Glycosylation of Branched Amino and Nitro Sugars. 2. Synthesis of the Cororubicin Trisaccharide

Lincoln Noecker, Franco Duarte, Scott A. Bolton, Wayne G. McMahon, Maria T. Diaz, and Robert M. Giuliano*

Department of Chemistry, Villanova University, Villanova, Pennsylvania 19085

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The synthesis of the nitro-sugar-containing trisaccharide found in the antibiotic cororubicin is described. This trisaccharide contains the nitro sugar L-decilonitrose which is attached to two digitoxose residues (a dideoxy sugar) by β-1,4 and α-1,4 linkages. The target trisaccharide synthesized was methyl 2,6-dideoxy-α-L-*lyxo*-hexopyranosyl-(1→4)-2,3,6-trideoxy-3-*C*-methyl-3-nitro-β-L-*ribo*-hexopyranosyl-(1→4)-2,6-dideoxy-α-L-*lyxo*-hexopyranoside. The principle features of the synthesis are the use of an *O*-benzylhydroxylamino sugar as the precursor to the nitro sugar decilonitrose and as both the acceptor and donor in glycosyations, a β-selective glycosylation by means of a thioglycoside donor, and novel functional group transformations carried out on the assembled trisaccharide. These include oxidative cleavage of the *O*-benzylhydroxylamino group to nitro, carried out with dimethyldioxirane in one step. This transformation proved critical in completing the synthesis, which is the first reported of one of the decilonitrose-containing trisaccharides found in antibiotics.

During the process of screening for antitumor antibiotics which generated active oxygen species in tumor cells, Seto and co-workers isolated cororubicin, a new anthracycline antibiotic, from *Micromonospora* sp. JY16.[1] Cororubicin was shown to produce superoxide radicals in N18-RE-105 neuronal hybridoma cells and was cytotoxic against KB human epidermoid cells. The aglycon of cororubicin resembles that found in the anthracycline antibiotics arugomycin,[2] avidinorubicin,[3] decilorubicin,[4] nogalamycin,[5] the respinomycins,[6] and viriplanin.[7] The novel benzoxocin ring system contains an amino sugar attached to an aromatic ring by two glycosidic linkages, one of them a *C*-glycoside. Glycosylation of the aglycon varies widely among these anthracycline antibiotics. Cororubicin contains a trisaccharide attached to the 4′-position in which the nitro sugar decilonitrose[8] is attached to two digitoxose residues by β-1,4 and α-1,4 linkages (Figure 1). Oligosaccharides that contain nitro sugars are also reported as components of arugomycin, decilorubicin, and respinomycin D, while branched amino and hydroxylamino sugars are reported in avidinorubicin, respinomycins A1 and A2, and viriplanin A. The nitrogen-containing sugar found in viriplanin A was initially thought to be the nitro sugar decilonitrose; however, its structure has been reassigned as the corresponding hydroxylamino sugar. The hydroxylamino sugar in viriplanin A undergoes photooxidation to decilonitrose in the formation of viriplanin D. Another nitro sugar, rubranitrose,[9] found in the antibiotic rubradirin, has also been shown to be formed oxidatively, from a methyl-branched nitroso sugar residue.[10]

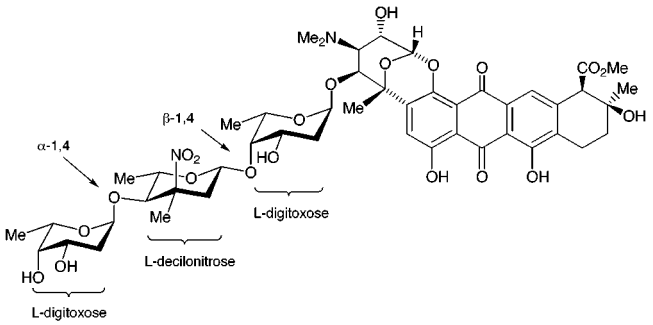

Figure 1. Structure of cororubicin.

Structure−activity studies across diverse classes of antibiotics have revealed strong effects of glycosylation on antibiotic and antitumor activity. In certain cases, synthetic modification of carbohydrates has provided a method for the development of drug analogues, as demonstrated for daunomycin, adriamycin, and other members of the anthracycline class.[11,12] In the case of the

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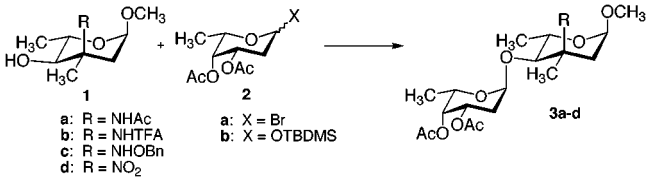
aureolic acid antibiotic chromomycin A_3, the trisaccharide stabilizes the dimeric drug−metal complex which binds to DNA.[12] A striking example of the effect of carbohydrates on biological activity of antibiotics occurs in rubradirin, a nitro-sugar-containing antibiotic. The parent antibiotic possesses a different mechanism of action than the aglycon, which lacks only the nitro sugar residue.[13] The antibiotic respinomycin D, which contains the nitro sugar decilonitrose instead of the amino sugar avidinosamine in respinomycin A2, is highly cytotoxic against leukemia K-562 cells while respinomycin A2 is not.[6] The recent isolation of nitroso and hydroxylamino sugars raises questions about the presence of nitro sugars in the antibiotics in which they were originally reported, and creates the need not only for confirmation of the antibiotic structures, but also for clarification of the influence of these unusual nitrogen-containing sugars on the biological activities of the antibiotics in which they occur.

There have been no reported syntheses of the cororubicin trisaccharide or of the related trisaccharides found in arugomycin and decilorubicin. Synthesis of the nitro sugar decilonitrose has been successfully carried out by several approaches, most of which are lengthy and produce mixtures of stereoisomers.[14] The synthesis of oligosaccharides that contain branched nitro or amino sugars has been limited to very few examples, not only by the difficult access to decilonitrose precursors, but also by the well-known problems encountered in the synthesis of oligosaccharides which contain 2-deoxy-β-glycosidic linkages, such as that found in cororubicin. The synthesis of oligosaccharides containing evernitrose, a naturally occurring nitro sugar found in the everninomicin antibiotics, has been described.[15] The first glycosylations involving nitro sugars were reported by Baer,[16] in which nitro hexopyranosides were glycosylated by the Koenigs−Knorr method. In a recent paper from our laboratory, we described the first synthesis of α-linked disaccharides containing the nitro sugar decilonitrose, in which derivatives (**1**) of the branched amino sugar methyl 3-amino-2,3,6-trideoxy-3-*C*-methyl-α-L-*ribo*-hexopyranoside and its 3-nitro analogue (decilonitrose) were coupled with glycosyl donors (**2**) of 3,4-di-*O*-acetyl-2,6-dideoxy-L-fucopyranose to give α-linked disaccharides.[17] Stereoselective glycosylations were developed using the fucosyl bromide, activated with silver triflate, and the fucosyl oxysilane, activated with trimethylsilyl triflate (Scheme 1).

In our analysis of the cororubicin trisaccharide problem, we considered that the most difficult problem would be the construction of the β-glycosidic linkage at C-1 of a protected branched amino sugar (**1a**−**c**) or nitro sugar (**1d**), and that this coupling would likely have to be carried out before attachment of the α-linked residue. This approach requires that any methods developed for the α-glycosylation of **1** at the C-4 hydroxyl group will

Scheme 1



apply to suitably protected β-disaccharides. In this paper, we describe the successful application of this strategy, which has resulted in the first synthesis of the cororubicin trisaccharide. Key elements of the synthesis are the use of an *O*-benzylhydroxylamino sugar as a precursor to the nitro sugar decilonitrose and as the acceptor and donor in the two glycosylation steps, β-selective glycosylation by means of a thioglycoside donor, and functional group transformations carried out on the assembled trisaccharide. These include an oxidative cleavage of the *O*-benzylhydroxylamino group to give a nitro sugar, and an oxidative debenzylation, both carried out in a single step with dimethyldioxirane.

A challenging problem in the synthesis of the cororubicin trisaccharide and related oligosaccharides is the development of glycosyl donors for the construction of the 2-deoxy-β-glycosidic linkage to the nitro sugar residue. The synthesis of 2-deoxy-β-glycosidic linkages has been addressed by several imaginative approaches, using a wide variety of glycosyl donors.[18] Some of the first solutions to this problem involved the use of 1,2-*trans*-dibromides in which the 2-bromo substituent[19] directs glycosylation from the opposite face. The use of sulfur,[20] selenium, or other groups[21] at the 2-position, which also function as temporary directing groups during the glycoside bond-forming step, has also been described. Glycosyl bromides lacking the substituent at C-2 have been shown to form β-glycosides stereoselectively in the presence of silver zeolite as the promoter.[22] Glycosyl fluorides can be activated with dicyclopentadienylzirconium dichloride−silver perchlorate to give β-glycosides selectively;[23] however, the method was not applied to 2-deoxy fluorides. Arylbis(arylthio)sulfonium salts undergo electrophilic addition to glycals in the presence of alcohols to give 2-arylthio-β-glycosides.[24] β-Selective glycosylations have recently been developed using glycosyl diethyl phosphites[25] and bicyclic glycosyl donors prepared by cycloaddition of 3-thiono-2,4-pentanedione to glycals to give bicyclic vinyl glycosides.[26] The latter two approaches as

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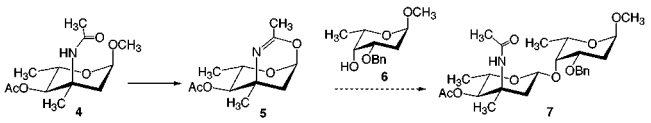
Scheme 2



well as the use of 1,2-*trans*-dibromides have been applied to the synthesis of oligosaccharides found in the aureolic acid antibiotics. Roush and co-workers have recently described a promising approach to the 2-deoxy-β-glycoside problem based on the use of 2-iodo glycosyl acetates.[27] For the synthesis of the cororubicin trisaccharide, we required a glyscosyl donor that would be accessible directly from a stable glycoside, on which the early steps necessary for the introduction of the C-3 functionality in decilonitrose could be carried out. Accessibility to the donors utilized in some of the aforementioned methods was one concern. The synthesis of the nitro sugars is already lengthy, and additional steps required to obtain the necessary anomeric substituent or glycal would be problematic in some cases. The stability of the donors was also questionable in certain cases, for example, 2-deoxy glycosyl halides, as evidenced by our previous studies of the glycosylation of digitoxose.[28]

Our initial approach was based on a bridged bicyclic donor, dihydrooxazine **5**. Coupling of **5** would be expected to proceed with high β-selectivity because of participation of the remote substutent at C-3 (Scheme 2). Since most methyl-branched sugars contain an amino or hydroxyl group in this position, this strategy might constitute a general β-glycosylation method for several members of this class of carbohydrates. Conceptually similar to the approach taken by Wiesner in the synthesis of the cardiac glycoside digitoxin,[29] it has the advantage that the donor is readily accessible from a stable carbohydrate derivative, in this case a methyl glycoside. During the course of our previous studies, an investigation by Binkley and Koholic concluded that the ability of 1,3-participation to control the stereochemistry of glycosidic bond formation appeared not to be significant for glycosyl chlorides and thioglycoside donors which were substituted with acyloxy groups at the C-3 position.[30] However, a successful application of a carbohydrate dihydrooxazine in glycoside synthesis was reported by Nicolaou in the synthesis of amphotericin B.[31] In the synthesis of oligosaccharides found in vancomycin, Danishefsky and co-workers obtained a 2-iododihydrooxazine similar in structure to **5**, but chose an alternative glycosylation method.[32]

Intrigued by these results, we decided to investigate the synthesis of **5** from the diacetyl derivative **4**, which was readily available in our laboratory from the synthesis of decilonitrose.[33] Treatment of **4** with HCl in acetic anhydride, conditions which were expected to produce a glycosyl chloride, led directly to the crystalline dihydrooxazine **5** in quantitative yield. Processing of the reaction proved to be important, as quenching with aqueous sodium bicarbonate solution produced rearranged products. The facile preparation of **5** prompted us to attempt glycosylation reactions with this novel donor, under a variety of conditions. Many attempts were made to couple **5** with the dideoxyfucose derivative **6**,[34] and with other acceptors. Catalysts which were attempted included camphorsulfonic acid, PPTS, trimethylsilyl triflate, copper triflate, mercuric nitrate, and ferric chloride. Alkylation of the nitrogen with benzyl chloride was also attempted, as this would give a potentially more reactive donor. None of these methods resulted in any evidence of disaccharide formation; unreacted **5** was recovered or decomposition was observed, depending on the catalyst used. Conversion of **6** to its tributyltin ether, in an effort to increase its reactivity, was carried out as described by Thiem,[35] but again, disaccharide formation was not observed. Potential acceptors in which the C-4 hydroxyl group is equatorially disposed and acceptors which contained primary hydroxyl groups also failed to undergo glycosylation with **5**. Activation of **5** by prior reduction of the C−N double bond was considered, but owing to difficulties with this system, our attention turned to the development of other glycosyl donors for decilonitrose and corresponding branched amino sugars.

Our success with the preparation of the α-linked disaccharides with branched amino and nitro sugar acceptors (Scheme 1) led us to consider using donors derived from monosaccharides of general type **1** for the synthesis of the 2-deoxy-β-glycosidic linkage. In the absence of neighboring-group participation, donors derived from **1** might still be expected to give higher amounts of β-glycoside because the α-glycoside is less favorable due to steric requirements of the C-3 substuent. We chose to prepare thioglycosides because of their stability and because many methods are now available for activating them.[36] Also, access to other donors such as glycals and glycosyl fluorides from thioglycosides expands their versatility. The use of thioglycosides as donors for decilonitrose or its precursor amino sugar was particularly attractive in the context of the trisaccharide problem for another reason. An efficient synthesis of decilonitrose based on the alkylation of *O*-benzyl oxime ethers had been developed by Scharf and co-workers,[37] and their route could be modified to allow for introduction of the thiophenyl group at the anomeric carbon at an early stage. Outlined in Scheme 3, this synthesis of the key thioglycosides **14** and **15** provided access to substrates for glycosylation reactions that could be activated for the synthesis of disaccharides, and easily deblocked at the C-4 hydroxyl group for subsequent assembly of the trisaccharide.

Deacylation of 3,4-di-*O*-acetyl-L-rhamnal **8** followed by silver carbonate-on-Celite oxidation[38] gave enone **10** in higher yields than that obtained with manganese dioxide[39] or pyridinium dichromate,[40] two methods which had

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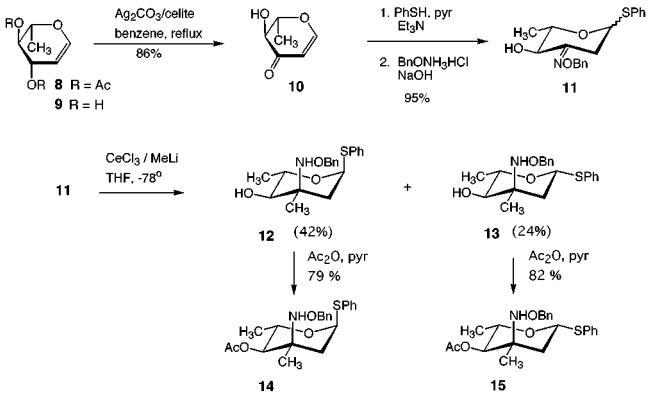
Scheme 3

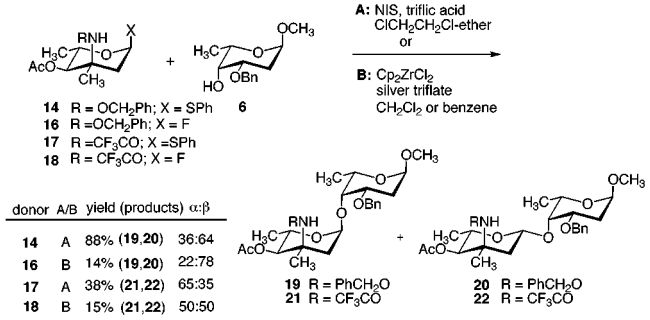


been reported previously. Conversion of **10** to *O*-benzyl oxime **11** was carried out by Michael addition of benzenethiol[41] followed by treatment with *O*-benzylhydroxylamine.[37] The thioglycosides were obtained as mixtures of anomers which were not separated. Scharf and co-workers had shown that methyl carbohydrate *O*-benzyl oxime ethers undergo alkylation with methylcerium to give branched-chain sugars.[37] Methylcerium addition to the oxime ether **11** took place stereoselectively to give branched sugars **12** and **13** in a combined yield of 66%, accompanied by a small amount (3%) of an elimination product. The diastereomeric addition product which would have resulted from addition of methylcerium to the α-face of **11** was not detected. Separation and acetylation of the C-4 hydroxyl group in **12** and **13** provided fully protected glycosyl donors **14** and **15** for synthesis of the *β*-1,4-disaccharide. Treatment of either thioglycoside **14** or **15** with DAST[42] gave glycosyl fluoride **16**, and **18** could similarly be prepared from **17**. Another advantage to the synthesis outlined in Scheme 3 is that methylcerium addition can be carried out without protection of the C-4 hydroxyl group in **12**, allowing ready access to an acceptor (**12** or **13**) for the construction of α-1,4 glycosides.

Our previous study of α-disaccharide synthesis using branched amino sugar derivatives revealed a dependence of stereoselectivity on the nitrogen protecting group; thus, it was desirable to have another derivative of general structure **1** for the glycosylation. Acetamido, trifluoroacetamido, and carbobenzyloxy derivatives of **1** had been prepared from the amino alcohol in our previous study.[17] The *N*-trifluoroacetyl derivative **1b** was chosen for this study because of the ease of protecting group manipulation. Acylation of **1b**, followed by treatment with TMS−SPh/TMSOTf, gave a fully protected thioglycoside, **17**, for investigation of the *β*-disaccharide synthesis.

Results of the disaccharide synthesis with amino sugar thioglycosides as donors are shown in Scheme 4. Coupling of the thioglycoside **14** with **6** using NIS/triflic acid[43] gave the best yields of *β*-disaccharide. While it has become

Scheme 4



standard practice to include molecular sieves in glycosylation reactions, significantly lower yields of disaccharide were obtained when couplings of **14** were carried out in the presence of sieves. Lower temperature (−50 °C) also resulted in lower yields of disaccharide. Lower selectivity for the *β*-disaccharide was observed when the trifluoroacetamido derivative **17** was used as the donor. The glycosyl fluorides **16** and **18** gave poor yields of disaccharide (<20%) in the presence of $CpZrCl_2$ and silver perchlorate,[23] conditions that have been successful in *β*-glycosylations in other systems. Anomeric thioglycosides **14** and **15** were used separately and as a mixture in coupling reactions with **6**. The anomeric configuration of the starting thioglycoside was found to have no effect on the yield or stereoselectivity of the glycosylation.

With *β*-disaccharide **20** in hand, we were able to address the question of whether the methods developed for glycosylation of **1** in our previous study would be applicable for the construction of the corresponding α-linkage in the trisaccharide. Fucosyl bromide **2a** had given the best overall results in terms of yield and selectivity in glycosylation reactions with derivatives of **1**, so it was decided to attempt coupling of the bromide to disaccharide **23**. Deacylation of *β*-disaccharide **20** and coupling of acceptor **23** with the fucosyl bromide **2a** gave the fully protected trisaccharide in high yield and stereoselectivity (Scheme 5). As was observed in the α-disaccharide, glycosylation of the C-4 hydroxyl group in the branched hydroxylamino residue of **23** with **2a** was completely stereoselective for the α-anomer.

Completion of the synthesis required deprotection of the trisaccharide **24** and oxidation of the amino group to nitro. These transformations proved to be challenging in that the two benzyl groups were removed only very slowly by hydrogenolysis. In an attempt to cleave the *O*-benzylhydroxylamino function oxidatively, it was discovered that treatment of **24** with dimethyldioxirane resulted in debenzylation of *both* the *O*-benzylhydroxylamino group and the hydroxyl group, as well as oxidation of the amine to nitro, to give trisaccharide **26** in 83% yield. Debenzylation of the hydroxylamino group in **24** followed by oxidation to nitro presumably occurs via hydroxylamino and nitroso intermediates; however, these species were not isolated from the reaction. To our knowledge, oxidative deprotection of an *O*-benzylhydroxylamino group with DMDO has not been reported. In a synthesis of evernitrose, Nicolaou and co-workers generated the nitro group from an *O*-benzylhydroxylamino precursor by ozonolysis.[44] There are other examples of oxidative N−O bond cleavage reactions described in the literature. In

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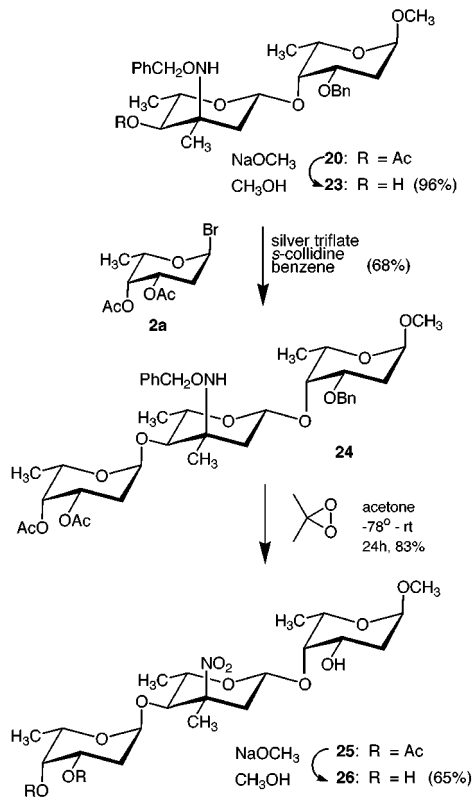
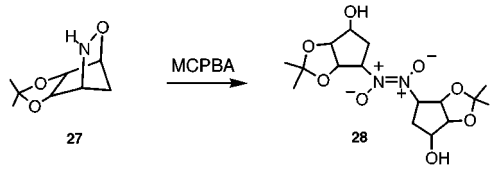
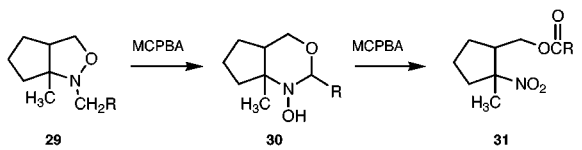
Scheme 5



studies of the oxidative transformations of bicyclo[2.2.1]-oxazine **27** by Yan and co-workers,[45] N−O bond cleavage and oxidation of the amino group occurred in the presence of a slight excess of MCPBA to give a dimeric bisnitroso compound, **28**.



In a study of oxidations of isoxazolines with peroxy acids, LeBel and co-workers[46] observed that treatment of **29** with stoichiometric MCPBA gave *N*-hydroxy-1,3-tetrahydrooxazines **30** by way of *N*-oxide and nitroso intermediates, and that further oxidation of **30** resulted in the formation of nitroso products and their dimers. Oxidation of **30** with excess MCPBA gave *nitro* ester **31**.



Dimerization of the intermediate nitroso compound formed by oxidation of **30** is hindered by the α-methyl group, so that further oxidation to nitro takes place. Similarly, dimerization of an intermediate nitroso compound derived from trisaccharide **24** would also be hindered by the branching methyl group, so further oxidation to nitro occurs readily. Dimeric nitroso compounds have been reported in the oxidation of primary amines with DMDO by Crandall,[47] while Murray described the preparation of nitro adamantane from the amine by DMDO oxidation.[48] Danishefsky and co-workers[49] have described the oxidation of several amino sugars to their hydroxylamino derivatives with DMDO; however, the substrates lacked the branching methyl group found in **24**. In a recent study of the oxidation of 2-amino sugars with MCPBA, the corresponding nitro sugars were obtained.[50] The oxidative deprotection of *O*-benzylhydroxylamines with DMDO, which we demonstrated in **24**, will be useful in approaches to other nitro sugars such as kijanose,[51] and also in the synthesis of branched amino sugars, as it complements the known reductive debenzylation.[37]

Oxidative cleavage of benzyl ethers with DMDO has been reported;[52] however, this transformation was unexpected in the reaction of **24** with DMDO. In an attempted application of this debenzylation to α-disaccharide **19**, a mixture of products was obtained in which the nitro disaccharide was present, but the reaction was not as clean as that observed for **24**, in that only partial *O*-debenzylation occurred. Zemplen deacylation[53] of **25** gave the fully deprotected cororubicin trisaccharide **26** in 65% yield, making the approach described in this paper the first successful synthesis of one of the trisaccharides which contain the nitro sugar decilonitrose. While the stereoselectivity of β-glycosylations in 2-deoxy sugars remains an issue, the methodology developed in the synthesis of **26** should be applicable to other problems of interest which involve amino- and nitro-sugar-containing antibiotics.

Experimental Section

General Methods. ^{1}H and ^{13}C NMR spectra were recorded on a Varian XL200 spectrometer at 200.06 and 50.3 MHz, respectively, in deuteriochloroform solution. Proton chemical shifts are relative to tetramethylsilane (0.00 ppm), and carbon chemical shifts are relative to deuteriochloroform (76.91 ppm). High-resolution mass spectra were measured at the University of Pennsylvania under electrospray conditions. Flash chromatography[54] was performed on Merck silica gel 60 using mixtures of ethyl acetate and hexane as indicated. Visualization of TLC plates was carried out with ceric sulfate−ammonium molybdate in 2 M sulfuric acid. Anhydrous DMF and THF were purchased as such from Aldrich Chemical Co. Dry benzene was purchased from Aldrich. Methanol was dried by distillation from magnesium. Dry dichloromethane was purchased from Aldrich and dried further by passing through a column of basic alumina (Woelm activity 1). Molecular sieves were dried overnight under vacuum at 130 °C.

2-Methyl-5,6-dihydro-(4-*O*-acetyl-1,2,3,6-tetradeoxy-3-methyl-α-L-*ribo*-hexopyranoso)[3,2,1-de]-4*H*-1,3-oxazine (5). Dry HCl gas was bubbled into a stirred solution of diacetate **4** (95 mg, 0.39 mmol) in distilled acetic anhydride (7.3 mL) at 0 °C for 10 min. The reaction mixture was then

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stirred at room temperature for 24 h, and concentrated to give a solid which was crystallized from ethyl acetate−hexanes to give 88 mg (quantitative) of **5** as a white solid: mp 182−183 °C; ^{1}H NMR (200 MHz) δ 5.84 (s, 1H), 4.83 (d, 1H), 3.58 (dq, 1H), 2.75 (s, 3H), 2.29 (s, 3H), 2.25−1.85 (m, 2H), 1.63 (s, 3H), 1.27 (d, 3H); HRMS calcd for $C_{11}H_{17}NO_4$ $(M + H)^+$ 228.1236, found 228.1230.

***O*-Benzyl Phenyl-2,6-dideoxy-1-thio-α,*β*-*erythro*-hexopyranosid-3-ulose Oxime (11).** To enone **10** (0.128 g, 1.0 mmol) in 0.12 mL of pyridine containing triethylamine (prepared by adding 3 drops of triethylamine to 5 mL of pyridine) was added thiophenol (0.11 mL, 1.1 mmol) at room temperature. Starting material was consumed after 3 h (TLC, R_f (ethyl acetate−hexanes, 2:3 v/v) 0.68, 0.63). The solution was diluted with methanol (0.5 mL). *O*-Benzylhydroxylamine hydrochloride (0.17 g, 1.1 mmol) was added, and the mixture was stirred overnight for 15 h. After removal of methanol in vacuo, the crude mixture was added to a Florisil column and eluted with ethyl acetate−hexanes (1:9 v/v) to give waxy white solid **11** (0.33 g, 95%) as a mixture of anomers (~60:40, α/*β*) which were not separated: R_f 0.63−0.68 (ethyl acetate−hexanes, 2:3). Anal. Calcd for $C_{19}H_{21}NO_3S$: C, 66.45; H, 6.16; N, 4.08. Found: C, 66.55; H, 6.31; N, 4.04.

α-Anomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55−7.25 (m, 10H), 5.64 (br d, 1H, J = 6.6 Hz, H1), 5.19 (s, 2H), 4.20 (m, 1H, J = 9.4, 6.2, 0.6 Hz, H5), 3.83 (dd, 1H, J = 9.4, 4.2 Hz, H4), 3.45 (d, 1H, OH), 3.63 (br d, 1H, J = 14.9 Hz, $H2_{eq}$), 2.56 (dd, 1H, J = 14.9, 6,6 Hz, $H2_{ax}$), 1.35 (d, 3H, J = 6.2 Hz, H6); ^{13}C NMR ($CDCl_3$) δ 153.0, 137.5−126.2 (12C), 82.6, 76.0, 72.3, 71.4, 30.8, 17.7.

***β*-Anomer:** ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55−7.25 (m, 10H), 5.10 (s, 2H), 4.72 (dd, 1H, J = 11.9, 2.6 Hz, H1), 3.80 (dd, 1H, J = 9.6, 3.5 Hz, H4), 3.62 (dd, 1H, J = 14.7, 2.6 Hz, $H2_{eq}$), 3.38 (d, 1H, J = 3.5 Hz, OH), 3.35 (dq, 1H, J = 9.4, 6.1 Hz, H5), 2.15 (dd,1H, J = 14.7, 11.9 Hz, $H2_{ax}$), 1.44 (d, 3H, J = 6.1 Hz, H6); ^{13}C NMR ($CDCl_3$) δ 154.5, 137.5−126.2 (12C), 82.1, 78.9, 76.1, 71.8, 31.5, 18.3.

A third isomer was identified in the ^{1}H 300 MHz spectra corresponding to α-thioglycoside, with the opposite syn/anti configuration on nitrogen: δ 5.49 (dd, 1H, J = 7.2, 6.4 Hz, H1), 5.15 (d, 1H, J = 11.9 Hz), 5.10 (d, 1H), 4.27 (dd, 1H, J = 9.7, 2.7 Hz, H4), 4.21 (m, 1H, H5), 3.80 (d, 1H, J = 2.7 Hz, OH), 2.87 (dd, 1H, J = 15.4, 6.4 Hz, $H2_{eq}$), 2.74 (dd, 1H, J = 15.4, 7.2 Hz, $H2_{ax}$), 1.32 (d, 3H, J = 6.0 Hz, H6).

Phenyl 3-(*O*-Benzylhydroxyamino)-2,3,6-trideoxy-3-*C*-methyl-1-thio- α,*β*-*ribo*-hexopyranoside (12, 13). Cerium trichloride (anhydrous, 31.3 g, 127 mmol) was slurried in dry THF (300 mL) and stirred for 17 h at room temperature under dry N_2. After the solution was cooled to −78 °C, MeLi (1.4 M solution in ether, 63.9 g, 122 mmol) was added with rapid stirring for 90 min. Oxime **11** (6.88 g, 20 mmol) dissolved in 150 mL of dry THF was added over 20 min, and stirring was continued for another 30 min. After the solution was warmed to −50 °C, saturated $NaHCO_3$ (50 mL) was slowly added. The reaction mixture was filtered on a pad of Celite and rinsed successively with diethyl ether, ethyl acetate, and ethyl acetate−methanol (9:1). The pooled filtrates were washed with water (3 × 300 mL) and saturated NaCl solution (100 mL) and dried (Na_2SO_4). After solvent was removed in vacuo, column chromatography on silica gel (ethyl acetate−hexanes, 15:85) gave (as syrups) 3.0 g of α-thioglycoside **12** (42%; R_f 0.63 (ethyl acetate−hexanes, 2:3)), 1.7 g of *β*-thioglycoside **13** (24%, R_f 0.56), and starting material (0.39 g, 6%, R_f 0.75).

12: $[a]^{22}_D$ −246° (*c*, 1.1, chloroform); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48−7.21 (m,10H), 6.35 (br s, NH), 5.44 (dd, 1H, J = 6.7, 1.8 Hz, H1), 4.80 (s, 2H, OBn), 4.14 (dq, 1H, J = 8.8, 6.3 Hz, H5), 3.22−3.13 (m, 2H, H4, OH), 2.23 (dd, 1H, J = 15.0, 1.8 Hz, $H2_{eq}$), 2.03 (dd, 1H, J = 15.0. 6.7 Hz, $H2_{ax}$), 1.36, (s, 3H, CH_3), 1.27 (d, 3H, J = 6.3 Hz, H6); ^{13}C NMR ($CDCl_3$) δ 135.8−127.0 (12C), 82.7, 78.6, 77.1, 66.0, 57.9 (C3), 38.7, 23.5, 18.1. Anal. Calcd for $C_{20}H_{25}NO_3S$: C, 66.82; H, 7.01; N, 3.90. Found: C, 66.96; H, 7.18, N, 3.82.

13: $[a]^{22}_D$ −9.2° (*c*, 3.2, $CHCl_3$); ^{1}H NMR (chloroform) δ 7.46−7.20 (m, 10H), 5.63 (br s, 1H, NH), 5.12 (dd, 1H, J = 11.9, 2.1 Hz, H1), 4.68, 4.62 (2d, 2H, J = 11.6 Hz, OBn), 3.76 (dq, 1H, J = 9.6, 6.2 Hz, H5), 3.14 (dd, 1H, J = 9.6, 4.0 Hz, H4), 2.70 (br d, 1H, J = 4.0 Hz, OH), 2.17 (dd, 1H, J = 14.0, 2.1 Hz, $H2_{eq}$), 1.64 (dd, 1H, J = 14.0, 11.9 Hz, $H2_{ax}$), 1.27 (s, 3H, CH_3), 1.27 (d, 3H, J = 6.2 Hz, H6); ^{13}C NMR ($CDCl_3$) δ 137.0−126.7 (12C), 80.1, 78.2, 76.7, 73.1, 58.6 (C3), 40.6, 23.4, 18.5. Anal. Calcd for $C_{20}H_{25}NO_3S$: C, 66.82; H, 7.01; N, 3.90. Found: C, 66.75; H, 7.24, N, 3.66.

Phenyl 4-*O*-Acetyl-3-(*O*-benzylhydroxyamino)-2,3,6-trideoxy-3-*C*-methyl-1-thio-α-*ribo*-hexopyranoside (14). To a solution of **12** (1.0 g, 2.4 mmol) in chloroform (3 mL) and pyridine (3 mL) at 5 °C was added acetic anhydride (3 mL). The solution was allowed to warm and stir for 6 h, then poured into ice and water, and extracted with $CHCl_3$ (3 × 20 mL). The extract was washed with cold 1 N HCl (25 mL), water (2 × 25 mL), and saturated $NaHCO_3$, dried (Na_2SO_4), and concentrated at reduced pressure. Purification by column chromatography on silica gel (ethyl acetate−hexanes, 1:9) gave syrupy **14** (0.89 g, 79%): R_f 0.87 (ethyl acetate−hexanes, 2:3); $[a]^{22}_D$ −189° (*c*, 1.0, chloroform); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51−7.21 (m, 10H), 5.64 (s, NH), 5.48 (dd, 1H, J = 6.9, 1.4 Hz, H-1), 5.08, 4.88 (2d, 2H, J = 11.4 Hz, OBn), 4.78 (d, 1H, J = 9.8 Hz, H4), 4.54 (dq, 1H, J = 9.8, 6.2 Hz, H5), 2.58 (dd, 1H, J = 14.8, 1.4 Hz, $H2_{eq}$), 2.07 (dd, 1H, J = 1.8, 6.9 Hz, $H2_{ax}$), 2.07 (s, 3H, CH_3CO), 1.19 (s, 3H), 1.13 (d, 3H, J = 6.2 Hz, H6); ^{13}C NMR ($CDCl_3$) δ 169.8, 137.8−126.5 (12C), 83.7, 78.1, 75.7, 63.4, 57.5 (C3), 38.8, 23.3, 20.6, 17.6. Anal. Calcd for $C_{22}H_{27}NO_4S$: C, 65.81; H, 6.78; N, 3.49. Found: C, 66.11; H, 6.72, N, 3.44.

Phenyl 4-*O*-Acetyl-3-(*O*-benzylhydroxyamino)-2,3,6-trideoxy-3-*C*-methyl-1-thio-*β*-*ribo*-hexopyranoside (15). Following the same procedure described for **14**, acetylated compound **15** (waxy solid, 0.85 g, 82%) was prepared from thioglycoside **13**: R_f 0.87 (ethyl acetate−hexanes, 2:3); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48−7.19 (m, 10H), 5.47 (br d, 1H), 5.10 (dd, 1H), 4.69 (d, 1H), 4.64 (s, 2H), 3.97 (dq, 1H), 2.37 (dd, 1H), 2.08 (s, 3H), 1.62 (ddd, 1H), 1.13 (s, 3H), 1.10 (d, 3H); ^{13}C NMR ($CDCl_3$) δ 169.7, 137.5−126.9 (12C), 80.1, 77.8, 76.9, 70.6, 59.0, 39.4, 23.0, 20.6, 18.1. Anal. Calcd for $C_{22}H_{27}NO_4S$: C, 65.81; H, 6.78; N, 3.49. Found: C, 65.71; H, 6.73, N, 3.22.

Phenyl 4-*O*-Acetyl-2,3,6-trideoxy-3-*C*-methyl-3-(*O*-trifluoroacetamido)-1-thio-α/*β*-L-*ribo*-hexopyranoside (17a, 17b). To a solution of methyl 4-*O*-acetyl-2,3,6-trideoxy-3-*C*-methyl-3-(*O*-trifluoroacetamido)-α-*ribo*-hexopyranoside (0.24 g, 0.77 mmol) and (phenylthiomethyl)trimethylsilane (0.73 mL, 3.8 mmol) in dry CH_2Cl_2 (3 mL) under dry N_2 at 0 °C was added TMSOTf (0.24 mL, 1.3 mmol) in two portions 3 h apart. The reaction was allowed to warm to room temperature and was stirred for an additional 15 h. After addition of $NaHCO_3$ (50 mg) and concentration under reduced pressure, the residue was purified by column chromatography on Florisil (ethyl acetate−hexanes, 15:85) to give an equal mixture of anomeric thioglycosides **17a** and **17b** (0.25 g, 83%) which were further purified by chromatography on silica gel with 1:3 ethyl acetate−hexanes.

17a: R_f 0.49 (ethyl acetate−hexanes, 1:3); $[a]^{22}_D$ −288° (*c*, 0.64, chloroform); ^{1}H NMR ($CDCl_3$) δ 7.46−7.26 (m, 5H), 6.67 (br s, 1H, NH), 5.46 (d, 1H, J = 6.0 Hz, H1), 4.75 (d, 1H, J = 10.1 Hz, H4), 4.42 (dq, 1H, J = 10.1, 6.2 Hz, H5), 3.37 (d, 1H, J = 15.2 Hz, $H2_{eq}$), 2.19 (s 3H, OAc), 2.15 (dd, 1H, J = 15.2, 6.0 Hz, $H2_{ax}$), 1.43 (s, 3H, Me), 1.20 (d, 3H, J = 6.2 Hz, H6); ^{13}C NMR ($CDCl_3$) δ 169.2, 156.8 (q, J = 37 Hz), 115.3 (q, J = 290 Hz), 135.4, 131.1 (2C), 128.8 (2C), 127.2, 83.1, 76.8, 62.8, 55.5, 37.6, 23.4, 20.5, 17.3. Anal. Calcd for $C_{17}H_{20}F_3NO_4S$: C, 52.17; H, 5.15; N, 3.58. Found: C, 52.40; H, 5.27, N, 3.45.

17b: R_f 0.44 (ethyl acetate−hexanes, 1:3); $[a]^{22}_D$ −44° (*c*, 0.62, chloroform); ^{1}H NMR ($CDCl_3$) δ 7.52−7.27 (m, 5H), 6.36 (br s, 1H, NH), 4.79 (dd, 1H, J = 11.9, 1.8 Hz, H1), 4.67 (dd, 1H, J = 9.9, 1.1 Hz, H4), 3.69 (dq, 1H, J = 9.9, 6.1 Hz, H5), 3.37 (dd, 1H, J = 14.5, 1.8 Hz, $H2_{eq}$), 2.17 (s, 3H, OAc), 1.73 (ddd, 1H, J = 14.5, 11.9, 1.1 Hz, $H2_{ax}$), 1.35 (s, 3H, Me), 1.22 (d, 3H, J = 6.1 Hz, H6); ^{13}C NMR ($CDCl_3$) δ 169.0, 156.5 (q, J = 289 Hz), 132.7, 132.3 (2C), 128.7 (2C), 127.7, 115.3 (q, J = 289 Hz), 80.1, 76.3, 71.0, 57.5, 38.5, 23.3, 20.5, 17.8. Anal. Calcd for $C_{17}H_{20}F_3NO_4S$: C, 52.17; H, 5.15; N, 3.58. Found: C, 52.31; H, 5.31, N, 3.42.

Methyl 4-*O*-Acetyl-3-(*O*-benzylhydroxyamino)-2,3,6-trideoxy-3-*C*-methyl-α/*β*-L-*ribo*-hexopyranosyl-(1→4)-3-*O*-benzyl-2,6-dideoxy-α-L-*lyxo*-hexopyranoside (19, 20). Thioglycoside **14** (234 mg, 0.58 mmol) and acceptor **6** (104 mg, 0.41 mmol) were dissolved in dry dichloroethane−ether (1:1, v/v, 5 mL) under dry nitrogen, and the solution was cooled to −20 °C. In a separate flask, triflic acid (5.2 mL, 0.058 mmol) was added to a mixture of *N*-iodosuccinimide (132 mg, 0.58 mmol) in dry dichloroethane−ether (1:1, 3 mL). The NIS−triflic acid suspension was added dropwise to the solution of **14** and **6** over 1 min, and the resulting mixture was stirred for an additional 2 h while being warmed to 10 °C. The reaction mixture was diluted with dichloromethane (20 mL), washed with aqueous sodium bisulfite solution (5%, 10 mL) and saturated sodium chloride solution (10 mL), dried (Na_2SO_4), and concentrated under reduced pressure. Purification of the product by flash chromatography on silica gel with ethyl acetate−hexanes (1:3) gave syrupy *β*-disaccharide **20** (127 mg, 0.23 mmol, 57%) and α-disaccharide **19** (70 mg, 0.13 mmol, 31%).

20: R_f 0.72 (ethyl acetate−hexanes, 2:3); $[a]^{22}_D$ −48.3° (*c*, 1.5, chloroform); ^{1}H NMR ($CDCl_3$) δ 7.31−7.15 (m, 10H), 5.42 (dd, 1H, J = 9.6, 2.1 Hz, H1′), 5.39 (br s, 1H, NH), 4.85 (dd, 1H, J = 3.5, 1.2 Hz, H1), 4.69 (d, 1H, J = 9.7 Hz, H4′), 4.54 (s, 2H, OBn), 4.52, 4.37 (2d, 1H each, J = 11.1 Hz, OBn), 3.96 (m, 1H, J = 2.6, 1.2, 0.7 Hz, H4), 3.96 (dq, 1H, J = 9.8, 6.3 Hz, H5′), 3.85 (ddd, 1H, J = 12.5, 4.9, 2.6, H3), 3.82 (dq, 1H, J = 6.5, 0.7 Hz, H5), 3.30 (s, 3H, OCH_3), 2.45 (dd, 1H, J = 13.9 Hz, $H2'_{eq}$), 2.10 (m, 1H, J = 12.6, 12.5, 3.5 Hz, $H2_{ax}$), 2.05 (s, 3H, CH_3CO), 1.94 (m, 1H, J = 12.6, 4.9, 1.2 Hz, $H2_{eq}$), 1.55 (dd, 1H, J = 13.9, 9.6 Hz, $H2'_{ax}$), 1.26 (d, 3H, J = 6.5 Hz, H6), 1.10 (s, 3H, CH_3), 1.09 (d, 3H, J = 6.3 Hz, H6′); ^{13}C NMR ($CDCl_3$) δ 169.8, 138.5−127.3 (12C), 98.8 (C1′), 98.1 (C1), 78.5, 76.9, 74.5, 73.5, 70.4, 67.7, 66.3, 59.1, 54.6, 39.3, 30.3, 23.2, 20.6, 17.9, 17.1. Anal. Calcd for $C_{30}H_{41}NO_8$: C, 66.28; H, 7.60; N, 2.58. Found: C, 66.49; H, 7.57; N, 2.44.

19: R_f 0.61 (ethyl acetate−hexanes, 2:3); $[a]^{22}_D$ −161° (*c*, 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 7.41−7.22 (m, 10H), 6.61 (br s, 1H, NH), 4.94 (d, 1H, J = 4.1 Hz, H1′), 4.82, 4.74 (2d, 1H each, J = 11.4 Hz, OBn), 4.76 (m, 1H, H1), 4.66 (d, 1H, J = 10.2 Hz, H4′), 4.56 (s, 2H, OBn), 4.38 (dq, 1H, J = 10.2, 6.0 Hz, H5′), 3.83−3.74 (m, 3H, H3, H4, H5), 3.27 (s, 3H, OCH_3), 2.44 (br d, 1H, J = 14.5 Hz, $H2'_{eq}$), 2.06 (s, 3H, CH_3CO), 1.96 (m, 1H, J = 13.0, 13.0, 3.6 Hz, $H2_{ax}$), 1.86 (dd, 1H, J = 13.0, 4.9 Hz, $H2_{eq}$), 1.60 (dd, 1H, 14.5, 4.5 Hz, $H2'_{ax}$), 1.21 (d, 3H, J = 6.6 Hz, H6), 1.16 (s, 3H, CH_3), 0.80 (d, 3H, J = 6.1 Hz, H6′); ^{13}C NMR ($CDCl_3$) δ 170.4, 138.6, 138.5, 128.4−127.2 (10C), 98.7 (C1′), 97.9 (C1), 76.9, 76.8, 74.6, 72.5, 70.0, 66.6, 62.4, 57.7, 54.5, 37.4, 30.6, 23.2, 20.7, 17.5, 17.5. Anal. Calcd for $C_{30}H_{41}NO_8$: C, 66.28; H, 7.60; N, 2.58. Found: C, 65.54; H, 7.41; N, 3.00.

Methyl 4-*O*-Acetyl-2,3,6-trideoxy-3-*C*-methyl-3-(trifluoroacetamido)-α/*β*-L-*ribo*-hexopyranosyl)-(1→4)-3-*O*-benzyl-2,6-dideoxy-α/*β*-L-*lyxo*-hexopyranoside (21, 22). Following the procedure described for the preparation of **19** and **20**, thioglycoside **17** (α-anomer, 55 mg, 0.14 mmol) and **6** (25 mg, 0.10 mmol) in 3 mL of dichloroethane−ether (1:1) were treated with a mixture of NIS (32 mg, 0.14 mmol) and TfOH (1.3 μL, 0.014 mmol) in 3 mL of dry dichloroethane−ether (1:1) for 3 h to give a mixture of disaccharides. Column chromatography on silica gel (ethyl acetate−hexanes, 15:85) gave *β*-anomer **22** (7 mg, 13%), α-anomer **21** (13 mg, 25%), and 11 mg of methyl 4-*O*-acetyl-2,3,6-trideoxy-3-*C*-methyl-3-trifluoroacetamido-α-L-hexopyranoside, formed by transglycosylation.

22: $[a]^{22}_D$ −49° (*c*, 0.48, chloroform); ^{1}H NMR ($CDCl_3$) δ 7.39−7.22 (m, 5H), 6.25 (br s, 1H), 4.93 (dd, 1H, J = 9.6, 1.8 Hz, H1′), 4.80 (br d, 1H, J = 2.6 Hz, H1), 4.67 (d, 1H, J = 9.9 Hz), 4.52 (AB_q, 2H, J = 12.4 Hz, $PhCH_2$), 3.83−3.77 (m, 3H), 3.58 (dq, 1H, J = 9.9, 6.2 Hz), 3.33 (dd, 1H, J = 14.4, 1.8 Hz, $H2'_{eq}$), 3.28 (s, 3H), 2.16 (s, 3H), 2.05−1.86 (m, 2H), 1.64 (dd, 1H, J = 14.4, 9.6 Hz, $H2'_{ax}$), 1.36 (s, 3H), 1.21 (d, 3H, J = 6.5 Hz, H6), 1.16 (d, 3H, J = 6.2 Hz, H6′); ^{13}C NMR ($CDCl_3$) δ 167.9, 130.8, 128.3, 127.3, 127.1, 98.8, 97.8, 76.9, 74.3, 73.8, 70.0, 67.8, 66.0, 57.2, 54.6, 38.4, 30.1, 23.6, 20.6, 17.7, 17.1.

21: $[a]^{22}_D$ −69° (*c*, 0.88, chloroform); ^{1}H NMR ($CDCl_3$) δ 8.10 (br s, 1H), 7.38−7.28 (m, 5H), 5.34 (dd, 1H, J = 2.9, 1.1 Hz), 4.82 (dd, 1H, J = 1.9, 1.9 Hz), 4.68 (d, 1H, J = 10.0 Hz), 4.59 (m, 2H), 4.12, (dq, 1H, J = 10.0, 6.2 Hz), 3.89−3.79 (m, 3H), 3.32 (s, 3H), 2.27 (dd, 1H, J = 14.8, 1.1 Hz), 2.12 (s, 3H), 1.96−1.92 (m, 2H), 1.78 (m, 1H), 1.59 (s, 3H), 1.31 (d, 3H, J = 6.6 Hz), 1.17 (d, 3H, J = 6.2 Hz); ^{13}C NMR ($CDCl_3$) δ 172.4, 130.8, 128.4, 127.7, 127.5, 98.6, 91.3, 77.1, 72.9, 70.0, 68.3, 68.1, 65.3, 62.7, 54.6, 40.3, 29.8, 23.7, 20.6, 17.4, 16.7.

Methyl 3-(*O*-Benzylhydroxyamino)-2,3,6-trideoxy-3-*C*-methyl-*β*-L-*ribo*-hexopyranosyl)-(1→4)-3-*O*-benzyl-2,6-dideoxy-α-L-*lyxo*-hexopyranoside (23). To *β*-disaccharide **20** (60 mg) dissolved in dry methanol (5 mL) was added dropwise NaOMe (0.1 mL, 1.0 M), and the mixture was stirred for 15 h. The volume was reduced to half in vacuo, and the residue was diluted into CH_2Cl_2, washed with water (5 mL × 2) and brine (5 mL), and dried (Na_2SO_4) to give syrupy **23** (51 mg, 92%): R_f 0.56 (ethyl acetate−hexanes, 2:3); $[a]^{22}_D$ −49.6° (*c*, 0.92, chloroform); ^{1}H NMR ($CDCl_3$) δ 7.37−7.19 (m, 10H), 5.42 (br s, 1H), 5.17 (dd, 1H, J = 9.6, 2.1 Hz, H1′), 4.81 (br d, 1H, J = 3.7 Hz, H1), 4.54 (s, 2H, OBn), 4.54, 4.49 (2d, 1H each, J = 11.4 Hz, OBn), 3.92 (br s, 1H, H4), 3.82 (ddd, 1H, J = 9.6, 4.9, 2.6 Hz, H3), 3.80 (bq, 1H, J = 6.6 Hz, H5), 3.66 (dq, 1H, J = 9.6, 6.2 Hz, H5′), 3.29 (s, 3H, OCH_3), 3.10 (dd, 1H, J = 9.6, 7.3 Hz, H4′), 2.84 (d, 1H, J = 7.3 Hz, OH), 2.10 (dd, 1H, J = 13.9, 2.1 Hz, $H2'_{eq}$), 2.06 (m, 1H, J = 12.6, 12.4, 3.7 Hz, $H2_{ax}$), 1.91 (br dd, 1H, J = 12.6, 4.9 Hz, H2), 1.55 (dd, 1H, J = 13.9, 9.6 Hz, $H2'_{ax}$), 1.25 (s 3H, CH_3), 1.25, 1.24 (2d, 3H each, H6, H6′); ^{13}C NMR ($CDCl_3$) δ 138.6, 137.0, 128.4−127.2(10C), 98.8 (C1′), 97.9 (C1), 78.7, 76.6, 74.4, 73.4, 70.4, 70.2, 66,2, 58.6, 54.6, 40.9, 30.4, 23.7, 18.3, 17.1.

Methyl 3,4-Di-*O*-acetyl-2,6-dideoxy-α-L-*lyxo*-hexopyranosyl-(1→4)-3-(*O*-benzylhydroxyamino)-2,3,6-trideoxy-3-*C*-methyl-*β*-L-*ribo*-hexopyranosyl)-(1→4)-3-*O*-benzyl-2,6-dideoxy-α-L-*lyxo*-hexopyranoside (24). To *β*-disaccharide **23** (143 mg, 0.29 mmol) dissolved in dry benzene (5 mL) and *s*-collidine (102 mg, 0.84 mmol), containing molecular sieves (4 Å, 200 mg) and silver triflate (215 mg, 0.84 mmol), at 5 °C under dry nitrogen was added a solution of 3,4-di-*O*-acetyl-2,6-dideoxy-α-L-*lyxo*-hexopyranosyl bromide **2a** (prepared fresh from $HBr_{(g)}$ and 3,4-di-*O*-acetyl-L-fucal, 184 mg 0.86 mmol) in dry benzene (5 mL) over 10 min. After 2 h, the reaction was allowed to warm to room temperature and stir for 24 h in the dark. The mixture was filtered through a Celite pad, and the solids were rinsed with dichloromethane and ethyl acetate (5 mL each). The organic phase was concentrated in vacuo, diluted with more dichloromethane (25 mL), washed with water (30 mL × 2) and brine (30 mL), and dried with Na_2SO_4. Column chromatography on silica gel (ethyl acetate−hexanes, 1:3) separated unreacted disaccharide and trisaccharide from other glycosyl bromide remnants. The recovered di- and trisaccharide mixture was then separated on a second silica column (methanol−dichloromethane, 1:99) to give unreacted disaccharide (53 mg, 106 mmol, 37% of original) and trisaccharide **24** (88 mg, 68% based on consumed disaccharide).

	R_f(ethyl acetate−hexanes (2:3))	R_f (methanol−CH_2Cl_2 (5:95))
disaccharide	0.49	0.20
trisaccharide	0.47	0.39
glycosyl bromide remnant	0.32	0.38

Careful column chromatography using 120 mg of silica gel on a 3.5 × 15 cm column with 2% methanol−dichloromethane gave a clean separation in a repeated preparation of **24**: $[a]^{22}_D$ −81.7°(*c*, 0.71, chloroform); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40−7.15 (m, 10H), 5.51(br s, 1H, NH), 5.39 (dd, 1H, J = 9.4, 2.0 Hz, H1′), 5.18 (ddd, 1H, J = 13.3, 4.9, 3.0 Hz H3″), 5.17 (dd, 1H, J = 3.0, 0.4 Hz, H4″), 5.05 (br d, 1H, J = 3.2 Hz, H1″), 4.83 (br d, 1H J = 3.0 Hz, H1), 4.54 and 4.50 (2d, 2H, J = 11.0 Hz, OBn), 4.50 and 4.34 (2d, 2H, J = 11.0 Hz, OBn), 4.14 (dq, 1H, J = 5.6, 0.4 Hz, H5″), 3.95 (br s, 1H, H4), 3.88 (dq, 1H, J = 9.3, 6.2 Hz, H5′), 3.84 (m, 1H, H3), 3.81 (bq, 1H, J = 6.5 Hz, H5), 3.30 (s, 3H, OCH_3), 3.22 (d, 1H, J = 9.3 Hz, H4′), 2.34 (dd, 1H, J = 13.8, 2.0 Hz, $H2_{eq}$), 2.14 (s, 3H, OAc), 1.99

(s, 3H, OAc), 2.13−2.02 (m, 2H, $H2_{eq}$, $H2''_{eq}$), 1.90 (m, 2H, $H2_{ax}$, $H2''_{ax}$), 1.46 (dd, 1H, J = 13.8, 9.4 Hz, $H2'_{ax}$), 1.25 (d, 3H, J = 6.5 Hz, H6), 1.24 (d, 3H, J = 6.2 Hz, H6′), 1.19 (s, 3H, CH_3), 1.10 (d, 3H, J = 6.6 Hz, H6″); ^{13}C NMR ($CDCl_3$) δ 170.5, 170.1, 138.4, 137.6, 128.4−127.3 (10C), 100.7 (C1″), 98.8 (C1), 98.1 (C1′), 88.2, 77.1, 74.5, 73.4, 70.5, 69.5, 68.6, 66.4, 66.3, 65.5, 60.1, 54.6, 39.3, 30.3, 30.0, 24.3, 20.8, 20.6, 18.7, 17.2, 16.2. Anal. Calcd for $C_{38}H_{53}NO_{12}$: C, 63.76; H, 7.46; N, 1.96. Found: C, 63.37; H, 7.38; N, 1.68.

Methyl 3,4-Di-*O*-acetyl-2,6-dideoxy-α-L-*lyxo*-hexopyranosyl-(1→4)-2,3,6-trideoxy-3-*C*-methyl-3-nitro-*β*-L-*ribo*-hexopyranosyl-(1→4)-2,6-dideoxy-α-L-*lyxo*-hexopyranoside (25). To a solution of dimethyldioxirane[55] in acetone (0.042 M, 20.7 mL) at −78 °C was added trisaccharide **24** (21.2 mg, 30 mmol) dissolved in acetone−ethyl acetate (6 mL, 1:1, v/v). The solution was allowed to warm and stir at room temperature for 16 h. Removal of the solvent under reduced pressure followed by purification of the product by column chromatography on Florisil using ethyl acetate−hexanes (1:3) gave syrupy **25** (13.5 mg, 83%): R_f 0.15 (ethyl acetate−hexanes, 2:3); $[a]^{22}_D$ −163.6° (*c*, 1.1, chloroform); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.41 (dd, 1H, J = 8.4, 3.0 Hz, H1′), 5.18, (br d, 1H, J = 2.9 Hz, H4″), 5.15 (br d, 1H, J = 3.9 Hz, H1″), 5.10 (ddd, 1H, J = 12.5, 5.2, 2.9 Hz, H3″), 4.79 (br d, 1H, J = 3.0 Hz, H1), 4.12−4.04 (m, 2H, H3, H5″), 3.95 (dq, 1H, J = 8.2, 6.3 Hz, H5′), 3.80 (br d, 1H, J = 2.5 Hz, H4), 3.49 (d, 1H, J = 8.2 Hz, H4′), 3.31 (s, 3H, OCH_3), 2.55 (dd, 1H, J = 14.9, 3.0 Hz, $H2'_{eq}$), 2.15, 1.98 (2s, 3H each, CH_3CO), 2.06 (ddd, 1H, J = 13.1, 12.5, 3.9 Hz, $H2''_{eq}$), 1.97 (dd, 1H, J = 14.9, 8.4 Hz, $H2'_{ax}$), 1.93−1.84 (m, 3H, $H2''_{ax}$, $H2_{eq}$, $H2_{ax}$), 1.71 (s, 3H, CH_3), 1.32 (d, 3H, J = 3.6 Hz, H6′), 1.27 (d, 3H, J = 6.6 Hz, H6), 1.11 (d, 3H, J = 6.6 Hz, H6″); ^{13}C NMR ($CDCl_3$) δ 170.5, 169.9, 100.4, 98.6, 98.3, 89.4, 83.2, 77.5, 69.9, 69.3, 66.2, 66.2, 65.9, 65.6, 54.7, 40.4, 33.4, 29.6, 25.9, 20.7, 20.5, 18.9, 17.2, 16.2. Anal. Calcd for $C_{24}H_{39}NO_{13}$: C, 52.45; H, 7.15; N, 2.55. Found: C, 52.73; H, 7.12; N, 2.37.

Methyl 2,6-dideoxy-α-L-*lyxo*-hexopyranosyl-(1→4)-2,3,6-trideoxy-3-*C*-methyl-3-nitro-*β*-L-*ribo*-hexopyranosyl)-(1→4)-2,6-dideoxy-α-L-*lyxo*-hexopyranoside (26). To a solution of **25** (28 mg, 50 mmol) in dry methanol (5.0 mL) was added freshly prepared sodium methoxide (0.7 M, 1.0 mL). The solution was stirred for 3 days and concentrated to half its original volume, and the residue was purified by column chromatography on Florisil using ethyl acetate as eluant to give deacylated nitro saccharide **26** (15.4 mg, 65%): R_f 0.42 (ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.40 (dd, 1H, J = 8.6, 2.8 Hz, H1′), 5.04 (br d, 1H, J = 3. 2 Hz, H1″), 4.78 (t, 1H, J = 1.9, 1.9 Hz, H1), 4.11−4.00 (m, 2H, H3, H3″), 3.94 (dq, 1H, J = 8.5, 6.2 3.2, 3.2 Hz, H4″), 3.42 (d, 1H, J = 8.5 Hz, H4′), 3.31 (s, 3H, OCH_3), 2.52 (dd, 1H, J = 14.8, 2.8 Hz, $H2'_{eq}$), 2.13−1.77 (m, 5H, $H2'_{ax}$, $H2_{eq}$, $H2_{ax}$, $H2''_{eq}$, $H2''_{ax}$), 1.70 (s, 3H, CH_3), 1.31 (d, 3H, J = 6.2 Hz, H6′), 1.26 (d, 3H, J = 6.6 Hz, H6), 1.24 (d, 3H, J = 6.6 Hz, H6″); ^{13}C NMR ($CDCl_3$) δ 101.1, 98.5, 98.2, 89.6, 83.6, 77.3, 70.7, 69.7, 66.8, 66.2, 65.5, 65.2, 54.7, 40.7, 33.4, 32.5, 25.7, 18.8, 17.2, 16.4; HRMS calcd for $C_{20}H_{35}NO_{11}Na$ $(M + Na)^+$ 488.2107, found 488.2122.

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Supporting Information Available: ^{1}H NMR spectra for compounds **11**−**15**, **17**, and **19**−**26** and ^{13}C NMR spectra for **11**, **24**, and **26**. This material is available free of charge via the Internet at http://pubs.acs.org.

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