From D-Glucose to Biologically Potent L-Hexose Derivatives: Synthesis of α-L-Iduronidase Fluorogenic Detector and the Disaccharide Moieties of Bleomycin A_2 and Heparan Sulfate

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Dedicated to Professor Sunney I. Chan on the occasion of his 67th birthday

Abstract: A novel and convenient route for the synthesis of biologically potent and rare L-hexose derivatives from D-glucose is described. Conversion of diacetone-α-D-glucose (**14**) into 1,2:3,5-di-*O*-isopropylidene-β-L-idofuranose (**19**) was efficiently carried out in two steps. Orthogonal isopropylidene rearrangement of compound **19** led to 1,2:5,6-di-*O*-isopropylidene-β-L-idofuranose (**27**), which underwent regioselective epimerization at the C3 position to give the L-talo- and 3-functionalized L-idofuranosyl derivatives. Hydrolysis of compound **19** under acidic conditions furnished 1,6-anhydro-β-L-idopyranose (**35**) in excellent yield, which was successfully transformed into the corresponding L-*allo*, L-*altro*, L-*gulo*, and L-*ido* derivatives via regioselective benzylation, benzoylation, triflation and nucleophilic substitution as the key steps. Applications of these 1,6-anhydro-β-L-hexopyranoses as valuable building blocks to the syntheses of 4-methylcoumarin-7-yl-α-L-iduronic acid and the disaccharide moieties of bleomycin A_2 as well as heparan sulfate are highlighted.

Keywords: 1,6-anhydro-β-L-hexopyranoses · bleomycin A_2 · carbohydrates · glycosides · heparan sulfate

Introduction

The rare L-hexoses are key components of numerous biologically potent oligosaccharides, antibiotics, glycopeptides, terpene glycosides, as well as steroid glycosides (Figure 1).[1] A remarkable example is presented by bleomycin A_2 **1**,[2] a significant antitumor drug exhibiting strong activity through DNA binding and metal-dependent oxidative cleavage of nucleotides in the presence of oxygen. It belongs to a family of glycopeptide antibiotics and contains a disaccharide moiety consisting of a α1→2 linked 3-*O*-carbamoyl-D-mannopyranose with L-gulopyranose. Amongst nucleoside antibiotics with potential antibacterial properties, adenomycin (**2**)[3] is composed of L-gulosamine as a basic subunit whereas capuramycin (**3**)[4] has a 3-*O*-methyl-L-talofuranosyl sugar. Other notable examples include L-altrose (**4**), which is a typical constituent of the extracellular polysaccharides from *Butyrivibrio fibrisolvens* strain CF3.[5]

Heparin and heparan sulfate, which are linear sulfated polysaccharides of glycosaminoglycans comprising of alternating D-glucosamine and hexuronic acid (L-iduronic acid or D-glucuronic acid) residues with 1→4 linkages, play important roles in a diverse set of biological processes, including blood coagulation, cell growth control, inflammation, wound healing, virus infection, tumor metastasis and diseases of nervous system.[6] Heparin, containing the disaccharide repeating unit **5** as a major component, can interact with a variety of proteins in many biological events.[7] The rare 3-*O*-sulfonated disaccharide residue **6** of cell surface heparan sulfate exhibits specific binding site to the glycoprotein gD of herpes simplex virus type-1 during virus entry.[8] The mucopolysaccharidosis are a group of heritable lysosomal storage disorders caused by lack of enzymes catalyzing the stepwise degradation of glycosaminoglycans.[9] α-L-Iduronidase

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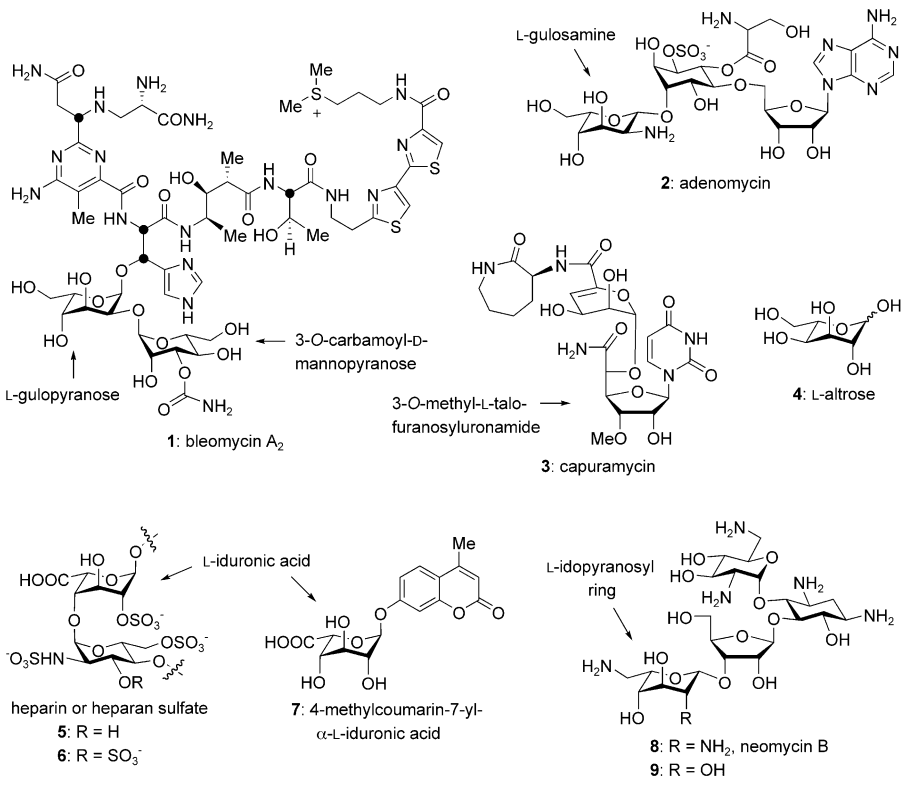


Figure 1. Biologically potent and rare L-hexoses and their related biomolecules.

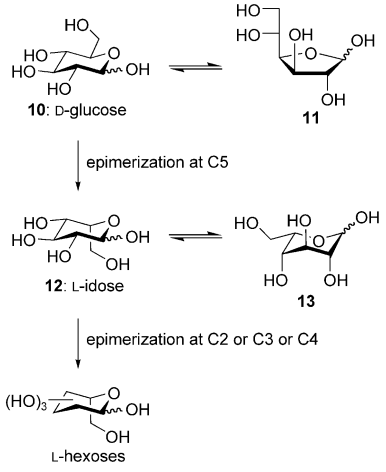
(EC 3.2.1.76),[10] a lysosomal hydrolase that cleaves terminal α-L-iduronic acid unit, is deficient in Hurler and Scheie syndromes. 4-Methylcoumarin-7-yl-α-L-iduronic acid (**7**) is a fluorogenic substrate for assay of its activity.[11] Neomycin B (**8**), an aminoglycoside antibiotic possessing specific binding to the A site of the prokaryotic 16S rRNA[12] and inhibition for the binding of the HIV Rev protein to its viral RNA recognition site (RRE),[13] has 2,6-diamino-2,6-dideoxy-L-idopyranose as the D ring. Modification of this D ring as the 6-amino-6-deoxy-L-idopyranosyl derivative **9** also presents similar antibacterial activity.[14]

As most of the structural information of carbohydrate–protein and carbohydrate–nucleotide complex at molecular level remains obscure, homogeneous materials with well-defined configurations are essential for the determination of biological activity and structure–function relationship. These frequently encountered L-hexoses, however, are not commercially available. This very fact coupled with practical difficulties in obtaining these rare sugars from nature sources has urged chemists to develop novel, cost effective, general, simple, and convenient routes for their syntheses. As a result, the literature documents an array of methodologies for this purpose,[15] each one having its own advantages and disadvantages.

The only difference between the structures of the most abundant D-glucose and rare L-idose is the stereochemistry at the C5 position. Our plan (Scheme 1) was to first achieve the conversion from D-*gluco* to L-*ido* configuration in a shortest possible way and then carry out the specific epimerization of the L-*ido* sugars at C2, C3 and/or C4 to get to the whole set of L-hexoses.[16] However simple this might appear at the first instance, several problems still need to be encountered, including 1) the stereoselective C5 inversion of commercially available compounds derived from D-glucopyranose **10** and its furanosyl form **11**, 2) the regioselective epimerization of the remaining individual chiral centers in L-idose, an equilibrating pyranosyl mixture of the $^4C_1$ conformer **12** and $^1C_4$ conformer **13**, without affecting other functional groups, 3) the control of regioselective protection in the D-*gluco* and L-*ido* sugars, and 4) the selection of appropriate protecting groups toward the synthesis of various L-hexoses and their related natural products. To tackle these problems, we have explored a straightforward route to prepare 1,2:5,6-di-*O*-isopropylidene-β-L-furanosyl and 1,6-anhydro-β-L-pyranosyl derivatives of L-idose from D-glucose followed by an efficient transformation of these L-*ido* sugars into the corresponding β-L-hexofuranosyl and 1,6-anhydro-β-L-hexopyranosyl sugars by manipulating the steric and stereoelectronic factors. Novel approaches toward the synthesis of α-L-iduronidase fluorogenic detector **7** and the disaccharide moieties of bleomycin A_2 and heparan sulfate employing 1,6-anhydro-β-L-hexopyranoses as valuable synthons are also described.

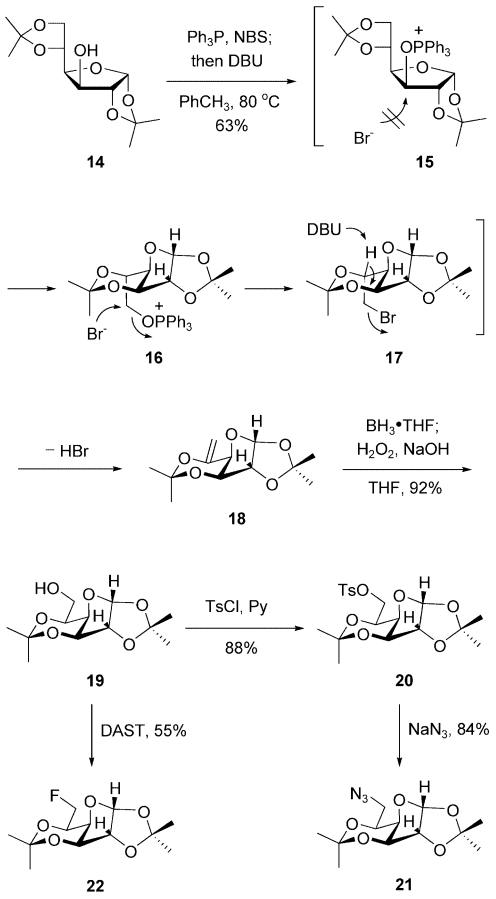
Results and Discussion

Synthesis of L-idose derivatives: Our idea for the preparation of the L-*ido* sugars is based on the model of double



Scheme 1.

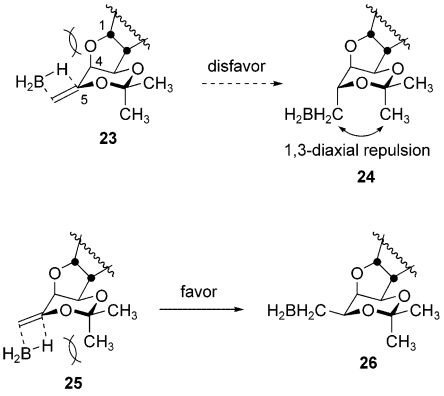
ketal fixation on the 1,2- and 3,5-hydroxy groups of D-glucose to form a *cis–anti–cis*-fused tricyclic D-glucofuranosyl derivative, which could undergo elimination to form a 5-*exo*-double bond followed by electrophilic addition to give the desired products. An efficient synthesis of 1,2:3,5-di-*O*-isopropylidene-β-L-idofuranose (**19**) from diacetone-α-D-glucose (**14**) in two steps is outlined in Scheme 2. Consecutive



Scheme 2.

treatment of compound **14** with triphenylphosphine (PPh_3), *N*-bromosuccinimide (NBS), and freshly distilled 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in toluene at 80 °C afforded the enol ether **18** in 63% yield in a one-pot manner. Mechanistically, PPh_3 first reacts with NBS to generate a phosphonium salt, which is readily attacked by the 3-hydroxy group of **14** resulting in the formation of alkoxyphosphonium intermediate **15**.[17] Due to the rigid *cis*-5,5-fused ring conformation, the isopropylidene rearrangement of **15** appears to precede over direct S_N2 substitution by bromide ion owing to the steric hindrance for the α-face attack. In contrast to this, the transition state in **16** is sterically favored for a facile nucleophilic displacement by bromide ion, which ends up in an overall regioselective bromination at C6. DBU then effects the dehydrobromination of **17** to furnish the enol ether **18**. As expected, hydroboration of compound **18** followed by oxidative work-up led to the desired L-idofuranosyl product **19** (92%) as a single diastereoisomer. The absolute configuration of compound **19** (see Supporting Information) was unambiguously determined through the single-crystal X-ray analysis of its 6-*O*-tosyl derivative **20** (TsCl, pyridine, 88%). The stereo ORTEP drawing illustrates that the C4–O4 and C3–C2 bonds are at the axial and equatorial positions, respectively. Nucleophilic substitution of **20** with NaN_3 gave the corresponding 6-azido derivative **21** (84%). Treatment of the alcohol **19** with diethylaminosulfur trifluoride (DAST) provided the 6-fluoro compound **22** in 55% yield.

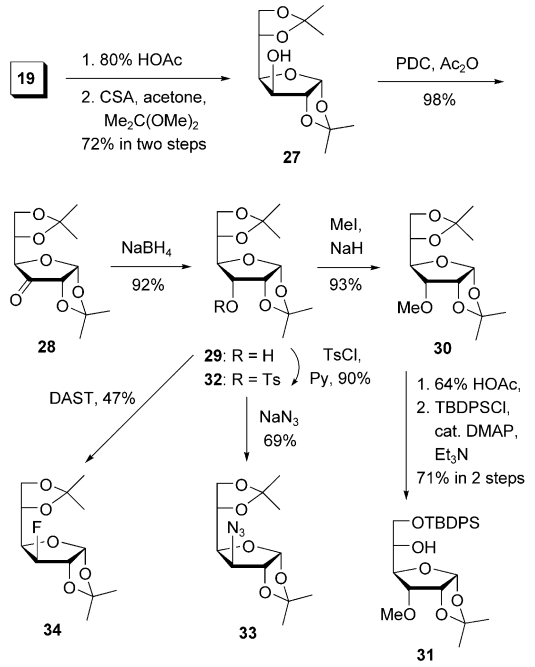
Apparently, the face selectivity of borane addition in this case is arising mainly through a combination of complementary steric factors (Scheme 3). The disposition of the axial



Scheme 3.

C4–O4 bond directs the addition of borane onto the 5-*exo* double bond from the less hindered α-face to form the intermediate **25** rather than **23**. As a result, the substituted group (CH_2BH_2) orients equatorially at the C5 position of **26**. Along with this, the 1,3-diaxial repulsion between the methyl and CH_2BH_2 groups in the boron complex **24** also seems to play a role, resulting in exclusive formation of the L-*ido* isomer **19** after oxidative work-up. It is evident that the transition state required for formation of **24** will be sterically encumbered and hence energetically disfavored.

Synthesis of L-talo- and 3-functionalized L-idofuranosyl compounds: As illustrated in Scheme 4, orthogonal isopropylidene rearrangement of compound **19** with a solution of 2,2-dimethoxypropane and acetone in the presence of catalytic amount of (±)-camphorsulfonic acid at room temperature yielded the 3-alcohol **27**[18] as a white solid (42% after recrystallization from hexane) and a mixture of unreacted **19** and its 6-*O*-C(OMe)Me_2 derivative in 52% yield. This mixture could be reutilized under the same conditions and similar results were obtained. Alternatively, regioselective hydrolysis of **19** in 60% aq HOAc at 40 °C followed by 5,6-*O*-isopropylidenation furnished the product **27** in 72% overall yield in two steps. Oxidation of **27** with pyridinium dichromate and acetic anhydride afforded the ketone **28** (98%), which was subjected to sodium borohydride reduction to give 1,2:5,6-di-*O*-isopropylidene-β-L-talofuranose (**29**) in 92% yield. Its absolute configuration was firmly secured by



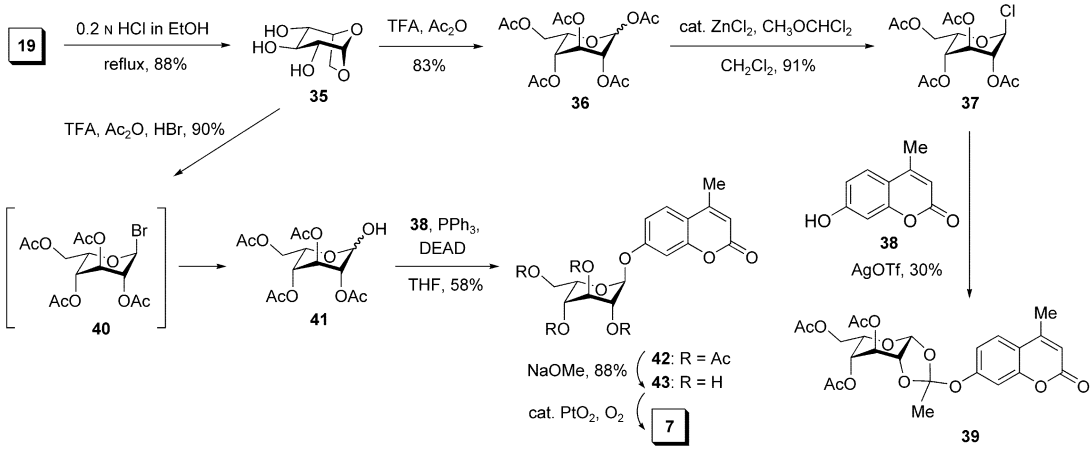
Scheme 4.

the single-crystal X-ray analysis (see Supporting Information). Methylation of **29** (NaH, MeI, 93%) led to the corresponding 3-OMe derivative **30** in excellent yield. Regioselective removal of the 5,6-*O*-isopropylidene group (64% $HOAc_{aq}$, 92%) followed by 6-*O*-silylation (TBDPSCl, cat. DMAP, Et_3N, 77%) fashioned the adduct **31**, a key intermediate for the total synthesis of capuramycin.[4]

The anticoagulant activity of heparin via a unique pentasaccharide sequence binding with antithrombin III (AT-III) has been an area of intense research directed towards probing the molecular level details of their interaction.[19] The affinity study of the 3-deoxy-L-idose-derived pentasaccharide with AT-III is reported by Sinaÿ and co-workers.[20] Since L-talose is a C3-epimer of L-idose, it was realized that the 3-alcohol **29** could be reutilized to prepare differentially 3-functionalized L-*ido* compounds. We first studied the nucleophilic substitution of the 3-triflate derivative of **29**. However, none of the desired products were obtained. Alternatively, the 3-tosylate **32** (TsCl, Py, 90%), upon treatment with sodium azide, underwent a facile S_N2 reaction to generate the 3-azido-L-idofuranosyl sugar **33** (69%). In a similar manner, reaction of compound **29** with DAST gave the corresponding 3-fluoro derivative **34** in 47% yield.

Synthesis of 4-methylcoumarin-7-yl-α-L-iduronic acid: The preparation of the fluorogenic substrate 4-methylcoumarin-7-yl-α-L-iduronic acid **7** has been reported.[21] However, the strategy not only involves tedious steps to synthesize the L-*ido* sugars but also is low yielding in the glycosylation reaction. In our synthetic plan of compound **7**, we needed L-idopyranosyl pentaacetates **36** as the building block. Peracetylation of L-idose gave a mixture of the corresponding pyranosyl and furanosyl pentaacetates together with their anomeric isomers. The purification of these four compounds was time-consuming and the furanosyl pentaacetates were not useful in the context of ongoing synthesis. To obviate these problems, we have employed 1,6-anhydro-β-L-idopyranose (**35**) as a potent synthon, which can undergo one-pot peracetylation–acetolysis to give only the pyranosyl pentaacetates **36**.

Scheme 5 depicts our approach toward the synthesis of target molecule **7**. Reflux of compound **19** in a 0.2 N ethanolic solution of HCl yielded the triol **35** (88%) as a single product. One-pot peracetylation–acetolysis of **35** (TFA, Ac_2O, 83%) furnished the pentaacetate **36**, which was converted to the corresponding α-glycosyl chloride **37** ($ZnCl_2$, CH_3OCHCl_2, 93%). An X-ray single-crystal analysis of compound **37** fully secured its structure (see Supporting Information). Unfortunately, AgOTf-promoted coupling of the donor **37** with 7-hydroxy-4-methylcoumarin (**38**) proved to be a futile exercise due to the formation of the orthoester **39** (30%). So, we opted for an equally concise and even more promising route. A one-pot synthesis of the alcohol **41** from compound **35** in 90% yield was successfully carried out via programmable peracetylation, acetolysis, and bromination. The reaction, monitored by ^1H NMR and TLC, revealed that the corresponding triacetate was initially formed in a short period and completely transformed into the pen-



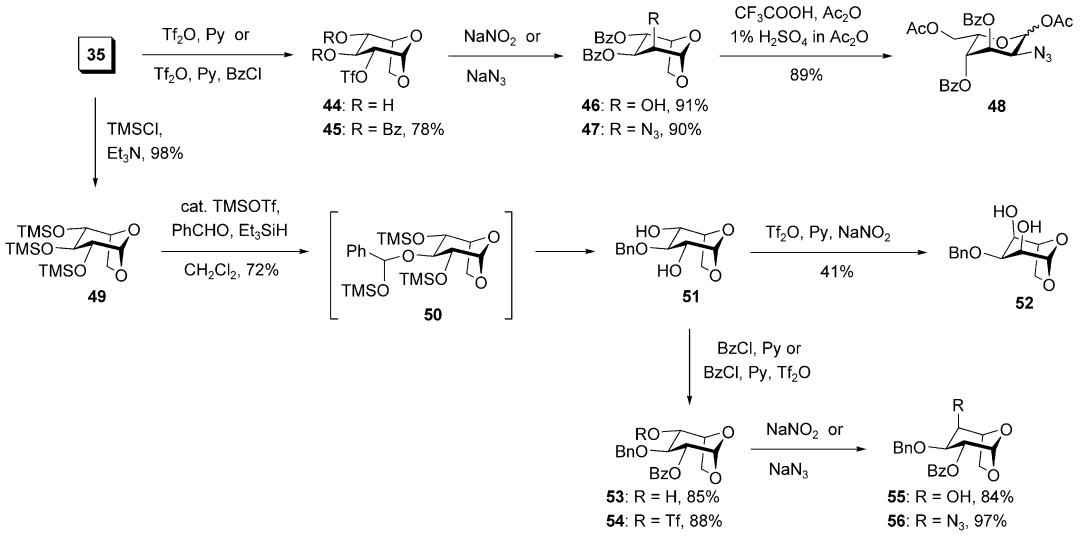
Scheme 5.

taacetate **36** after stirring for 24 h. It is evident from this observation that acetylation of three hydroxyl groups is faster than the opening of 1,6-anhydro ring. Addition of HBr into the reaction mixture in the same pot gave the unstable glycosyl bromide **40**, which was hydrolyzed to the corresponding alcohol **41** after neutralization with saturated aqueous sodium bicarbonate solution. Mitsunobu-type glycosylation of **41** with the acceptor **38** in the presence of triphenylphosphine and diethyl azodicarboxylate led to the desired α-adduct **42** and its β-isomer in 58 and 24% yield, respectively. The detailed structure of **42** via the single-crystal X-ray analysis (see Supporting Information) clearly indicated that all substituted groups orient toward the axial positions except the CH_2OAc group at C5. Saponification of compound **42** with sodium methoxide in methanol produced the tetraol **43** (88%), which was identical with the literature report with respect to ^1H NMR spectrum.[21b] This constitutes a more convenient route to 4-methylcoumarin-7-yl-α-L-iduronic acid **7**, since it has been previously obtained from compound **43** by regioselective C6-oxidation.[21]

Synthesis of 1,6-anhydro-β-L-hexopyranoses: 1,6-Anhydro-β-hexopyranoses are valuable synthons in the synthesis of oligosaccharides, glycoconjugates as well as natural products.[22] The advantages of their [3.2.1]bicyclic skeleton in comparison with the corresponding pyranoses include 1) the regio- and stereoselectivities are highly controlled by the rigid conformation, 2) the reactivity is affected because of equatorial-axial conversion of various substituted groups at the C2, C3, and C4 positions, 3) two less protecting groups at C1 and C6 are needed, and 4) only one anomeric isomer is obtained which by-passes time-consuming purification and identification of two α- and β-epimers. Moreover, once the requisite functionalities are properly installed, the internal acetal can be cleaved and the free hydroxyls can be utilized for further elaboration of sugar by functional group modification or glycosylation.

With the key molecule **35** in hand, we further studied the regioselective protection and epimerization to generate various 1,6-anhydro-β-L-hexopyranoses (Scheme 6). Reaction of the triol **35** with one equivalents of trifluoromethanesulfonic anhydride in pyridine led to the 2-OTf derivative **44** as a single isomer. The high regioselectivity is perhaps a direct consequence of the inductive effect exerted by two oxygen atoms at C1 to increase the acidity of O2-proton, forming the alkoxide at C2 under basic conditions that reacts preferentially with various electrophiles. This result prompted us to study the one-pot triflation–benzoylation and the corresponding ester **45** was successfully isolated in 78% yield. Treatment of **45** with $NaNO_2$ and NaN_3 gave the 1,6-anhydro-β-L-gulopyranosyl sugar **46** (91%) and its 2-azido derivative **47** (90%), respectively. The single-crystal X-ray analyses of **46** and **47** (see Supporting Information) confirmed their absolute configurations. Acetolysis of compound **47** using a combination of trifluoroacetic acid, acetic anhydride, and 1% solution of conc. H_2SO_4 in acetic anhydride yielded the corresponding diacetate **48** (89%). It should be noted that the typical acetolysis conditions failed to deliver the expected ring-opened product in this case and extra addition of 1% conc. H_2SO_4 turned out to be a crucial factor effecting this transformation. The fully protected L-gulosamine derivative **48** is believed to be a potential precursor in the synthesis of adenomycin **2**.[3]

Towards this end, a highly regioselective 3-*O*-benzylation of the potent synthon **35** to the corresponding 2,4-diol **51** (72%) was achieved employing TMSOTf-catalyzed Et_3SiH reductive etherification of its *O*-trimethylsilylated ether **49** (TMSCl, Et_3N, 98%). The high selectivity in this case stems out from steric interactions. The C2- and C4-trimethylsilyloxy groups being adjacent to the bridgehead carbon atoms are less accessible as compared to the C3-OTMS, allow exclusive formation of the TMS-acetal intermediate **50** that can be further reduced by Et_3SiH in the presence of TMSOTf as an efficient Lewis acid to produce the 3-OBn compound **51**. Triflation (Tf_2O, Py) of **51** followed by nucleophilic substitution ($NaNO_2$, HMPA) furnished the corresponding L-*allo* derivative **52** in 41% overall yield. Regioselective O2-benzoylation of the diol **51** with BzCl in pyridine

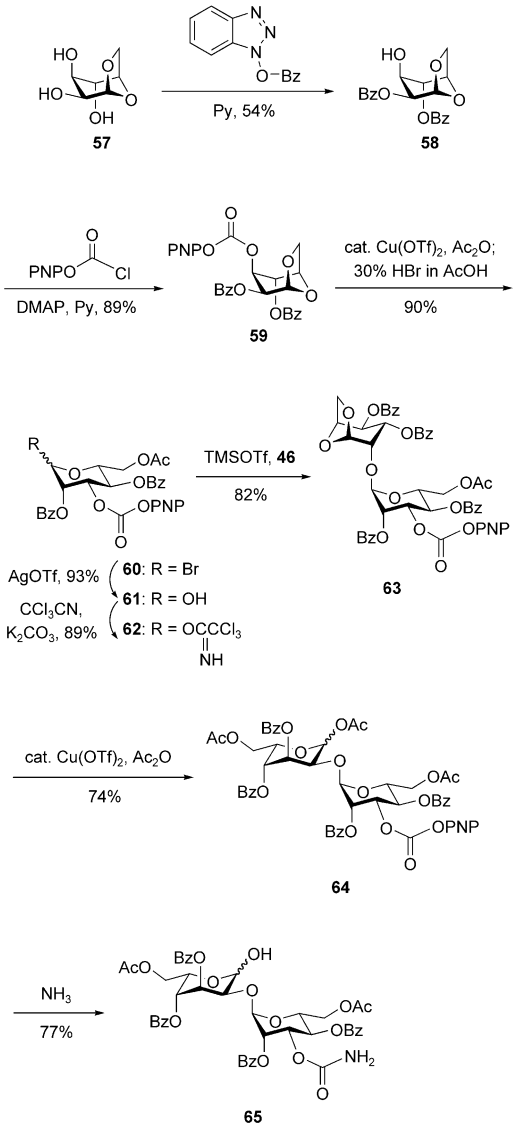


Scheme 6.

at 0 °C led to the alcohol **53** as a single isomer (85 %). One-pot benzoylation–triflation of **51** provided the 2-OBz,4-OTf derivative **54** (88 %), which was subjected to S_N2 substitutions with $NaNO_2$ and NaN_3 to afford the corresponding L-altropyranosyl sugar **55** (84 %) and its 4-azido derivative **56** (97 %), respectively. The absolute configurations of compounds **51**, **53**, and **56** were unambiguously assigned through their single-crystal X-ray analyses (see Supporting Information).

Synthesis of the carbohydrate moiety of bleomycin A_2: The construction of the disaccharide subunit in bleomycin A_2 requires the coupling of 3-*O*-carbamoyl-D-mannopyranosyl donor and L-gulopyranosyl acceptor with a $\alpha1\rightarrow2$ linkage.[2] A D-mannopyranosyl derivative bearing well-distinguished hydroxy group at C3 should suffice for this purpose. The rare L-gulose residue, which has to serve a dual function of a glycosyl acceptor in the disaccharide formation at O2 and finally as a donor for assembly with the aglycon moiety of bleomycin A_2, is the real key building block for this synthesis.

Our preparation of this carbohydrate moiety is summarized in Scheme 7. Treatment of commercially available 1,6-anhydro-β-D-mannopyranose (**57**) with benzoyl chloride in pyridine gave a mixture of mono-, di- and tri-OBz derivatives without any regioselectivity. Use of benzoyloxybenzotriazole (BzOBT) as a mild reagent dramatically enhanced the simplicity and overall efficiency of the synthetic route, delivering the expected 2,4-di-OBz adduct **58** in 54 % yield. From this reaction, the corresponding 2-OBz (15 %) and 2,3,4-tri-OBz (26 %) were also obtained and both compounds could be recycled by removing the benzoyl groups (cat. NaOMe, MeOH) to recover the starting material **57** back. An X-ray crystal analysis of **58** assured its absolute structure (See supporting information). The high regioselectivity in this mild benzoylation reaction is perhaps governed by the 1,3-diaxial repulsion between the C3-OH group and the C6-methylene group.[22] With the alcohol **58** in hand, it was successfully converted into the desired carbonate **59** in 89 % yield. Ring opening of **59** with TFA and Ac_2O gave the corresponding 1,6-diacetate in low yield. We recently found that metal trifluoromethanesulfonates are effective and mild catalysts in acetolysis of 1,6-anhydrohexopyranoses.[23] Consecutive treatment of **59** with Ac_2O in the presence of 5 mol % $Cu(OTf)_2$ followed by addition of 30 % HBr in acetic acid yielded the glycosyl bromide **60** (90 %) in a one-pot manner. AgOTf-promoted coupling of the donor **60** with the alcohol **46** provided the disaccharide **63**, albeit in low yields, along with the orthoester as a major side product. Alternatively, Schmidt's glycosylation method was thought to be a good solution for our purpose. Hydrolysis of the crude glycosyl bromide **60** in an acetone/water solution of AgOTf and 2,6-di-*tert*-butyl-4-methylpyridine was smoothly carried out and the alcohol derivative **61** was obtained in excellent yield (93 %). Reaction of compound **61** with K_2CO_3 and CCl_3CN led to the corresponding trichloroacetimidate **62** (89 %), which was subjected to coupling with **46** to furnish the α-linked disaccharide **63** (82 %), exclusively. $Cu(OTf)_2$-catalyzed acetolysis of **63** afforded the

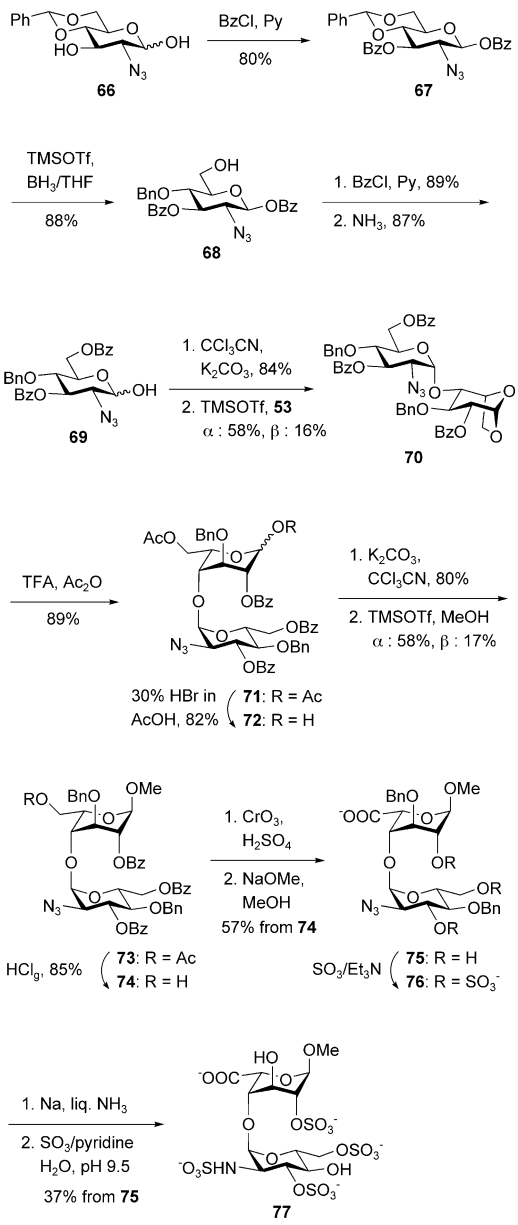


Scheme 7.

expected diacetate **64** (74 %), which upon one-pot nucleophilic displacement with ammonia, produced the title compound **65** (77 %), a suitable precursor for the total synthesis of the antibiotic as reported first by Boger[2c] and Hecht.[2f]

Synthesis of a rare and potent disaccharide subunit in heparan sulphate: The 3-*O*-sulfonated disaccharide moiety **6** found in heparan sulfate chain as a minor component exhibits specific binding site during herpes simplex virus entry.[8] Its mimetics may serve as potential pharmaceutical agents to block virus entry into target cells. We have explored herein the synthesis of a disaccharide analogue **77** employing the 1,6-anhydro-β-L-idopyranosyl sugar **53** as a valuable building block (Scheme 8).

2-Azido-4,6-*O*-benzylidene-2-deoxy-D-glucose (**66**), derived from D-glucosamine hydrochloride in two steps,[24] was dibenzoylated to furnish the ester **67** (80 %), which underwent ring opening of benzylidene acetal at the O6 position via a combination of TMSOTf and borane to deliver the primary alcohol **68** (88 %) in very high selectivity. Benzoylation



Scheme 8.

of **68** (BzCl, Py, 89%) followed by regioselective removal of the anomeric benzoyl group with ammonia gave the alcohol **69** (87%, α/β 3:1, determined by its ^{1}H NMR spectrum). Interestingly, only the β-form isomer **69** was obtained upon recrystallization using vapor diffusion process. Its ORTEP drawing of X-ray single-crystal diffraction analysis indicates that the anomeric hydroxy group orients toward the equatorial position (see Supporting Information). Compound **69** was treated with CCl_3CN and K_2CO_3 at −78°C to get the corresponding trichloroacetimidate (84%, α/β 1:4), which was coupled with the glycosyl acceptor **53** in the presence of TMSOTf as a catalyst to yield the α-linked disaccharide **70** (58%, $J_{1',2'}$ = 3.8 Hz) and its β-isomer (16%), respectively. The 1,6-anhydro ring of **70** was smoothly opened under typical acetolysis conditions (TFA, Ac_2O), generating the diacetate derivative **71** in 89% yield. Since regioselective deacetylation of **71** at the anomeric position under the basic conditions [NH_3, $BnNH_2$, $(NH_4)_2CO_3$] was low yielding, we decided to convert it into the corresponding glycosyl bromide via treatment with 30% HBr in acetic acid. When the mixture was quenched with saturated sodium bicarbonate aqueous solution, the expected alcohol **72** (82%) was isolated in a one-pot manner. Transformation of **72** into the corresponding trichloroacetimidate (80%) followed by coupling with methanol produced the methyl α-glycoside **73** and its β-isomer in 58 and 17% yield, respectively. Selective deacetylation of **73** with HCl_g in 1,4-dioxane without affecting the benzoyl groups provided the primary alcohol **74** (85%) which, upon sequential Jones oxidation and debenzoylation (NaOMe, MeOH) afforded the triol **75** in 57% overall yield in two steps. Reaction of **75** with sulfur trioxide/triethylamine complex led to the tri-*O*-sulfonated carboxylate **76**. One-pot Birch reduction of the azido and two benzyl groups in compound **76** furnished the amino alcohol, which underwent selective N-sulfonation with sulfur trioxide/pyridine complex at pH 9.5 to give the desired target molecule **77** in 37% overall yield from **75**.

Conclusion

We have successfully developed a short and convenient route to prepare the biologically important and rare L-hexoses from the most abundant D-glucose via their corresponding furanosyl and 1,6-anhydropyranosyl derivatives as key intermediates. In this synthetic endeavor, we have discovered some interesting facets and reactivity patterns exhibited by these conformationally biased synthons. Applications of these new developments in the efficient syntheses of the α-L-iduronidase fluorogenic detector **7** and the disaccharide moieties of bleomycin A_2 and heparan sulfate are demonstrated.

Experimental Section

General procedures: Solvents were purified and dried from a safe purification system.[25] Flash column chromatography[26] was carried out as recommended with silica gel 60 (230–400 mesh, E. Merck). TLC was performed on pre-coated glass plates of Silica Gel 60 F254 (0.25 mm, E. Merck); detection was executed by spraying with a solution of $Ce(NH_4)_2(NO_3)_6$, $(NH_4)_6Mo_7O_{24}$, as well as H_2SO_4 in water and subsequent heating on a hot plate. Melting points were determined with a Büchi B-540 apparatus and are uncorrected. Optical rotations were measured with a Jasco DIP-370 polarimeter at ~25°C. ^{1}H and ^{13}C NMR spectra were recorded with Bruker AC300 and AMX400 MHz instruments. Chemical shifts are in ppm from Me_4Si, generated from the $CHCl_3$ lock signal at δ 7.24. Mass spectra were obtained with a VG 70-250S mass spectrometer in the EI and FAB modes. IR spectra were taken with a Perkin-Elmer Paragon 1000 FT-IR spectrometer. Elemental analyses were measured with a Perkin–Elmer 2400CHN instrument.

6-Deoxy-1,2:3,5-di-*O*-isopropylidene-α-D-*xylo*-hex-5-enofuranose (18): *N*-Bromosuccinimide (5.13 g, 28.8 mmol) was added at room temperature under nitrogen to a solution of **14** (5.00 g, 19.2 mmol) and triphenylphosphine (8.31 g, 31.7 mmol) in anhydrous toluene (50 mL). The reaction flask was immersed in an oil bath at 90°C for 45 min, DBU (20 mL, 134 mmol, freshly distilled from CaH_2) was added, and the stirring was continued at the same temperature for another 2 h. After cooling to room temperature, the mixture was filtered through Celite followed by wash with hexane. Water (50 mL) was added to the filtrate, and the aque-

ous phase was extracted with hexane (3×50 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography (EtOAc/Hex 1:15) to afford the enol ether **18** (2.95 g, 63%) as a colorless oil. $[\alpha]_D^{25}=+163.7$ ($c=1.0$, $CHCl_3$); IR ($CHCl_3$): $\tilde{\nu}=2988$, 1660, 1375, 1082, 1017 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta=5.98$ (d, $J=3.7$ Hz, 1H, H-1), 4.76 (d, $J=0.6$ Hz, 1H, H-6a), 4.69 (d, $J=0.6$ Hz, 1H, H-6b), 4.56 (d, $J=3.7$ Hz, 1H, H-2), 4.37 (d, $J=2.3$ Hz, 1H, H-3), 4.34 (d, $J=2.3$ Hz, 1H, H-4), 1.52 (s, 3H, CH_3), 1.47 (s, 3H, CH_3), 1.40 (s, 3H, CH_3), 1.33 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=150.31$ (C), 111.80 (C), 105.20 (CH), 101.37 (CH_2), 100.53 (C), 84.27 (CH), 74.66 (CH), 72.34 (CH), 28.01 (CH_3), 26.72 (CH_3), 26.11 (CH_3), 21.90 (CH_3); HRMS (FAB): calcd for $C_{12}H_{18}O_5$: 242.1154; found: 242.1152; elemental analysis calcd (%) for $C_{12}H_{18}O_5$: C 59.49, H 7.49; found: C 59.19, H 7.38.

1,2:3,5-Di-*O*-isopropylidene-β-L-idofuranose (19): A 1M solution of borane/THF complex in THF (5.53 mL, 5.53 mmol) was added to a mixture of **18** (1.44 g, 5.53 mmol) in THF (15 mL) at room temperature under nitrogen. After stirring for 3 h, the reaction flask was cooled in an ice-bath, and a mixed solution of 30% H_2O_2 (6 mL) and 3N NaOH (6 mL) was slowly added to the mixture. The aqueous phase was extracted with EtOAc (3×15 mL), and the combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo to give a liquid residue. Purification of this residue through flash column chromatography (EtOAc/Hex 1:2) led to the 6-alcohol **19** (1.42 g, 92%) as a colorless oil. $[\alpha]_D^{32}=-3.2$ ($c=1.0$, $CHCl_3$); IR ($CHCl_3$): $\tilde{\nu}=$ 3491, 2991, 2939, 1653, 1212, 1164, 1090, 1019, 861 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta=5.94$ (d, $J=3.7$ Hz, 1H, H-1), 4.49 (d, $J=3.7$ Hz, 1H, H-2), 4.31 (d, $J=2.2$ Hz, 1H, H-3), 4.12 (m, 1H, H-5), 4.01 (t, $J=$ 2.2 Hz, 1H, H-4), 3.88 (dd, $J=11.6$, 6.9 Hz, 1H, H-6a), 3.78 (dd, $J=11.6$, 4.6 Hz, 1H, H-6b), 1.48 (s, 3H, CH_3), 1.44 (s, 3H, CH_3), 1.40 (s, 3H, CH_3), 1.31 (s, 3H, CH_3); elemental analysis calcd (%) for $C_{12}H_{20}O_6$: C 55.37, H 7.74; found: C 55.01, H 7.69.

6-Azido-6-deoxy-1,2:3,5-di-*O*-isopropylidene-β-L-idofuranose (21): Compound **19** (0.15 g, 0.58 mmol) was dissolved in pyridine (1.5 mL) at room temperature under nitrogen, *p*-toluenesulfonyl chloride (0.12 g, 0.63 mmol) was added to the reaction solution, and the mixture was kept stirring for 4 h. The reaction was quenched by addition of water (5 mL), and the mixture was extracted with EtOAc (3×5 mL). The combined organic layers were consecutively washed with 1N aq HCl, aq sat $NaHCO_3$, and brine. The organic phase was dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was recrystallized via vapor diffusion method to yield the corresponding 6-tosylate **20** (0.20 g, 88%) as colorless crystals. ^1H NMR (300 MHz, $CDCl_3$): $\delta=7.79$ (d, $J=8.2$ Hz, 2H, ArH), 7.33 (d, $J=8.2$ Hz, 2H, ArH), 5.86 (d, $J=3.4$ Hz, 1H, H-1), 4.45 (d, $J=3.4$ Hz, 1H, H-2), 4.28–4.09 (m, 4H), 3.93 (s, 1H), 2.44 (s, 3H, CH_3), 1.46 (s, 3H, CH_3), 1.39 (s, 3H, CH_3), 1.32 (s, 3H, CH_3), 1.30 (s, 3H, CH_3).

Sodium azide (0.16 g, 2.5 mmol) was added to a solution of compound **20** (0.20 g, 0.51 mmol) in DMF (2 mL), and the mixture was kept stirring at 90°C for 3 d. After cooling to room temperature, water (5 mL) was added to the solution, and the mixture was extracted with EtOAc (3× 5 mL). The combined organic layers were sequentially washed with water and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by column chromatography (EtOAc/Hex 1:9) to provide **21** (0.12 g, 84%) as a white solid. $[\alpha]_D^{25}=+7.3$ ($c=1.1$, $CHCl_3$); IR (neat): $\tilde{\nu}$ = 2925, 2101,1374, 1088 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta=5.93$ (d, $J=3.6$ Hz, 1H, H-1), 4.49 (d, $J=3.6$ Hz, 1H, H-2), 4.31 (d, $J=2.2$ Hz, 1H, H-3), 4.14 (ddd, $J=8.1$, 4.5, 2.2 Hz, 1H, H-5), 3.92 (t, $J=2.2$ Hz, 1H, H-4), 3.58 (dd, $J=12.8$, 8.1 Hz, 1H, H-6a), 3.36 (dd, $J=12.8$, 4.5 Hz, 1H, H-6b), 1.48 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.40 (s, 3H, CH_3), 1.31 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=$ 111.82, 105.14, 98.31, 83.91, 73.80, 71.33, 68.29, 51.72, 28.98, 26.63, 26.08,19.07; HRMS (FAB): calcd for $C_{12}H_{20}O_5N_3$: 286.1402; found: 286.1405 [M+H$^+$].

6-Deoxy-1,2:3,5-di-*O*-isopropylidene-6-fluoro-β-L-idofuranose (22): *N,N*-Diethylaminosulfur trifluoride (0.47 mL, 3.5 mmol) was added at −40°C under nitrogen to a solution of **19** (150 mg, 0.58 mmol) in dichloromethane (4 mL). The cooling bath was removed, and the mixture was kept stirring at room temperature for 6 h. Methanol (2 mL) was slowly added to the reaction mixture at −10°C, the resulting solution was concentrated in vacuo, and the residue was purified by flash column chromatography (EtOAc/Hex 1:9) to afford **22** (83 mg, 55%). $[\alpha]_D^{25}=+13.1$ ($c=1.0$, $CHCl_3$); IR ($CHCl_3$): $\tilde{\nu}=2991$, 1375, 1204, 1163, 1016 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta=5.94$ (d, $J=3.6$ Hz, 1H, H-1), 4.66 (ddd, $J=48.2$, 9.8, 4.2 Hz, 1H, H-6a), 4.55 (ddd, $J=48.2$, 7.0, 4.2 Hz, 1H, H-6b), 4.50 (d, $J=3.6$ Hz, 1H, H-2), 4.37–4.30 (m, 2H, H-3, H-5), 3.96 (t, $J=2.0$ Hz, 1H, H-4), 1.45 (s, 3H, CH_3), 1.44 (s, 3H, CH_3), 1.39 (s, 3H, CH_3), 1.29 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=111.84$(C), 105.30 (CH), 98.21 (C), 83.82 (CH), 83.32 (d, $J=251.8$ Hz, CH_2), 73.74 (CH), 70.61 (d, $J=$ 11.2 Hz, CH), 67.88 (d, $J=32.2$ Hz, CH), 29.03 (CH_3), 26.65 (CH_3), 26.09 (CH_3), 19.06 (CH_3); HRMS (FAB): calcd for $C_{12}H_{20}O_5F$: 263.1295; found: 263.1288 [M+H$^+$]; elemental analysis calcd (%) for $C_{12}H_{19}O_5F$: C 54.96, H 7.25; found: C 55.03, H 7.40.

1,2:5,6-Di-*O*-isopropylidene-β-L-idofuranose (27): A solution of **19** (133 mg, 0.51 mmol) in 60% aq HOAc (1.3 mL) was stirred at 40°C for 9 h, and the mixture was coevaporated with toluene (5×5 mL) under reduced pressure to furnish the corresponding 3,5,6-triol. This crude triol was dissolved in anhydrous acetone (0.5 mL) at room temperature under nitrogen, and 2,2-dimethoxypropane (0.25 mL) and camphorsulfonic acid (5.0 mg) were consecutive added to the solution. After stirring for 5 min, the reaction was quenched with aq sat $NaHCO_3$ (5 mL), and the mixture was extracted with CH_2Cl_2 (3×5 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was recrystallized in hexane to afford **27** (95 mg, 72% in two steps) as a white solid. $[\alpha]_D^{29}=-21.5$ ($c=0.5$, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): $\delta=5.94$ (d, $J=3.6$ Hz, 1H, H-1), 4.45–4.48 (m, 2H), 4.22 (m, 1H, OH), 4.12–4.06 (m, 3H), 3.70 (d, $J=3.3$ Hz, 1H), 1.47 (s, 3H, CH_3), 1.45 (s, 3 H, CH_3), 1.42 (s, 3H, CH_3), 1.29 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=111.65$, 110.38, 104.86, 85.19, 78.02, 76.36, 74.74, 66.09, 26.74, 26.13, 25.83, 25.67; HRMS (FAB): calcd for $C_{12}H_{21}O_6$: 261.1338; found: 261.1335 [M+H$^+$].

1,2:5,6-Di-*O*-isopropylidene-β-L-*lyxo*-hex-3-ulose (28): A solution of **27** (1.00 g, 3.84 mmol) in dichloromethane (6 mL) was added to a mixture of pyridinium dichromate (1.08 g, 2.87 mmol) and acetic anhydride (1.1 mL, 11.6 mmol) in dichloromethane (12 mL) at room temperature under nitrogen. The whole mixture was refluxed for 2 h, then cooled to room temperature, and the solvent was evaporated under reduced pressure. EtOAc (10 mL) was added to dissolve the solid residue, and the resulting solution was filtered through Celite. The filtrate was concentrated in vacuo to obtain ketone **28** (0.97 g, 98%), which could be used for further reactions. ^1H NMR (400 MHz, $CDCl_3$): $\delta=6.10$ (d, $J=4.2$ Hz, 1H, H-1), 4.38 (d, $J=4.2$ Hz, 1H, H-2), 4.32 (s, 1H, H-4), 4.27 (t, $J=7.8$ Hz, 1H, H-5), 4.06 (t, $J=7.8$ Hz, 1H, H-6a), 4.01 (t, $J=7.8$ Hz, 1H, H-6b), 1.45 (s, 3 H, CH_3), 1.42 (s, 3H, CH_3), 1.40 (s, 3H, CH_3), 1.31 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=208.63$ (C), 114.18 (C), 109.84 (C), 103.52 (CH), 78.61 (CH), 76.58 (CH), 75.28 (CH), 64.74 (CH_2), 27.32 (CH_3), 26.86 (CH_3), 25.76 (CH_3), 25.18 (CH_3).

1,2:5,6-Di-*O*-isopropylidene-β-L-talofuranose (29): A solution of sodium borohydride (0.18 g, 4.8 mmol) in water (5 mL) was added at room temperature to a solution of **28** (0.97 g, 3.8 mmol) in 56% aq EtOH (4.3 mL). After stirring for 3 h, the mixture was extracted with dichloromethane (3×8 mL), and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was recrystallized via vapor diffusion method to afford **29** (0.90 g, 92%) as colorless crystals. $[\alpha]_D^{28}=+20.7$ ($c=1.0$, $CHCl_3$); m.p. 77–78°C; IR ($CHCl_3$): $\tilde{\nu}$ = 453, 2986, 2930, 1210, 1008 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta=5.84$ (d, $J=4.2$, 1H, H-1), 4.58 (dd, $J=5.2$, 4.2 Hz, 1H, H-2), 4.20 (dt, $J=6.8$, 8.4 Hz, 1H, H-5), 4.08 (dd, $J=8.4$, 6.8 Hz, 1H, H-6a), 3.98 (t, $J=8.4$ Hz, 1H, H-6b), 3.90 (ddd, $J=10.4$, 8.4, 5.2 Hz, 1H, H-3), 3.75 (dd, $J=8.4$, 5.2 Hz, 1H, H-4), 2.39 (d, $J=10.4$ Hz, 1H, 3-OH), 1.54 (s, 3H, CH_3), 1.43 (s, 3H, CH_3), 1.38 (s, 6H, 2×CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=$ 112.75 (C), 109.44 (C), 104.21 (CH), 80.34 (CH), 78.47 (CH), 75.50 (CH), 72.29 (CH), 65.16 (CH_2), 26.53 (CH_3), 26.45 (CH_3), 26.23 (CH_3), 25.47 (CH_3); HRMS (FAB): calcd for $C_{12}H_{21}O_6$: 261.1338; found: 261.1339 [M+H$^+$]; elemental analysis calcd (%) for $C_{12}H_{20}O_6$: C 55.37, H 7.74; found: C 55.48, H 7.74.

1,2:5,6-Di-*O*-isopropylidene-3-*O*-methyl-β-L-talofuranose (30): Compound **29** (400 mg, 1.46 mmol) was dissolved in THF (4 mL) under nitrogen, the reaction flask was immersed in an ice-bath, and 60% sodium hydride in mineral oil (148 mg, 6.17 mmol) was added to the solution. After 30 min, methyl iodide (300 μL, 4.82 mmol) was added to the mixture, the ice-bath was removed, and the whole solution was gradually warmed up to room temperature and kept stirring for 2 h. Water (2.4 mL) was added

to quench the reaction, and the mixture was extracted with EtOAc (3× 5 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography (EtOAc/Hex 1:2) to give the product **30** (390 mg, 93%). $[\alpha]_D^{28}=+84.4$ ($c=0.6$, $CHCl_3$); IR ($CHCl_3$): $\tilde{\nu}=2988$, 2936, 1372, 1068 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): $\delta=5.75$ (d, $J=4.9$ Hz, 1H), 4.65 (t, $J=4.9$ Hz, 1H), 4.18–4.12 (m, 1H), 4.02–3.89 (m, 3H), 3.60 (dd, $J=12.0$, 5.6 Hz, 1H), 3.45 (s, 3H), 1.55 (s, 3H), 1.40 (s, 3H), 1.35 (s, 3H), 1.33 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta=113.1$ (C), 109.4 (C), 104.3 (CH), 81.2 (CH), 77.9 (CH), 76.7 (CH), 75.4 (CH), 65.4(CH_2), 58.2 (CH_3), 26.8 (CH_3), 26.5 (CH_3), 26.1 (CH_3), 25.8 (CH_3); elemental analysis calcd (%) for $C_{13}H_{22}O_6$: C 56.92, H 8.08; found: C 56.97, H 8.15.

6-*O*-*tert*-Butyldiphenylsilyl-1,2-*O*-isopropylidene-3-*O*-methyl-β-L-talofuranose (31): A mixture of compound **30** (390 mg, 1.42 mmol) in 64% aq HOAc (4 mL) was stirred at 40°C for 10 h. The solution was cooled in an ice-bath, and aq sat $NaHCO_3$ was added to neutralize the reaction mixture. The mixture was extracted with chloroform (5×15 mL), and the combined organic layers were washed by brine, dried over $MgSO_4$, filtered, and concentrated in vacuo to provide the 5,6-diol (306 mg, 92%). $[\alpha]_D^{28}=+45.3$ ($c=1.0$, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): $\delta=5.76$ (d, $J=3.8$ Hz, 1H), 4.66 (t, $J=3.8$ Hz, 1H), 3.98 (dd, $J=8.8$, 1.7 Hz, 1H), 3.79–3.70 (m, 4H), 3.49 (s, 3H), 1.34 (s, 3H), 1.23 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta=113.3$ (C), 104.3 (CH), 80.2 (CH), 79.7 (CH), 76.6 (CH), 69.9 (CH), 64.8 (CH_2), 58.3 (CH_3), 26.7 (CH_3), 26.4 (CH_3).

To a solution of this diol (306 mg, 1.30 mmol) in dichloromethane (3 mL) was sequentially added triethylamine (219 μL, 1.58 mmol), DMAP (6 mg, 45 μmol), and TBDPSCl (394 mg, 1.44 mmol) at room temperature under nitrogen atmosphere. After stirring for 16 h, the reaction was diluted by dichloromethane (10 mL), and the mixture was consecutively washed with water (2×3 mL) followed by aq sat NH_4Cl (2×3 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo, and residue was purified by flash column chromatography (EtOAc/Hex 1:2) to furnish the product **31** (472 mg, 77%). $[\alpha]_D^{28}=+35.6$ ($c=0.5$, $CHCl_3$); IR ($CHCl_3$): $\tilde{\nu}=3473$, 2931.2, 1428, 1113 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): $\delta=7.67$–7.63 (m, 4H, Ph-H), 7.43–7.33 (m, 6H, Ph-H), 5.75 (d, $J=3.8$ Hz, 1H, H-1), 4.65 (t, $J=3.8$ Hz, 1H, H-2), 4.04 (dd, $J=10.0$, 1.8 Hz, 1H, H-6a), 3.86–3.83 (m, 1H, H-5), 3.79 (dd, $J=6.6$, 3.8 Hz, 1H, H-3), 3.77 (dd, $J=7.4$, 6.6 Hz, 1H, H-4), 3.68 (dd, $J=10.0$, 5.4 Hz, 1H, H-6b), 3.47 (s, 3H, CH_3), 2.29 (d, $J=6.4$ Hz, 1H, 5-OH), 1.53 (s, 3H, CH_3), 1.34 (s, 3H, CH_3), 1.04 (s, 9H, *t*Bu); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta=135.56$ (CH), 133.13 (C), 129.74 (CH), 127.74 (CH), 113.08 (C), 104.25 (CH), 79.92 (CH), 77.32 (CH), 76.68 (CH), 69.75 (CH), 65.37 (CH_2), 58.42 (CH_3), 26.80 (4×CH_3), 26.48 (CH_3), 19.18 (C); HRMS (FAB): calcd for $C_{26}H_{37}O_6Si$: 473.2360; found: 473.2354 [$M+H^+$]; elemental analysis calcd (%) for $C_{26}H_{36}O_6Si$: C 66.07, H 7.68; found: C 65.92, H 7.46.

1,2:5,6-Di-*O*-isopropylidene-3-*O*-(*p*-toluenesulfonyl)-β-L-talofuranose (32): *p*-Toluenesulfonyl chloride (422 mg, 2.21 mmol) was added to a solution of **29** (204 mg, 0.78 mmol) in pyridine (2 mL) at room temperature under nitrogen. The mixture was stirred for 3 d, and water (0.4 mL) was added to quench the reaction. After stirring for 20 min, the resulting solution was poured into ice-water (20 mL), the mixture was filtered, and the collected solid was recrystallized via vapor diffusion method to yield **32** (292 mg, 90%) as colorless crystals. $[\alpha]_D^{28}=+82.3$ ($c=1.0$, $CHCl_3$); m.p. 143–144°C; IR ($CHCl_3$): $\tilde{\nu}=2988$, 1623, 1371 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta=7.83$ (d, $J=8.4$ Hz, 2H, Ar-H), 7.33 (d, $J=8.4$ Hz, 2H, Ar-H), 5.73 (d, $J=3.2$ Hz, 1H, H-1), 4.62–4.56 (m, 2H, H-2, H-3), 4.01 (dd, $J=8.0$, 2.8 Hz, 1H, H-4), 3.90–3.82 (m, 3H, H-5, H-6a, H-6b), 2.43 (s, 3H, CH_3), 1.50 (s, 3H, CH_3), 1.30 (s, 3H, CH_3), 1.28 (s, 3H, CH_3), 1.21 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=145.27$ (C), 132.88 (C), 129.79 (CH), 128.20 (CH), 113.70 (C), 109.48 (C), 104.20 (CH), 77.61 (CH), 76.95 (CH), 76.42 (CH), 73.68 (CH), 65.17 (CH_2), 26.66 (CH_3), 26.51 (CH_3), 25.91 (CH_3), 25.61 (CH_3), 21.64 (CH_3); HRMS (FAB): calcd for $C_{19}H_{27}O_8S$: 415.1427; found: 415.1460 [$M+H^+$].

3-Azido-3-deoxy-1,2:5,6-di-*O*-isopropylidene-β-L-idofuranose (33): A mixture of **32** (100 mg, 0.24 mmol), [15]crown-5 (96 μL, 0.48 mmol), and sodium azide (235 mg, 3.62 mmol) in DMF (1 mL) was heated at 140°C for 14 h. After cooling to room temperature, water (3 mL) was added to the solution, and the mixture was extracted with chloroform (3×3 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography (EtOAc/Hex 1:5) to give **33** (47 mg, 69%). $[\alpha]_D^{28}=-80.7$ ($c=1.0$, $CHCl_3$); m.p. 68–69°C; IR ($CHCl_3$): $\tilde{\nu}=2989$, 2937, 2107, 1216, 1076, 1022 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta=5.99$ (d, $J=3.6$ Hz, 1H, H-1), 4.71 (d, $J=3.6$ Hz, 1H, H-2), 4.33 (q, $J=7.2$ Hz, 1H, H-5), 4.18 (dd, $J=7.2$, 4.8 Hz, 1H, H-4), 4.16 (dd, $J=8.4$, 4.2 Hz, 1H, H-6a), 3.83 (d, $J=3.6$ Hz, 1H, H-3), 3.69 (dd, $J=8.4$, 7.2 Hz, 1H, H-6b), 1.52 (s, 3H, CH_3), 1.47 (s, 3H, CH_3), 1.39 (s, 3H, CH_3), 1.36 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=112.43$ (C), 110.25 (C), 105.01 (CH), 83.44 (CH), 80.83 (CH), 74.89 (CH), 65.88 (CH), 65.74 (CH_2), 26.65 (CH_3), 25.64 (CH_3), 26.32 (CH_3), 25.30 (CH_3); HRMS (FAB): calcd for $C_{12}H_{20}N_3O_5$: 286.1403; found: 286.1391 [$M+H^+$].

3-Deoxy-1,2:5,6-di-*O*-isopropylidene-3-fluoro-β-L-idofuranose (34): Pyridine (0.27 mL, 3.31 mmol) was added at 0°C under nitrogen to a solution of **29** (43 mg, 0.17 mmol) in dichloromethane (0.4 mL). After 10 min, *N*,*N*-diethylaminosulfur trifluoride (0.22 mL, 1.65 mmol) was added dropwise to the solution, the ice-bath was removed, and the mixture was kept stirring at room temperature for 24 h. Methanol (3 mL) was added to quench the reaction, then the mixture was evaporated under reduced pressure. Water (5 mL) was added to the residue, and the mixture was extracted with EtOAc (3×5 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. Purification of the resulting residue through flash column chromatography (EtOAc/Hex 1:4) provided **34** (20.4 mg, 47%) as a colorless oil. $[\alpha]_D^{28}=-37.3$ ($c=1.0$, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): $\delta=6.02$ (d, $J=3.8$ Hz, 1H, H-1), 4.84 (dd, $J=50.7$, 2.4 Hz, 1H, H-3), 4.66 (dd, $J=11.6$, 3.8 Hz, 1H, H-2), 4.33 (q, $J=7.6$ Hz, 1H, H-5), 4.17 (ddd, $J=30.2$, 7.6, 2.4 Hz, 1H, H-4), 4.12 (t, $J=7.6$ Hz, 1H, H-6a), 3.72 (t, $J=7.6$ Hz, 1H, H-6b), 1.47 (s, 3H, CH_3), 1.44 (s, 3H, CH_3), 1.36 (s, 3H, CH_3), 1.30 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=112.39$ (C), 110.13 (C), 105.22 (CH), 94.58 (d, $J=182.8$ Hz, CH), 82.70 (d, $J=31.5$ Hz, CH), 81.56 (d, $J=18.2$ Hz, CH), 74.25 (d, $J=8.9$ Hz, CH), 65.68 (CH_2), 26.71 (CH_3), 26.69 (CH_3), 26.26 (CH_3), 25.31 (CH_3).

1,6-Anhydro-β-L-idopyranose (35): A solution of **19** (503 mg, 1.93 mmol) in 0.2 N HCl_{EtOH} (15 mL) was heated at 95°C for 18 h. After cooling to room temperature, the reaction was neutralized by $Ag_2CO_{3(s)}$ (400 mg), and the mixture was filtered through Celite to remove AgCl. The filtrate was concentrated in vacuo, and the residue was purified by flash column chromatography using EtOAc to give **35** (275 mg, 88%) as a white solid. $[\alpha]_D^{33}=+106.47$ ($c=1.0$, $CHCl_3$); ^1H NMR (400 MHz, CD_3COCD_3): $\delta=5.15$ (d, $J=1.6$ Hz, 1H, H-1), 4.42 (d, $J=4.2$ Hz, 1H, 4-OH), 4.32 (t, $J=4.6$ Hz, 1H, H-5), 4.19 (d, $J=4.6$ Hz, 1H, 3-OH), 4.00 (d, $J=6.6$ Hz, 1H, 2-OH), 3.96 (d, $J=7.4$ Hz, 1H, H-6a), 3.66–3.62 (m, 1H. H-4), 3.60–3.56 (m, 1H, H-6b), 3.48–3.45 (m, 1H, H-3), 3.33 (ddd, $J=8.2$, 6.6, 1.6 Hz, 1H, H-2); ^1H NMR (400 MHz, CD_3COCD_3 + 1 drop of D_2O): $\delta=5.14$ (d, $J=1.7$ Hz, 1H, H-1), 4.32 (t, $J=4.6$ Hz, 1H, H-5), 3.96 (d, $J=7.4$ Hz, 1H, H-6a), 3.64 (dd, $J=8.2$, 4.6 Hz, 1H, H-4), 3.56 (dd, $J=7.4$, 4.6 Hz, 1H, H-6b), 3.47 (t, $J=8.2$ Hz, 1H, H-3), 3.34 (dd, 1H, $J=8.2$, 1.7 Hz, H-2); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=102.9$ (CH), 76.4 (CH), 76.1 (CH), 72.4 (CH), 65.4 (CH_2); elemental analysis calcd (%) for $C_6H_{10}O_5$: C 44.45, H 6.22; found: C 44.05, H 6.16.

1,2,3,4,6-Penta-*O*-acetyl-L-idopyranose (36): Compound **35** (75 mg, 0.46 mmol) was dissolved in acetic anhydride (1.5 mL) under nitrogen, and the reaction flask was immersed in an ice-bath. Trifluoroacetic acid (0.38 mL) was added to the reaction solution, the ice-bath was removed, and the mixture was kept stirring at room temperature for 24 h. After cooling to 0°C, the reaction was quenched by slow addition of methanol (4 mL), and the mixture was coevaporated with toluene and ethanol in vacuo. The residue was purified by flash column chromatography (EtOAc/Hex 1:1) to afford **36** (0.15 g, 83%, α/β 1:1, determined by ^1H NMR) as a colorless oil.

Isomer 36α: IR ($CHCl_3$): $\tilde{\nu}=2990$, 2938, 1374, 1204, 1164, 1090, 1016 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta=6.04$ (d, $J=1.8$ Hz, 1H, H-1), 5.05 (ddd, $J=3.9$, 3.0, 0.5 Hz, 1H, H-3), 4.92 (t, $J=3.0$ Hz, 1H, H-4), 4.86 (ddd, $J=3.9$, 1.8, 0.5 Hz, 1H, H-2), 4.17 (ddd, $J=9.1$, 6.0, 3.0 Hz, 1H, H-5), 4.26–4.14 (m, 2H, H-6a, H-6b), 2.13–2.01 (m, 15H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=170.47$ (C), 169.67 (C), 169.02 (C), 168.79 (C), 168.42 (C), 90.61 (CH), 66.69 (CH), 66.30 (CH), 66.23 (CH), 66.14 (CH), 61.76 (CH_2), 20.83 (CH_3), 20.69 (CH_3); elemental analysis calcd (%) for $C_{16}H_{22}O_{11}$: C 49.23, H 5.68; found: C 49.44, H 5.80.

Isomer 36β: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 6.06$ (d, $J = 2.2$ Hz, 1H, H-1), 5.24 (t, $J = 4.8$ Hz, 1H, H-3), 4.99 (dd, $J = 4.8$, 2.2 Hz, 1H, H-2), 4.89 (dd, $J = 4.8$, 2.4 Hz, 1H, H-4), 4.44 (ddd, $J = 8.8$, 6.3, 2.4 Hz, 1H, H-5), 4.23 (d, $J = 6.3$ Hz, 2H, H-6a, H-6b), 2.13–2.01 (m, 15H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 170.33$ (C), 169.35 (C), 168.30 (C), 168.53 (C), 168.46 (C), 89.75 (CH), 71.84 (CH), 67.04 (CH), 66.26 (CH), 66.11 (CH), 62.05 (CH_2), 20.71 (CH_3), 20.58 (CH_3), 20.54 (CH_3), 20.48 (CH_3), 20.44 (CH_3).

2,3,4,6-Tetra-*O*-acetyl-α-L-idopyranosyl chloride (37): Dichloromethyl methyl ether (2.2 mL) was added to a mixture of **36** (520 mg, 1.33 mmol) and freshly fused zinc chloride (19 mg, 0.14 mmol) in dichloromethane (2.2 mL) at room temperature under nitrogen. The mixture was refluxed for 0.5 h, cooled in an ice-bath, and neutralized by aq sat $NaHCO_3$ (3 mL). The whole mixture was extracted with dichloromethane (3× 3 mL), and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by flash column chromatography (Et_3N/EtOAc/Hex 1:8:11), the solid residue was recrystallized via vapor diffusion method to provide **37** (444 mg, 91%) as colorless crystals. $[\alpha]_D^{31} = -114.3$ ($c = 1.3$, $CHCl_3$); m.p. 115–116°C; IR ($CHCl_3$): $\tilde{\nu}$ = 2973, 1747, 1372, 1218, 1047 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 6.02$ (s, 1H, H-1), 5.03–4.99 (m, 2H, H-2, H-3), 4.93–4.92 (m, 1H, H-4), 4.69–4.66 (m, 1H, H-5), 4.27–4.19 (m, 2H, H-6a, H-6b), 2.16 (s, 3H, CH_3), 2.14 (s, 3H, CH_3), 2.13 (s, 3H, CH_3), 2.10 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 170.47$ (C), 169.54 (C), 168.89 (C), 168.80 (C), 88.23 (CH), 68.46 (CH), 66.35 (CH), 65.87 (CH), 65.60 (CH), 61.74 (CH_2), 20.79 (CH_3), 20.68 (CH_3), 20.59 (CH_3); elemental analysis calcd (%) for $C_{14}H_{19}ClO_9$: C 45.85, H 5.22; found: C 45.85, H 5.26.

2,3,4,6-Tetra-*O*-acetyl-L-idopyranose (41): Trifluoroacetic acid (0.28 mL) was added at room temperature under nitrogen to a solution of compound **35** (69 mg, 0.43 mmol) in acetic anhydride (1.4 mL). After stirring for 24 h, a solution of 30% HBr in acetic acid (1 mL, 4.2 mmol) was added, and the mixture was kept stirring at room temperature for another 6 h. The reaction was quenched with aq sat $NaHCO_3$ at 0°C, and the whole mixture was extracted with EtOAc (3×5 mL). The combined organic layers were consecutively washed with aq sat $NaHCO_3$ twice followed by brine. The organic phase was dried over $MgSO_4$, filtered, and concentrated in vacuo, and the resulting residue was purified by flash column chromatography (EtOAc/Hex 2:3) to produce **41** (133 mg, 90%) as a colorless oil.

4-Methylcoumarin-7-yl-2,3,4,6-tetra-*O*-acetyl-α-L-idopyranoside (42): A solution of diethyl azodicarboxylate (0.16 mL, 1.0 mmol) in THF (3.6 mL) was added to a mixture of **41** (0.26 g, 0.76 mmol), triphenylphosphine (0.25 g, 0.95 mmol), and 7-hydroxy-4-methylcoumarin (**38**; 0.27 g, 1.5 mmol) in THF (4 mL) at 0°C under nitrogen. After stirring for 2 h, the ice-bath was removed, and the reaction was quenched with aq sat $NaHCO_3$. The solution was diluted with EtOAc (5 mL), and the mixture was sequentially washed by aq 0.2 N NaOH (3×5 mL), water (2×5 mL), then brine. The organic layer was dried over $MgSO_4$, filtered and concentrated in vacuo. Purification of the residue through flash column chromatography (EtOAc/Hex 3:2) gave **42** (225 mg, 58%) and its β-isomer (93 mg, 24%).

Compound 42: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.53$ (d, $J = 8.8$ Hz, 1H, Ar-H), 7.08 (d, $J = 2.4$ Hz, 1H, Ar-H), 6.97 (dd, $J = 8.8$, 2.4 Hz, 1H, Ar-H), 6.20 (d, $J = 1.2$ Hz, 1H), 5.59 (s, 1H), 5.10 (t, $J = 3.4$ Hz, 1H), 5.07–5.06 (m, 1H), 4.95 (t, $J = 2.6$ Hz, 1H), 4.50 (ddd, $J = 6.3$, 6.3, 1.9 Hz, 1H), 4.18 (d, $J = 6.3$ Hz, 2H), 2.42 (d, $J = 1.2$ Hz, 3H, CH_3), 2.18–2.14 (m, 9H, CH_3), 1.93 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 169.93$ (C), 169.23 (C), 168.79 (C), 168.53 (C), 160.37 (C), 158.13 (C), 154.41 (C), 151.69 (C), 125.157 (CH), 114.76 (C), 113.02 (CH), 112.63 (CH), 104.15 (CH), 95.43 (CH), 66.32 (CH), 66.07 (CH), 65.66 (CH), 65.03 (CH), 61.44 (CH_2), 20.36 (CH_3), 20.34 (CH_3), 20.21 (CH_3), 20.08 (CH_3), 18.19 (CH_3); elemental analysis calcd (%) for $C_{24}H_{26}O_{12}$: C 55.92, H 5.17; found: C 55.62, H 5.29.

Isomer 42β: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.52$ (d, $J = 8.8$ Hz, 1H, Ar-H), 7.05 (d, $J = 2.4$ Hz, 1H, Ar-H), 6.97 (dd, $J = 8.8$, 2.4 Hz, 1H, Ar-H), 6.19 (d, $J = 1.2$ Hz), 5.59 (d, $J = 2.4$ Hz, 1H), 5.45 (t, $J = 5.6$ Hz, 1H), 5.15 (dd, $J = 5.6$, 2.4 Hz, 1H), 5.03 (dd, $J = 3.6$, 5.6 Hz, 1H), 4.49–4.46 (m, 1H), 4.32–4.19 (m, 1H), 2.41 (d, $J = 1.2$ Hz, 3H), 2.19–2.07 (m, 9H), 2.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 170.29$ (C), 169.53 (C), 169.39 (C), 168.52 (C), 154. 74 (C), 151.97 (C), 125.48 (CH), 115.16 (C), 113.65 (CH), 113.00 (CH), 103.74 (CH), 95.36 (CH), 71.67 (CH), 67.37 (CH), 67.04 (CH), 66.73 (CH), 62.49 (CH_2), 20.57 (CH_3), 20.44 (CH_3), 18.52 (CH_3); HRMS (FAB): calcd for $C_{24}H_{27}O_{12}$: 507.1502; found: 507.1517 [M+H$^+$].

4-Methylcoumarin-7-yl-α-L-Idopyranoside (43): A mixture of **42** (0.15 g, 0.31 mmol) and sodium methoxide (2.4 mg, 45 μmol) in methanol (1.5 mL) was stirred at room temperature for 3 h under nitrogen. The reaction solution was neutralized with Amberlite-120 acidic resin, and the mixture was filtered to remove the resin followed by washings with methanol. The filtrate was concentrated in vacuo, and the resulting solid was recrystallized in a mixed solvent (EtOAc/MeOH/Hex 1:1:10) to furnish **43** (89 mg, 88%) as a white solid. ^{1}H NMR (400 MHz, [D_6]acetone): $\delta =$ 7.69 (d, $J = 9.4$ Hz, 1H, Ar-H), 7.19–7.16 (m, 2H, Ar-H), 6.20 (s, 1H), 5.55 (d, $J = 3.4$ Hz, 1H), 4.77 (d, $J = 7.2$ Hz, 1H), 4.58 (d, $J = 5.8$ Hz, 1H), 4.33 (d, $J = 4.8$ Hz, 1H), 4.20 (ddd, $J = 5.7$, 5.7, 2.3 Hz, 1H), 4.04 (t, $J =$ 5.8 Hz, 1H), 3.95 (q, $J = 4.6$ Hz, 1H), 3.85–3.79 (m, 4H), 2.45 (d, $J =$ 1.2 Hz, 3H); HRMS (FAB): calcd for $C_{16}H_{19}O_8$: 339.1080; found: 339.1084 [M+H$^+$]; elemental analysis calcd (%) for $C_{16}H_{18}O_8$: C 56.80, H 5.36; found: C 56.63, H 5.38.

1,6-Anhydro-3,4-di-*O*-benzoyl-2-*O*-trifluoromethanesulfonyl-β-L-idopyranose (45): Trifluoromethanesulfonic anhydride (0.25 mL, 1.48 mmol) was added to a solution of **35** (201 mg, 1.24 mmol) in pyridine (2 mL) at 0°C under nitrogen. After stirring at the same temperature for 30 min, benzoyl chloride (0.58 mL, 5.0 mmol) was added to the mixture, the ice-bath was removed. The reaction solution was kept stirring for another 16 h, and methanol (0.4 mL) was added to quench the reaction. The mixture was coevaporated with toluene under reduced pressure, and the residue was dissolved in EtOAc (10 mL). The solution was consecutively washed with aq 2 N HCl, aq sat $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by column chromatography (EtOAc/Hex 1:4) to provide **45** (485 mg, 78%). $[\alpha]_D^{23} = -29.2$ ($c = 1.0$, $CHCl_3$); m.p. 156–157°C; IR ($CHCl_3$): $\tilde{\nu} =$ 3090, 2922, 2834, 1476, 1412, 1346, 1209, 1141, 1139, 1099, 1017, 963, 890, 754 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.92 (d, $J = 7.6$ Hz, 2H, Bz-H), 7.90 (d, $J = 7.2$ Hz, 2H, Bz-H), 7.49 (dd, $J = 7.6$, 7.2 Hz, 2H, Bz-H), 7.37 (d, $J = 7.6$ Hz, 2H, Bz-H), 7.33 (d, $J = 7.2$ Hz, 2H, Bz-H), 5.92 (t, $J =$ 8.8 Hz, 1H, H-3), 5.63 (s, 1H, H-1), 5.31 (dd, $J = 8.8$, 4.6 Hz, 1H, H-4), 4.87 (d, $J = 8.8$ Hz, 1H, H-2), 4.84 (t, $J = 4.6$, 1H, H-5), 4.32 (d, $J = 8.0$ Hz, 1H, H-6a), 3.86 (dd, $J = 8.0$, 4.6 Hz, 1H, H-6b); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 165.25$ (C), 165.09 (C), 133.86 (CH), 133.66 (CH), 118.23 (quant, $J = 253.3$ Hz, C), 99.09 (CH), 84.61 (CH), 72.86 (CH_2), 71.58 (CH), 69.38 (CH), 65.20 (CH).

1,6-Anhydro-3,4-di-*O*-benzoyl-β-L-gulopyranose (46): Sodium nitrite (123 mg, 1.8 mmol) and [15]crown-5 (0.36 mL, 1.8 mmol) at room temperature were sequentially added to a solution of **45** (300 mg, 0.60 mmol) in HMPA (3 mL). After stirring overnight, the reaction was quenched with H_2O (4 mL) and extracted with EtOAc (3×30 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash column chromatography (EtOAc/Hex 1:2) to afford **46** (205 mg, 91%) as a white solid. $[\alpha]_D^{25} = -131.3$ ($c = 1.0$, $CHCl_3$); m.p. 151–152°C; ^{1}H NMR (400 MHz, CD_3Cl_3): $\delta = 8.03$ (dd, $J = 8.1$, 1.1 Hz, 2H, Bz-H), 7.59–7.52 (m, 2H, Bz-H), 7.99 (dd, $J = 8.1$, 1.1 Hz, 2H, Bz-H), 7.42 (td, $J = 8.1$, 2.0 Hz, 4H, Bz-H), 5.65 (ddd, $J = 9.7$, 4.5, 0.8 Hz, 1H, H-4), 5.57 (d, $J = 2.4$ Hz, 1H, H-1), 5.54 (dd, $J = 9.7$, 4.5 Hz, 1H, H-3), 4.83 (t, $J = 4.5$ Hz, 1H, H-5), 4.31 (ddd, $J = 7.5$, 4.5, 2.4 Hz, 1H, H-2), 4.26 (d, $J = 8.0$ Hz, 1H, H-6a), 3.82 (d, $J = 8.0$, 4.5 Hz, 1H, H-6b), 2.16 (d, $J = 7.5$ Hz, 1H, 2-OH); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 165.62$ (C), 165.59 (C), 133.57 (CH), 133.56 (CH), 129.80 (CH), 129.19 (C), 128.88 (C), 128.50 (CH), 101.53 (CH), 72.57 (CH), 70.30 (CH), 69.72 (CH), 69.49 (CH), 64.26 (CH_2); HRMS (FAB): calcd for $C_{20}H_{17}O_7$: 371.1130; found: 371.1136 [M^+]; elemental analysis calcd (%) for $C_{20}H_{18}O_7$: C 64.86, H 4.90; found: C 64.80, H 4.91.

1,6-Anhydro-2-azido-3,4-di-*O*-benzoyl-2-deoxy-β-L-gulopyranose (47): A mixture of **45** (3.04 g, 6.05 mmol), sodium azide (1.97 g, 0.03 mol), and [15]crown-5 (126 μL, 0.63 mmol) in DMF (30 mL) was stirred at room temperature for 16 h. Water (25 mL) was added to the reaction solution, and the mixture was extracted with EtOAc (3×30 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. After purification via flash column chromatography (EtOAc/Hex 1:6), the solid residue was recrystallized through vapor diffusion method to give **47** (2.15 g, 90%) as colorless crystals. $[\alpha]_D^{33} =$

−69.12 (c = 1.0, $CHCl_3$); IR ($CHCl_3$): $\tilde{\nu}$ = 2109, 1727, 1272, 1112 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.06 (dd, J = 8.0, 1.4 Hz, 2H, Bz-H), 7.98 (dd, J = 8.0, 1.4 Hz, 2H, Bz-H), 7.56–7.54 (m, 2H, Bz-H), 7.45–7.40 (m, 4H, Bz-H), 5.75 (dd, J = 9.6, 5.3 Hz, 1H, H-3), 5.65 (dd, J = 9.6, 4.2 Hz, 1H, H-4), 5.56 (d, J = 2.2 Hz, 1H, H-1), 4.85 (t, J = 4.2 Hz, 1H, H-5), 4.27 (d, J = 8.1 Hz, 1H, H-6a), 4.18 (dd, J = 5.3, 2.2 Hz, 1H, H-2), 3.82 (dd, J = 8.1, 4.2 Hz, 1H, H-6b); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.59 (C), 165.30 (C), 133.67 (CH), 130.00 (CH), 129.79 (CH), 128.83 (C), 128.55 (CH), 100.58 (CH), 72.59 (CH), 69.69 (CH), 69.44 (CH), 64.84 (CH_2), 61.92 (CH); HRMS (FAB): calcd for $C_{20}H_{17}N_3O_6$: 396.1196; found: 396.1209 [M^+].

6-*O*-Acetyl-2-azido-3,4-di-*O*-benzoyl-2-deoxy-L-gulopyranosyl acetate (48): Compound **47** (0.10 g, 0.25 mmol) was dissolved in dichloromethane (1 mL) followed by consecutive addition of acetic anhydride (2 mL), trifluoroacetic acid (0.4 mL), and a solution of 1% H_2SO_4 in acetic anhydride (0.5 mL) at room temperature under nitrogen. The mixture was kept stirring for 2 h, the reaction flask was immersed in an ice-bath, and the reaction was quenched by aq sat $NaHCO_3$ (10 mL). The mixture was extracted with dichloromethane (3×10 mL), and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo to afford **48** (112 mg, 89%). **48β**: ^1H NMR (400 MHz, $CDCl_3$): δ = 8.10–8.06 (m, 4H, Bz-H), 7.65–7.60 (m, 2H, Bz-H), 7.51–7.47 (m, 4H, Bz-H), 6.12 (d, J = 8.6 Hz, 1H, H-1), 5.73 (t, J = 4.0 Hz, 1H, H-3), 5.35 (dd, J = 4.0, 1.4 Hz, 1H, H-4), 4.48 (dt, J = 6.4, 1.4 Hz, 1H, H-5), 4.26–4.18 (m, 2H, H-6a, H-6b), 4.00 (dd, J = 8.6, 4.0 Hz, 1H, H-2), 2.23 (s, 3H, CH_3), 1.98 (s, 3H, CH_3).

1,6-Anhydro-2,3,4-tri-*O*-trimethylsilyl-β-L-idopyranose (49): Triethylamine (5.5 mL, 40 mmol) at room temperature under nitrogen was added to a solution of compound **35** (1.28 g, 7.89 mmol) in dichloromethane (26 mL). The mixture was cooled to 0°C, and trimethylsilyl chloride (4.0 mL, 32 mmol) was slowly added to the reaction solution. The ice-bath was removed, and the reaction was kept stirring at room temperature for 3.5 h. The mixture was evaporated under reduced pressure, the residue was diluted with hexane (20 mL), and the salt was filtered followed by washings with hexane. The filtrate was concentrated in vacuo, and the resulting residue was recrystallized in ethanol to get **49** as a white solid (2.93 g, 98%). $[\alpha]_D^{30}$ = +43.3 (c = 1.0, $CHCl_3$); m.p. 65–66°C; IR ($CHCl_3$): $\tilde{\nu}$ = 3476, 3303, 2955, 1129, 1062, 1027, 956 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 5.18 (d, J = 1.6 Hz, 1H, H-1), 4.26 (t, J = 4.6 Hz, 1H, H-5), 4.08 (d, J = 7.5 Hz, 1H, H-6a), 3.69 (dd, J = 7.5, 4.6 Hz, 1H, H-4), 3.68 (dd, J = 7.5, 4.6 Hz, 1H, H-6b), 3.56 (t, J = 7.5 Hz, 1H, H-3), 3.47 (dd, J = 7.5, 1.6 Hz, 1H, H-2), 0.17 (s, 9H, $SiMe_3$), 0.14 (s, 9H, $SiMe_3$), 0.13 (s, 9H, $SiMe_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 102.06 (CH), 76.35 (CH), 75.72 (CH), 72.91 (CH), 65.07 (CH_2), 0.87 (CH_3), 0.35 (CH_3); elemental analysis calcd (%) for $C_{15}H_{34}O_5Si_3$: C 47.62, H 8.99; found: C 47.50, H 9.03.

1,6-Anhydro-3-*O*-benzyl-β-L-idopyranose (51): TMSOTf (18 μL, 0.10 mmol) was added to a mixture of compound **49** (0.38 g, 1.0 mmol), benzaldehyde (0.15 mL, 1.5 mmol), and freshly dried 3 Å molecular sieves (0.76 g) in dichloromethane (8 mL) at −78°C under nitrogen. The solution was stirred at the same temperature for 1 h, triethylsilane (0.24 mL, 1.5 mmol) was added to the mixture, and the reaction was kept stirring for another 1 h. A 1 M solution of tetra-*n*-butylammonium fluoride in THF (4 mL, 4 mmol) was added to the reaction mixture, and the resulting solution was further stirred for 1.5 h followed by addition of aq sat NH_4Cl (15 mL). The mixture was extracted with ethyl acetate (3× 15 mL), and the combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (EtOAc/Hex 3:2) to give a white solid, which was further recrystallized via vapor diffusion method to produce **51** (181 mg, 72%) as colorless crystals. $[\alpha]_D^{27}$ = +69.2 (c = 1.0, MeOH); m.p. 158–159°C; IR ($CHCl_3$): $\tilde{\nu}$ = 3301, 1128, 1028, 949 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.36–7.28 (m, 5H, Ph-H), 5.27 (d, J = 1.8 Hz, 1H, H-1), 4.93 (d, J = 11.7 Hz, 1H, CH_2Ph), 4.72 (d, J = 11.7 Hz, 1H, CH_2Ph), 4.41 (t, J = 4.9 Hz, 1H, H-5), 4.01 (d, J = 7.8 Hz, 1H, H-6a), 3.85 (ddd, J = 7.8, 4.9, 3.3 Hz, 1H, H-4), 3.71 (dd, J = 7.8, 4.9 Hz, 1H, H-6b), 3.64 (dt, J = 7.8, 1.8 Hz, 1H, H-2), 3.37 (t, J = 7.8 Hz, 1H, H-3), 2.09 (d, J = 3.3 Hz, 1H, 4-OH), 1.89 (d, J = 7.8 Hz, 1H, 2-OH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 138.40 (C), 128.68 (CH), 128.03 (CH), 127.88 (CH), 101.82 (CH), 84.19 (CH), 75.44 (CH), 74.99 (CH), 74.50 (CH_2), 71.07 (CH), 65.05 (CH_2); HRMS (FAB): calcd for $C_{13}H_{16}O_5$: 252.0997; found: 252.0992 [M^+]; elemental analysis calcd (%) for $C_{13}H_{16}O_5$: C 61.90, H 6.39; found: C 61.65, H 6.35.

1,6-Anhydro-3-*O*-benzyl-β-L-allopyranose (52): Compound **51** (0.50 g, 1.98 mmol) was dissolved in pyridine (10 mL) at room temperature under nitrogen, the mixture was cooled to 0°C, trifluoromethanesulfonic anhydride (1.0 mL, 5.95 mmol) was added to the solution, and the ice-bath was removed. After stirring for 16 h, the reaction was quenched with water (1 mL), and the solvent was coevaporated with toluene under reduced pressure. The residue was dissolved in EtOAc (15 mL), and the mixture was consecutively washed with aq 2 N HCl, aq sat $NaHCO_3$, and brine. The organic phase was dried over $MgSO_4$, filtered, and concentrated in vacuo to give a residue, which was recrystallized in ethanol to yield the corresponding 2,4-di-OTf derivative as a white solid (927 mg, 88%). $[\alpha]_D^{23}$ = +32.8 (c = 1.1, $CHCl_3$); m.p. 117–118°C; IR ($CHCl_3$): $\tilde{\nu}$ = 2974, 3076, 1723, 1415, 1274, 1211, 1246, 1241, 1203, 1139, 1100, 927, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.42–7.28 (m, 5H, Ar-H), 5.62 (s, 1H, H-1), 4.99 (dd, J = 8.0, 4.0, H-2), 4.80 (ddd, J = 4.8, 4.0, 1.2 Hz, H-5), 4.79 (s, 1H, CH_2Ph), 4.78 (s, 1H, CH_2Ph), 4.75 (d, J = 8.0, 1.2 Hz, H-4), 4.21 (d, J = 8.6 Hz, H-6a), 4.13 (t, J = 8.0 Hz, H-3), 3.95 (dd, J = 8.6, 4.8 Hz, H-6b); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.81 (CH), 128.68 (CH), 28.64 (CH), 28.53 (CH), 118.43 (q, J = 299.8 Hz, C), 98.97 (CH), 86.35 (CH), 83.06 (CH), 76.39 (CH_2), 75.95 (CH), 73.05 (CH), 65.91 (CH_2); HRMS (FAB): calcd for $C_{15}H_{15}F6O_9S_2$: 517.00617; found: 517.0233 [M+H$^+$]; elemental analysis calcd (%) for $C_{14}H_{15}F6O_9S_2$: C 34.89, H 2.73; found: C 34.89, H 2.69.

A mixture of this 2,4-di-OTf compound (50 mg, 0.09 mmol), $NaNO_2$ (67 mg, 1.0 mmol), and [15]crown-5 (0.22 mL, 1.0 mmol) in HMPA (1 mL) was stirred at room temperature for 24 h. Water (3 mL) was added to the reaction solution, and the mixture was extracted with EtOAc (2×5 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo, and the residue was purified by flash column chromatography on silica gel (EtOAc/Hex 2:1) to provide **52** (11.5 mg, 47%) as a colorless oil. $[\alpha]_D^{23}$ = −18.6 (c = 0.25, $CHCl_3$); IR ($CHCl_3$): $\tilde{\nu}$ = 3412, 3052, 2949, 1413, 1211, 1138, 946 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.62–7.28 (m, 5H, Ar-H), 5.47 (d, J = 1.5 Hz, 1H, H-1), 4.89 (dd, J = 8.2, 1.5 Hz, 1H, H-2), 4.76 (d, J = 11.7 Hz, 1H, CH_2Ph), 4.60 (dd, J = 5.5, 2.5 Hz, 1H, H-4), 4.54 (d, J = 11.7 Hz, 1H, CH_2Ph), 3.89–3.82 (m, 3H, H-3, H-5, H-6a), 3.62 (d, J = 8.2 Hz, H-6b), 2.15–1.91 (br, 2H, 2-OH, 4-OH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.45 (C), 128.77 (CH), 128.35 (CH), 128.00 (CH), 78.14 (CH), 74.18 (CH), 71.86 (CH_2), 68.94 (CH), 67.87 (CH), 63.58 (CH_2).

1,6-Anhydro-2-*O*-benzoyl-3-*O*-benzyl-β-L-idopyranose (53): Pyridine (3.0 mL, 37.2 mmol) at room temperature under nitrogen was added to a solution of compound **51** (3.00 g, 11.9 mmol) in dichloromethane (35 mL). The reaction flask was immersed in an ice-bath, and benzoyl chloride (1.45 mL, 12.5 mmol) was slowly added to the mixture. After stirring at the same temperature for 4 h, the reaction was quenched by methanol (2 mL), and the solvent was evaporated with toluene under reduced pressure. The residue was dissolved in EtOAc (30 mL), and the mixture was sequentially washed with aq 2 N HCl, aq sat $NaHCO_3$, water, and brine. The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo to furnish a solid residue, which was recrystallized via vapor diffusion method to get **53** (3.60 g, 85%) as colorless crystals. $[\alpha]_D^{27}$ = +127.5 (c = 1.2, $CHCl_3$); m.p. 142–143°C; IR ($CHCl_3$): $\tilde{\nu}$ = 3473, 2904, 1722, 1452, 1272, 1113, 1027, 712 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.08 (dd, J = 7.6, 1.3 Hz, 2H, Bz-H), 7.59 (tt, J = 7.6, 1.3 Hz, 1H, Bz-H), 7.46 (t, J = 7.6 Hz, 2H, Bz-H), 7.29–7.24 (m, 5H, Ar-H), 5.53 (d, J = 1.6 Hz, 1H, H-1), 5.07 (dd, J = 8.2, 1.6 Hz, 1H, H-2), 4.80 (d, J = 11.6 Hz, 1H, CH_2Ph), 4.65 (d, J = 11.6 Hz, 1H, CH_2Ph), 4.51 (t, J = 4.6 Hz, 1H, H-5), 4.15 (d, J = 7.5 Hz, 1H, H-6a), 4.00 (ddd, J = 8.2, 4.6, 3.0 Hz, 1H, H-4), 3.87 (t, J = 8.2 Hz, 1H, H-3), 3.76 (dd, J = 7.5, 4.6 Hz, 1H, H-6b), 2.22 (d, J = 3.0 Hz, 1H, 4-OH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.77 (C), 137.94 (C), 133.38 (CH), 129.81 (CH), 129.40 (C), 128.53 (CH), 128.45 (CH), 127.96 (CH), 127.84 (CH), 99.41 (CH), 80.24 (CH), 76.71 (CH), 75.07 (CH), 74.58 (CH_2), 71.33 (CH), 65.27 (CH); HRMS (FAB): calcd for $C_{20}H_{21}O_6$: 357.1338; found: 357.1353 [M+H$^+$]; elemental analysis calcd (%) for $C_{20}H_{20}O_6$: C 67.41, H 5.61; found: C 67.20, H 5.44.

1,6-Anhydro-2-*O*-benzoyl-3-*O*-benzyl-4-*O*-trifluoromethanesulfonyl-β-L-idopyranose (54): A solution of benzoyl chloride (49 μL, 0.42 mmol) in dichloromethane (0.7 mL) was added to a mixture of compound **51**

(0.10 g, 0.40 mmol) in pyridine (0.5 mL) at 0 °C under nitrogen. After stirring at the same temperature for 4 h, trifluoromethanesulfonic anhydride (0.20 mL, 1.2 mmol) was added to the reaction solution, the ice-bath was removed, and the mixture was kept stirring at room temperature for another 1 h. The reaction was quenched by addition of MeOH (0.5 mL), and the mixture was coevaporated with toluene under reduced pressure. The solid residue was dissolved in water (4 mL), the mixture was extracted with EtOAc (3×5 mL), and the combined organic layers were washed with aq 2 N HCl, then brine. The organic phase was dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (EtOAc/Hex 1:4) to furnish a white solid, which was recrystallized through vapor diffusion method to afford **54** (0.17 g, 88 %) as colorless crystals. $[\alpha]_D^{25} = +147.1$ ($c = 1.0$, $CHCl_3$); m.p. 125–126 °C; IR ($CHCl_3$): $\tilde{\nu} = 1726$, 1417, 1270, 1245, 1212, 1142, 937 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.99$ (dd, $J = 8.4$, 1.3 Hz, 2H, Bz-H), 7.58 (tt, $J = 8.4$, 1.3 Hz, 1H, Bz-H), 7.44 (t, $J = 8.4$ Hz, 2H, Bz-H), 7.23 (s, 5H, Ar-H), 5.56 (d, $J = 1.8$ Hz, 1H, H-1), 5.10 (dd, $J = 8.2$, 1.8 Hz, H-2), 5.01 (dd, $J = 8.2$, 4.6 Hz, H-4), 4.77 (t, $J = 4.6$ Hz, 1H, H-5), 4.73 (d, $J = 11.0$ Hz, 1H, CH_2Ph), 4.66 (d, $J = 11.0$ Hz, 1H, CH_2Ph), 4.18 (d, $J = 8.1$ Hz, 1H, H-6a), 4.12 (t, $J = 8.2$ Hz, H-3), 3.88 (dd, $J = 8.1$, 4.6 Hz, 1H, H-6b); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 165.34$ (C), 136.65 (C), 133.67 (CH), 129.88 (CH), 128.91 (C), 128.54 (CH), 128.39 (CH), 128.06 (CH), 127.96 (CH), 120.84 (q, $J = 317.5$ Hz, CF_3), 99.40 (CH), 83.77 (CH), 76.78 (CH), 76.58 (CH), 75.23 (CH_2), 73.03 (CH), 65.42 (CH_2); HRMS (FAB): calcd for $C_{21}H_{20}F_3O_8S$: 489.0830; found: 489.0854 [$M+H^+$]; elemental analysis calcd (%) for $C_{21}H_{19}F_3O_8S$: C 51.64, H 3.89; found: C 51.15, H 3.73.

1,6-Anhydro-2-*O*-benzoyl-3-*O*-benzyl-β-L-altropyranose (55): Compound **54** (50 mg, 0.10 mmol) was dissolved in HMPA (1 mL) at room temperature, $NaNO_2$ (70 mg, 1.0 mmol) and [15]crown-5 (40 μL, 0.20 mmol) were consecutively added to the reaction solution, and the mixture was kept stirring for 3 d. The resulting solution was filtered through Celite, and the filtrate was diluted with EtOAc (10 mL), which was sequentially washed by water (4×6 mL) and brine. The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography (EtOAc/Hex 1:1) to yield **55** (30.6 mg, 84 %) as a white solid. $[\alpha]_D^{25} = +199.5$ ($c = 1.0$, $CHCl_3$); m.p. 99–100 °C; IR ($CHCl_3$): $\tilde{\nu} = 3481$, 2918, 1718, 1453, 1273, 1110, 1030, 713 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 8.01$ (dd, $J = 8.5$, 1.1 Hz, 2H, Bz-H), 7.57 (tt, $J = 8.5$, 1.1 Hz, 1H, Bz-H), 7.43 (t, $J = 8.5$ Hz, 2H, Bz-H), 7.23 (s, 5H, Ar-H), 5.53 (d, $J = 1.7$ Hz, 1H, H-1), 5.21 (dd, $J = 8.6$, 1.7 Hz, H-2), 4.71 (dd, $J = 5.4$, 2.2 Hz, H-5), 4.68 (d, $J = 12.1$ Hz, 1H, CH_2Ph), 4.60 (d, $J = 12.1$ Hz, 1H, CH_2Ph), 3.98 (dd, $J = 4.5$, 2.2 Hz, 1H, H-4), 3.88 (dd, $J = 8.6$, 4.5, 1H, H-3), 3.80 (dd, $J = 7.9$, 5.4 Hz, 1H, H-6a), 3.71 (d, $J = 7.9$, 1H, H-6b), 2.98–2.89 (bs, 1H, 4-OH); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 165.77$ (C), 137.06 (C), 133.30 (CH), 129.85 (CH), 129.50 (C), 128.55 (CH), 128.38 (CH), 128.16 (CH), 127.85 (CH), 99.30 (CH), 75.97 (CH), 74.31 (CH), 74.09 (CH), 72.14 (CH_2), 68.41 (CH), 65.46 (CH_2); HRMS (FAB): calcd for $C_{21}H_{20}O_6$: 357.1338; found: 357.1327 [$M+H^+$]; elemental analysis calcd (%) for $C_{20}H_{19}O_6$: C 67.57, H 5.57; found: C 67.40, H 5.66.

1,6-Anhydro-4-azido-2-*O*-benzoyl-3-*O*-benzyl-4-deoxy-β-L-altropyranose (56): A mixture of **54** (60 mg, 0.12 mmol) and NaN_3 (33 mg, 0.51 mmol) in DMF (1 mL) was stirred at 50 °C for 18 h. The solvent was coevaporated with toluene under reduced pressure, the syrup was dissolved in water (3 mL), and the mixture was extracted with EtOAc (3×5 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography (EtOAc/Hex 1:4) to give a white solid, which was recrystallized via vapor diffusion method to yield **56** (45.4 mg, 97 %) as colorless crystals. $[\alpha]_D^{25} = +193.4$ ($c = 1.0$, $CHCl_3$); m.p. 132–133 °C; IR ($CHCl_3$): $\tilde{\nu} = 2904$, 2111, 1717, 1453, 1271, 1113, 1030, 980, 715 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 8.01$ (dd, $J = 8.5$, 1.4 Hz, 2H, Bz-H), 7.57 (tt, $J = 8.5$, 1.4 Hz, 1H, Bz-H), 7.43 (t, $J = 8.5$ Hz, 2H, Bz-H), 7.28–7.23 (m, 5H, Ar-H), 5.55 (d, $J = 1.7$ Hz, 1H, H-1), 5.23 (dd, $J = 8.9$, 1.7 Hz, H-2), 4.70 (d, $J = 12.2$ Hz, 1H, CH_2Ph), 4.64 (d, $J = 12.2$ Hz, 1H, CH_2Ph), 4.62 (dd, $J = 4.7$, 2.1 Hz, H-5), 4.09 (dd, $J = 8.9$, 5.0 Hz, 1H, H-3), 3.80 (dd, $J = 5.0$, 2.1 Hz, 1H, H-4), 3.78 (dd, $J = 8.1$, 4.7 Hz, 1H, H-6a), 3.71 (d, $J = 8.1$ Hz, 1H, H-6b); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 165.63$ (C), 137.15 (C), 133.36 (CH), 129.88 (CH), 129.44 (C), 128.55 (CH), 128.42 (CH), 128.13 (CH), 127.90 (CH), 99.61 (CH), 75.68 (CH), 74.39 (CH), 74.16 (CH), 72.53 (CH_2), 66.32 (CH_2), 60.99 (CH); HRMS (FAB): calcd for $C_{20}H_{20}O_5N_3$: 382.1429; found: 382.1439 [$M+H^+$]; elemental analysis calcd (%) for $C_{20}H_{19}N_3O_5$: C 62.98, H 5.02, N 11.01; found: C 63.23, H 5.01, N 11.09.

1,6-Anhydro-2,4-di-*O*-benzoyl-β-D-mannopyranose (58): *N*-Benzoyloxybenzotriazole (5.31 g, 22.2 mmol) at room temperature under nitrogen was added to a solution of **57** (3.00 g, 18.5 mmol) in pyridine (60 mL). The reaction mixture was stirred for 28 h, the same amount of *N*-benzoyloxybenzotriazole (5.31 g, 22.2 mmol) was added to the solution, and the mixture was kept stirring for another 48 h. The solvent was coevaporated with toluene under reduced pressure, water (80 mL) was added to the solid residue, and the mixture was extracted with EtOAc (2×150 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash column chromatography (EtOAc/Hex 1:2→2:1) to furnish a white solid, which was recrystallized through vapor diffusion method to afford **58** (3.70 g, 54 %) as colorless crystals. IR ($CHCl_3$): $\tilde{\nu} = 3552$, 2963, 1720, 1601, 1451, 1317, 1266, 1108, 1071, 1028, 986, 710 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 8.08$ (d, $J = 7.8$ Hz, 4H, Bz-H), 7.58 (t, $J = 8.1$ Hz, 2H, Bz-H), 7.47–7.43 (m, 4H, Bz-H), 5.66 (s, 1H, H-1), 5.24 (d, $J = 1.6$ Hz, 1H, H-4), 5.18 (dd, $J = 5.2$, 1.6 Hz, 1H, H-2), 4.78 (d, $J = 5.4$ Hz, 1H, H-5), 4.44 (d, $J = 7.6$ Hz, 1H, H-6a), 4.37 (t, $J = 1.6$ Hz, 1H, H-3), 3.86 (dd, $J = 7.6$, 5.4 Hz, 1H, H-6b), 3.00 (s, 1H, 3-OH); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 165.29$ (C), 165.27 (C), 133.67 (CH), 133.57 (CH), 133.52 (CH), 129.31 (C), 128.99 (C), 128.36 (CH), 100.07 (CH), 74.32 (CH), 73.74 (CH), 69.90 (CH), 68.58 (CH), 65.58 (CH_2); HRMS (FAB): calcd for $C_{20}H_{19}O_7$: 371.1131; found: 371.1154 [$M+H^+$]; elemental analysis calcd (%) for $C_{20}H_{18}O_7$: C 64.86, H 4.90; found: C 64.98, H 4.78.

1,6-Anhydro-2,4-di-*O*-benzoyl-3-*O*-[(*p*-nitrophenyl)formyl]-β-D-mannopyranose (59): A mixture of compound **58** (90 mg, 0.24 mmol) and DMAP (0.12 g, 0.97 mmol) in pyridine (0.90 mL) was stirred at room temperature under nitrogen, *p*-nitrophenyl chloroformate (0.20 g, 0.97 mmol) was added to the solution, and the reaction was kept stirring for 48 h. The solvent was coevaporated with toluene under reduced pressure, the residue was partitioned between EtOAc (5 mL) and H_2O (3 mL), and the aqueous phase was extracted with EtOAc (2×5 mL). The combined organic layers were consecutively washed by aq 2 N HCl, aq 5 % K_2CO_3, and brine. The organic phase was dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography (EtOAc/Hex 2:5) to provide **59** (117 mg, 89 %) as a syrup. ^1H NMR (400 MHz, $CDCl_3$): $\delta = 8.15$ (t, $J = 9.2$, 1.4 Hz, 2H, Ph-H), 8.08 (dd, $J = 8.6$, 1.2 Hz, 2H, *p*-NO_2Ph-H), 7.64 (dd, $J = 7.5$, 1.4 Hz, 2H, Ph-H), 7.51 (t, $J = 7.9$ Hz, 2H, Ph-H), 7.46 (t, $J = 7.9$ Hz, 2H, Ph-H), 7.14 (d, $J = 8.6$, 1.2 Hz, 2H, *p*-NO_2Ph-H), 5.71 (d, $J = 1.7$ Hz, 1H, H-1), 5.51 (ddd, $J = 5.4$, 3.3, 1.0 Hz, 1H, H-3), 5.44 (dd, $J = 5.4$, 1.7 Hz, 1H, H-2), 5.33 (t, $J = 3.3$ Hz, 1H, H-4), 4.85 (d, $J = 5.3$ Hz, 1H, H-5), 4.41 (dd, $J = 7.9$, 1.0 Hz, 1H, H-6a), 4.01 (dd, $J = 7.9$, 5.3 Hz, 1H, H-6b); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 165.35$ (C), 165.25 (C), 155.25 (C), 151.88 (C), 145.60 (C), 134.07(CH), 133.89 (CH), 130.17(CH), 129.99 (CH),129.12 (CH), 128.74 (CH), 125.34 (CH), 121.70 (CH), 99.50 (CH), 74.11(CH), 72.89 (CH), 72.05 (CH), 67.61 (CH), 65.61 (CH_2); HRMS (FAB): calcd for $C_{27}H_{22}O_{11}N$: 536.1194; found: 536.1205 [$M+H^+$]; elemental analysis calcd (%) for $C_{27}H_{17}O_{11}N$: C 60.56, H 4.95, N 3.62; found: C 60.74, H 4.18, N 5.31.

6-*O*-Acetyl-2,4-di-*O*-benzoyl-3-*O*-[(*p*-nitrophenyl)fomyl]-α-D-mannopyranosyl bromide (60): $Cu(OTf)_2$ (1.1 mg, 3.0 μmol) was added to a solution of **59** (32.6 mg, 61 μmol) in acetic anhydride (115 μL) at room temperature under argon, and the mixture was kept stirring for 24 h. The reaction flask was immersed in an ice-bath, a 30 % solution of HBr in acetic acid (164 μL, 0.61 mmol) was added to the reaction solution, and the mixture was gradually warmed up to room temperature and kept stirring overnight. The whole solution was poured into ice-water (5 mL), the mixture was extracted with EtOAc (3×10 mL), and the combined organic layers were washed with aq sat $NaHCO_3$ twice, then brine. The resulting organic phase was dried over $MgSO_4$, filtered, and concentrated in vacuo. Purification of the residue via flash column chromatography (EtOAc/Hex 1:3) led to the bromide **60** (36.1 mg, 90 %). ^1H NMR (400 MHz, $CDCl_3$): δ = 8.18–8.07 (m, 6H, Ar-H), 7.65 (t, $J = 7.4$ Hz, 2H, Ar-H), 7.54–7.50 (m, 4H, Ar-H), 7.18 (d, $J = 9.1$ Hz, 2H, Ar-H), 6.54 (d, $J = 1.4$ Hz, 1H, H-1), 5.99–5.89 (m, 3H, H-2, H-3, H-4), 4.49 (dt, $J = 7.2$, 3.5 Hz, 1H, H-5), 4.40–4.32 (m, 2H, H-6a, H-6b), 2.10 (s, 3H, CH_3); ^{13}C NMR (100 MHz,

$CDCl_3$): δ = 170.32 (C), 165.09 (C), 155.05 (C), 151.44 (C), 145.57 (C), 134.16 (CH), 134.07 (CH), 130.03 (CH), 129.99 (CH), 129.02 (CH), 128.75 (C), 125.18 (CH), 121.78 (CH), 82.67 (CH), 73.49 (CH), 72.83 (CH), 72.01 (CH), 65.99 (CH), 61.58 (CH_2), 20.57 (CH_3); HRMS (FAB): calcd for $C_{29}H_{24}BrO_{12}NNa$: 658.0560; found: 658.0563 [M+Na^+].

6-*O*-Acetyl-2,4-di-*O*-benzoyl-3-*O*-[(*p*-nitrophenyl)formyl]-D-mannopyranose (61): Compound **60** (20.3 mg, 30 μmol) was dissolved in 0.5% wet acetone (0.50 mL) at room temperature. AgOTf (8.7 mg, 30 μmol) and 2,6-di-*tert*-butyl-4-methylpyridine (3.6 mg, 18 μmol) were consecutively added to the solution, and the mixture was kept stirring for 1 h followed by addition of 2,6-di-*tert*-butyl-4-methylpyridine (3.6 mg, 18 μmol). The whole reaction mixture was filtered through Celite, and the filtrate was concentrated in vacuo to give a residue, which was purified by flash column chromatography (EtOAc/Hex 1:2) to furnish the product **61** (17.1 mg, 93%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01 (d, J = 9.2 Hz, 2H, Bz-H), 7.56 (t, J = 7.6 Hz, 2H, Ar-H), 7.60–7.42 (m, 4H, Ar-H), 7.05 (d, J = 9.2 Hz, 2H, Ar-H), 5.75 (t, J = 10.0 Hz, 1H, H-4), 5.67 (dd, J = 3.2, 1.6 Hz, 1H, H-2), 5.58 (dd, J = 10.0, 3.2 Hz, 1H, H-3), 5.41 (dd, J = 4.1, 1.6 Hz, 1H, H-1), 4.41 (ddd, J = 10.0, 7.7, 4.2 Hz, 1H, H-5), 4.30–4.20 (m, 2H, H-6a, H-6b), 3.32 (d, J = 4.1 Hz, 1H, 1-OH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.84 (C), 165.61 (C), 165.30 (C), 155.16 (C), 151.50 (C), 145.43 (C), 133.83 (CH), 129.89 (CH), 128.90 (C), 128.76 (CH), 128.65 (CH), 128.59 (CH), 125.10 (CH), 121.81 (CH), 92.18 (CH), 74.33 (CH), 69.96 (CH), 68.44 (CH), 66.98 (CH), 62.68 (CH_2), 20.62 (CH_3); HRMS (MALDI): calcd for $C_{29}H_{25}NO_{13}Na$: 618.1224; found: 618.1200 [M+Na^+].

6-*O*-Acetyl-2,4-di-*O*-benzoyl-3-*O*-[(*p*-nitrophenyl)formyl]-α-D-mannopyranosyl trichloroacetimidate (62): Potassium carbonate (249 mg, 1.81 mmol) at room temperature under nitrogen was added to a mixture of **61** (215 mg, 0.36 mmol) and trichloroacetonitrile (362 μL, 3.61 mmol) in dichloromethane (2 mL). After stirring for 6 h, the reaction mixture was filtered through Celite, and the organic layer was washed with water (2 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo to give **62** (238 mg, 89%). $[\alpha]_D^{24} = -82.0$ (c = 0.25, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.89 (s, 1H, NH), 8.17 (d, J = 9.2 Hz, 2H, Bz-H), 8.15 (d, J = 9.2 Hz, 2H, Ar-H), 8.07 (d, J = 7.6 Hz, 2H, Ar-H), 7.65 (dd, J = 7.6, 7.2 Hz, 2H, Ar-H), 7.29 (d, J = 7.2 Hz, 2H, Ar-H), 7.19 (d, J = 9.2 Hz, 2H, Ar-H), 6.54 (s, 1H, H-1), 5.96 (d, J = 3.1 Hz, 1H, H-2), 5.93 (t, J = 10.1 Hz, 1H, H-4), 5.61 (dd, J = 10.1, 3.1 Hz, 1H, H-3), 4.45 (ddd, J = 10.1, 6.8, 3.6 Hz, 1H, H-5), 4.33 (dd, J = 12.3, 6.8 Hz, 1H, H-6a), 4.32 (dd, J = 12.3, 3.6 Hz, 1H, H-6b), 2.08 (s, 1H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.37 (C), 165.28 (C), 165.12 (C), 159.70 (C), 155.12 (C), 151.56 (C), 145.62 (C), 134.05(CH), 133.95 (CH), 130.04 (CH), 130.00 (CH), 128.69 (CH), 128.59 (C), 125.18 (CH), 121.88 (CH), 94.59 (CH), 74.33 (CH), 71.25 (CH), 67.77 (CH), 66.03 (CH), 62.68 (CH_2), 20.54 (CH_3).

1,6-Anhydro-2-*O*-{6-*O*-acetyl-2,4-di-*O*-benzoyl-3-*O*-[(*p*-nitrophenyl)formyl]-α-D-mannopyranosyl}-3,4-di-*O*-benzoyl-β-L-gulopyranoside (63): A mixture of the trichloroacetimidate **62** (26.9 mg, 36.4 μmol), compound **46** (11.2 mg, 30.2 μmol), and freshly dried 4 Å molecular sieves (150 mg) in dichloromethane (0.5 mL) was stirred at room temperature for 30 min under nitrogen. The mixture was cooled to −40 °C, trimethylsilyl trifluoromethanesulfonate (2.7 μL, 14.9 μmol) was added to the reaction mixture, and the resulting solution was gradually warmed up to room temperature. After stirring for 20 h, the reaction was quenched by addition of triethylamine (6 μL), and the mixture was filtered through Celite followed by wash with dichloromethane. The filtrate was concentrated in vacuo, and the residue was purified by flash column chromatography (EtOAc/Hex 2:5) to afford **46** (2.7 mg) and **63** (17.8 mg, 62%, recovery yield: 82%). $[\alpha]_D^{24} = -237.4$ (c = 0.15, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.15 (d, J = 9.2 Hz, 2H, Ar-H), 8.10–7.94 (m, 6H, Ar-H), 7.7–7.38 (m, 10H, Ar-H), 7.32 (t, J = 7.4 Hz, Ar-H), 5.82–7.74 (m, 3H, H-3, H-4, H-3′), 5.72 (dd, J = 3.2, 1.8 Hz, 1H, H-2), 5.71 ~ 5.69 (m, 2H, H-1′, H-4), 5.10 (d, J = 1.8 Hz, 1H, H-1), 4.91 (dd, J = 4.6, 3.4 Hz, 1H, H-5′), 4.56 (ddd, J = 8.6, 5.0, 3.2 Hz, 1H, H-5), 4.34–4.31 (m, 2H, H-6a, H-2′), 4.27 (d, J = 8.1 Hz, 1H, H-6a′), 4.25 (d, J = 10.1, 3.2 Hz, 1H, H-6b), 3.81 (dd, J = 8.1, 4.6 Hz, 1H, H-6b′); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.41 (C), 165.66 (C), 165.52 (C), 165.33 (C), 165.10 (C), 155.30 (C), 151.29 (C), 145.46 (C), 133.87 (CH), 133.78 (CH), 133.64 (CH), 133.46 (CH), 130.13 (CH), 129.90 (CH), 129.84 (CH), 128.88 (C), 128.68 (CH), 128.58 (CH), 128.56 (CH), 125.09 (CH), 121.90 (CH), 100.35 (CH), 99.55 (CH), 77.80 (CH), 74.48 (CH), 72.36 (CH), 70.20 (CH), 69.42 (CH), 69.04 (CH), 68.52 (CH), 66.50 (CH), 64.57 (CH_2), 62.62 (CH_2), 20.61 (CH_3); HRMS (MALDI): calcd for $C_{49}H_{41}NO_{19}Na$: 970.2170; found: 970.2168 [M+Na^+].

6-*O*-Acetyl-2-*O*-{6-*O*-acetyl-2,4-di-*O*-benzoyl-3-*O*-[(*p*-nitrophenyl)formyl]-α-D-mannopyranosyl}-3,4-di-*O*-benzoyl-L-gulopyranosyl acetate (64): $Cu(OTf)_2$ (0.9 mg, 2.5 μmol) was added to a solution of compound **63** (20.3 mg, 21.4 μmol) in acetic anhydride (203 μL) at room temperature under argon. After stirring for 4 d, the reaction was quenched with aq sat $NaHCO_3$ (3 mL), and the mixture was extracted with EtOAc (3 × 5 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. Purification of the residue via flash column chromatography (EtOAc/Hex 2:5) provided **63** (3.5 mg) and **64** (13.8 mg, 61%, recovery yield = 74%). $[\alpha]_D^{28} = -59.02$ (c = 0.61, $CHCl_3$); IR ($CHCl_3$): $\tilde{\nu}$ = 2919, 1728, 1247, 1087, 708 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.22 (dd, J = 8.5, 1.4 Hz, 0.9H, Ar-H), 8.15 (dd, J = 8.5, 1.4 Hz, 2.3H, Ar-H), 8.13–8.05 (m, 10.4H, Ar-H), 7.96 (dd, J = 8.0, 1.4 Hz, 2.1H, Ar-H), 7.67–7.59 (m, 6.4H, Ar-H), 7.53–7.42 (m, 13.1H, Ar-H), 7.14–7.08 (m, 3.0H, Ar-H), 6.56 (d, J = 4,0 Hz, 0.4H), 6.15 (d, J = 8.2 Hz, 1.0H), 5.94 (t, J = 3.7 Hz, 1.0H), 5.82 (t, J = 3.5 Hz, 0.4H), 5.76–5.70 (m, 1.4H), 5.61 (dd, J = 3.2, 1.9 Hz, 1.0H), 5.56 (dd, J = 3.2, 1.9 Hz, 0.4H), 5.54 (d, J = 3.5 Hz, 0.4H), 5.48 (dd, J = 4,0, 1.5 Hz, 1.0H), 5.36–5.33 (m, 2.5H), 5.20 (dd, J = 10.1, 3.2 Hz, 0.4H), 4.85 (t, J = 6.4 Hz, 0.4H), 4.68 (dt, J = 1.3, 6.4 Hz, 1.0H), 4.47 (t, J = 3.9 Hz, 0.4H), 4.39 (m, 9.1H), 2.23 (s, 3.0H, CH_3), 2.09–2.08 (m, 6.0H, CH_3), 2.05 (s, 1.5H, CH_3), 2.03 (s, 3.0H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.44 (C), 170.39 (C), 169.60 (C), 168.71 (C), 165.15 (C), 165.10 (C), 165.04 (C), 165.00 (C), 164.87 (C), 155.25 (C), 155.17 (C), 151.16 (C), 151.10 (C), 145.40 (C), 145.36 (C), 133.97 (CH), 133.89 (CH), 133.76 (CH), 130.12 (CH), 130.02 (CH), 129.97 (CH), 129.93 (CH), 129.78 (CH), 128.84 (C), 128.70 (CH), 128.61 (CH), 128.54 (CH), 125.03 (CH), 121.82 (CH), 95.67 (CH), 95.39 (CH), 90.99 (CH), 89.54 (CH), 74.16 (CH), 71.90 (CH), 70.74 (CH), 69.61 (CH), 69.29 (CH), 68.56 (CH), 68.48 (CH), 68.34 (CH), 68.23 (CH), 67.68 (CH), 66.66 (CH), 66.37 (CH), 66.10 (CH), 64.32 (CH), 62.42 (CH_2), 62.33 (CH_2), 61.91 (CH_2), 61.79 (CH_2), 20.97 (CH_3), 20.92 (CH_3), 20.69 (CH_3), 20.65 (CH_3), 20.57 (CH_3); HRMS (MALDI): calcd for $C_{53}H_{47}NO_{22}Na$: 1072.2487; found: 1072.2478 [M+Na^+].

6-*O*-Acetyl-2-*O*-(6-*O*-acetyl-2,4-di-*O*-benzoyl-3-*O*-carbamoyl-α-D-mannopyranosyl)-3,4-di-*O*-benzoyl-L-gulopyranose (65): A solution of compound **64** (11.2 mg, 10.7 μmol) in THF (3 mL) was saturated with ammonia gas at room temperature, and the mixture was kept stirring for 5 h. Evaporation of the mixture in vacuo furnished a residue followed by purification through flash column chromatography (EtOAc/Hex 1:1) to yield **65** (7.3 mg, 77%). $[\alpha]_D^{28} = -79.4$ (c = 0.14, $CHCl_3$); IR ($CHCl_3$): $\tilde{\nu}$ = 3448, 2913, 1723, 1257, 1116, 709 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.14–8.11 (m, 4.2H, Bz-H), 8.07 (d, J = 7.2 Hz, 2.4H, Bz-H), 7.98 (dd, J = 8.4, 1.2 Hz, Bz-H), 7.66–7.58 (m, 3.7H, Bz-H), 7.56–7.52 (m, 3.2H, Bz-H), 7.51–7.41 (m, 8.1H, Bz-H), 5.85 (t, J = 3.6 Hz, 1H), 5.66 (t, J = 10.0 Hz, 0.9H), 5.49–5.43 (m, 3.2H), 5.31–5.27 (m, 2.2H), 4.62–4.58 (m, 1H), 4.55 (t, J = 6.4 Hz, 1.1H), 4.34–4.26 (m, 5.1H), 4.06 (dd, J = 7.9, 3.3 Hz, 1.1H), 3.79 (d, J = 5.4 Hz, 0.8H), 2.09 (s, 3.4H, CH_3), 2.06 (s, 4.5H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.79 (C), 170.57 (C), 165.68 (C), 164.99 (C), 164.95 (C), 164.87 (C), 155.07 (C), 133.83 (CH), 133.65 (CH), 133.46 (CH), 129.96 (CH), 129.87 (CH), 129.42 (C), 129.06 (C), 128.65 (CH), 128.47 (CH), 95.57 (CH), 93.47 (CH), 73.26 (CH), 71.17 (CH), 69.98 (CH), 69.90 (CH), 68.92 (CH), 68.68 (CH), 67.23 (CH), 66.72 (CH), 62.75 (CH_2), 20.74 (CH_3); HRMS (MALDI): calcd for $C_{45}H_{43}NO_{18}Na$: 908.2377; found: 908.2357 [M+Na^+].

2-Azido-3-*O*-benzoyl-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranosyl benzoate (67): A mixture of compound **66** (100 mg, 0.34 mmol) and pyridine (0.19 mL, 2.0 mmol) in dichloromethane (2 mL) was cooled to 0 °C under nitrogen. Benzoyl chloride (0.13 mL, 1.1 mmol) was slowly added to the solution, the ice-bath was removed, and the mixture was kept stirring at room temperature for 18 h. Methanol (2 mL) was added to quench the reaction, and the resulting solution was evaporated under reduced pressure. Water (2 mL) was added to the solid residue, the mixture was extracted with ethyl acetate (3 × 3 mL), and the combined organic layers were sequentially washed with aq 1 N HCl, aq sat $NaHCO_3$ and brine. The organic portion was dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography (EtOAc/Hex 1:3) to get the 1,3-dibenzoate **67** (137 mg, 80%) as a white solid. $[\alpha]_D^{29} = -111.0$ (c = 1.0, $CHCl_3$); m.p. 129–130 °C; IR ($CHCl_3$):

$\tilde{\nu}$ = 2880, 2113, 1746, 1724, 1289 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.11–8.08 (m, 4H, Bz-H), 7.64–7.56 (m, 2H, Bz-H), 7.49–7.44 (m, 4H, Bz-H), 7.40–7.37 (m, 2H, Ph-H), 7.31–7.28 (m, 3H, Ph-H), 5.98 (d, J = 8.4 Hz, 1H, H-1), 5.58 (t, J = 9.6 Hz, 1H, H-3), 5.51 (s, 1H, PhCH), 4.42 (dd, J = 15.9, 10.3 Hz, 1H, H-6a), 4.40 (dd, J = 9.6, 8.4 Hz, 1H, H-2), 3.88 (dt, J = 9.6, 1.7 Hz, 1H, H-4), 3.80 (m, 2H, H-5, H-6b); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.17 (C), 164.22 (C), 136.51 (C), 134.07 (CH), 133.44 (CH), 130.09 (CH), 129.90 (CH), 129.24 (C), 129.09 (CH), 128.64 (CH), 128.47 (CH), 128.40 (C), 128.19 (CH), 126.08 (CH), 101.62 (CH), 93.89 (CH), 78.56 (CH), 71.85 (CH), 68.27 (CH_2), 67.26 (CH), 64.18 (CH); HRMS (FAB): calcd for $C_{27}H_{23}N_3O_7$: 502.1615; found: 502.1624 [M+H^+]; elemental analysis calcd (%) for $C_{27}H_{23}N_3O_7$: C 64.67, H 4.62, N 8.38; found: C 64.55, H 4.51, N 8.17.

2-Azido-3-*O*-benzoyl-4-*O*-benzyl-2-deoxy-β-D-glucopyranosyl benzoate (68): A 1 M solution of BH_3/THF complex in THF (1.6 mL, 1.6 mmol) was added at 0 °C under nitrogen to a mixture of **67** (100 mg, 0.20 mmol) in dichloromethane (2 mL). After 10 min, TMSOTf (18 μL, 0.10 mmol) was added to the solution, the ice-bath was removed, and the mixture was kept stirring for 3 h. The reaction was quenched by triethylamine (50 μL) followed by slow addition of methanol at 0 °C, till the evolution of hydrogen gas stopped. The resulting mixture was coevaporated with methanol, and the residue was purified through flash column chromatography (EtOAc/Hex 1:3) to give the 6-alcohol **68** (88.4 mg, 88%) as a white solid. $[\alpha]_D^{30}$ = +46.3 (c = 1.0, $CHCl_3$); m.p. 137–138 °C; IR ($CHCl_3$): $\tilde{\nu}$ = 3372, 2950, 2097, 1720, 1646, 1538, 1259, 1082 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.09–8.04 (m, 4H, Bz-H), 7.62–7.58 (m, 2H, Bz-H), 7.48–7.44 (m, 4H, Bz-H), 7.17–7.12 (m, 5H, Ar-H), 5.87 (d, J = 8.4 Hz, 1H, H-1), 5.49 (dd, J = 10.2, 9.2 Hz, 1H, H-3), 4.59 (s, 2H, CH_2Ph), 3.95–3.91 (m, 2H, H-4, H-6a), 3.85 (dd, J = 9.2, 8.4 Hz, 1H, H-2), 3.70 (m, 1H, H-5), 3.65 (d, J = 8.1 Hz, 1H, H-6b), 1.77 (s, 1H, 6-OH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.01 (C), 133.99 (CH), 133.51 (CH), 130.09 (CH), 129.87 (CH),129.11 (C), 128.63 (CH), 128.56 (CH), 128.41 (CH), 128.21 (CH), 128.05 (CH), 93.61 (CH), 76.25 (CH), 74.80 (CH_2), 74.70 (CH), 63.39 (CH), 61.01 (CH_2).

2-Azido-4-*O*-benzyl-2-deoxy-3,6-di-*O*-benzoyl-D-glucopyranose (69): Benzoyl chloride (54 μL, 0.44 mmol) was slowly added to a solution of **68** (147 mg, 0.29 mmol) in pyridine (1.5 mL) at 0 °C under nitrogen. The ice-bath was removed, and the mixture was kept stirring at room temperature for 1.5 h. Methanol (5 mL) was added to quench the reaction, and the resulting solution was evaporated under reduced pressure. Water (2 mL) was added to the solid residue, and the mixture was extracted with ethyl acetate (3×3 mL). The combined organic layers were sequentially washed with aq 1 N HCl, aq sat $NaHCO_3$, and finally with brine. The organic portion was dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo, and the resulting residue was purified by flash column chromatography (EtOAc/Hex 1:6) to provide the 1,3,6-tribenzoate (158 mg, 89%). $[\alpha]_D^{30}$ = −26.1 (c = 1.0, $CHCl_3$); IR ($CHCl_3$): $\tilde{\nu}$ = 2921, 2106, 1725, 1597, 1494, 1259, 1062 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.07–8.02 (m, 6H, Bz-H), 7.67–7.54 (m, 3H, Bz-H), 7.44–7.38 (m, 6H, Bz-H), 7.06–7.05 (m, 5H, Ar-H), 5.92 (d, J = 8.4 Hz, 1H, H-1), 5.55 (dd, J = 10.1, 8.8 Hz, 1H, H-3), 4.63–4.57 (m, 2H, H-6a, H-6b), 4.57 (d, J = 10.8, 1H, CH_2Ph), 4.52 (d, J = 10.8, 1H, CH_2Ph), 4.02–3.90 (m, 3H, H-2, H-4, H-5); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 66.03 (C), 165.25 (C), 164.25 (C), 136.51 (C), 133.90 (CH), 133.61 (CH), 133.17 (CH), 130.12 (CH), 129.90 (CH), 129.77 (CH), 129.53 (CH), 129.22 (C), 128.61 (CH), 128.56 (CH), 128.41 (CH), 128.26 (CH), 128.14 (CH), 93.56 (CH), 75.39 (CH), 74.86 (CH_2), 74.16 (CH), 63.73 (CH), 62.76 (CH_2); HRMS (FAB): calcd for $C_{36}H_{29}N_3O_8$: 608.2034; found: 608.2053 [M+H^+].

Ammonia gas was passed through a solution of the 1,3,6-tribenzoate (27 mg, 44 μmol) in a mixed solvent (THF/MeOH 7:3, 1.4 mL) at 0 °C for 20 min. The reaction was monitored by TLC till the consumption of starting material (ca. 1.5 h). The solvent was concentrated under reduced pressure, and the residue was purified by flash column chromatography (EtOAc/Hex 1:3) to afford **69** (19.5 mg, 87%, α/β 3:1). Recrystallization of the white solid via vapor diffusion method produced **69β** as colorless crystals. $[\alpha]_D^{29}$ = +46.9 (c = 1.0, $CHCl_3$); IR ($CHCl_3$): $\tilde{\nu}$ = 3435, 2901, 2106, 1720, 1601, 1582, 1263, 1091 cm^{-1}; ^1H NMR (400 MHz,$CDCl_3$): δ = 8.10–8.01 (m, 4H, Bz-H), 7.60–7.56 (m, 2H, Bz-H), 7.49–7.43 (m, 4H, Bz-H), 7.15–7.07 (m, 5H, Ph-H), 5.92 (dd, J = 10.3, 9.0 Hz, 1H, H-3), 5.42 (dd, J = 8.0, 5.0 Hz, 1H, H-1), 4.85–4.36 (m, 4H, 2×CH_2Ph, H-6a, H-6b), 3.85–3.79 (m, 2H, H-4, H-5), 3.55 (dd, J = 10.3, 8.0 Hz, 1H, H-2), 3.41 (d, J = 5.0, 1H, 1-OH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.22 (C), 165.41 (C), 136.61 (C), 133.54 (CH), 133.28 (CH), 129.89 (C), 129.76 (CH), 129.33 (C), 128.58 (CH), 128.45 (CH), 128.24 (CH), 128.12 (CH), 96.35 (CH), 75.72 (CH), 74.88 (CH_2), 74.73 (CH), 73.49 (CH), 65.56 (CH), 62.97 (CH_2); HRMS (FAB): calcd for $C_{27}H_{25}N_3O_7Na$: 526.1593; found: 526.1570 [M+Na^+]; elemental analysis calcd (%) for $C_{27}H_{25}N_3O_7$: C 64.41, H 5.00, N 8.35; found: C 64.24, H 4.91, N 8.00.

1,6-Anhydro-4-*O*-(2-azido-4-*O*-benzyl-2-deoxy-3,6-di-*O*-benzoyl-α-D-glucopyranosyl)-2-*O*-benzoyl-3-*O*-benzyl-β-L-idopyranoside (70): A mixture of **69** (0.47 g, 0.93 mmol) and freshly dried 4 Å molecular sieves (3 g) in dichloromethane (4.7 mL) was stirred at room temperature for 30 min under nitrogen. Anhydrous potassium carbonate (0.20 g, 1.4 mmol) and trichloroacetonitrile (0.93 mL, 9.27 mmol) were sequentially added to the mixture at −78 °C, and the reaction was gradually warmed up to room temperature. After stirring for 2 h, the resulting mixture was filtered through Celite, and the filtrate was washed with water, dried over $MgSO_4$, filtered, and concentrated in vacuo to give the crude trichloroacetimidate derivative (0.51 g, 84%, α/β 1:4 determined by the ^1H NMR spectrum), which was directly used for subsequent reaction without further purification.

A mixture of this crude trichloroacetimidate (374 mg, 0.58 mmol), compound **53** (138 mg, 0.39 mmol), and freshly dried 4 Å molecular sieves (1.5 g) in dichloromethane (5 mL) was stirred at room temperature for 30 min under nitrogen. The reaction flask was cooled to −78 °C, trimethylsilyl trifluoromethanesulfonate (50 μL, 0.30 mmol) was added to the mixture, and the resulting solution was gradually warmed up to room temperature and kept stirring overnight. The reaction was quenched with triethylamine (100 μL), the mixture was filtered through Celite, the filtrate was concentrated in vacuo, and the residue was purified by flash column chromatography (EtOAc/Hex 1:5) to afford **70** (189 mg, 58%) and its corresponding β-isomer (52 mg, 16%). $[\alpha]_D^{30}$ = +74.4 (c = 0.5, $CHCl_3$); m.p. 185–186 °C; IR ($CHCl_3$): $\tilde{\nu}$ = 3245, 2097, 1690, 1612, 1504, 1268, 1106 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.10 (dd, J = 8.5, 1.4 Hz, 2H, Bz-H), 8.05 (dd, J = 8.5, 1.4 Hz, 2H, Bz-H), 8.02 (dd, J = 8.5, 1.3 Hz, 2H, Bz-H), 7.62–7.55 (m, 3H, Ar-H), 7.49–7.42 (m, 6H, Ar-H), 7.22–7.10 (m, 10H, Ar-H), 5.85 (dd, J = 10.8, 9.2 Hz, 1H, H-3′), 5.53 (d, J = 1.7 Hz, 1H, H-1), 5.45 (d, J = 3.8 Hz, 1H, H-1′), 5.06 (dd, J = 8.0, 1.7 Hz, 1H, H-2), 4.79 (d, J = 10.8 Hz, 1H, CH_2Ph), 4.74 (d, J = 10.8 Hz, 1H, CH_2Ph), 4.64–4.50 (m, 5H, 2×CH_2Ph, H-6a, H-6a′, H-6b′), 4.24 (d, J = 7.9 Hz, 1H, H-6b), 4.17 (t, J = 8.0 Hz, 1H, H-3), 4.12–4.09 (m, 2H, H-4, H-5′), 3.81 (dd, J = 7.9, 5.0 Hz, 1H, H-5), 3.76 (t, J = 9.2, 1H, H-4′), 3.37 (dd, J = 10.8, 3.8 Hz, 1H, H-2′); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.14 (C), 165.71 (C), 165.46 (C), 137.70 (C), 136.47 (C), 133.61 (CH), 133.45 (CH), 133.38 (CH), 129.88 (CH), 129.62 (CH), 129.54 (C), 129.31 (C), 129.25 (C), 128.60 (CH), 128.52 (CH), 128.50 (CH), 128.31 (CH), 127.81 (CH), 127.70 (CH), 99.43 (CH), 99.34 (CH), 79.80 (CH), 77.54 (CH), 77.24 (CH), 76.40 (CH), 75.31 (CH_2), 74.90 (CH_2), 74.28 (CH), 72.53 (CH), 69.75 (CH), 65.84 (CH_2), 63.18 (CH_2), 61.42 (CH).

6-*O*-Acetyl-4-*O*-(2-azido-4-*O*-benzyl-2-deoxy-3,6-di-*O*-benzoyl-α-D-glucopyranosyl)-2-*O*-benzoyl-3-*O*-benzyl-L-idopyranosyl acetate (71): Trifluoroacetic acid (0.64 mL) at room temperature under nitrogen was added to a solution of **70** (159 mg, 0.19 mmol) in acetic anhydride (3.2 mL). After stirring for 24 h, the reaction was quenched by aq sat $NaHCO_3$ (10 mL), and the mixture was extracted with EtOAc (3×10 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. Purification of the residue via flash column chromatography (EtOAc/Hex 1:3) yielded the diacetate **71** (160 mg, 89%). $[\alpha]_D^{30}$ = +75.1 (c = 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 8.11–8.03 (m, 13H, Bz-H), 7.62–7.58 (m, 5H, Bz-H), 7.54–7.41 (m, 16H, Bz-H), 7.32–7.24 (m, 3H, Ar-H), 7.17–7.12 (m, 10H, Ar-H), 6.36 (d, J = 3.3 Hz, 1H, H-1β), 6.23 (d, J = 2.8 Hz, 1H, H-1α), 5.80 (dd, J = 10.6 Hz, 9.0 Hz, 1H, H-3′β), 5.75 (dd, J = 10.6, 9.1 Hz, 1H, H-3′α), 5.31 (d, J = 3.7 Hz, 1H, H-1′β), 5.27 (dd, J = 11.1, 3.3 Hz, 1H, H-2β), 5.24 (t, J = 3.5 Hz, 1H, H-2α), 5.01 (d, J = 3.7 Hz, 1H, H-1′α), 4.87–4.83 (m, 3H), 4.63–4.50 (m, 13H), 4.40–4.33 (m, 2H), 4.26(ddd, J = 5.8, 3.6, 2.1 Hz, 1H, H-6′β), 4.21 (ddd, J = 6.4, 4.2, 2.2 Hz, 1H, H-6′α), 4.16 (t, J = 3.9 Hz, 1H, H-3), 3.98 (t, J = 3.1 Hz, 1H, H-4), 3.94(s, 2H), 3.45 (dd, J = 10.7, 3.7 Hz, 1H, H-2′α), 3.38 (dd, J = 10.1, 3.7 Hz, 1H, H-2′β), 2.15 (s, 3H), 2.15 (s, 3H), 2.11 (s, 3H), 2.09 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.76 (C), 169.04 (C), 168.95 (C), 166.12 (C), 165.66 (C), 165.23 (C), 137.22 (C), 136.64 (C), 133.52 (CH), 133.42 (CH), 133.33 (CH),

137.22 (CH), 136.64 (CH), 133.52 (CH), 133.42 (CH), 133.33 (CH), 133.25 (CH), 129.85 (CH), 129.73 (CH), 129.66 (CH),129.28 (C), 129.14 (C), 128.56 (CH), 128.51 (CH), 128.41 (CH), 128.31 (CH), 128.25 (CH), 128.13 (CH), 127.90 (CH), 98.55 (CH), 97.43 (CH), 91.48 (CH), 90.16 (CH), 77.35 (CH), 76.13 (CH), 75.00 (CH_2), 74.93 (CH_2), 74.77 (CH), 73.72 (CH), 73.33 (CH), 73.06 (CH), 72.99 (CH), 72.70 (CH), 70.89 (CH), 70.09 (CH), 68.07 (CH), 63.80 (CH_2), 63.04 (CH_2), 62.92 (CH_2), 61.68 (CH), 61.48 (CH), 21.09 (CH_3), 20.95 (CH_3), 20.79 (CH_3); HRMS (FAB): calcd for $C_{51}H_{49}N_3O_{15}$: 943.3164; found: 943.3149 [M^+].

6-*O*-Acetyl-4-*O*-(2-azido-4-*O*-benzyl-2-deoxy-3,6-di-*O*-benzoyl-α-D-glucopyranosyl)-2-*O*-benzoyl-3-*O*-benzyl-L-idopyranose (72): Compound **71** (0.41 g, 0.43 mmol) was dissolved in dichloromethane (8.2 mL) at room temperature under nitrogen, acetic anhydride (83 μL, 0.88 mmol) was added to the mixture, and the reaction flask was immersed in an ice-bath. A 30% solution of HBr in acetic acid (0.47 mL) was added to the mixture, the ice-bath was removed, and the reaction was kept stirring at room temperature for 0.5 h. The resulting solution was poured into ice-water (8 mL), and the aqueous phase was extracted with dichloromethane (3×10 mL). The combined organic layers were consecutively washed by aq sat $NaHCO_3$ (3×15 mL), and finally with brine. The organic portion was dried over $MgSO_4$, filtered, and concentrated in vacuo, and the residue was purified by flash column chromatography (EtOAc/Hex 1:2) to provide **72** (0.32 g, 82%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.08–7.98 (m, 10H, Bz-H), 7.59–7.52 (m, 4H, Bz-H), 7.45–7.33 (m, 16H, Bz-H), 7.27–7.26 (m, 8H, Ar-H), 7.13–7.07 (m, 10 H, Ar-H), 5.68 (dd, J=19.5, 9.9 Hz, 2H, H-3′α, H-3′β), 5.31 (dd, J=8.1, 2.4 Hz, 1H), 5.24 (dd, J=8.4, 3.0 Hz, 1H), 5.08 (t, J=4.0 Hz, 1H), 5.06 (t, J=2.5 Hz, 1H, H-1α), 4.98 (d, J=3.6 Hz, 1H, H-1β), 4.94 (d, J=3.7 Hz), 4.85–4.70 (m, 4H), 4.62 (dd, J=10.4, 5.4 Hz, 2H), 4.31–4.25 (m, 2H), 4.18–4.14 (m, 3H), 3.92–3.89 (m, 1H), 3.86 (t, J=4.8 Hz, 1H), 3.71 (dt, J=13.0, 3.8 Hz, 2H), 3.65 (s, 1H), 3.40 (t, J=3.4 Hz, 1H), 3.38 (t, J=3.5 Hz, 1H), 2.09 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.08 (C), 170.63 (C), 166.28 (C), 166.03 (C), 164.98 (C), 137.24 (C), 136.61 (C), 133.42 (CH), 133.24 (CH), 133.18 (CH), 132.88 (CH), 129.77 (CH), 129.65 (CH), 129.25 (C), 128.47 (CH), 128.37 (CH), 128.29 (CH), 128.26 (CH), 128.19 (CH), 128.09 (CH), 128.00 (CH), 97.64 (CH), 92.78 (CH), 91.93 (CH), 77.22 (CH), 76.03 (CH), 74.90 (CH_2), 73.81 (CH_2), 73.49 (CH), 73.33 (CH), 73.02 (CH), 72.84 (CH), 71.09 (CH), 70.42 (CH), 70.17 (CH), 66.61 (CH), 64.12 (CH_2), 62.89 (CH_2), 62.60 (CH_2), 61.62 (CH), 20.92 (CH_2), 20.87 (C); HRMS (FAB): calcd for $C_{49}H_{47}N_3O_{14}$: 901.3058; found: 901.3044 [M+H$^+$].

Methyl 6-*O*-acetyl-4-*O*-(2-azido-4-*O*-benzyl-2-deoxy-3,6-di-*O*-benzoyl-α-D-glucopyranosyl)-2-*O*-benzoyl-3-*O*-benzyl-β-L-idopyranoside (73): A mixture of **72** (70 mg, 78 μmol) and freshly dried 4 Å molecular sieves (0.14 g) in dichloromethane (0.7 mL) was stirred at room temperature for 30 min under nitrogen. The reaction flask was cooled to −78°C, anhydrous potassium carbonate (23 mg, 0.17 mmol) and trichloroacetonitrile (83 μL, 0.83 mmol) were sequentially added to the solution, and the whole mixture was gradually warmed up to room temperature. After 8 h, the mixture was filtered through Celite followed by wash with dichloromethane. The filtrate was concentrated in vacuo to afford the crude trichloroacetimidate derivative (65 mg, 80%), which was directly used for the ensuing reaction without further purification.

A mixture of the crude trichloroacetimidate (100 mg, 0.10 mmol), methanol (80 μL, 1.98 mmol), and freshly dried 4 Å molecular sieves (200 mg) in dichloromethane (1 mL) was stirred at room temperature for 30 min under nitrogen. Trimethylsilyl trifluoromethanesulfonate (3.6 μL, 0.02 mmol) was added to the reaction solution at −78°C, the reaction flask was gradually warmed up to room temperature, and the mixture was kept stirring overnight. Triethylamine (8 μL) was added to quench the reaction, the whole mixture was filtered through Celite, the filtrate was concentrated in vacuo, and the residue was purified by flash column chromatography (EtOAc/Hex 1:5) to give **73** (51 mg, 58%) and its corresponding β-isomer (15 mg, 17%). $[\alpha]_D^{32}$=+47.8 (c=1.0, $CHCl_3$); m.p. 117–118°C; IR ($CHCl_3$): $\tilde{\nu}$=3029, 2918, 2108, 1724, 1452, 1268, 1094, 1069 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.05 (d, J=7.6 Hz, 2H, Bz-H), 8.00 (d, J=7.6 Hz, 4H, Bz-H), 7.59–7.54 (m, 2H, Ar-H), 7.44–7.33 (m, 8H, Ar-H), 7.29–7.19 (m, 5H, A-H), 7.11–7.09 (m, 4H, Ar-H), 5.71 (t, J=8.3 Hz, 1H, H-3′), 5.14 (t, J=2.8 Hz, 1H, H-2), 4.89 (d, J=3.7 Hz, 1H, H-1′), 4.84 (d, J=2.8 Hz, 1H, H-1), 4.80 (d, J=11.6 Hz, 1H, CH_2Ph), 4.67 (d, J=11.6 Hz, 1H, CH_2Ph), 4.58–4.47 (m, 5H, 2×CH_2Ph, H-6a, H-6b, H-6a′), 4.41–4.37 (m, 1H, H-5), 4.32 (dd, J=11.4, 4.4 Hz, 1 H, H-6b′), 4.17–4.15 (m, 1H, H-5′), 4.00 (dd, J=4.2, 2.8 Hz, 1H, H-3), 3.89 (t, J=4.2 Hz, 1H, H-4), 3.71 (t, J=8.3 Hz, 1H, H-4′), 3.42 (s, 3H, CH_3), 3.35 (dd, J=8.3, 3.7 Hz, 1H, H-2′), 2.06 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.51 (C), 166.05 (C), 165.79 (C), 165.04 (C), 137.37 (C), 136.62 (C), 133.40 (CH), 133.21 (CH), 133.05 (CH), 129.78 (CH), 129.66 (CH), 129.44 (C), 129.31 (C), 129.16 (CH), 128.48 (CH), 128.37 (CH), 128.34 (CH), 128.28 (CH), 128.29 (CH), 127.85 (CH), 126.31 (CH), 99.32 (CH), 97.43 (CH), 76.09 (CH), 74.88 (CH_2), 73.74 (CH), 73.38 (CH), 73.02 (CH), 72.90 (CH_2), 70.21 (CH), 70.04 (CH), 66.58 (CH), 62.99 (CH_2), 62.71 (CH_2), 61.65 (CH), 55.70 (CH_3), 20.80 (CH_3); HRMS (FAB): calcd for $C_{50}H_{50}N_3O_{14}$: 916.3294; found: 916.3311 [M+H$^+$].

Methyl 4-*O*-(2-azido-4-*O*-benzyl-2-deoxy-3,6-di-*O*-benzoyl-α-D-glucopyranosyl)-2-*O*-benzoyl-3-*O*-benzyl-β-L-idopyranoside (74): Compound **73** (171 mg, 0.19 mmol) was dissolved in a 0.5% solution of HCl in methanol (3.5 mL) at room temperature under nitrogen. After stirring for 5 h, the reaction was neutralized by silver carbonate, and the mixture was filtered through Celite. The filtrate was concentrated in vacuo, and the residue was recrystallized in ethanol to provide **74** (139 mg, 85%) as a white solid. $[\alpha]_D^{32}$=+51.4 (c=1.0, $CHCl_3$); m.p. 113–114°C; IR ($CHCl_3$): $\tilde{\nu}$= 3400, 3019, 2921, 2108, 1722, 1601, 1316 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.06 (dd, J=8.3, 1.7 Hz, 2H, Bz-H), 8.02–7.99 (m, 4H, Bz-H), 7.59–7.54 (m, 2H, Ar-H), 7.46–7.41 (m, 5H, Ar-H), 7.39–7.32 (m, 3 H, Ar-H), 7.30–7.19 (m, 4H, Ar-H), 7.13–7.07 (m, 5H, Ar-H), 5.71 (dd, J=10.6, 9.4 Hz, 1H, H-3′), 5.15 (dd, J=3.5, 2.4 Hz, 1H, H-2), 4.88 (d, J=2.4 Hz, 1H, H-1), 4.85 (d, J=3.8 Hz, 1H, H-1′), 4.80 (d, J=11.6 Hz, 1 H, CH_2Ph), 4.67 (d, J=11.6 Hz, 1H, CH_2Ph), 4.58–4.46 (m, 4H, 2× CH_2Ph, 2×H-6′), 4.30–4.26 (m, 1H, H-4), 4.16 (ddd, J=9.4, 4.8, 2.4 Hz, 1 H, H-5′), 4.06–4.00 (m, 2H, H-3, H-6a), 3.89 (t, J=3.7 Hz, 1H, H-6b), 3.87–3.82 (m, 1H, H-5), 3.68 (t, J=9.4 Hz, 1H, H-4′), 3.43 (s, 3H, CH_3), 3.36 (dd, J=10.6, 3.8 Hz, 1H, H-2′), 1.99 (dd, J=7.8, 4.3 Hz, 1H, 6-OH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.14 (C), 165.87 (C), 165.10 (C), 137.47 (C), 136.60 (C), 133.43 (CH), 133.25 (CH), 133.15 (CH), 133.02 (CH), 129.78 (CH), 129.64 (CH), 129.50 (C), 129.30 (C), 128.49 (CH), 128.40 (CH), 128.32 (CH), 128.10 (CH), 127.87 (CH), 127.81 (CH), 99.58 (CH), 97.00 (CH), 76.23 (CH), 74.88 (CH_2), 73.45 (CH), 73.07 (CH), 72.85 (CH), 72.62 (CH_2), 70.25 (CH), 69.96 (CH), 68.32 (CH), 63.17 (CH_2), 61.93 (CH_2), 61.69 (CH), 55.66 (CH_3).

Methyl 4-*O*-(2-azido-4-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-3-*O*-benzyl-β-L-idopyranosiduronic acid (75): Jones reagent was slowly added to a mixture of **74** (361 mg, 0.41 mmol) and Celite (110 mg) in acetone (4 mL) at 0°C. When the solution turned orange color, the reaction was re-titrated by isopropanol. The whole mixture was filtered through Celite, and the filtrate evaporated under reduced pressure. Water (8 mL) was added to the syrup, the mixture was extracted with dichloromethane (3×8 mL), and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography (MeOH/$CHCl_3$ 1:10) to afford the corresponding carboxylic acid (315 mg). $[\alpha]_D^{31}$=+35.2 (c=1.0, DMSO); IR ($CHCl_3$): $\tilde{\nu}$=3400, 2931, 2104, 1720, 1623, 1268 cm^{-1}; ^{13}C NMR (100 MHz, $CDCl_3$): δ=166.07 (C), 165.51 (C), 138.64 (C), 137.71 (C), 134.22 (CH), 133.88 (CH), 133.72 (CH), 131.68 (CH), 131.04 (CH), 129.89 (CH), 129.82 (CH), 129.49 (CH), 129.31 (CH), 129.05 (CH), 128.56 (CH), 128.48 (CH), 128.33 (CH), 128.18 (CH), 127.76 (CH), 98.91 (CH), 97.99 (CH), 76.20 (CH), 74.18 (CH_2), 73.77 (CH), 73.20 (CH_2), 68.98 (CH), 63.60 (CH_2), 61.75 (CH), 55.68 (CH_3).

The above carboxylic acid (315 mg, 0.35 mmol) was dissolved in methanol (3.4 mL) at room temperature under nitrogen, sodium methoxide (41 mg, 0.93 mmol) was added to the reaction solution, and the mixture was kept stirring overnight. The reaction was acidified by Amberlite IR-120 acidic resin to pH 2, then the whole mixture was filtered through paper. The filtrate was concentrated in vacuo, and the residue was purified by flash column chromatography (MeOH/$CHCl_3$ 1:10) to yield **75** (133 mg, 56% in two steps) as a colorless oil. $[\alpha]_D^{31}$=+6.8 (c=1.0, MeOH); ^{1}H NMR (400 MHz, CD_3OD): δ = 7.40–7.26 (m, 10H, Ar-H), 5.13 (s, 1H, H-1), 4.99 (d, J=3.8 Hz, 1H, H-1′), 4.93 (d, J=10.9 Hz, 1H, CH_2Ph), 4.72–4.58 (m, 4H, 3×CH_2Ph, H-5), 4.24 (s, 1H, H-4), 4.00 (t, J=9.8 Hz, 1H, H-3′), 3.89–3.86 (m, 2H, H-5′, H-6a′), 3.81 (s, 1H, H-3), 3.73–3.69 (m, 2H, H-2, H-6b′), 3.52 (dd, J=9.8, 3.8 Hz, 1H, H-2′), 3.40 (s, 3H, CH_3), 3.40–3.32 (m, 1H, H-4′); ^{13}C NMR (100 MHz, MeOH): δ=

176.64 (C), 139.99 (C), 139.55 (C), 129.69 (CH), 129.53 (CH), 129.41 (CH), 129.34 (CH), 129.15 (CH), 128.95 (CH), 128.86 (CH), 103.64 (CH), 97.03 (CH), 80.10 (CH), 76.19 (CH_2), 74.68 (CH), 74.57 (CH), 74.35 (CH), 73.13 (CH), 72.79 (CH_2), 69.84 (CH), 67.90 (CH), 66.31 (CH), 62.83 (CH_2), 56.31 (CH_3); HRMS (MALDI): calcd for $C_{27}H_{33}N_3O_{11}Na$: 598.2013; found: 598.2015 [$M+Na^+$].

Methyl 4-*O*-(2-azido-4-*O*-benzyl-2-deoxy-3,6-di-*O*-sulfonato-α-D-glucopyranosyl)-3-*O*-benzyl-2-*O*-sulfonato-β-L-idopyranosiduronic acid (76): Sulfur trioxide-triethylamine complex (470 mg, 2.60 mmol) was added at room temperature under nitrogen to a solution of **75** (33.2 mg, 56.3 mmol) in DMF (0.66 mL). The mixture was gradually warmed up to 50 °C, then kept stirring overnight. After cooling to room temperature, a solution of sodium bicarbonate (874 mg) in water (10.4 mL) was added to the reaction solution, and the mixture was stirred for another 16 h. The solvent was removed in vacuo, and the residue was dissolved in a mixed solvent (CH_2Cl_2/MeOH 1:1, 2 mL). The mixture was filtered through paper, and the filtrate was concentrated in vacuo. The residue was again dissolved in a mixed solvent (CH_2Cl_2/MeOH 4:1, 1 mL), the mixture was filtered, and the filtrate was concentrated in vacuo to furnish the crude **76** (46.8 mg) as a white powder. MS-ESI (negative mode): calcd for $C_{27}H_{32}N_3O_{20}S_3$: 814.07, found 813.94 $[M-H]^{-1}$.

Methyl 4-*O*-(2-deoxy-3,6-di-*O*-sulfonato-2-*N*-sulfonato-α-D-glucopyranosyl)-2-*O*-sulfonato-β-L-idopyranosiduronate, pentasodium salt (77): Ammonia gas was condensed in a reaction flask containing a mixture of sodium (60.0 mg, 2.61 mmol) in tetrahydrofuran (3 mL), and a solution of the crude **76** (46.8 mg, 57.7 μmol) in a mixed solvent (EtOH/THF 1:1, 3 mL) was added. When the deep blue color was disappeared, the mixture was gradually warmed up to room temperature followed by concentration in vacuo.

The above residue was dissolved in water (5 mL) at room temperature, and aq 2 N NaOH was slowly added to the solution till pH 9.5. Sulfur trioxide/pyridine complex (29.3 mg, 18.4 μmol) was added to the mixture, and the pH value was maintained at 9.5 by addition of aq 2 N NaOH. After 1 h, the same amount of sulfur trioxide/pyridine complex (29.3 mg, 18.4 μmol) was added to the reaction solution, and the mixture was kept stirring for another 5 h. The mixture was concentrated in vacuo, and the residue was purified by column chromatography on Sephadex G-25 (0.2 N aq NaCl). Desalting through a Sephadex G-25 column eluted with water gave compound **77** (14.6 mg, 37% in three steps). MS-ESI (negative mode): calcd for $C_{13}H_{23}NO_{23}S_4$: 686.93; found: 686.76 $[M-2H]^{2-}$.

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