxy-(2*R*,3*S*,4*R*,5*R*)-hexanamide (26): Compound **25** (30.9 mg, 0.06 mmol) was converted into **26** (34.6 mg, 0.05 mmol, 92 %). $[\alpha]_D^{24}$ = +29.4 (*c* = 1.00 in EtOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36–7.13 (m, 20H), 4.87 (s, 2H), 4.78 (d, *J* = 11.6 Hz, 1H), 4.70 (d, *J* = 10.8 Hz, 1H), 4.56 (m, 2H), 4.46 (s, 2H), 4.32 (d, *J* = 3.6 Hz, 1H), 4.06 (dd, *J* = 3.6, 6.0 Hz, 1H), 3.80 (dd, *J* = 6.0, 7.6 Hz, 1H), 3.76 (d, *J* = 3.2, 9.6 Hz, 1H), 3.72 (m, 1H); 3.62 (dd, *J* = 5.2, 9.6 Hz, 1H), 0.90 (s, 9H), 0.07 (s, 3H), 0.06 ppm (s, 3H); ^{13}C NMR (150 MHz, [D$_6$]acetone): δ = 168.78, 138.24, 137.64, 136.59, 135.37, 128.94, 128.66, 128.61, 128.51, 128.49, 128.40, 128.38, 128.33, 128.19, 128.01, 127.85, 127.67, 80.83, 79.60, 78.15, 77.69, 75.59, 74.33, 73.78, 72.19, 64.04, 25.90, 18.41, −5.37, −5.31 ppm. IR (neat): $\tilde{\nu}$ = 3378, 1680 cm^{-1}; HRMS (FAB-NBA+NaI): calcd for $C_{40}H_{51}O_7NSiNa$: 708.3332; found: 708.3328.

2*N*-Benzyloxy-3,4,5-tris(benzyloxy)-6-*tert*-butyldimethylsilyloxymethyl-(3*R*,4*S*,5*R*,6*S*)-tetrahydro-2*H*-pyran-2-imine (27): Compound **26** (32.6 mg, 0.05 mmol) was converted into **27** (30.3 mg, 0.045 mmol, 95 %). $[\alpha]_D^{24}$ = +20.9 (*c* = 0.35 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35–7.23 (m, 20H), 5.09 (s, 2H), 4.75 (d, *J* = 11.72 Hz, 1H), 4.62 (d, *J* = 11.72 Hz, 1H), 4.57 (d, *J* = 11.72 Hz, 1H), 4.49 (d, *J* = 11.96 Hz, 2H), 4.41 (d, *J* = 11.96 Hz, 1H), 4.32 (m, 1H), 4.10 (d, *J* = 5.37 Hz, 1H), 3.95 (m, 2H), 3.89 (dd, *J* = 3.17, 5.37 Hz, 1H), 3.78 (dd, *J* = 3.17, 2.69 Hz, 1H), 0.89 (s, 9H), 0.06 (s, 3H), 0.05 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.22, 138.66, 137.85, 137.82, 128.57, 128.48, 128.39, 128.36, 128.30, 128.04, 128.02, 127.91, 127.80, 127.69, 78.73, 76.47, 75.43, 72.35, 61.26, 77.43, 75.01, 72.75, 72.32, 26.35, 26.34, 26.31, 18.68, −4.85, −4.93 ppm; IR (neat): $\tilde{\nu}$ = 3387, 1738, 1684 cm^{-1}; HRMS (EI): calcd for $C_{40}H_{49}NO_6Si$: 667.3329; found: 667.3333.

2,3,4-Tri-*O*-benzyl-L-idono-1,5-lactone (28): *p*-TsOH·H_2O (7.5 mg, 0.04 mmol) was added to a solution of **27** (26.4 mg, 0.04 mmol) in acetone (2.8 mL) at 0 °C. The solution was stirred at RT for 6.5 d and was then poured into saturated $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 and the combined organic extracts were dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by chromatography on silica gel with (hexane/AcOEt 1:1) to give **28** (14.1 mg 0.03 mmol) as a white solid. M.p. 107 °C (hexane/AcOEt); $[\alpha]_D^{24}$ = +45.6 (*c* = 0.98 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.44–7.22 (m, 15H), 5.07 (d, *J* = 11.48 Hz, 1H), 4.69–4.57 (m, 4H), 4.47 (m, 1H), 4.30 (d, *J* = 12.2 Hz, 1H), 4.20 (d, *J* = 6.35 Hz, 1H), 3.97 (dd, *J* = 6.84, 11.96 Hz, 1H), 3.92 (dd, *J* = 1.22, 6.35 Hz, 1H), 3.72 (dd, *J* = 1.22, 1.46 Hz, 1H), 3.65 ppm (dd, *J* = 4.88, 11.96 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.30, 137.07, 136.81, 136.53, 136.96, 128.47, 128.44, 128.42, 128.40, 128.05, 128.02, 127.95, 127.92, 127.84, 127.82, 79.84, 78.54, 75.10, 73.43, 64.51, 72.60, 72.59, 71.17 ppm; IR (KBr): $\tilde{\nu}$ = 3357, 1746 cm^{-1}; HRMS (EI): calcd for $C_{27}H_{28}O_6$: 448.1886; found: 448.1891.

6-*O*-Acetyl-2,3,4-tri-*O*-benzyl-L-idono-1,5-lactone (29): Excess acetic anhydride (0.1 mL) was added to a solution of **28** (5.0 mg, 0.011 mmol) in pyridine (0.1 mL) at RT. The solution was stirred at RT for 12 h and was then poured into water. The aqueous layer was extracted with CH_2Cl_2 and the combined organic extracts were dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by chromatography on silica gel with (hexane/AcOEt 2:1) to give **29** (5.4 mg, 0.011 mmol, 99.1 %) as a white solid. M.p. 99 °C (hexane/AcOEt); $[\alpha]_D^{26}$ = +35.3 (*c* = 0.94 in $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.43–7.21 (m, 15H), 5.06 (d, *J* = 11.5 Hz, 1H), 4.67 (d, *J* = 12.1 Hz, 1H), 4.65 (d, *J* = 11.5 Hz, 1H), 4.60 (d, *J* = 12.1 Hz, 1H), 4.57 (d, *J* = 12.1 Hz, 1H), 4.56 (m, 1H), 4.33 (dd, *J* = 7.2, 11.6 Hz, 1H), 4.30 (d, *J* = 12.1, 1H), 4.20–4.17 (m, 2H), 3.91 (dd, *J* = 1.7, 6.6 Hz, 1H), 3.69 (dd, *J* = 1.7, 1.7 Hz, 1H), 1.99 ppm (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.4, 169.0, 137.2, 136.9, 136.5, 128.6, 128.5, 128.4, 128.3, 128.1, 128.0, 79.5, 78.4, 74.9, 74.6, 73.4, 72.6, 62.4, 20.7 ppm; IR (KBr): $\tilde{\nu}$ = 1750 cm^{-1}; HRMS (EI): calcd for $C_{29}H_{30}O_7$: 490.1991; found: 490.1981.

2,3,4-Tri-*O*-benzyl-L-idose (30): DIBAL-H (0.45 mL, 0.43 mmol, 0.95 M in *n*-hexane) was added to a solution of **29** (70.3 mg, 0.14 mmol) in CH_2Cl_2 (1.4 mL) at 0 °C. The solution was stirred at RT for 15 min and was then poured into saturated NH_4Cl. The aqueous layer was extracted with CH_2Cl_2 and the combined extracts were dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by chromatography on silica gel with (hexane/AcOEt 2:1) to give 56.8 mg (0.13 mmol, 88 %) of the L-idose derivative **30** as the α/β-mixture. ^{1}H NMR (600 MHz, $CDCl_3$) major: δ = 7.43–7.19 (m, 15H), 4.95 (s, 1H), 4.64 (d, *J* = 12.1 Hz, 1H), 4.61 (d, *J* = 12.1 Hz, 1H), 4.56 (d, *J* = 12.1 Hz, 1H), 4.43 (d, *J* = 12.1 Hz, 1H), 4.40 (d, *J* = 12.1 Hz, 1H), 4.33 (d, *J* = 12.1 Hz, 1H), 3.94 (dd, *J* = 7.7, 11.5, 1H), 3.92–3.90 (m, 1H), 3.76 (dd, *J* = 3.3, 3.9 Hz, 1H), 3.56 (dd, *J* = 3.9, 11.5 Hz, 1H), 3.45–3.43 (m, 1H), 3.33–3.32 ppm (m, 1H); minor: δ = 7.43–7.19 (m, 15H), 4.68 (d, *J* = 12.1 1H), 4.63 (d, *J* = 11.5 Hz, 1H), 4.58 (d, *J* = 12.1 Hz, 1H), 4.54 (d, *J* = 11.5 Hz, 1H), 4.47 (d, *J* = 11.5 Hz, 1H), 4.39 (d, *J* = 11.5 Hz, 1H), 4.19 (ddd, *J* = 2.8, 5.0, 7.7 Hz, 1H), 3.97–3.92 (m, 1H), 3.79–3.77 (m, 1H), 3.69 (dd, *J* = 4.8, 11.6 Hz, 1H), 3.51–3.50 (m, 1H), 3.46–3.45 (m, 1H), 3.33–3.32 ppm (m, 1H); HRMS (EI): calcd for $C_{27}H_{30}O_6$: 450.2040; found: 450.2044.

Methyl 2,3,4-tri-*O*-benzyl-β-L-idopyranoside (31) and methyl 2,3,4-tri-*O*-benzyl-α-L-idopyranoside (32): Saturated HCl in MeOH (1.33 mL) was added to a solution of **30** (530 mg, 1.18 mmol) in MeOH (10 mL) at RT. The solution was stirred at reflux for 5 h and was then poured into saturated $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 and the combined organic extracts were dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by chromatography on silica gel with (hexane/AcOEt 2:1) to give β-anomer **31** (289.2 mg, 0.62 mmol, 53 %) and α-anomer **32** (243.8 mg, 0.55 mmol, 45 %).

*Compound (**31**)*: M.p. 97 °C (hexane/AcOEt); $[\alpha]_D^{23}$ = −10.1 (*c* = 0.96 in $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.34–7.23 (m, 15H), 4.75 (d, *J* = 3.3 Hz 1H), 4.74 (d, *J* = 11.5 Hz, 1H), 4.70 (d, *J* = 12.1 Hz, 1H), 4.69 (d, *J* = 12.1 Hz, 1H), 4.59 (d, *J* = 12.1 Hz, 1H), 4.57 (d, *J* = 11.5 Hz, 1H), 4.45 (d, *J* = 12.1 Hz, 1H), 4.05 (ddd, *J* = 4.4, 6.6, 7.7 Hz, 1H), 3.90 (dd, *J* = 6.6, 12.1 Hz, 1H), 3.78 (dd, *J* = 5.5, 6.6 Hz, 1H), 3.71 (dd, *J* = 4.4, 12.1 Hz, 1H), 3.63 (dd, *J* = 5.5, 7.7 Hz, 1H), 3.61 (dd, *J* = 3.3, 6.6 Hz, 1H), 3.43 (s, 3H), 1.92 ppm (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 138.1, 138.0, 137.7, 128.5, 128.4, 128.1, 128.0, 127.9, 127.8, 127.7, 101.7, 78.6, 77.2, 73.6, 73.3, 73.2, 69.6, 62.1, 55.6 ppm; IR (KBr): $\tilde{\nu}$ = 3308 cm^{-1}; HRMS (EI): calcd for $C_{28}H_{32}O_6$: 464.2199; found: 464.2198.

*Compound (**32**)*: $[\alpha]_D^{23}$ = +30.2 (*c* = 1.02 in $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.36–7.27 (m, 15H), 4.80 (d, *J* = 12.1 Hz, 1H), 4.76 (d, *J* = 12.1 Hz, 1H), 4.75 (d, *J* = 12.1 Hz, 1H), 4.72 (d, *J* = 11.5 Hz, 1H), 4.68 (d, *J* = 12.1 Hz, 1H), 4.56 (d, *J* = 12.1 Hz, 1H), 4.54 (d, *J* = 3.9 Hz, 1H), 4.04

(dd, $J=7.7$, 8.3 Hz, 1H), 3.97 (dd, $J=5.5$, 11.0 Hz, 1H), 3.89 (dd, $J=5.5$, 12.1 Hz, 1H), 3.83 (dd, $J=5.5$, 12.1 Hz, 1H), 3.63 (dd, $J=5.5$, 7.7 Hz, 1H), 3.48 (s, 3H), 3.47 ppm (dd, $J=3.9$, 8.3 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta=138.4$, 138.2, 137.8, 128.5, 128.4, 128.1, 128.0, 127.9, 127.8, 99.0, 78.1, 77.8, 74.9, 73.7, 75.0, 73.8, 63.1, 56.9 ppm; IR (KBr): $\tilde{\nu}=3467$ cm^{-1}; HRMS (FAB-NBA+NaI): calcd for $C_{28}H_{32}O_6Na$I: 487.2097; found: 487.2099.

Methyl 2,3,4-tri-*O*-benzyl-β-L-idopyranosiduronate (33): CrO_3 69.7 mg (0.70 mmol) dissolved in H_2SO_4 (3.5 M, 1 mL) was added to a solution of **31** (120 mg, 1.18 mmol) in acetone (3 mL). The solution was stirred at 0°C for 10 min before being filtered. The aqueous layer was extracted with $CHCl_3$ and the combined organic extracts were dried over Na_2SO_4, filtered, and concentrated in vacuo to give the crude product **33** (76.3 mg, 0.16 mmol, 60%), which was applied to the next reaction without further purification.

Dimethyl 2,3,4-tri-*O*-benzyl-β-L-idopyranosiduronate (34): Excess CH_2N_2 in Et_2O was added to a solution of **33** (104.5 mg, 0.22 mmol) in CH_2Cl_2 (2 mL) at 0°C. The solution was stirred at RT for 2 h and was then concentrated in vacuo. The residue was purified by chromatography on silica gel with (hexane/AcOEt 10:1) to give the L-idose derivative **34** (76.3 mg, 0.16 mmol, 60%). $[\alpha]_D^{26}=+29.0$ ($c=1.10$ in $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): $\delta=7.26$–7.15 (m, 15H), 4.68 (d, $J=12.7$ Hz 1H), 4.58 (d, $J=12.7$ Hz, 1H), 4.57 (d, $J=12.1$ Hz, 1H), 4.50–4.48 (m, 3H), 4.41 (d, $J=12.1$ Hz, 1H), 4.23 (d, $J=3.6$ Hz, 1H), 3.97–3.95 (dd, $J=5.5$, 7.6 Hz, 1H), 3.65 (s, 3H), 3.61 (dd, $J=3.6$, 5.5 Hz, 1H), 3.41–3.39 ppm (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta=169.5$, 138.5, 138.0, 137.9, 128.5, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 100.9, 75.7, 74.5, 73.7, 73.5, 72.9, 56.92, 51.87 ppm; IR (neat): $\tilde{\nu}=1688$ cm^{-1}; HRMS (EI): calcd for $C_{29}H_{32}O_7$: 492.2148; found: 492.2132.

Dimethyl β-L-idopyranosiduronate (35): $Pd(OH)_2/C$ (14.4 mg) was added to a solution of **34** (71.9 mg, 0.15 mmol) in MeOH (1.5 mL) and the mixture was stirred under a H_2 atmosphere for 22 h at RT. After this time, the mixture was filtered and concentrated to give **35** (31.9 mg, 0.15 mmol, quant). $[\alpha]_D^{22}=+80.7$ ($c=0.23$ in MeOH); ^{1}H NMR (600 MHz, $CDCl_3$): $\delta=4.67$ (d, $J=1.7$ Hz, 1H), 4.54 (d, $J=2.2$ Hz, 1H), 4.00 (dd, $J=3.3$, 3.9 Hz, 1H), 3.81–3.79 (m, 1H), 3.77 (s, 3H), 3.61 (dd, $J=1.7$, 3.9 Hz, 1H), 3.55 ppm (s, 3H); ^{13}C NMR (150 MHz, CD_3OD): $\delta=171.8$, 101.7, 75.1, 71.6, 71.3, 70.7, 57.4, 52.5 ppm; IR (neat): $\tilde{\nu}=3488$, 1734 cm^{-1}; HRMS (EI): calcd for $C_8H_{14}O_7$: 222.0740; found: 222.0739.

1*N*-Benzyloxy-2,3,4,6-tetra-*tert*-butyldimethylsilyloxy-5-hydroxy-(2*R*,3*S*,4*R*,5*R*)-hexanamide (37): A mixture of **36** (790 mg, 1.25 mmol) and benzylhydroxyamine (1.23 g, 9.96 mmol) in CH_2Cl_2 (10 mL) was stirred at room temperature for 30 min, after which time, a solution of trimethylaluminum (9.96 mL of 1.00 M solution in *n*-hexane, 9.96 mmol) was added. The resulting solution was stirred at room temperature for a period of 2 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, filtered, and the solvent was removed in vacuo. Purification by silica-gel chromatography (hexane/Et_2O 10:1) gave **37** 814 mg (86%). $[\alpha]_D^{24}=+98.5$ ($c=0.85$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=8.62$ (s, 1H), 7.36–7.30 (m, 5H), 5.06 (d, $J=11.96$ Hz, 1H), 4.82 (d, $J=11.96$ Hz, 1H), 4.58 (s, 1H), 4.02 (d, $J=4.63$ Hz, 1H), 3.86 (dd, 1H, $J=4.63$, 9.28 Hz, 1H), 3.81 (m, 1H), 3.63 (m, 2H), 3.49 (s, 1H), 0.91 (s, 9H), 0.90 (s, 9H), 0.87 (s, 9H), 0.79 (s, 9H), 0.15 (s, 3H), 0.14 (s, 3H), 0.11 (s, 3H), 0.07 (s, 6H), 0.04 (s, 3H), 0.03 (s, 3H), −0.07 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=170.86$, 135.63, 128.47, 128.32, 127.86, 77.98, 76.72, 74.05, 72.48, 68.85, 64.21, 26.15, 25.98, 25.96, 25.67, 18.63, 18.10, 18.04, 17.78, −3.84, −4.20, −4.75, −4.77, −4.78, −5.11, −5.41 ppm; IR (neat): $\tilde{\nu}=3416$, 1711 cm^{-1}; HRMS (FAB-NBA+NaI): exact mass calcd for $C_{37}H_{75}NO_7Si_4Na$: 780.4518; found: 780.4515 $[M+Na]^+$.

2,3,4-Tri-*O*-*tert*-butyldimethylsilyl-L-idono-1,5-lactone (38′) and 3,4,5-tris(*tert*-butyldimethylsilyloxy)-6-*tert*-butyldimethylsilyloxymethyl-1-(benzyloxy)-(3*R*,4*S*,5*R*,6*S*)-tetrahydropyridin-2(1*H*)-one (39): *p*-TsOH·H_2O (17.5 mg, 0.09 mmol) was added to a mixture of **38** and **39** (67.9 mg, **38**/**39** 1.4:1) in acetone (4.5 mL) at 0°C. The solution was stirred at 5°C for 6 d and was then poured into saturated $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 and the combined organic extracts were dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by chromatography on silica gel with (hexane/AcOEt 10:1→4:1) to give the lactone compound **38′**, which was derived from **38**, and remaining **39**.

Compound (38′): $[\alpha]_D^{24}=+10.1$ ($c=0.72$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=4.62$ (dd, $J=5.12$, 7.57 Hz, 1H), 4.08 (d, $J=1.47$ Hz, 1H), 3.92 (dd, $J=7.57$, 11.47 Hz 1H), 3.84 (m, 1H), 3.71 (d, $J=2.93$ Hz, 1H), 3.64 (dd, $J=5.12$, 11.47 Hz, 1H), 0.91 (s, 9H), 0.90 (s, 9H), 0.87 (s, 9H), 0.18 (s, 3H), 0.14 (s, 3H), 0.12 (s, 3H), 0.11 (s, 3H), 0.08 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=170.90$, 78.67, 77.36, 75.80, 69.32, 62.36, 26.03, 25.81, 25.77, 25.63, 18.46, 18.06, 17.93, −3.89, −3.93, −4.03, −4.42, −4.77, −5.22 ppm; IR (neat): $\tilde{\nu}=3411$, 1750 cm^{-1}; HRMS (FAB-NBA+NaI): exact mass calcd for $C_{24}H_{52}O_6Si_3$: 520.3072; found: 520.3063.

Compound (39): $[\alpha]_D^{24}=+13.4$ ($c=0.36$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.35$–7.20 (m, 5H), 5.19 (dd, $J=7.81$, 11.72 Hz, 1H), 4.98 (d, $J=15.13$ Hz, 1H), 4.94 (d, $J=15.13$ Hz, 1H), 4.27 (d, $J=5.13$ Hz, 1H), 3.92 (m, 1H), 3.85 (m, 1H), 3.78–3.76 (m, 2H), 0.91 (s, 9H), 0.89 (s, 9H), 0.83 (s, 18H), 0.12 (s, 3H), 0.10 (s, 3H), 0.08 (s, 3H), 0.07 (s, 3H), 0.05 (s, 3H), 0.02 (s, 3H), 0.01 (s, 3H), −0.02 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=153.24$, 138.74, 127.89, 127.01, 78.58, 75.75, 75.51, 73.12, 71.71, 67.98, 26.25, 26.22, 26.06, 25.72, 18.52, 18.42, 18.40, 18.02, −3.67, −4.35, −4.37, −4.59, −4.62, −4.73, −5.00, −5.08 ppm; IR (neat): $\tilde{\nu}=1642$ cm^{-1}; HRMS (EI): exact mass calcd for $C_{37}H_{73}NO_6Si_4$: 739.4515; found: 739.4520 $[M]^+$.

1*N*-Methoxy-2,3,4,6-tetra-*tert*-butyldimethylsilyloxy-5-hydroxy-(2*R*,3*S*,4*R*,5*R*)-hexanamide (40a): Compound **36** (68.9 mg, 0.10 mmol) was converted into **40a** (46.4 mg, 0.068 mmol, 63%). M.p. 87°C (hexane/AcOEt); $[\alpha]_D^{24}=+75.3$ ($c=1.03$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=8.58$ (s, 1H), 4.61 (s, 1H), 4.03 (d, $J=4.63$ Hz, 1H), 3.90 (dd, $J=4.63$, 9.28 Hz, 1H), 3.87 (m, 1H), 3.79 (s, 3H), 3.70–3.67 (m, 2H), 3.53 (s, 1H), 0.99 (s, 9H), 0.93 (s, 9H), 0.92 (s, 1H), 0.90 (m, 9H), 0.16 (s, 12H), 0.12 (s, 3H), 0.07 (s, 3H), 0.06 (s, 3H), 0.05 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=170.50$, 76.58, 74.14, 72.47, 68.82, 64.27, 64.24, 26.16, 25.99, 25.98, 25.96, 25.89, 18.66, 18.11, 18.05, 18.01, −3.88, −4.01, −4.74, −4.76, −4.78, −5.10, −5.46 ppm; IR (KBr): $\tilde{\nu}=3418$, 1711, 1468 cm^{-1}; HRMS (FAB-NBA+NaI): calcd for $C_{31}H_{72}NO_7Si_4$: 682.4386; found: 682.4391.

1*N*-Ethoxy-2,3,4,6-tetra-*tert*-butyldimethylsilyloxy-5-hydroxy-(2*R*,3*S*,4*R*,5*R*)-hexanamide (40b): Compound **36** (83.4 mg, 0.12 mmol) was converted into **40b** (56.7 mg, 0.081 mmol, 74%). $[\alpha]_D^{24}=+86.4$ ($c=1.02$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=8.51$ (s, 1H), 4.60 (d, $J=1.10$ Hz, 1H), 4.03 (dd, $J=1.10$, 6.88 Hz, 1H), 3.89 (dd, $J=6.88$, 9.07 Hz, 1H), 3.87–3.85 (m, 3H), 3.68 (dd, $J=1.92$, 10.72 Hz, 1H), 3.64 (dd, $J=3.58$, 10.72 Hz, 1H), 2.69 (s, 1H), 1.27 (dd, $J=6.6$, 6.6 Hz, 1H), 0.98 (s, 9H), 0.91 (s, 18H), 0.89 (s, 9H), 0.14 (s, 12H), 0.12 (s, 3H), 0.07 (s, 3H), 0.05 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=170.64$, 76.61, 74.08, 72.43, 72.13, 64.21, 60.38, 13.73, 26.13, 25.96, 25.93, 25.85, 21.14, 18.62, 17.96, 17.93, −3.87, −3.91, −4.05, −4.08, −4.77, −4.81, −4.95, −5.13 ppm; IR (neat): $\tilde{\nu}=3416$, 1709, 1464 cm^{-1}; HRMS (FAB-NBA+NaI): calcd for $C_{32}H_{73}NO_7Si_4Na$: 718.4362; found: 718.4363.

1*N*-*tert*-Butoxy-2,3,4,6-tetra-*tert*-butyldimethylsilyloxy-5-hydroxy-(2*R*,3*S*,4*R*,5*R*)-hexanamide (40c): Compound **36** (114 mg, 0.18 mmol) was converted into **40c** (82.4 mg, 0.11 mmol, 63%). $[\alpha]_D^{24}=+71.5$ ($c=0.12$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=8.14$ (s, 1H), 4.69 (s, 1H), 4.08 (d, $J=3.66$, 1H), 3.96–3.92 (m, 2H), 3.76–3.69 (m, 2H), 3.62 (s, 1H), 1.33 (s, 9H), 1.05 (s, 9H), 0.98 (s, 18H), 0.98 (s, 9H), 0.95 (s, 9H), 0.24 (s, 3H), 0.22 (s, 9H), 0.17 (s, 3H), 0.12 ppm (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=177.94$, 77.11, 74.01, 72.72, 68.95, 64.30, 29.07, 26.59, 26.20, 26.19, 26.06, 26.05, 25.96, 25.95, 25.89, 25.88, −81.24, 18.69, 18.14, 18.04, 17.91, −3.50, −3.57, −3.77, −4.66, −4.74, −5.06, −5.56 ppm; IR (neat): $\tilde{\nu}=3382$, 1719, 1464 cm^{-1}; HRMS (FAB-NBA+NaI): calcd for $C_{34}H_{78}NO_7Si_4$: 724.4855; found: 724.4857.

1*N*-*tert*-Butoxy-2,3,4,6-tetra-*tert*-butyldimethylsilyloxy-5-hydroxy-(2*R*,3*S*,4*R*,5*R*)-hexanamide (40d): Compound **36** (542 mg, 0.10 mmol) was converted into **40d** (553 mg, 0.71 mmol, 83%). $[\alpha]_D^{24}=+56.8$ ($c=1.32$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=8.38$ (s, 1H), 4.63 (s, 1H), 4.06 (dd, $J=1.22$, 4.44 Hz, 1H), 3.95 (m, 1H), 3.92 (dd, $J=4.44$, 9.28 Hz, 1H), 3.71–3.66 (m, 2H), 3.61 (s, 1H), 1.00 (s, 9H), 0.97 (s, 9H), 0.94 (s, 18H), 0.92 (s, 9H), 0.23 (s, 3H), 0.18 (s, 3H), 0.17 (s, 6H), 0.16 (s, 3H), 0.14 (s, 3H), 0.10 (s, 6H), 0.09 (s, 3H), 0.08 ppm (s, 3H); ^{13}C NMR

(100 MHz, $CDCl_3$): δ = 180.39, 85.04, 84.73, 82.14, 81.03, 72.33, 29.09, 28.94, 28.88, 28.80, 28.76, 21.57, 21.02, 20.96, 20.89, 20.83, −0.77, −0.82, −0.94, −1.73, −1.85, −1.87, −1.98, −2.18, −2.25 ppm; IR (neat): $\tilde{\nu}$ = 3387, 1719, 1464 cm^{-1}; HRMS (EI): calcd for $C_{36}H_{83}NO_7Si_5$: 781.5016; found: 781.4999.

3,4,5-Tris(*tert*-butyldimethylsilyloxy)-6-*tert*-butyldimethylsilyloxymethyl-1-methoxy-(3*R*,4*S*,5*R*,6*S*)-tetrahydropyridin-2(1*H*)-one (42a): *p*-TsOH•H_2O (11.6 mg, 0.06 mmol) was added to a mixture of **41a** and **42a** (40.2 mg, **41a**/**42a** 1.3:1) in acetone (3.0 mL) at 0°C. The solution was stirred at 5°C for 4 d and was then poured into saturated $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 and the combined extracts were dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by chromatography on silica gel with (hexane/AcOEt 10:1∼4:1) to give the lactone compound (**38′**) (21.2 mg, 0.03 mmol), which was derived from **41a**, and unreacted **42a** (11.9 mg, 0.02 mmol).

Compound (42a): M.p. 65°C (hexane/AcOEt); $[\alpha]_D^{24}$ = +13.4 (*c* = 0.36 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.35–7.20 (m, 5H), 5.19 (dd, *J* = 7.81, 11.72 Hz, 1H), 4.98 (d, *J* = 15.13 Hz, 1H), 4.94 (d, *J* = 15.13 Hz, 1H), 4.27 (d, *J* = 5.13 Hz, 1H), 3.92 (m, 1H), 3.85 (m, 1H), 3.78–3.76 (m, 2H), 0.91 (s, 9H), 0.89 (s, 9H), 0.83 (s, 18H), 0.12 (s, 3H), 0.10 (s, 3H), 0.08 (s, 3H), 0.07 (s, 3H), 0.05 (s, 3H), 0.02 (s, 3H), 0.01 (s, 3H), −0.02 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.24, 138.74, 127.89, 127.01, 78.58, 75.75, 75.51, 73.12, 71.71, 67.98, 26.25, 26.22, 26.06, 25.72, 18.52, 18.42, 18.40, 18.02, −3.67, −4.35, −4.37, −4.59, −4.62, −4.73, −5.00, −5.08 ppm; IR (neat): $\tilde{\nu}$ = 1642 cm^{-1}; HRMS (FAB): exact mass calcd for $C_{41}H_{42}NO_6$: 644.3012; found: 644.3011 $[M+H]^+$.

3,4,5-Tris(*tert*-butyldimethylsilyloxy)-6-*tert*-butyldimethylsilyloxymethyl-1-ethoxy-(3*R*,4*S*,5*R*,6*S*)-tetrahydropyridin-2(1*H*)-one (42b): *p*-TsOH•H_2O (9.2 mg, 0.04 mmol) was added to a mixture of **41b** and **42b** (32.5 mg, **41b**/**42b** 1.1:1) in acetone (2.5 mL) at 0°C. The solution was stirred at 5°C for 5 d and was then poured into saturated $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 and the combined organic extracts were dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by chromatography on silica gel with (hexane/AcOEt 10:1→4:1) to give the lactone compound **38′** (9.4 mg, 0.02 mmol), which was derived from **41b**, and unreacted **42b** (12.4 mg, 0.02 mmol).

Compound (42b): $[\alpha]_D^{24}$ = +16.8 (*c* = 0.98 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 5.19 (dd, *J* = 7.81, 11.47 Hz, 1H), 4.34 (d, *J* = 5.13, 1H), 4.00 (q, 2H), 3.92 (m, 1H), 3.87 (m, 1H), 3.81 (dd, *J* = 3.17, 5.13 Hz, 1H), 3.76 (m, 1H), 1.25 (t, 3H), 0.92–0.90 (m, 36H), 0.12–0.07 ppm (m, 24H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.69, 78.55, 75.66, 73.10, 71.68, 69.37, 67.84, 15.07, 26.26, 26.21, 26.13, 25.77, 18.51, 18.48, 18.43, 18.06, −3.64, −4.27, −4.38, −4.59, −4.60, −4.69, −4.93, −4.93 ppm; IR (neat): $\tilde{\nu}$ = 1639 cm^{-1}; HRMS (EI): exact mass calcd for $C_{32}H_{71}NO_6Si_4$: 677.4358; found: 677.4362.

3,4,5-Tris(*tert*-butyldimethylsilyloxy)-6-*tert*-butyldimethylsilyloxymethyl-1-(benzyloxy)-(3*R*,4*S*,5*R*,6*S*)-tetrahydropyridin-2(1*H*)-one (42c): *p*-TsOH•H_2O (13.5 mg, 0.04 mmol) was added to a mixture of **41c** and **42c** (49.1 mg, **41c**/**42c** 1:5.1) in acetone (3.6 mL) at 0°C. The solution was stirred at 5°C for 6 d and was then poured into saturated $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 and the combined extracts were dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by chromatography on silica gel with (hexane/AcOEt 10:1→4:1) to give the lactone compound **38′** (6.4 mg, 0.02 mmol), which was derived from **41b**, and unreacted **42c** (38.4 mg, 0.056 mmol).

Compound (42c): $[\alpha]_D^{24}$ = +3.78 (*c* = 0.43 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 5.13 (dd, *J* = 7.81, 11.72 Hz, 1H), 4.36 (d, *J* = 4.89, 1H), 3.89 (m, 1H), 3.84 (m, 1H), 3.79 (dd, *J* = 2.93, 4.89 Hz, 1H), 3.75 (m, 1H), 1.25 (s, 9H), 0.90–0.88 (m, 36H), 0.10–0.07 ppm (m, 24H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.46, 77.71, 76.08, 73.62, 71.85, 67.60, 27.71, 26.25, 26.21, 26.13, 25.83, 78.76, 18.54, 18.50, 18.42, 18.10, −3.73, −4.38, −4.44, −4.57, −4.63, −4.69, −4.72, −4.97 ppm; IR (KBr): $\tilde{\nu}$ = 1638 cm^{-1}; HRMS (EI): exact mass calcd for $C_{34}H_{75}NO_6Si_4$: 705.4671; found: 705.4672.

1,3,4,5-Tetrakis(*tert*-butyldimethylsilyloxy)-6-*tert*-butyldimethylsilyloxymethyl-(3*R*,4*S*,5*R*,6*S*)-tetrahydropyridin-2(1*H*)-one (42d): Compound **40d** (65.5 mg, 0.08 mmol) was converted into **42d** (39.4 mg, 0.05 mmol, 61%). $[\alpha]_D^{24}$ = +6.50 (*c* = 0.37 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 5.13 (dd, *J* = 7.57, 11.72 Hz, 1H), 4.36 (d, *J* = 4.64, 1H), 3.86–3.83 (m, 2H), 3.80 (dd, *J* = 2.69, 4.64, 1H), 3.77 (d, *J* = 11.72, 1H), 0.93–0.87 (m, 45H), 0.12–0.00 ppm (m, 30H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 180.39, 85.04, 84.73, 82.14, 81.03, 72.33, 29.09, 28.94, 28.88, 28.76, 21.57, 21.02, 20.96, 20.89, 20.83, −0.77, −0.82, 0.94, −1.73, −1.85, −1.87, −1.98, −2.18, −2.25 ppm; IR (neat): $\tilde{\nu}$ = 1634 cm^{-1}; HRMS (EI): exact mass calcd for $C_{36}H_{81}NO_6Si_5$: 763.4910; found: 763.4918.

1,3,4,5-Tetrakis(*tert*-butyldimethylsilyloxy)-6-hydroxymethyl-(3*R*,4*S*,5*R*,6*S*)-2-piperidinone (42d′): *p*-TsOH•H_2O (10.6 mg, 0.06 mmol) was added to a mixture of **41d** and **42d** (42.7 mg, **41d**/**42d** 1:1.8) in acetone (2.8 mL) at 0°C. The solution was stirred at 5°C for 6.5 d and was then poured into saturated $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 and the combined organic extracts were dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by chromatography on silica gel with (hexane/AcOEt 10:1→4:1) to give the lactone compound **38′** (6.9 mg, 0.01 mmol), which was derived from **41d**, and desilylated **42d′** (18.7 mg, 0.03 mmol).

Compound (42d′): $[\alpha]_D^{24}$ = +8.56 (*c* = 0.33 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 5.25 (dd, *J* = 7.81, 11.72 Hz, 1H), 4.37 (dd, *J* = 0.98, 5.13, 1H), 3.94–3.81 (m, 4H), 0.93–0.90 (m, 36H), 0.12–0.09 ppm (m, 24H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.54, 78.50, 75.45, 73.02, 71.54, 68.14, 26.25, 26.20, 26.08, 25.80, 18.52, 18.46, 18.42, 18.03, −3.63, −4.31, −4.42, −4.60, −4.65, −4.74, −4.94, −5.03 ppm; IR (neat): $\tilde{\nu}$ = 1680, 3349 cm^{-1}; HRMS (EI): exact mass calcd for $C_{30}H_{67}NO_6Si_4$: 649.4045; found: 649.4042.

1*N*-Benzyloxy-2,3,4,6-tetra-*tert*-butyldimethylsilyloxy-5-hydroxy-(2*R*,3*S*,4*S*,5*R*)-hexanamide (44a): Compound **43** (324 mg, 0.51 mmol) was converted into **44a** (335 mg, 0.44 mmol, 87%). $[\alpha]_D^{24}$ = +16.4 (*c* = 0.47 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 8.71 (s, 1H), 7.40–7.33 (m, 5H), 4.93 (s, 2H), 4.14 (d, *J* = 4.64 Hz, 1H), 4.04 (dd, *J* = 2.68, 4.39 Hz, 1H), 4.00 (dd, *J* = 2.68, 4.64 Hz, 1H), 3.79 (m, 1H), 3.59 (dd, *J* = 5.86, 9.52 Hz, 1H), 3.55 (dd, *J* = 8.06, 9.52 Hz, 1H), 2.99 (s, 1H), 0.92 (s, 9H), 0.90 (s, 9H), 0.89 (s, 9H), 0.86 (s, 9H), 0.14 (s, 9H), 0.10 (s, 3H), 0.09 (s, 3H), 0.06 (s, 6H), 0.04 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.83, 135.73, 128.55, 128.34, 128.27, 78.47, 77.88, 71.14, 71.03, 63.41, 73.31, 26.32, 26.12, 26.02, 25.87, 18.66, 18.39, 18.30, 18.22, −2.89, −4.21, −4.54, −4.63, −4.79, −4.87, −5.15, −5.21 ppm; IR (neat): $\tilde{\nu}$ = 3418, 1705, 1472 cm^{-1}; HRMS (FAB-NBA+NaI): exact mass calcd for $C_{37}H_{75}NO_7Si_4Na$: 780.4518; found: 780.4517 $[M+Na]^+$.

1*N*-*tert*-Butyldimethylsilyloxy-2,3,4,6-tetra-*tert*-butyldimethylsilyloxy-5-hydroxy-(2*R*,3*S*,4*S*,5*R*)-hexanamide (44b): Compound **43** (165 mg, 0.26 mmol) was converted into **44b** (179 mg, 0.23 mmol, 88%). $[\alpha]_D^{24}$ = −7.10 (*c* = 1.01 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 8.36 (s, 1H), 4.15 (d, *J* = 4.40 Hz, 1H), 4.05 (dd, *J* = 2.44, 4.64 Hz, 1H), 3.95 (dd, *J* = 2.44, 4.40 Hz, 1H), 3.75 (dd, *J* = 5.37, 10.01 Hz, 1H), 3.62 (dd, *J* = 8.06, 10.01 Hz, 1H), 3.55 (m, 1H), 3.09 (s, 1H), 0.97 (s, 9H), 0.96 (s, 9H), 0.95 (s, 9H), 0.93 (s, 9H), 0.90 (s, 9H), 0.19 (s, 3H), 0.16 (s, 15H), 0.14 (s, 3H), 0.11 (s, 3H), 0.07 (s, 3H), 0.06 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.49, 78.40, 72.96, 72.46, 71.14, 63.38, 26.46, 26.14, 26.10, 26.01, 25.95, 18.80, 18.44, 18.39, 18.36, 18.19, −2.98, −4.00, −4.61, −4.69, −4.88, −5.07, −5.10, −5.15, −5.26, −5.28 ppm; IR (neat): $\tilde{\nu}$ = 1740, 1472 cm^{-1}; HRMS (FAB-NBA+NaI): calcd for $C_{36}H_{84}NO_7Si_5$: 782.5094; found: 782.5087 $[M+Na]^+$.

2*N*-Benzyloxy-3,4,5-tris(*tert*-butyldimethylsilyloxy)-6-*tert*-butyldimethylsilyloxymethyl-(3*R*,4*S*,5*S*,6*S*)-tetrahydro-2*H*-pyran-2-imine (45a) and 3,4,5-tris(*tert*-butyldimethylsilyloxy)-6-*tert*-butyldimethylsilyloxymethyl-1-(benzyloxy)-(3*R*,4*S*,5*S*,6*S*)-tetrahydropyridin-2(1*H*)-one (46a): Compound **44a** (68.9 mg, 0.442 mmol) was converted into products **45a**/**46a** 1.6:1 (54.0 mg, 0.07 mmol, 80%).

Compound (45a): $[\alpha]_D^{24}$ = −41.6 (*c* = 0.78 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.46–7.32 (m, 5H), 5.12 (d, *J* = 12.70 Hz, 1H), 5.06 (d, *J* = 12.70 Hz, 1H), 4.59 (dd, *J* = 1.95, 9.52 Hz, 1H), 4.25 (d, *J* = 9.28, Hz, 1H), 4.16 (d, *J* = 3.91 Hz, 1H), 4.19 (dd, *J* = 1.95, 11.96 Hz, 1H), 3.98–3.95 (m, 2H), 1.02 (s, 9H), 1.00 (s, 9H), 0.96 (s, 18H), 0.26 (s, 3H), 0.22 (s, 6H), 0.18 (s, 6H), 0.17 (s, 3H), 0.15 (s, 3H), 0.04 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.41, 138.62, 127.85, 127.80, 127.06, 77.97, 75.80, 73.12, 70.63, 64.21, 61.36, 26.17, 26.09, 25.82, 18.68, 18.22, 18.18, 18.14, −3.52, −4.30, −4.33, −4.57, −4.66, −4.82, −5.23, −5.27 ppm; IR (neat):

$\tilde{\nu}$ = 1649 cm^{-1}; HRMS (EI): exact mass calcd for $C_{37}H_{73}NO_6Si_4$: 739.4515; found: 739.4519 $[M]^+$.

*Compound (**46a**)*: $[\alpha]_D^{24} = -4.82$ (c = 1.03 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34–7.25 (m, 5H), 4.99 (s, 2H), 4.57 (dd, J = 3.66, 6.10 Hz, 1H), 4.37 (d, J = 3.66 Hz, 1H), 4.15 (dd, J = 3.18, 6.10 Hz, 1H), 4.10 (m, 1H), 3.90 (dd, J = 3.66, 10.99, 1H), 3.76 (dd, J = 4.88, 10.99 Hz, 1H), 0.89 (s, 9H), 0.88 (s, 18H), 0.84 (s, 9H), 0.15–0.01 ppm (s, 24H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.30, 138.34, 127.89, 127.18, 76.17, 75.95, 75.09, 69.99. 64.39, 56.35, 26.06, 26.02, 25.97, 25.72, 18.49, 18.33, 18.12, 18.06, −3.76, −4.04, −4.09, −4.32, −4.34, −4.63, −5.20 ppm; IR (neat): $\tilde{\nu}$ = 1741 cm^{-1}; HRMS (EI): exact mass calcd for $C_{37}H_{73}NO_6Si_4$: 739.4515; found: 739.4520.

2*N*-*tert*-Butyldimethylsilyloxy-3,4,5-tris(*tert*-butyldimethylsilyloxy)-6-*tert*-butyldimethylsilyloxymethyl-(3*R*,4*S*,5*S*,6*S*)-tetrahydro-2*H*-pyran-2-imine (45b) and 1,3,4,5-tetrakis(*tert*-butyldimethylsilyloxy)-6-*tert*-butyldimethylsilyloxymethyl-(3*R*,4*S*,5*S*,6*S*)-tetrahydropyridin-2(1*H*)-one (46b): Compound **44b** (162 mg, 0.442 mmol) was converted into products **45b**/**46b** 1.6:1 (111 mg, 0.15 mmol, 70%).

*Compound (**45b**)*: $[\alpha]_D^{24} = +2.11$ (c = 0.59 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.14 (dd, J = 7.56, 11.72 Hz, 1H), 4.35 (d, J = 4.64 Hz, 1H), 3.86–3.83 (m, 2H), 3.79 (dd, J = 4.64, 2.69 Hz, 1H), 3.76 (d, J = 11.72, Hz, 1H), 0.92 (s, 9H), 0.89 (s, 9H), 0.88 (s, 18H), 0.87 (s, 9H), 0.12–0.02 ppm (m, 30H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.54, 78.94, 75.91, 74.16, 71.90, 67.66, 26.47, 26.24, 26.22, 26.09, 26.00, 26.20, 18.62, 18.44, 18.43, 18.33, −3.77, −4.37, −4.49, −4.52, −4.67, −4.72, −4.90, 4.96 ppm; IR (neat): $\tilde{\nu}$ = 1636 cm^{-1}; HRMS (EI): exact mass calcd for $C_{36}H_{81}NO_6Si_5$: 763.4910; found: 763.4918 $[M]^+$.

*Compound (**46b**)*: $[\alpha]_D^{24} = -7.42$ (c = 0.19 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.54 (dd, J = 3.17, 5.61 Hz, 1H); 4.33 (d, J = 1.71 Hz, 1H); 4.16–4.10 (m, 2H); 3.91 (dd, J = 3.17, 10.99 Hz, 1H); 3.78 (dd, J = 5.61, 10.99 Hz, 1H); 0.92–0.87 (m, 45H); 0.17–0.07 ppm (m, 30H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.37, 76.05, 75.26, 71.71, 64.93, 26.41, 26.14, 26.09, 25.77, 25.82, 18.54, 18.39, 18.16, 18.09, −4.01, −4.29, −4.86, −5.08, −5.10 ppm, IR (neat): $\tilde{\nu}$ = 1746 cm^{-1}; HRMS (EI): exact mass calcd for $C_{36}H_{81}NO_6Si_5$: 763.4910; found: 763.4908.

General procedure for the reduction of 39, 42, and 46: $Pd(OH)_2/C$ (67.6 mg) was added to a solution of **42d** (67.6 mg, 0.09 mmol) in MeOH (5.0 mL) and the resulting mixture was stirred under a H_2 atmosphere for 12 h at RT. After this time, the mixture was filtered and concentrated. Purification by column chromatography on silica gel (hexane/Et_2O 4:1) afforded **47** (42.3 mg, 0.07 mmol, 76%).

3,4,5-Tris(*tert*-butyldimethylsilyloxy)-6-*tert*-butyldimethylsilyloxymethyl-(3*R*,4*S*,5*R*,6*S*)-2-piperidinone (47): $[\alpha]_D^{24} = +6.12$ (c = 1.07 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.29 (s, 1H), 5.21 (dd, J = 8.06, 11.72 Hz, 1H), 4.37 (dd, J = 0.98, 5.13 Hz, 1H), 3.88 (m, 1H), 3.84 (m, 1H), 3.80–3.78 (m, 2H), 0.93 (s, 9H), 0.92 (s, 18H), 0.91 (s, 9H), 0.17 (s, 3H), 0.16 (s, 3H), 0.15 (m, 9H), 0.13 (s, 3H), 0.11 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.58, 76.10, 75.09, 71.40, 64.50, 26.06, 26.03, 25.93, 25.73, 18.50, 18.38, 18.16, 18.05, −3.54, −3.98, −4.30, −4.70, −5.19, −5.24 ppm; IR (neat): $\tilde{\nu}$ = 1752, 1472 cm^{-1}; HRMS (EI): exact mass calcd for $C_{30}H_{67}NO_5Si_4$: 633.4096; found: 633.4094.

3,4,5-Tris(*tert*-butyldimethylsilyloxy)-6-*tert*-butyldimethylsilyloxymethyl-(3*R*,4*S*,5*S*,6*S*)-2-piperidinone (48): Compound **46a** (60.3 mg, 0.07 mmol) was converted into **48** (43.6 mg, 0.07 mmol, 86%). $[\alpha]_D^{24} = +0.09$ (c = 0.37 in $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.11 (s, 1H), 4.61 (dd, J = 3.18, 6.59 Hz, 1H), 4.35 (m, 1H), 4.17–4.13 (m, 2H), 3.90 (dd, J = 3.18, 10.99 Hz, 1H), 3.80 (dd, J = 4.64, 10.99 Hz, 1H), 0.90 (s, 9H), 0.89 (s, 18H), 0.88 (s, 9H), 0.14–0.10 ppm (m, 24H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 158.64, 76.05, 75.04, 71.38, 64.47, 60.43, 26.05, 26.02, 25.93, 25.69, 18.49, 18.37, 18.16, 8.05, −3.57, −3.99, −4.02, −4.32, −4.71, −5.21, −5.25 ppm; IR (neat): $\tilde{\nu}$ = 1703 cm^{-1}; HRMS (EI): exact mass calcd for $C_{30}H_{67}NO_5Si_4$: 633.4096; found: 633.4087.

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