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Stereoselective Synthesis of Iminosugar 2-Deoxy(thio)glycosides from Bicyclic Iminoglycal Carbamates Promoted by Cerium(IV) Ammonium Nitrate and Cooperative Brønsted Acid-Type Organocatalysis

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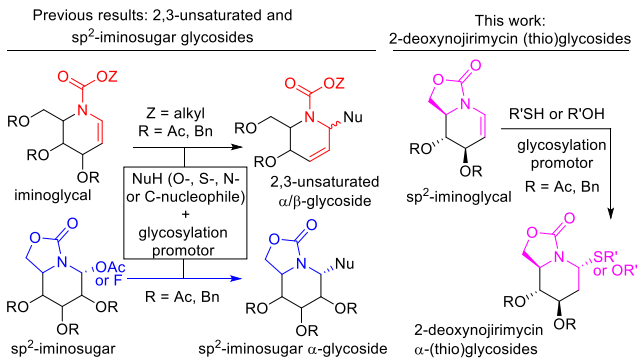
KEYWORDS. 2-deoxyglycosides • iminosugars • cerium ammonium nitrate • organocatalysis • iminoglycal.

ABSTRACT: The first examples of iminosugar-type 2-deoxy(thio)glycoside mimetics are reported. The key step is the activation of a bicyclic iminoglycal carbamate to generate a highly reactive acyliminium cation. Cerium(IV) ammonium nitrate efficiently promoted the formation of 2-deoxy *S*-glycosides in the presence of thiols, probably by in situ generation of catalytic HNO_3, with complete α-stereoselectivity. Cooperative phosphoric acid/Schreiner's thiourea organocatalysis proved better suited for generating 2-deoxy *O*-glycosides, significantly broadening the scope of the approach.

INTRODUCTION

The synthesis of 2-deoxyglycosides has drawn considerable attention from carbohydrate, organic and medicinal chemists since these motifs are present in a broad variety of natural products and clinically relevant agents displaying antitumor, antimicrobial or anti-HIV activities, among others.[1-3] The incorporation of 2-deoxyglycosides and their analogs in drug discovery is hindered, however, by the difficulties associated with their stereoselective preparation and the insufficient metabolic stability of the glycosides. The absence of a neighboring participant group at the C-2 position in 2-deoxyglycosyl donors, such as in a glycal (1,2-unsaturated sugar), to bias the stereochemical outcome, makes notoriously challenging the control of the anomeric configuration in the glycosylation reaction. In addition, the resulting C-2 unsubstituted products are more susceptible to acid-catalyzed hydrolysis and henceforth are more difficult to handle. The total or partial cleavage of the saccharide moieties by the action of glycosidases or acid medium is particularly problematic since it often results in toxicity and reduced bioactivity, thwarting any pharmacological use.[4] The substitution of the *O*-glycosidic linkage in 2-deoxyglycosides by a thioether bond has been proposed, but the reported methodologies likewise suffer from stereoselectivity issues.[5] A converse approach consisting in the replacement of the endocyclic oxygen atom in the 2-deoxysugar glycone unit by nitrogen, to afford a member of the archetypic iminosugar glycomimetic family, is conceptually more appealing.[6] In principle, the anticipated lability of amino(thio)acetal functional groups can be alleviated by the installation of N-alkoxycarbonyl substituents, which further allows nucleophilic additions to the α-carbon via acyliminium ion intermediates.[7] Notwithstanding, attempts to access 2-deoxyiminosugar glycosides from the corresponding iminoglycal donors obstinately proceeded with concomitant double bond migration (Ferrier rearrangement)[8] to afford 2,3-unsaturated compounds (Scheme 1, left panel).[9]

Scheme 1. Glycosidation Reactions of Iminoglycals and sp^2-Iminosugars and Proposed Strategy for the Synthesis of 2-Deoxyiminosugar Glycosides.

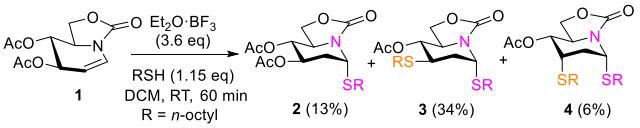


In previous work, we found that installing a five-membered carbamate ring in the iminosugars, thereby imparting high sp^2-hybridation character to the endocyclic nitrogen, affords bicyclic monosaccharide surrogates (sp^2-iminosugars) that emulate both the function and chemistry of the parent carbohydrates.[10] The carbamate segment is a key integral part of the sp^2-iminosugar glycomimetic structure, not a protecting group, that fixes the conformation about the exocyclic C-5—C-6 bond in the *gauche-trans* conformation (C-4 and O-6 in *anti* disposition). Notably, this subtle structural difference enables glycosylation reactions upon activation of glycosyl acetate or fluoride donors with Brønsted or Lewis acid promotors and drastically stabilizes axially-oriented anomeric heteroatom substituents (Scheme 1, left panel).[11] The stereochemical outcome is then strictly governed by stereoelectronic effects, mainly the anomeric effect, independently of the presence or lack of a stereodirecting group at the C-2 position. We wondered if such favorable features could be extended to the more demanding 2-deoxyiminosugars. This endeavor has been addressed in the present study, where we have developed an efficient method to access the first representatives of this hitherto elusive type of glycomimetics. Specifically, we show that *gluco*-configured bicyclic iminoglycal carbamates (*sp^2-iminoglycals*) can be efficiently transformed into 2-deoxynojirimycin *S*- and *O*-glycosides with absolute α-stereoselectivity (Scheme 1, right panel).

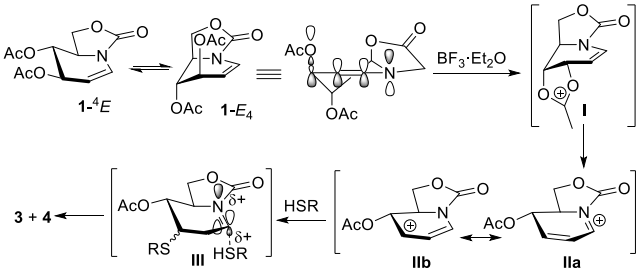
RESULTS AND DISCUSSION

We initiate our study on the reaction of the diacetylated iminoglycal carbamate **1**[12] with octanethiol in the presence of $BF_3{\cdot}Et_2O$. This promotor has been found previously to efficiently activate peracetylated sp^2-iminosugar donors to give iminosugar octyl α-thiogycosides with remarkable antiproliferative activity.[11] Indeed, exclusively α-*S*-glycosides were detected in the reaction mixture. However, after screening a series of reaction conditions we ultimately determined that the target 2-deoxyiminosugar thioglycoside **2** was always accompanied by major proportions of compounds **3** and **4**, bearing a second octylthio substituent at position C-3 (Scheme 2). It became apparent that formation of a Ferrier-type allylic carbocation followed by nucleophilic attack of the thiol at C-3, to give a transient 2,3-addition product, is favored over the 1,2-addition pathway. We reasoned that the π-symmetry of the p orbital hosting the lone electron pair in the sp^2-hybridized carbamate nitrogen in **1** enhances the vinylogous anomeric effect, as compared with classical glycals, by efficiently overlapping with the π-system of the double bond and the σ* antibonding orbital of the axially-oriented C-3—O-3 bond in a conformation close to an envelope E_4.[8] Departure of the allylic acetate group upon coordination to the Lewis acid is then likely favored by the anchimeric assistance of the vicinal O-4 acetyl (**I**). The electron withdrawing effect of the N-alkoxycarbonyl segment zipping the five-membered ring disfavors the acyliminium resonant form (**IIa**) in the resulting cationic intermediate, driving thiol attack at position C-3. The liberated proton can then activate the 1,2-double bond to give a transient acyliminium cation. Addition of a second thiol molecule through the α-face is then strongly favored, given the enhanced negative hyperconjugation contribution to the anomeric effect in sp^2-iminosugars (**III**),[11,12] affording the α-thioglycoside as a mixture of the corresponding C-3 epimers **3** and **4** (Scheme 3). This result is in agreement with the longtime known principles of stereoelectronic control governing the condensation reactions of iminium ions.[13]

Scheme 2. Reaction of Iminoglycal Carbamate 1 with Octanethiol using $BF_3{\cdot}Et_2O$ as promotor.

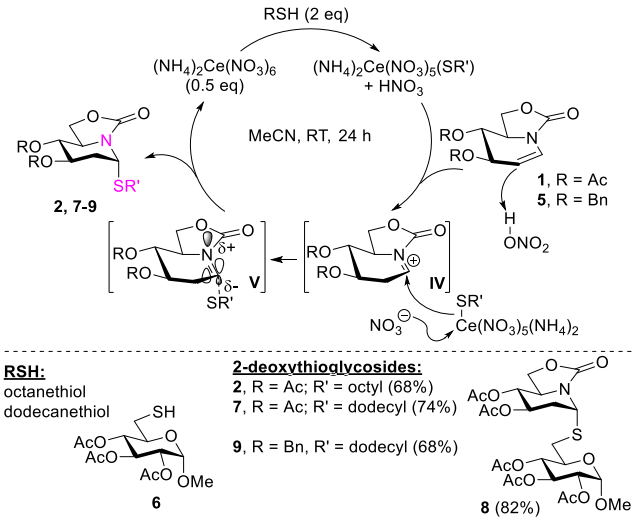


Scheme 3. Reaction Pathway Leading to 3 and 4.



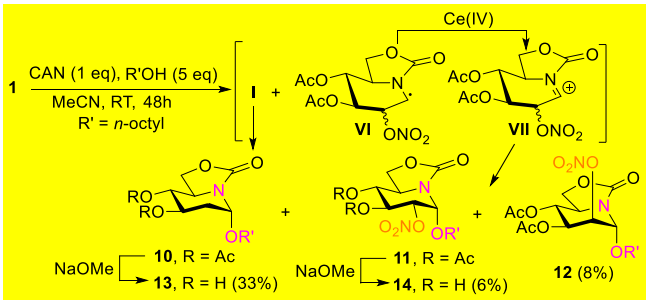
The fact that no iminoglycal products resulting from the addition of a single octylthio substituent at C-3 could be isolated from the above reaction mixtures indicates that thiol addition to the acyliminium cation is kinetically favored. In the glycal series, It has been reported that CAN in the presence of alcohols preferentially supplies 2-deoxyglycosides over 2,3-unsaturated derivatives, which is notably different from that observed with most Lewis or protic acids.[14] The proposed mechanism implies the *in situ* generation of HNO_3, which efficiently promotes the formation of an oxacarbenium cation and the subsequent transfer of the alkoxide moiety from cerium to the anomeric carbon.[14,15] We conceived that the higher acidity of thiols as compared to alcohols will facilitate HNO_3 development and iminoglycal activation to the corresponding acyliminium species (**IV**), whereas the lower stability of the Ce(IV)—SR bond (hard acid—soft base) will speed thioglycoside formation. The exacerbated anomeric effect in sp^2-iminosugars was then expected to drive thiol addition through the α-face (**V**).[11,12] To our delight, the reaction of **1** with octanethiol, dodecanethiol and methyl 2,3,4-tri-*O*-acetyl-6-thio-α-D-glucopyranoside[16] (**6**) in the presence of CAN (0.5 eq) proceeded smoothly in MeCN at room temperature to afford the target 2-deoxynojirimycin α-thioglycoside derivatives **2, 7** and **8** in 68-82% isolated yield after 24-48 h. The benzylated iminoglycal **5** likewise provided the dodecyl 2-deoxy-α-thioglycoside **9** using this protocol (see the SI, Table S1). Oxidation of the thiol to the corresponding disulfide by CAN was an anticipated potential side reaction that would also lead to the liberation of HNO_3. Although in some of the crude reaction mixtures using the octyl and dodecyl thiols the corresponding disulfide was detected by MS, it was always in a very low proportion, discarding that this is a preferred reaction pathway. Neither Ferrier products nor the respective β-anomer were detected in the crude reaction mixtures by MS or NMR (Scheme 4).

Scheme 4. CAN-Mediated Synthesis of 2-Deoxynojirimycin α-Thioglycosides.



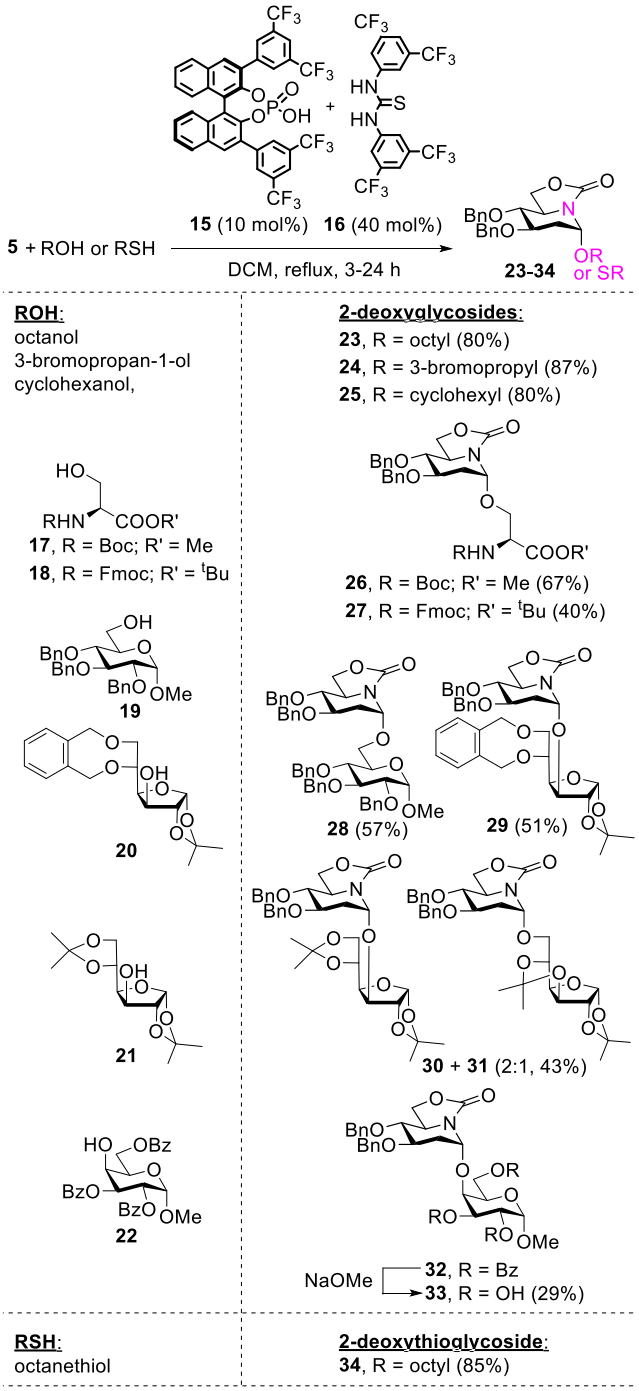
We next attempted translation of the CAN methodology for the purpose of accessing 2-deoxynojirimycin *O*-glycosides. TLC and MS monitoring of the reaction of iminoglycal **1** with octanol evidenced that the rate of formation of the corresponding octyl 2-deoxyglycoside was significantly slower when compared with octanethiol. An equimolecular proportion of CAN and a five-fold excess of the alcohol were required to achieve total consumption of **1** in 48 h at room temperature. Moreover, the presence of products incorporating a nitrate group was detected in the crude material. Column chromatography afforded an inseparable mixture of the 3,4-di-*O*-acetyl-2-deoxyiminosugar octyl α-glycoside derivative **10** and the nojirimycin 2-nitrate ester **11**, together with the pure mannojirimycin 2-nitrate epimer **12** (8%). The mixture of **10** and **11** was subjected to catalytic (NaOMe/MeOH) deacetylation to afford diols **13** and **14**, which could then be separated (33% and 6%, respectively) and fully characterized, confirming the structural assignment. The results can be rationalized assuming that sequential proton addition (→**I**)/alkoxyde anion addition to the iminoglycal (→**10**) competes with oxidation of nitrate anion to nitrate radical by Ce(IV). Anti-Markovnikov nitrate radical addition to the double bond can then occur either through the α or β face, a mechanism that is reminiscent of the classical azidonitration reaction of glycals.[17] The resulting transient imine radical **VI** can be oxidized by Ce(IV) to the corresponding highly reactive acyliminium cation **VII**, which finally undergoes glycosidation (→**11** and **12**; Scheme 5).

Scheme 5. CAN-Mediated Reaction of the sp^2-Iminoglycal 1 with Octanol.

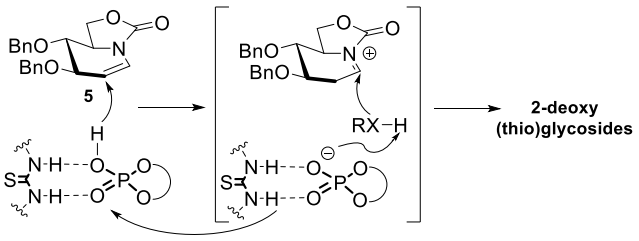


A range of different promotors for glycal activation were screened aiming to improve the yield of the 2-deoxyiminosugar glycoside targets. These include trifluoroacetic acid (TFA), [(pCF$_3$Ph)$_3$P)-AuCl]/AgOTf,[2j] Cu(OTf)$_2$·C$_6$H$_6$,[18] B(C$_6$F$_5$)$_3$,[2d] bis(*p*-nitrophenyl) hydrogen phosphate ((O$_2$NC$_6$H$_4$O)$_2$P(O)OH),[2i] (*R*)-3,3′-bis[3,5-bis(trifluoromethyl)phenyl]-1,1′-binaphthyl-2,2′-diyl hydrogen phosphate (**15**), N,N'-bis[3,5-bis(trifluoromethyl)phenyl]thiourea (Schreiner's thiourea; **16**), and the combination of (O$_2$NC$_6$H$_4$O)$_2$P(O)OH or **15** and **16** (see the SI, Table S2).[2i] None of them were effective at mediating the reaction of **1** with octanol. The TFA, copper(II) and borane promoters were instead active on the benzylated iminoglycal carbamate **5**, affording **23** as the only reaction product (Scheme 6). Regrettably, in all three cases the conversion did not progress beyond 40% even using high promotor loadings and prolonged reaction times. The gold catalyst as well as the thiourea **16** remained inefficient. In sharp contrast, the phosphoric acid derivatives (O$_2$NC$_6$H$_4$O)$_2$P(O)OH and **16** in DCM under reflux allowed glycosidation of **5** with octanol to go to completion (TLC) in 24 h. The combined use of the achiral (O$_2$NC$_6$H$_4$O)$_2$P(O)OH promotor and thiourea **16**, previously found advantageous for the activation of trichloroacetimidate glycosyl donnors,[19] did not afford any further improvement in our case. However, the combination of **15** and **16** in 1:4 relative proportion led to a significant increase in the reaction rate, highlighting the benefit of thiourea-induced acid amplification to favor the formation of the acyliminium intermediate and assisting the subsequent attack of the glycosyl acceptor. Following previous observations in the use of this system for glycosylation reactions,[2i, 19] the mechanism depicted in Scheme 7 is proposed. Using the optimized conditions, yields over 80% on the alkyl 2-deoxy-α-glycoside mimics **23**-**25** were achieved with octanol, 3-bromopropan-1-ol and cyclohexanol, respectively. The potential of the methodology to access 2-deoxyiminosugar conjugates and oligosaccharides was further confirmed by using the selectively protected serine and monosaccharide derivatives **17**, **18** and **19**,[20] **20**,[21] respectively, as acceptors: the corresponding glycopeptide and disaccharide adducts **26**, **27** and **28**, **29** were thus obtained in about 50% yield. The choice of protecting groups is important. Thus, 1,2:5,6-diisopropylidene-α-D-glucofuranose (**21**) underwent concomitant rearrangement to the 1,2:3,5-diisopropylidene isomer under the reaction conditions, affording an inseparable mixture of the α(1→3) and α(1→6) disaccharide mimetics **30** and **31**. The 2,3,6-tri-*O*-benzoyl-α-D-galactopyranoside derivative **22**[22] provided the corresponding α(1→4)-linked pseudodisaccharide **32**, which could be separated from the excess of **22** after catalytic (NaOMe/MeOH) debenzoylation (→**33**). Finally, the suitability of **15**/**16** cooperative catalysis to access 2-deoxythioglycosides was investigated. No reaction was observed in the case of the acetylated iminoglycal **1** and octanethiol. However, the benzylated precursor **5** afforded the expected octyl 2-deoxy-α-thioglycoside **34** in 85% yield (Scheme 6).

Scheme 6. Synthesis of 2-Deoxynojirimycin *O*- and *S*-Glycosides by Cooperative Organocatalysis.



Scheme 7. Proposed Acid Amplification Mechanism in Cooperative Organocatalysis.



It is worth highlighting that no β-liked derivatives were detected in the reactions depicted in Schemes 2, 4, 5 and 6 (see also the SI, Tables S1 ans S2), even after short reaction times. In previous work regarding the synthesis of thioglycosides from sp^2-iminosugar (not 2-deoxy) donors, only in a single case the β-anomer could be isolated, though in a very minor proportion (α:β 20:1).[11a] In such case, the NMR data supported that the piperidine ring adopted a boat conformation with the β-anomeric group in pseudoaxial disposition to fit the anomeric effect. Further on, computational calculations supported that formation of sp^2-iminosugar α-*O*-glycosides, which can fulfil the anomeric effect in the more stable chair conformation, through acyliminium intermediates is both kinetically and thermodynamically favored over the corresponding β-*O*-glycosides.[12] We can thus reasonably assume that in the 2-deoxy series here reported the situation is similar and that once generated the acyliminium cation from the glycal precursor, the extremely strong anomeric effect stabilizes both the transition state leading to the α-anomer and the final 2-deoxy α-glycoside.

CONCLUSIONS

In summary, we have achieved the synthesis of a series of 2-deoxynojirimycin (thio)glycosides, the first representatives of the iminosugar-type 2-deoxyglycoside mimetics. Unlike previous attempts using monocyclic iminoglycal precursors, which led to 2,3-unsaturated products, the reaction of bicyclic iminoglycal carbamates (sp^2-iminoglycals) with thiols or alcohols enables efficient access to the target N,S- or N,O-acetals, upon activation with CAN or by cooperative catalysis between the chiral (*R*)-BINOL phosphoric acid derivative **15** and Schreiner's thiourea **16**, under conditions that prevent intramolecular rearrangements. The two methods are complementary: CAN activation tolerates acetate or benzyl protecting groups in the sp^2-iminoglycal, but is restricted to thiol partners, whereas cooperative organocatalysis is equally efficient for thiols or alcohols, but is incompatible with ester protecting groups in the iminoglycal substrate. In all cases, we believe that the reaction proceeds via the corresponding short-lived N-acyliminium ion intermediate that is rapidly trapped by the SH or OH nucleophile under strict control of the anomeric effect, affording exclusively the α-*S*- or *O*-glycosidic linkage. Altogether, our results open new avenues for the synthesis of 2-deoxyglycoside mimics resistant to acid-mediated or enzymatic hydrolysis.

EXPERIMENTAL SECTION

Materials and General Methods. Reagents and solvents were purchased from commercial sources and used without further purification. Optical rotations were measured with a JASCO P-2000 Polarimeter, using a sodium lamp (λ = 589 nm) at 22 ˚C in 1 cm or 1 dm tubes. ^{1}H (^{13}C) NMR experiments were performed at 300 (75.5), 400 (100.1) and 500 (125.7) MHz. 2-D COSY, HSQC and 1D-TOCSY experiments were carried out to assist on signal assignment. For ESI mass spectra, 0.1 pm sample concentrations were used, the mobile phase consisting of 50% aq MeCN at 0.1 mL/min. Thin-layer chromatography was performed on precoated TLC plates, silica gel 30F-245, with visualization by UV light and by carring with 10% H_2SO_4 or 0.2% w/v cerium (IV) sulphate-5% ammonium molybdate in 2 M H_2SO_4 or 0.1% ninhydrin in EtOH. Column chromatography was performed on Silica Gel 60 AC.C (63-200 mm) Sigma Aldrich and Geduran Si 60 Merck (40-63 mm). All com-

pounds were purified to ≥95% purity as determined by elemental microanalysis results obtained on a CHNS-TruSpect® Micro elemental analyzer (Instituto de Investigaciones Químicas de Sevilla, Spain) from vacuum-dried samples. The analytical results for C, H, N and S were within ±0.4 of the theoretical values. Conventional deacetylation was conducted by addition of NaOMe (0.1 eq/Ac mol) in MeOH at room temperature, followed by neutralization with solid CO_2, evaporation of the solvent and purification by column chromatography. The starting derivatives 3,4-di-*O*-acetyl-5*N*,6*O*-(oxomethylidene)nojirimycin iminoglycal (**1**),[12] methyl 2,3,4-tri-*O*-acetyl-6-thio-α-D-glucopyranoside (**6**),[23] Fmoc-Ser-O^{t}Bu (**18**),[24] methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (**19**),[21] 1,2-*O*-isopropylidene-5,6-*O*-(*o*-xylylene)-α-D-glucofuranose (**20**),[18] and methyl 2,3,6-tri-*O*-benzoyl-α-D-galactopyranoside (**22**)[22] were prepared according to previously reported protocols.

3,4-Di-*O*-benzyl-5*N*,6*O*-oxomethylidenenojirimycin Iminoglycal (5). To a solution of iminoglycal **1** (193 mg, 0.76 mmol) in MeOH (4 mL), NaOMe (1 M) (152 μL, 0.152 mmol) was added and the reaction mixture was stirred for 20 min, neutralized with solid CO_2 and concentrated under reduced pressure. The resulting residue was purified by column chromatography (EtOAc) to yield the fully unprotected iminoglycal, namely 5*N*,6*O*-oxomethylidenenojirimycin iminoglycal. Yield: 125 mg (96%). R_f 0.23 (9:1 EtOAc-cyclohexane). $[\alpha]_D$ +73.7 (*c* 1.0 in MeOH). ^{1}H NMR (300 MHz, CD_3OD) δ 6.50 (dd, 1 H, $J_{1,2}$ = 7.8 Hz, $J_{1,3}$ = 2.1 Hz, H-1), 4.99 (dd, 1 H, $J_{2,3}$ = 2.1 Hz, H-2), 4.64 (t, 1 H, $J_{6a,6b}$ = $J_{5,6a}$ = 9.0 Hz, H-6a), 4.28-4.19 (m, 2 H, H-3, H-6b), 4.00 (bq, 1 H, $J_{4,5}$ = $J_{5,6b}$ = 9.0 Hz, H-5), 3.55 (dd, 1 H, $J_{3,4}$ = 7.8 Hz, H-4). ^{13}C NMR (75.5 MHz, CD_3OD) δ 155.9 (CO), 122.0 (C-1), 112.8 (C-2), 74.4 (C-4), 72.0 (C-3), 69.1 (C-6), 56.8 (C-5). ESIMS: *m/z* 194.0 $[M + Na]^+$. Anal. Calcd for $C_7H_9NO_4$: C, 49.12; H, 5.30; N, 8.18. Found: C, 49.19; H, 5.54; N, 7.90.

To a solution of the above 5*N*,6*O*-oxomethylidenenojirimycin iminoglycal (130 mg, 0.76 mmol) in dry DMF (4 mL) under Ar atmosphere, NaH (95%, 91 mg, 3.80 mmol) was added at 0 ºC and the mixture was stirred for 10 min. Benzyl bromide (362 μL, 3.04 mmol) was then added dropwise and the reaction mixture was stirred for 17 h. Water (20 mL) was then added and the aqueous phase was extracted with Et_2O (5 x 30 mL), dried ($MgSO_4$) and concentrated under reduced pressure. The resulting residue was purified by column chromatography (1:3 EtOAc-cyclohexane). Yield: 200 mg (75%). R_f 0.76 (1:1 EtOAc-cyclohexane). $[\alpha]_D$ +45.2 (*c* 1.0 in DCM). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50-7.20 (m, 10 H, Ph), 6.60 (dd, 1 H, $J_{1,2}$ = 7.8 Hz, $J_{1,3}$ = 1.5 Hz, H-1), 5.13 (dd, 1 H, $J_{2,3}$ = 2.1 Hz, H-2), 4.94 (d, 1 H, $^2J_{H,H}$ = 11.7 Hz, OC*H*Ph), 4.76 (d, 1 H, $^2J_{H,H}$ = 11.7 Hz, OC*H*Ph), 4.71 (d, 1 H, OC*H*Ph), 4.66 (d, 1 H, OC*H*Ph), 4.48 (dd, 1 H, $J_{6a,6b}$ = 8.7 Hz, $J_{5,6a}$ = 7.8 Hz, H-6a), 4.42 (dt, 1 H, $J_{3,4}$ = 7.5 Hz, H-3), 4.03-3.91 (m, 1 H, H-5), 3.80 (t, 1 H, $J_{5,6b}$ = 8.7 Hz, H-6b), 3.68 (dd, 1 H, $J_{4,5}$ = 10.0 Hz, H-4). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 153.4 (CO), 137.8-127.9 (OCH_2*Ph*), 122.2 (C-1), 107.3 (C-2), 79.0 (C-3), 77.6 (C-4), 74.0, 71.4 (CH_2Ph), 67.6 (C-6), 54.4 (C-5). ESIMS: *m/z* 374.2 $[M + Na]^+$. Anal. Calcd for $C_{21}H_{21}NO_4$: C, 71.78; H, 6.02; N, 3.99. Found: C, 71.90; H, 6.19; N, 3.81.

Thioglycosylation Procedure Using BF_3·Et_2O. To a solution of 3,4-di-*O*-acetyl-5*N*,6*O*-(oxomethylidene)nojirimycin glucal (**1**; 54 mg, 0.21 mmol) in dry DCM (5 mL) under Ar atmosphere, 1-octanethiol (42 μL, 0.24 mmol, 1.15 eq) and BF_3·Et_2O (95 μL, 0.76 mmol, 3.6 eq) were added at 0 ºC and the reaction was stirred for 60 min at RT, diluted with DCM, washed with aqueous $NaHCO_3$ (2 x 10 mL), brine (10 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting mixture was purified by column chromatography (1:5 EtOAc-cyclohexane) to afford compounds **2-4** as amorphous solids.

(1R)-3,4-Di-O-acetyl-1-octylthio-5N,6O-oxomethylidene-2-deoxynojirimycin (2). Yield: 11 mg (13%). R_f 0.53 (1:1 EtOAc-cyclohexane). $[\alpha]_D$ +71.3 (*c* 1.1 in DCM). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.28 (dd, 1 H, $J_{1,2a}$ = 5.7 Hz, $J_{1,2b}$ = 1.2 Hz, H-1), 5.22 (ddd, 1 H, $J_{2a,3}$ = 11.7 Hz, $J_{3,4}$ = 9.3 Hz, $J_{2b,3}$ = 4.8 Hz, H-3), 4.80 (t, 1 H, $J_{4,5}$ = 9.3 Hz, H-4), 4.37 (t, 1 H, $J_{6a,6b}$ = $J_{5,6a}$ = 8.5 Hz, H-6a), 4.20 (dd, 1 H, $J_{5,6b}$ = 6.0 Hz, H-6b), 4.09 (ddd, 1 H, H-5), 2.57 (ddd, 1 H, $^2J_{H,H}$ = 12.9 Hz, $^3J_{H,H}$ = 8.1 Hz, $^3J_{H,H}$ = 6.3 Hz, SCH_2), 2.43 (ddd, 1 H, SCH_2), 2.20 (ddd, 1 H, $J_{2a,2b}$ = 13.2 Hz, H-2b), 2.00-1.96 (2 s, 6 H, MeCO), 2.05-1.93 (m, 1 H, H-2a), 1.66-1.10 (m, 12 H, CH_2), 0.81 (t, 3 H, $^3J_{H,H}$ = 7.0 Hz, CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 170.2-169.7 (CO ester), 155.7 (CO carbamate), 73.5 (C-4), 68.9 (C-3), 66.2 (C-6), 54.4 (C-1), 51.9 (C-5), 34.6 (C-2), 31.7-22.6 (CH_2), 20.8-20.6 (*Me*CO), 14.1 (CH_3). ESIMS: *m/z* 424.2 $[M + Na]^+$. Anal. Calcd for $C_{19}H_{31}NO_6S$: C, 56.84; H, 7.78; N, 3.49; S, 7.98. Found: C, 56.98; H, 7.85; N, 3.57; S, 7.72.

(1R)-4-O-Acetyl-1,3-di-octylthio-5N,6O-oxomethylidene-2-deoxynojirimycin (3). Yield: 35 mg (34%). R_f 0.61 (1:4 EtOAc-cyclohexane). $[\alpha]_D$ +36.3 (*c* 1.0 in DCM). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.28 (d, 1 H, $J_{1,2a}$ = 5.0 Hz, H-1), 4.70 (t, 1 H, $J_{4,5}$ = $J_{3,4}$ = 9.6 Hz, H-4), 4.40 (t, 1 H, $J_{6a,6b}$ = $J_{5,6a}$ = 8.7 Hz, H-6a), 4.19 (dd, 1 H, $J_{5,6b}$ = 6.6 Hz, H-6b), 4.06 (td, 1 H, H-5), 3.01 (ddd, 1 H, $J_{2a,3}$ = 13.0 Hz, $J_{2b,3}$ = 3.9 Hz, H-3), 2.64 (ddd, 1 H, $^2J_{H,H}$ = 12.9 Hz, $^3J_{H,H}$ = 8.1 Hz, $^3J_{H,H}$ = 6.1 Hz, SCH_2), 2.56-2.45 (m, 3 H, SCH_2), 2.27 (dd, 1 H, $J_{2a,2b}$ = 14.0 Hz, H-2b), 2.12 (s, 3 H, MeCO), 2.16-2.07 (m, 1 H, H-2a), 1.74-1.19 (m, 24 H, CH_2), 0.87 (t, 6 H, $^3J_{H,H}$ = 6.5 Hz, CH_3). ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 170.2 (CO ester), 155.8 (CO carbamate), 74.2 (C-4), 66.6 (C-6), 55.5 (C-1), 53.0 (C-5), 42.5 (C-3), 37.3 (C-2), 31.8 (SCH_2), 31.1-22.6 (CH_2), 20.8 (*Me*CO), 14.1 (CH_3). ESIMS: *m/z* 510.1 $[M + Na]^+$. Anal. Calcd for $C_{25}H_{45}NO_4S_2$: C, 61.56; H, 9.30; N, 2.87; S, 13.15. Found: C, 61.39; H, 8.99; N, 2.84; S, 12.82

(1R)-4-O-Acetyl-1,3-di-octylthio-5N,6O-oxomethylidene-2-deoxyallonojirimycin (4). Yield: 6 mg (6%). R_f 0.53 (1:2 EtOAc-cyclohexane). $[\alpha]_D$ +65.5 (*c* 1.0 in DCM). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.22 (dd, 1 H, $J_{1,2a}$ = 7.0 Hz, $J_{1,2b}$ = 2.5 Hz, H-1), 4.75 (dd, 1 H, $J_{4,5}$ = 9.0 Hz, $J_{3,4}$ = 4.0 Hz, H-4), 4.46 (t, 1 H, $J_{6a,6b}$ = $J_{5,6a}$ = 9.0 Hz, H-6a), 4.32 (td, 1 H, $J_{5,6b}$ = 5.5 Hz, H-5), 4.15 (dd, 1 H, H-6b), 3.38 (q, 1 H, $J_{2a,3}$ = $J_{2b,3}$ = 4.0 Hz, H-3), 2.68 (ddd, 1 H, $^2J_{H,H}$ = 12.8 Hz, $^3J_{H,H}$ = 8.3 Hz, $^3J_{H,H}$ = 6.1 Hz, SCH), 2.59-2.46 (m, 4 H, SCH_2, SCH, H-2a), 2.22 (ddd, 1 H, $J_{2a,2b}$ = 15.0 Hz, H-2b), 2.11 (s, 3 H, MeCO), 1.70-1.20 (m, 24 H, CH_2), 0.88 (t, 3 H, $^3J_{H,H}$ = 6.7 Hz, CH_3), 0.87 (t, 3 H, $^3J_{H,H}$ = 6.7 Hz, CH_3). ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 170.3 (CO ester), 156.1 (CO carbamate), 74.5 (C-4), 66.1 (C-6), 55.0 (C-1), 49.6 (C-5), 42.8 (C-3), 35.2 (C-2), 34.2-22.6 (CH_2), 20.8 (*Me*CO), 14.1 (CH_3). ESIMS: *m/z* 510.5 $[M + Na]^+$. HRFABMS Calcd for $C_{25}H_{45}NO_4S_2Na$ $[M + Na]^+$ 510.2688, found 510.2689.

General Thioglycosylation Procedure Using CAN. To a stirred solution of the di-*O*-acetyl- or di-*O*-benzyl glucal (**1** or **5**; 0.20 mmol) and CAN (0.5 eq) in dry MeCN (2 mL) under Ar atmosphere, the corresponding thiol derivative (0.40 mmol, 2.0 eq) was added and the reaction mixture was stirred for 24-48 h at RT (see the SI Table S1, entries 1-7, for a full account of the assayed reaction conditions). Et_2O (20 mL) and H_2O (20 mL) were then added and the aqueous phase was extracted with Et_2O (2 x 10 mL) and the organic layer was dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography using the solvent indicated in each case

*(1R)-3,4-Di-O-acetyl-1-octylthio-5N,6O-oxomethylidene-2-deoxynojirimycin (**2**)*. Column chromatography (1:4 → 1:2 EtOAc-cyclohexane). Yield: 152 mg (68%).

*(1R)-3,4-Di-O-acetyl-1-dodecylthio-5N,6O-oxomethylidene-2-deoxynojirimycin (**7**)*. Column chromatography (1:3 → 1:2 EtOAc-cyclohexane). Yield: 59 mg (74%). R_f 0.62 (1:1 EtOAc-cyclohexane). $[\alpha]_D$ +65.3 (*c* 1.0 in DCM). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.30 (dd, 1 H, $J_{1,2a}$ = 5.6 Hz, $J_{1,2b}$ = 1.5 Hz, H-1), 5.25 (ddd, 1 H, $J_{2a,3}$ = 11.7 Hz, $J_{3,4}$ = 9.5 Hz, $J_{2b,3}$ = 4.8 Hz, H-3), 4.83 (t, 1 H, $J_{4,5}$ = 9.5 Hz, H-4), 4.40 (dd, 1 H, $J_{6a,6b}$ = 9.0 Hz, $J_{5,6a}$ = 8.4 Hz, H-6a), 4.23 (dd, 1 H, $J_{5,6b}$ = 6.0 Hz, H-6b), 4.11 (ddd, 1 H, H-5), 2.70-2.40 (m, 2 H, SCH_2), 2.23 (ddd, 1 H, $J_{2a,2b}$ = 13.2 Hz, H-2b), 2.04-1.99 (2 s, 6 H, MeCO), 2.10-1.95 (m, 1 H, H-2a), 1.70-1.10 (m, 20 H, CH_2), 0.84 (t, 3 H, $^3J_{H,H}$ = 6.7 Hz, CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 170.2-169.7 (CO ester), 155.6 (CO carbamate), 73.5 (C-4), 68.9 (C-3), 66.1 (C-6), 54.4 (C-1), 51.9 (C-5), 34.6 (C-2), 31.9-22.6 (CH_2), 20.8-20.6 (*Me*CO), 14.1 (CH_3). ESIMS: *m/z* 480.2 $[M + Na]^+$. Anal. Calcd for $C_{23}H_{39}NO_6S$: C, 60.37; H, 8.59; N, 3.06; S, 7.01. Found: C, 60.49; H, 8.71; N, 2.90; S, 6.84.

*(1R)-3,4-Di-O-acetyl-1-(methyl-2,3,4-tri-O-acetyl-6-thio-α-D-glucopyranosid-6-yl)-5N,6O-oxomethylidene-2-deoxynojirimycin (**8**)*. Column chromatography (1:4 → 1:2 EtOAc-cyclohexane). Yield: 111 mg (82%). R_f 0.18 (1:1 EtOAc-cyclohexane). $[\alpha]_D$ +110.3 (*c* 1.5 in DCM). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.44 (t, 1 H, $J_{2,3}$ = $J_{3,4}$ = 9.6 Hz, H-3), 5.37 (bd, 1 H, $J_{1',2a'}$ = 4.8 Hz, H-1'), 5.22 (ddd, 1 H, $J_{2a',3'}$ = 11.7 Hz, $J_{3',4'}$ = 9.6 Hz, $J_{2b',3'}$ = 4.8 Hz, H-3'), 5.04 (t, 1 H, $J_{4,5}$ = 9.6 Hz, H-4), 4.92-4.78 (m, 3 H, H-1, H-2, H-4'), 4.50-4.40 (m, 1 H, H-6a'), 4.25-4.11 (m, 2 H, H-5', H-6b'), 3.99 (ddd, 1 H, $J_{5,6b}$ = 6.0 Hz, $J_{5,6a}$ = 3.3 Hz, H-5), 3.41 (s, 3 H, OMe), 3.03 (dd, 1 H, $J_{6a,6b}$ = 14.0 Hz, H-6a), 2.63 (dd, 1 H, H-6b), 2.28 (ddd, 1 H, $J_{2a',2b'}$ = 13.5 Hz, $J_{1,2b}$ = 1.5 Hz, H-2b'), 2.06-1.98 (5 s, 15 H, MeCO), 2.11-2.04 (m, 1 H, H-2a'). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 170.3-169.7 (CO ester), 156.0 (CO carbamate), 96.6 (C-1), 73.6 (C-4'), 70.8 (C-2), 70.6 (C-4), 70.0 (C-3), 68.7 (C-3'), 68.3 (C-5), 66.5 (C-6'), 55.5 (OMe), 55.0 (C-1'), 51.9 (C-5'), 34.6 (C-2'), 32.0 (C-6), 20.8-20.6 (*Me*CO). ESIMS: *m/z* 614.2 $[M + Na]^+$. Anal. Calcd for $C_{24}H_{33}NO_{14}S$: C, 48.73; H, 5.62; N, 2.37; S, 5.42. Found: C, 48.87; H, 5.73; N, 2.12; S, 5.19.

*(1R)-3,4-Di-O-benzyl-1-dodecylthio-5N,6O-oxomethylidene-2-deoxynojirimycin (**9**)*. Column chromatography (1:4 EtOAc-cyclohexane). Yield: 18 mg (68%). R_f 0.50 (1:3 EtOAc-cyclohexane). $[\alpha]_D$ +93.6 (*c* 1.0 in DCM). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29-7.19 (m, 10 H, Ph), 5.21 (d, 1 H, $J_{1,2a}$ = 6.0 Hz, H-1), 4.89 (d, 1 H, $^2J_{H,H}$ = 11.4 Hz, OC*H*$_2$Ph), 4.61 (d, 1 H, $^2J_{H,H}$ = 11.4 Hz, OC*H*$_2$Ph), 4.58 (d, 1 H, OC*H*$_2$Ph), 4.55 (d, 1 H, OC*H*$_2$Ph), 4.29 (t, 1 H, $J_{6a,6b}$ = $J_{5,6a}$ = 8.5 Hz, H-6a), 3.94-3.80 (m, 2 H, H-3, H-5), 3.75 (dd, 1 H, $J_{5,6b}$ = 6.0 Hz, H-6b), 3.21 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 9.0 Hz, H-4), 2.54 (ddd, 1 H, $^2J_{H,H}$ = 12.9 Hz, $^3J_{H,H}$ = 8.1 Hz, $^3J_{H,H}$ = 6.0 Hz, SCH_2), 2.38 (ddd, 1 H, SCH_2), 2.21 (ddd, 1 H, $J_{2a,2b}$ = 13.5 Hz, $J_{2b,3}$ = 4.5 Hz, $J_{1,2b}$ = 1.5 Hz, H-2b), 1.81 (ddd, 1 H, $J_{2a,3}$ = 11.7 Hz, H-2a), 1.60-1.10 (m, 20 H, CH_2), 0.81 (t, 3 H, $^3J_{H,H}$ = 7.0 Hz, CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 156.0 (CO), 137.9-127.8 (Ph), 81.6 (C-4), 78.2 (C-3), 74.8, 72.2 (*C*H$_2$Ph), 66.6 (C-6), 54.9 (C-1), 52.5 (C-5), 35.0 (C-2), 31.9-22.7 (CH_2), 14.1 (CH_3). ESIMS: *m/z* 576.4 $[M + Na]^+$. Anal. Calcd for $C_{33}H_{47}NO_4S$: C, 71.57; H, 8.55; N, 2.53; S, 5.79. Found: C, 71.38; H, 8.30; N, 2.22; S, 5.57.

Glycosylation Procedure Using CAN. To a stirred solution of the sp^2-iminoglycal derivative **1** (111 mg, 0.43 mmol) and CAN (236 mg, 0.43 mmol, 1.0 eq) in dry MeCN (3 mL) under Ar atmosphere, 1-octanol (0.34 mL, 2.15 mmol, 5.0 eq) was added and the reaction mixture was stirred for 48 h at RT (see the SI Table S2, entry 10). Et_2O (20 mL) and H_2O (20 mL) were next added, the aqueous phase was extracted with Et_2O (2 x 10 mL) and the organic layer was dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography (1:3 EtOAc-cyclohexane) to afford the 1-*O*-octyl-2-nitrate ester **12** (15 mg; 8%) together with a mixture of **10** and **11** in a 3:1 ratio. Conventional *O*-deacetylation reaction of the later fraction as described in General Methods and column chromatography (1:2 EtOAc-cyclohexane) of the resulting fully unprotected product afforded the pure diols **13** (33%) and **14** (6**%)**.

(*1R)-3,4-Di-O-acetyl-2-nitrate-1-O-octyl-5N,6O-oxomethylidenemannojirimycin (**12**)*. Yield: 15 mg (8%). R_f 0.35 (1:2 EtOAc-cyclohexane). $[\alpha]_D$ -5.2 (*c* 1.3 in DCM). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.51-5.43 (m, 2H, H-2, H-3), 5.23 (d, 1H, $J_{1,2}$ = 2.1 Hz, H-1), 5.12 (t, 1H, $J_{3,4}$ = $J_{4,5}$ = 9.5 Hz, H-4), 4.46 (dd, 1H, $J_{6a,6b}$ = 9.0 Hz, $J_{5,6a}$ = 8.0 Hz, H-6a), 4.34 (dd, 1H, $J_{5,6b}$ = 6.6 Hz, H-6b), 3.90 (ddd, 1 H, H-5), 3.64-3.50 (m, 2H, OCH_2), 2.07-2.06 (2 s, 6H, MeCO), 1.70-1.20 (m, 12 H, CH_2), 0.88 (t, 3 H, $^3J_{H,H}$ = 7.0 Hz, CH_3). ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 169.9-169.6 (CO ester), 156.1 (CO carbamate), 79.6 (C-1), 77.2 (C-2), 69.7 (C-4), 69.3 (OCH_2), 68.0 (C-3), 66.8 (C-6), 52.5 (C-5), 31.8-22.6 (CH_2), 20.5 (*Me*CO), 14.1 (CH_3). ESIMS: *m/z* 469.2 $[M + Na]^+$. ESI-HRMS Calcd for $C_{19}H_{30}N_2O_{10}Na$ $[M + Na]^+$ 469.1793, found 469.1794.

(*1R)-1-O-Octyl-5N,6O-oxomethylidene-2-deoxynojirimycin (**13**)*. Yield: 43 mg (33%, two steps). R_f 0.30 (2:1 EtOAc-cyclohexane). $[\alpha]_D$ +36.3 (*c* 1.4 in MeOH). ^{1}H NMR (300 MHz, CD_3OD) δ 5.09 (d, 1 H, $J_{1,2a}$ = 3.6 Hz, $J_{1,2b}$ = 1.5 Hz, H-1), 4.54 (t, 1 H, $J_{6a,6b}$ = $J_{5,6a}$ = 9.0 Hz, H-6a), 4.26 (dd, 1 H, $J_{5,6b}$ = 6.0 Hz, H-6b), 3.79 (ddd, 1 H, $J_{2a,3}$ = 11.7 Hz, $J_{3,4}$ = 9.0 Hz, $J_{2b,3}$ = 4.5 Hz, H-3), 3.69 (td, 1 H, $J_{4,5}$ = 9.0 Hz, H-5), 3.55-3.35 (m, 2 H, OCH_2), 3.22 (t, 1 H, H-4), 2.15 (ddd, 1 H, $J_{2a,2b}$ = 13.5 Hz, H-2b), 1.66-1.50 (m, 3 H, H-2a, CH_2), 1.45-1.20 (m, 10 H, CH_2), 0.91 (t, 3 H, $^3J_{H,H}$ = 7.0 Hz, CH_3). ^{13}C NMR (75.5 MHz, CD_3OD) 158.8 (CO), 81.2 (C-1), 77.2 (C-4), 69.6 (C-3), 68.9 (OCH_2), 68.3 (C-6), 55.5 (C-5), 38.4 (C-2), 33.1-23.7 (CH_2), 14.4 (CH_3). ESIMS: *m/z* 324.1 $[M + Na]^+$. Anal. Calcd for $C_{15}H_{27}NO_5S$: C, 59.78; H, 9.03; N, 4.65. Found: C, 59.54; H, 8.87; N, 4.41.

*(1R)-2-Nitrate-1-O-octyl-5N,6O-oxomethylidenenojirimycin (**14**)*. Yield: 11 mg (6% in two steps). R_f 0.29 (2:1 EtOAc-cyclohexane). $[\alpha]_D$ +58.7 (*c* 0.9 in MeOH). ^{1}H NMR (300 MHz, CD_3OD) δ 5.36 (d, 1 H, $J_{1,2}$ = 4.2 Hz, H-1), 4.92 (dd, 1 H, $J_{2,3}$ = 10.0 Hz, H-2), 4.60 (t, 1 H, $J_{6a,6b}$ = $J_{5,6a}$ = 9.0 Hz, H-6a), 4.29 (dd, 1 H, $J_{5,6b}$ = 6.3 Hz, H-6b), 3.79 (t, 1 H, $J_{3,4}$ = 10.0 Hz, H-3), 3.78-3.70 (m, 1 H, H-5), 3.66-3.39 (m, 3 H, H-4, OCH_2), 1.70-1.20 (m, 12 H, CH_2), 0.91 (t, 3 H, $^3J_{H,H}$ = 7.0 Hz, CH_3). ^{13}C NMR (75.5 MHz, CD_3OD) δ 158.4 (CO), 82.0 (C-2), 79.9 (C-1), 75.8 (C-4), 71.0 (C-3), 69.6 (OCH_2), 68.6 (C-6), 54.3 (C-5), 32.9-23.7 (CH_2), 14.0 (CH_3). ESIMS: *m/z* 385.1 $[M + Na]^+$. ESI-HRMS Calcd for $C_{15}H_{26}N_2O_8Na$ $[M + Na]^+$ 385.1581, found 385.1577.

General Glycosylation/Thioglycosylation Procedure by Cooperative Organocatalysis. The benzylated iminoglycal donor **5** (20 mg, 57 μmol) and the corresponding acceptor (86 μmol, 1.5 eq) were placed into a microwave vial under vacuum for 1 h under N_2 atmosphere. A mixture of the BINOL-derived phosphoric acid (R)-**15** (6 μmol) and Schreiner's thiourea **16** (23 μmol) in anhydrous DCM (~1 mL, 0.1 M) were stirred for 30 min and then added to the microwave vial containing the donor and acceptor. The reaction mixture was refluxed for 3-24 h, concentrated under reduced pressure and purified by column chromatography using the solvent indicated in each case (see the SI Table S1, entries 8 and 9, and Table S2 for a full account of the assayed reaction conditions).

*(1R)-3,4-Di-O-benzyl-1-O-octyl-5N,6O-oxomethylidene-2-deoxynojirimycin (**23**)*. Column chromatography (1:6 → 1:4 EtOAc-cyclohexane). Yield: 22 mg (80%). R_f 0.7 (1:2 EtOAc-cyclohexane). $[\alpha]_D$ +44.7 (*c* 1.0 in DCM). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28-7.18 (m, 10 H, Ph), 5.05 (dd, 1 H, $J_{1,2b}$ = 3.7 Hz, $J_{1,2a}$ = 1.8 Hz, H-1), 4.89, 4.58 (2 d, 2 H, $^2J_{H,H}$ = 11.6 Hz, C*H*Ph), 4.63,

4.57 (2 d, 1 H, $^2J_{H,H}$ = 11.4 Hz, C*H*Ph), 4.29 (t, 1 H, $J_{6a,6b}$ = $J_{5,6a}$ = 8.6 Hz, H-6a), 3.90 (m, 1 H, H-3), 3.75 (dd, 1 H, $J_{5,6b}$ = 6.3 Hz, H-6b), 3.70-3.65 (m, 1 H, H-5), 3.38-3.29 (m, 2 H, OCH_2), 3.24 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 9.0 Hz, H-4), 2.30 (ddd, 1 H, $J_{2a,2b}$ = 13.2 Hz, $J_{2a,3}$ = 4.7 Hz, H-2a), 1.54 (ddd, 1 H, $J_{2b,3}$ = 11.2 Hz, H-2b), 1.47-1.43 (m, 1 H, OCH_2CH_2), 1.20 (m, 10 H, CH_2), 0.81 (t, 3 H, $J_{H,H}$ = 7.0 Hz, CH_3). ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 156.7 (CO), 138.4-138.3 (Ph), 128.9-128.0 (Ph), 81.7 (C-4), 79.7 (C-1), 77.9 (C-3), 75.0, 72.4 (*C*H_2Ph), 68.3 (OCH_2), 67.2 (C-6), 53.4 (C-5), 35.3 (C-2), 32.1-23.0 (CH_2), 14.3 (CH_3). ESIMS: *m/z* 504.3 $[M + Na]^+$. ESI-HRMS Calcd for $C_{29}H_{39}NO_5Na$ $[M + Na]^+$ 504.2720, found 504.2716.

*(1R)-3,4-Di-O-benzyl-1-O-(3-bromopropyl)-5N,6O-oxomethylidene-2-deoxynojirimycin (**24**)*. Column chromatography (1:4 EtOAc-hexane). Yield: 21 mg (87%). R_f 0.5 (1:2 EtOAc-cyclohexane). $[\alpha]_D$ +54.3 (*c* 1.0 in DCM). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30-7.18 (m, 10 H, Ph), 5.07 (dd, 1 H, $J_{1,2b}$ = 4.0 Hz, $J_{1,2a}$ = 1.8 Hz, H-1), 4.89, 4.59 (2 d, 2 H, $^2J_{H,H}$ = 11.5 Hz, C*H*Ph), 4.63, 4.59 (2 d, 1 H, $^2J_{H,H}$ = 11.5 Hz, C*H*Ph), 4.30 (t, 1 H, $J_{6a,6b}$ = $J_{5,6a}$ = 8.24 Hz, H-6a), 3.86 (m, 1 H, H-3), 3.76-3.67 (m, 2 H, H-5, H-6b), 3.57 (m, 1 H, OCH_2), 3.44 (m, 1 H, OCH_2), 3.39 (t, 2 H, $J_{H,H}$ = $J_{H,H}$ = 6.7 Hz, CH_2Br), 3.25 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 9.2 Hz, H-4), 2.29 (ddd, 1 H, $J_{2a,2b}$ = 13.2 Hz, $J_{2a,3}$ = 4.7 Hz, H-2a), 2.08-1.99 (m, 1 H, CH_2), 1.98-1.90 (m, 1 H, CH_2), 1.56 (ddd, 1 H, $J_{2b,3}$ = 11.3 Hz, H-2b). ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 156.7 (CO), 138.3-139.1 (Ph), 128.8-127.9 (Ph), 81.5 (C-4), 79.6 (C-1), 77.6 (C-3), 75.0-72.3 (*C*H_2Ph), 67.1 (C-6), 65.0 (OCH_2), 53.4 (C-5), 35.0 (C-2), 32.2 (CH_2), 30.4 (CH_2Br). ESIMS: *m/z* 512.1 $[M + Na]^+$. ESI-HRMS Calcd for $C_{24}H_{28}BrN_4NaO_5$ $[M + Na]^+$ 512.1043, found 512.1036.

*(1R)-3,4-Di-O-benzyl-1-O-(cyclohexyl)-5N,6O-oxomethylidene-2-deoxynojirimycin (**25**)*. Column chromatography (1:30 → 1:20 → 1:10 EtOAc-toluene). Yield: 21 mg (80%). R_f 0.7 (1:2 EtOAc-toluene). $[\alpha]_D$ +41.0 (*c* 1.0 in DCM). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30-7.18 (m, 10 H, Ph), 5.22 (dd, 1 H, $J_{1,2}$ = 4.1 Hz, $J_{1,2a}$ = 1.9 Hz, H-1), 4.90, 4.58 (2 d, 2 H, $^2J_{H,H}$ = 11.6 Hz, C*H*Ph), 4.63, 4.57 (2 d, 1 H, $^2J_{H,H}$ = 11.2 Hz, C*H*Ph), 4.28 (t, 1 H, t, $J_{5,6a}$ = $J_{6a,6b}$ = 8.2 Hz, H-6a), 3.96-3.91 (m, 1 H, H-3), 3.76 (dd, 1 H, $J_{6a,6b}$ = 8.7 Hz, $J_{5,6b}$ = 5.6 Hz, H-6b), 3.73-3.68 (m, 1 H, H-5), 3.34-3.30 (m, 1 H, OCH), 3.24 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 8.9 Hz, H-4), 2.25 (ddd, 1 H, $J_{2a,2b}$ = 13.2 Hz, $J_{2a,3}$ = 4.6 Hz, H-2a), 1.86 (m, 1 H, CH_2), 1.62 (m, 3 H, CH_2), 1.54 (ddd, 1 H, H-2b), 1.43 (m, 1 H, CH_2), 1.18 (m, 4 H, CH_2). ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 156.6 (CO), 138.6-138.4 (Ph), 128.9-128.1 (Ph), 81.9 (C-4), 78.0 (C-3), 77.3 (C-1), 75.2 (*C*H_2Ph), 74.9 (OCH), 72.4 (*C*H_2Ph), 67.1 (C-6), 53.5 (C-5), 35.8 (C-2), 33.6, 31.6, 26.0, 24.4, 24.1 (CH_2). ESIMS: *m/z* 474.2 $[M + Na]^+$. ESI-HRMS Calcd for $C_{27}H_{33}NO_5Na$ $[M + Na]^+$ 474.2251, found 474.2244.

*(1R)-3,4-Di-O-benzyl-1-O-(Boc-l-Ser-OMe)-5N,6O-oxomethylidene-2-deoxynojirimycin (**26**)*. Column chromatography (1:4 → 1:3 → 1:2 EtOAc-cyclohexane). Yield: 11 mg (67%). R_f 0.5 (1:2 EtOAc-hexane). $[\alpha]_D$ +80.0 (*c* 1.0 in DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.26 (m, 10 H, Ph), 5.20 (d, 1 H, $J_{NH,CH}$ = 9.3Hz, NH), 5.11 (dd, 1 H, dd, 1 H, $J_{1,2b}$ = 4.0 Hz, $J_{1,2a}$ = 1.8 Hz, H-1), 4.96, 4.64 (2 d, 2 H, $^2J_{H,H}$ = 11.3 Hz, C*H*Ph), 4.68, 4.65 (2 d, 1 H, $^2J_{H,H}$ = 11.5 Hz, C*H*Ph), 4.45 (d, 1 H, C*H*NH), 4.36 (t, 1 H, $J_{6a,6b}$ = $J_{5,6a}$ = 8.6 Hz, H-6a), 3.88 (m, 1 H, H-3), 3.83-3.78 (m, 2 H, OCH_2, H-6b), 3.76 (s, 3 H, OCH_3), 3.73-3.68 (m, 2 H, H-5, OCH_2), 3.29 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 9.1 Hz, H-4), 2.30 (ddd, 1 H, $J_{2a,2b}$ = 13.3 Hz, $J_{2a,3}$ = 4.7 Hz, H-2a), 1.63-1.59 (ddd, 1 H, H-2b), 1.46 (s, 9 H, CH_3). ^{13}C NMR (101.1 MHz, $CDCl_3$) δ 171.2 (CO ester), 156.5, 155.6 (CO carbamate), 138.2 (Ph), 128.9-128.1 (Ph), 81.4 (C-4), 80.37 (C-1), 77.5 (C-3), 75.1-72.4 (*C*H_2Ph), 68.4 (OCH_2), 67.1 (C-6), 54.0 (CHNH), 53.3 (C-5), 52.9 (OCH_3), 34.9 (C-2), 28.6 (CH_3). ESIMS: *m/z* 593.3 $[M + Na]^+$. ESI-HRMS Calcd for $C_{30}H_{38}N_2O_9Na$ $[M + Na]^+$ 593.2470, found 593.2456.

*(1R)-3,4-Di-O-benzyl-1-O-(Fmoc-l-Ser-O^{t}Bu)-5N,6O-oxomethylidene-2-deoxynojirimycin (**27**)*. Column chromatography (1:6 → 1:4 EtOAc-cyclohexane). Yield: 21 mg (40%). R_f 0.4 (1:2 EtOAc-cyclohexane). $[\alpha]_D$ +36.1 (*c* 1.0 in DCM). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (d, 2 H, *J* = 7.8 Hz, Fmoc), 7.53 (d, 2 H, *J* = 7.0 Hz, Fmoc), 7.32-7.18 (m, 14 H, Fmoc, Ph), 5.47 (d, 1 H, $J_{NH,CH}$ = 7.6 Hz, NH), 5.07 (m, 1 H, H-1), 4.87, 4.57 (2 d, 2 H, $^2J_{H,H}$ = 11.7 Hz, C*H*Ph), 4.58-4.56 (2 d, 1 H, $^2J_{H,H}$ = 11.6 Hz, C*H*Ph), 4.37-4.27 (m, 3 H, C*H*NH, CH_2Fmoc), 4.22 (t, 1 H, $J_{6a,6b}$ = $J_{5,6a}$ = 8.4 Hz, H-6a), 4.17 (t, 1 H, $J_{H,H}$ = 7.3 Hz, CHFmoc) 3.85-3.81 (m, 1 H, H-3), 3.85-3.76 (m, 2 H, OCH_2), 3.72-3.69 (m, 1 H, H-6b), 3.66-3.62 (m, 1 H, H-5), 3.22 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 8.8 Hz, H-4), 2.21 (m, 1 H, H-2a), 1.56-1.51 (m, 1 H, H-2b), 1.42 (s, 9 H, CH_3). ^{13}C NMR (125.75 MHz, $CDCl_3$) δ 167.2 (CO ester), 156.5, 156.1 (CO carbamate), 144.2, 141.6 (Fmoc), 138.2 (Ph), 132.6-127.4 (Ph), 125.4, 120.3 (Fmoc), 83.0 (C-4), 81.5 (C-1), 80.6 (C-3), 75.1-72.5 (*C*H_2Ph), 68.9 (OCH_2), 67.6 (*C*H_2Fmoc), 67.2 (C-6), 55.0 (CHNH), 53.5 (C-5), 47.5 (*C*HFmoc), 35.0 (C-2), 28.4 (CH_3). ESIMS: *m/z* 757.3 $[M + Na]^+$. ESI-HRMS Calcd for $C_{43}H_{48}N_2NaO_9$ $[M + Na]^+$ 757.3096, found 757.3087.

*(1R)-3,4-Di-O-benzyl-1-O-(methyl 2,3,4-tri-O-benzyl-α-D-glucopyranosyd-6-yl)- 5N,6O-oxomethylidene-2-deoxynojirimycin (**28**)*. Column chromatography (1:6 EtOAc-toluene). Yield: 26 mg (57%). R_f 0.5 (1:2 EtOAc-toluene). $[\alpha]_D$ +60.8 (*c* 1.0 in DCM). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24-7.15 (m, 15 H, Ph), 5.10 (dd, 1 H, $J_{1',2'}$ = 3.7 Hz, $J_{1',2a'}$ = 1.8 Hz, H-1'), 4.92, 4.72 (2 d, 2 H, $^2J_{H,H}$ = 10.6 Hz, C*H*Ph), 4.86, 4.42 (2 d, 1 H, $^2J_{H,H}$ = 11.6 Hz, C*H*Ph), 4.84, 4.52 (2 d, 2 H, $^2J_{H,H}$ = 11.6 Hz, C*H*Ph), 4.72,4.61 (d, 1 H, $^2J_{H,H}$ = 12.8 Hz, CHPh), 4.60, 4.53 (d, 1 H, $^2J_{H,H}$ = 11.9 Hz, CHPh), 4.54 (d, 1 H, $J_{1,2}$ = 3.6 Hz, H-1), 3.92 (t, 1 H, $J_{2,3}$ = $J_{3,4}$ = 8.9 Hz, H-3), 3.92 (t, 1 H, $J_{5,6a}$ = $J_{6a,6b}$ = 9.3 Hz, H-6a), 3.82-3.76 (m, 1 H, H-3'), 3.66 (m, 1 H, H-5), 3.63-3.57 (m, 2 H, H-6a', H-6b), 3.51 (dd, 1H, $J_{5',6b'}$ = 5.87 Hz, H-6b'), 3.48-3.44 (m, 2 H, H-2, H-5'), 3.39 (t, 1 H, $J_{4,5}$ = 9.4 Hz, H-4), 3.28 (s, 3 H, OMe), 3.17 (t, 1H, $J_{4',5'}$ = 9.1 Hz, H-4'), 2.32 (ddd, 1 H $J_{2a',2b'}$ = 13.4 Hz, $J_{2a',3'}$ = 4.7 Hz, H-2a'), 1.52 (ddd, 1 H, H-2b'). ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 156.5 (CO), 138.1-137.9 (Ph), 128.5-127.2 (Ph), 98.3 (C-1), 82.5 (C-3), 81.7 (C-4'), 80.4 (C-1'), 80.3 (C-2), 78.0 (C-4),77.3 (C-3'), 76.0-72.3 (*C*H_2Ph), 69.9 (C-5), 67.1 (C-6'), 66.9 (C-6), 55.5 (OMe), 53.3 (C-5'), 35.0 (C-2'). ESIMS: *m/z* 838.4 $[M + Na]^+$. ESI-HRMS Calcd for $C_{49}H_{53}NNaO_{10}$ $[M + Na]^+$ 838.3526, found 838.3562.

*(1R)-3,4-di-O-benzyl-1-O-(1,2-O-isopropylidene-5,6-O-(o-xylylene)-α-D-glucofuranos-3-yl)-5N,6O-oxomethylidene-2-deoxynojirimycin (**29**)*. Column chromatography (1:6 → 1:4 → 1:2 EtOAc-cyclohexane). Yield: 17 mg (51%). R_f 0.7 (1:1 EtOAc-cyclohexane). $[\alpha]_D$ +12.0 (*c* 1.0 in DCM). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39-7.22 (m, 14 H, Ph), 5.89 (d, 1 H, $J_{1,2}$ = 3.8 Hz, H-1), 5.22 (dd, 1 H, $J_{1',2'}$ = 4.0 Hz, $J_{1',2a'}$ = 1.8 Hz, H-1'), 4.94, 4.74 (2 d, 2 H, $^2J_{H,H}$ = 12.5 Hz, C*H*Ph), 4.92, 4.62 (2 d, 1 H, $^2J_{H,H}$ = 12.5 Hz, C*H*Ph), 4.88, 4.60 (2 d, 1 H, $^2J_{H,H}$ = 12.0 Hz, C*H*Ph), 4.55 (1 d, 1 H, $^2J_{H,H}$ = 11.7 Hz, C*H*Ph), 4.60 (d, 1 H, H-2), 4.43 (t, 1 H, $J_{5',6a'}$ = $J_{6a',6b'}$ = 7.0 Hz, H-6a'), 4.31 (dd, 1 H, $J_{4,5}$ = 9.3 Hz, $J_{3,4}$ = 3.4 Hz ,H-4), 4.10 (d, 1 H, H-3), 4.04-3.95 (m, 1H, H-3'), 3.93-3.84 (m, 2 H, H-5', H-6a), 3.80 (dd, 1 H, $J_{5',6b'}$ = 10.8 Hz, $J_{6a',6b'}$ = 2.0 Hz, H-6b'), 3.73-3.68 (m, 1H, H-5), 3.80 (dd, 1 H, $J_{6a,6b}$ = 11.0 Hz, $J_{5,6b}$ = 4.5 Hz, H-6b), 3.34 (t, 1 H, $J_{4',5'}$ = 9.2 Hz, H-4'), 2.52 (ddd, 1 H $J_{2a',2b'}$ = 13.7 Hz, $J_{2a',3'}$ = 4.7 Hz, H-2a'), 1.66 (ddd, 1 H, H-2b'). ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 156.9 (CO), 138.6-136.4 (Ph), 131.3-128.0 (Ph), 112.0 ($C(CH_3)_2$), 106.1 (C-1), 84.4 (C-2), 83.6 (C-3), 82.0 (C-4'), 79.9 (C-1'), 79.6 (C-4), 78.2 (C-3'), 76.6 (C-5), 75.0-72.5 (*C*H_2Ph), 67.2 (C-6), 67.1 (C-6'), 53.2 (C-5'), 35.2 (C-2'), 27.3, 26.7 (CH_3). ESIMS: *m/z* 696.3 $[M + Na]^+$. ESI-HRMS Calcd for $C_{38}H_{43}NNaO_{10}$ $[M + Na]^+$ 696.2779, found 696.2769.

*(1R)-3,4-Di-O-benzyl-1-O-(1,2:5,6-di-O-isopropylidene-α-D-glucofuranos-3-yl)-5N,6O-oxomethylidene-2-deoxynojirimycin (**30**) and (1R)-3,4-Di-O-benzyl-1-O-(1,2:3,5-di-O-isopropylidene-α-D-glucofuranos-6-yl)-5N,6O-oxomethylidene-2-deoxynojirimycin (**31**)*. Compounds **30** and **31** were obtained as a 2:1 mixture from **5** (20 mg, 57 μmol) and the commercially available 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose **21** (22 mg, 86 μmol) following the general *O*-glycosylation procedure. After 24 h the resulting residue was purified by column chromatography (1:4 → 1:2 EtOAc-toluene). Yield: 15 mg (43%). R_f 0.5 (1:2 EtOAc-toluene). ESIMS: *m/z* 634.2 $[M + Na]^+$. ESI-HRMS Calcd for $C_{33}H_{41}NNaO_{10}$ $[M + Na]^+$ 634.2623, found 634.2610.

Data for **30**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37-7.26 (m, 10 H, Ph), 5.83 (d, 1 H, $J_{1,2}$ = 5.6 Hz, H-1), 5.39 (m, 1 H, H-1'), 4.96, 4.65 (2 d, 2 H, $^2J_{H,H}$ = 11.5 Hz, C*H*Ph), 4.70, 4.65 (2 d, 1 H, $^2J_{H,H}$ = 11.6 Hz, C*H*Ph), 4.43 (d, 1 H, $J_{1,2}$ = 3.40 Hz, H-2), 4.40 (t, 1 H, $J_{5,'6a'}$ = $J_{6a',6b'}$ = 7.1 Hz, H-6a'), 4.33 (t, 1 H, H-6b'), 4.14 (d, 1 H, $J_{3,4}$ = 2.9 Hz, H-3), 4.11 (dd, 1 H, $J_{6a,\,6b}$ = 5.8 Hz, $J_{5,6a}$ = 8.3 Hz, H-6a), 4.07 (dd, 1 H, $J_{4,3}$ = 8.9 Hz, $J_{4,5}$ = 3.0 Hz, H-4), 4.00 (dd, 1 H, $J_{5,6b}$ = 4.9 Hz, H-6b), 3.98-3.91 (m, 1 H, H-3'), 3.98-3.91 (m, 1 H, H-3), 3.82-3.77 (m, 1 H, H-5'), 3.34 (t, 1 H, $J_{4',5'}$ = 8.9 Hz, H-4'), 2.40 (ddd, 1 H $J_{2a',2b'}$ = 13.5 Hz, $J_{2a',3'}$ = 4.8 Hz, H-2a'), 1.60 (ddd, 1 H, H-2b'). ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 155.9 (CO), 138.1-137.8 (Ph), 128.6-127.7 (Ph), 112.22-109.4 (CH_3), 105.4 (C-1), 83.8 (C-2), 81.2 (C-4'), 80.4 (C-1'), 79.8 (C-4), 77.5 (C-3'), 74.8-72.3 (*C*H_2Ph), 72.3 (C-3), 67.7 (C-6), 67.0 (C-6'), 53.6 (C-5'), 34.0 (C-2').

Data for **31**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37-7.26 (m, 10 H, Ph), 5.99 (d, 1 H, $J_{1,2}$ = 3.6 Hz, H-1), 5.18 (dd, 1 H, H-1'), 4.96, 4.65 (2 d, 2 H, $^2J_{H,H}$ = 11.5 Hz, C*H*Ph), 4.70, 4.65 (2 d, 1 H, $^2J_{H,H}$ = 11.6 Hz, C*H*Ph), 4.56 (d, 1 H, H-2), 4.40 (t, 1 H, $J_{5',6a'}$ = $J_{6a',6b'}$ = 7.1 Hz, H-6a'), 4.33 (t, 1 H, H-6b'), 4.24 (dd, 1 H, $J_{4,3}$ = 6.9 Hz, $J_{4,5}$ = 3.7 Hz, H-4), 4.19 (d, 1 H, H-3), 3.82-3.77 (m, 1 H, H-5'), 3.71-3.66 (m, 2 H, H-5, H-6a), 3.58 (dd, 1 H, $J_{5,6a}$ = 10.1 Hz , $J_{5,6a}$ = 6.2 Hz, H-6b), 3.29 (t, 1H, $J_{4',5'}$ = 8.9 Hz, H-4'), 2.40 (ddd, 1 H, $J_{2a',2b'}$ = 13.5 Hz, $J_{2a',3'}$ = 4.8 Hz, H-2a'), 1.60 (ddd, 1 H, H-2b'). ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 156.4 (CO), 138.1-137.8 (Ph), 128.6-127.7 (Ph), 112.22-109.4 (CH_3), 106.4 (C-1), 84.0 (C-2), 81.4 (C-4'), 80.5 (C-1'), 79.21 (C-4), 77.5 (C-3'), 75.0 (C-3), 74.8-72.3 (*C*H_2Ph), 71.0 (C-5), 68.3 (C-6'), 66.9 (C-6), 53.0 (C-5'), 34.9 (C-2').

*(1R)-3,4-Di-O-benzyl-1-O-(1-methyl α-D-galactopyranosyd-4-yl)-5N,6O-oxomethylidene-2-deoxynojirimycin (**33**)*. Compound **33** was obtained from glucal **5** (20 mg, 57 μmol) and methyl 2,3,6-tri-*O*-benzyl-α-D-galactopyranoside **(22)** (35 mg, 86 μmol) following the general procedure above described. After 24 h the resulting crude residue containing **32** and partially debenzoylated derivatives was concentrated and deprotected under Zemplén conditions (see General Methods). The resulting fully deacylated product was purified by column chromatography (1:2 EtOAc-cyclohexane → 9:1 → 4:1 EtOAc-MeOH) to give **33**. Yield: 9 mg (29%, two steps). R_f 0.6 (9:1 EtOAc-MeOH). $[\alpha]_D$ +71.0 (*c* 0.65 in MeOH). ^{1}H NMR (300 MHz, CD_3OD) δ 7.40-7.27 (m, 10 H, Ph), 5.26 (dd, 1 H, $J_{1',2b'}$ = 4.0 Hz, $J_{1',2a'}$ = 1.7 Hz, H-1'), 4.91, 4.65 (2 d, 2 H, $^2J_{H,H}$ = 11.7 Hz, C*H*Ph), 4.73, 4.68 (2 d, 1 H, $^2J_{H,H}$ = 11.7 Hz, C*H*Ph), 4.72 (d, 1 H, $J_{1,2}$ = 2.9 Hz, H-1), 4.42 (t, 1 H, $J_{6a',6b'}$ = $J_{5',6a'}$ = 8.3 Hz, H-6'), 4.40-4.31 (m, 1 H, H-5'), 4.08-4.03 (m, 2 H, H-3, H-3'), 3.96-3.91 (t, 1 H, $J_{5',6b'}$ = $J_{6a',6b'}$ = 7.8 Hz, H-6b'), 3.87 (t, 1 H, $J_{5,6a}$ = $J_{5,6b}$ = 6.9 Hz, H-5), 3.84-3.75 (m, 4 H, H-2, H-4, H-6), 3.44 (t, 2 H, $J_{3',4'}$ = $J_{4',5'}$ = 9.6 Hz, H-4'), 3.41 (s, 3 H, OMe), 2.48 (ddd, 1 H $J_{2a',2b'}$ = 13.4 Hz, $J_{2a',3'}$ = 4.7 Hz, H-2a'), 1.64 (ddd, 1 H, H-2b'). ^{13}C NMR (125.1 MHz, $CDCl_3$) δ 156.9 (CO), 140.7-140.6 (Ph), 130.3-129.9 (Ph), 102.4 (C-1), 84.1 (C-4'), 82.7 (C-1'), 79.5, 79.3 (C-3', C-3), 76.2, 73.9 (*C*H_2Ph), 73.2 (C-5), 71.4 (C-2), 71.4 (C-4), 69.6 (C-6'), 62.7 (C-6), 56.7 (OMe), 55.4 (C-5'), 36.7 (C-2'). ESIMS: *m/z* 568.2 $[M + Na]^+$. ESI-HRMS Calcd for $C_{28}H_{35}NNaO_{10}$ $[M + Na]^+$ 568.2153, found 568.2146.

*(1R)-3,4-Di-O-benzyl-1-octylthio-5N,6O-oxomethylidene-2-deoxynojirimycin (**34**)*. Column chromatography (1:3 EtOAc-toluene). Yield: 24 mg (85%). R_f 0.6 (1:2 EtOAc-toluene). $[\alpha]_D$ +63.7 (*c* 0.6 in DCM). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41-7.30 (m, 10 H, Ph), 5.30 (dd, 1 H, $J_{1,2b}$ = 4.9 Hz, $J_{1,2a}$ = 1.7 Hz, H-1), 4.98, 4.68 (2 d, 2 H, $^2J_{H,H}$ = 11.7 Hz, C*H*Ph), 4.70, 4.65 (2 d, 1 H, $^2J_{H,H}$ = 11.5 Hz, C*H*Ph), 4.40 (t, 1 H, $J_{6a,6b}$ = $J_{5,6a}$ = 8.6 Hz, H-6a), 4.05-3.91 (m, 2 H, H-3, H-5), 3.84 (dd, 1 H, $J_{5,6b}$ = 6.7 Hz, H-6b), 3.30 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 8.9 Hz, H-4), 2.66-2.57 (m, 1 H, SCH_2), 2.52-2.43 (m, 1 H, SCH_2), 2.30 (ddd, 1 H, $J_{2a,2b}$ = 13.6 Hz, $J_{2a,3}$ = 4.6 Hz, H-2a), 1.91 (ddd, 1 H, $J_{2b,3}$ = 11.2 Hz, H-2b), 1.69-1.51 (m, 2 H, CH_2), 1.36-1.28 (m, 7 H, CH_2), 0.90 (t, 3 H, $^3J_{H,H}$ = 6.5 Hz, CH_3). ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 156.3 (CO), 138.3-138.2 (Ph), 129.0-128.2 (Ph), 82.0 (C-4), 78.5 (C-3), 75.1, 72.5 (*C*H_2Ph), 67.0 (C-6), 55.3 (C-1), 52.9 (C-5), 35.4 (C-2), 35.4 (SCH_2), 32.3-28.9 (CH_2), 23.0 (CH_3). ESIMS: *m/z* 520.3 $[M + Na]^+$. ESI-HRMS Calcd for $C_{29}H_{39}NO_4NaS$ $[M + Na]^+$ 520.2492, found 520.2487.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Tables S1 and S2 with detailed description of the tested reaction conditions for thioglycosylation/glycosylation and copies of NMR spectra (PDF).

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The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

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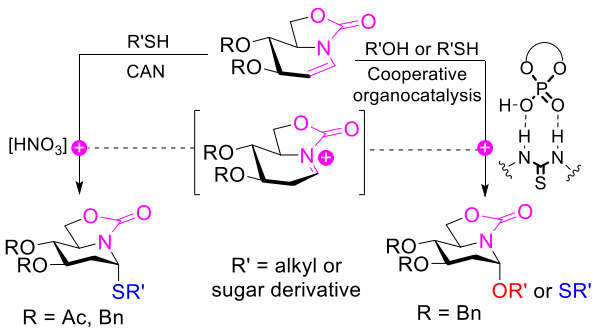
R'SH
CAN
R'OH or R'SH
Cooperative
organocatalysis
[HNO3]
RO
RO
SR'
R = Ac, Bn
R' = alkyl or
sugar derivative
OR' or SR'
R = Bn