Development of an Efficient, Regio- and Stereoselective Route to Libraries Based on the β-D-Glucose Scaffold

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The design and execution of an efficient synthetic route for the sequential functionalization of the five hydroxyl substituents of β-D-glucose has been achieved. This strategy, based on the stereoselective glycosidation of thioglycosides, provides a new approach for the parallel construction of a wide variety of β-D-glucose analogues and as such holds promise for solid-support library syntheses.

In the early 1990s we reported that β-D-glucose derivatives that lack the amide backbone of peptides but retain peptidal side chains can serve as competent nonpeptidal peptidomimetics[1] of the hormone somatostatin (SRIF).[2] This and more recent observations demonstrate that monosaccharides possess many characteristics which afford them particularly attractive scaffolds. They are readily available, chiral, conformationally rigid, highly functionalized, displaying the five hydroxyl groups in a well defined, three-dimensional arrangement as vectors for the introduction of diverse side-chains. In addition they possess pseudo symmetry,[2a] a potential advantage in the evaluation of new compounds in diverse screens.[2c] They have also been shown to be stable in gastric acid (pH 1.2 at 37 °C) and to glycosidases,[2d] thus offering a potential advantage to the limitations of peptidal therapeutic agents, such as low metabolic stability. The recent discovery that some congeners of β-D-glucose are also potent β-adrenergic and NK-1 antagonists[2b] suggested that β-D-glucose, and more generally monosaccharides, are *privileged* platforms for the design of therapeutically important agents. Taken together these observations raised our interest in the development of an efficient route for the selective functionalization of all five hydroxyl groups of the β-D-glucose scaffold. In this full account we describe a new approach for the preparation of carbohydrate-based libraries for broad screening.

Solid-support synthesis is presently the most widely used method to generate a library for lead discovery.[3] Our goal, therefore, was to develop a viable synthetic sequence in solution that could later be extended to solid-support. Much of the recent progress in carbohydrate solid-phase chemistry involves oligosaccharides or glycopeptides[4] and relies on two broad strategies.[5] In the first, the saccharide is anchored to the support via the C(6) hydroxyl group and functions as a donor in the coupling event. Alternatively, the saccharide can be linked to the resin via the C(1) hydroxyl group and serves as a glycosyl acceptor. For our purposes both protocols suffer from a common limitation: removal from the resin at the end of the on-resin synthetic sequence would reveal a free hydroxyl group, either at C(1) or at C(6), that would require additional solution-phase functionalization. A related strategy consists of attaching the monosaccharide scaffold to the solid support through a prelinked diversity element; this approach, however, restricts the choice for this side-chain (e.g., amino acids).[6] We instead envisaged use of a thioglycoside anchor that would serve as glycosyl donor, thus permitting glycosidation to remove the monosaccharide from the resin with simultaneous introduction of a diversity element at C(1).[7]

The use of thiol linkers has been used previously for oligosaccharide synthesis,[8,9] as well as for the sequential functionalization of D-galactose wherein an orthogonally protected[10] thioglycoside **1** was attached to a polystyrene resin via formation of an amide linkage (Scheme 1).[11] The requirement of monosaccharides with orthogonal protecting groups, however, would increase the synthetic complexity and the cost of such a library. We therefore devised a different strategy in which a thiol-functional-

(1) (a) Hirschmann, R. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1278−1301. (b) Giannis, A.; Kolter, T. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1244−1267. (c) Gante, J. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1699−1720.

(2) (a) Hirschmann, R.; Nicolaou, K. C.; Pietranico, S.; Leahy, E. M.; Salvino, J.; Arison, B.; Cichy, M. A.; Spoors, P. G.; Shakespeare, W. C.; Sprengeler, P. A.; Hamley, P.; Smith, A. B., III; Reisine, T.; Raynor, K.; Maechler, L.; Donaldson, C.; Vale, W.; Freidinger, R. M.; Cascieri, M. R.; Strader, C. D. *J. Am. Chem. Soc.* **1993**, *115*, 12550−12568. (b) Hirschmann, R.; Hynes, J., Jr.; Cichy-Knight, M. A.; van Rijn, R. D.; Sprengeler, P. A.; Spoors, P. G.; Shakespeare, W. C.; Pietranico-Cole, S.; Barbosa, J.; Liu, J.; Yao, W.; Rohrer, S.; Smith, A. B., III. *J. Med. Chem.* **1998**, *41*, 1382−1391. (c) Liu, J.; Underwood, D. J.; Cascieri, M. A.; Rohrer, S. P.; Cantin, L.-D.; Chicchi, G.; Smith, A. B, III.; Hirschmann, R. Manuscript in preparation. (d) Prasad, V. Manuscript in preparation.

(3) (a) Thompson, L. A.; Ellman, J. A. *Chem. Rev.* **1996**, *96*, 555−600. (b) Obrecht, D.; Villalgordo, J. M. *Solid-Supported Combinatorial and Parallel Synthesis of Small-Molecular-Weight Compound Libraries*; Tetrahedron Organic Chemistry Series Vol. 17; Pergamon: Oxford, 1998.

(4) (a) Osborn, H. M. I.; Khan, T. H. *Tetrahedron* **1999**, *55*, 1807−1850. (b) Sofia, M. J. *Mol. Diversity* **1998**, *3*, 75−94.

(5) Seeberger, P. H.; Danishefsky, S. J. *Acc. Chem. Res.* **1998**, *31*, 685−695.

(6) Sofia, M. J.; Hunter, R.; Chan, T. Y.; Vaughan, A.; Dulina, R.; Wang, H.; Gange, D. *J. Org. Chem.* **1998**, *63*, 2802−2803.

(7) For a review on glycosidation, see: Toshima, K.; Tatsuta, K. *Chem. Rev.* **1993**, *93*, 1503−1531.

(8) (a) Rademann, J.; Schmidt, R. R. *Tetrahedron Lett.* **1996**, *37*, 3989−3990. (b) Rademann, J.; Schmidt, R. R. *J. Org. Chem.* **1997**, *62*, 3650−3653.

(9) Yan, L.; Taylor, C. M.; Goodnow, R., Jr.; Kahne, D. *J. Am. Chem. Soc.* **1994**, *116*, 6953−6954.

(10) For orthogonal protection−deprotection strategies, see: (a) Wunberg, T.; Kallus, C.; Opatz, T.; Henke, S.; Schmidt, W.; Kunz, H. *Angew. Chem., Int. Ed.* **1998**, *37*, 2503−2505. (b) Wong, C.-H.; Ye, X.-S.; Zhang, Z. *J. Am. Chem. Soc.* **1998**, *120*, 7137−7138.

(11) Kallus, C.; Opatz, T.; Wunberg, T.; Schmidt, W.; Henke, S.; Kunz, H. *Tetrahedron Lett.* **1999**, *40*, 7783−7786.

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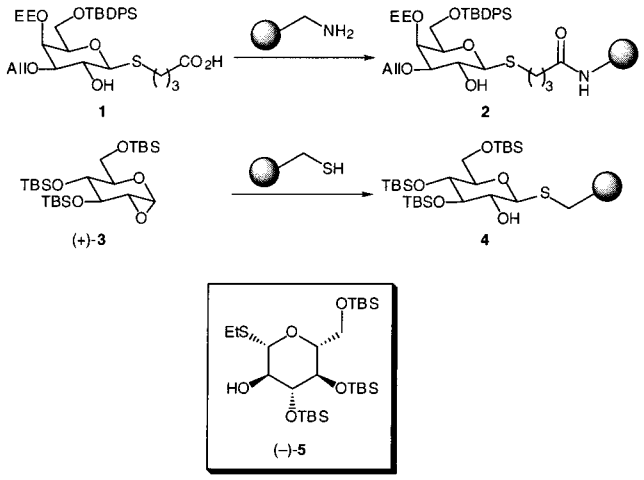
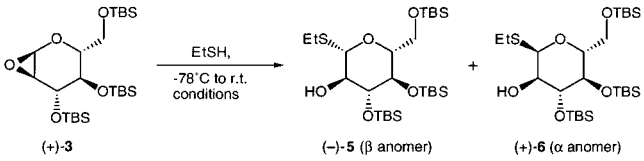
Scheme 1



ized resin would be employed as the nucleophile to react with an 1,2-α-anhydro sugar [e.g., (+)-**3**]. This tactic has the advantage of starting from the known epoxide (+)-**3**, readily available from tri-*O*-acetyl-D-glucal.[12] What remained was to design a short, efficient route to functionalize selectively the four hydroxyl substituents of the resin-bound thioglycoside **4**, noting that at this stage three of the hydroxyls were not differentiated. Toward this end, we explored the solution functionalization of (−)-**5** as a model for **4**. These studies permitted both the optimization of the individual steps and validation of our overall strategy for the diversity-oriented derivatization of the β-D-glucose scaffold.

Validation of the Solution-Phase Synthetic Strategy. Ethanethiol was used as the nucleophile for the opening of epoxide (+)-**3**, to mimic the thiol-functionalized resin (Scheme 2). Initial attempts employed zinc chloride as a Lewis acid promoter; the reaction, however, only proceeded in low yield (27%) and with no diastereoselectivity.[12] In contrast, use of trifluoroacetic anhydride in

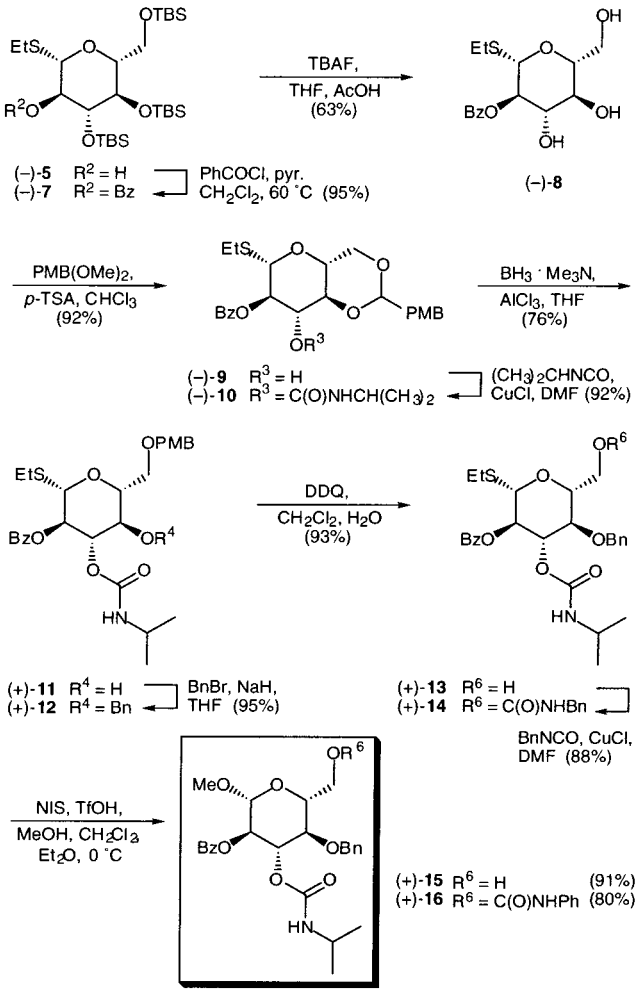
Scheme 2



reagent	solvent	reaction time	yield	5 / 6
$ZnCl_2$	THF	24 h	27%	~ 1 : 1
TFAA	CH_2Cl_2	2-4 days	85%	19 : 1
TFAA	toluene	36 h	81%	9 : 1

dichloromethane[13] furnished the desired β-anomer (−)-**5** in 85% yield together with 4% of the α-anomer (+)-**6** (19:1 selectivity). Toluene also proved effective as solvent, providing similar yields with good selectivity; the faster reaction time also facilitated reaction scale-up. We next introduced an ester group at C(2) to ensure formation of a β-D-glycosidic linkage (e.g., neighboring-group participation) in the final glycosidation reaction. Treatment of (−)-**5** with benzoyl chloride in pyridine/dichloromethane

Scheme 3



furnished (−)-**7** in 95% yield (Scheme 3). The silyl protecting groups in thioglycoside (−)-**7** were then removed with tetrabutylammonium fluoride (TBAF) under acidic conditions[14] so as to avoid benzoyl group migration from one hydroxyl to another. Both the C(4) and C(6) hydroxyls of (−)-**8** were then protected as the *p*-methoxybenzylidene (PMB) acetal. Unfortunately, alkylation of the remaining C(3) hydroxyl in (−)-**9** proved difficult; basic conditions (NaH) led to migration of the benzoyl group, while acidic reagents such as trichloroacetimidates[15] failed to react, presumably due to steric congestion. The C(3) hydroxyl group was therefore functionalized via a Cu(I)-mediated reaction with isopropyl isocyanate to afford carbamate (−)-**10** in good yield.[16] The *p*-methoxybenzylidene acetal in (−)-**10** was then reduced with borane−trimethylamine/aluminum(III) chloride in THF,[17] to install selectively a PMB ether at C(6) and to liberate a free hydroxyl group at C(4), while maintaining the benzoyl group intact. It is particularly noteworthy that reduction of benzylidene acetals under these conditions furnished substrates with a benzyl ether at C(4)

(12) Halcomb, R. L.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1989**, *111*, 6661−6666.

(13) Seeberger, P. H.; Eckhardt, M.; Gutteridge, C. E.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1997**, *119*, 10064−10072.

(14) Smith, A. B., III; Ott, G. R. *J. Am. Chem. Soc.* **1996**, *118*, 13095−13096 and references therein.

(15) (a) Iversen, T.; Bundle, D. R. *J. Chem. Soc., Chem. Commun.* **1981**, 1240−1241. (b) Wessel, H.-P.; Iversen, T.; Bundle, D. R. *J. Chem. Soc., Perkin Trans. 1* **1985**, 2247−2250.

(16) Duggan, M. E.; Imagire, J. S. *Synthesis* **1989**, 131−132.

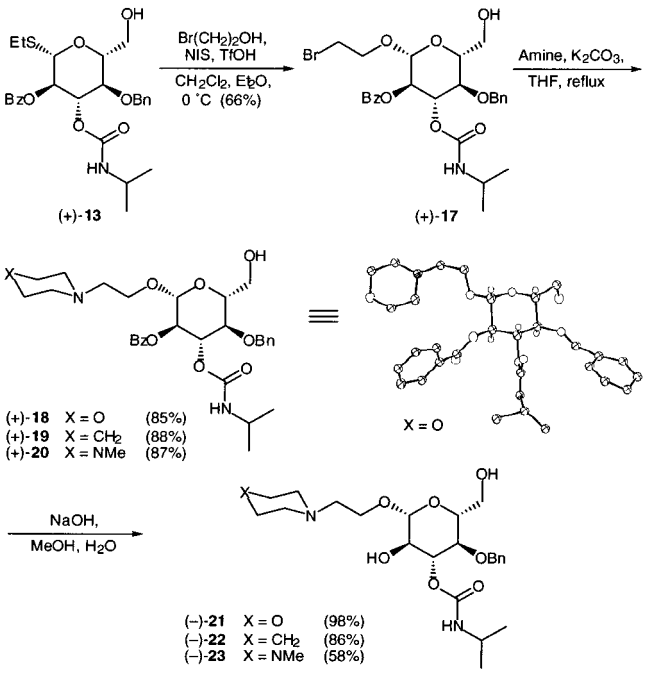
(17) (a) Ek, M.; Garegg, P. J.; Hultberg, H.; Oscarson, S. *J. Carbohydr. Chem.* **1983**, *2*, 305−311. (b) As reported in Smith, A. B., III; Hale, K. J.; Vaccaro, H. A.; Rivero, R. A. *J. Am. Chem. Soc.* **1991**, *113*, 2112−2122; in this case, however, the solvent was CH_2Cl_2.

and a hydroxyl group at C(6),[17] a result expected due to the large steric demand of the Lewis acid (kinetic product),[18] whereas *p*-methoxybenzylidene acetals under the same conditions lead to the opposite regioselectivity.[19] Presumably, the *p*-methoxy group decreases the reactivity of the acetal sufficiently via resonance to permit equilibration of the Lewis acid. Coordination of $AlCl_3$ to the more acidic C(4)-oxygen would then result in the formation of the thermodynamic product.

Continuing with the functionalization of (+)-**11**, alkylation afforded benzyl ether (+)-**12** in 95% yield. Oxidative-removal of the PMB group with 1,2-dichloro-4,5-dicyanobenzoquinone (DDQ) then gave alcohol (+)-**13**. Next, a second carbamate side-chain was introduced, yielding (+)-**14**, thereby illustrating that functionalization at C(6) is possible. In most cases, however, the C(6)-hydroxyl group was retained unfunctionalized partly to keep the molecular weight of the final products below 600 Da, while increasing water-solubility. Maintaining a free hydroxyl at C(6) could also be beneficial for binding.[20] Finally, glycosidation can be reliably accomplished with methanol, using promoters such as *N*-iodosuccinimide (NIS) and trifluorosulfonic acid,[21] to furnish the desired β-anomers (+)-**15** and (+)-**16** in 91% and 80% yield, respectively. Retention of configuration at the anomeric position through double inversion (anchimeric assistance) accounts for the observed greater than 9:1 β-stereoselectivity (^{1}H NMR). The fully substituted β-D-glucose derivative (+)-**16** is thus available in 10 steps and in 17.7% overall yield, corresponding to an average yield of 84% for each step.

Synthesis of a Small Library of β-D-Glucosides. To explore the scope of this reaction sequence as well as building block compatibility, we devised a small library of β-D-glucosides with potentially interesting biological properties. We were in particular interested in introducing side-chains that are not found among the coded amino acids. After replacement of the peptidic backbone by the β-D-glucose scaffold, this approach takes us one step further away from peptides in order to establish monosaccharides not only as peptidomimetics, but as an independent class of potentially important therapeutic agents. Glucoside (+)-**18**, incorporating a morpholine functionality, was selected as our first target. Attempted direct glycosidation of (+)-**13** with 4-(2-hydroxyethyl)morpholine afforded only unchanged starting material. Presumably the basic tertiary amine inhibits the acid-promoted glycosidation. To circumvent this difficulty, we employed a two-step sequence consisting of glycosidation with 2-bromoethanol as the nucleophile to furnish bromide (+)-**17** (Scheme 4); the reaction proceeded with greater than 9:1 β-selectivity. Substitution of the terminal bromide with morpholine then led to (+)-**18** as a beautifully crystalline solid. Single-crystal X-ray analysis confirmed the structure and stereochemistry. Glycosides (+)-**19** and (+)-**20** were similarly prepared from (+)-**17**, using piperidine and *N*-methylpiperazine as nucleophiles. Hydrolytic removal of the benzoyl groups then furnished the

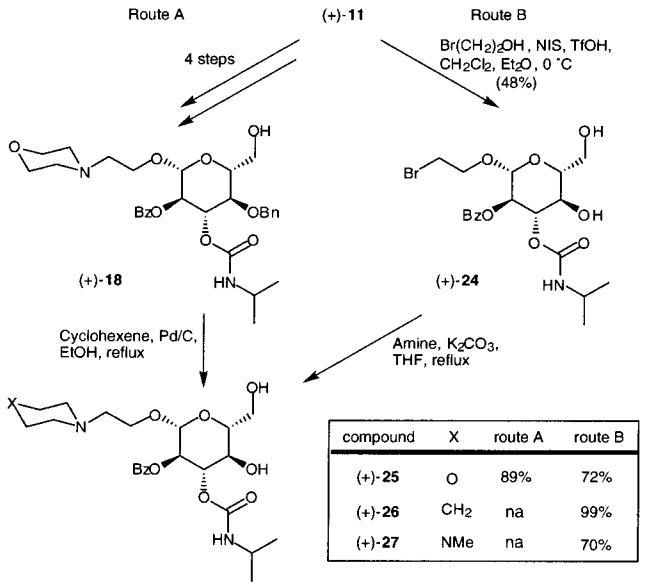
Scheme 4



more hydrophilic glycosides (+)-**21**, (+)-**22**, and (+)-**23**, with molecular weights of 468, 466, and 481 Da, respectively.

Derivatives lacking the C(4)-benzyl groups were also targeted to increase the diversity of our library while again reducing molecular weights. Toward this end, reductive removal of the benzyl group in (+)-**18** furnished (+)-**25** in 89% yield (Scheme 5). Interestingly, we discovered that glycosidation of (+)-**11** under the same conditions as previously presented simultaneously removed

Scheme 5



compound	X	route A	route B
(+)-**25**	O	89%	72%
(+)-**26**	CH_2	na	99%
(+)-**27**	NMe	na	70%

the PMB group at C(6) to give diol (+)-**24** in 48% yield (4:1 β-selectivity), thus offering an alternative route toward C(6)-unfunctionalized derivatives. Substitution of the bromide with morpholine, piperidine, and *N*-methylpiperazine generated (+)-**25**, (+)-**26** and (+)-**27** respectively, in yields ranging from 70 to 99%. This result also enabled us to convert thioglycoside (+)-**12** directly to (+)-

(18) Garegg, P. J.; Hultberg, H.; Wallin, S. *Carbohydr. Res.* **1982**, *108*, 97−101.
(19) Sanders, W. J.; Manning, D. D.; Koeller, K. M.; Kiessling, L. L. *Tetrahedron* **1997**, *53*, 16391−16422.
(20) Dinh, T. Q.; Smith, C. D.; Du, X.; Armstrong, R. W. *J. Med. Chem.* **1998**, *41*, 981−987.
(21) (a) Veeneman, G. H.; van Leeuwen, S. H.; van Boom, J. H. *Tetrahedron Lett.* **1990**, *31*, 1331−1334. (b) Konradsson, P.; Udodong, U. E.; Fraser-Reid, B. *Tetrahedron Lett.* **1990**, *31*, 4313−4316.

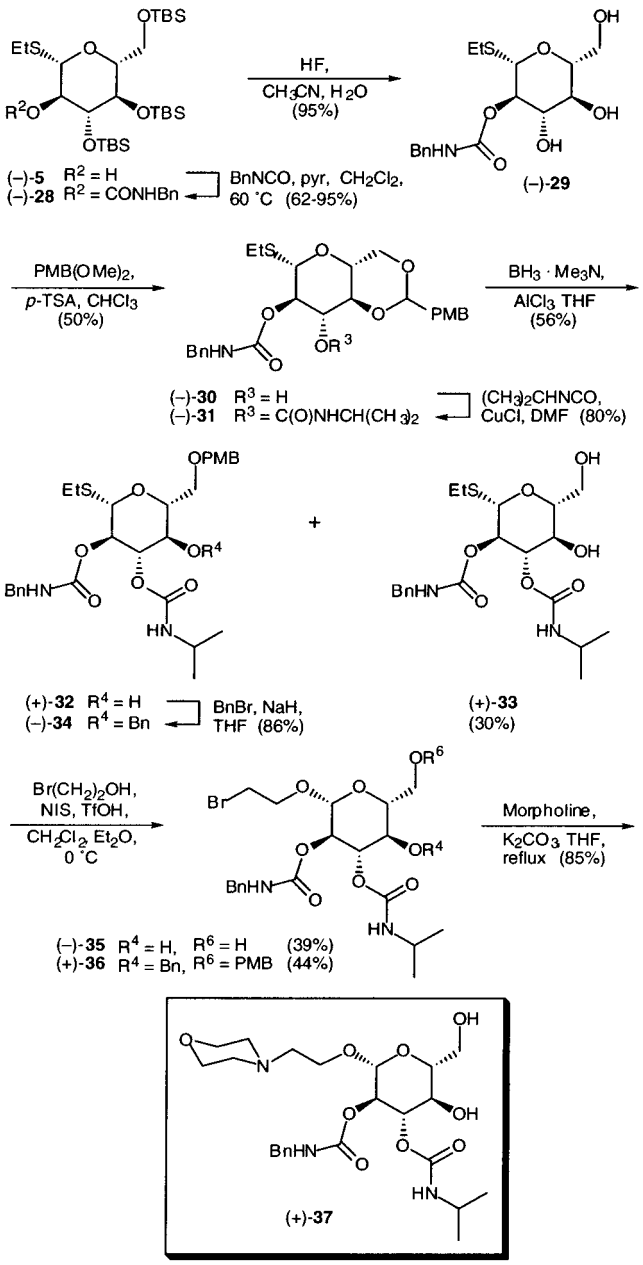
17 in 70% yield, with greater than 9:1 β-selectivity. Interestingly removal of the PMB group in (+)-**12** was faster than the glycosidation reaction, as evidenced by the isolation of thioglycoside (+)-**13** as the only product, upon premature quenching of the reaction. This observation supports NIS-mediated PMB oxidation of (+)-**12**, as opposed to deprotection via the in situ generated thiol.[22] *N*-Bromosuccinimide (NBS) has been reported to remove the *p*-methoxybenzyl moiety from ethers,[23] but to the best of our knowledge this is the first use of NIS. It is also notable that the benzyl moiety at C(4) remains intact under these conditions, illustrating that this protocol is selective for *p*-methoxybenzyl over benzyl ethers.

Anchimeric Assistance at C(2) via the Carbamate Group. A key element of our strategy for β-glucosides is the use of a participating group at C(2) to ensure formation of the desired 1,2-trans-β-glycoside in the final glycosidation. As discussed above, esters are well-known to furnish β-selective glucosidation. A participating group at C(2) that, unlike esters,[24] cannot be removed by proteases would be highly desirable. Although amides would fulfill this criteria, conversion of the C(2)-hydroxyl to the corresponding primary amine would significantly lengthen the synthetic sequence.[25] Carbamates appeared to be a better choice since they combine stability toward hydrolytic enzymes with ease of introduction. Moreover the effectiveness of C(2)-carbamates for stereoselective Koenigs−Knorr glycosidation of altrosyl fluorides has been reported.[26] Encouraged by this observation, a benzyl carbamate was installed at the C(2)-hydroxyl of (−)-**5** via reaction with benzyl isocyanate in pyridine/dichloromethane on the way to (+)-**37**. On small scale (ca. 100 mg) the reaction proved near quantitative; however, on larger scale complete conversion could not be achieved leading to significant recovered starting material (34%).

Continuing with the synthesis of (+)-**37** (Scheme 6), removal of the three TBS groups in carbamate (−)-**28** proved much faster and more efficient with hydrogen fluoride (HF) than with TBAF, as used previously (Scheme 3). Formation of the PMB acetal then permitted selective functionalization of the C(3)-hydroxyl again as a carbamate; reduction of the PMB acetal led to (+)-**32** in 56% isolated yield, along with 30% of the diol (+)-**33**. *O*-Benzylation of alcohol (+)-**32** next generated ether (−)-**34** in 86% yield. We were pleased to discover that both (+)-**33** and (−)-**34** could be glycosidated selectively (>95:5), albeit both in moderate yield (39% and 44%, respectively). Presumably the increased stability of the cyclic imminium intermediate compared to the cyclic oxonium species accounts for the better stereoselectivity but lower conversion. Substitution of (−)-**35** with morpholine then furnished diol (+)-**37** in 85% yield.

Summary. A new reaction pathway for the regio- and stereoselective functionalization of β-D-glucosides has been developed. This work sets the stage for the preparation of monosaccharide libraries in which β-D-glucose will serve as platform with the groups attached to the hydroxyls as diversity elements. The efficacy of the solution protocols has been demonstrated via the preparation of a small library of monosaccharides. We anticipate that the reaction sequence will prove easily amenable to solid-phase synthesis thereby facilitating the construction of diverse monosaccharide libraries. Studies toward this end are currently underway in our laboratory.

Scheme 6



Experimental Section[27]

Thioethyl 3,4,6-Tri-*O*-(*tert*-butyldimethylsilyl)-β-D-glucopyranrose (−)-5. To a solution of epoxide (+)-**3** (1.0 g, 1.98 mmol) and ethanethiol (1.47 mL, 19.84 mmol) in toluene (25 mL) at −78 °C under argon atmosphere was added trifluoroacetic anhydride (28 μL, 0.20 mmol). The reaction mixture was slowly allowed to warm to rt and stirred for 48 h. The excess ethanethiol was evaporated in vacuo and the resulting solution

(22) For thiol-mediated PMB deprotection, see for example: (a) Bouzide, A.; Sauvé, G. *Tetrahedron Lett.* **1999**, *40*, 2883−2886. (b) Yu, W.; Xiaobang, G.; Yang, Z.; Jin, Z. *Tetrahedron Lett.* **2000**, *41*, 4015−4017.

(23) Classon, B.; Garegg, P. J.; Samuelsson, B. *Acta Chem. Scand. B* **1984**, *38*, 419−422.

(24) Wermuth, C. G., Testa, B. In *The Practice of Medicinal Chemistry*; Wermuth, C. G., Ed.; Academic Press: London, 1996; pp 615−641.

(25) A new method to install a C(2)-*N*-acetylamino functionality directly from glucal derivatives has recently been published: Di Bussolo, V.; Liu, J.; Huffman, L. G., Jr.; Gin, D. Y. *Angew. Chem., Int. Ed.* **2000**, *39*, 204−207.

(26) Miethchen, R.; Rentsch, R. *Liebigs Ann. Chem.* **1996**, 539−543.

purified by flash chromatography (hexane/EtOAc 99:1) on silica gel to give (−)-**5** as a colorless oil (828 mg, 74%) and α-anomer (+)-**6** as a colorless oil (80 mg, 7%):

(−)-**5**: $[\alpha]_D^{25} = -49.0$ (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 2980 (w), 2960 (w), 2880 (w), 1270 (w), 850 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.62 (d, *J* = 7.0 Hz, 1 H), 4.05 (dd, *J* = 10.4, 6.2 Hz, 1 H), 3.76−3.71 (m, 3 H), 3.56−3.53 (m, 1 H), 3.45−3.41 (m, 1 H), 2.83 (d, *J* = 5.3 Hz, 1 H), 2.73−2.64 (m, 2 H), 1.31−1.27 (m, 3 H), 0.91 (s, 9 H), 0.89 (s, 9 H), 0.88 (s, 9 H), 0.13 (s, 3 H), 0.12 (s, 3 H), 0.11 (s, 3 H), 0.10 (s, 3 H), 0.04 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 84.83, 81.64, 75.97, 73.63, 70.78, 63.41, 26.29, 26.00, 25.93, 25.36, 18.49, 18.33, 18.02, 15.31, −3.49, −3.78, −3.95, −4.36, −5.19, −5.26; high-resolution mass spectrum (ES) *m*/*z* 589.3216 [(M + Na)$^+$; calcd for $C_{26}H_{58}O_5SSi_3Na$: 589.3211].

(+)-**6**: $[\alpha]_D^{25} = +28.6$ (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3040 (m), 2980 (w), 2940 (w), 2420 (w), 1430 (w), 1260 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.01 (s, 1 H), 3.95−3.84 (m, 4 H), 3.73 (d, *J* = 3.3 Hz, 1 H), 3.62 (d, *J* = 11.2 Hz, 1 H), 3.53−3.51 (m, 1 H), 2.72 (q, *J* = 7.3 Hz, 2 H), 1.29 (t, *J* = 7.3 Hz, 3 H), 0.89 (s, 9 H), 0.88 (s, 9 H), 0.87 (s, 9 H), 0.10 (s, 3 H), 0.08 (s, 9 H), 0.03 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 80.75, 78.01, 72.39, 71.47, 68.87, 60.86, 25.86, 25.79, 25.76, 25.21, 18.19, 17.97, 17.93, 15.15, −4.73, −4.85 (2×), −4.98, −5.35, −5.37; high-resolution mass spectrum (ES) *m*/*z* 589.3195 [(M + Na)$^+$; calcd for $C_{26}H_{58}O_5SSi_3Na$: 589.3211].

Thioethyl 2-*O*-Benzoyl-3,4,6-tri-*O*-(*tert*-butyldimethylsilyl)-β-D-glucopyranose (−)-**7.** A solution of thioglycoside (−)-**5** (2.04 g, 3.60 mmol) and benzoyl chloride (4.18 mL, 36.04 mmol) in pyridine (25 mL) and CH_2Cl_2 (50 mL) was heated at 50−60 °C for 36 h. The reaction mixture was allowed to cool, quenched with 1 M aq HCl (100 mL), and extracted with CH_2Cl_2 (3 × 100 mL). The combined organic extracts were dried (Na_2SO_4), evaporated in vacuo, and purified by flash chromatography (hexane/EtOAc 99:1) on silica gel to give (−)-**7** as a colorless oil (2.29 g, 95%): $[\alpha]_D^{25} = -0.7$ (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 2980 (m), 2960 (m), 2880 (m), 1735 (m), 1270 (m), 1120 (s), 850 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.04−8.02 (m, 2 H), 7.55−7.52 (m, 1 H), 7.42−7.39 (m, 2 H), 5.11−5.08 (m, 1 H), 4.90 (d, *J* = 9.0 Hz, 1 H), 3.91−3.84 (m, 3 H), 3.78−3.74 (m, 2 H), 2.76−2.60 (m, 2 H), 1.25−1.22 (m, 3 H), 0.89 (s, 9 H), 0.88 (s, 9 H), 0.86 (s, 9 H), 0.09 (s, 6 H), 0.07 (s, 3 H), 0.05 (s, 6 H), 0.04 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.43, 132.96, 130.22, 129.93, 128.22, 83.26, 80.62, 75.78, 74.87, 70.49, 63.74, 25.93, 25.91, 25.90, 24.17, 18.34, 18.02, 17.96, 14.94, −3.94, −4.21, −4.39, −4.43, −5.26 (2×); high-resolution mass spectrum (ES) *m*/*z* 693.3499 [(M + Na)$^+$; calcd for $C_{33}H_{62}O_6SSi_3Na$: 693.3473].

Thioethyl 2-*O*-Benzoyl-β-D-glucopyranose (−)-**8.** To a solution of thioglycoside (−)-**7** (2.29 g, 3.42 mmol) in THF (48.5 mL) and glacial acetic acid (1.5 mL) was added a 1 M tetrabutylammonium fluoride solution in THF (20.41 mL, 20.41 mmol), and the solution was stirred at rt for 5 days. The reaction was quenched with ice/water (10 mL), and the THF was evaporated in vacuo. The solution was diluted with EtOAc (100 mL) and washed with a saturated aqueous NaCl solution (100 mL), 1 M aq HCl (100 mL), a saturated aqueous $NaHCO_3$ solution (100 mL), and water (100 mL). The organic phase was dried (Na_2SO_4), evaporated in vacuo, and purified by flash chromatography (hexane/EtOAc 15:85) on silica gel to give (−)-**8** as a colorless solid (704 mg, 63%): mp 145−146 °C; $[\alpha]_D^{25} = -11.7$ (*c* 1.0, MeOH); IR ($CHCl_3$) 3040 (s), 2420 (m), 1530 (w), 1440 (w) cm^{-1}; ^1H NMR (500 MHz, CD_3OD) δ 8.05−8.02 (m, 2 H), 7.60−7.58 (m, 1 H), 7.49−7.46 (m, 2 H), 5.00−4.96 (m, 1 H), 4.66 (d, *J* = 10.0 Hz, 1 H), 3.91−3.87 (m, 1 H), 3.71−3.68 (m, 2 H), 3.46−3.37 (m, 2 H), 3.31−3.29 (m, 1 H), 2.77−2.67 (m, 2 H), 1.20 (t, *J* = 7.4 Hz, 3 H); ^{13}C NMR (125 MHz, CD_3OD) δ 167.42, 134.40, 131.72, 130.90, 129.62, 84.85, 82.46, 77.65, 74.76, 71.86, 63.04, 25.03, 15.38; ES-MS *m*/*z* 351 [100, (M + Na)$^+$]. Anal. Calcd for $C_{15}H_{20}O_6S$: C, 54.86; H, 6.14. Found: C, 55.06; H, 6.12.

Thioethyl 2-*O*-Benzoyl-4,6-*O*-(4-methoxybenzylidene)-β-D-glucopyranose (−)-**9.** A solution of thioglycoside (−)-**8** (1.25 g, 3.81 mmol), *p*-methoxybenzaldehyde dimethylacetal (3.25 mL, 19.05 mmol), and *p*-toluenesulfonic acid monohydrate (72 mg, 0.38 mmol) in $CHCl_3$ (200 mL) was stirred at rt for 3 h. The reaction mixture was evaporated in vacuo and purified by flash chromatography (hexane/EtOAc 75:25) on silica gel to give (−)-**9** as a colorless solid (1.56 g, 92%): mp 99−102 °C; $[\alpha]_D^{25} = -35.0$ (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3020 (s), 2420 (m), 1750 (w), 1530 (m), 1440 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.06 (d, *J* = 7.4 Hz, 2 H), 7.58−7.55 (m, 1 H), 7.46−7.42 (m, 2 H), 7.40 (d, *J* = 8.7 Hz, 2 H), 6.88 (d, *J* = 8.7 Hz, 2 H), 5.51 (s, 1 H), 5.23−5.20 (m, 1 H), 4.66 (d, *J* = 10.0 Hz, 1 H), 4.36 (dd, *J* = 10.5, 4.9 Hz, 1 H), 4.05−4.02 (m, 1 H), 3.78 (s, 3 H), 3.78−3.75 (m, 1 H), 3.64−3.61 (m, 1 H), 3.59−5.53 (m, 1 H), 2.73−2.67 (m, 3 H), 1.23 (t, *J* = 7.4 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.77, 160.33, 133.32, 129.97, 129.61, 129.37, 128.41, 127.60, 113.74, 101.88, 84.04, 80.80, 73.59, 73.07, 70.56, 68.53, 55.31, 24.10, 14.84; ES-MS *m*/*z* 469 [100, (M + Na)$^+$]. Anal. Calcd for $C_{23}H_{26}O_7S$: C, 61.87; H, 5.87. Found: C, 61.84; H, 6.05.

Thioethyl 2-*O*-Benzoyl-3-*O*-isopropylcarbamoyl-4,6-*O*-(4-methoxybenzylidene)-β-D-glucopyranose (−)-**10.** To a mixture of thioglycoside (−)-**9** (1.56 g, 3.50 mmol) and copper-(I) chloride (346 mg, 3.50 mmol) in DMF (50 mL) was added isopropyl isocyanate (360 μL, 3.67 mmol), and the reaction mixture was stirred at rt for 5 h. The reaction mixture was evaporated in vacuo and purified by flash chromatography (hexane/EtOAc 8:2) on silica gel to give (−)-**10** as a colorless solid (1.70 g, 92%): mp 190−192 °C; $[\alpha]_D^{25} = -19.8$ (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 1750 (s), 1280 (m), 1260 (m), 1110 (s), 1080 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, *J* = 7.2 Hz, 2 H), 7.56−7.53 (m, 1 H), 7.44−7.40 (m, 2 H), 7.38 (d, *J* = 8.7 Hz, 2 H), 6.85 (d, *J* = 8.7 Hz, 2 H), 5.47 (s, 1 H), 5.40−5.35 (m, 1 H), 5.26−5.21 (m, 1 H), 4.72 (d, *J* = 10.0 Hz, 1 H), 4.46−4.40 (m, 1 H), 4.36 (dd, *J* = 10.5, 4.8 Hz, 1 H), 3.82−3.70 (m, 1 H), 3.78 (s, 3 H), 3.68−3.50 (m, 3 H), 2.74−2.68 (m, 2 H), 1.22 (t, *J* = 7.5 Hz, 3 H), 0.98 (d, *J* = 6.5 Hz, 3 H), 0.73−0.72 (m, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.51, 160.15, 133.29, 130.01, 129.43, 128.38, 127.57, 113.57, 101.50, 84.39, 78.64, 73.28, 71.61, 71.05, 68.52, 55.27, 43.08, 24.45, 22.56, 22.38, 14.83; high-resolution mass spectrum (ES) *m*/*z* 554.1841 [(M + Na)$^+$; calcd for $C_{27}H_{33}NO_8SNa$: 554.1826].

Thioethyl 2-*O*-Benzoyl-3-*O*-isopropylcarbamoyl-6-*O*-(4-methoxybenzyl)-β-D-glucopyranose (+)-**11.** A solution of thioglycoside acetal (−)-**10** (322 mg, 0.61 mmol) and borane−trimethylamine complex (266 mg, 3.64 mmol) in THF (200 mL) was stirred at rt for 30 min. Aluminum chloride (485 mg, 3.64 mmol) was added, and the mixture was stirred at rt for 2 h. The reaction was quenched with a saturated aqueous NaCl solution (50 mL) and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic extracts were dried (Na_2SO_4), evaporated in vacuo, and purified by flash chromatography (hexane/EtOAc

(27) **Materials and Methods:** All reactions were carried out in oven- or flame-dried glassware under an argon atmosphere, unless otherwise noted. All solvents were reagent grade. Diethyl ether and tetrahydrofuran (THF) were freshly distilled from sodium/benzophenone under argon. Triethylamine (TEA) was distilled from calcium hydride and stored over potassium hydroxide. Anhydrous pyridine, *N*,*N*-dimethylformamide (DMF), toluene, and dimethyl sulfoxide (DMSO) were purchased from Aldrich and used without purification. Except as otherwise indicated, all reactions were magnetically stirred and monitored by thin-layer chromatography with Whatman 0.25-mm precoated silica gel plates. Flash column chromatography was performed using silica gel 60 (particle size 0.023−0.040 mm) supplied by E. Merck. Yields refer to chromatographically and spectroscopically pure compounds, unless otherwise stated. All melting points were obtained on a Thomas-Hoover apparatus and are corrected. Infrared spectra were recorded on a Perkin-Elmer Model 283B spectrometer with polystyrene as external standard. Proton and carbon-13 NMR spectra were recorded on a Bruker AM-500 spectrometer. Chemical shifts are reported relative to internal chloroform (δ 7.24) or methanol (δ 4.78) for ^1H and chloroform (δ 77.0) or methanol (δ 49.0) for ^{13}C. Optical rotations were measured with a Perkin-Elmer Model 241 polarimeter. High-resolution mass spectra were obtained at the University of Pennsylvania Mass Spectrometry Service Center with either a VG Micromass 70/70H or VG ZAB-E spectrometer. Microanalyses were performed at the University of Pennsylvania. Single-crystal X-ray structure determinations were performed at the University of Pennsylvania with an Enraf Nonius CAD-4 automated diffractometer.

6:4 to 5:5) on silica gel to give (+)-**11** as a colorless solid (245 mg, 76%): mp 105−106 °C; $[\alpha]_D^{25} = +27.6$ (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 1750 (s), 1530 (m), 1390 (s), 1360 (m), 1200 (s), 1090 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, $J = 7.4$ Hz, 2 H), 7.55−7.52 (m, 1 H), 7.43−7.40 (m, 2 H), 7.25 (d, $J = 8.9$ Hz, 2 H), 6.86 (d, $J = 8.9$ Hz, 2 H), 5.19−5.15 (m, 1 H), 4.99 (t, $J = 9.3$ Hz, 1 H), 4.59 (d, $J = 10.0$ Hz, 1 H), 4.52 (s, 2 H), 3.80−3.72 (m, 3 H), 3.78 (s, 3 H), 3.64−3.57 (m, 3 H), 2.71−2.67 (m, 2 H), 1.22 (t, $J = 7.5$ Hz, 3 H), 1.04 (d, $J = 6.2$ Hz, 3 H), 0.81 (d, $J = 6.3$ Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.47, 159.25, 155.76, 133.22, 129.98, 129.85, 129.48, 129.29, 128.34, 113.79, 83.40, 79.16, 77.95, 73.27, 70.59, 69.73, 55.22, 43.25, 24.22, 22.47, 22.40, 14.87; ES-MS *m/z* 556 [100, $(M + Na)^+$]. Anal. Calcd for $C_{27}H_{35}NO_8S$: C, 60.77; H, 6.61; N, 2.62. Found: C, 60.93; H, 6.41; N, 2.03.

Thioethyl 2-*O*-Benzoyl-4-*O*-benzyl-3-*O*-isopropylcarbamoyl-6-*O*-(4-methoxybenzyl)-*β*-D-glucopyranose (+)-**12.** To a 0 °C solution of thioglycoside (+)-**11** (100 mg, 0.19 mmol) and benzyl bromide (224 μL, 1.88 mmol) in anhydrous THF (5 mL) was added 60% sodium hydride (11 mg, 0.28 mmol), and the solution was stirred at rt for 3 h. The reaction was quenched with 1 M aq HCl (20 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were dried (Na_2SO_4), evaporated in vacuo, and purified by flash chromatography (hexane/EtOAc 9:1 to 7:3) on silica gel to give (+)-**12** as a colorless solid (111 mg, 95%): mp 123−125 °C; $[\alpha]_D^{25} = +22.4$ (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3040 (s), 2420 (m), 1750 (m), 1530 (m), 1520 (m), 1440 (m), 1280 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, $J = 7.8$ Hz, 2 H), 7.54−7.51 (m, 1 H), 7.42−7.39 (m, 2 H), 7.28−7.23 (m, 5 H), 7.19−7.18 (m, 2 H), 6.86 (d, $J = 8.5$ Hz, 2 H), 5.31−5.27 (m, 1 H), 5.17−5.13 (m, 1 H), 4.61−4.56 (m, 3 H), 4.50−4.46 (m, 2 H), 4.35 (d, $J = 7.4$ Hz, 1 H), 3.79 (s, 3 H), 3.75−3.69 (m, 3 H), 3.60−3.56 (m, 2 H), 2.74−2.66 (m, 2 H), 1.23 (t, $J = 7.4$ Hz, 3 H), 0.99 (d, $J = 6.3$ Hz, 3 H), 0.72 (d, $J = 6.0$ Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.63, 159.27, 154.35, 137.88, 133.14, 130.23, 129.98, 129.61, 129.46, 128.31, 128.27, 128.03, 127.71, 113.80, 83.43, 79.41, 76.55, 75.72, 74.31, 73.14, 71.42, 68.39, 55.26, 43.06, 24.24, 22.72, 22.39, 14.92; ES-MS *m/z* 646 [100, $(M + Na)^+$]. Anal. Calcd for $C_{34}H_{41}NO_8S$: C, 65.47; H, 6.63; N, 2.25. Found: C, 65.55; H, 6.41; N, 1.91.

Thioethyl 2-*O*-Benzoyl-4-*O*-benzyl-3-*O*-isopropylcarbamoyl-*β*-D-glucopyranose (+)-**13.** To a solution of thioglycoside (+)-**12** (120 mg, 0.19 mmol) in CH_2Cl_2 (10 mL) and water (0.5 mL) was added 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (48 mg, 0.21 mmol), and the solution was stirred at rt for 5 h. The reaction was quenched with a saturated aqueous $NaHCO_3$ solution (20 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were dried (Na_2SO_4), evaporated in vacuo, and purified by flash chromatography (hexane/EtOAc 8:2 to 6:4) on silica gel to give (+)-**13** as a colorless solid (90 mg, 93%): mp 178−180 °C; $[\alpha]_D^{25} = +32.1$ (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3040 (s), 2420 (m), 1750 (s), 1520 (m), 1280 (m), 1110 (m), 1090 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.03 (d, $J = 7.7$ Hz, 2 H), 7.55−7.52 (m, 1 H), 7.42−7.39 (m, 2 H), 7.32−7.24 (m, 5 H), 5.35−5.31 (m, 1 H), 5.14−5.10 (m, 1 H), 4.69−4.65 (m, 2 H), 4.60 (d, $J = 11.2$ Hz, 1 H), 4.46 (d, $J = 7.2$ Hz, 1 H), 3.93−3.90 (m,1 H), 3.76−3.69 (m, 2 H), 3.59−3.52 (m, 2 H), 2.72−2.67 (m, 2 H), 1.21 (t, $J = 7.4$ Hz, 3 H), 0.99 (d, $J = 6.3$ Hz, 3 H), 0.71 (d, $J = 6.1$ Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.61, 154.29, 137.67, 133.21, 129.96, 129.47, 128.37, 128.33, 128.10, 127.89, 83.61, 79.56, 76.42, 75.38, 74.46, 71.38, 61.84, 43.07, 24.45, 22.69, 22.34, 14.87; ES-MS *m/z* 526 [60, $(M + Na)^+$], 504 [70, $(M + H)^+$], 277 (100). Anal. Calcd for $C_{26}H_{33}NO_7S$: C, 62.01; H, 6.60; N, 2.78. Found: C, 61.94; H, 6.68; N, 2.65.

Thioethyl 2-*O*-Benzoyl-4-*O*-benzyl-6-*O*-benzylcarbamoyl-3-*O*-isopropylcarbamoyl-*β*-D-glucopyranose (+)-**14.** To a solution of thioglycoside (+)-**13** (45 mg, 0.09 mmol) and copper(I) chloride (9 mg, 0.09 mmol) in DMF (5 mL) was added benzyl isocyanate (22 μL, 0.18 mmol), and the solution was stirred at rt for 24 h. The DMF was evaporated in vacuo and the residue purified by flash chromatography (hexane/EtOAc 9:1 to 7:3) on silica gel to give (+)-**14** as a colorless solid (50 mg, 88%): mp 152−154 °C; $[\alpha]_D^{25} = +21.4$ (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3018 (m), 1729 (m), 1602 (w), 1509 (w), 1267 (w), 1224 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, $J = 8.3$ Hz, 2 H), 7.54−7.52 (m, 1 H), 7.42−7.39 (m, 2 H), 7.32−7.24 (m, 10 H), 5.35−5.29 (m, 1 H), 5.14−5.08 (m, 1 H), 5.04−5.00 (m, 1 H), 4.65−4.52 (m, 3 H), 4.44−4.30 (m, 5 H), 3.68−3.54 (m, 3 H), 2.68−2.65 (m, 2 H), 1.20 (t, $J = 7.4$ Hz, 3 H), 1.00 (d, $J = 6.0$ Hz, 3 H), 0.72 (d, $J = 5.8$ Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.59, 156.02, 154.21, 138.33, 137.39, 133.20, 129.94, 129.46, 128.66, 128.35, 128.32, 128.23, 127.90, 127.50, 83.51, 77.50, 76.48, 75.52, 74.36, 71.35, 63.53, 45.13, 43.09, 24.45, 22.68, 22.33, 14.83; high-resolution mass spectrum (ES) *m/z* 659.2427 $[(M + Na)^+$; calcd for $C_{34}H_{40}N_2O_8SNa$: 659.2403].

Methyl 2-*O*-Benzoyl-4-*O*-benzyl-3-*O*-isopropylcarbamoyl-*β*-D-glucopyranose (+)-**15.** To a solution of thioglycoside (+)-**13** (14 mg, 0.03 mmol) in CH_2Cl_2 (4.75 mL) and methanol (0.25 mL) at 0 °C was added a solution of *N*-iodosuccinimide (13 mg, 0.06 mmol) and trifluoromethane sulfonic acid (1 drop) in CH_2Cl_2/Et_2O 1:1 (2 mL), and the solution was stirred at 0 °C for 15 min. The reaction was quenched with a 10% aq $Na_2S_2O_3$ solution (20 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were dried (Na_2SO_4), evaporated in vacuo, and purified by flash chromatography (hexane/EtOAc 7:3) on silica gel to give (+)-**15** as a colorless solid (12 mg, 91%): mp 184−185 °C; $[\alpha]_D^{25} = +30.4$ (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3040 (s), 2420 (m), 1740 (s), 1520 (m), 1280 (m), 1110 (m), 1090 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.03 (d, $J = 7.3$ Hz, 2 H), 7.55−7.52 (m, 1 H), 7.42−7.39 (m, 2 H), 7.32−7.25 (m, 5 H), 5.33−5.29 (m, 1 H), 5.11−5.07 (m, 1 H), 4.68 (d, $J = 11.2$ Hz, 1 H), 4.60 (d, $J = 11.2$ Hz, 1 H), 4.55 (d, $J = 7.9$ Hz, 1 H), 4.42 (d, $J = 6.9$ Hz, 1 H), 3.92 (d, $J = 11.9$ Hz, 1 H), 3.79−3.70 (m, 2 H), 3.60−3.50 (m, 2 H), 3.47 (s, 3 H), 1.93 (br s, 1 H), 1.00 (d, $J = 6.2$ Hz, 3 H), 0.73 (d, $J = 6.0$ Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.65, 154.32, 137.68, 133.14, 129.95, 129.64, 128.41, 128.31, 128.15, 127.93, 101.87, 75.44, 75.30, 75.17, 74.50, 72.54, 61.69, 57.14, 43.10, 22.72, 22.38; high-resolution mass spectrum (ES) *m/z* 496.1967 $[(M + Na)^+$; calcd for $C_{25}H_{31}NO_8Na$: 496.1947].

Methyl 2-*O*-Benzoyl-4-*O*-benzyl-6-*O*-benzylcarbamoyl-3-*O*-isopropylcarbamoyl-*β*-D-glucopyranose (+)-**16.** To a solution of thioglycoside (+)-**14** (28 mg, 0.04 mmol) in CH_2Cl_2 (4.75 mL) and methanol (0.25 mL) at 0 °C was added a solution of *N*-iodosuccinimide (20 mg, 0.09 mmol) and trifluoromethane sulfonic acid (1 drop) in CH_2Cl_2/Et_2O 1:1 (2 mL), and the solution was stirred at 0 °C for 15 min. The reaction was quenched with a 10% aq $Na_2S_2O_3$ solution (20 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were dried (Na_2SO_4), evaporated in vacuo, and purified by flash chromatography (hexane/EtOAc 7:3) on silica gel to give (+)-**16** as a colorless solid (21 mg, 80%): mp 183−184 °C; $[\alpha]_D^{25} = +32.9$ (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3018 (m), 1730 (s), 1509 (m), 1270 (m), 1220 (s), 1093 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.03−8.01 (m, 2 H), 7.54−7.51 (m, 1 H), 7.42−7.39 (m, 2 H), 7.33−7.20 (m, 10 H), 5.33−5.28 (m, 1 H), 5.12−5.07 (m, 1 H), 5.04−4.99 (m, 1 H), 4.63 (d, $J = 10.5$ Hz, 1 H), 4.54 (d, $J = 10.5$ Hz, 1 H), 4.50 (d, $J = 7.8$ Hz, 1 H), 4.43−4.34 (m, 5 H), 3.65−3.55 (m, 3 H), 3.44 (s, 3 H), 1.00 (d, $J = 6.3$ Hz, 3 H), 0.73 (d, $J = 6.2$ Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.63, 156.06, 154.24, 138.32, 137.42, 133.13, 130.05, 129.95, 129.65, 128.70, 128.39, 128.31, 127.94, 127.56, 101.72, 75.51, 75.31, 74.38, 73.44, 72.47, 63.28, 56.99, 45.20, 43.12, 22.72, 22.37; ES-MS *m/z* 629 [100, $(M + Na)^+$]. Anal. Calcd for $C_{33}H_{38}N_2O_9$: C, 65.33; H, 6.31; N, 4.62. Found: C, 65.58; H, 6.48; N, 4.40.

2-Bromoethyl 2-*O*-Benzoyl-4-*O*-benzyl-3-*O*-isopropylcarbamoyl-*β*-D-glucopyranose (+)-**17. Method A.** To a solution of thioglycoside (+)-**13** (50 mg, 0.10 mmol) in CH_2Cl_2 (4.75 mL) and 2-bromoethanol (0.25 mL) at 0 °C was added a solution of *N*-iodosuccinimide (45 mg, 0.20 mmol) and trifluoromethane sulfonic acid (1 drop) in CH_2Cl_2/Et_2O 1:1 (2 mL), and the solution was stirred at 0 °C for 30 min. The reaction was quenched with a 10% aq $Na_2S_2O_3$ solution (50 mL) and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic extracts were dried (Na_2SO_4), evaporated in vacuo, and puri-

fied by flash chromatography (hexane/EtOAc 8:2 to 6:4) on silica gel to give (+)-**17** as a colorless solid (37 mg, 66%).

Method B. To a solution of thioglycoside (+)-**12** (100 mg, 0.16 mmol) in CH_2Cl_2 (9 mL) and 2-bromoethanol (1 mL) at 0 °C was added a solution of *N*-iodosuccinimide (90 mg, 0.40 mmol) and trifluoromethane sulfonic acid (3 drops) in CH_2Cl_2/Et_2O 1:1 (2 mL), and the solution was stirred at 0 °C for 2 h. The reaction was quenched with a 10% aq $Na_2S_2O_3$ solution (30 mL) and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic extracts were dried (Na_2SO_4), evaporated in vacuo, and purified by flash chromatography (hexane/EtOAc 8:2 to 6:4) on silica gel to give (+)-**17** as a colorless solid (64 mg, 70%).

(+)-**20**: mp 158−160 °C; $[\alpha]_D^{25}$ = +25.8 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3040 (s), 2420 (m), 1750 (s), 1520 (m), 1440 (w), 1430 (w), 1270 (s), 1110 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.0 Hz, 2 H), 7.49−7.46 (m, 1 H), 7.37−7.34 (m, 2 H), 7.27−7.19 (m, 5 H), 5.28−5.25 (m, 1 H), 5.08−5.05 (m, 1 H), 4.66 (d, *J* = 8.0 Hz, 1 H), 4.64 (d, *J* = 11.6 Hz, 1 H), 4.55 (d, *J* = 11.6 Hz, 1 H), 4.46 (d, *J* = 7.4 Hz, 1 H), 4.06−4.01 (m, 1 H), 3.87−3.84 (m, 1 H), 3.79−3.66 (m, 3 H), 3.56−3.52 (m, 1 H), 3.49−3.46 (m, 1 H), 3.30 (app. t, *J* = 6.3 Hz, 2 H), 1.96 (br s, 1 H), 0.95 (d, *J* = 6.3 Hz, 3 H), 0.70 (d, *J* = 6.1 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.87, 154.56, 137.88, 133.40, 130.15, 129.84, 128.65, 128.56, 128.39, 128.18, 101.32, 75.75, 75.53, 75.30, 74.76, 72.60, 69.94, 61.84, 43.35, 29.79, 22.95, 22.63; ES-MS *m*/*z* 590/588 [100, $(M + Na)^+$]. Anal. Calcd for $C_{26}H_{32}BrNO_8$: C, 55.21; H, 5.71; N, 2.48. Found: C, 55.56; H, 5.81; N, 2.40.

2-(Morpholin-4-yl)ethyl 2-*O*-Benzoyl-4-*O*-benzyl-3-*O*-isopropylcarbamoyl-β-D-glucopyranose (+)-**18.** A solution of glycoside (+)-**17** (28 mg, 0.05 mmol), potassium carbonate (68 mg, 0.49 mmol), and morpholine (43 μL, 0.49 mmol) in THF (5 mL) was heated at reflux for 7 h. The reaction was allowed to cool, quenched with a saturated aqueous $NaHCO_3$ solution (25 mL), and extracted with CH_2Cl_2 (3 × 25 mL). The combined organic extracts were dried (Na_2SO_4), evaporated in vacuo, and purified by flash chromatography (CH_2Cl_2/MeOH/Et_3N 90:9:1) on silica gel to give (+)-**18** as a colorless solid (24 mg, 85%): mp 138−140 °C; $[\alpha]_D^{25}$ = +15.6 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 2960 (w), 1750 (s), 1520 (m), 1470 (m), 1280 (s), 1120 (s), 1110 (s), 1100 (s), 1090 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, *J* = 7.4 Hz, 2 H), 7.55−7.52 (m, 1 H), 7.42−7.39 (m, 2 H), 7.32−7.25 (m, 5 H), 5.32−5.29 (m, 1 H), 5.11−5.07 (m, 1 H), 4.68 (d, *J* = 11.2 Hz, 1 H), 4.67 (d, *J* = 7.9 Hz, 1 H), 4.60 (d, *J* = 11.2 Hz, 1 H), 4.46 (d, *J* = 7.4 Hz, 1 H), 3.99−3.95 (m, 1 H), 3.89 (dd, *J* = 12.1, 2.5 Hz, 1 H), 3.76 (dd, *J* = 12.1, 4.1 Hz, 1 H), 3.73−3.69 (m, 1 H), 3.67−3.62 (m, 1 H), 3.62−3.56 (m, 1 H), 3.53−3.50 (m, 1 H), 3.47−3.38 (m, 4 H), 2.51−2.49 (m, 2 H), 2.36−2.31 (m, 4 H), 2.20 (br s, 1 H), 1.00 (d, *J* = 6.3 Hz, 3 H), 0.74 (d, *J* = 6.1 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.46, 154.33, 137.67, 133.27, 129.82, 129.52, 128.40 (2×), 128.14, 127.93, 100.87, 75.52, 75.42, 75.05, 74.47, 72.46, 67.97, 66.64, 61.70, 57.82, 53.93, 43.11, 22.72, 22.41; ES-MS *m*/*z* 573 [100, $(M + H)^+$]. Anal. Calcd for $C_{30}H_{40}N_2O_9$: C, 62.91; H, 7.04; N, 4.89. Found: C, 62.62; H, 7.12; N, 4.61.

2-(Piperidin-1-yl)ethyl 2-*O*-Benzoyl-4-*O*-benzyl-3-*O*-isopropylcarbamoyl-β-D-glucopyranose (+)-**19.** A solution of glycoside (+)-**17** (17 mg, 0.03 mmol), potassium carbonate (41 mg, 0.30 mmol), and piperidine (30 μL, 0.30 mmol) in THF (5 mL) was heated at reflux for 8 h. The reaction was allowed to cool, quenched with a saturated aqueous $NaHCO_3$ solution (25 mL), and extracted with CH_2Cl_2 (3 × 25 mL). The combined organic extracts were dried (Na_2SO_4), evaporated in vacuo, and purified by flash chromatography (CH_2Cl_2/MeOH/Et_3N 90:9:1) on silica gel to give (+)-**19** as a colorless solid (15 mg, 88%): mp 105−106 °C; $[\alpha]_D^{25}$ = +13.9 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 2960 (m), 1750 (s), 1520 (w), 1480 (w), 1290 (s), 1100 (s), 1080 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.02−8.01 (m, 2 H), 7.54−7.51 (m, 1 H), 7.42−7.38 (m, 2 H), 7.32−7.25 (m, 5 H), 5.31−5.28 (m, 1 H), 5.10−5.07 (m, 1 H), 4.70−4.66 (m, 2 H), 4.60 (d, *J* = 11.2 Hz, 1 H), 4.43 (d, *J* = 7.5 Hz, 1 H), 3.97−3.93 (m, 1 H), 3.88 (dd, *J* = 11.1, 2.5 Hz, 1 H), 3.76 (dd, *J* = 11.1, 4.2 Hz, 1 H), 3.73−3.66 (m, 2 H), 3.63−3.57 (m, 1 H), 3.54−3.51 (m, 1 H), 2.51 (t, *J* = 5.5 Hz, 2 H), 2.31 (br s, 5 H), 1.42−1.36 (m, 4 H), 1.28−1.25 (m, 2 H), 1.00 (d, *J* = 6.3 Hz, 3 H), 0.75 (d, *J* = 6.1 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.53, 154.35, 137.72, 133.14, 129.88, 129.62, 128.39, 128.32, 128.13, 127.89, 100.84, 75.60, 75.45, 75.08, 74.40, 72.58, 67.70, 61.72, 58.12, 54.75, 43.09, 25.54, 23.88, 22.72, 22.41; high-resolution mass spectrum (ES) *m*/*z* 571.2993 [$(M + H)^+$; calcd for $C_{31}H_{43}N_2O_8$: 571.3019].

2-(4-Methylpiperazin-1-yl)ethyl 2-*O*-Benzoyl-4-*O*-benzyl-3-*O*-isopropylcarbamoyl-β-D-glucopyranose (+)-**20.** A solution of glycoside (+)-**17** (20 mg, 0.04 mmol), potassium carbonate (48 mg, 0.35 mmol), and *N*-methylpiperazine (39 μL, 0.35 mmol) in THF (5 mL) was heated at reflux for 8 h. The reaction was allowed to cool, quenched with a saturated aqueous $NaHCO_3$ solution (25 mL), and extracted with CH_2Cl_2 (3 × 25 mL). The combined organic extracts were dried (Na_2SO_4), evaporated in vacuo, and purified by flash chromatography (CH_2Cl_2/MeOH/Et_3N 90:9:1 to 80:19:1) on silica gel to give (+)-**20** as a colorless solid (18 mg, 87%): mp 115−117 °C; $[\alpha]_D^{25}$ = +20.0 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 2960 (w), 1750 (s), 1520 (m), 1470 (w), 1290 (s), 1120 (m), 1100 (s), 1040 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, *J* = 7.5 Hz, 2 H), 7.54−7.51 (m, 1 H), 7.42−7.39 (m, 2 H), 7.31−7.25 (m, 5 H), 5.31−5.28 (m, 1 H), 5.10−5.07 (m, 1 H), 4.68−4.66 (m, 2 H), 4.60 (d, *J* = 11.2 Hz, 1 H), 4.45 (d, *J* = 7.1 Hz, 1 H), 3.98−3.94 (m, 1 H), 3.89 (dd, *J* = 12.1, 2.3 Hz, 1 H), 3.77 (dd, *J* = 12.1, 4.0 Hz, 1 H), 3.73−3.70 (m, 1 H), 3.67−3.63 (m, 1 H), 3.60−3.57 (m, 1 H), 3.52−3.50 (m, 1 H), 2.56 (t, *J* = 5.3 Hz, 2 H), 2.49 (br s, 4 H), 2.29 (br s, 4 H), 2.20 (s, 3 H), 1.00 (d, *J* = 6.1 Hz, 3 H), 0.74 (d, *J* = 5.9 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.46, 154.34, 137.71, 133.16, 129.88, 129.61, 128.38 (2×), 128.12, 127.89, 100.85, 75.57, 75.41, 75.05, 74.45, 72.53, 67.58, 61.55, 57.16, 54.58, 52.67, 45.53, 43.09, 22.71, 22.40; high-resolution mass spectrum (ES) *m*/*z* 586.3128 [$(M + H)^+$; calcd for $C_{31}H_{44}N_3O_8$: 586.3142].

2-(Morpholin-1-yl)ethyl 4-*O*-Benzyl-3-*O*-isopropylcarbamoyl-β-D-glucopyranose (−)-**21.** A solution of glycoside (+)-**18** (10 mg, 0.02 mmol) in methanol (2 mL) and 1 M aq NaOH (2 mL) was stirred at rt for 12 h. The reaction mixture was diluted with a saturated aqueous NaCl solution (20 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were dried (Na_2SO_4), evaporated in vacuo, and purified by flash chromatography (CH_2Cl_2/MeOH/Et_3N 90:9:1 to 80:19:1) on silica gel to give (−)-**21** as a colorless solid (8 mg, 98%): mp 51−53 °C; $[\alpha]_D^{25}$ = −20.3 (*c* 0.75, $CHCl_3$); IR ($CHCl_3$) 3040 (s), 2420 (m), 1740 (m), 1520 (m), 1090 (s), 1070 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.33−7.25 (m, 5 H), 4.94−4.90 (m, 1 H), 4.66 (d, *J* = 11.1 Hz, 1 H), 4.59 (d, *J* = 11.1 Hz, 1 H), 4.52 (d, *J* = 7.0 Hz, 1 H), 4.37 (d, *J* = 7.7 Hz, 1 H), 4.05−4.00 (m, 1 H), 3.86 (dd, *J* = 12.1, 2.6 Hz, 1 H), 3.85−3.77 (m, 1 H), 3.76−3.69 (m, 6 H), 3.59−3.55 (m, 1 H), 3.44−3.40 (m, 2 H), 2.68−2.63 (m, 1 H), 2.56−2.48 (m, 5 H), 1.14 (d, *J* = 6.5 Hz, 3 H), 1.12 (d, *J* = 6.4 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.58, 137.88, 128.41, 128.11, 127.90, 103.63, 78.08, 75.50, 75.45, 74.58, 73.06, 66.58, 66.44, 61.78, 57.86, 53.52, 43.33, 23.05, 22.79; high-resolution mass spectrum (ES) *m*/*z* 491.2387 [$(M + Na)^+$; calcd for $C_{23}H_{36}N_2O_8Na$: 491.2369].

2-(Piperidin-1-yl)ethyl 4-*O*-Benzyl-3-*O*-isopropylcarbamoyl-β-D-glucopyranose (−)-**22.** A solution of glycoside (+)-**19** (10 mg, 0.02 mmol) in methanol (2 mL) and 1 M aq NaOH (2 mL) was stirred at rt for 12 h. The reaction mixture was diluted with a saturated aqueous NaCl solution (10 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were dried (Na_2SO_4), evaporated in vacuo, and purified by preparative thin-layer chromatography (CH_2Cl_2/MeOH 80:20) on silica gel to give (−)-**22** as a colorless solid (7 mg, 86%): mp 58−60 °C; $[\alpha]_D^{25}$ = −15.6 (*c* 0.8, $CHCl_3$); IR ($CHCl_3$) 2960 (m), 1730 (s), 1510 (m), 1460 (m), 1240 (m), 1100 (s), 1060 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.33−7.25 (m, 5 H), 4.94−4.90 (m, 1 H), 4.67 (d, *J* = 11.1 Hz, 1 H), 4.58 (d, *J* = 11.1 Hz, 1 H), 4.58−4.55 (m, 1 H), 4.37 (d, *J* = 7.7 Hz, 1 H), 4.09−4.04 (m, 1 H), 3.86 (dd, *J* = 12.1, 2.6 Hz, 1 H), 3.85−3.74 (m, 2 H), 3.72 (dd, *J* = 12.1, 4.2 Hz, 1 H), 3.58−3.54 (m, 1 H), 3.44−3.41 (m, 2 H), 2.66−2.61 (m, 2 H), 2.56 (br s, 4 H), 1.66−1.62 (m, 4 H), 1.44 (br s, 2 H), 1.14 (d, *J* = 6.4 Hz, 3 H),

1.11 (d, $J = 6.4$ Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.59, 137.94, 128.39, 128.12, 127.85, 103.76, 78.15, 75.63, 75.50, 74.52, 72.81, 65.89, 61.80, 57.97, 54.36, 43.27, 24.84, 23.74, 23.06, 22.80; high-resolution mass spectrum (ES) *m/z* 467.2764 [$(M + H)^+$; calcd for $C_{24}H_{39}N_2O_7$: 467.2757].

2-(4-Methylpiperazin-1-yl)ethyl 4-*O*-Benzyl-3-*O*-isopropylcarbamoyl-*β*-D-glucopyranose (−)-**23.** A solution of glycoside (+)-**20** (21 mg, 0.04 mmol) in methanol (2 mL) and 1 M aq NaOH (2 mL) was stirred at rt for 12 h. The reaction mixture was diluted with a saturated aqueous NaCl solution (20 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were dried (Na_2SO_4), evaporated in vacuo, and purified by preparative thin-layer chromatography (CH_2Cl_2/MeOH 80:20) on silica gel to give (−)-**23** as a colorless solid (10 mg, 58%): mp 57−59 °C; $[\alpha]_D^{25} = -29.8$ (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 2960 (m), 2830 (m), 1740 (s), 1520 (m), 1470 (m), 1240 (m), 1180 (m), 1160 (m), 1090 (s), 1070 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34−7.25 (m, 5 H), 4.95−4.92 (m, 1 H), 4.66 (d, $J = 11.1$ Hz, 1 H), 4.58 (d, $J = 11.1$ Hz, 1 H), 4.55 (d, $J = 6.1$ Hz, 1 H), 4.37 (d, $J = 7.7$ Hz, 1 H), 4.04−3.99 (m, 1 H), 3.86 (dd, $J = 12.1$, 2.5 Hz, 1 H), 3.85−3.77 (m, 1 H), 3.75−3.70 (m, 1 H), 3.73 (dd, $J = 12.1$, 3.7 Hz, 1 H), 3.60−3.56 (m, 1 H), 3.43−3.40 (m, 2 H), 2.69−2.63 (m, 1 H), 2.57−2.52 (m, 5 H), 2.45 (br s, 4 H), 2.27 (s, 3 H), 1.14 (d, $J = 6.5$ Hz, 3 H), 1.11 (d, $J = 6.4$ Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.55, 137.92, 128.38, 128.09, 127.85, 103.58, 78.04, 75.53, 75.46, 74.53, 72.95, 66.45, 61.68, 57.34, 54.61, 52.80, 45.85, 43.28, 23.05, 22.81; high-resolution mass spectrum (ES) *m/z* 482.2844 [$(M + H)^+$; calcd for $C_{24}H_{40}N_3O_7$: 482.2866].

2-Bromoethyl 2-*O*-Benzoyl-3-*O*-isopropylcarbamoyl-*β*-D-glucopyranose (+)-**24.** To a solution of thioglycoside (+)-**11** (200 mg, 0.38 mmol) in CH_2Cl_2 (9.0 mL) and 2-bromoethanol (1.0 mL) at 0 °C was added a solution of *N*-iodosuccinimide (169 mg, 0.75 mmol) and trifluoromethane sulfonic acid (2 drops) in CH_2Cl_2/Et_2O 1:1 (5 mL), and the solution was stirred at 0 °C for 1 h. The reaction was quenched with a 10% aq $Na_2S_2O_3$ solution (30 mL) and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic extracts were dried (Na_2SO_4), evaporated in vacuo, and purified by flash chromatography (hexane/EtOAc 5:5 to 3:7) on silica gel to give (+)-**24** as a colorless solid (85 mg, 48%): mp 157−159 °C; $[\alpha]_D^{25} = +36.8$ (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 2940 (m), 1740 (s), 1280 (s), 1130 (s), 1100 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, $J = 7.5$ Hz, 2 H), 7.57−7.54 (m, 1 H), 7.44−7.41 (m, 2 H), 5.19−5.16 (m, 1 H), 4.97−4.93 (m, 1 H), 4.81 (d, $J = 7.6$ Hz, 1 H), 4.71 (d, $J = 8.0$ Hz, 1 H), 4.14−4.09 (m, 1 H), 3.98−3.74 (m, 5 H), 3.67−3.60 (m, 1 H), 3.52−3.48 (m, 1 H), 3.39−3.32 (m, 2 H), 2.28 (br s, 1 H), 1.06 (d, $J = 6.3$ Hz, 3 H), 0.87 (d, $J = 6.3$ Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.49, 156.20, 133.31, 129.85, 129.51, 128.39, 101.09, 76.07, 71.53, 69.99, 69.63, 62.29, 43.42, 29.60, 22.51, 22.45; high-resolution mass spectrum (ES) *m/z* 498.0738 [$(M + Na)^+$; calcd for $C_{19}H_{26}BrNO_8$-Na: 498.0740].

2-(Morpholin-4-yl)ethyl 2-*O*-Benzoyl-3-*O*-isopropylcarbamoyl-*β*-D-glucopyranose (+)-**25. Route A.** A solution of benzylglycoside (+)-**18** (8 mg, 0.01 mmol) and 10% Pd/C (2 mg) in cyclohexene (0.1 mL) and ethanol (2 mL) was heated at reflux for 12 h. The reaction mixture was filtered over Celite to give (+)-**25** as a colorless solid (6 mg, 89%).

Route B. A solution of glycoside (+)-**24** (30 mg, 0.06 mmol), potassium carbonate (87 mg, 0.63 mmol), and morpholine (55 μL, 0.63 mmol) in THF (5 mL) was heated at reflux for 8 h. The reaction was allowed to cool, quenched with a saturated aqueous $NaHCO_3$ solution (20 mL), and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were dried (Na_2SO_4), evaporated in vacuo, and purified by flash chromatography (CH_2Cl_2/MeOH/Et_3N 90:9:1) on silica gel to give (+)-**25** as a colorless solid (22 mg, 72%).

(+)-**25**: mp 140−142 °C; $[\alpha]_D^{25} = +21.2$ (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 2900 (m), 1740 (s), 1280 (s), 1270 (s), 1100 (s), 1080 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, $J = 7.4$ Hz, 2 H), 7.58−7.55 (m, 1 H), 7.45−7.42 (m, 2 H), 5.18−5.14 (m, 1 H), 4.96−4.92 (m, 1 H), 4.73 (d, $J = 7.4$ Hz, 1 H), 4.66 (d, $J = 7.9$ Hz, 1 H), 4.05−4.01 (m, 1 H), 3.95 (dd, $J = 11.9$, 3.2 Hz, 1 H), 3.85 (dd, $J = 11.9$, 4.9 Hz, 1 H), 3.77−3.74 (m, 1 H), 3.69−3.61 (m, 2 H), 3.57−3.44 (m, 5 H), 2.55 (br s, 2 H), 2.38 (br s, 4 H), 1.07 (d, $J = 6.4$ Hz, 3 H), 0.88 (d, $J = 6.4$ Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.33, 156.15, 133.43, 129.76, 129.44, 128.50, 100.84, 76.12, 71.72, 69.96, 67.68, 66.50, 62.25, 57.79, 53.88, 43.40, 22.54, 22.48; high-resolution mass spectrum (ES) *m/z* 483.2323 [$(M + H)^+$; calcd for $C_{23}H_{35}N_2O_9$: 483.2342].

2-(Piperidin-1-yl)ethyl 2-*O*-Benzoyl-3-*O*-isopropylcarbamoyl-*β*-D-glucopyranose (+)-**26.** A solution of glycoside (+)-**24** (11 mg, 0.02 mmol), potassium carbonate (32 mg, 0.23 mmol), and piperidine (23 μL, 0.23 mmol) in THF (3 mL) was heated at reflux for 8 h. The reaction was allowed to cool, quenched with a saturated aqueous $NaHCO_3$ solution (20 mL), and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were dried (Na_2SO_4), evaporated in vacuo, and purified by flash chromatography (CH_2Cl_2/MeOH/Et_3N 90:9:1) on silica gel to give (+)-**26** as a colorless solid (11 mg, 99%): mp 120 °C (dec); $[\alpha]_D^{25} = +23.4$ (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 2940 (m), 1740 (s), 1290 (s), 1100 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, $J = 7.2$ Hz, 2 H), 7.57−7.53 (m, 1 H), 7.44−7.41 (m, 2 H), 5.17−5.13 (m, 1 H), 4.97−4.93 (m, 1 H), 4.79 (d, $J = 7.8$ Hz, 1 H), 4.68 (d, $J = 7.9$ Hz, 1 H), 4.05−4.01 (m, 1 H), 3.95 (dd, $J = 11.9$, 3.1 Hz, 1 H), 3.85 (dd, $J = 11.9$, 5.0 Hz, 1 H), 3.78−3.70 (m, 2 H), 3.67−3.61 (m, 1 H), 3.50−3.47 (m, 1 H), 2.58 (t, $J = 5.5$ Hz, 2 H), 2.40 (br s, 4 H), 1.47−1.38 (m, 4 H), 1.31−1.27 (m, 2 H), 1.06 (d, $J = 6.4$ Hz, 3 H), 0.87 (d, $J = 6.4$ Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.45, 156.03, 133.34, 129.81, 129.50, 128.44, 100.69, 76.41, 71.94, 69.71, 66.52, 62.06, 57.66, 54.48, 45.73, 43.32, 24.66, 23.29, 22.56, 22.50; high-resolution mass spectrum (ES) *m/z* 481.2532 [$(M + H)^+$; calcd for $C_{24}H_{37}N_2O_8$: 481.2550].

2-(4-Methylpiperazin-1-yl)ethyl 2-*O*-Benzoyl-3-*O*-isopropylcarbamoyl-*β*-D-glucopyranose (+)-**27.** A solution of glycoside (+)-**24** (11 mg, 0.02 mmol), potassium carbonate (32 mg, 0.23 mmol), and *N*-methylpiperazine (26 μL, 0.23 mmol) in THF (3 mL) was heated at reflux for 8 h. The reaction was allowed to cool, quenched with a saturated aqueous $NaHCO_3$ solution (20 mL), and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were dried (Na_2SO_4), evaporated in vacuo, and purified by flash chromatography (CH_2Cl_2/MeOH/Et_3N 90:9:1 to 80:19:1) on silica gel to give (+)-**27** as a colorless solid (8 mg, 70%): mp 160 °C (dec); $[\alpha]_D^{25} = +14.0$ (*c* 0.8, $CHCl_3$); IR ($CHCl_3$) 2960 (m), 1740 (s), 1280 (s), 1270 (m), 1100 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, $J = 7.4$ Hz, 2 H), 7.57−7.54 (m, 1 H), 7.44−7.41 (m, 2 H), 5.17−5.14 (m, 1 H), 4.96−4.92 (m, 1 H), 4.77 (d, $J = 7.8$ Hz, 1 H), 4.67 (d, $J = 7.9$ Hz, 1 H), 4.00−3.96 (m, 1 H), 3.94 (dd, $J = 11.9$, 3.1 Hz, 1 H), 3.85 (dd, $J = 11.9$, 4.8 Hz, 1 H), 3.78−3.75 (m, 1 H), 3.66−3.62 (m, 2 H), 3.49−3.46 (m, 1 H), 2.54 (t, $J = 5.5$ Hz, 2 H), 2.43 (br s, 4 H), 2.22 (br s, 4 H), 2.15 (s, 3 H), 1.06 (d, $J = 6.4$ Hz, 3 H), 0.87 (d, $J = 6.4$ Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.34, 156.19, 133.29, 129.82, 129.58, 128.45, 100.94, 77.37, 76.09, 71.82, 69.96, 67.68, 62.28, 57.28, 54.75, 53.04, 45.78, 43.39, 22.57, 22.50; high-resolution mass spectrum (ES) *m/z* 496.2664 [$(M + H)^+$; calcd for $C_{24}H_{38}N_3O_8$: 496.2659].

Thioethyl 2-*O*-Benzylcarbamoyl-3,4,6-tri-*O*-(*tert*-butyldimethylsilyl)-*β*-D-glucopyranose (−)-**28.** To a solution of thioglycoside (−)-**5** (2.00 g, 3.53 mmol) and benzyl isocyanate (4.35 mL, 35.27 mmol) in pyridine (10 mL) and CH_2Cl_2 (40 mL) was added 60% sodium hydride (141 mg, 3.53 mmol), and the mixture was heated at reflux for 5 days. The reaction mixture was allowed to cool, quenched with 1 M aq HCl (50 mL), and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic extracts were dried (Na_2SO_4), evaporated in vacuo, and purified by flash chromatography (hexane/EtOAc 95:5) on silica gel to give (−)-**28** as a colorless solid (1.52 g, 62%): mp 89−90 °C; $[\alpha]_D^{25} = -12.0$ (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3040 (s), 2940 (m), 2420 (m), 1740 (m), 1540 (m), 1480 (m), 1440 (m), 1120 (m), 940 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34−7.23 (m, 5 H), 4.87−4.85 (m, 2 H), 4.74 (dd, $J = 8.8$, 3.2 Hz, 1 H), 4.63 (d, $J = 9.1$ Hz, 1 H), 4.40 (dd, $J = 14.8$, 5.9 Hz, 1 H), 4.35 (dd, $J = 14.8$, 5.9 Hz, 1 H), 3.84−3.78 (m, 2 H), 3.73−3.69 (m, 1 H), 3.62−3.59 (m, 1 H), 2.73−2.63 (m, 2 H), 1.24 (t,

J = 7.4, 3 H), 0.87 (s, 18 H), 0.87 (s, 9 H), 0.11 (s, 3 H), 0.08 (s, 3 H), 0.07 (s, 3 H), 0.06 (s, 3 H), 0.04 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.37, 138.44, 128.58, 127.52, 127.43, 82.97, 81.27, 76.06, 74.69, 70.67, 63.53, 45.16, 25.96, 25.92, 25.90, 24.02, 18.31, 18.05, 17.97, 14.86, −3.68, −3.91, −4.19, −4.32, −5.27 (2×); ES-MS m/z 722 [100, $(M + Na)^+$]. Anal. Calcd for $C_{34}H_{65}NO_6SSi_3$: C, 58.32; H, 9.36; N, 2.00. Found: C, 58.62; H, 9.56; N, 2.11.

Thioethyl 2-*O*-Benzylcarbamoyl-β-D-glucopyranose (−)-29. To a solution of thioglycoside (−)-**28** (1.92 g, 2.74 mmol) in acetonitrile (100 mL) at 0 °C was added 49% aq hydrofluoric acid (0.86 mL, 27.43 mmol), and the solution was stirred at rt for 1 h. The reaction mixture was evaporated in vacuo and purified by flash chromatography (EtOAc/MeOH 100:0 to 90:10) on silica gel to give (−)-**29** as a colorless solid (930 mg, 95%): mp 195−197 °C; $[\alpha]_D^{25}$ = −23.2 (c 1.0, MeOH); IR ($CHCl_3$) 3040 (s), 2420 (m), 1540 (m), 1530 (m), 1440 (m), 940 (m) cm^{-1}; ^{1}H NMR (500 MHz, CD_3OD) δ 7.38−7.24 (m, 5 H), 4.65−4.61 (m, 1 H), 4.51 (d, J = 10.0 Hz, 1 H), 4.41 (d, J = 15.4 Hz, 1 H), 4.32 (d, J = 15.4 Hz, 1 H), 3.91 (dd, J = 12.0, 1.9 Hz, 1 H), 3.70 (dd, J = 12.0, 5.8 Hz, 1 H), 3.58−3.54 (m, 1 H), 3.43−3.39 (m, 1 H), 3.36−3.31 (m, 2 H), 2.81−2.71 (m, 2 H), 1.28 (t, J = 7.4, 3 H); ^{13}C NMR (125 MHz, CD_3OD) δ 158.47, 140.54, 129.36, 128.23, 128.03, 85.10, 82.23, 77.64, 74.80, 71.70, 62.92, 45.50, 24.86, 15.17; ES-MS m/z 380 [100, $(M + Na)^+$]. Anal. Calcd for $C_{16}H_{23}NO_6S$: C, 53.77; H, 6.49; N, 3.92. Found: C, 54.08; H, 6.25; N, 3.85.

Thioethyl 2-*O*-Benzylcarbamoyl-4,6-*O*-(4-methoxybenzylidene)-β-D-glucopyranose (−)-30. To a solution of thioglycoside (−)-**29** (280 mg, 0.78 mmol) and p-toluenesulfonic acid monohydrate (15 mg, 0.08 mmol) in chloroform (75 mL) was added p-methoxybenzaldehyde dimethylacetal (0.67 mL, 3.92 mmol), and the solution was stirred at rt for 5 h. The reaction mixture was evaporated in vacuo without heating and purified by flash chromatography (hexane/EtOAc 5:5) on silylated silica gel to give (−)-**30** as a colorless solid (185 mg, 50%): mp 183−185 °C; $[\alpha]_D^{25}$ = −43.8 (c 1.0, $CHCl_3$); IR ($CHCl_3$) 3050 (s), 2430 (m), 1740 (w), 1530 (m), 1440 (m), 1110 (m), 1060 (m), 980 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (d, J = 7.9 Hz, 2 H), 7.34−7.25 (m, 5 H), 6.87 (d, J = 7.9 Hz, 2 H), 5.50 (s, 1 H), 5.11−5.09 (m, 1 H), 4.83−4.80 (m, 1 H), 4.49 (d, J = 10.0 Hz, 1 H), 4.48−4.43 (m, 1 H), 4.38−4.31 (m, 1 H), 3.90−3.88 (m, 1 H), 3.78 (s, 3 H), 3.76−3.72 (m, 1 H), 3.60−3.56 (m, 1 H), 3.48−3.44 (m, 1 H), 2.95 (br s, 1 H), 2.75−2.71 (m, 2 H), 1.26 (t, J = 7.5, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.28, 155.95, 138.05, 129.42, 128.67, 127.61, 127.57, 127.45, 113.69, 101.81, 84.04, 80.81, 73.99, 73.68, 70.47, 68.51, 55.30, 45.27, 24.00, 14.81; ES-MS m/z 973 [65, $(2M + Na)^+$], 539 [100, $(M + Na + MeCN)^+$], 498 [50, $(M + Na)^+$]. Anal. Calcd for $C_{24}H_{29}NO_7S$: C, 60.62; H, 6.15; N, 2.95. Found: C, 60.95; H, 6.32; N, 2.87.

Thioethyl 2-*O*-Benzylcarbamoyl-3-*O*-Isopropylcarbamoyl-4,6-*O*-(4-methoxybenzylidene)-β-D-glucopyranose (−)-31. To a solution of thioglycoside (−)-**30** (500 mg, 1.05 mmol) and copper(I) chloride (104 mg, 1.05 mmol) in DMF (25 mL) was added isopropyl isocyanate (124 μL, 1.26 mmol), and the solution was stirred at rt for 12 h. The DMF was evaporated in vacuo, and the mixture was purified by flash chromatography (hexane/EtOAc 6:4) on silica gel to give (−)-**31** as a colorless solid (470 mg, 80%): mp 205−207 °C; $[\alpha]_D^{25}$ = −42.1 (c 1.0, $CHCl_3$); IR ($CHCl_3$) 3050 (s), 2420 (m), 1750 (s), 1530 (s), 1120 (m), 1100 (m), 1090 (m), 1050 (m), 940 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (d, J = 8.5 Hz, 2 H), 7.31−7.24 (m, 5 H), 6.84 (d, J = 8.5 Hz, 2 H), 5.44 (s, 1 H), 5.20−5.14 (m, 1 H), 5.14−5.09 (m, 1 H), 4.95−4.88 (m, 1 H), 4.60−4.55 (m, 1 H), 4.54 (d, J = 10.0 Hz, 1 H), 4.42 (dd, J = 14.8, 5.9, 1 H), 4.34−4.31 (m, 2 H), 3.77 (s, 3 H), 3.77−3.72 (m, 2 H), 3.64−3.59 (m, 1 H), 3.55−3.50 (m, 1 H), 2.73 (q, J = 7.3 Hz, 2 H), 1.25 (t, J = 7.3, 3 H), 1.09−1.07 (m, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.05, 155.23, 154.63, 138.14, 129.43, 128.54, 127.46, 127.40, 127.28, 113.49, 101.28, 84.49, 78.66, 73.42, 71.77, 70.76, 68.44, 55.23, 45.06, 43.17, 24.17, 22.75, 22.66, 14.77; ES-MS m/z 583 [100, $(M + Na)^+$]. Anal. Calcd for $C_{28}H_{36}N_2O_8S$: C, 59.98; H, 6.47; N, 5.00. Found: C, 59.97; H, 6.50; N, 4.89.

Thioethyl 2-*O*-Benzylcarbamoyl-3-*O*-isopropylcarbamoyl-6-*O*-(4-methoxybenzyl)-β-D-glucopyranose (+)-32. A solution of thioglycoside acetal (−)-**31** (90 mg, 0.16 mmol) and borane−trimethylamine complex (70 mg, 0.96 mmol) in anhydrous THF (20 mL) was stirred at rt for 30 min. Aluminum chloride (128 mg, 0.96 mmol) was then added and the mixture stirred at rt for 12 h. The reaction was quenched with a saturated aqueous NaCl solution (20 mL), the THF evaporated in vacuo, and the residual solution extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were dried (Na_2SO_4), evaporated in vacuo, and purified by flash chromatography (hexane/EtOAc 6:4 to 5:5) on silica gel to give (+)-**32** as a colorless solid (51 mg, 56%) and (+)-**33** as a colorless solid (21 mg, 30%):

(+)-**32**: mp 146−148 °C; $[\alpha]_D^{25}$ = +15.4 (c 1.0, $CHCl_3$); IR ($CHCl_3$) 3020 (w), 3000 (w); 2940 (w), 2900 (w), 2420 (w), 1750 (s), 1620 (w), 1530 (s), 1470 (w), 1430 (w), 1090 (m), 1060 (m), 940 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28−7.21 (m, 7 H), 6.84 (d, J = 8.6 Hz, 2 H), 5.21−5.18 (m, 1 H), 4.86−4.76 (m, 2 H), 4.48 (s, 2 H), 4.42 (d, J = 9.5 Hz, 1 H), 4.36−4.32 (m, 1 H), 3.77 (s, 3 H), 3.77−3.66 (m, 4 H), 3.64−3.59 (m, 1 H), 3.53−3.48 (m, 1 H), 2.73−2.67 (m, 2 H), 1.24 (t, J = 7.4, 3 H), 1.11 (d, J = 6.0 Hz, 3 H), 1.08 (d, J = 6.2 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.22, 156.16, 155.31, 138.24, 130.03, 129.26, 128.55, 127.41, 127.28, 113.77, 83.50, 79.19, 78.27, 73.22, 70.83, 70.63, 69.69, 55.22, 45.03, 43.36, 24.03, 22.74, 22.58, 14.85; ES-MS m/z 585 [100, $(M + Na)^+$]. Anal. Calcd for $C_{28}H_{38}N_2O_8S$: C, 59.77; H, 6.81; N, 4.98. Found: C, 59.72; H, 7.03; N, 4.97.

(+)-**33**: mp 160−162 °C; $[\alpha]_D^{25}$ = +28.9 (c 1.0, $CHCl_3$); IR ($CHCl_3$) 3013 (w), 2974 (w), 2932 (w), 2875 (w), 1731 (s), 1515 (s), 1456 (w), 1226 (s), 1078 (m), 1050 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32−7.24 (m, 5 H), 5.12−5.08 (m, 1 H), 4.91−4.88 (m, 1 H), 4.86−4.81 (m, 1 H), 4.75−4.70 (m, 1 H), 4.44 (d, J = 10.0 Hz, 1 H), 4.42−4.33 (m, 2 H), 3.92 (dd, J = 12.0, 3.3 Hz, 1 H), 3.80−3.74 (m, 2 H), 3.67−3.64 (m, 1 H), 3.44−3.41 (m, 1 H), 2.72−2.69 (m, 2 H), 1.25 (t, J = 7.4, 3 H), 1.13 (d, J = 6.4 Hz, 3 H), 1.10 (d, J = 6.3 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.58, 155.30, 138.18, 128.65, 127.57, 127.36, 83.67, 80.08, 78.89, 70.61, 70.36, 62.63, 45.16, 43.52, 24.10, 22.76, 22.61, 14.83; ES-MS m/z 465 [100, $(M + Na)^+$]. Anal. Calcd for $C_{20}H_{30}N_2O_7S$: C, 54.28; H, 6.83; N, 6.33. Found: C, 54.26; H, 7.04; N, 6.18.

Thioethyl 4-*O*-Benzyl-2-*O*-benzylcarbamoyl-3-*O*-isopropylcarbamoyl-6-*O*-(4-methoxybenzyl)-β-D-glucopyranose (−)-34. To a 0 °C solution of thioglycoside (+)-**32** (25 mg, 0.04 mmol) and benzyl bromide (52 μL, 0.44 mmol) in anhydrous THF (5 mL) was added 60% sodium hydride (2 mg, 0.05 mmol), and the solution was stirred at rt for 1 h. The reaction was quenched with 1 M aq HCl (20 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were dried (Na_2SO_4), evaporated in vacuo, and purified by flash chromatography (hexane/EtOAc 8:2) on silica gel to give (−)-**34** as a colorless solid (25 mg, 86%): mp 148−151 °C; $[\alpha]_D^{25}$ = −1.8 (c 1.0, $CHCl_3$); IR ($CHCl_3$) 3019 (s), 1732 (s), 1513 (s), 1224 (s), 1082 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28−7.16 (m, 12 H), 6.86−6.83 (m, 2 H), 5.15−5.05 (m, 2 H), 4.86−4.79 (m, 1 H), 4.60−4.29 (m, 9 H), 3.78 (s, 3 H), 3.71−3.63 (m, 3 H), 3.52−3.49 (m, 1 H), 2.74−2.68 (m, 2 H), 1.25 (t, J = 7.2 Hz, 3 H), 1.09−1.06 (m, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.23, 155.37, 154.68, 138.21, 137.82, 130.22, 129.42, 128.55, 128.26, 128.06, 127.71, 127.39, 127.30, 113.77, 83.55, 79.26, 75.83, 74.36, 73.10, 71.55, 68.37, 55.24, 45.06, 43.18, 23.98, 22.86, 22.80, 14.88; high-resolution mass spectrum (ES) m/z 675.2732 [$(M + Na)^+$; calcd for $C_{35}H_{44}N_2O_8SNa$: 675.2716].

2-Bromoethyl 2-*O*-Benzylcarbamoyl-3-*O*-isopropylcarbamoyl-β-D-glucopyranose (−)-35. To a solution of thioglycoside (+)-**33** (50 mg, 0.11 mmol) in CH_2Cl_2 (4.75 mL) and 2-bromoethanol (0.25 mL) at 0 °C was added a solution of *N*-iodosuccinimide (52 mg, 0.23 mmol) and trifluoromethane sulfonic acid (1 drop) in CH_2Cl_2/Et_2O 1:1 (2 mL), and the solution was stirred at 0 °C for 30 min. The reaction was quenched with a 10% aq $Na_2S_2O_3$ solution (20 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic

extracts were dried (Na_2SO_4), evaporated in vacuo, and purified by flash chromatography (hexane/EtOAc 4:6 to 2:8) on silica gel to give (−)-**35** as a colorless solid (22 mg, 39%): mp 188−189 °C; $[\alpha]_D^{25} = -4.4$ (*c* 1.0, MeOH); IR ($CHCl_3$) 3014 (m), 1732 (m), 1699 (m), 1517 (m), 1212 (s), 1086 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.32−7.24 (m, 5 H), 5.11−5.06 (m, 1 H), 4.92 (d, $J = 6.6$ Hz, 1 H), 4.84−4.79 (m, 1 H), 4.73−4.69 (m, 1 H), 4.52 (d, $J = 7.9$ Hz, 1 H), 4.40−4.32 (m, 2 H), 4.14−4.09 (m, 1 H), 3.92 (dd, $J = 11.9$, 3.3 Hz, 1 H), 3.84−3.64 (m, 3 H), 3.81 (dd, $J = 11.9$, 4.8 Hz, 1 H), 3.44−3.37 (m, 3 H), 1.14 (d, $J = 6.5$ Hz, 3 H), 1.11 (d, $J = 6.7$ Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.62, 155.39, 138.16, 128.68, 127.62, 127.48, 101.19, 77.69, 75.94, 71.84, 70.28, 69.48, 62.39, 45.22, 43.53, 29.90, 22.75, 22.61; high-resolution mass spectrum (ES) *m/z* 527.1026 [$(M + Na)^+$; calcd for $C_{20}H_{29}BrN_2O_8Na$: 527.1005].

2-Bromoethyl 4-*O*-Benzyl-2-*O*-benzylcarbamoyl-3-*O*-isopropylcarbamoyl-*β*-D-glucopyranose (+)-**36.** To a solution of thioglycoside (−)-**34** (10 mg, 0.02 mmol) in CH_2Cl_2 (2.30 mL) and 2-bromoethanol (0.20 mL) at 0 °C was added a solution of *N*-iodosuccinimide (9 mg, 0.04 mmol) and trifluoromethane sulfonic acid (1 drop) in CH_2Cl_2/Et_2O 1:1 (2 mL), and the solution was stirred at 0 °C for 4 h and at rt for 2 h. The reaction was quenched with a 10% aq $Na_2S_2O_3$ solution (20 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were dried (Na_2SO_4), evaporated in vacuo, and purified by flash chromatography (hexane/EtOAc 6:4) on silica gel to give (+)-**36** as a colorless amorphous solid (4 mg, 44%): $[\alpha]_D^{25} = +2.7$ (*c* 0.5, $CHCl_3$); IR ($CHCl_3$) 3019 (s), 1732 (m), 1514 (m), 1220 (s), 1208 (s), 1082 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.32−7.21 (m, 10 H), 5.15−5.08 (m, 2 H), 4.77 (d, $J = 9.2$ Hz, 1 H), 4.66 (d, $J = 10.8$ Hz, 1 H), 4.61−4.54 (m, 2 H), 4.52 (d, $J = 7.9$ Hz, 1 H), 4.41−4.29 (m, 2 H), 4.12−4.07 (m, 1 H), 3.89−3.70 (m, 4 H), 3.67−3.62 (m, 1 H), 3.45−3.39 (m, 3 H), 1.11 (d, $J = 6.5$ Hz, 3 H), 1.09 (d, $J = 6.7$ Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.42, 154.68, 137.59, 128.64, 128.51, 128.44, 128.21, 127.99, 127.53, 127.44, 101.26, 75.33, 74.59, 69.64, 61.64, 45.16, 43.29, 29.74, 29.70, 22.90, 22.88; high-resolution mass spectrum (ES) *m/z* 617.1480 [$(M + Na)^+$; calcd for $C_{27}H_{35}BrN_2O_8Na$: 617.1475].

2-(Morpholin-4-yl)ethyl 2-*O*-Benzylcarbamoyl-3-*O*-isopropylcarbamoyl-*β*-D-glucopyranose (+)-**37.** A solution of glycoside (−)-**35** (14 mg, 0.03 mmol), potassium carbonate (39 mg, 0.28 mmol), and morpholine (24 μL, 0.28 mmol) in THF (5 mL) was heated at reflux for 7 h. The reaction was allowed to cool, quenched with a saturated aqueous $NaHCO_3$ solution (20 mL), and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were dried (Na_2SO_4), evaporated in vacuo, and purified by flash chromatography (CH_2Cl_2/MeOH/Et_3N 90:9:1) on silica gel to give (+)-**37** as a colorless solid (12 mg, 85%): mp 181−183 °C; $[\alpha]_D^{25} = +15.6$ (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3018 (s), 1732 (m), 1702 (m), 1517 (m), 1224 (s), 1207 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.32−7.24 (m, 5 H), 5.17−5.13 (m, 1 H), 4.96 (d, $J = 7.1$ Hz, 1 H), 4.82−4.78 (m, 1 H), 4.75−4.70 (m, 1 H), 4.49 (d, $J = 7.7$ Hz, 1 H), 4.37−4.30 (m, 2 H), 4.05−4.00 (m, 1 H), 3.91 (dd, $J = 11.9$, 2.5 Hz, 1 H), 3.80 (dd, $J = 11.9$, 4.8 Hz, 1 H), 3.74−3.65 (m, 7 H), 3.41−3.38 (m, 1 H), 2.64 (br s, 2 H), 2.55 (br s, 4 H), 1.13 (d, $J = 6.3$ Hz, 3 H), 1.09 (d, $J = 6.2$ Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.39, 155.53, 138.21, 128.68, 127.60, 127.36, 100.93, 76.06, 72.34, 69.68, 66.76, 66.46, 62.05, 57.89, 53.88, 45.10, 43.38, 22.75, 22.58; high-resolution mass spectrum (ES) *m/z* 512.2586 [$(M + H)^+$; calcd for $C_{24}H_{37}N_3O_9$: 512.2608].

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Supporting Information Available: Spectroscopic data for glycosides (+)-**15**, (+)-**16**, (+)-**25**, and (+)-**37**. This material is available free of charge via the Internet at http://pubs.acs.org.

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