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Use of Cyclic Sulfamidates Derived from D-Allosamine in Nucleophilic Displacements: Scope and Limitations

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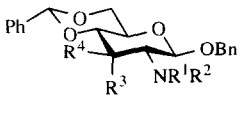
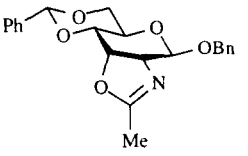
Abstract: A cyclic 2,3-sulfamidate derived from *N*-acetyl-D-allosamine has been treated with a variety of S-, N-, O-, and C-nucleophiles, leading to nucleophilic displacement at C-3, elimination, or deacetylation reactions depending on the type of nucleophile used. Nucleophilic displacement is achieved with thio-nucleophiles and NaN_3, allowing the preparation of 3-thio- or 3-azido glucosamine derivatives difficult to obtain by use of sulfonates.

Nucleophilic displacement of sulfonates is a useful reaction for the synthesis and transformation of carbohydrates.[1] In particular, the synthesis of oligosaccharides containing an interglycosidic sulfur linkage can be achieved by S_N2 reaction of a sugar sulfonate with a glycosylthio anion.[2] Within a project addressed to the synthesis of oligosaccharide inhibitors of neural cell division,[3,4] we were interested[5] in the preparation of a 3-S-α-fucosyl-glucosaminide derivative **9** (Scheme 1). This compound could be an appropriate intermediate for the synthesis of thioglycosidic analogs of the biologically active oligosaccharides. It is known[2] that S-linked oligosaccharides are resistant to glycosidase-catalysed hydrolysis, and more stable at acidic pH than the corresponding O-glycoside. For the synthesis of **9**, we proposed the introduction of the desired thioglycosidic bond through nucleophilic displacement at C-3 of an allosamine 3-sulfonate derivative with a sulfur nucleophile. All the attempts, however, to displace triflate or tosylate derivatives **1-3** with KSAc failed (Figure 1). Triflate **1** was highly unstable, leading rapidly to oxazoline **5**[6], and could not be used. Triflate **2**, with a phthalimide group instead of the acetamide group, when treated with potassium thioacetate gave mainly the elimination product **6** along with the desired susbtitution product **4**. Finally, tosylate **3** gave no reaction with KSAc at even 80 °C for 24 h.



1 R^1= H, R^2= Ac, R^3= TfO, R^4= H
2 R^1, R^2= Phth, R^3= TfO, R^4= H
3 R^1= H, R^2= Ac, R^3= TsO, R^4= H
4 R^1, R^2= Phth, R^3= H, R^4= SAc



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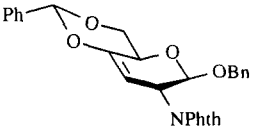
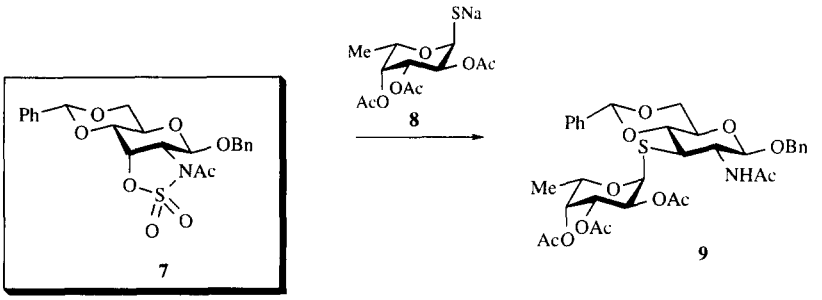


6

Figure 1

Recently, the synthesis of cyclic sulfamidates derived from (*S*)-serine and their regioselective ring opening by several nucleophiles has been reported.[7,8] We hypothesized[5] that such a methodology could be applicable to our problem. Thus, nucleophilic displacement of sulfamidate **7** with **8**[9] furnished the desired thiodisaccharide **9** (Scheme 1). Prompted by this succesful result, we decided to explore the synthetic potential of this methodology for the preparation of glucosamine derivatives modified at C-3 position. In this paper full details about the preparation of **7** and its treatment with several nucleophiles is described.



Scheme 1

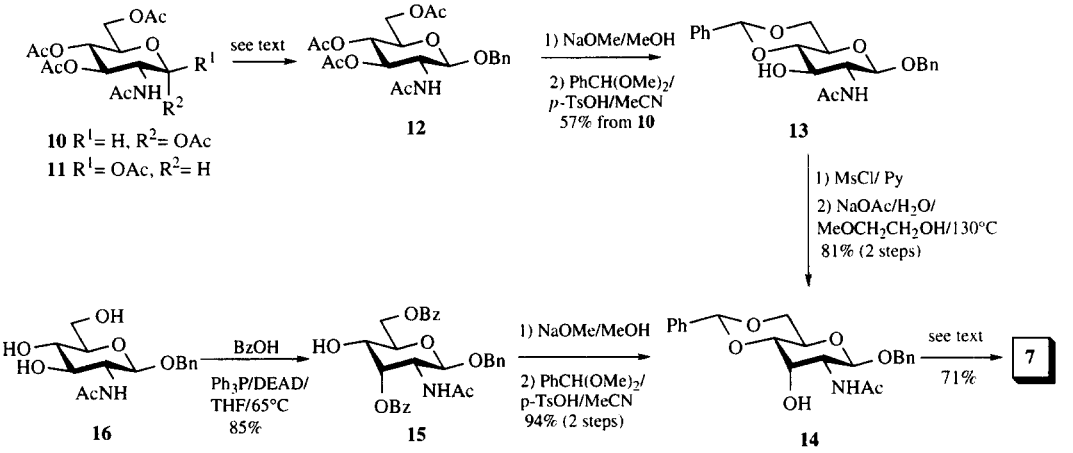
RESULTS AND DISCUSSION

Preparation of 2,3-sulfamidate 7

For the synthesis of **7**, D-allosamine derivative **14** (Scheme 2) was first required. This compound was prepared starting from the known peracetylated benzyl β-glucosaminide **12**, which on turn can be obtained by glycosylation of BnOH with peracetylated β-glucosamine **11** using $FeCl_3$,[10] $ZnCl_2$,[11] or CSA[12] as acid promotors. However, these glycosylations are not convenient for large-scale syntheses, since the preparation of glycosyl donor **11** from D-glucosamine hydrochloride proceeds in low yield unless a multistep route is used.[13] Therefore, a new glycosylation from the α-anomer **10**, easily obtained from D-glucosamine hydrochloride in high yield,[14] was sought. The reaction of **10** with BnOH was screened under different conditions, varying solvent (CH_2Cl_2, 1,2-dichloroethane, CH_3CN), glycosylation promotor ($BF_3{\cdot}Et_2O$, TMSOTf, $SnCl_4$) and temperature. The best result, in terms of yield and stereoselectivity, was obtained with 1.2 eq. of $SnCl_4$ in CH_3CN at 65°C. Under these conditions large-scale synthesis of **12** was achieved yielding, after deacetylation and subsequent benzylidenation, benzyl glucosaminide **13** in 57% overall yield. Further inversion of hydroxyl group at position 3 was carried out via a two-step sequence[15] affording benzyl allosaminide **14**. On the other hand, **14** can be obtained by selective inversion at C-3 of benzyl glucosaminide **16** using Mitsunobu reaction conditions.[16] This reaction afforded dibenzoate **15** in high yield, which after debenzoylation and subsequent benzylidenation provided allosamine derivative **14**. However, this alternative is not convenient for large-scale preparation of **14** since side-products arising from the Mitsunobu reaction make the purification of **15** difficult.

Direct formation of cyclic sulfamidate **7** from **14** by reaction with sulfuryl chloride[7] failed, the starting material remaining unaltered. The two-step procedure, *i.e.* reaction with thionyl chloride followed by oxidation,[7,8] gave under the best conditions only a 45% yield of **7**. We found that **7** could be obtained in higher

yield if **14** is treated with 1,1'-sulfonyl diimidazole followed by acetyl chloride to reinstall the acetyl group on the nitrogen atom, which is cleaved during the reaction. The N-deacetylation on **14** could be due to the presence of sodium imidazolate released during the reaction (see below). When DMF was used as solvent in the first step, **7** was obtained in 74% yield; however, this result could not be reproduced when the reaction was carried out in gram quantities. After much experimentation, we found that using THF as solvent in the sulfamidation, **7** could be prepared in 71% overall yield in gram-scale.



10 R^1= H, R^2= OAc
11 R^1= OAc, R^2= H

12 **13** **14** **15** **16**

Scheme 2

Nucleophilic Displacements on Sulfamidate 7

Compound **7** in a polar aprotic solvent, such as DMF or THF, was treated with different nucleophiles. Three types of products were formed, arising from nucleophilic displacement of sulfamidate at C-3 (**9** and **17**), proton abstraction at C-2 (**19**) or C-4 (**18**), and N-deacetylation (**20**). The results, summarized in Table 1, show that S-nucleophiles KSAc and **8**, and the N-nucleophile NaN_3, produce effectively the regioselective ring opening of the sulfamidate functionality, to afford the 3-thio derivatives **17a** and **9**, and the 3-azido glucosaminide **17b**, respectively. However, the other N-nucleophile, sodium imidazolate (NaIm), attacked to the carbonyl group and gave **20**. This result explains the need of the reacetylation step when the formation of **7** was performed with 1,1'-sulfonyl diimidazole. When oxyanions were used as nucleophiles, elimination was the main pathway, but also products coming from nucleophilic displacement or deacetylation were isolated, depending on the reagent used, NaOAc or sodium cyclohexanolate, respectively. Finally, all C-nucleophiles tested, i.e. NaCN, Li–C≡C–TMS, or vinylmagnesium bromide, led to N-deacetylation.

The results showed in Table 1 indicate that sulfamidate **7** possesses several electrophilic centers sensitive to the attack of nucleophiles. The reactions can, therefore, proceed in one or other direction depending on the reactivity of the reagent, i.e. nucleophilicity and basicity of the S-, N-, O-, or C-nucleophile. A schematic summary of the reactions observed on **7** is depicted in Scheme 3.

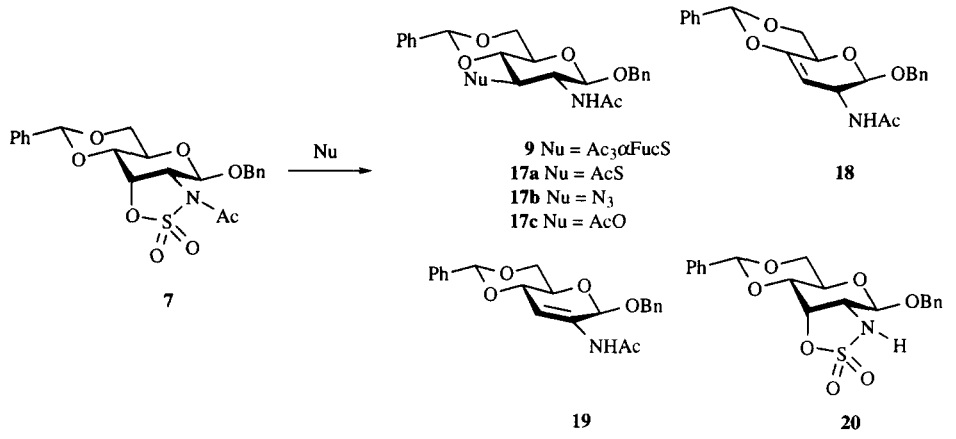
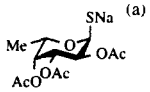
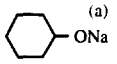
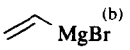
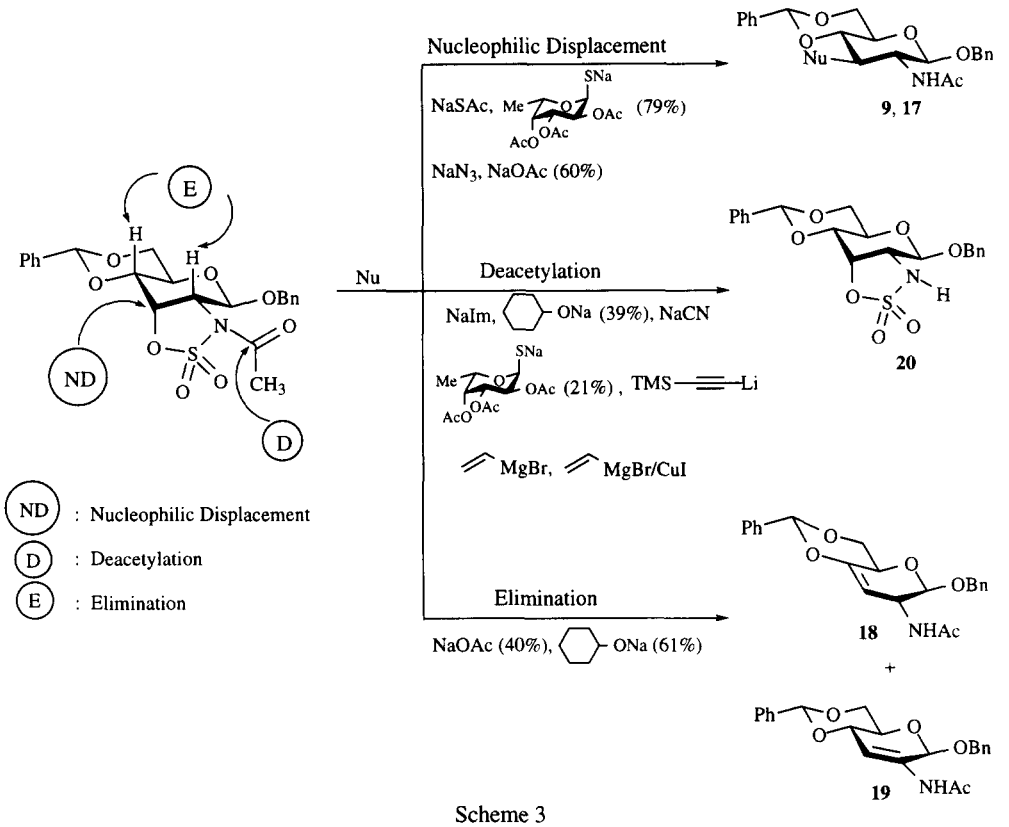


Table 1. Treatment of Sulfamidate **7** with different Nucleophiles

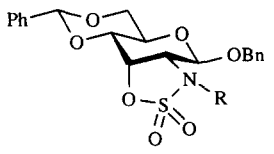
Nucleophile (Nu)	T (°C)	Time (h)	Yield (%) of Products from: Nucleophilic Displacement (**17** or **9**)	Elimination (**18** : **19**)	Deacetylation (**20**)
$KSAc^{(a)}$	20	0.5	82 (**17a**)	—	—
 $^{(a)}$	20	0.5	61 (**9**)	—	17
$NaN_3{}^{(a)}$	20	2	92 (**17b**)	—	—
$NaIm^{(b)}$	20	0.1	—	—	94
$NaOAc^{(a)}$	40	48	47 (**17c**)	31 (1:0)	—
 $^{(a)}$	20	3	—	51 (1:0.8)	33
$NaCN^{(a)}$	20	0.5	—	—	97
 $^{(b)}$	-78	1	—	—	86
 $^{(b)}$	0	0.1	—	—	99
 $^{(b)}$	-40→50	72	Complex mixture		

[a] DMF or [b] THF was used as solvent

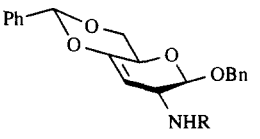


Scheme 3

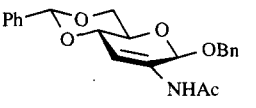
A final attempt to effect a displacement with a C-nucleophile was carried out using sulfamidates **21** and **22**, where the acetyl group is replaced by allyl or *t*-butoxycarbonyl (Boc) protecting groups. Treatment of **21** with NaCN gave, however, elimination products **23** and **25**, indicating that in the absence of the carbonyl attached to the sulfamidate functionality the cyanide is behaving as a base. With **22** almost equimolecular formation of elimination and N-de-*t*-butoxycarbonylation products, **24** and **20** respectively, was observed. These unsuccessful attempts contrast with recently reported examples about the regioselctive ring opening of sufamidates by different reagents, including C-nucleophiles such as NaCN[7] or $LiCHBr_2$.[17] Nevertheless, simple sulfamidates were used in both cases, in which the attack of the nucleophile takes place at a primary carbon atom. In our case the ring opening must proceed at a secondary carbon, and this is only feasible with strong non-carbon nucleophiles of low basicity, such as thio derivatives, azide or, in a lesser extent, acetate .



21 R = All
22 R = Boc

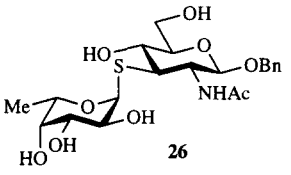


23 R = All
24 R = Boc



25

In summary, allosamine derived sulfamidate **7** allows the synthesis of thiodisaccharides such as compound **9**, which are difficult to obtain using sulfonates. Transformation of **9**, which is currently being used in synthesis of Lewis X oligosaccharide analogs,[18] furnished the unprotected thio-disaccharide **26**. A similar α(1→3) linked thiodisaccharide has been shown to be an inhibitor of fucosidases,[9] interestingly, its inhibition constant was better than the observed for the α(1→4), and α(1→6) regioisomers.



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Finally, the 3-azido glucosamine derivative **17b** can be a useful intermediate for the synthesis of pseudooligosaccharides as inhibitors of glycosidases.[19]

ACKNOWLEDGEMENTS

Financial support by Ministerio de Educación y Cultura and CSIC (to B. A. and C. J., respectively), and Comunidad de Madrid (Grant AE00049/95) and DGICYT (Grant PB93-0127-C02-01), is gratefully acknowledged.

EXPERIMENTAL PART

General. Separation and purification of all synthesized compounds was carried out by flash chromatography (FC) using silicagel Merck (230-400 mesh). The eluent used is indicated, and solvent ratios refer to volume. Tlc was performed using tlc plates GF_{234} Merck (0.2 mm), detecting with 5% PMA in EtOH or 5% H_2SO_4 in EtOH. Solvents were dried and distilled as follows: THF and MeCN (Na/benzophenone), CH_2Cl_2 (CaH_2), DMF (BaO, 3Å molecular sieves), Py (NaOH). Those used in work-ups were further dried with anh Na_2SO_4, and evaporated in vacuo. Melting points were determined in a Kofler hot-stage apparatus and are not corrected. ^{1}H-RMN and ^{13}C-RMN were registered with a Varian Unity-500 (500 MHz and 125 MHz, respectively), a Varian XL-300 (300 MHz and 75 MHz, respectively) spectrometer, a Varian-Gemini 200 (200 MHz and 50 MHz, respectively) spectrometer, or a Bruker AM-200 (200 MHz and 50 MHz, respectively) spectrometer, in $CDCl_3$ or in the solvent indicated. IR spectra were recorded with a Perkin Elmer 257 spectrophotometer. Optical rotations, $[\alpha]_D$,were measured at r.t. in a Perkin Elmer 241 MC polarimeter in quartz cells (d = 1 dm), using Na 589 light, with the solvent and concentration indicated. Elemental analysis were determined in an Perkin Elmer 240 analyzer, and refer to %.

2-Acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-α-D-glucopyranose (10). A solution of 2-amino-2-deoxy-D-glucose hydrochloride (**8**, 22.0 g, 102 mmol) in Py (100 ml) was treated with Ac_2O (94 ml, 101 g, 996 mmol, 9.8 eq), and stirred at r.t. for 14 h. After this time, the mixture was poured into H_2O (100 ml), and extracted with CH_2Cl_2 (1 x 200 ml, 1 x 100 ml). The combined organics were dried, and the solvent was evaporated. The residue was crystallized from CH_2Cl_2/Et_2O (275 ml, 1:10) to give **10** (32.9 g, 83%). Mother liquors were evaporated, and the residue was purified by FC (EtOAc) to give additionally 4.77 g of **9** (12%; overall yield, 95%). R_f (hexane/EtOAc 1:3) 0.23; m.p. 138-140°C (lit.[14] 136-137°C); $[\alpha]_D$ +88.5 (*c* 2.0, $CHCl_3$) (lit.[14] +91, *c* 0.6, MeOH); ^{1}H-NMR (200 MHz): δ 6.16 (d, 1 H, $J_{1,2}$ = 3.6 Hz, H-1), 5.65 (d, 1 H, $J_{NH,2}$ = 8.8 Hz, NH), 5.30-5.20 (m, 2 H, H-3, H-4), 4.48 (ddd, 1 H, $J_{2,3}$ = 10.2 Hz, H-2), 4.25 (dd, 1 H,

$J_{5,6a}$ = 4.1 Hz, $J_{6a,6b}$ = 12.4 Hz, H-6_a), 4.09-3.97 (m, 2 H, H-5, H-6_b), 2.19 (s, 3 H, CH_3), 2.09 (s, 3 H, CH_3), 2.05 (s, 3 H, CH_3), 2.04 (s, 3 H, CH_3), 1.94 (s, 3 H, CH_3); ^{13}C-NMR (50 MHz): δ 171.61 (C=O), 170.54 (C=O), 169.84 (C=O), 168.99 (C=O), 168.47 (C=O), 90.73 (C-1), 70.76, 69.77, 67.70, 61.64 (C-6), 51.16 (C-2), 22.91 (CH_3), 20.77 (CH_3), 20.57 (2 CH_3), 20.44 (CH_3).

Benzyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranoside (12). To a solution of **10** (66.7 g, 171 mmol) and BnOH (43.7 ml, 45.7 g, 422 mmol, 2.5 eq) in MeCN (500 ml), under argon, was added 4Å molecular sieves (11.4 g). After 10 min, $SnCl_4$ (24.1 ml, 53.6 g, 206 mmol, 1.2 eq) was added dropwise, and the mixture was heated at 75°C for 14 h. After this time, the reacion mixture was cooled to r.t., quenched with Et_3N (145 ml), and filtered through a pad of celite. The solid was washed with CH_2Cl_2 (2 x 300 ml), and the combined organics were evaporated. The residue was dissolved in CH_2Cl_2 (300 ml), washed with H_2O (100 ml), dried and concentrated to give a solid which was crystallized from CH_2Cl_2/Et_2O (330 ml, 1:10) to give **12** (34.0 g, 45%), slightly impurified by its α-anomer. Mother liquors were evaporated, and the residue was purified by FC (EtOAc) to give additionally 11.6 g (16%; overall yield, 61%) of **12**, which contained traces of the α-anomer, and was used without further purification in the next step. A sample was recrystallized for analysis: R_f (hexane/EtOAc 1:4) 0.26; m.p. 165-166°C (lit.[20] 170°C); $[\alpha]_D$ -44.3 (*c* 1.0, MeOH), (lit.[20] -40, *c* 0.7, MeOH); ^{1}H-NMR (200 MHz): δ 7.28-7.26 (m, 5 H, aromatic), 5.78 (d, 1 H, $J_{NH,2}$ = 9.4 Hz, NH), 5.21 (t, 1 H, $J_{3,4} \approx J_{4,5}$ = 9.3 Hz, H-4), 5.04 (t, 1 H, $J_{2,3}$ = 9.6 Hz, H-3), 4.85 (d, 1 H, *J* = 12.8 Hz, CH_2Ph), 4.64 (d, 1 H, $J_{1,2}$ = 8.3 Hz, H-1), 4.56 (d, 1 H, CH_2Ph), 4.24 (dd, 1 H, $J_{5,6a}$ = 4.8 Hz, $J_{6a,6b}$ = 12.2 Hz, H-6_a), 4.12 (dd, 1 H, H-6_b, $J_{5,6b}$ = 2.6 Hz), 3.92 (ddd, 1 H, H-2), 3.66 (ddd, 1 H, H-5), 2.05 (s, 3 H, CH_3), 1.97 (s, 6 H, 2 CH_3), 1.85 (s, 3 H, CH_3); ^{13}C-NMR (50 MHz): δ 170.73 (C=O), 170.59 (C=O), 170.13 (C=O), 169.28 (C=O), 136.92 (C-ipso), 128.35 (aromatic), 127.88 (aromatic), 99.48 (C-1), 72.44, 71.73, 70.56 (CH_2Ph), 68.74, 62.15 (C-6), 54.39 (C-2), 23.11 (CH_3), 20.83 (CH_3), 20.55 (2 CH_3), 20.49 (CH_3).

Benzyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside (13): To a solution of **12**, 45.6 g, 104 mmol) in MeOH (400 ml) was added NaOMe (2 M in MeOH, 26.0 ml, 52.0 mmol, 0.50 eq), and the mixture was stirred at r.t. for 1 h. After this time, the reaction mixture was neutralized with Amberlite® IR-120 (H^+), and filtered. The solvent was evaporated, and crude **16** was suspended in MeCN (500 ml) and treated with $PhCH(OMe)_2$ (40.0 ml, 40.6 g, 267 mol, 2.6 eq) and *p*-TsOH·H_2O (5.00 g, 26.3 mol, 0.25 eq) at r.t. for 14 h. After this time, the reacion mixture was quenched with Et_3N (4.0 ml), and hexane (100 ml) and MeOH (100 ml) were added. The crystals were filtered, and treated with boiling hexane/CH_2Cl_2/Et_2O (550 ml, 10:1:2) to give **13** (33.5 g, 81%). The combined filtrates were concentrated, and the residue was purified by FC (hexane/CH_2Cl_2 1:1 → CH_2Cl_2 → CH_2Cl_2/MeOH 5:1) to give additionally 5.0 g (12%; overall yield, 93%) of **13**: R_f (CH_2Cl_2/MeOH 18:1) 0.21; m.p. 265-268°C (lit.[15] 270-271°C); $[\alpha]_D$ -92.0 (*c* 0.5, Py), (lit.[15] -89, *c* 0.8, Py); ^{1}H-NMR (200 MHz, d_6-DMSO/d_6-acetone 2:1): δ 7.83 (d, 1 H, aromatic), 7.51-7.26 (m, 9 H, aromatic), 5.62 (s, 1 H, CHPh), 5.24 (d, 1 H, $J_{NH,2}$ = 4.8 Hz, NH), 4.80 (d, 1 H, *J* = 12.4 Hz, CH_2Ph), 4.65 (d, 1 H, $J_{1,2}$ = 8.1 Hz, H-1), 4.56 (d, 1 H, CH_2Ph), 4.25 (dd, 1 H, $J_{5,6e}$ = 4.7 Hz, $J_{6a,6e}$ = 10.1 Hz, H-6_e), 3.78 (t, 1 H, $J_{5,6a}$ = 10.0 Hz, H-6_a), 3.78-3.64 (m, 2 H, H-2, H-4), 3.49 (t, 1 H, $J_{2,3} \approx J_{3,4}$ = 9.0 Hz, H-3), 3.38 (ddd, 1 H, $J_{4,5}$ = 9.4 Hz, H-5), 1.84 (s, 3 H, CH_3). ^{13}C-NMR (50 MHz, d_6-DMSO/d_6-acetone 2:1): δ 169.20 (C=O), 137.98 (C-ipso), 137.86 (C-ipso), 128.70 (aromatic), 128.07 (aromatic), 127.90 (aromatic), 127.29 (aromatic), 127.16 (aromatic), 126.32 (aromatic), 101.46 (PhCH), 100.78 (C-1), 81.45, 70.46, 70.04

(CH_2Ph), 67.97 (C-6), 66.09, 56.35 (C-2), 22.86 (CH_3).

Benzyl 2-acetamido-3,6-di-*O*-benzoyl-β-D-allopyranoside (15): To a mixture of **16**, prepared as described above, (2 g, 6.43 mmol), triphenylphosphine (5.07 g, 19.3 mmol, 3 eq) and benzoic acid (2.37 g, 19.3 mmol, 3 eq) in dry THF at 65 °C under argon, was added dropwise DEAD (3.05 mL, 19.3 mmol, 3 eq) and the mixture was stirred at 65 °C for 1.5 h. After cooling, the reaction mixture was diluted with EtOAc (200 ml), washed with sat. $NaHCO_3$ solution (100 ml), H_2O (100 ml) and brine (100 ml), dried (Na_2SO_4) and concentrated. The residual syrup was purified by FC (hexane/EtOAc 1:2) to give **15** (2.81 g, 85 %). R_f (EtOAc) 0.53; m.p. 137-139°C; $[\alpha]_D$ - 52.0 (*c* 1, $CHCl_3$); ^{1}H-NMR (300 Mz): δ 8.1-7.3 (m, 15 H, aromatic), 5.85 (t, 1 H, $J_{2,3} \approx J_{3,4}$= 2.7 Hz, H-3), 5.5 (d, 1 H, $J_{NH,2}$ = 8.0 Hz, NH), 4.95 (d, 1 H, *J* = 12.0 Hz, CH_2Ph), 4.87 (d, 1 H, $J_{1,2}$ = 7.9 Hz, H-1), 4.65 (m, 3 H, H-6_a, H-6_b, CH_2Ph), 4.4 (ddd, 1 H, $J_{1,2}$ = 7.9 Hz, $J_{2,3}$ = 2.7 Hz, H-2), 4.1 (m, 2 H, H-4, H-5), 2.88 (d, 1 H, $J_{OH,4}$ = 3.4 Hz, OH), 1.9 (s, 3 H, CH_3); ^{13}C-NMR (50 MHz): δ 170.0 (C=O), 166.7 (C=O), 166.2 (C=O), 137.1 (C-ipso), 133.5 (C-ipso), 133.2 (C-ipso), 129.7 (aromatic), 129.3 (aromatic), 128.6 (aromatic), 128.5 (aromatic), 128.4 (aromatic), 127.9 (aromatic), 98.1 (C-1), 73.4, 72.4, 70.1, 67.1, 64.1, 51.3 (C-2), 23.1 (CH_3). Anal.: Calc. for $C_{27}H_{29}NO_8$: C, 67.05; H, 5.59; N, 2.69. Found: C, 67.31; H, 5.81; N, 2.80.

Benzyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-allopyranoside (14):

a) *From* **13**: To a suspension of **13** (26.7 g, 66.8 mmol) in CH_2Cl_2 (200 ml) at r.t. was added Py (100 ml, 97.8 g, 1.24 mol, 18 eq). After 10 min, MsCl (7.50 ml, 11.1 g, 96.9 mmol, 1.4 eq) was added dropwise, and the mixture was stirred for 28 h. The reaction mixture was then diluted with CH_2Cl_2 (500 ml) and washed with H_2O (400 ml). The aqueous phase was extracted with CH_2Cl_2 (3 x 200 ml), and the combined organics[†] were evaporated to give a residue which was suspended in 2-methoxyethanol/H_2O (550 ml, 10:1) and treated with NaOAc·$3H_2O$ (28.0 g, 206 mmol, 3.1 eq) at 130°C for 18 h. After this time, the mixture was cooled to r.t., and the solvents were evaporated. The residue was dissolved in CH_2Cl_2 (1 l), washed with H_2O (500 ml), dried, and concentrated to give a solid which was crystallized from MeOH/hexane/CH_2Cl_2 (520 ml, 12:12:1) to give **14** (9.00 g, 34%). A second crop, obtained from MeOH/hexane/CH_2Cl_2 (320 ml, 15:15:1) gave further 5.93 g (22%) of **14**. Mother liquors were evaporated, and the residue was purified by FC (CH_2Cl_2/MeOH 70:1 → 60:1→ 40:1) to give additionally 6.80 g (16%; overall yield, 81%) of **14**. A sample was recrystallized for analysis. R_f (CH_2Cl_2/MeOH 18:1) 0.30; m.p. 265°C (lit.[15] 260-265°C); $[\alpha]_D$ -108.1 (*c* 1, $CHCl_3$), (lit.[15] -115.6, *c* 1.3, $CHCl_3$); ^{1}H-NMR (200 MHz):δ 7.52-7.30 (m, 10 H, aromatic), 5.85 (d, 1 H, $J_{NH,2}$ = 8.8 Hz, NH), 5.62 (s, 1 H, CHPh), 4.93 (d, 1 H, *J* = 12.5 Hz, CH_2Ph), 4.70 (d, 1 H, $J_{1,2}$ = 7.9 Hz, H-1), 4.60 (d, 1 H, CH_2Ph), 4.43 (dd, 1 H, $J_{5,6e}$ = 4.4 Hz, $J_{6a,6e}$ = 9.8 Hz, H-6_e), 4.31-4.21 (m, 2 H, H-2, H-3), 3.98 (ddd, 1 H, $J_{4,5}$ = 9.1 Hz, $J_{5,6b}$ = 9.6 Hz, H-5), 3.83 (t, 1 H, H-6_b), 3.69 (dd, 1 H, $J_{3,4}$ = 2.1 Hz, H-4), 2.39 (d, 1 H, $J_{OH,3}$ = 1.5 Hz, HO-3), 2.00 (s, 3 H, CH_3); ^{13}C-NMR (50 MHz, $CDCl_3$/CD_3OD 4:1): δ 170.23 (C=O), 137.27 (C-ipso), 136.99 (C-ipso), 129.11 (aromatic), 128.21 (aromatic), 127.58 (aromatic), 126.01 (aromatic), 101.58 (CHPh), 98.92 (C-1), 78.86; 70.49 (CH_2Ph), 68.94 (C-6), 68.23, 63.09, 52.08 (C-2), 22.82 (CH_3).

b) *From* **15**: Compound **15** (1.94 g, 3.73 mmol) was treated with a 0.1M solution of NaOMe in MeOH (107.5 ml) at r.t. for 1h. The mixture was neutralized with Amberlite® IR-120 (H^+) and filtered. The solvent was evaporated, the residue was suspended in dry CH_3CN (19 ml) and treated with $PhCH(OMe)_2$ (2.64 ml,

[†] The organic phase was not dried to prevent loss of material, which starts to crystallize upon standing.

17.5 mmol, 4.7 eq) and *p*-TsOH·H_2O (33.4 mg, 0.17 mmol, 0.045 eq) at room temperature for 2h. After this time, the reaction mixture was diluted with CH_2Cl_2 (20 ml), neutralized with Et_3N and evaporated to dryness. The residue was purified as above to give **14** (1.32 g, 94 %), identical to the material prepared from **13**.

Benzyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-3-*O*-*p*-toluenesulfonyl-β-D-allopyranoside (3): A mixture of **14** (169 mg, 0.42 mmol) and *p*-toluensulfonyl chloride (202 mg, 1.06 mmol, 2.5 eq) in CH_2Cl_2/Py 1:1 (4 ml) was stirred at room temperature for 6 h. After this time, the reaction mixture was diluted with CH_2Cl_2 (50 ml), washed with H_2O (50 ml), dried (Na_2SO_4) and concentrated. The residue was purified by FC (CH_2Cl_2/EtOAc 20:1) to give **3** (185 mg, 79%). R_f (CH_2Cl_2/MeOH 20:1) 0.65; m.p. 98-100°C; $[\alpha]_D$ -50.9 (*c* 1, $CHCl_3$); ^{1}H-NMR (300 MHz): δ 7.72-7.06 (m, 14 H, aromatic), 5.71 (d, 1 H, $J_{NH,2}$ = 8.2 Hz, NH), 5.65 (t, 1 H, $J_{2,3} \approx J_{3,4}$ = 2.9 Hz, H-3), 5.49 (s, 1 H, CHPh), 4.73 (d, 1 H, J = 11.6 Hz, CH_2Ph), 4.68 (d, 1 H, $J_{1,2}$ = 8.3 Hz, H-1), 4.40 (d, 1 H, CH_2Ph), 4.31 (dd, 1 H, $J_{5,6e}$ = 4.2 Hz, $J_{6a,6e}$ = 9.9 Hz, H-6_e), 3.82 (ddd, 1 H, H-5), 3.72 (t, 1 H, $J_{5,6a}$= 10.0 Hz, H-6_a), 3.65 (dd, 1 H, $J_{3,4}$ = 2.6 Hz, $J_{4,5}$ = 9.3 Hz, H-4), 3.54 (ddd, 1 H, H-2), 2.33 (s, 3 H, CH_3), 2.12 (s, 3 H, CH_3); ^{13}C-NMR (50 MHz): δ 169.1 (C=O), 143.3 (C-ipso), 137.3 (C-ipso), 136.8 (C-ipso), 136.7 (C-ipso), 129.6 (aromatic), 129.5 (aromatic), 129.4 (aromatic), 128.8 (aromatic), 128.7 (aromatic), 128.6 (aromatic), 128.5 (aromatic), 128.4 (aromatic), 128.2 (aromatic), 128.1 (aromatic), 127.9 (aromatic), 127.6 (aromatic), 127.4, 127.1 (aromatic), 125.8 (aromatic), 101.1 (CHPh), 98.9 (C-1), 76.9, 70.9, 69.7, 68.7, 64.1, 56.3 (C-2), 21.3 (CH_3), 20.6 (CH_3).

Treatment of triflate 2 with KSAc: To a solution of benzyl 4,6-*O*-benzylidene-2-deoxy-2-phthalimido-β-D-allopyranoside, obtained[21] from **14**, (167 mg, 0.34 mmol) in dry CH_2Cl_2 (3 ml) under Ar at -30°C, were successively added Py (138 µl, 1.7 mmol, 5 eq) and Tf_2O (173 µl, 1.03 mmol, 3 eq) dropwise. The reaction was stirred for 1h from -30°C to 0°C; then, the mixture was poured onto ice-H_2O and extracted with CH_2Cl_2 (3 x 25 ml), dried (Na_2SO_4) and concentrated. Crude **2** was dissolved under Ar in dry DMF (3 ml) and treated with KSAc (77.5 mg, 0.68 mmol, 2 eq) for 1 h at r.t. The reaction mixture was diluted with CH_2Cl_2 (50 ml), washed with sat. $NaHCO_3$ solution (30 ml) and H_2O (30 ml), dried (Na_2SO_4) and concentrated. The residue was purified by FC (hexane/EtOAc 4:1) to give **4** (26 mg, 14%) and **6** (119 mg, 75%).

4: R_f (hexane:EtOAc 2:1) 0.48; ^{1}H-NMR (200 MHz): δ 7.78-7.03 (m, 14 H, aromatic), 5.55 (s, 1 H, CHPh), 5.43 (d, 1 H, $J_{1,2}$ = 7.9 Hz, H-1), 4.84 (d, 1 H, J = 12.2 Hz, CH_2Ph), 4.66-4.39 (m, 4 H, CH_2Ph, H-2, H-5, H-6_e), 3.85-3.71 (m, 3 H, H-3, H-4, H-6_a), 2.14 (s, 3 H, CH_3); ^{13}C-NMR (50 MHz): δ 193.34 (SC=0), 167.59 (C=O), 137.07 (C-ipso), 136.82 (C-ipso), 134.00 (C-ipso), 131.46 (C-ipso), 129.03 (aromatic), 128.21 (aromatic), 127.72 (aromatic), 127.64 (aromatic), 126.21 (aromatic), 123.49 (aromatic), 101.84 (CHPh), 98.71 (C-1), 78.69, 71.34, 69.61, 68.79, 54.57 (C-2), 44.96 (C-3), 30.36 (CH_3).

6: R_f (hexane:EtOAc 2:1) 0.59; m.p. 57-59 °C; $[\alpha]_D$ -133.2 (*c* 0.4, $CHCl_3$); ^{1}H-NMR (300 MHz): δ 7.84-7.02 (m, 14 H, aromatic), 5.62 (s, 1 H, CHPh), 5.30 (d, 1 H, $J_{1,2}$ = 7.2 Hz, H-1), 5.18-5.11 (m, 2 H, H-2, H-3), 4.88 (d, 1 H, J = 12.3 Hz, CH_2Ph), 4.67-4.59 (m, 1 H, H-5), 4.56 (d, 1 H, CH_2Ph), 4.47 (dd, 1 H, $J_{5,6e}$ = 6.5 and $J_{6a,6e}$ = 10.3 Hz, H-6_e), 3.88 (t, 1 H, $J_{5,6a}$ = 10.3 Hz, H-6_a); ^{13}C-NMR (50 MHz): δ 167.47 (C=O), 152.90 (C-4), 137.05 (C-ipso), 136.41 (C-ipso), 133.42 (aromatic), 131.79 (C-ipso), 129.47 (aromatic), 128.33 (aromatic), 128.20 (aromatic), 127.63 (aromatic), 126.24 (aromatic), 123.26 (aromatic), 103.29 (C-3), 102.92 (CHPh), 96.67 (C-1), 70.88 (CH_2Ph), 69.51 (C-6), 66.17, 49.62 (C-2).

Benzyl 4,6-*O*-benzylidene-2-deoxy-β-D-allopyranoside 2,3-sulfamidate (20): To a suspension of **14** (1.00 g, 2.50 mmol) in THF (15 ml) at r.t. was added NaH (190 mg, 7.52 mol, 3.0 eq). After 15 min, a solution of 1,1'-sulfonyldiimidazole (640 mg, 3.23 mmol, 1.3 eq) in THF (7 ml) was added dropwise during 10 min, and the mixture was stirred for 15 h. The reaction mixture was then quenched with MeOH, the solvents were evaporated, and the residue was purified by FC (CH_2Cl_2 →CH_2Cl_2/MeOH 100:1) to give 760 mg (72%) of **20**. A sample was crystallized (CH_2Cl_2/MeOH/hexane 10:1:10, 3 ml) for analysis: R_f (CH_2Cl_2/ EtOAc 4:1) 0.80; m.p. 167-169°C. $[\alpha]_D$ -61.4 (*c* 1.0, $CHCl_3$); ^{1}H-NMR (200 MHz): δ 7.48-7.38 (m, 10 H, aromatic), 5.57 (s, 1 H, CHPh), 5.13 (dd, 1 H, $J_{2,3}$ = 4.5, $J_{3,4}$ = 3.0 Hz, H-3), 5.07 (bs, 1 H, NH), 4.99 (d, 1 H, $J_{1,2}$ = 7.4 Hz, H-1), 4.93 (d, 1 H, *J* = 11.4 Hz, CH_2Ph), 4.65 (d, 1 H, CH_2Ph), 4.47 (dd, 1 H, $J_{5,6e}$ = 4.8 Hz, $J_{6a,6e}$ = 10.2 Hz, H-6_e), 4.00 (ddd, 1 H, $J_{4,5}$ = 9.3 Hz, $J_{5,6a}$ = 9.7 Hz, H-5), 3.89 (dd, 1 H, H-4), 3.79 (dd, 1 H, H-6_b), 3.61 (dd, 1 H, H-2). ^{13}C-NMR (50 MHz): δ 136.38 (C-ipso), 136.31 (C-ipso), 129.50 (aromatic), 128.67 (aromatic), 128.42 (aromatic), 128.15 (aromatic), 126.26 (aromatic), 102.70 (PhCH), 100.06 (C-1), 80.10, 75.52, 72.15 ($PhCH_2$), 68.77 (C-6), 63.02, 59.40 (C-2). Anal.: Calc. for $C_{20}H_{21}NO_7S$: C, 57.27; H, 5.05; N, 3.34; S, 7.64. Found: C, 56.57; H, 4.80; N, 3.50; S, 7.53.

Benzyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-allopyranoside 2,3-sulfamidate (7): To a suspension of **20** (970 mg, 2.31 mmol) in CH_2Cl_2 (30 ml) at r.t. was added Py (0.60 ml, 587 mg, 7.42 mol, 3.2 eq). After 5 min, AcCl (0.25 ml, 276 mg, 3.52 mmol, 1.5 eq) was added dropwise, and the mixture was stirred for 30 min. After this time, the reaction mixture was diluted with CH_2Cl_2 (160 ml), washed with H_2O (80 ml), and concentrated to give a residue which was purified by FC (CH_2Cl_2 → CH_2Cl_2/EtOAc 250:1 → 100:1) to give 1.05 g (98%) of **7**. R_f (CH_2Cl_2/ EtOAc 40:1) 0.34; m.p. 162-165°C; $[\alpha]_D$ -55.2 (*c* 1, $CHCl_3$); IR (KBr): 1100, 1370 cm^{-1} (-SO_2-); ^{1}H-NMR (200 MHz): δ 7.47-7.32 (m, 10 H, aromatic), 5.61 (s, 1 H, CHPh), 5.23 (dd, 1 H, $J_{2,3}$ = 4.3, $J_{3,4}$ = 2.3 Hz, H-3), 4.97 (d, 1 H, $J_{1,2}$ = 7.0 Hz, H-1), 4.94 (d, 1 H, *J* = 11.9 Hz, CH_2Ph), 4.78-4.64 (m, 1 H, H-2), 4.63 (d, 1 H, CH_2Ph), 4.49 (dd, 1 H, $J_{5,6e}$ = 4.7 Hz, $J_{6a,6e}$ = 9.6 Hz, H-6_e), 4.05 (ddd, 1 H, $J_{4,5}$ = 9.4 Hz, $J_{5,6a}$ = 9.6 Hz, H-5), 3.98 (dd, 1 H, H-4), 3.83 (dd, 1 H, H-6_a), 2.38 (s, 3 H, CH_3); ^{13}C-NMR (50 MHz): δ 136.19 (C-ipso), 129.60 (aromatic), 128.64 (aromatic), 128.45 (aromatic), 128.34 (aromatic), 127.95 (aromatic), 126.22 (aromatic), 102.84 (CHPh), 99.74 (C-1), 77.91, 75.00, 71.74, 68.86, 63.27, 58.82 (C-2), 22.52 (CH_3). Anal.: Calc. for $C_{22}H_{23}NO_8S$: C, 57.26; H, 5.02; N, 3.04; S, 6.95. Found: C, 58.31; H, 5.12; N, 3.02; S, 6.76.

Benzyl 2-allylamino-4,6-*O*-benzylidene-2-deoxy-β-D-allopyranoside 2,3-sulfamidate (21): To a suspension of **14** (1.13 g, 2.83 mmol) in THF (20 ml) at r.t. was added NaH (225 mg, 8.91 mol, 3.1 eq). After 15 min, a solution of 1,1'-sulfonyldiimidazole (860 mg, 4.34 mmol, 1.5 eq) in THF (8 ml) was added dropwise, and the mixture was stirred for 14 h. A solution of AllBr (0.62 ml, 867 mg, 7.16 mmol, 2.5 eq) in DMF (4.5 ml) was then added dropwise, and stirring was continued for 5 additional h. After this time, the reaction mixture was quenched with MeOH, diluted with CH_2Cl_2 (75 ml), filtered through cotton, and washed with H_2O (50 ml). The solvent was evaporated, and the residue was purified by FC (hexane/EtOAc 6:1 → 4:1) to give 930 mg (72%) of **21**. A sample was crystallized (hexane/EtOAc 4:1) for analysis: R_f (hexane/EtOAc 4:1) 0.22; m.p. 165-166°C; $[\alpha]_D$ -55.1 (*c* 1.3, $CHCl_3$); ^{1}H-NMR (200 MHz): δ 7.48-7.37 (m, 10 H, aromatic), 5.98-5.78 (m, 1 H, -CH=CH_2), 5.58 (s, 1 H, CHPh), 5.32-5.29 (m, 1 H, -CH=CH_2), 5.25-5.22 (m, 1 H, -CH=CH_2), 5.11 (dd, 1 H, $J_{2,3}$ = 4.7, $J_{3,4}$ = 3.0 Hz, H-3), 5.09 (d, 1 H, $J_{1,2}$ = 7.0 Hz, H-1), 4.94 (d, 1 H, *J* =

11.4 Hz, CH_2Ph), 4.66 (d, 1 H, CH_2Ph), 4.47 (dd, 1 H, $J_{5,6e}$ = 4.8 Hz, $J_{6a,6e}$ = 10.3 Hz, H-6_e), 4.02 (ddd, 1 H, $J_{4,5}$ = 9.5 Hz, $J_{5,6a}$ = 9.7 Hz, H-5), 3.95-3.72 (m, 2 H, -OCH_2), 3.89 (dd, 1 H, H-4), 3.79 (dd, 1 H, H-6_b), 3.61 (dd, 1 H, H-2). ^{13}C-NMR (50 MHz): δ 136.36 (2 C-ipso), 131.06 (=CH), 129.38 (aromatic), 128.53 (aromatic), 128.33 (aromatic), 128.24 (aromatic), 128.01 (aromatic), 126.18 (aromatic), 121.04 (=CH_2), 102.52 (CHPh), 100.40 (C-1), 77.25, 75.33, 71.80 (CH_2Ph), 68.76 (C-6), 62.64, 61.47 (C-2), 49.63 (NCH_2). Anal.: Calc. for $C_{23}H_{25}NO_7S$: C, 60.12; H, 5.48; N, 3.05; S, 6.98. Found: C, 60.37; H, 5.43; N, 3.11; S, 7.08.

Benzyl 2-*t*-butyloxycarbonylamino-4,6-*O*-benzylidene-2-deoxy-β-D-allopyranoside 2,3-sulfamidate (22): To a solution of **14** (500 mg, 1.19 mmol) in MeCN (15 ml) at r.t. was added DMAP (470 mg, 1.78 mol, 1.5 eq). After 5 min, Boc_2O (322 mg, 1.48 mmol, 1.2 eq) was added, and the mixture was stirred for 45 min. After this time, the reaction mixture was diluted with CH_2Cl_2 (40 ml), washed with H_2O (20 ml), and concentrated to give a residue which was purified by FC (hexane/EtOAc 7:1) to give 517 mg (84%) of **22**: R_f (hexane/EtOAc 4:1) 0.31; ^{1}H-NMR (200 MHz): δ 7.54-7.33 (m, 10 H, aromatic), 5.59 (s, 1 H, CHPh), 5.20 (dd, 1 H, $J_{2,3}$ = 4.3, $J_{3,4}$ = 2.7 Hz, H-3), 4.99 (d, 1 H, $J_{1,2}$ = 7.1 Hz, H-1), 4.97 (d, 1 H, J = 11.9 Hz, CH_2Ph), 4.66 (d, 1 H, CH_2Ph), 4.49 (dd, 1 H, H-2), 4.47 (dd, 1 H, $J_{5,6e}$ = 4.6 Hz, $J_{6a,6e}$ = 9.7 Hz, H-6_e), 4.02 (ddd, 1 H, $J_{4,5}$ = 9.5 Hz, $J_{5,6a}$ = 9.7 Hz, H-5), 3.92 (dd, 1 H, H-4), 3.81 (dd, 1 H, H-6_a), 1.55 (s, 9 H, $(CH_3)_3$); ^{13}C-NMR (50 MHz): δ 147.92 (C=O), 136.35 (C-ipso), 136.25 (C-ipso), 129.50 (aromatic), 128.45 (aromatic), 128.38 (aromatic), 128.04 (aromatic), 127.53 (aromatic), 126.22 (aromatic), 102.67 (CHPh), 100.45 (C-1), 85.86 ($(CH_3)_3$), 77.00, 74.91, 71.63, 68.75, 63.15, 59.17 (C-2), 27.72 (3 CH_3).

Treatment of sulfamidate 7 with nucleophiles (General procedure):

To a 0.02-0.10 M solution of sulfamidate **7** was added the nucleophile (2-10 eq) with stirring at the temperatures and for the times shown in Table 1. Then, the solvent was evaporated. For the cases in which compound **20** was the only product, the residue was purified by FC to give **20.** Otherwise, the residue was suspended in THF (0.10M), and treated with a solution (4 ml/mmol of substrate) of 96% H_2SO_4 (220 µl) and H_2O (70µl) in THF (5 ml) for 30-60 min. The reaction mixture was then diluted with CH_2Cl_2, washed with sat. $NaHCO_3$, and concentrated to give a residue which was purified by FC. Selected data of representative products are given below.

Benzyl 2-acetamido-3-*S*-acetyl-4,6-*O*-benzylidene-2-deoxy-3-thio-β-D-glucopyranoside (17a): R_f (CH_2Cl_2/acetone 10:1) 0.46; m.p. 242-244°C; $[\alpha]_D$ -112 (*c* 0.4, $CHCl_3$). ^{1}H-NMR (500 MHz, d_6-acetone): δ 7.42 - 7.25 (m, 10 H, aromatic), 5.62 (s, 1 H, CHPh), 5.60 (d, 1 H, J = 7.1 Hz, NH), 4.85 (d, 1 H, $J_{1,2}$ = 8.2 Hz, H-1), 4.84 (d, 1 H, J = 12.3 Hz, CH_2Ph), 4.63 (d, 1H, CH_2Ph), 4.28 (dd, 1 H, $J_{5,6e}$ = 4.9 and $J_{6a,6e}$ = 10.4 Hz, H-6_e), 4.09 (m, 1 H, H-2), 3.87 (t, 1 H, $J_{2,3} \approx J_{3,4}$ = 10.8 Hz, H-3), 3.80 (t, 1 H, $J_{5,6a}$ = 10.2 Hz, H-6a), 3.68 (dd, 1 H, $J_{4,5}$ = 8.9 Hz, H-4), 3.56 (m, 1 H, H-5), 2.24 (s, 3 H, CH_3), 1.8 (s, 3 H, CH_3); ^{13}C-NMR (50 MHz, $CDCl_3$: CD_3OD 7:1): δ 196.17 (SC=O), 170.87 (CO), 136.93 (C-ipso), 136.76 (C-ipso), 128.79 (aromatic), 128.10 (aromatic), 127.89 (aromatic), 127.59 (aromatic), 127.51 (aromatic), 125.82 (aromatic), 101.67 (CHPh), 101.31 (C-1), 77.92, 70.47, 69.44, 68.43, 53.38 (C-2), 47.10 (C-3), 30.32 (CH_3), 22.38 (CH_3). Anal.: Calc. for $C_{24}H_{27}NO_6S$: C, 63.0; H, 5.95; N, 3.06; S, 7.01. Found: C, 61.9; H, 5.76; N, 3.14; S, 6.83.

Benzyl 2-acetamido-3-azido-4,6-*O*-benzylidene-2,3-dideoxy-β-D-glucopyranoside (17b): R_f (CH_2Cl_2/acetone 10:1) 0.51; m.p. 262-265°C; $[\alpha]_D$ -63.8 (*c* 0.22, $CHCl_3$); IR (KBr): 2100 cm^{-1} (N_3; ^{1}H-NMR (300 MHz): δ 7.51-7.30 (m, 10 H, aromatic), 5.62 (d, 1 H, $J_{NH,2}$ = 7.5 Hz, NH), 5.59 (s, 1 H, CHPh), 5.1 (d, 1 H, $J_{1,2}$ = 8.3 Hz, H-1), 4.89 (d, 1 H, *J* = 11.8 Hz, CH_2Ph), 4.58 (d, 1 H, CH_2Ph), 4.44 (dd, 1 H, $J_{2,3}$ = 10.7 Hz, H-3), 4.41 (dd, 1 H, $J_{5,6e}$ = 4.7, $J_{6a,6e}$ = 10.7 Hz, H-6_e), 3.81 (t, 1 H, $J_{3,4} \approx J_{4,5}$ = 9.8 Hz, H-4), 3.61-3.49 (m, 2 H, H-5, H-6_a), 3.22 (ddd, 1 H, H-2), 1.97 (s, 3 H, CH_3); ^{13}C-NMR (50 MHz, $CDCl_3$: CD_3OD 2:1): δ 172.27 (C=O), 137.31 (C-ipso), 137.07 (C-ipso), 129.39 (aromatic), 128.65 (aromatic), 128.51 (aromatic), 128.19 (aromatic), 128.09 (aromatic), 126.28 (aromatic), 101.73 (CHPh), 100.57 (C-1), 80.41, 78.24, 71.31, 68.92, 67.31, 62.58, 55.34 (C-2), 22.83 (Ac). Anal.: Calc. for $C_{22}H_{24}N_5O_4$: C, 62.25; H, 5.7; N, 13.2. Found: C, 63.08; H, 5.62; N, 13.39.

Benzyl 2-acetamido-3-*O*-acetyl-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside (17c): R_f (hexane/EtOAc 1:2) 0.41. It was characterized as **12** after conventional deacetylation with NaOMe/MeOH.

Benzyl 2-acetamido-4,6-*O*-benzylidene-2,3-dideoxy-β-D-*erythro*-hex-3-enopyranoside (19): R_f (hexane/EtOAc 1:2) 0.48, ^{1}H-NMR (200 MHz): δ 7.46-7.35 (m, 10 H, aromatic); 5.58 (s, 1 H, CHPh); 5.42-5.39 (m, 2 H, H-3, NH); 4.84 (d, 1 H, *J* = 12.1 Hz, CH_2Ph); 4.77-4.67 (m, 2 H, H-1, H-2); 4.61 (d, 1 H, CH_2Ph); 4.43 (dddd, 1 H, $J_{2,5}$ = 1.4 Hz, $J_{3,5}$ = 1.8 Hz, $J_{5,6e}$ = 6.1 Hz, $J_{5,6a}$ = 10.5 Hz, H-5); 4.32 (dd, 1 H, $J_{6a,6e}$ = 9.6 Hz, H-6_e); 3.82 (dd, 1 H, H-6_a); 1.96 (s, 3 H, CH_3).

Benzyl 2-Acetamido-4,6-*O*-benzylidene-2,3-dideoxy-β-D-*erythro*-hex-2-enopyranoside (18): R_f (hexane/EtOAc 2:1) 0.26; ^{1}H-NMR (200 MHz): δ 7.39-7.35 (m, 10 H, aromatic), 6.83-6.75 (m, 2 H, H-3, NH), 5.63 (s, 1 H, CHPh), 5.33 (dd, 1 H, $J_{1,3}$ = 1.1 Hz, $J_{1,4}$ = 1.3 Hz, H-1), 4.84 (d, 1 H, *J* = 11.5 Hz, CH_2Ph), 4.64 (d, 1 H, CH_2Ph), 4.43 (ddd, 1 H, $J_{3,4}$ = 2.0 Hz, $J_{4,5}$ = 8.0 Hz, H-4), 4.33 (dd, 1 H, $J_{5,6e}$ = 3.8 Hz, $J_{6a,6e}$ = 9.5 Hz, H-6_e), 3.91 (dd, 1 H, $J_{5,6a}$ = 10.1 Hz), H-6_a; 3.80 (ddd, 1 H, H-5), 1.97 (s, 3 H, CH_3).

Benzyl 2 Acetamido-3-*S*-(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-4,6-*O*-benzylidene-2-deoxy-3-thio-β-D-glucopyranoside (9): To a solution of 2,3,4-tri-*O*-acetyl-1-thio-α-L-fucopyranose (1.5 g, 4.9 mmol, 1.5 eq) in dry DMF (8.5 ml) was added NaH (123.6 mg, 5.15 mmol, 1.65 eq) at 0°C for 5 min. After this time, a solution of compound **7** (1.44 g, 3.12 mmol) in dry DMF (12 ml) was added slowly at 0 °C to the reaction mixture. Then, the mixture was stirred at r.t. for 30 min. and worked-up as described in the general procedure. R_f (hexane:EtOAc 1:1) 0.36; m.p. 132-134°C; $[\alpha]_D$ -122 (*c* 1, $CHCl_3$); ^{1}H-NMR (500 MHz): δ 7.48-7.28 (10 H, m, aromatic), 5.73 (d, 1 H, $J_{1,2}$ = 5.6 Hz, H-1'), 5.52 (d, 1 H, $J_{NH,2}$ = 6.9 Hz, NH), 5.51 (s, 1 H, CHPh), 5.14 (dd, 1 H, $J_{2',3'}$ = 10.8 Hz, $J_{3',4'}$ = 3.1 Hz, H-3'), 5.08 (d, 1 H, H-4'), 5.03 (dd, 1 H, H-2'), 4.85 (d, 1 H, *J* = 11.9 Hz, CH_2Ph), 4.83 (d,1 H, $J_{1,2}$ = 7.8 Hz, H-1), 4.56 (1H, d, CH_2Ph), 4.39 (m, 1H, H-5'), 4.33 (dd, 1 H, $J_{5,6e}$ = 4.7 Hz, $J_{6a,6e}$= 10.6 Hz, H-6_e), 3.74 (t, 1 H, $J_{5,6a}$ = 10.5 Hz, H-6a), 3.52-3.60 (m, 2 H, H-2, H-5), 3.40-3.37 (m, 2 H, H-3, H-4), 2.05 (s, 3 H, CH_3), 1.98 (s, 3 H, CH_3), 1.95 (s, 6 H, 2 CH_3), 0.64 (d, 3 H, *J* = 6.6 Hz, CH_3-Fuc); ^{13}C-NMR (50 MHz): δ 171.09 (C=O), 171.04 (C=O), 170.71 (C=O), 137.79 (C-ipso), 129.84 (aromatic), 129.12 (aromatic), 128.83 (aromatic), 128.69 (aromatic), 127.00 (aromatic), 102.85 (CHPh), 101.27 (C-1), 82.60 (C-1'), 79.56, 71.70, 71.52, 70.37, 69.38, 69.14, 68.89,

65.62, 58.78 (C-2) , 46.44 (C-3), 24.04 (CH_3), 21.37 (CH_3), 21.26 (CH_3), 21.12 (CH_3), 15.87 (CH_3-Fuc). Anal.: Calc. for $C_{34}H_{41}NO_{12}S$: C, 79.38 ; H, 6.01; N, 2.04; S, 4.66. Found: C, 59.35; H, 6.12; N, 2.03; S, 4.86.

Benzyl 2-acetamido-3-*S*-(2,3,4-tri-*O*-acetil-α-L-fucopyranosyl)-2-deoxy-3-thio-β-D-glucopyranoside (27): A mixture of **9** (270 mg, 0.39 mmol) and camphorsulfonic acid (22.7 mg, 0.078 mmol, 0.2 eq) in MeOH (5.5 ml) was stirred at 50 °C for 1.5 h. After cooling at r.t., the reaction mixture was diluted with CH_2Cl_2 (25 ml), washed with sat. $NaHCO_3$ solution (25 ml) and H_2O (25 ml), dried (Na_2SO_4) and concentrated. The residue was purified by FC (hexane/EtOAc 1:2→1:4), to give **26** (172 mg, 73%). R_f (hexane/acetone 1:1) 0.24; m.p. 125 -127°C; $[\alpha]_D$ -172 (*c* 1, $CHCl_3$); ^{1}H-NMR (300 MHz): δ 7.37 -7.29 (m, 5 H, aromatic), 5.74 (d, 1 H, $J_{1',2'}$ = 5.3 Hz, H-1'), 5.55 (d, 1 H, $J_{NH,2}$ = 8.2 Hz, NH), 5.29 (dd, 1 H, $J_{3',4'}$ = 3.0, $J_{4',5'}$= 1.0 Hz, H-4'), 5.19 (dd, 1 H,$J_{2',3'}$ =11.0, H-2'), 5.12 (dd, 1 H, H-3'), 4.87 (d, 1 H, J = 11.9 Hz, CH_2Ph), 4.80 (d, 1 H, $J_{1,2}$ = 7.9 Hz, H-1), 4.61 (d, 1 H, CH_2Ph), 4.58 (q, 1 H, H-5'), 3.92- 3.72 (m, 3 H, H-6_a, H-6_b, H-5), 3.44- 3.53 (m, 3 H, H-2, OH, OH), 3.32- 3.28 (m, 2 H, H-3, H-4), 2.15 (s, 3 H, CH_3), 2.06 (s, 3 H, CH_3), 1.99 (s, 3 H, CH_3), 1.95 (s, 3 H, CH_3), 1.16 (d, 1 H, J = 6.4 Hz, CH_3-Fuc); ^{13}C-NMR (50 MHz): δ 169.73 (C=O), 169.72 (C=O), 169.63 (C=O), 169.22 (C=O), 136.65 (C-ipso), 127.84 (aromatic), 127.37 (aromatic), 99.72 (C-1), 82.81 (C-1'), 77.17, 70.36, 69.92, 69.73, 67.53, 67.34, 65.11, 62.25, 55.38, 52.29, 22.75 (CH_3), 20.15 (CH_3), 20.0 (CH_3), 19.9 (CH_3), 15.25 (CH_3-Fuc). Anal.: Calc for C_{27} $H_{37}NO_{12}S$: C, 54.08; H, 6.22; N, 2.32; S, 5.35. Found: C, 53.75; H, 6.02; N, 2.34; S, 5.29.

Benzyl 2-Acetamido-3-*S*-(α-L-fucopyranosyl)-2-deoxy-3-thio-β-D-glucopyranoside (26): Compound **27** (80 mg, 0.13 mmol) was treated with a 0.1 M solution of NaOMe in MeOH (2.6 ml). After 30 min, the reaction mixture was diluted with MeOH (25 mL) and neutralized with Amberlite® IR-120 (H^+) and filtered. The filtrate was concentrated and the residue was purified by FC (CH_2Cl_2/MeOH 5:1) to give **27** (59 mg, 94%). R_f (CH_2Cl_2/MeOH 5:1) 0.22; m.p. 261-263°C; $[\alpha]_D$ -200.6 (*c* 0.2, MeOH); ^{1}H-NMR (300 MHz, D_2O): δ 7.23-7.14 (m, 5 H, aromatic), 5.1 (d, 1 H, $J_{1',2'}$ = 5.8 Hz, H-1'), 4.44 (d, 1 H, J = 11.9 Hz, CH_2Ph), 4.30 (d, 1 H, $J_{1,2}$ = 8.4 Hz, H-1), 4.21 (q, 1 H, H-5'), 3.80-3.70 (m, 2 H, H-2', H-6a), 3.59-3.51 (m, 3 H, H-2, H-6b, H-4'), 3.45 (dd, 1 H, $J_{2',3'}$ = 10.3 and $J_{3',4'}$ = 3.2 Hz, H-3'), 3.28- 3.19 (m, 2 H, H-4, H-5), 2.5 (dd, 1 H, J = 9.3, J = 11.8 Hz, H-3), 1.7 (s, 3 H, CH_3), 0.95 (d, 1 H, J = 6.5 Hz, CH_3-Fuc). ^{13}C-NMR (50 MHz,CD_3OD): δ 173.41 (CO), 139.18 (C-ipso), 129.32, 128.87, 128.68 (aromatics), 102.84 (C-1), 88.52 (C-1'), 80.55, 73.41, 72.30, 71.47, 70.31, 69.59, 68.98, 63.14, 56.51(C-2) , 54.54 (C-3), 22.99 (CH_3), 16.53 (CH_3-Fuc). Anal.: Calc. for $C_{21}H_{31}NO_9S$: C, 33.27; H, 6.6; N, 6.77; S, 2.96. Found: C, 53.51; H, 6.83; N, 3.16; S, 6.60.

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