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Note

Differently N-protected 3,4,6-tri-*O*-acetyl-2-amino-2-deoxy-D-glucopyranosyl chlorides and their application in the synthesis of diosgenyl 2-amino-2-deoxy-β-D-glucopyranoside

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ABSTRACT

Four differently N-protected 3,4,6-tri-*O*-acetyl-2-amino-2-deoxy-D-glucopyranosyl chlorides were synthesized and used as glycosyl donors in reactions with diosgenin. The following amine group protections were tested: trifluoroacetyl (TFA), 2,2,2-trichloroethoxycarbonyl (Troc), phthaloyl (Phth), and tetrachlorophthaloyl (TCP). Products of glycosylation were deprotected to yield diosgenyl 2-amino-2-deoxy-β-D-glucopyranoside. The efficiency of the procedures is discussed. Additionally, a single-crystal X-ray diffraction analysis for 3,4,6-tri-*O*-acetyl-2-deoxy-2-tetrachlorophthalimido-β-D-glucopyranosyl chloride is reported. Orientations of the pyranose substituents as well as the planarity of the acetoxy and phthalimide groups in the crystal lattice are discussed. Structural evidence is presented for a mesomeric effect in both groups. The preference of the *cis* over *trans* orientation of the acetoxy group is confirmed in the crystal lattice.

2-Amino-2-deoxy-D-glucose is widely distributed in living organisms where it is an important component of oligosaccharides and glycoconjugates.[1] Because of the abundance and biological importance of 2-amino-2-deoxy-D-glucose, much effort has been put into developing chemical methods of its glycosidation.[2,3] These methods are often derived from those reported for the 'usual' carbohydrates. However, the presence of the 2-amino group complicates the typical approach to glycoside bond formation, since this demands suitable protection of the amino group. Unfortunately, glycoside bond formation with donors derived from naturally occurring *N*-acetyl-2-amino-2-deoxy-D-glucose is unsatisfactory. This usually results in the formation of relatively stable oxazolines that cannot be converted into aminosugars under mild conditions. Therefore, various glucosamine donors, with modified or latent amino functionalities, have been investigated.[3,4]

Our research aims to synthesize derivatives of diosgenyl 2-amino-2-deoxy-β-D-glucopyranoside (**18**), a compound with promising antitumor and antimicrobial activity.[5,6] Naturally occurring diosgenyl glycosides belong to the group of saponins. These are steroid or triterpenoid glycosides, widely distributed in plants and certain marine organisms.[7–9] As their name suggests, saponins are natural surfactants and have been used as detergents, foaming agents, and emulsifiers. But these natural glycosides also display a wide range of biological activities, including anti-inflammatory, antibacterial, antiparasitic, antifungal, and antitumor activities.[10–13] The yields of homogenous saponins isolated from nature are rather small. Therefore, chemical synthesis is necessary to investigate structure–activity relationships and the mechanisms of action of saponins.[14–20]

Diosgenyl 2-amino-2-deoxy-β-D-glucopyranoside (**18**) is a synthetic saponin, which has not yet been found in nature. The presence of the amine group in this promising antitumor and antimicrobial compound creates the opportunity to synthesize its new analogues with better cytotoxic activity.[21] To find the best procedure for the synthesis of **18** we studied different glycosyl donors, different amine group protections, and a variety of other conditions. Here, we compare the results of diosgenin glycosylation with differently N-protected 3,4,6-tri-*O*-acetyl-2-amino-2-deoxy-D-glucopyranosyl chlorides. These are glycosyl donors typical of the Koenigs–Knorr procedure, the best known method for the preparation of 1,2-*trans*-glycosides, which requires silver salts as promoters. The following N-protection groups were tested (Fig. 1): trifluoroacetyl (TFA), 2,2,2-trichloroethoxycarbonyl (Troc), phthaloyl (Phth), and tetrachlorophthaloyl (TCP). Importantly, the results are useful for the glycosidation of 2-amino-2-deoxysugars in general. Additionally, a single-crystal X-ray diffraction analysis for 3,4,6-tri-*O*-acetyl-2-tetrachlorophthalimido-β-D-glucopyranosyl chloride is reported. This enables studies of the geometries of

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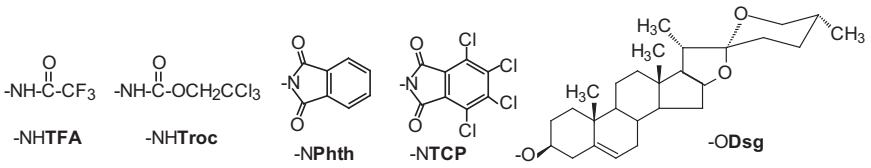
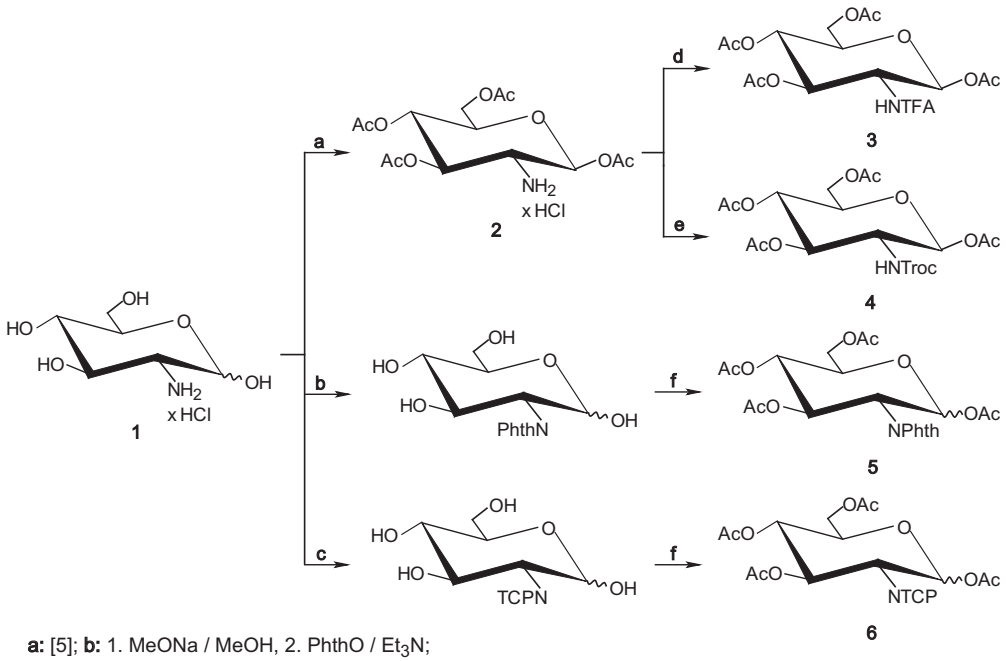


Figure 1. The abbreviations used.

pyranose ring substituents. Such studies are important and extensively carried out usually by theoretical calculations.[22]

To introduce the TFAc and Troc protecting groups onto the amine function of D-glucosamine, D-glucosamine hydrochloride (**1**) was first converted into 1,3,4,6-tetra-*O*-acetyl-β-D-glucosamine hydrochloride (**2**) as previously reported.[5] Product **2** was next acylated with trifluoroacetic anhydride to give 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-trifluoroacetamido-β-D-glucopyranose (**3**). Acylation of **2** with 2,2,2-trichloroethoxycarbonyl chloride, performed according to the literature procedure,[23] yielded 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranose (**4**). The protecting Phth and TCP groups were introduced onto D-glucosamine directly by reaction with phthalic anhydride and with 3,4,5,6-tetrachlorophthalic anhydride, respectively, followed by acetylation with acetic anhydride and pyridine. In the first case we adopted the procedure described for D-galactosamine[24] and after column chromatography obtained 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-phthalimido-D-glucopyranose (**5**) as a mixture of anomers (α:β = 1:4), yield 50%. Crystallization of this mixture with ethanol provided pure β-anomer, yield 34%. Another methodology, described by Dasgupta and Garegg, for obtaining **5** produced only the β anomer yield 44%.[25] 1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-(3,4,5,6-tetrachlorophthalimido)-D-glucopyranose (**6**) was synthesized from the latter (**5**, **6**). Additionally, the overall yields are better when the acetylation is carried out first. The final amounts of **3**–**6** calculated with reference to 1 mmol of **1** are 0.81 mM of **3** (pure β), 0.68 mM of **4** (pure β), 0.5 mM of **5** (α + β), and 0.62 mM of **6** (α + β). These observations clearly also depend on the protecting groups used.

To synthesize N-protected 3,4,6-tri-*O*-acetyl-2-amino-2-deoxy-D-glucopyranosyl chlorides (**7**–**10**) Magnusson's procedure described for 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-phthalimido-α,β-D-galactopyranose was adopted.[26] Thus, acetates **3** and **4** were treated with 1,1-dichloromethyl methyl ether (~9 equiv) and zinc chloride (~0.06 equiv), which gave solely the α chloride **7** ($J_{1,2}$ 3.6 Hz) (yield 90%) and the α chloride **8** ($J_{1,2}$ 3.6 Hz) (yield 98%), respectively. Both **7** and **8** were of sufficient purity for use in the glycosylation reaction. In turn, treatment of **5** with 1,1-dichloromethyl methyl ether (~9 equiv) and boron trifluoride etherate (~4 equiv) yielded 91% of the β chloride **9** ($J_{1,2}$ 9.6 Hz) of sufficient purity for use in the glycosylation reaction. Recrystallization from diethyl ether/petroleum ether yielded 80% of crystalline **9**. The analogous reaction of **6** yielded 98% of the β chloride **10** ($J_{1,2}$ 9.2 Hz) of sufficient purity for use in the glycosylation reaction. Recrystallization from diethyl ether/petroleum ether yielded 67% of crystalline **10**.



a: [5]; **b:** 1. MeONa / MeOH, 2. PhthO / Et_3N;
c: 1. MeONa / MeOH, 2. TCPO / Et3N; **d:** TFAA / Py; **e:** TrocCl / Py; **f:** Ac_2O / Py.

1 as previously reported.[5] Comparing these two procedures of obtaining N-protected acetates **3**–**6**, one may see that when the acetylation is carried out first the final products are the pure β anomers (**3**, **4**). When the N-protection is carried out first the final products are the mixtures of α and β anomers with the clear dominance of

In the next step, the coupling reactions of N-protected 3,4,6-tri-*O*-acetyl-2-deoxy-2-amino-D-glucopyranosyl chlorides (**7**–**10**) and diosgenin were carried out to obtain the respective N-protected diosgenyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-amino-β-D-glucopyranosides (**11**–**14**). All glycosylations of diosgenin were carried out in

the presence of AgOTf used in conjunction with activated and finally powdered 4 Å molecular sieves in a mixture of CH_2Cl_2/Et_2O for **11** and **12** and in CH_2Cl_2 for **13** and **14**. In such conditions the glycosidations were efficient and stereoselective, providing solely diosgenyl β-glycosides in yields of 69%, 86%, 99%, and 87% respectively. The duration of these reactions does not depend on the N-protecting group or on the anomeric configuration of the respective chlorides. In all cases glycosylation took about 20 h.

The final steps in the synthesis of **18** require deprotection of the hydroxyl and amine functions. In principle, the N-protected per-*O*-acetyl-D-glucosamine glycosides (**11**–**14**) should be O-deacetylated first. Otherwise, *O*→*N* acetyl migration will take place. Thus, MeONa in MeOH was used to remove *O*-acetyl groups in **11** and **13**. In this way, **15** and **17** were obtained in yields of 98% and 76% respectively. The analogous O-deacetylation of **12** was not carried out since it was previously reported that the *N*-Troc group is converted into the corresponding carbamate in such basic conditions.[27] Therefore, two other procedures were attempted. One of them involves Et_3N in MeOH and produces **16** (yield 69%) without affecting the *N*-Troc group. In the second method, adopted from other *N*-Troc protected 2-amino-2-deoxy sugars,[27] MeONa was applied together with a guanidine/guanidinium nitrate buffer in the mixture of $MeOH/CH_2Cl_2$. Such O-deacetylation also took place without affecting the *N*-Troc group and led to **16** (yield 57%). Compounds **15**–**17** were N-deprotected in accordance with the groups to be removed. Thus, the trifluoroacetyl group was readily removed by basic hydrolysis with NaOH in acetone to give diosgenyl 2-amino-2-deoxy-β-D-glucopyranoside (**18**) (yield 80%). The 2,2,2-trichloroethoxycarbonyl group was removed with zinc in acetic acid, as reported for other *N*-Troc protected compounds.[28–30] Unfortunately, this removal of the *N*-Troc group from **16** was problematic and yielded a homogeneous mixture of **18** and an unidentified product. The phthaloyl group was removed by treatment of **17** with excess of ethylenediamine in ethanol to give **18** (yield 81%).

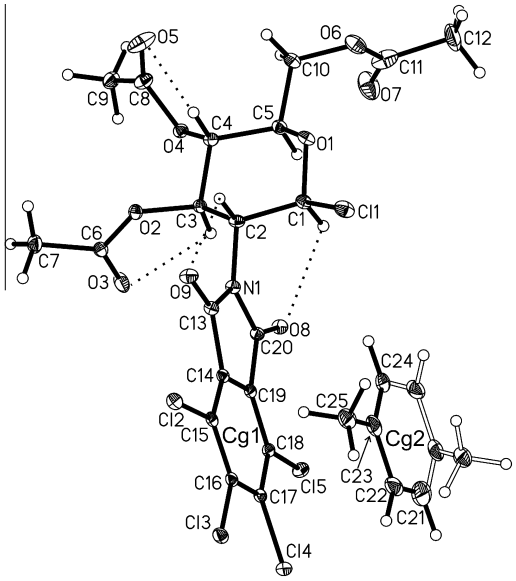
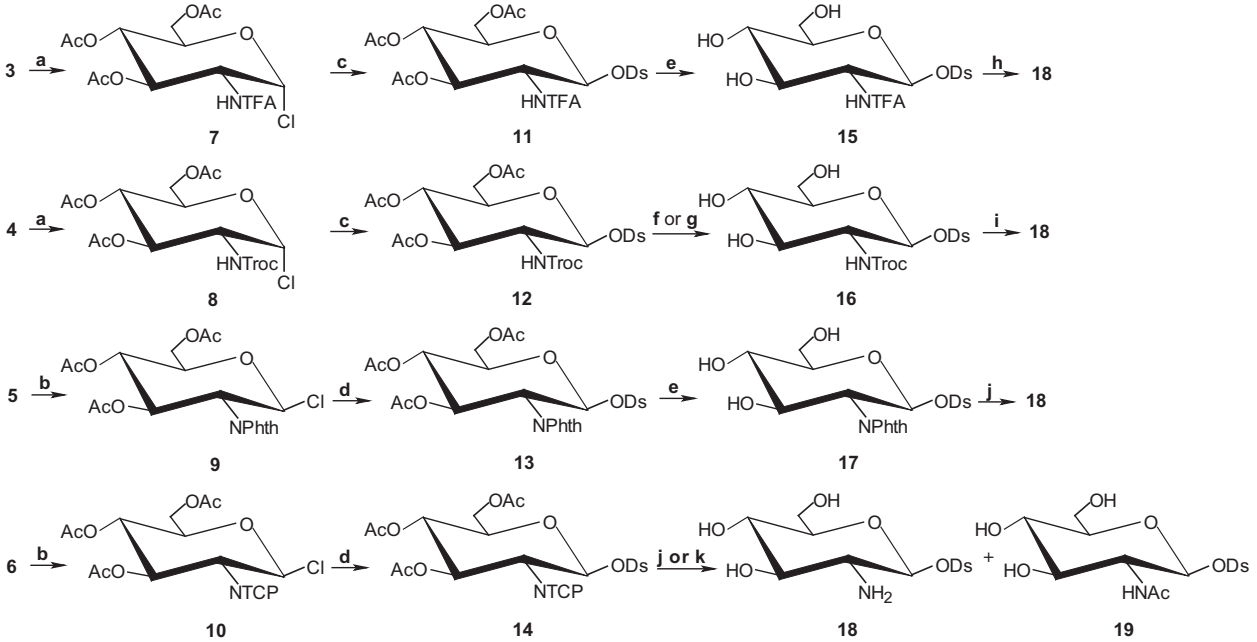


Figure 2. Structure of **10** showing 25% probability displacements for ellipsoids. The intramolecular C–H···O interactions are represented by dotted lines; Cg1 and Cg2 denote the ring centroids.

In the case of diosgenyl glycoside **14** we tried to remove the O- and N-protective groups under the same reaction conditions. With this end in view, six equivalents of ethylenediamine in ethanol were used, which led to **18** and **19** in yields of 70% and 29% respectively.[5] Such a result indicates that the *O*→*N* acetyl migration occurs in the conditions applied. To avoid this, we tested different excesses of ethylenediamine, but in all cases both **18** and **19** were obtained. The use of the mixture of $CH_3CN/THF/EtOH$ (2:1:1) instead of ethanol, which was reported for selective *N*-TCP



a: $Cl_2CHCOCH_3$ / $ZnCl_2$ / $CHCl_3$; **b:** $Cl_2CHCOCH_3$ / BF_3 x Et_2O / $CHCl_3$; **c:** DsOH / AgOTf / CH_2Cl_2 / Et_2O; **d:** DsOH / AgOTf / CH_2Cl_2;
e: MeONa / MeOH; **f:** Et_3N / MeOH; **g:** guanidine / guanidine x HNO_3; **h:** NaOH / acetone / H_2O; **i:** Zn / CH_3COOH;
j: $H_2NCH_2CH_2NH_2$ / EtOH; **k:** H_2NNH_2 x H_2O / EtOH.

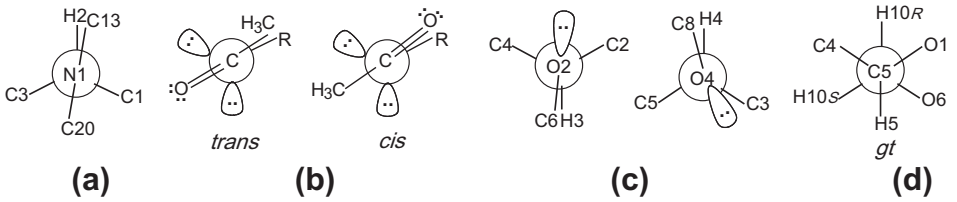


Figure 3. Newman projections: along the N1–C2 bond in the crystal lattice of **10** (a), along the Ac–O bond of the two orientations of the acetoxy group (R = sugar residue) (b), along the AcO2–C3 and AcO4–C4 bonds in the crystal lattice of **10** (c), along the C5–C10 bond in the crystal lattice of **10** (d).

deprotection in the presence of *O*-acetyl groups,[31] caused substrate **14** not to react at all. Exclusive synthesis of **18** from **14** was achieved using hydrazine hydrate in ethanol. In such conditions **18** was obtained in a yield of 97% after column chromatography and with a 74% yield after crystallization from methanol.

In the crystal structure, the asymmetric part of 3,4,6-tri-*O*-acetyl-2-deoxy-2-(3,4,5,6-tetrachlorophthalimido)-β-D-glucopyranosyl chloride (**10**) consists of one molecule of sugar and half a molecule of disordered solvent (toluene), which lies on the crystallographic mirror plane (Fig. 2). The arrangement of chloride **10** and toluene in the crystal lattice is determined by the π–π interactions of the aromatic rings (Fig. S2, Table S4 in Supplementary data). In the crystal chloride **10** adopts the $^4C_1$ conformation (Fig. 2) with ring-puckering parameters[32,33] $Q = 0.602(4)$ Å, $\theta = 7.9(4)$ Å, and $\varphi = 334(3)°$.

Starting analysis of the geometry of **10** from the chloride it is worth pointing out that the Cl1–C1 bond length of 1.777 Å (Table S2) is typical of the β chlorides in the $^4C_1$ conformation, where an *endo*-anomeric effect does not operate. The α chlorides are characterized by the Cl1–C1 bond length >1.8 Å.[34]

The tetrachlorophthalimide group is almost planar and the C2 sugar carbon atom belongs to the plane created by the two fused rings of the NTCP. This is illustrated by the respective torsion angles, for example, the C2–N1–C13–C14 torsion angle of −172.7° (Table S2). The observed planarity implies sp^2 hybridization of the N1 nitrogen atom. Indeed, the C13–N1–C2 (122.8°), C20–N1–C2 (124.3°), and C20–N1–C13 (112.4°) valence angles confirm the trigonal planar geometry of this part of the NTCP group. This planarity is necessary for the delocalization of nitrogen lone pair of electrons onto the carbonyl oxygen atoms. The fact that such delocalization occurs is demonstrated by the N1–C13 and N1–C20 bond lengths, which are 1.392 and 1.388 Å respectively. These are significantly shorter than the N1–C2 bond length of 1.467 Å, which is due to the partial double-bond character of the shorter bonds resulting from the mesomeric effect and delocalization of the electrons.

The planar tetrachlorophthalimide group of **10** in the crystal lattice is arranged in such a way that the C13 carbon atom of the TCP is eclipsed by the glucosamine H2 proton (Fig. 3a). This orientation is confirmed by the C13–N1–C2–C3 torsion angle of −122.3° and the C13–N1–C2–C1 torsion angle of 114.4° (Table S2). Thus, the NTCP group is almost perpendicular to the pyranose ring. In this way steric strain is minimized and, moreover, C–H···O interactions between the O8 and pyranose H1 atoms and between the O9 and pyranose H2 atoms are possible.

In our previous papers, both crystallographic[35] and theoretical,[36] we consistently demonstrated that the acetoxy group is planar starting from the respective pyranose carbon atom. Being planar, the acetoxy group may adopt two orientations with regard to the Ac–O bond rotation, in which the carbonyl oxygen is oriented *trans* or *cis* to the respective sugar carbon atom (Fig. 3b). Our studies of peracetylated glycals, based on DFT calculations, have indicated that the *trans* orientation of the acetoxy group is unfavourable, which is due to both electronic and steric interactions.[37] This paper provides an additional reason why the acetoxy group in carbohydrate derivatives prefers the *cis* over the *trans* orientation. Thus, the C3–O2–C6–O3 (7.4°), C4–O4–C8–O5 (8.7°), and C10–O6–C11–O7 (−2.5°) torsion angles (Table S2) confirm that the acetoxy groups are almost planar and *cis* oriented in the crystal lattice of **10**. Besides the previously discussed steric and electronic factors, X-ray analysis of **10** reveals that the *cis* orientation of the acetoxy groups enables the carbonyl oxygen atoms to interact preferentially with the pyranose ring hydrogen atoms. These intramolecular C–H···O interactions are illustrated in Figure 2 and Table S3. Because of them the 3-OAc and 4-OAc groups are oriented in such a way that the C6 and C8 carbonyl atoms are almost eclipsed by the H3 and H4 atoms respectively (Fig. 3c). This is indicated by the C6–O2–C3–C2 torsion angle of −124.6° and the C8–O4–C4–C3 torsion angle of 130.9°.

The planarity of the acetoxy groups is necessary for the delocalization of the non-carbonyl oxygen lone pair of electrons onto the carbonyl oxygen atom. Hence, this planarity provides evidence of the mesomeric effect in the acetoxy group. This effect is additionally illustrated in the crystal lattice of **10** by the C6–O2 (1.337 Å), C8–O4 (1.353 Å), and C11–O6 (1.200 Å) bond lengths, which are significantly shorter than the similar C3–O2 (1.435 Å), C4–O4 (1.441 Å), and C10–O6 (1.426 Å) bond lengths. These differences are due to the partial double-bond character of the shorter bonds resulting from the mesomeric effect and delocalization of the electrons.

With regard to the rotation about the exocyclic C5–C10 bond, the acetoxymethyl group of **10** adopts the staggered *gt* conformation in the crystal lattice (Fig. 3d), which is confirmed by the O1–C5–C10–O6 torsion angle of 51.2°. Such a conformation is typical of D-hexopyranoses, which have the C4 substituent oriented both equatorially and axially.[33]

1. Experimental

1.1. General methods

The melting points were uncorrected. The optical rotations were determined at rt with a Perkin–Elmer polarimeter in a 1-dm tube at the D line of sodium for solution in $CHCl_3$, CH_3OH, or $CHCl_3/CH_3OH$ (1:1, v/v). The IR spectra were recorded as Nujol mulls with a Bruker IFS 66 spectrophotometer; ^1H and ^{13}C NMR spectra on a Varian Mercury 400 (400/100 MHz) instrument for solution in $CDCl_3$, CD_3OD, $CDCl_3/CD_3OD$ (1:1, v/v), or DMSO (internal Me_4Si); elemental analyses were done on a Carlo Erba EA 1108 instrument. Thin-layer chromatography (TLC) was performed on E. Merck Kieselgel 60 F-254 plates using the eluent systems (v/v) A, 5:1 toluene–ethyl acetate; B, 2:1 toluene–ethyl acetate; C, 1:3 $CHCl_3$–MeOH; D, 4:1 CCl_4–acetone; E, 6:1 toluene–ethyl acetate; F, 10:1 $CHCl_3$–MeOH; G, 8:1 $CHCl_3$–MeOH; H, 7:1 $CHCl_3$–MeOH; I, 5:1 $CHCl_3$–MeOH, and column chromatography on MN Kieselgel 60 (<0.08 mm) with one of the eluent systems listed above.

1.2. 1,3,4,6-Tetra-*O*-acetyl-β-D-glucosamine hydrochloride (2)

This was synthesized from **1** as previously reported.[5]

1.3. 1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-trifluoroacetamido-β-D-glucopyranose (3)

This was synthesized from **2** as previously reported.[5]

1.4. 1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranose (4)

This was synthesized from **2** (2.22 g, 5.8 mM) according to the literature procedure.[23] Purification with column chromatography (solvent A) gave **4** (2.33 g, 77%): mp 123–125 °C, lit.[23] mp 125–126 °C; $[\alpha]_D^{20}$ +15 (*c* 0.5, $CHCl_3$), lit.[21] +14 (*c* 0.9, $CHCl_3$); R_f 0.53 (solvent B); IR: *ν* 3379 (N–H), 1751 (acetyl C=O), 1718 (Troc C=O), 1536 cm^{-1} (–NH, C–N); the ^1H NMR (400 MHz, $CDCl_3$) data were identical with those of presented in Ref. 22; ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 171.11, 170.65, 169.65, 169.50, (4 × acetyl C=O), 154.40 (Troc C=O), 92.50 (C-1), 74.68 (Troc CH_2), 72.99 (C-5), 72.29 (C-3), 68.18 (C-4), 61.81 (C-6), 55.27 (C-2), 21.06, 20.94, 20.83, 20.80 (4 × acetyl CH_3); Anal. Calcd for $C_{17}H_{22}Cl_3NO_{11}$: C, 39.06; H, 4.24; N, 2.68. Found: C, 39.10; H, 4.24; N, 2.65.

1.5. 1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-phthalimido-α,β-D-glucopyranose (5)

D-Glucosamine hydrochloride (2.73 g, 12.6 mmol) was added to a NaOMe solution prepared from Na (0.29 g, 12.6 mmol) and MeOH (12.6 mL) with simultaneous stirring. After 7 min the resultant NaCl was filtered and washed with MeOH. The filtrate was treated with phthalic anhydride (0.93 g, 6.3 mmol) and stirred. After 15 min the reaction mixture was treated again with the anhydride (1 g, 6.7 mmol) and with Et_3N (1.8 mL, 13 mmol). Then the mixture was stirred for 2 h at 50 °C; the end of reaction was detected by TLC (solvent C). After cooling to about 5 °C diethyl ether (50 mL) was added to the reaction mixture. The precipitate was treated with pyridine (40 mL) and Ac_2O (23 mL) at rt for 20 h. Then the solution was poured into ice-water and the aqueous mixture extracted with $CHCl_3$ (3 × 50 mL). The organic extracts were combined and washed with H_2O (30 mL), satd aq $NaHCO_3$ (2 × 50 mL), and H_2O (50 mL). The organic layer was dried with Na_2SO_4, filtered, and the solvent evaporated. The residue was chromatographed (solvent A) to yield **5** as a mixture of anomers (*α*:*β* = 1:4) (3.0 g, 50%). Crystallization of **5** with EtOH yielded the β anomer (2.06 g, 34%): mp 90–94 °C, lit.[25] mp 90–94 °C; $[\alpha]_D^{20}$ +59 (*c* 0.5, $CHCl_3$), lit.[25] +65.5 (*c* 1.0, $CHCl_3$); R_f 0.38 (solvent A); ^1H NMR (100 MHz, $CDCl_3$): *δ* 7.87, 7.76 (2 m, 4H, Phth), 6.52 (d, 1H, $J_{1,2}$ 9.2 Hz, H-1), 5.89 (dd, 1H, $J_{3,4}$ 9.2 Hz, H-3), 5.22 (dd, 1H, $J_{4,5}$ 10.4 Hz, H-4), 4.48 (dd, 1H, $J_{2,3}$ 10.8 Hz, H-2), 4.38 (dd, 1H, $J_{6,6'}$ 12.4 Hz, H-6), 4.15 (dd, 1H, H-6′), 4.03 (m, 1H, $J_{5,6}$ 4.4, $J_{5,6'}$ 2.0 Hz, H-5), 2.12, 2.05, 2.00, 1.87 (4 s, 12H, 4 × OAc); ^{13}C NMR (400 MHz, $CDCl_3$): *δ* 170.87, 170.22, 169.67, 168.84, 167.56 (6 × C=O), 134.69, 123.98 (Phth), 89.91 (C-1), 72.77 (C-5), 70.65 (C-3), 68.12 (C-4), 61.68 (C-6), 53.64 (C-2), 20.95, 20.92, 20.79, 20.57 (4 × acetyl CH_3); Anal. Calcd for $C_{22}H_{23}NO_{11}$: C, 55.35; H, 4.86; N, 2.93. Found: C, 55.51; H, 5.08; N, 2.89. The α anomer remained in the mixture (syrup): ^1H NMR (400 MHz, $CDCl_3$): *δ* 7.85, 7.75 (2 m, 4H, Phth), 6.57 (dd, 1H, $J_{3,4}$ 9.2 Hz, H-3), 6.29 (d, 1H, $J_{1,2}$ 3.2 Hz, H-1), 5.17 (dd, 1H, $J_{4,5}$ 10.4 Hz, H-4), 4.72 (dd, 1H, $J_{2,3}$ 11.6 Hz, H-2), 4.37 (dd, 1H, $J_{6,6'}$ 12.4 Hz, H-6), 4.14 (dd, 1H, H-6′), 3.86 (m, 1H, $J_{5,6}$ 3.6, $J_{5,6'}$ 2.0 Hz, H-5), 2.13, 2.09, 2.06, 1.88 (4 s, 12 H, 4 × OAc); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 170.94, 170.02, 169.79, 169.56 (6 × C=O), 134.68, 123.95 (Phth), 90.72 (C-1), 70.36 (C-5), 69.56 (C-4), 67.18 (C-3), 61.70 (C-6), 52.99 (C-2), 21.20, 20.95, 20.86 (4 × $COCH_3$).

1.6. 1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-(3,4,5,6-tetrachlorophthalimido)-α,β-D-glucopyranose (6)

This was synthesized from **1** as previously reported.[5]

1.7. 3,4,6-Tri-*O*-acetyl-2-deoxy-2-trifluoroacetamido-α-D-glucopyranosyl chloride (7)

Cl_2HCOCH_3 (0.97 mL, 10.9 mmol) followed by freshly fused $ZnCl_2$ (10 mg, 0.073 mmol) were added to a solution of **3** (0.5 g, 1.25 mmol) in dry $CHCl_3$ (1.5 mL). After being stirred for 10 min under N_2, the reaction mixture was heated for 1 h at 40 °C. Then it was diluted with $CHCl_3$ (50 mL), washed with H_2O and satd aq $NaHCO_3$, dried over $MgSO_4$, and concentrated to give crude **7** (0.47 g, 90%, foam) of sufficient purity for use in the glycosylation reaction: $[\alpha]_D^{20}$ −88 (*c* 0.5, $CHCl_3$); R_f 0.63 (solvent B); IR: *ν* 3310 (N–H), 1748 (acetyl C=O), 1729 (TFAc C=O), 1554 cm^{-1} (–NH, C–N); ^1H NMR (400 MHz, $CDCl_3$): *δ* 7.29 (d, 1H, NH), 6.19 (d, 1H, $J_{1,2}$ 3.6 Hz, H-1), 5.41 (dd, 1H, $J_{3,4}$ 10.0 Hz, H-3), 5.16 (dd, 1H, $J_{4,5}$ 9.6 Hz, H-4), 4.49 (m, 1H, $J_{2,3}$ 10.8 Hz, H-2), 4.27 (dd, 1H, $J_{6,6'}$ 13.6 Hz, H-6), 4.27 (m, 1H, $J_{5,6}$ 4.0, $J_{5,6'}$ 2.8 Hz, H-5), 4.08 (dd, 1H, H-6′), 2.04, 1.98, 1.97 (3 s, 9H, 3 × OAc); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 171.54, 170.63, 169.30 (3 × $COCH_3$), 157.57 (q, $J_{C,F}$ 37.8 Hz, $COCF_3$), 115,55 (q, $J_{C,F}$ 285.6 Hz, $COCF_3$), 92.00 (C-1), 71.10 (C-5), 69.82 (C-3), 67.10 (C-4), 61.13 (C-6), 53.94 (C-2), 20.68, 20.48, 20.37 (3 × $COCH_3$).

1.8. 3,4,6-Tri-*O*-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranosyl chloride (8)

Cl_2HCOCH_3 (0.5 mL, 5.62 mmol) followed by freshly fused $ZnCl_2$ (5 mg, 0.037 mmol) were added to a solution of **4** (0.3 g, 0.57 mmol) in dry $CHCl_3$ (0.8 mL). After being stirred for 10 min under N_2, the reaction mixture was stirred for 1 h at rt. Then it was diluted with $CHCl_3$ (50 mL), washed with H_2O and satd aq $NaHCO_3$, dried over $MgSO_4$, and concentrated to give crude **8** (0.28 g, 98%, foam) of sufficient purity for use in the glycosylation reaction: $[\alpha]_D^{20}$ −81 (*c* 0.5, $CHCl_3$); R_f 0.67 (solvent B); IR: *ν* 3329 (N–H), 1749 (acetyl and Troc C=O), 1536 cm^{-1} (–NH, C–N); ^1H NMR (400 MHz, $CDCl_3$): *δ* 6.20 (d, 1H, $J_{1,2}$ 3.6 Hz, H-1), 5.41 (d, 1H, NH), 5.37 (dd, 1H, $J_{3,4}$ 10.0 Hz, H-3), 5.21 (dd, 1H, $J_{4,5}$ 9.6 Hz, H-4), 4.82 (d, 1H, Cl_3CCH_2), 4.46 (d, 1H, Cl_3CCH_2), 4.30 (m, 3H, $J_{2,3}$ 10.0 Hz, $J_{5,6}$ 4.0, $J_{6,6'}$ 11.6 Hz, H-2, H-5, H-6), 4.14 (dd, 1H, H-6′), 2.11, 2.06, 2.05 (3 s, 9H, 3 × OAc); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 171.22, 170.75, 169.46 (3 × ester C=O), 154.28 (amide C=O), 93.54 (C-1), 74. 96 (Troc CH_2), 71.16 (C-5), 70.10 (C-3), 67.27 (C-4), 61.33 (C-6), 55.71 (C-2), 20.75 (ester CH_3).

1.9. 3,4,6-Tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl chloride (9)

Cl_2HCOCH_3 (0.97 mL, 10.9 mmol) and then $BF_3{\cdot}Et_2O$ (0.62 mL, 5 mmol) were added to a solution of **5** (0.6 g, 1.25 mmol) in dry $CHCl_3$ (1.5 mL). After being stirred for 10 min under N_2, the reaction mixture was heated for 3 h at 65 °C. This was then diluted with $CHCl_3$ (50 mL), washed with H_2O and satd aq $NaHCO_3$, dried over $MgSO_4$, and concentrated to give crude **9** (0.52 g, 91%, white power) of sufficient purity for use in the glycosylation reaction. Recrystallization from diethyl ether/petroleum ether yielded **9** (0.45 g, 80%): mp 151–152 °C, lit.[38] mp 148–151 °C; $[\alpha]_D^{20}$ +61 (*c* 0.5, $CHCl_3$), lit.[38] +62 (*c* 1, $CHCl_3$); R_f 0.57 (solvent D); IR: *ν* 1751, 1767 (acetyl C=O), 1714 cm^{-1} (Phth C=O); ^1H NMR (400 MHz, $CDCl_3$): *δ* 7.89, 7.78 (2 m, 4H, Phth), 6.20 (d, 1H, $J_{1,2}$ 9.6 Hz, H-1), 5.80 (dd, 1H, $J_{3,4}$ 8.8 Hz, H-3), 5.25 (dd, 1H, $J_{4,5}$ 10.4 Hz, H-4), 4.53 (dd, 1H, $J_{2,3}$ 10.4 Hz, H-2), 4.34 (dd, 1H, $J_{6,6'}$ 12.4 Hz, H-6), 4.21 (dd, 1H, H-6′), 3.98 (m, 1H, $J_{5,6}$ 4.8, $J_{5,6'}$ 2.0 Hz, H-5), 2.14, 2.05,

1.88 (3 s, 9H, 3 × OAc); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.86, 170.19, 169.52 (5 × C=O), 134.79, 124.08 (Phth), 85.75 (C-1), 75.93 (C-5), 70.80 (C-3), 68.34 (C-4), 61.88 (C-6), 57.71 (C-2), 20.97, 20.79, 20.59 (3 × acetyl CH_3); Anal. Calcd for $C_{20}H_{20}NO_9Cl$: C, 52.93; H, 4.44; N, 3.09. Found: C, 53.01; H, 4.29; N, 3.02.

1.10. 3,4,6-Tri-*O*-acetyl-2-deoxy-2-(3,4,5,6-tetrachlorophthalimido)-β-D-glucopyranosyl chloride (10)

This was synthesized from **6** as previously reported.[5]

1.11. Diosgenyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-trifluoroacetamido-β-D-glucopyranoside (11)

A mixture of diosgenin (0.18 g, 0.435 mmol) and 4 Å molecular sieves (1.2 g) in anhyd CH_2Cl_2 and Et_2O (21 mL, 8:13 v/v) was stirred at rt under N_2 for 10 min. Next AgOTf (0.22 g, 0.86 mmol) was added and stirring was continued for 10 min. Then, a solution of **7** (0.27 g, 0.65 mmol) in CH_2Cl_2 (7 mL) was allowed to drip on to the reaction mixture. After stirring for 20 h at rt, the mixture was neutralized with Et_3N (0.4 mL, 2.9 mmol), diluted with $CHCl_3$, filtered over the gel layer (MN Kieselgel 60), and concentrated. The addition of MeOH precipitated **11** (0.24 g, powder, 69%); all analyses are in agreement with those previously reported for the reaction with bromide.[5]

1.12. Diosgenyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside (12)

A mixture of diosgenin (0.148 g, 0.36 mmol) and 4 Å molecular sieves (1.4 g) in anhyd CH_2Cl_2 and Et_2O (16 mL, 3:5 v/v) was stirred at rt under N_2 for 10 min. Next, AgOTf (0.18 g, 0.72 mmol) was added and stirring was continued for 10 min. Then, a solution of **8** (0.27 g, 0.54 mmol) in CH_2Cl_2 (8 mL) was allowed to drip on to the reaction mixture. After stirring for 20 h at rt, the mixture was neutralized with Et_3N (0.4 mL, 2.9 mmol), diluted with $CHCl_3$, filtered over the gel layer (MN Kieselgel 60), and concentrated. The addition of MeOH caused the precipitation of **12** (0.27 g, white powder, 86%): mp >184 °C (dec); $[\alpha]_D^{20}$ −53 (*c* 0.5, $CHCl_3$); R_f 0.57 (solvent B); IR: *v* 3301 (N–H), 2874–2950 (C–H), 1745 (acetyl C=O), 1704 (Troc C=O), 1559 cm^{-1} (–NH, C–N); ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.37 (dd, 1H, $J_{3,4}$ 9.6 Hz, H-3), 5.20 (d, 1H, NH), 5.05 (dd, 1H, $J_{4,5}$ 9.2 Hz, H-4), 4.81 (d, 1H, $J_{1,2}$ 8.0 Hz, H-1), 4.78 (d, 1H, Cl_3CCH_2), 4.68 (d, 1H, Cl_3CCH_2), 4.27 (dd, 1H, $J_{6,6'}$ 12.0 Hz, H-6), 4.10 (dd, 1H, H-6′), 3.69 (m, 1H, $J_{5,6}$ 4.8 Hz, H-5), 3.50 (m, 1H, $J_{2,3}$ 10.4 Hz, H-2), 2.08, 2.04, 2.03 (3 s, 9H, 3 × OAc); diosgenyl protons: 5.32 (m, C_6-H), 4.41 (dd, C_{16}-H), 3.50 (m, C_{26}-H_e), 3.37 (t, C_{26}-H_a), 2.24 (m, C_4-2H), 0.99 (s, CH_3), 0.97 (d, CH_3), 0.79 (d, CH_3), 0.78 (s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.95, 170.84, 169.75 (3 × ester C=O), 154.14 (amide C=O), 99.44 (C-1), 74.62 (Troc CH_2), 71.85 (C-5 and C-3), 69.08 (C-4), 62.43 (C-6), 56.68 (C-2), 20.99, 20.90, 20.86 (3 × ester CH_3); diosgenyl carbons: 140.32 (C-5), 122.23 (C-6), 109.51 (C-22), 81.02 (C-16), 80.08 (C-3), 67.06 (C-26), 62.28 (C-17), 56.84 (C-14), 50.25 (C-9), 41.81 (C-20), 40.47 (C-13), 39.96 (C-12), 38.96 (C-4), 37.33 (C-1), 37.05 (C-10), 32.26 (C-7), 32.04 (C-15), 28.99, 29.64, 30.50, 31.58 (C-8, C-24, C-25, C-23, C-2,), 21.03 (C-11), 19.57 (C-19), 17.34 (C-27), 16.48 (C-18), 14.72 (C-21); Anal. Calcd for $C_{42}H_{60}NO_{12}Cl_3$: C, 57.50; H, 6.89; N, 1.60. Found: C, 57.31; H, 6.97; N, 1.59.

1.13. Diosgenyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (13)

A mixture of diosgenin (0.15 g, 0.37 mmol) and 4 Å molecular sieves (1 g) in anhyd CH_2Cl_2 (10 mL) was stirred at rt under N_2 for 10 min. Next, *s*-collidine (0.19 mL, 1.44 mmol) and AgOTf (0.25 g, 0.97 mmol) were added and stirring was continued for 10 min. Then, a solution of **9** (0.25 g, 0.55 mmol) in CH_2Cl_2 (5 mL) was dripped on to the reaction mixture. After stirring for 20 h at rt, the mixture was diluted with $CHCl_3$, filtered over the gel layer (MN Kieselgel 60), and concentrated. The addition of MeOH caused the precipitation of **13**, which was filtered. The filtrate was chromatographed (solvent A) to yield an additional portion of **13** (totally 0.3 g, white solid, 99%): mp 193–196 °C; $[\alpha]_D^{20}$ −22 (*c* 0.5, $CHCl_3$); R_f 0.59 (solvent E); IR: *v* 2872–2950 (C–H), 1750 (acetyl C=O), 1717 cm^{-1} (Phth C=O); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86, 7.75 (2 m, 4H, Phth), 5.77 (dd, 1H, $J_{3,4}$ 9.2 Hz, H-3), 5.47 (d, 1H, $J_{1,2}$ 8.4 Hz, H-1), 5.16 (dd, 1H, $J_{4,5}$ 10.0 Hz, H-4), 4.33 (dd, 1H, $J_{6,6'}$ 12.4 Hz, H-6), 4.30 (dd, 1H, $J_{2,3}$ 10.4 Hz, H-2), 4.15 (dd, 1H, H-6′), 3.86 (m, 1H, $J_{5,6}$ 4.4, $J_{5,6'}$ 2.4 Hz, H-5), 2.10, 2.03, 1.86 (3 s, 9H, 3 × OAc); diosgenyl protons: 5.22 (m, C_6-H), 4.38 (dd, C_{16}-H), 3.46 (m, C_{26}-H_e), 3.36 (t, C_{26}-H_a), 2.06 (m, C_4-2H), 0.95 (d, CH_3), 0.88 (s, CH_3), 0.78 (d, CH_3), 0.74 (s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.96, 170.43, 169.71 (5 × C=O), 134.51, 123.83 (Phth), 97.00 (C-1), 71.90 (C-5), 71.09 (C-3), 69.33 (C-4), 62.26 (C-6), 55.05 (C-2), 20.98, 20.87, 20.69 (3 × acetyl CH_3); diosgenyl carbons: 140.41 (C-5), 122.04 (C-6), 109.48 (C-22), 81.98 (C-16), 79.63 (C-3), 67.04 (C-26), 62.40 (C-17), 56.63 (C-14), 50.17 (C-9), 41.79 (C-20), 40.43 (C-13), 39.90 (C-12), 38.76 (C-4), 37.27 (C-1), 36.93 (C-10), 32.20 (C-7), 32.01 (C-15), 31.57 (C-23), 31.54 (C-25), 30.48 (C-2), 29.52 (C-24), 28.99 (C-8), 21.02 (C-11), 19.50 (C-19), 17.34 (C-27), 16.44 (C-18), 14.71 (C-21); Anal. Calcd for $C_{47}H_{61}NO_{12}$: C, 67.85; H, 7.39; N, 1.68. Found: C, 67.89; H, 7.42; N, 1.59.

1.14. Diosgenyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-(3,4,5,6-tetrachlorophthalimido)-β-D-glucopyranoside (14)

A mixture of diosgenin (0.094 g, 0.25 mmol) and 4 Å molecular sieves (0.9 g) in anhyd CH_2Cl_2 (10 mL) was stirred at rt under N_2 for 10 min. Next, *s*-collidine (0.12 mL, 0.91 mmol) and AgOTf (0.16 g, 0.61 mmol) were added and stirring was continued for 10 min. Then a solution of **10** (0.20 g, 0.34 mmol) in CH_2Cl_2 (5 mL) was dripped on to the reaction mixture. After stirring for 20 h at rt, the mixture was diluted with $CHCl_3$, filtered over the gel layer (MN Kieselgel 60), and concentrated. The addition of MeOH caused **14** to precipitate (0.19 g, white solid, 87%); all analyses are in agreement with previously reported for the reaction with bromide.[39]

1.15. Diosgenyl 2-deoxy-2-trifluoroacetamido-β-D-glucopyranoside (15)

This was synthesized from **11** as previously reported.[5]

1.16. Diosgenyl 2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside (16)

Procedure f: Et_3N (1.2 mL, 8.55 mmol) was added to a solution of **12** (0.3 g, 0.34 mmol) in MeOH (7 mL). The mixture was stirred at rt for 20 h and then evaporated. The residue was purified by column chromatography (solvent F) to yield **16** (0.18 g, white powder, 69%): mp 205–207 °C ; $[\alpha]_D^{20}$ −60 (*c* 0.5, 1:1 $CHCl_3$:MeOH); R_f 0.58 (solvent G); IR: *v* 3200–3550 (O–H and N–H), 2850–2951 (C–H), 1719 (Troc C=O), 1545 cm^{-1} (–NH, C–N); ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.49 (d, 1H, NH), 4.96 (m, 2H, 3-OH, 4-OH), 4.88, 4.68 (2 d, 2H, Cl_3CCH_2), 4.40 (m, 1H, 6-OH), 4.39 (d, 1H, $J_{1,2}$ 8.0 Hz, H-1), 3.67 (dd, 1H, $J_{6,6'}$ 11.2 Hz, H-6), 3.41 (m, 2H, H-4, H-6′), 3.07 (m, 3H, H-2, H-3, H-5); diosgenyl protons: 5.28 (d, C_6-H), 4.28 (dd, C_{16}-H), 3.42 (m, C_{26}-H_e), 3.21 (t, C_{26}-H_a), 2.33, 2.20 (m, C_4-2H), 0.93 (s, CH_3), 0.90 (d, CH_3), 0.73 (s, 2 × CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 154.24 (amide C=O), 99.19 (C-1), 76.90 (C-3), 73.69 (Troc CH_2), 73.23 (C-4), 70.69 (C-5), 61.00

(C-6), 57.76 (C-2); diosgenyl carbons: 140.43 (C-5), 122.94 (C-6), 108.35 (C-22), 80.13 (C-16), 77.28 (C-3), 65.87 (C-26), 61.76 (C-17), 55.68 (C-14), 49.48 (C-9), 41.04 (C-20), 40.14 (C-13), 38.88 (C-12), 38.34 (C-4), 36.68 (C-1), 36.31 (C-10), 31.49, 31.40, 30.93, 29.74, 29.11, 28.43 (C-2, C-7, C-8, C-15, C-23, C-24, C-25), 20.32 (C-11), 19.02 (C-19), 17.01 (C-27), 15.91 (C-18), 14.58 (C-21); Anal. Calcd for $C_{36}H_{54}NO_9Cl_3$: C, 57.56; H, 7.25; N, 1.86. Found: C, 57.27; H, 7.56; N, 1.84.

Procedure g: Compound **12** (0.2 g, 0.23 mmol) was added to a solution of guanidine nitrate (0.12 g, 1 mmol) and MeONa (0.2 mmol) in a mixture of MeOH and CH_2Cl_2 (5 mL; 9:1 v/v). The mixture was stirred at rt for 1 h and then evaporated. The residue was purified by column chromatography (solvent H) to give **16** (0.10 g, white powder, 57%).

1.17. Diosgenyl 2-deoxy-2-phthalimido-β-D-glucopyranoside (17)

A 1 M solution of NaOMe in MeOH (1.4 mL) was added to a solution of **13** (0.4 g, 0.48 mmol) in MeOH (80 mL). The mixture was stirred at rt for 1 h and then neutralized with Dowex-50 W (H^+) ion-exchange resin, filtered, and the solvent was evaporated. The yellow residue was purified by column chromatography (solvent F) to give **17** (0.26 g, white powder, 76%): mp >271 °C (dec); $[\alpha]_D^{20}$ −29 (*c* 0.5, 1:1 $CHCl_3$:MeOH); R_f 0.60 (solvent G); IR: *ν* 3456 (O–H), 2872–2949 (C–H), 1714 cm^{-1} (Phth C=O); ^1H NMR (400 MHz, $CDCl_3$): *δ* 7.83, 7.71 (2 m, 4H, Phth), 5.33 (d, 1H, $J_{1,2}$ 8.4 Hz, H-1), 4.29 (dd, 1H, $J_{3,4}$ 8.4 Hz, H-3), 4.20 (m, 1H, 4-OH), 4.08 (dd, 1H, $J_{2,3}$ 10.8 Hz, H-2), 3.90 (m, 3H, H-6, H-6′, 3-OH), 3.71 (dd, 1H, $J_{4,5}$ 9.2 Hz, H-4), 3.48 (m, 1H, H-5); diosgenyl protons: 5.21 (m, C_6-H), 4.28 (dd, C_{16}-H), 3.39 (m, C_{26}-H_e), 3.36 (t, C_{26}-H_a), 2.03, 1.80 (2 m, C_4-2H), 0.95 (d, CH_3), 0.85 (s, CH_3), 0.78 (d, CH_3), 0.74 (s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 168.69 (2 × C=O), 134.36, 131.85, 123.73 (Phth), 97.16 (C-1), 75.59 (C-5), 71.96 (C-3), 71.83 (C-4), 62.11 (C-6), 57.07 (C-2); diosgenyl carbons: 140.38 (C-5), 122.04 (C-6), 109.49 (C-22), 81.00 (C-16), 79.35 (C-3), 67.05 (C-26), 62.28 (C-17), 56.63 (C-14), 50.17 (C-9), 41.80 (C-20), 40.44 (C-13), 39.92 (C-12), 38.78 (C-4), 37.27 (C-1), 36.90 (C-10), 32.20 (C-7), 32.01 (C-15), 31.57 (C-23), 31.55 (C-25), 30.49 (C-2), 29.60 (C-24), 29.00 (C-8), 20.98 (C-11), 19.48 (C-19), 17.33 (C-27), 16.44 (C-18), 14.72 (C-21); MALDI-TOFMS: *m/z* 728.7 $(M+Na)^+$; Anal. Calcd for $C_{41}H_{55}NO_9 \times 1.5\ H_2O$: C, 67.19; H, 7.98; N, 1.91. Found: C, 67.61; H, 8.04; N, 1.84.

1.18. Diosgenyl 2-amino-2-deoxy-β-D-glucopyranoside (18) from 15

An 0.1 M aq solution of NaOH (23 mL) was added to a solution of **15** (0.32 g, 0.48 mmol) in acetone. The mixture was stirred at rt for 3 h, neutralized with Dowex-50 W (H^+) ion-exchange resin and filtered, after which the solvent was azeotropically evaporated with toluene and ethanol. The crude residue was purified by column chromatography (solvent H containing 0.2% Et_3N) to give **18** (0.22 g, 80%); all data as reported for other procedures.[5]

1.19. Diosgenyl 2-amino-2-deoxy-β-D-glucopyranoside (18) from 16

Zinc dust (0.8 g, 7.14 mmol) was added to a solution of **16** (0.22 g, 0.29 mmol) in glacial acetic acid (5 mL). The mixture was stirred at rt for 2 h, diluted with toluene, and the zinc filtered off. The filtrate was evaporated. The white residue was purified by column chromatography (solvent H) to give a chromatographically homogeneous mixture of **18** and an unidentified product (0.18 g).

Table 1
Crystal data and structure refinement for **10**

Empirical formula	2 $[C_{20}\ H_{16}O_9Cl_5N]\cdot C_7H_7$
Formula weight	1274.3
Temperature (K)	295(2)
Wavelength (Å)	1.54178
Crystal system	orthorhombic
Space group	$C222_1$
Unit cell dimensions	
a (Å)	10.818(2)
b (Å)	19.765(4)
c (Å)	25.910(5)
V (Å^3)	5540.0(2)
Z	4
D_{calcd} (Mg m^{-3})	1.528
Absorption coefficient (mm^{-1})	5.232
F(000)	2596
Crystal size (mm)	0.55 × 0.15 × 0.10
Θ Range for data collection (°)	3.41–67.72
Limiting indices	$-11 \leqslant h \leqslant 11$, $-11 \leqslant k \leqslant 22$, $0 \leqslant l \leqslant 30$
Reflections collected/unique	4862/4640 [R_{int} = 0.0191]
Completeness 2*Θ* = 50.24° (%)	96.5
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	4640/0/357
Goodness-of-fit on F^2	1.117
Final *R* indices [$I > 2\sigma(I)$]	R_1 = 0.0484
	wR_2 = 0.1381
R Indices (all data)	R_1 = 0.0538
	wR_2 = 0.1437
Absolute structure parameter	0.003(2)
Largest diff. peak and hole (e Å^{-3})	0.617 and −0.275

1.20. Diosgenyl 2-amino-2-deoxy-β-D-glucopyranoside (18) from 17

Ethylenediamine (1.08 mL, 16 mmol) was added to a solution of **17** (0.225 g, 0.32 mmol) in ethanol (3 mL). The mixture was stirred at 60 °C for 2.5 h and evaporated. The yellow residue was purified by column chromatography (solvent H containing 0.2% Et_3N) to give **18** (0.15 g, 81%); all data as reported for other procedures.[5]

1.21. Diosgenyl 2-amino-2-deoxy-β-D-glucopyranoside (18) and diosgenyl 2-acetamido-2-deoxy-β-D-glucopyranoside (19) from 14

These were synthesized as previously reported.[5]

1.22. Diosgenyl 2-amino-2-deoxy-β-D-glucopyranoside (18) from 14

An 85% solution of hydrazine hydrate (0.35 mL, 16 mmol) was added to a solution of **14** (0.2 g, 0.21 mmol) in ethanol (4 mL). The mixture was stirred at 80 °C for 24 h and evaporated. The residue was purified using two procedures. One involved column chromatography (solvent I containing 0.2% Et_3N) and provided pure **18** with a yield of 97% (0.12 g). The other involved dilution of the crude residue in a mixture of $CHCl_3$/MeOH (7:1, v/v), filtration over a layer of silica gel, evaporation, and crystallization from methanol. This gave pure **18** (yield 74%) (0.09 g); all data as reported for other procedures.[5]

1.23. Description of the crystal structure of 10

Diffraction data were collected at room temperature (293 K) on a KUMA KM-4 four circle diffractometer[40] Cu Kα radiation (*λ* = 1.54184 Å) using the 2Θ/ω scan mode. Phase angles were initially determined with the SHELXS program.[41] All H atoms bound to C atoms were placed geometrically and refined using a riding model with C–H = 0.96 Å and $U_{iso}(H) = 1.2U_{eq}(C)$ ($U_{iso}(H) = 1.5\ U_{eq}(C)$ for

the methyl H atoms). Table 1 summarizes the crystallographic data, data collection, and structure refinement, Table S1 sets out the coordinates of atoms and their isotropic temperature factors, Table S2 lists a selection of the crystal's important geometric parameters, Table S3 summarizes the intra- and intermolecular short contacts and Table S4 shows the π–π interactions.

The crystal structure was refined to $R_1 = 0.0538$ (4640 reflections, all unique) and $R_1 = 0.0484$ (4179 reflections with $F_0 > 2\sigma(F_0)$) by the full-matrix least-squares method using the SHELXL-97 program[42] based on 120 parameters. Figure 2 illustrates the compound's structure, showing the conformation and atom numbering system. Figure S1 shows the molecular packing in the crystal. Figure S2 shows the π–π interactions in the crystal lattice.

All interactions demonstrated were found by the PLATON program.[43] The programs used to prepare the molecular graphics were ORTEPII,[44] PLUTO-78,[45] and Mercury.[46]

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Supplementary data

Full crystallographic details, excluding structures features, have been deposited (Deposition No. CCDC 901908) with the Cambridge Crystallographic Data Center. These data may be obtained, on request, from The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (tel.: +44 1223 336408; fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.carres.2012.11.020.

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