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A Moenomycin-type Structural Analogue of Lipid II
Some Possible Mechanisms of the Mode of Action of Transglycosylase Inhibitors can be Discarded

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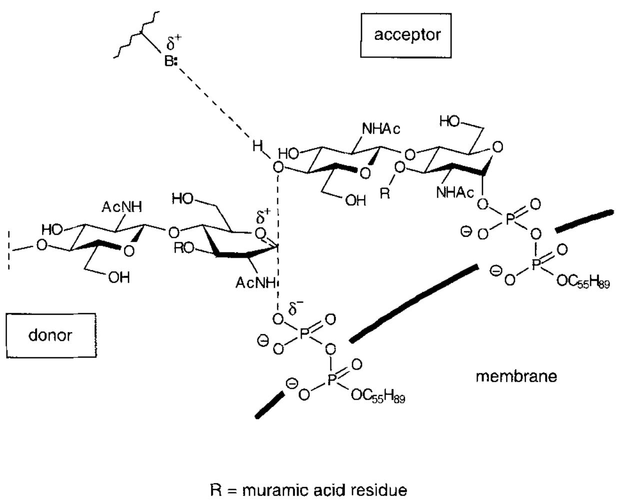
Dedicated with great Appreciation to Professor Ekkehard Winterfeldt on the Occasion of his 65th Birthday

Abstract. The transglycosylation step in the peptidoglycan biosynthesis belongs to the general class of glycosyltransferase-catalyzed reactions. The structural analogue **2** of moenomycin A has been synthesized and has been found to be antibiotically *inactive*. The assumption that moenomycin-type transglycosylase inhibitors such as **1** bind at the donor site of the enzyme and that their mode of action is the result of the high stability of the sugar→ phosphate bond seems to be ruled out by the present results.

Glycosyltransferases catalyze the transfer of sugar residues from activated glycosyl-phosphate derivatives to specific acceptors [1]. In bacterial peptidoglycan and in eukaryotic asparagine-linked glycoprotein biosynthesis the glycosyl donor leaving group is a pyrophosphate or phosphate group linked to a lipid moiety. The lipid unit in bacteria is a C_{55} isoprenoid (bacterioprenol) whereas in the eukaryotic dolichol cycle long-chain polyprenol alcohols (dolichols) of varying chain lengths (C_{40}–C_{120}) are used. Similar cycles are found in the biosyntheses of other complex carbohydrates [2].

We are interested in compounds which inhibit the assembly of uncross-linked polysaccharide strands in peptidoglycan biosynthesis from a disaccharide intermediate. The reaction is called transglycosylation reaction and is believed to proceed in such a way that the growing peptidoglycan chain linked to bacterioprenol *via* a pyrophosphate bridge acts as the glycosyl donor whereas a disaccharide intermediate, the so-called lipid II, is the glycosyl acceptor (see Scheme 1).

This mode of glycan chain elongation is not explicitly proven for *E. coli* but has been demonstrated for a poorly lytic mutant of *Bacillus licheniformis* [3]. In *E. coli* the transglycosylation reaction is catalyzed by the high-molecular weight penicillin-binding proteins such as the PBPs 1a and 1b. These are bifunctional enzymes



Scheme 1 Mechanism of the transglycosylation reaction in peptidoglycan biosynthesis (speculative).

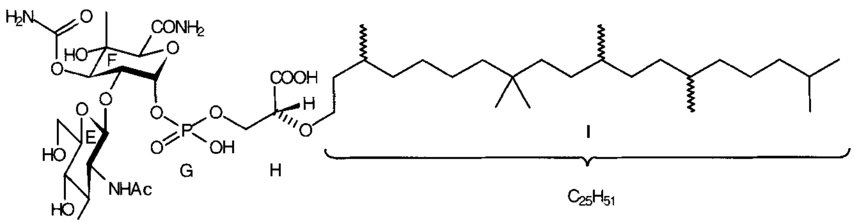
which catalyze in addition to the transglycosylation the so-called transpeptidation reaction, in which the sugar strands are cross-linked *via* short peptide chains [4]. The transpeptidase active site is located in the C-terminal module and its study has been greatly facilitated by the covalent binding of radiolabeled penicillin. The *N*-terminal module (at the outer surface of the cytoplasmic membrane) catalyzes the transglycosylation reaction. The active site is still unknown and the mechanism of the transglycosylation reaction is poorly understood.

Two groups of antibiotics are known to interfere with the transglycosylation step. The glycopeptides such as vancomycin act by binding to peptidoglycan precursors terminating in Lys-D-Ala-D-Ala (gram-positive bacteria) and prevent the approach of the transglycosylase [5].

On the other hand moenomycin-type antibiotics reversibly bind to the enzyme [6]. But what is their exact mode of action? Research in this field is still in its infancy but studies of structure-activity relations have demonstrated that antibiotically active moenomycin A degradation product **1** most probably contains all the essential structural informations of a transglycosylase inhibitor [7]. The structural similarities between moenomycin A and structural analogues such as **1** on the one hand and the donor and acceptor components of the transglycosylation reaction (see Scheme 1) on the other are striking and have been taken as a hint that the moenomycins are competitive inhibitors. However, until now this assumption is not substantiated by experiment.

It has been shown in a number of cases that glycosyltransferases recognize *both* the glycosyl donor and the glycosyl acceptor [8]. Accepting this view, **1** may be a structural analogue of lipid II and bind at the lipid II (acceptor) binding site. The accepting 4-OH group (in unit E) may then spacially not be available to react with the donor because of the 1→ 2-connection of the two sugar units in **1** instead of the 1→ 4-link in lipid II. Equally well **1** could bind at the binding site of the growing peptidoglycan chain (the donor binding site) mimicking the lipid diphosphate and the first two sugar units. The inhibition of the enzyme could then be attributed to the stronger bond between C-1^F and the phosphate group due to the presence of the electron-withdrawing uronamide group in unit F making **1** an unreactive substrate [9]. It is also conceivable that the phosphoglycerate unit is an unsuitable leaving group in the transglycosylation reaction when compared with the pyrophosphate bridge which is present in the donor (the growing peptidoglycan chain, Scheme 1). Another view recognizes again the 1→ 2-connection of the two sugar units in **1** *vs.* the 1→ 4-link in the biosynthetic donor intermediate and attributes the inhibitory properties to the fact that at the active site of the enzyme the phosphate leaving group is spacially not available [10].

Finally, the inhibitory properties of **1** and similar compounds might be related to the fact that its lipid chain is appreciably shorter than that of the peptidoglycan intermediates. The inhibitors may thus bind at either of the enzyme binding sites but in an unsuitable way for being used in the transglycosylation reaction due to the differences in the lipid moieties. It has been shown that in the dolichol cycle the glycosyltransferases investigated did not accept glycosyl donors with too short a lipid moiety [11]. To answer some of the questions raised above we set out to synthesize **2**, the 1→ 4-linked di-



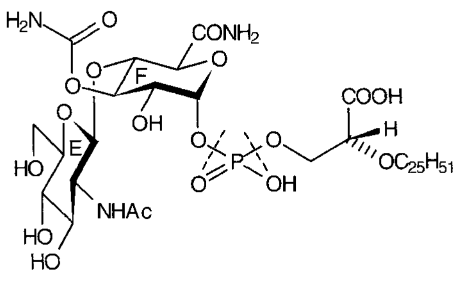
1

Scheme 2 The smallest moenomycin A degradation product with full antibiotic activity.

saccharide “isomer” of **1** which is the closest moenomycin-type structural analogue of lipid II conceivable.

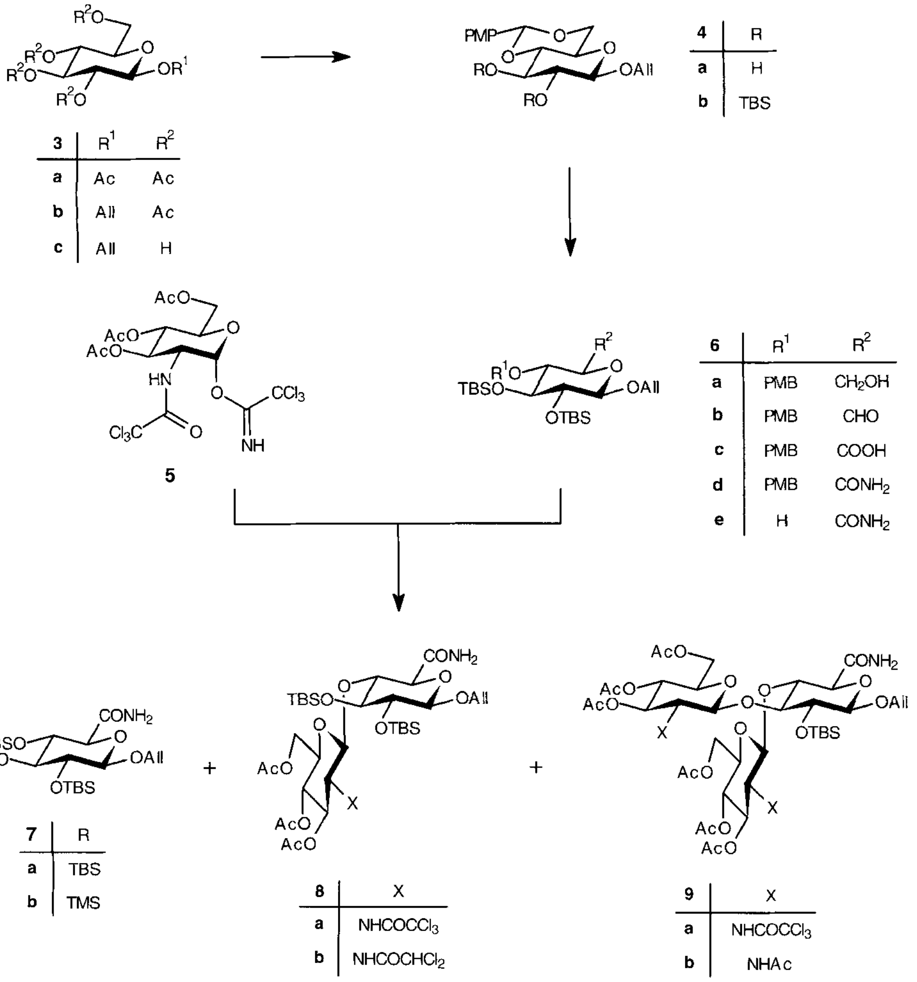
Retrosynthetic Disconnection of the Moenomycin-type Lipid II Analogue 2 and Synthesis of the Disaccharide Intermediate 11e

The retrosynthetic analysis as indicated in Formula 1 (dashed lines) led to three precursors for **2**: (i) an E–F disaccharide, (ii) an electrophilic phosphoric acid equivalent, and (iii) the 2-*O*-alkylglyceric acid moiety which is available by degradation of moenomycin [12].



2 (1)

We started from *β*-D-glucose pentaacetate which was converted into the known allyl glycoside **3b** making use of Magnusson’s method [13, 14]. Zemplén deacetylation [15] followed by acetal formation with 4-methoxybenzaldehyde dimethyl acetal furnished the 4,6-*O*-(4-methoxybenzylidene)-protected compound **4a**. Of several methods that we tried [16], only the Johansson–Samuelsson [17] variant gave gratifying results (89% for both steps).



3	R^1	R^2
a	Ac	Ac
b	All	Ac
c	All	H

4	R
a	H
b	TBS

6	R^1	R^2
a	PMB	CH_2OH
b	PMB	CHO
c	PMB	COOH
d	PMB	$CONH_2$
e	H	$CONH_2$

7	R
a	TBS
b	TMS

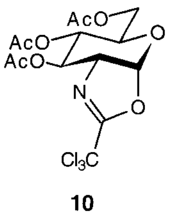
8	X
a	$NHCOCCl_3$
b	$NHCOCHCl_2$

9	X
a	$NHCOCCl_3$
b	NHAc

Scheme 3 Synthesis of a disaccharide precursor of **2** (PMP = 4-methoxyphenyl; PMB = 4-methoxybenzyl, TBS = *tert*-butyldimethylsilyl).

Then, the remaining two hydroxy groups were protected as *tert*-butyldimethylsilyl ethers [18, 19] making use of the imidazole method [20, 21]. For the regioselective opening of 4,6-*O*-benzylidene acetals a number of methods are available [22–26]. We used the reductive opening with sodium cyanoborohydride in the presence of trimethylsilyl chloride with good success. The desired 4-*O*-(4-methoxybenzyl) derivative **6a** was obtained in 97% yield whereas only 2% of the isomeric 6-*O*-PMB ether (formula not shown) were isolated. The FAB mass spectra of **6a** as well as of all other compounds containing the PMB group displayed peaks formally at $[M-H]^+$ in addition to the expected molecular ion at $[M+H]^+$. Linked-scan MS (MIKE) demonstrated loss of H_2 from $[M+H]^+$ [27].

The oxidation of the 6-OH group in **6a** was accomplished by a two-step procedure. First the primary alcohol was oxidized to give the corresponding aldehyde with sodium hypobromite [28] in the presence of the 2,2,6,6-tetramethyl-1-piperidinyloxy radical (TEMPO) [29] under the conditions reported by Flitsch *et al.* [30]. In contrast to other reports [30–32], in our system the reaction was stopping quite selectively at the aldehyde stage even in the presence of an excess of oxidant. The uronic acid was formed only to a minor extent as shown by TLC. It may be mentioned that the Swern oxidation [33] and the use of 4-acetylamino-TEMPO [34] gave less satisfying results [16]. The aldehyde then was oxidized with sodium chlorite [35] to furnish the uronic acid which was immediately converted into the uronamide using Staab's method [36]. The overall yield (**6a→6d**) was 90%. For the removal of the PMB protecting group a number of methods are known. In the present case oxidation with ceric ammonium nitrate (CAN) [17, 37, 38] proceeded smoothly and provided **6e** in 72% yield.



10

(2)

At that stage a critical reaction, the glycosidation with a *N*-acetyl-glucosamine equivalent, was expected. We tried several of the well-established methods without success [16]. Finally, the Jacquinet method [39], which uses the 2-trichloromethyl-oxazoline **10** (prepared *in situ* from **5**) as glycosyl donor, provided **8a** in 31% yield, accompanied by **7a** (12%) and trisaccharide **9a** (15%). The formation of the latter two compounds is indicative of a silyl group migration under the conditions of the glycosylation reaction (1,2-dichloroethane, TMS-triflate, molecular sieves). On the basis of results reported by Jacquinet [40] silyl group migration is rather unexpected and may be a special feature of our system as will be discussed below. The conditions of the reaction of **6e** with **5** had to be optimized carefully. On longer reaction times the amount of trisaccharide **9a** increased. Both the glycosyl acceptor (free and as TMS ether) and the glycosyl donor were not completely consumed under these conditions. The latter was partly re-isolated in the form of **10**.

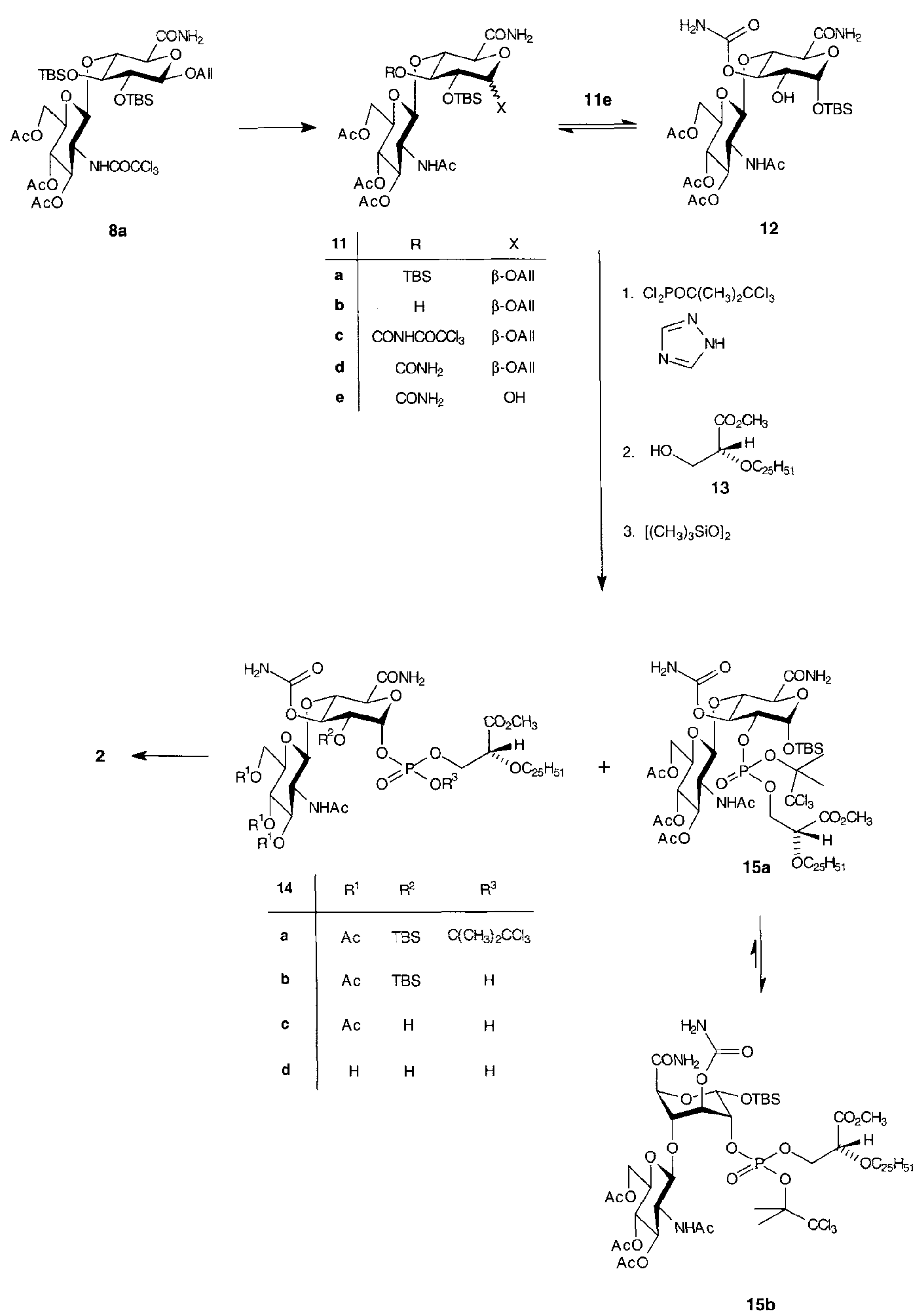
The dehalogenation of chloro-substituted acetamides can be achieved with activated zinc-acetic acid in THF [41] or by a radical process with tributyltin hydride/AIBN [39, 42]. We used the latter method with good success. After 1.5 h at 80 °C **11a** was obtained in 77% yield accompanied by the monosilyl derivative **11b** (23%). **11b** was the desired product of the next step of the synthesis. The exact mechanism by which it is formed during the dehalogenation reaction was not studied, probably chloride ion is the nucleophilic species in this reaction.

In a related case we found that deprotection at C-3 was possible with TBAF in 95:5 THF-water under carefully selected conditions [19]. In the present synthesis the silyl ether was much more reluctant and could only be cleaved with TBAF in the "absence" of water. As in the previous example the reaction was selective and the desired monosilyl compound **11b** was isolated in 67% yield, accompanied by 8% of the corresponding diol (formula not shown). The modest yield is probably the result of difficulties in the work-up procedure.

For the introduction of the carbamoyl group the trichloroacetyl isocyanate (TAI) method was employed [43]. Thus, **11b** on reaction with TAI in dichloromethane solution at 20 °C furnished **11c** which on reductive removal of the trichloroacetyl group (zinc dust in methanol) provided **11d** (91% overall yield). For the cleavage of allyl ethers a large number of methods exist. However, many of them have been shown not to be applicable in the moenomycin field [19, 44]. In the present case, the Nakayama method (tetrakis(triphenylphosphin)palladium(0) in acetic acid [45]) gave nice results. The deprotection product **11e** was isolated in 92% yield.

Discussion of the Structure of 11e and the Merits of the Silyl Protecting Groups

The NMR spectra of **11e** were taken in $[D_5]$pyridine. At the beginning two sets of resonances were observed corresponding to the two anomers. In the course of the measurements a third compound was formed with clearly visible $COCH_3$, $SiCH_3$ und $SiC(CH_3)_3$ ^1H NMR signals. Based on $^1H,^1H$ COSY it could be shown that the newly formed compound was **12** formed by 2-*O*→1-*O* silyl group migration. Three OH signals could be iden-



11	R	X
a	TBS	β-OAll
b	H	β-OAll
c	CONHCOCCl$_3$	β-OAll
d	CONH$_2$	β-OAll
e	CONH$_2$	OH

14	R^1	R^2	R^3
a	Ac	TBS	C(CH$_3$)$_2$CCl$_3$
b	Ac	TBS	H
c	Ac	H	H
d	H	H	H

Scheme 4 Completion of the synthesis of **2** (for abbreviations, see Scheme 3).

tified in the spectrum, two of which had cross peaks to the 1^F-H signals of α-**11e** and β-**11e**, respectively. The third OH proton was correlated to 2^F-H proving the silyl group migration. The ratio of the three compounds in the sample was α-**11e**:β-**11e**:**12** = 1:1:0.5 (integrals of the OH and $SiC(CH_3)_3$ ^1H NMR signals). Examples of this type of silyl migrations are known both in furanoid [18] and pyranoid [46, 47] carbohydrates, although most of them require bases stronger than pyridine. Mulzer has shown these silyl group migrations of 1,2-diol systems to be intramolecular and reversible [46].

As has been discussed above, under the conditions of the disaccharide formation and the dehalogenation the *tert*-butyldimethylsilyl ethers were not completely stable. In addition to these synthetic shortcomings the silyl protecting groups caused further complications by forcing ring F out of the normal $^4C_1$ conformation into another one with completely different coupling constants. Table 1 displays the ring proton coupling constants of a number of synthetic intermediates. Using the Karplus equation, from the coupling constants it may be concluded that ring F in compounds **6d**, **7a**, **7b**, **8a**, **8b**, **9a** and **11a** adopts a twist conformation. Obviously the accumulation of two *O*-silyl substituents in positions 2 and 3 and a further substituent at 4-*O* induces the conformational shift. In **6e** and **11b** as well as in urethanes **11c** and **11d** the common $^4C_1$ conformation prevails. We believe that the selective removal of the 3-*O*-silyl group in reaction **11a**→**11b** benefits from the altered conformation.

Table 1 Unit F coupling constants in some synthetic intermediates.

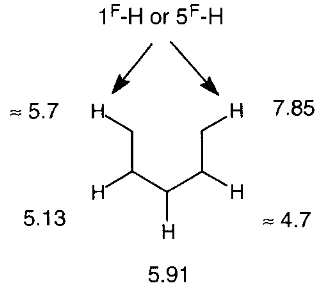
comp.	$^3J_{1F,2F}$ (Hz)	$^3J_{2F,3F}$ (Hz)	$^3J_{3F,4F}$ (Hz)	$^3J_{4F,5F}$ (Hz)
6d	6.8	3.3	5.3	3.9
6e	7.5	7.8	8.1	9.1
7a	6.8	0.7	3.5	
7b	6.6	3.9	≈ 1.1	
8a	6.8	≈ 1.1		
8b	6.7	≈ 1.1		2.4
9a	6.3	1.9	4.4	2.4
11a	6.8	2.6	4.6	3.1
11b	7.7	8.6	8.0	
11c	7.4		9.6	
11d	7.7	9.2	9.1	9.4

Completion of the Synthesis of 2

The phosphoric acid diester grouping was installed making use of our version [48] of the Ugi procedure [49]. Thus, the dichlorophosphite (see Scheme 4) was converted into the corresponding bistriazolide and this in turn was treated with **11e**/**12**. The reaction product was then allowed to react with the moenomycin derived glyceric acid derivative **13** [12] to furnish the corresponding phosphorous acid triester which was oxidized with bis(trimethylsilyl) peroxide [50] to provide **14a** in 23%, accompanied by **15** (26% yield). The product ratio indicates that α-**11e** reacts much faster than β-**11e** (in agreement with previous results) whereas the reaction rates of α-**11e** and **12** are similar.

The structure of **14a** was confirmed by NMR and FAB mass spectra. Two signals in the ^{31}P NMR spectrum were indicative of two diastereomers (isomeric at phosphorus). The glyceric acid moiety displayed even three OCH_3 signals as a result of the stereogenic centres in the lipid part. The coupling constants $^3J_{1F,2F}$ = 3.4 Hz and 3.5 Hz (for the two diastereomers) clearly indicated that **14a** was the desired α-phosphate.

The second compound was **15a**, the phosphorylation product of **12**. The anomeric carbon resonances appeared at δ=102.2 ppm (C-1^E) and 99.9/100.1 ppm (C-1^F, two P diastereomers) and that of 1^F-H at 5.71–5.74. In the isomeric 1-phosphate the corresponding chemical shifts are: 97.6/98.2 for C-1^F and 6.10/6.17 for 1^F-H. Interestingly, **15a** slowly (in the course of the NMR measurements in [D_5]pyridine) suffered a conformational change to give **15b** with ring F in the $^1C_4$ conformation. First, according to the NMR spectrum, in the solution **15a** predominated ($^3J_{2F,3F}$ = 7.0 Hz and $^3J_{3F,4F}$ = 7.4 Hz). Later on, gradually the resonances of **15b** appeared dominating the spectrum after a few days. The coupling constants of the ring F protons then were in the range of 2.0 and 3.5 Hz.



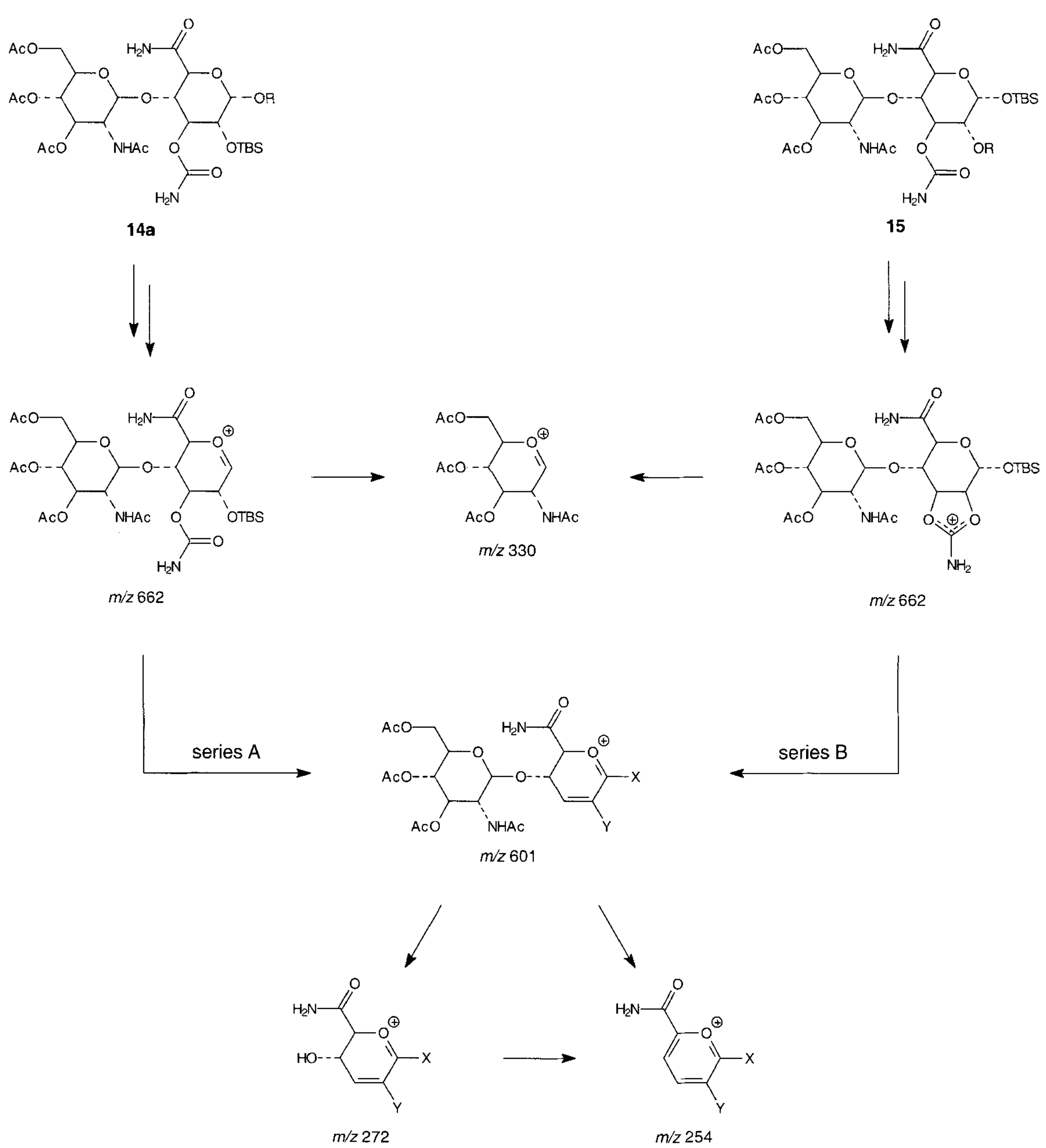
(3)

The structural assignment of **15b** rests on a careful analysis of one- and two-dimensional NMR spectra. The $^1H,^1H$ COSY spectrum of **15b** revealed that in the 5-spin system of the ring F protons the two signals at δ 5.7 and 7.85 were each correlated to only one other signal. They must, therefore, correspond to 1^F-H and 5^F-H, respectively (see Formula 3). Since in the ^{13}C, ^1H COSY the signal at δ 7.85 had a cross peak with δ 90.7 (C-1^F), it clearly belonged to 1^F-H. Thus, this proton has a very unusual chemical shift probably caused by some anisotropy effect. The 1^F-H signal is a sharp doublet with $^3J_{1F,2F}$ = 2.6 Hz. A $^1H,^{31}P$ coupling was not detected.

Interestingly, the FAB mass spectra of **14a** and **15** were almost identical. An explanation is given in Scheme 5. Most notably the fragmentation of **15** starts with the loss of the 2-substituent presumably assisted by the carbamoyl group (cf. **15** →→ m/z = 662).

On reduction with zinc-copper couple (Imai conditions [51]) **14a** was converted into **14b** (61% yield, only one ^{31}P NMR signal) accompanied by some **14c** (8%). The removal of the silyl protecting group from **14b** then was achieved with 3:1:1 acetic acid-THF-water (100% based on consumed **14b**) [20]. TBAF was not used because we have found previously that the carbamoyl group is quite labile under these deprotection conditions [19].

As usual [43] the final basic ester hydrolysis was problematic and had to be performed in two steps. The acetyl groups were removed easily whereas the methyl glycerate was quite reluctant. The final reaction had to be carefully monitored to avoid cleavage of the carb-



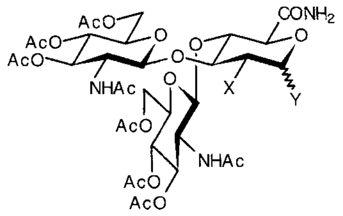
Scheme 5 Mass spectrometric fragmentation of **13a** and **14** (series A: X = H, Y = OTBS series B: X = OTBS, Y = H).

amoyl group. The NMR and mass spectra of the hydrolysis products were well in accord with structures **14d** and **2** (the target compound of the synthesis).

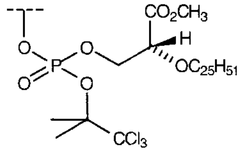
Some Observation in the Trisaccharide Series

Radical dehalogenation of **9a** provided **9b** (86%). At this stage the connectivity of the sugar units could be established. The $^{13}C,^{1}H$-LRHC spectrum demonstrated correlations 1^{E}-H → C-3^{F} and $1^{E'}$-H → C-4^{F} proving the (1→3)- and (1→4)-glycosidic bonds. Again, ring F did *not* adopt the $^{4}C_{1}$ conformation due to steric repulsion of the substituents ($^{3}J_{2F,3F}$ = 3.5 Hz).

For the cleavage of the allyl glycoside bond a number of methods were tested: (i) palladium(II) chloride in acetate buffer, (ii) palladium(II) acetate in aqueous acetic acid, tetrakis(triphenylphosphine)palladium(0) [45] in degassed acetic acid. Only the latter method gave reasonably good results and furnished a single compound as immediate reaction product (according to TLC). After flash chromatography or standing in pyridine solution a second TLC spot was visible. The compounds could be separated, and it turned out (TLC analysis) that in pyridine solution they were in equilibrium. The NMR spectra revealed that the mixture contained in fact three compounds. Two of them were the



(4)

16	X	Y
a	OTBS	OH
b	OH	α-OTBS
c		α-OTBS

expected deallylation products α-**16a** and β-**16a**, and the third, **16b**, was a rearrangement product formed by silyl group migration as in the disaccharide series. **16b** was the main component of the mixture ($\approx$ 80%).

In **16b** ring F adopts the $^4C_1$ conformation. We believe that in this case the rearrangement product is preferred because it allows ring F to return into the more stable conformation from the twist conformation, which has been demonstrated for **9b**. In **16b** the compression of the bulky substituents at positions 2, 3, and 4 is released.

The construction of the phosphoric acid triester was performed as described above. The 2-phosphate **16c** was isolated in 48% yield whereas the 1-phosphate was not found. The structural assignment was performed in analogy to **14a**. The MS fragmentation behaviour cannot be straightforwardly explained inasmuch as the 2-substituent is lost rather than the silyloxy group from the anomeric position.

Antibiotic Activity of 2

The biological activities of **2** were tested in the following assays:

(i) Inhibition of the UDP-*N*-acetylmuramyl pentapeptide-dependent incorporation of [^{14}C]UDP-*N*-acetylglucosamine into cross-linked high-molecular weight peptidoglycan (studied with a slightly modified [52] version of the assay described by Izaki, Matsuhashi, and Strominger [53])

(ii) the inhibitory effect of **2** directly on the transglycosylation reaction (determined by the in vitro assay developed earlier in one of our laboratories [54] using a crude extract from an over-producer of polymerase PBP 1b (*E. coli JA200 plc19-19)* and as substrate lipid II which is the immediate precursor of uncrosslinked peptidoglycan)

(iii) the minimum inhibitory concentrations (MIC) of compound **2** against various microorganisms (determined by a serial two fold agar dilution method, Müller Hinton Agar). The results are collected in Tables 2–4.

In all test systems **2** was of very low activity when compared with active transglycosylase inhibitors such as moenomycin A.

Table 2 Minimum inhibitory concentrations (in μgxml^{-1}) of **2** and of moenomycin A (for comparison) against various test organisms.

strain	MIC (μgxml^{-1}) moenomycin A	2
S. aureus SG 511	0.049	>50
S. aureus 503	0.049	>50
Strept. pyog. A77	<0.002	3.125
Ps. aerug. 1771M	12.5	>50
E. coli DC2	50	>50

Table 3 Effect of **2** and of moenomycin A (for comparison) on the in vitro UDP-*N*-acetylmuramylpentapeptide-dependent incorporation of [^{14}C]UDP-*N*-acetylglucosamine into cross-linked high-molecular weight peptidoglycan.

final concentration (μgxml^{-1})	% inhibition moenomycin A	2
100	97	56
10	96	12
1	95	0
0.1	55	0
0.01	8	0
IC$_{50}$ (μgxml^{-1})	0.08	78.0

Table 4 Effect of **2** and of moenomycin A (for comparison) on the in vitro formation of uncrosslinked peptidoglycan by transglycosylation.

final concentration (μgxml^{-1})	% inhibition moenomycin A	2
10	100	95
1	100	66
0.1	54	0

Discussion

In the introductory part of this paper a number of possible mechanisms for the moenomycin-type transglycosylation inhibitors have been discussed. Two of them can now be eliminated. Obviously, the idea can be discarded that the moenomycin-type compounds bind at the donor site and inhibit the enzyme as a result of the stronger bond to the leaving group (caused by the electron-withdrawing effect of the uronamide group) or because the phosphoglycerate is a poor leaving group when compared with the diphosphate in the natural donor substrate. In this case **2** should be a better inhibitor than **1**, and obviously this is not the case.

The present results lend credence to our recently reported [10b, 10c] mechanistic considerations which rely on the different linkage between the first two sugars (compare **1** and the donor in Scheme 1).

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Experimental

NMR: Gemini 200 (Varian, ^1H NMR 200 MHz, ^{13}C NMR 50.3 MHz), Gemini 2000 (Varian, ^1H NMR 200 MHz, ^{13}C NMR 50.3 MHz, ^{31}P NMR 81.0 MHz), Gemini 300 (Varian, ^1H NMR 300 MHz, ^{13}C NMR 75.5 MHz, ^{31}P NMR 121.5 MHz), Unity 400 (Varian, ^1H NMR 400 MHz, ^{13}C NMR 100.6 MHz, ^{31}P NMR 161.9 MHz). Chemical shifts are given in δ values, the ^{31}P NMR chemical shifts are based on external phosphoric acid. When identified by APT (attached proton test), CH_3, CH_2, CH groups and quaternary carbons are indicated by "+"(C_q and CH_2) and "–" (CH and CH_3). – IR: Specord M80 grating spectrophotometer (Carl Zeiss Jena) and FT-IR spectrometer (ATI Mattson, Genesis Series). The concentrations were about 5 mg per 0.2 ml solution. – FAB MS: Fisons VG. Matrices were lactic acid and 3-nitrobenzyl alcohol, respectively. Two molecular masses are always communicated, the first was calculated using the International Atomic Masses, the second refers to ^{12}C, ^1H, ^{16}O, ^{14}N, ^{28}Si, ^{35}Cl, and ^{31}P (mono-isotopic masses). Carbon and proton numbering in the subunits (see NMR data) as well as naming of the MS fragments follows the moenomycin nomenclature [55]. – Micro analyses were performed by the laboratory Ilse Beetz, Kronach. – Melting points (corrected): Boëtius apparatus (VEB Wägetechnik RAPIDO, Radebeul). – Analytical TLC: Merck precoated silica gel 60 F_{254} plates (0.2 mm), spots were identified under a UV lamp (λ = 254 nm and λ = 366 nm) and with a 2.22 mol l^{-1} H_2SO_4 solution which contained $Ce(SO_4)_2 \cdot 4H_2O$ (10 g l^{-1}) and $H_3[PO_4(Mo_3O_9)_4] \cdot H_2O$ (25 g l^{-1}) and heating at 140 °C [56]. LC (preparative gravitational liquid chromatography): silica gel (ICN Biomedicals Silica 63–100 µm). FC (flash chromatography) was performed as described by Still [57] (ICN Biomedicals Silica 32–63 µm and 63–100 µm, respectively). – Solvents were dried using standard procedures, molecular sieves were dried at 320 °C for 18 h at 10 Pa. If necessary, solvents were degassed by sonication (Bandelin, Sonorex Super RK 106). – All O_2- or moisture-sensitive reactions were performed in oven-dried glassware under a positive pressure of argon. Liquids and solutions were transferred by syringe. Small-scale reactions were performed in Wheaton serum bottles sealed with aluminum caps with open top and Teflon®-faced septum (Aldrich). For the phosphorylation reactions the educts were dried by dissolving them in dry pyridine and solvent removal in a flow of dry argon. The cation exchange resin was freshly regenerated. – Glycosyl donor **5** [39] and bis(trimethylsilyl) peroxide [50c] were prepared as described in the literature. Organic solvent evaporations were performed *in vacuo* at 40 °C using a rotatory evaporator, water was removed by lyophilization using the Leybold-Heraeus GT2 and the Christ Alpha 1-2 apparatus.

Allyl 4,6-O-(4-methoxybenzylidene)-β-D-glucopyranoside (**4a**)

To a solution of **3b** (6.34 g, 16.3 mmol) in methanol (163 ml) 2.8 ml of a solution of sodium methoxide (1.0 mol l^{-1} in methanol, 3 mmol) were added. The mixture was stirred at 20 °C for 1 h. After addition of acetic acid (2.8 ml) solvents were evaporated. In a 250 ml round-bottomed flask to the residue (4.46 g, max. 16.3 mmol of **3c**), dissolved in DMF (19 ml, 250 ml), 4-methoxybenzaldehyde dimethylacetal (9.5 ml, 56 mmol) and p-TsOH·H_2O (0.93 g, 4.9 mmol) were added and the flask was attached to a rotavapor and left there for 4 h (bath temp. 40 °C, p = 10000 Pa, 60 rpm). After addition of triethylamine (5 ml) the mixture was directly applied to the top of a FC column. Elution with petroleum ether-ethyl acetate 3:2 → pure ethyl acetate) provided **4a** (4.91 g, 89%).

M.p. 158–159 °C (ethyl acetate-petroleum ether). – R_f = 0.42 (petroleum ether-$CHCl_3$-ethanol 5:2:2). – ^1H NMR (300 MHz, [D_5]pyridine): δ 3.66 (s, 3 H, OCH_3), 3.74 (ddd, 1 H, 5-H), 3.94 (dd, 1 H, 6-H_{ax}), 3.95 (dd, 1 H, 4-H), 4.11 (dd, 1 H, 2-H), 4.33 (ddt, 1 H, allyl-1-H), 4.34 (dd, 1 H, 3-H), 4.50 (dd, 1 H, 6-H_{eq}), 4.57 (ddt, 1 H, allyl-1-H'), 4.90 (d, 1 H, 1-H), 5.16 (dq, 1 H, allyl-3-H_{trans}), 5.46 (dq, 1 H, allyl-3-H_{cis}), 5.77 (s, 1 H, acetal-H), 6.01–6.14 (m, 1 H, allyl-2-H), 6.99–7.04 (m, 2 H, Ar-3-H), 7.64–7.70 (m, 2 H, Ar-2-H), $^3J_{1,2}$ = 7.7 Hz, $^3J_{2,3}$ = 8.5 Hz, $^3J_{3,4}$ = 9.1 Hz, $^3J_{4,5}$ = 9.4 Hz, $^3J_{5,6ax}$ = 9.9 Hz, $^3J_{5,6eq}$ = 5.0 Hz, $^2J_{6ax,6eq}$ = 10.2 Hz; allyl group coupling constants: $^2J_{1,1'}$ = 13.2 Hz, $^3J_{1,2}$ = 5.8 Hz, $^3J_{1',2}$ = 4.9 Hz, $^4J_{1,3}$ = 1.5 Hz, $^3J_{2,3cis}$ = 17.3 Hz, $^3J_{2,3trans}$ = 10.5 Hz, $^2J_{3cis,3trans}$ = 3.5 Hz [58, 59]. – ^{13}C NMR (75.5 MHz, ^{13}C,^1H COSY, APT, 50.3 MHz, [D_5]pyridine): δ 55.06 (–, OCH_3), 66.93 (–, C-5), 69.11 (+, C-6), 70.17 (+, allyl-C-1), 74.33 (–, C-3), 75.63 (–, C-2), 82.24 (–, C-4), 101.94 (–, acetal-C), 104.24 (–, C-1), 113.69 (–, Ar-C-3), 116.64 (+, allyl-C-3), 128.32 (–, Ar-C-2), 131.07 (+, Ar-C-1), 135.05 (–, allyl-C-2), 160.38 (+, Ar-C-4). – FAB-MS: m/z 339.1 [M+H]$^+$, 281.1 [f]$^+$.

$C_{17}H_{22}O_7$ calcd.: C 60.35 H 6.55;
(338.36, 338.14) found: C 60.25 H 6.47.

Allyl 2,3-di-O-tert-butyldimethylsilyl-4,6-O-(4-methoxybenzylidene)-β-D-glucopyranoside (**4b**)

A solution of **4a** (1.88 g, 5.56 mmol), imidazole (4.54 g, 66.69 mmol), and *tert*-butyldimethylsilyl chloride (5.04 g, 33.44 mmol) in DMF (20 ml) was stirred at 40 °C for 3 d. Excess reagent was destroyed with methanol (15 ml). Solvent evaporation and LC (petroleum ether-ethyl acetate 7:1) furnished **4b** (3.11 g, 99%).

R_f = 0.54 (petroleum ether-$CHCl_3$-ethanol 5:2:0.4). – ^1H NMR (200 MHz, [D_5]pyridine): δ 0.18, 0.20, 0.27, 0.30 (4 s, 4×3 H, $SiCH_3$), 0.97, 1.06 [2 s, 2×9 H, $SiC(CH_3)_3$], 3.65 (s, 3 H,

OCH_3), 3.55–3.70 (m, 2 H, 4-H, 5-H), 3.72 (dd, 1 H, 2-H), 3.85 (dd, 1 H, 6-H_{ax}), 3.99 (dd, 1 H, 3-H), 4.18 (ddt, 1 H, allyl-1-H), 4.44 (dd, 1 H, 6-H_{eq}), 4.48 (ddt, 1 H, allyl-1-H'), 4.57 (d, 1 H, 1-H), 5.22 (dq, 1 H, allyl-3-H_{trans}), 5.38 (dq, 1 H, allyl-3-H_{cis}), 5.63 (s, 1 H, acetal-H), 6.00–6.19 (m, 1 H, allyl-2-H), 7.07 (AA'BB' system, 2 H, Ar-3-H, Ar-3'-H), 7.66–7.70 (AA'BB' system, 2 H, Ar-2-H, Ar-2'-H), $^3J_{1,2}$ = 7.3 Hz, $^3J_{2,3}$ = 8.1 Hz, $^3J_{3,4}$ = 8.5 Hz, $^3J_{5,6ax}$ = 9.0 Hz, $^3J_{5,6eq}$ = 4.6 Hz, $^2J_{6ax,6eq}$ = 10.3 Hz. – ^{13}C NMR (50.3 MHz, [D_5]pyridine): δ –4.46, –4.43, –4.00, –3.79 ($SiCH_3$), 17.33, 17.44 [$Si\underline{C}(CH_3)_3$], 25.30 [$SiC(\underline{C}H_3)_3$] [60], 53.90 (OCH_3), 65.16 (C-5), 67.94 (C-6), 69.33 (allyl-C-1), 75.04, 75.82 (C-2, C-3), 80.81 (C-4), 101.32 (acetal-C), 102.07 (C-1), 112.63 (Ar-C-3), 116.37 (allyl-C-3), 127.40 (Ar-C-2), 129.61 (Ar-C-1), 133.60 (allyl-C-2), 159.40 (Ar-C-4). – $C_{29}H_{50}O_7Si_2$ [566.88, 566.31], FAB-MS: *m/z* (%) = 567.3 $[M+H]^+$, 551.2 $[M+H–CH_4]^+$, 509.2 $[f]^+$.

Reductive opening of the 4-methoxybenzylidene acetal of 4b

In a 250 ml round-bottomed flask powdered molecular sieves 3Å and sodium cyanoborohydride (1.67 g, 26.58 mmol) were placed and a solution of **4b** (3.00 g, 5.29 mmol) in acetonitrile (120 ml) was added at once. Trimethylsilyl chloride (4.0 ml, 31.7 mmol) was added dropwise. At 20 °C the mixture was stirred for 28.5 h, then triethylamine (5.2 ml) and methanol (21 ml) were added. After solvent evaporation the residue was redissolved in methanol (100 ml), acetic acid (10 ml) was added and the mixture was stirred at 20 °C for 6.5 h. Addition of triethylamine (4.0 ml), solvent evaporation, and FC (petroleum ether-ethyl acetate 14:1 → petroleum ether-ethyl acetate 5:1 → pure ethyl acetate) furnished **6a** (2.93 g, 97%) and the isomeric 6-*O*-PMB ether (74.4 mg, 2%).

Allyl 2,3-di-O-tert-butyldimethylsilyl-4-O-(4-methoxybenzyl)-β-D-glucopyranoside (**6a**)

R_f = 0.28 (petroleum ether-$CHCl_3$-ethanol 5:2:0.4). – ^1H NMR (300 MHz, [D_5]pyridine): δ 0.28, 0.31 (2 s, 9 H and 3 H, $SiCH_3$), 1.07, 1.08 [2 s, 2×9 H, $SiC(CH_3)_3$], 3.68 (s, 3 H, OCH_3), 3.66–3.95 (m, 4 H, 2-H, 3-H, 4-H, 5-H), 4.09 (ddt, 1 H, allyl-1-H), 4.22 (br. t, 2 H, CH_2-6), 4.48 (ddt, 1 H, allyl-1-H'), 4.52 (d, 1 H, 1-H), 5.01, 5.04 (AB system, 2 H, Ar-CH_2), 5.18 (dq, 1 H, allyl-3-H_{trans}), 5.32 (dq, 1 H, allyl-3-H_{cis}), 6.00–6.14 (m, 1 H, allyl-2-H), 6.71 (br. s, 1 H, OH), 7.04 (AA'BB' system, 2 H, Ar-3-H, Ar-3'-H), 7.54 (AA'BB' system, 2 H, Ar-2-H, Ar-2'-H), $^3J_{1,2}$ = 7.2 Hz, J_{AB} = 11.3 Hz. – ^{13}C NMR (75.5 MHz, ^{13}C,^1H COSY, APT, 50.3 MHz, [D_5]pyridine): δ –3.24, –3.21, –2.67, –2.13 (–, $SiCH_3$), 18.17, 18.50 (+, $Si\underline{C}(CH_3)_3$), 26.58 (–, $SiC(\underline{C}H_3)_3$) [60], 54.98 (–, OCH_3), 61.46 (+, C-6), 70.07 (+, allyl-C-1), 73.36 (+, Ar-CH_2), 76.36, 77.21, 77.60, 78.83 (–, C-2, C-3, C-4, C-5), 102.69 (–, C-1), 114.00 (–, Ar-C-3), 117.14 (+, allyl-C-3), 128.94 (–, Ar-C-2), 131.53 (+, Ar-C-1), 134.83 (–, allyl-C-2), 159.31 (+, Ar-C-4). – $C_{29}H_{52}O_7Si_2$ (568.90, 568.33). FAB-MS (including MIKE mode): *m/z* (%) = 591.1 $[M+Na]^+$, 569 $[M+H]^+$, 567.2 $[M+H–H_2]^+$, 511 $[f]^+$, 509.1 $[f–H_2]^+$, 373.1 $[f–PMBOH]^+$.

Allyl 2,3-di-O-tert-butyldimethylsilyl-6-O-(4-methoxybenzyl)-β-D-glucopyranoside (formula not shown)

R_f = 0.38 (petroleum ether-$CHCl_3$-ethanol 5:2:0.4). – ^1H NMR (300 MHz, [D_5]pyridine): δ 0.29, 0.31, 0.35, 0.42 (4 s, 4×3 H, $SiCH_3$), 1.08, 1.09 [2 s, 2×9 H, $SiC(CH_3)_3$], 3.66 (s, 3 H, OCH_3), 3.74 (dd, 1 H, 2-H), 3.80–3.99 (m, 4 H, 3-H, 4-H, 5-H, 6-H), 4.12 (dd, 1 H, 6-H'), 4.16 (ddt, 1 H, allyl-1-H), 4.51 (d, 1 H, 1-H), 4.54 (ddt, 1 H, allyl-1-H'), 4.57 (s, 2 H, Ar-CH_2), 5.17 (dq, 1 H, allyl-3-H_{trans}), 5.33 (dq, 1 H, allyl-3-H_{cis}), 6.03–6.16 (m, 1 H, allyl-2-H), 6.70 (d, 1 H, OH), 6.93–6.96 (AA'BB' system, 2 H, Ar-3-H, Ar-3'-H), 7.33–7.36 (AA'BB' system, 2 H, Ar-2-H, Ar-2'-H), $^3J_{1,2}$ = 7.3 Hz, $^3J_{2,3}$ = 7.9 Hz, $^3J_{4,OH}$ = 5.8 Hz, $^3J_{5,6'}$ = 1.9 Hz, $^2J_{6,6'}$ = 10.7 Hz. – ^{13}C NMR (APT, 75.5 MHz, [D_5]pyridine): δ –3.17, –2.76, –2.63, –2.57 (–, $SiCH_3$), 18.51, 18.68 (+, $Si\underline{C}(CH_3)_3$), 26.52, 26.69 (–, $SiC(\underline{C}H_3)_3$), 54.98 (–, OCH_3), 70.20, 72.98 (+, allyl-C-1, Ar-CH_2, C-6) [60], 71.40, 76.42, 76.58, 79.75 (–, C-2, C-3, C-4, C-5), 102.77 (–, C-1), 113.95 (– Ar-C-3), 117.21 (+, allyl-C-3), 129.38 (–, Ar-C-2), 131.04 (+, Ar-C-1), 134.94 (–, allyl-C-2), 159.43 (+, Ar-C-4). – $C_{29}H_{52}O_7Si_2$ [568.90, 568.33], FAB-MS: *m/z* (%) = 591.2 $[M+Na]^+$, 569 $[M+H]^+$, 567.2 $[M+H–H_2]^+$, 511 $[f]^+$, 509.1 $[f–H_2]^+$, 431.1 $[M+H–PMBOH]^+$, 373.1 $[f–PMBOH]^+$.

Conversion of 6a into 6d

To a mixture of **6a** (1.37 g, 2.41 mmol), TEMPO (0.40 g, 2.55 mmol), tetrabutylammonium chloride (0.67 g, 2.42 mmol), potassium bromide (0.29 g, 2.43 mmol) and dichloromethane (22.5 ml) at 0 °C a mixture of satd. aq. sodium chloride (25.9 ml), satd. aq. sodium hydrogencarbonate (27.8 ml) and aq. sodium hypochlorite (25.9 ml, 12–14% active chlorine) was added during 45 min. The reaction mixture was vigorously stirred at 20 °C for 3.5 h (TLC control: petroleum ether–$CHCl_3$–ethanol 5:2:0.4). The pH was adjusted to 2–3 with concd. HCl. The organic layer was separated and the aqueous phase was extracted five times with dichloromethane. The combined organic extracts were dried (sodium sulfate). After solvent removal, the crude product (2.36 g, max. 2.41 mmol), sodium chlorite (2.17 g, 23.99 mmol), and sodium dihydrogenphosphate monohydrate (2.49 g, 18.04 mmol) were placed in a reaction flask and with stirring successively 2-methyl-2-butene (11.0 ml), *tert*-butanol (46.5 ml), and water (18.6 ml) were added. The reaction mixture was stirred at 20 °C for 4 h (TLC control: petroleum ether-$CHCl_3$-ethanol 5:2:2), then it was diluted with water (10 ml) and dichloromethane (100 ml). The organic phase was separated and the aqueous phase extracted twice with dichloromethane. The aqueous phase was then adjusted to pH 2 with concd. HCl and extracted three times with dichloromethane. After drying, solvent evaporation, and drying of the residue at 10 Pa, the crude acid (2.84 g, max. 2.41 mmol) and CDI (0.99 g, 6.11 mmol) were dissolved in dichloromethane (38 ml) and the mixture was stirred at 20 °C for 6 h. Through this solution at 0 °C gaseous ammonia was bubbled for 45 min. Then the mixture was stirred at 20 °C for 45 min. Solvent evaporation and FC (petroleum ether-ethyl acetate 3:1 → 1:1) furnished **6d** (1.27 g, 90% based on **6a**).

Allyl 2,3-di-O-tert-butyldimethylsilyl-4-O-(4-methoxybenzyl)-b-D-glucopyranosiduronic acid (**6c**)

R_f = 0.14 (petroleum ether–$CHCl_3$-ethanol 5:2:0.4). – IR ($CHCl_3$): $\tilde{\nu}$ = 3400, 2930, 1770, 1715, 1615, 1510 cm^{-1}. –

^{1}H NMR (200 MHz, CDCl$_3$) of the crude product: δ 0.00, 0.04, 0.10, 0.14 (4 s, 12 H, SiCH$_3$), 0.86, 0.91 [2 s, 18 H, SiC(CH$_3$)$_3$], 3.61–4.01 (m, 3 H, 2-H, 3-H, 4-H), 3.81 (s, 3 H, OCH$_3$), 4.05 (ddt, 1 H, allyl-1-H), 4.38 (ddt, 1 H, allyl-1-H'), 4.51, 4.63 (AB system, 2 H, Ar-CH$_2$), 4.53 (d, 1 H, 5-H), 4.94 (d, 1 H, 1-H), 5.22 (dq, 1 H, allyl-3-H$_{trans}$), 5.32 (dq, 1 H, allyl-3-H$_{cis}$), 5.89–6.03 (m, 1 H, allyl-2-H), 6.88 (AA'BB' system, 2 H, Ar-3-H, Ar-3'-H), 7.29 (AA'BB' system, 2 H, Ar-2-H, Ar-2'-H), $^3J_{1,2}$ = 6.3 Hz, J_{AB} = 10.4 Hz. – C$_{29}$H$_{50}$O$_8$Si$_2$ (582.88, 582.30), FAB-MS: *m/z* (%) = 605.2 [M+Na]$^+$, 583 [M+H]$^+$, 581.2 [M+H–H$_2$]$^+$, 547.2 [M+Na–*t*BuH]$^+$, 387.1 [f–PMBOH]$^+$.

Allyl 2,3-di-O-tert-butyldimethylsilyl-4-O-(4-methoxybenzyl)-β-D-glucopyranosiduronamide (**6d**)

R_f = 0.27 (petroleum ether–CHCl$_3$-ethanol 5:2:0.4). – ^{1}H NMR (300 MHz, [D$_5$]pyridine): δ 0.18, 0.19, 0.27, 0.28 (4 s, 4×3 H, SiCH$_3$), 0.98, 1.04 [2 s, 2×9 H, SiC(CH$_3$)$_3$], 3.66 (s, 3 H, OCH$_3$), 3.92 (dd, 1 H, 2-H), 4.07 (ddt, 1 H, allyl-1-H), 4.16 (dd, 1 H, 3-H), 4.34 (dd, 1 H, 4-H), 4.47 (ddt, 1 H, allyl-1-H'), 4.66 (d, 1 H, 5-H), 4.82, 4.87 (AB system, 2 H, Ar-CH$_2$), 4.95 (d, 1 H, 1-H), 5.16 (dq, 1 H, allyl-3-H$_{trans}$), 5.33 (dq, 1 H, allyl-3-H$_{cis}$), 5.93-6.13 (m, 1 H, allyl-2-H), 7.01 (AA'BB' system, 2 H, Ar-3-H, Ar-3'-H), 7.57 (AA'BB' system, 2 H, Ar-2-H, Ar-2'-H), 8.00, 8.36 (2×br. s, 2×1 H, CONH), $^3J_{1,2}$ = 6.8 Hz, $^3J_{2,3}$ = 3.3 Hz, $^3J_{3,4}$ = 5.3 Hz, $^3J_{4,5}$ = 3.9 Hz, J_{AB} = 10.8 Hz. – ^{13}C NMR (^{13}C,^{1}H COSY, APT, 50.3 MHz, [D$_5$]pyridine): δ –5.33, –5.25, –5.02, –4.81 (–, SiCH$_3$), 17.02, 17.20 (+, Si<u>C</u>(CH$_3$)$_3$), 25.00, 25.07 (–, SiC(<u>C</u>H$_3$)$_3$), 53.90 (–, OCH$_3$), 69.17 (+, allyl-C-1), 71.10 (+, Ar-CH$_2$), 74.69 (–, C-3), 76.10 (–, C-2), 77.41 (–, C-5), 78.45 (–, C-4), 101.18 (–, C-1), 112.85 (–, Ar-C-3), 115.90 (+, allyl-C-3), 128.66 (–, Ar-C-2), 129.79 (+, Ar-C-1), 133.63 (–, allyl-C-2), 158.46 (+, Ar-C-4), 171,21(+, CONH$_2$). – C$_{29}$H$_{51}$NO$_7$Si$_2$ (581.90, 581.32). – FAB-MS: *m/z* (%) = 604.3 [M+Na]$^+$, 582.3 [M+H]$^+$, 580 [M+H–H$_2$]$^+$, 566.3 [M+H–CH$_4$]$^+$, 524.3 [f]$^+$, 466.2 [M+Na–PMBOH]$^+$, 444.3 [M+H–PMBOH]$^+$, 386.2 [f–PMBOH]$^+$.

Allyl 2,3-di-O-tert-butyldimethylsilyl-β-D-glucopyranosiduronamide (**6e**)

To a solution of **6d** (1.27 g, 2.18 mmol) in 9:1 acetonitrile-water (30 ml) CAN (2.39 g, 4.36 mmol) was added and the mixture was stirred for 30 min at 0 °C. Aqueous work-up including a sodium hydrogencarbonate solution wash (dichloromethane) followed by FC (petroleum ether-ethyl acetate 6:1 → 3:1) yielded **6e** (0.73 g, 72%). 0.12 g of **6d** (9%) were recovered.

R_f = 0.18 (petroleum ether–CHCl$_3$-ethanol 5:2:0.4). – ^{1}H NMR (300 MHz, [D$_5$]pyridine): δ 0.28, 0.30, 0.34, 0.41 (4 s, 4 ×3 H, SiCH$_3$), 1.06, 1.10 (2 s, 2×9 H, SiC(CH$_3$)$_3$), 3.73 (dd, 1 H, 2-H), 3.94 (dd, 1 H, 3-H), 4.03 (dd, 1 H, 4-H), 4.13 (ddt, 1 H, allyl-1-H), 4.20 (d, 1 H, 5-H), 4.47 (ddt, 1 H, allyl-1-H'), 4.60 (d, 1 H, 1-H), 5.16 (dq, 1 H, allyl-3-H$_{trans}$), 5.28 (dq, 1 H, allyl-3-H$_{cis}$), 5.98–6.07 (m, 1 H, allyl-2-H), 6.39 (br. s, 1 H, OH), 8.27, 8.76 (2×br. s, 2×1 H, CONH), $^3J_{1,2}$ = 7.5 Hz, $^3J_{2,3}$ = 7.8 Hz, $^3J_{3,4}$ = 8.1 Hz, $^3J_{4,5}$ = 9.1 Hz. – ^{13}C NMR (^{13}C,^{1}H COSY, APT, 50.3 MHz, [D$_5$]pyridine): δ –2.87, –2.62, –2.39, –2.24 (–, SiCH$_3$), 18.88, 19.15 (+, Si<u>C</u>(CH$_3$)$_3$), 26.85, 27.08 (–, SiC(<u>C</u>H$_3$)$_3$), 70.93 (+, allyl-C-1), 73.80 (–, C-4), 75.56 (–, C-5), 76.32 (–, C-2), 79.57 (–, C-3), 103.03 (–, C-1), 117.84 (+, allyl-C-3), 135.05 (–, allyl-C-2), 174.26 (+, CONH$_2$). – C$_{21}$H$_{43}$NO$_6$Si$_2$ (461.75, 461.26). – FAB-MS: *m/z* (%) = 945.5 [2xM+Na]$^+$, 865.5 [2xM+H–AllOH]$^+$, 484.2 [M+Na]$^+$, 462.2 [M+H]$^+$, 404.2 [f]$^+$, 386.2 [f–H$_2$O]$^+$, 346.1 [f–*t*BuH]$^+$, 272.1 [f–*t*BuMe$_2$SiOH]$^+$.

Reaction of 6e with 5

A mixture of **6e** (429 mg, 0.93 mmol), **5** (547 mg, 0.92 mmol), molecular sieves 4Å, and 1,2-dichloroethane (10.0 ml) was stirred at 20 °C for 45 min. Then TMS triflate (30 µl, 0.17 mmol) was added. After 4 h at 20 °C (TLC control: petroleum ether-ethyl acetate 1:2) the reaction was quenched with triethylamine (0.5 ml). Solvent evaporation and FC (petroleum ether-ethyl acetate 4:1 → petroleum ether-ethyl acetate 1:2 → ethyl acetate) furnished **8a** (259 mg, 31%, based on **6e**) besides **9a** (171 mg, 15%), **7a** (65 mg, 12%), **10** (99 mg, 25%, based on **5**), and a fraction (296 mg) containing probably **6e** and trichloroacetamide.

In another experiment from **6e** (57.9 mg, 125 µmol), **5** (82.4 mg, 138 µmol) and TMS triflate (1.0 mol l^{-1} in toluene, 25 µl, 25 µmol) in dichloromethane (0.35 ml) the following products were isolated by FC (petroleum ether-ethyl acetate 5:1 → petroleum ether-ethyl acetate 1:1 → pure ethyl acetate): **7b** (8.2 mg, 60% based on TMS triflate), disaccharide **8a** (14.9 mg, 14%, based on **6e**), trisaccharide **9a** (23.6 mg, 15%), **7a** (8.5 mg, 12%). 18.3 mg of **10** (42% based on **5**) were isolated and 23.2 mg (40%) of **6e** were recovered.

Allyl 4-O-(3,4,6-tri-O-acetyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranosyl)-2,3-di-O-tert-butyldimethylsilyl-β-D-glucopyranosiduronamide (**8a**)

R_f = 0.32 (petroleum ether-ethyl acetate 1:2). – IR (CHCl$_3$): $\tilde{\nu}$ = 1749, 1696, 1521 cm^{-1}. – ^{1}H NMR (^{1}H,^{1}H COSY, 400 MHz, [D$_5$]pyridine): δ 0.25, 0.28, 0.29, 0.31 (4 s, 4×3 H, SiCH$_3$), 0.99, 1.08 [2 s, 2×9 H, SiC(CH$_3$)$_3$], 2.01, 2.07, 2.09 (3 s, 3×3 H, COCH$_3$), 3.92 (ddd, 1 H, 5^E-H), 3.99 (dd, 1 H, 2^F-H), 4.21 (ddt, 1 H, allyl-1-H), 4.36 (s, 1 H, 3^F-H), 4.38 (dd, 1 H, 6^E-H), 4.49 (dd, 1 H, 6^E-H'), 4.53 (ddt, 1 H, allyl-1-H'), 4.66 (ddd, 1 H, 2^E-H), 4.69 (s, 1 H, 4^F-H), 4.84 (s, 1 H, 5^F-H), 5.02 (d, 1 H, 1^F-H), 5.20 (dq, 1 H, allyl-3-H$_{trans}$), 5.37 (dq, 1 H, allyl-3-H$_{cis}$), 5.44 (d, 1 H, 1^E-H), 5.48 (dd, 1 H, 4^E-H), 5.84 (dd, 1 H, 3^E-H), 6.02–6.11 (m, 1 H, allyl-2-H), 8.10, 8.67 (2×s, 2×1 H, CONH), 10.44 (d, 1 H, NHCOCCl$_3$), $^3J_{1E,2E}$ = 8.4 Hz, $^3J_{2E,3E}$ = 10.5 Hz, $^3J_{3E,4E}$ = 10.3 Hz, $^3J_{4E,5E}$ = 10.2 Hz, $^3J_{5E,6E}$ = 2.2 Hz, $^3J_{5E,6'E}$ = 4.4 Hz, $^2J_{6E,6'E}$ = 12.5 Hz, $^3J_{1F,2F}$ = 6.8 Hz, $^3J_{2F,3F}$ ≈ 1.1 Hz, $^3J_{NH,2E}$ = 8.8 Hz. – ^{13}C NMR (^{13}C,^{1}H COSY, APT, 50.3 MHz, CDCl$_3$, [61]): δ –4.57, –4.51, –4.23, –3.72 (–, SiCH$_3$), 18.32, 18.45 (+, Si<u>C</u>(CH$_3$)$_3$), 21.10, 21.21 (–, CO<u>C</u>H$_3$) [60], 26.22 (–, SiC(<u>C</u>H$_3$)$_3$) [60], 55.80 (–, C-2^E), 62.90 (+, C-6^E), 68.84 (–, C-4^E), 71.44 (+, allyl-C-1), 72.68 (–, C-5^E), 72.93 (–, C-3^E), 76.56 (–, C-3^F or C-5^F), 76.73 (–, C-2^F), 79.26 (–, C-4^F), 80.82 (–, C-5^F or C-3^F), 93.34 (+, CCl$_3$), 101.97 (–, C-1^E), 102.52 (–, C-1^F), 118.08 (+, allyl-C-3), 134.29 (–, allyl-C-2), 162.46 (+, <u>C</u>OCCl$_3$), 169.70, 170.98, 171.88 (+, <u>C</u>OCH$_3$), 174.13 (+, CONH$_2$).- C$_{35}$H$_{59}$Cl$_3$N$_2$O$_{14}$Si$_2$ (894.39, 892.26). – FAB-MS: *m/z* (%) = 931.1 [M+K]$^+$, 915 [M+Na]$^+$, 893.1 [M+H]$^+$, 835 [f]$^+$, 777 [f–*t*BuH]$^+$, 703 [f–*t*BuMe$_2$SiOH]$^+$, 431.9 [e]$^+$, 311.9 [e–2xAcOH]$^+$.

Allyl 3,4-di-O-(3,4,6-tri-O-acetyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranosyl)-2-O-tert-butyldimethylsilyl-β-D-glucopyranosiduronamide (**9a**)

M.p. 234–237 °C (ethanol-petroleum ether). – R_f = 0.12 (petroleum ether-ethyl acetate 1:2). – IR (CHCl$_3$): $\tilde{\nu}$ = 1752, 1691, 1525 cm^{-1}. – ^{1}H NMR (^{1}H,^{1}H COSY, 400 MHz, [D$_5$]pyridine) [62]: δ 0.31 (s, 3 H, SiCH$_3$) [60], 1.09 [s, 9 H, SiC(CH$_3$)$_3$)], 1.99, 2.02, 2.05, 2.06, 2.13, 2.17 (6 s, 6×3 H, COCH$_3$), 4.07–4.12 (m, 2 H, 5^{E}-H, $5^{\mathrm{E'}}$-H), 4.20 (ddt, 1 H, allyl-1-H), 4.30 (dd, 1 H, 2^{F}-H), 4.33 (dd, 1 H, 6^{E}-H), 4.39 (ddd, 1 H, 2^{E}-H), 4.49 (ddt, 1 H, allyl-1-H'), 4.58 (dd, 1 H, $6^{\mathrm{E'}}$-H), 4.59 (dd, 1 H, 3^{F}-H), 4.66 (dd, 1 H, $6^{\mathrm{F'}}$-H'), 4.69 (dd, 1 H, 6^{E}-H'), 4.71 (ddd, 1 H, $2^{\mathrm{E'}}$-H), 4.84 (d, 1 H, 5^{F}-H), 5.02 (d, 1 H, 1^{F}-H), 5.03–5.04 (m, 1 H, 4^{F}-H), 5.21 (dq, 1 H, allyl-3-H$_{\mathrm{trans}}$), 5.40 (dq, 1 H, allyl-3-H$_{\mathrm{cis}}$), 5.46 (dd, 1 H, 4^{E}-H), 5.52 (d, 1 H, $1^{\mathrm{E'}}$-H), 5.54 (dd, 1 H, $4^{\mathrm{E'}}$-H), 5.59 (d, 1 H, 1^{E}-H), 5.88 (dd, 1 H, $3^{\mathrm{E'}}$-H), 6.02 (dd, 1 H, 3^{E}-H), 6.01–6.10 (m, 1 H, allyl-2-H), 7.44, 8.65 (2 d, 2×1 H, CONH), 10.25 (d, 1 H, Cl$_3$CCONH$^{\mathrm{E}}$), 10.56 (d, 1 H, Cl$_3$CCONH$^{\mathrm{E'}}$), $^3J_{\mathrm{1E,2E}}$ = 8.4 Hz, $^3J_{\mathrm{2E,3E}}$ = 10.7 Hz, $^3J_{\mathrm{3E,4E}}$ = 9.4 Hz, $^3J_{\mathrm{4E,5E}}$ = 9.9 Hz, $^3J_{\mathrm{5E,6E}}$ = 3.4 Hz, $^3J_{\mathrm{5E,6'E}}$ = 2.6 Hz, $^2J_{\mathrm{6E,6'E}}$ = 12.3 Hz, $^3J_{\mathrm{1E',2E'}}$ = 8.4 Hz, $^3J_{\mathrm{2E',3E'}}$ = 10.6 Hz, $^3J_{\mathrm{3E',4E'}}$ = 9.4 Hz, $^3J_{\mathrm{4E',5E'}}$ = 9.9 Hz, $^3J_{\mathrm{5E',6E'}}$ = 2.6 Hz, $^3J_{\mathrm{5E',6'E'}}$ = 3.6 Hz, $^2J_{\mathrm{6E',6'E'}}$ = 12.3 Hz, $^3J_{\mathrm{1F,2F}}$ = 6.3 Hz, $^3J_{\mathrm{2F,3F}}$ = 1.9 Hz, $^3J_{\mathrm{3F,4F}}$ = 4.4 Hz, $^3J_{\mathrm{4F,5F}}$ = 2.4 Hz, $^3J_{\mathrm{NH,2E}}$ = 8.6 Hz, $^3J_{\mathrm{NH,2E'}}$ = 9.1 Hz, $^2J_{\mathrm{CONH,CONH}}$ = 2.6 Hz. – ^{13}C NMR (^{13}C,^{1}H COSY, 75.5 MHz, APT, 50.3 MHz, [D$_5$]pyridine) [62]: δ –4.72, –4.42 (–, SiCH$_3$), 18.09 (+, Si$\underline{\mathrm{C}}$(CH$_3$)$_3$), 20.27, 20.59, 20.65 (–, CO$\underline{\mathrm{C}}$H$_3$), 25.87 (–, SiC($\underline{\mathrm{C}}$H$_3$)$_3$), 56.12 (–, C-$2^{\mathrm{E'}}$), 56.56 (–, C-2^{E}), 61.18 (+, C-6^{E}), 61.81 (+, C-$6^{\mathrm{E'}}$), 68.94 (–, C-$4^{\mathrm{E'}}$), 69.17 (–, C-4^{E}), 70.34 (+, allyl-C-1), 72.00 (two signals according to ^{13}C, ^{1}H COSY), 72.35 (–, C-3^{E}, C-5^{E}, C-$5^{\mathrm{E'}}$), 72.98 (–, C-$3^{\mathrm{E'}}$), 74.63 (–, C-2^{F}), 77.79 (–, C-4^{F}), 79.86 (–, C-5^{F}), 81.03 (–, C-3^{F}), 93.51, 93.74 (+, CCl$_3$), 99.25 (–, C-1^{E}), 101.23 (–, C-$1^{\mathrm{E'}}$), 102.81 (–, C-1^{F}), 116.85 (+, allyl-C-3), 134.46 (–, allyl-C-2), 162.80, 162.91 (+, $\underline{\mathrm{C}}$OCCl$_3$), 169.48, 170.16, 170.25, 170.33, 170.45 (+, $\underline{\mathrm{C}}$OCH$_3$), 172.32 (+, CONH$_2$). – FAB-MS: *m/z* (%) = 1232 [M+Na]$^+$, 1210 [M+H]$^+$, 1152 [f]$^+$, 779 [M+2×H–e]$^+$, 721 [M+2×H–e–*t*BuH]$^+$, 721 [M+2×H–e–*t*BuH–H$_2$O]$^+$, 431.9 [e]$^+$, 311.9 [e–2×AcOH]$^+$.

C$_{43}$H$_{61}$Cl$_6$N$_3$O$_{22}$Si calcd.: C 42.59 H 5.07;
(1212.77, 1209.16) found: C 42.47 H 5.03.

Allyl 2,3,4-tri-O-tert-butyldimethylsilyl-β-D-glucopyranosiduronamide (**7a**)

R_f = 0.61 (petroleum ether–ethyl acetate 1:1). – ^{1}H NMR (200 MHz, [D$_5$]pyridine): δ 0.21, 0.23, 0.25, 0.27, 0.28, 0.32 (6 s, 6×3 H, SiCH$_3$), 0.93, 1.029, 1.034 (3 s, 3×9 H, SiC(CH$_3$)$_3$), 3.97 (dd, 1 H, 2-H), 4.04 (dd, 1 H, 3-H), 4.11 (ddt, 1 H, allyl-1-H), 4.51 (ddt, 1 H, allyl-1-H'), 4.61 (s, 1 H, 5-H), 4.74 (d, 1 H, 4-H), 5.19 (d, 1 H, 1-H), 5.20 (dq, 1 H, allyl-3-H$_{\mathrm{trans}}$), 5.37 (dq, 1 H, allyl-3-H$_{\mathrm{cis}}$), 5.96–6.16 (m, 1 H, allyl-2-H), 7.64, 8.38 (2 br. s, 2×1 H, CONH), $^3J_{1,2}$ = 6.8 Hz, $^3J_{2,3}$ ≈ 0.7 Hz, $^3J_{3,4}$ = 3.5 Hz. – ^{13}C NMR (50.3 MHz, [D$_5$]pyridine): δ –5.04, –4.94, –4.84, –4.77, –4.14 (SiCH$_3$) [60], 17.87, 17.91, 18.07 (Si$\underline{\mathrm{C}}$(CH$_3$)$_3$), 25.68, 25.78, 25.93 (SiC($\underline{\mathrm{C}}$H$_3$)$_3$), 70.06, 72.79, 77.95, 78.19, 81.71 (allyl-C-1, C-2, C-3, C-4, C-5), 101.18 (C-1), 116.95 (allyl-C-3), 134.73 (allyl-C-2), 172.52 (C=O). – C$_{27}$H$_{57}$NO$_6$Si$_3$ (576.01, 575.35). – FAB-MS: *m/z* (%) = 598.4 [M+Na]$^+$, 576 [M+H]$^+$, 574.4 [M+H–H$_2$]$^+$, 560.4 [M+H–CH$_4$]$^+$, 518.3 [f]$^+$ and [M+H–*t*BuH]$^+$, 502.3 [f–CH$_4$]$^+$, 460.3 [f–*t*BuH]$^+$, 386.2 [f–*t*BuMe$_2$SiOH]$^+$.

Allyl 2,3-di-O-tert-butyldimethylsilyl-4-O-trimethylsilyl-β-D-glucopyranosiduronamide (**7b**)

R_f = 0.56 (petroleum ether–ethyl acetate 1:1). – ^{1}H NMR (200 MHz, [D$_5$]pyridine): δ 0.20, 0.22, 0.24, 0.25 (4 s, 4×3 H, Si(CH$_3$)$_2$), 0.31 (s, 9 H, Si(CH$_3$)$_3$), 0.93, 1.02 (2 s, 2×9 H, SiC(CH$_3$)$_3$), 3.95 (d, 1 H, 2-H), 4.01 (d, 1 H, 3-H), 4.07 (ddt, 1 H, allyl-1-H), 4.49 (ddt, 1 H, allyl-1-H'), 4.61 (d, 1 H, 5-H), 4.72 (dd, 1 H, 4-H), 5.12–5.17 (m, 2 H, 1-H, allyl-3-H$_{\mathrm{trans}}$), 5.34 (dq, 1 H, allyl-3-H$_{\mathrm{cis}}$), 5.94–6.12 (m, 1 H, allyl-2-H), 7.66, 8.33 (2 br. s, 2×1 H, CONH), $^3J_{1,2}$ = 6.6 Hz, $^3J_{3,4}$ = 3.9 Hz, $^3J_{4,5}$ ≈ 1.1 Hz. – ^{13}C NMR (50.3 MHz, [D$_5$]pyridine, [61]): δ –5.84, –5.72, –5.11 (Si(CH$_3$)$_2$) [60], –1.01 (Si(CH$_3$)$_3$), 16.97, 17.03 (Si$\underline{\mathrm{C}}$(CH$_3$)$_3$), 24.74, 24.81 (SiC($\underline{\mathrm{C}}$H$_3$)$_3$), 69.03, 71.53, 76.51, 76.82, 80.52 (allyl-C-1, C-2, C-3, C-4, C-5), 100.77 (C-1), 115.55 (allyl-C-3), 134.55 (allyl-C-2), 171.47 (C=O). – C$_{24}$H$_{51}$NO$_6$Si$_3$ (533.93, 533.30). – FAB-MS: *m/z* (%): 556.3 [M+Na]$^+$, 534 [M+H]$^+$, 532.3 [M+H–H$_2$]$^+$, 518.3 [M+H–CH$_4$]$^+$, 476.3 [f]$^+$ and [M+H–*t*BuH]$^+$, 460.2 [f–CH$_4$]$^+$, 418.2 [f–*t*BuH]$^+$, 386.2 [f–Me$_3$SiOH]$^+$, 344.2 [f–*t*Bu Me$_2$SiOH]$^+$.

2-Trichloromethyl-(3,4,6-tri-O-acetyl-1,2-dideoxy-α-D-glucopyrano)-[2,1-d]-2-oxazoline (**10**)

The spectroscopic data were identical with those reported in ref. [39].

Allyl 4-O-(2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-2,3-di-O-tert-butyldimethylsilyl-β-D-glucopyranosiduronamide (**11a**)

A solution of **8a** (838 mg, 0.94 mmol), freshly distilled tributyltin hydride (1.25 ml, 4.7 mmol) and AIBN (58 mg, 0.35 mmol) in toluene (31 ml) was heated in a sealed reaction vial to 80 °C for 1.5 h under stirring. Solvent evaporation followed by FC (petroleum ether → petroleum ether-CHCl$_3$-ethanol 5:2:0.5 → petroleum ether–CHCl$_3$-ethanol 5:2:1) furnished **11a** (568 mg, 77%) and **11b** (147 mg, 23%).

R_f = 0.45 (petroleum ether-CHCl$_3$-ethanol 5:2:2). – IR (CHCl$_3$): $\tilde{\nu}$ =1745, 1682, 1516 cm^{-1}. – ^{1}H NMR (200 MHz, ^{1}H, ^{1}H COSY [61], 400 MHz, [D$_5$]pyridine): δ 0.22, 0.25, 0.27, 0.28 (4×s, 4×3 H, SiCH$_3$), 0.97, 1.04 [2 s, 2×9 H, SiC(CH$_3$)$_3$], 1.99, 2.02, 2.07 (3 s, 3×3 H, OCOCH$_3$), 2.12 (s, 3 H, NHCO C$\underline{\mathrm{H}}_3$), 3.89 (ddd, 1 H, 5^{E}-H), 3.94 (dd, 1 H, 2^{F}-H), 4.13 (ddt, 1 H, allyl-1-H), 4.29 (dd, 1 H, 3^{F}-H), 4.33 (dd, 1 H, 6^{E}-H), 4.45–4.55 (m, 2 H, allyl-1-H', 6^{E}-H'), 4.57 (ddd, 1 H, 2^{E}-H), 4.64 (dd, 1 H, 4^{F}-H), 4.74 (d, 1 H, 5^{F}-H), 4.98 (d, 1 H, 1^{F}-H), 5.17 (dq, 1 H, allyl-3-H$_{\mathrm{trans}}$), 5.33 (d, 1 H, 1^{E}-H), 5.34 (dq, 1 H, allyl-3-H$_{\mathrm{cis}}$), 5.44 (dd,1 H, 4^{E}-H), 5.73 (dd, 1 H, 3^{E}-H), 5.92–6.14 (m, 1 H, allyl-2-H), 8.12, 8.62 (2×br. d, 2×1 H, CONH), 8.94 (d, 1 H, NHAc), $^3J_{\mathrm{1E,2E}}$ = 8.5 Hz, $^3J_{\mathrm{2E,3E}}$ = 10.3 Hz, $^3J_{\mathrm{3E,4E}}$ = 9.6 Hz, $^3J_{\mathrm{4E,5E}}$ = 9.7 Hz, $^3J_{\mathrm{5E,6E}}$ = 2.2 Hz, $^3J_{\mathrm{5E,6'E}}$ = 5.0 Hz, $^2J_{\mathrm{6E,6'E}}$ = 12.4 Hz, $^3J_{\mathrm{1F,2F}}$ = 6.8 Hz, $^3J_{\mathrm{2F,3F}}$ = 2.6 Hz, $^3J_{\mathrm{3F,4F}}$ = 4.4 Hz, $^3J_{\mathrm{4F,5F}}$ = 3.0 Hz, $^3J_{\mathrm{NH,2E}}$ = 8.8 Hz, $^2J_{\mathrm{CONH,CONH}}$ = 1.5 Hz. – ^{13}C NMR (^{13}C,^{1}H COSY, APT, 50.3 MHz, [D$_5$]pyridine, [61]): δ –4.10, –3.81, –3.75, –3.47 (–, SiCH$_3$), 18.41, 18.63 (+, Si$\underline{\mathrm{C}}$(CH$_3$)$_3$), 20.74, 20.85, 20.96 (–, OCO$\underline{\mathrm{C}}$H$_3$), 23.47 (–, NHCO$\underline{\mathrm{C}}$H$_3$), 26.43, 26.49 (–, SiC($\underline{\mathrm{C}}$H$_3$)$_3$), 55.05 (–, C-2^{E}), 62.94 (+, C-6^{E}), 69.67 (–, C-4^{E}), 70.76 (+, allyl-C-1), 72.66 (–, C-5^{E}), 74.15 (–, C-3^{E}), 76.96 (–, C-3^{F}), 77.34 (–, C-2^{F}), 79.06 (–, C-5^{F}), 79.97 (–, C-

4^F), 101.65 (–, C-1^E), 102.85 (–, C-1^F), 117.33 (+, allyl-C-3), 135.02 (–, allyl-C-2), 170.00, 170.36, 170.67, 170.88 (+, $\underline{\mathrm{C}}\mathrm{OCH_3}$), 173.27 (+, $\mathrm{CONH_2}$). –FAB-MS: *m/z* (%): 813.3 [M+Na]$^+$, 791.3 [M+H]$^+$,789 [M+H–H$_2$]$^+$, 733.2 [f]$^+$, 601.1 [f–*t*BuMe$_2$SiOH]$^+$, 462.1 [M+2×H–e]$^+$, 330.0 [e]$^+$.
$\mathrm{C_{35}H_{62}N_2O_{14}Si_2}$ calcd.: C 53.14 H 7.90;
(791.05, 790.37) found: C 53.01 H 7.82.

Allyl 4-O-(3,4,6-tri-O-acetyl-2-deoxy-2-dichloroacetamido-β-D-glucopyranosyl)-2,3-di-O-tert-butyldimethylsilyl-β-D-glucopyranosiduronamide (**8b**)

A solution of **8a** (49 mg, 55 µmol), tributyltin hydride (73 µl, 0.28 mmol), and AIBN (2 mg, 12 µmol) in toluene (1.8 ml) was stirred at 80 °C for 1 h. Solvent evaporation and FC (petroleum ether-ethyl acetate 3:2) furnished **8b** (22 mg, 47%). R_f = 0.24 (petroleum ether–ethyl acetate 1:2). – ^{1}H NMR (^{1}H,^{1}H COSY, 400 MHz, [D$_5$]pyridine, [61]): δ 0.25, 0.27, 0.28, 0.30 (4 s, 4×3 H, SiCH$_3$), 0.98, 1.07 (2 s, 2×9 H, SiC(CH$_3$)$_3$), 2.01, 2.04, 2.09 (3 s, 3×3 H, COCH$_3$), 3.92 (ddd, 1 H, 5^E-H), 3.99 (br. dd, 1 H, 2^F-H), 4.19 (ddt, 1 H, allyl-1-H), 4.35–4.37 (m, 1 H, 3^F-H), 4.38 (dd, 1 H, 6^E-H), 4.49 (dd, 1 H, 6^E-H'), 4.52 (ddt, 1 H, allyl-1-H), 4.65 (ddd, 1 H, 2^E-H), 4.69–4.70 (m, 1 H, 4^F-H), 4.85 (d, 1 H, 5^F-H), 5.04 (d, 1 H, 1^F-H), 5.18 (dq, 1 H, allyl-3-H$_{\mathrm{trans}}$), 5.36 (dq, 1 H, allyl-3-H$_{\mathrm{cis}}$), 5.38 (d, 1 H, 1^E-H), 5.47 (dd, 1 H, 4^E-H), 5.79 (dd, 1 H, 3^E-H), 6.00–6.09 (m, 1 H, allyl-2-H), 6.84 (s, 1 H, CHCl$_2$), 8.07, 8.63 (2×br. s, 2×1 H, CONH), 10.28 (d, 1 H, N$\underline{\mathrm{H}}$COCHCl$_2$), $^3J_{1E,2E}$ = 8.3 Hz, $^3J_{2E,3E}$ = 10.6 Hz, $^3J_{3E,4E}$ = 9.5 Hz, $^3J_{4E,5E}$ = 9.8 Hz, $^3J_{5E,6E}$ = 2.4 Hz, $^3J_{5E,6'E}$ = 4.4 Hz, $^2J_{6E,6'E}$ = 12.1 Hz, $^3J_{1F,2F}$ = 6.7 Hz, $^3J_{2F,3F} \approx$ 1.1 Hz, $^3J_{4F,5F}$ = 2.4 Hz, $^3J_{NH,2E}$ = 8.9 Hz. – ^{13}C NMR (APT, 50.3 MHz, CDCl$_3$, [61]): δ –4.38, –4.13 (–, SiCH$_3$) [60], 18.36, 18.49 (+, Si$\underline{\mathrm{C}}$(CH$_3$)$_3$), 21.13, 21.24 (–, CO$\underline{\mathrm{C}}$H$_3$) [60], 26.29 (–, SiC($\underline{\mathrm{C}}$H$_3$)$_3$) [60], 54.55 (–, C-2^E), 62.87 (+, C-6^E), 67.03 (–, CHCl$_2$), 68.84 (–, C-4^E), 71.36 (+, allyl-C-1), 72.69, 73.18, 76.52, 76.63, 78.79, 80.72 (–, C-3^E, C-5^E, C-2^F, C-3^F, C-4^F, C-5^F), 101.86, 102.68 (–, C-1^E, C-1^F), 117.95 (+, allyl-C-3), 134.42 (–, allyl-C-2), 164.88 (+, $\underline{\mathrm{C}}$OCHCl$_2$), 169.78, 171.09, 171.80 (+, $\underline{\mathrm{C}}$OCH$_3$), 174.01 (+, CONH$_2$).
– $\mathrm{C_{35}H_{60}Cl_2N_2O_{14}Si_2}$ (859.94, 858.30). – FAB-MS: *m/z* 881 [M+Na]$^+$, 859.3 [M+H]$^+$, 857 [M+H–H$_2$]$^+$, 801.3 [f]$^+$, 669.1 [f–*t*BuMe$_2$ SiOH]$^+$.

Removal of the 3^F-*O*-silyl protective group from 11a

To a solution of **11a** (193 mg, 0.24 mmol) in THF (8.5 ml) 220 µl of a TBAF solution (1.1 mol l^{-1} in THF, 0.24 mmol) were added. The mixture was stirred at 20 °C for 25 min, then ethyl acetate (10 ml) was added and the resulting solution was filtered through a small Florisil® column. Solvent evaporation and FC (petroleum ether-CHCl$_3$-ethanol 5:2:1) furnished **11b** (107 mg, 67%) and the corresponding diol (14 mg, 8%).

Allyl 4-O-(2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-2-O-tert-butyldimethylsilyl-β-D-glucopyranosiduronamide (**11b**)

M.p. 189–190 °C (ethyl acetate-petroleum ether). – R_f = 0.31 (petroleum ether–CHCl$_3$-ethanol 5:2:2). – IR (CHCl$_3$): $\tilde{\nu}$ = 1752, 1684 cm^{-1}. – ^{1}H NMR (^{1}H,^{1}H COSY, 400 MHz, homo decoupling, 200 MHz, [D$_5$]pyridine): δ 0.28, 0.33 (2 s, 2×3 H, SiCH$_3$), 1.05 [s, 9 H, SiC(CH$_3$)$_3$], 1.98, 2.05, 2.07 (3 s, 3×3 H, OCOCH$_3$), 2.17 (s, 3 H, NHCOC$\underline{\mathrm{H}}_3$), 3.76 (dd, 1 H, 2^F-H), 3.90 (dd, 1 H, 3^F-H), 4.06 (ddd, 1 H, 5^E-H), 4.15 (ddt, 1 H, allyl-1-H), 4.28–4.46 (m, 5 H, 6^E-H, 6^E-H', 4^F-H, 5^F-H, allyl-1-H'), 4.61 (d, 1 H, 1^F-H), 4.67 (m, 1 H, 2^E-H), 5.17 (dq, 1 H, allyl-3-H$_{\mathrm{trans}}$), 5.32 (dq, 1 H, allyl-3-H$_{\mathrm{cis}}$), 5.34 (d, 1 H, 1^E-H), 5.41 (dd, 1 H, 4^E-H), 5.58 (br. s, 1 H, 3^F-OH, correlation with 3^F-H), 5.72 (dd, 1 H, 3^E-H), 5.97–6.05 (m, 1 H, allyl-2-H), 8.62, 8.81 (2 br. s, 2×1 H, CONH), 8.82 (d, 1 H, NHAc), $^3J_{1E,2E}$ = 7.7 Hz, $^3J_{2E,3E}$ = 10.3 Hz, $^3J_{3E,4E}$ = 9.4 Hz, $^3J_{4E,5E}$ = 9.9 Hz, $^3J_{1F,2F}$ = 7.7 Hz, $^3J_{2F,3F}$ = 8.6 Hz, $^3J_{3F,4F}$ = 8.0 Hz, $^3J_{NH,2E}$ = 8.4 Hz. – ^{13}C NMR (^{13}C,^{1}H COSY, APT, 50.3 MHz, [D$_5$]pyridine): δ –3.90, –3.84 (–, SiCH$_3$), 18.93 (+, Si$\underline{\mathrm{C}}$ (CH$_3$)$_3$), 20.81, 20.89 (–, OCO$\underline{\mathrm{C}}$H$_3$)`[60], 23.59 (–, NHCO $\underline{\mathrm{C}}$H$_3$), 26.46 (–, SiC($\underline{\mathrm{C}}$H$_3$)$_3$), 54.93 (–, C-2^E), 62.93 (+, C-6^E), 69.88 (–, C-4^E), 70.78 (+, allyl-C-1), 72.39 (–, C-5^E), 74.42 (–, C-3^E), 75.21 (–, C-5^F), 75.61 (–, C-2^F), 76.27 (–, C-3^F), 83.29 (–, C-4^F), 102.61 (–, C-1^F), 103.22 (–, C-1^E), 117.46 (+, allyl-C-3), 135.00 (–, allyl-C-2), 170.09, 170.61, 170.78, 171.10 (+, COCH$_3$), 171.92 (+, CONH$_2$). – $\mathrm{C_{29}H_{48}N_2O_{14}Si}$ (676.79, 676.29). – FAB-MS: *m/z* (%): 699.2 [M+Na]$^+$, 677.2 [M+H]$^+$, 619.1 [f]$^+$, 330.0 [e]$^+$.

Allyl 4-O-(2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-β-D-glucopyranosiduronamide (formula not shown)

R_f = 0.12 (petroleum ether–CHCl$_3$-ethanol 5:2:2). – ^{1}H NMR (^{1}H,^{1}H COSY, 400 MHz, [D$_5$]pyridine, [61]): δ 1.97, 1.99, 2.06 (3 s, 3×3 H, OCOCH$_3$), 2.17 (s, 3 H, NHCOC$\underline{\mathrm{H}}_3$), 4.02–4.08 (m, 2 H, 5^E-H, 2^F-H), 4.18–4.25 (m, 2 H, allyl-1-H, 3^F-H), 4.34 (dd, 1 H, 6^E-H), 4.44–4.49 (m, 3 H, 6^E-H', 4^F-H, 5^F-H), 4.50 (ddt, 1 H, allyl-1-H'), 4.68 (ddd, 1 H, 2^E-H), 4.83 (d, 1 H, 1^F-H), 5.11 (dq, 1 H, allyl-3-H$_{\mathrm{trans}}$), 5.39 (dq, 1 H, allyl-3-H$_{\mathrm{cis}}$), 5.41 (d, 1 H, 1^E-H), 5.44 (dd, 1 H, 4^E-H), 5.74 (dd, 1 H, 3^E-H), 5.82 (br. s, 1 H, 3^F-OH), 5.95–6.04 (m, 1 H, allyl-2-H), 7.50 (br. s, 1 H, 2^F-OH, correlation with 2^F-H), 8.60, 8.77 (2 s, 2×1 H, CONH), 8.87 (d, 1 H, NHAc), $^3J_{1E,2E}$ = 8.5 Hz, $^3J_{2E,3E}$ = 10.1 Hz, $^3J_{3E,4E}$ = 9.7 Hz, $^3J_{4E,5E}$ = 10.1 Hz, $^3J_{5E,6E}$ = 2.4 Hz, $^2J_{6E,6'E}$ = 12.1 Hz, $^3J_{1F,2F}$ = 7.7 Hz, $^3J_{NH,2E}$ = 8.4 Hz. – $\mathrm{C_{23}H_{34}N_2O_{14}}$ (562.53, 562.20). – FAB-MS: *m/z* (%): 585.3 [M+Na]$^+$, 563.3 [M+H]$^+$, 330.2 [e]$^+$.

Allyl 4-O-(2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-2-O-tert-butyldimethylsilyl-3-O-trichloroacetylcarbamoyl-β-D-glucopyranosiduronamide (**11c**)

To a solution of **11b** (147 mg, 0.22 mmol) in dichloromethane (5.4 ml) trichloroacetyl isocyanate (40 µl, 0.34 mmol) was added and the reaction mixture was stirred at 20 °C for 45 min. Excess reagent was destroyed with methanol (2 ml). Solvent evaporation and FC (petroleum ether-CHCl$_3$-ethanol 5:2:1) gave **11c** (154 mg, 82%).
R_f = 0.16 (CH$_2$Cl$_2$–MeOH 20:1). – ^{1}H NMR (^{1}H,^{1}H COSY, 400 MHz, [D$_5$]pyridine, [61]): δ 0.14, 0.15 (2 s, 2×3 H, SiCH$_3$), 0.95 [s, 9 H, SiC(CH$_3$)$_3$], 1.95, 2.01, 2.03 (3 s, 3×3 H, OCOCH$_3$), 2.14 (s, 3 H, NHCOC$\underline{\mathrm{H}}_3$), 3.94 (ddd, 1 H, 5^E-H), 4.09 (ddt, 1 H, allyl-1-H), 4.28 (dd, 1 H, 6^E-H), 4.40 (ddt, 1 H, allyl-1-H'), 4.44 (d, 1 H, 5^F-H), 4.55 (ddd, 1 H, 2^E-H), 4.59 (d, 1 H, 1^F-H), 4.67 (br. m, 1 H, 4^F-H), 4.85 (dd, 1 H, 6^E-

H'), 5.16 (dq, 1 H, allyl-3-H_{trans}), 5.27 (dq, 1 H, allyl-3-H_{cis}), 5.38 (t, 1 H, 4^{E}-H), 5.48 (d, 1 H, 1^{E}-H), 5.72 (dd, 1 H, 3^{E}-H), 5.91–6.01 (m, 1 H, allyl-2-H), 8.72 (d, 1 H, NHAc), 8.76, 8.89 (2 s, 2×1 H, CONH), $^{3}J_{1E,2E}$ = 8.4 Hz, $^{3}J_{2E,3E}$ = 10.0 Hz, $^{3}J_{3E,4E}$ = 9.8 Hz, $^{3}J_{4E,5E}$ = 9.8 Hz, $^{3}J_{5E,6E}$ = 2.5 Hz, $^{3}J_{5E,6'E}$ = 4.5 Hz, $^{2}J_{6E,6'E}$ = 12.3 Hz, $^{3}J_{1F,2F}$ = 7.4 Hz, $^{3}J_{4F,5F}$ = 9.6 Hz, $^{3}J_{NH,2E}$ = 8.4 Hz [63]. – ^{13}C NMR (50.3 MHz, [D_5]pyridine, [61]): δ –4.69, –3.64 ($SiCH_3$), 18.54 ($Si\underline{C}(CH_3)_3$), 20.73, 20.92, 21.07 ($OCO\underline{C}H_3$), 23.67 ($NHCO\underline{C}H_3$), 26.23 ($SiC(\underline{C}H_3)_3$), 55.46 (C-2^{E}), 62.70 (br., C-6^{E}), 69.66 (br., C-4^{E}), 70.86 (allyl-C-1), 72.75 (br., C-5^{E}), 73.63 (br., C-2^{F}), 74.28 (C-3^{E}), 75.42 (C-5^{F}), 75.88 (C-3^{F}), 78.30 (br., C-4^{F}), 93.92 (CCl_3), 102.12, 102.64 (C-1^{E}, C-1^{F}), 117.99 (allyl-C-3), 134.49 (allyl-C-2), 151.53 ($OCONH\underline{C}OCCl_3$), 159.85 ($O\underline{C}ONHCOCCl_3$), 170.04, 170.75, 170.90, 171.07 ($\underline{C}OCH_3$), 171.44 ($CONH_2$). – $C_{32}H_{48}Cl_3N_3O_{16}Si$ (865.19, 863.19). – FAB-MS: *m/z* (%): 902 $[M+K]^+$, 886 $[M+Na]^+$, 864 $[M+H]^+$, 806.3 $[f]^+$, 330.2 $[e]^+$.

Allyl 4-O-(2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-2-O-tert-butyldimethylsilyl-3-O-carbamoyl-β-D-glucopyranosiduronamide (**11d**)

To a solution of **11b** (221 mg, 0.33 mmol) in dichloromethane (8.0 ml) trichloroacetyl isocyanate (60 μl, 0.51 mmol) was added and the reaction mixture was stirred at 20 °C for 50 min. Excess reagent was destroyed with methanol (2 ml). Solvents were evaporated and the sample was dried at 10 Pa. The resulting crude **11c** was dissolved in methanol (15 ml), zinc dust (250 mg) was added and the mixture was stirred at 20 °C for 5 h. After filtration and washing the residue with methanol the organic solutions were combined. Solvent evaporation and FC (CH_2Cl_2-MeOH 20:1 → 10:1) provided **11d** (216 mg, 91%).

M.p. 132–134 °C (dichloromethane-petroleum ether). – R_f = 0.11 (CH_2Cl_2-MeOH 20:1). – IR ($CHCl_3$): $\tilde{\nu}$ = 1749, 1696, 1685, 1570, 1542 cm^{-1}. – ^{1}H NMR (^{1}H,^{1}H COSY, 400 MHz, [D_5]pyridine): δ 0.23, 0.27 (2 s, 2×3 H, $SiCH_3$), 1.02 [s, 9 H, $SiC(CH_3)_3$], 1.96, 1.99, 2.02 (3 s, 3×3 H, $OCOCH_3$), 2.14 (s, 3 H, $NHCOC\underline{H}_3$), 3.87–3.94 (m, 2 H, 5^{E}-H, 2^{F}-H), 4.12 (ddt, 1 H, allyl-1-H), 4.37–4.40 (m, 2 H, 5^{F}-H, 6^{E}-H), 4.42 (ddt, 1 H, allyl-1-H'), 4.48 (ddd, 1 H, 2^{E}-H), 4.57 (dd, 1 H, 4^{F}-H), 4.60 (d, 1 H, 1^{F}-H), 4.69 (dd, 1 H, 6^{E}-H'), 5.17 (dq, 1 H, allyl-3-H_{trans}), 5.30 (dq, 1 H, allyl-3-H_{cis}), 5.39 (dd, 1 H, 4^{E}-H), 5.43 (d, 1 H, 1^{E}-H), 5.50 (dd, 1 H, 3^{F}-H), 5.74 (dd, 1 H, 3^{E}-H), 5.95–6.04 (m, 1 H, allyl-2-H), 8.64 (d, 1 H, NHAc), 8.65, 8.79 (2 s, 2×1 H, CONH), $^{3}J_{1E,2E}$ = 8.5 Hz, $^{3}J_{2E,3E}$ = 10.1 Hz, $^{3}J_{3E,4E}$ = 9.6 Hz, $^{3}J_{4E,5E}$ = 9.9 Hz, $^{3}J_{5E,6E}$ = 2.4 Hz, $^{3}J_{5E,6'E}$ = 4.6 Hz, $^{2}J_{6E,6'E}$ = 12.1 Hz, $^{3}J_{1F,2F}$ = 7.7 Hz, $^{3}J_{2F,3F}$ = 9.2 Hz, $^{3}J_{3F,4F}$ = 9.1 Hz, $^{3}J_{4F,5F}$ = 9.4 Hz, $^{3}J_{NH,2E}$ = 8.4 Hz. – ^{13}C NMR (75.5 MHz, ^{13}C,^{1}H COSY, APT, 50.3 MHz, [D_5]pyridine): δ –4.85, –4.10 (–, $SiCH_3$), 18.25 (+, $Si\underline{C}(CH_3)_3$), 20.30, 20.47, 20.52 (–, $OCO\underline{C}H_3$), 23.25 (–, $NHCO\underline{C}H_3$), 25.88 (–, $SiC(\underline{C}H_3)_3$), 55.24 (–, C-2^{E}), 62.44 (+, C-6^{E}), 69.44 (–, C-4^{E}), 70.45 (+, allyl-C-1), 72.08 (–, C-5^{E}), 73.71 (–, C-2^{F}), 74.24 (–, C-3^{E}), 75.27 (–, C-5^{F}), 76.12 (–, C-3^{F}), 78.53 (–, C-4^{F}), 101.57 (–, C-1^{E}), 102.63 (–, C-1^{F}), 117.34 (+, allyl-C-3), 134.34 (–, allyl-C-2), 157.06 (+, $OCONH_2$), 169.56, 170.36, 170.44, 170.60 (+, $\underline{C}OCH_3$), 171.48 (+, $CONH_2$). – FAB-MS: *m/z* 742.3 $[M+Na]^+$, 720.4 $[M+H]^+$, 662.3 $[f]^+$, 330.1 $[e]^+$.

$C_{30}H_{49}N_3O_{15}Si$	calcd.:	C 50.06	H 6.86;
(719.82, 719.29)	found:	C 50.04	H 6.96.

4-O-(2-Acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-2-O-tert-butyldimethylsilyl-3-O-carbamoyl-D-glucopyranuronamide (11e) and *tert-butyldimethylsilyl-4-O-(2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-3-O-carbamoyl-α-D-glucopyranosiduronamide* (**12**) by deallylation of **11d**

Under careful exclusion of oxygen in a light-protected vial to **11d** (152.0 mg, 211 μmol) and commercial tetrakis(triphenylphosphine)palladium(0) (260.0 mg, 225 μmol) degassed acetic acid (7.0 ml) was added. The suspension was stirred at 20 °C for 1.5 h. Subsequently ethyl acetate (3.5 ml) was added. Solvent evaporation (codistillation with toluene) and FC ($CHCl_3$-MeOH 20:1 → 5:1) furnished **11e** (131.6 mg, 92 %).

R_f = 0.29 ($CHCl_3$–MeOH 5:1). IR ($CHCl_3$): $\tilde{\nu}$ = 3519–3304, 1745, 1689, 1367 cm^{-1}. – ^{1}H NMR (^{1}H,^{1}H COSY, 400 MHz, [D_5]pyridine, in the course of the NMR experiments partly rearrangement of **11e** into **12** occurred, final composition: 1:1:0.5 mixture of *α*-**11e** – *β*-**11e**–**12** as calculated from the OH and *tert*-butyl signal integrals) [64]: δ 0.15, 0.16, 0.16, 0.24, 0.36, 0.38 (6×s, $SiCH_3$), 0.87, 0.96, 1.08 (3 s, $SiC(CH_3)_3$), 1.95–2.03 ($OCOCH_3$ signals), 2.10, 2.126, 2.131 (3×s, $NHCOC\underline{H}_3$), 3.89–4.02 [m, 2^{F}-H (*β*-**11e**), 3×5^{E}-H], 4.12–4.15 (m, 2×2^{F}-H, *α*-**11e** and **12**), 4.38 (dd, 6^{E}-H, $^{3}J_{5E,6E}$ = 2.1 Hz, $2J_{6E,6'E}$ = 12.2 Hz), 4.45 (d, 5^{F}-H, $^{3}J_{4F,5F}$ = 9.8 Hz, *β*-**11e**), 4.40–4.47 (m, 2×2^{E}-H and 2×6^{E}-H), 4.49 (ddd, 2^{E}-H), 4.60 (dd, 4^{F}-H, *β*-**11e**), 4.65 (dd, 2×4^{F}-H, *α*-**11e** and **12**), 4.70 (dd, 3×6^{E}-H', $^{3}J_{5E,6'E}$ = 4.6 Hz, $^{2}J_{6E,6'E}$ = 12.2 Hz), 4.90 (d, 5^{F}-H, **12**), 5.09 (dd, 1^{F}-H, $^{3}J_{1F,2F}$ = 6.7 Hz, *β*-**11e**), 5.15 (d, 5^{F}-H, $^{3}J_{4F,5F}$ = 9.8 Hz, *α*-**11e**), 5.39 (dd, 4^{E}-H), 5.43 (d, 1^{E}-H, $^{3}J_{1E,2E}$ = 8.6 Hz), 5.51 (d, 1^{E}-H, $^{3}J_{1E,2E}$ = 8.4 Hz), 5.52 (d, 1^{E}-H, $^{3}J_{1E,2E}$ = 8.6 Hz, **12**), 5.55 (d, 1^{F}-H, $^{3}J_{1F,2F}$ = 3.2 Hz, **12**), 5.57 (dd, 3^{F}-H, $^{3}J_{2F,3F}$ = 8.9 Hz, $^{3}J_{3F,4F}$ = 9.3 Hz, *β*-**11e**), 5.66 (br. d, 1^{F}-H, *α*-**11e**), 5.73 (dd, 3^{E}-H, $^{3}J_{2E,3E}$ = 10.2 Hz, $^{3}J_{3E,4E}$ = 9.5 Hz), 5.77 (dd, 3^{E}-H, $^{3}J_{2E,3E}$ = 10.3 Hz, $^{3}J_{3E,4E}$ = 9.4 Hz, **12**), 5.78 (dd, 3^{E}-H, $^{3}J_{2E,3E}$ = 10.3 Hz, $^{3}J_{3E,4E}$ = 9.4 Hz), 5.86 (dd, 3^{F}-H, *J* = 9.2 Hz, *J* = 9.7 Hz, **12**), 6.08 (t, 3^{F}-H, $^{3}J_{2F,3F}$ = $^{3}J_{3F,4F}$ = 9.4 Hz, *α*-**11e**), 6.50 (d, 2^{F}-OH, $^{3}J_{OH,2F}$ = 6.4 Hz, **12**), 8.48, 8.57 (2 br. s, CONH), 8.64 (d, NHAc, $^{3}J_{NH,2E}$ = 7.9 Hz), 8.68 (br. s, CONH), 8.70 (d, NHAc, $^{3}J_{NH,2E}$ = 8.6 Hz), 8.82 (d, NHAc, $^{3}J_{NH,2E}$ = 8.1 Hz), 9.03 (br. s, 1^{F}-OH, *α*-**11e**), 9.50 (d, 1^{F}-OH, $^{3}J_{OH,1F}$ = 5.7 Hz, *β*-**11e**). – ^{13}C NMR (^{13}C,^{1}H COSY, APT, 50.3 MHz, [D_5]pyridine) [64]: δ –4.41, –3.42 (–, $SiCH_3$), 18.59, 18.63, 18.88 [+, $Si\underline{C}(CH_3)_3$], 20.76, 20.98 (–, $OCO\underline{C}H_3$), 23.67, 23.71 (–, $NHCO\underline{C}H_3$), 26.07, 26.18, 26.45 [–, $SiC(\underline{C}H_3)_3$], 55.67, 55.90 (–, C-2^{E}), 62.90 (+, C-6^{E}), 69.90 (–, C-4^{E}), 71.41 (–, C-5^{F}, *α*-**11e** and **12**), 72.48, 72.57 (–, C-5^{E}), 73.38 (–, C-2^{F}, *α*-**11e** and **12**), 74.04 (–, C-3^{F}, *α*-**11e** and **12**), 74.70 (–, C-3^{E}), 75.78 (–, C-2^{F}, C-5^{F}, *β*-**11e**, identified by ^{13}C,^{1}H COSY), 76.73 (–, C-3^{F}, *β*-**11e**), 79.24 (–, C-4^{F}, *β*-**11e**), 79.60 (–, C-4^{F}, **12**), 79.87 (–, C-4^{F}, *α*-**11e**), 94.10 (–, C-1^{F}, *α*-**11e** and **12**), 98.43 (–, C-1^{F}, *β*-**11e**), 101.92, 102.00 (–, C-1^{E}), 157.76, 158.68 (+, $OCONH_2$), 170.03, 170.82, 170.95, 171.01, 171.07 (+, $\underline{C}OCH_3$) , 172.44, 172.85, 173.30 (+, $CONH_2$). – $C_{27}H_{45}N_3O_{15}Si$ (679.75, 679.26). – FAB-MS: *m/z* (%): 718.0 $[M+K]^+$, 702.0 $[M+Na]^+$, 680.0 $[M+H]^+$, 622.0 $[M+H–tBuH]^+$, 351.0 $[M+2×H–e]^+$, 330.0 $[e]^+$.

Phosphorylation of 11e/12

To a suspension of 1*H*-1,2,4-triazol (56.6 mg, 819 µmol) in 1:4 pyridine-dichloromethane (1.2 ml) at 0 °C 2,2,2-trichloro-1,1-dimethylethyl dichlorophosphite (39.5 µl, 0.20 mmol) was added. The mixture was stirred at 0 °C for 35 min. Then a solution of the **11e/12** mixture (111.1 mg, 163 µmol) in 1:4 pyridine-dichloromethane (1.5 ml) was added dropwise and the mixture was stirred at 0 °C for 70 min. Within 1.5 h a solution of **13** (224.2 mg, 476 µmol) in 1:4 pyridine–dichloromethane (2.0 ml) was added in four portions. Stirring at 0 °C was continued for 3 h. At 0 °C bis(trimethylsilyl) peroxide (69 µl, 0.33 mmol) was added, and the mixture was stirred at 20 °C for 17.5 h. Then the solvents were removed by evaporation at 25 °C and drying at 10 Pa. FC ($CHCl_3$–MeOH 20:1) followed by FC ($CHCl_3$-MeOH 30:1) of the fractions containing both **14a** and **15** furnished pure **14a** (50.1 mg, 23%) and **15** (58.3 mg, 26%).

4-O-(2-Acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-2-O-tert-butyldimethylsilyl-3-O-carbamoyl-1-O-{[(R)-2-methoxycarbonyl-2-(3,8,8,11,14,18-hexamethylnonadecyloxy)-ethoxy]-(2,2,2-trichloro-1,1-dimethylethyloxy)-phosphoryl}-β-D-glucopyranuronamide (**14a**)*, mixture of diastereomers* (isomeric at P)

R_f = 0.24 ($CHCl_3$–MeOH 15:1). – ^{1}H NMR (^{1}H,^{1}H COSY, 400 MHz, [D_5]pyridine): δ 0.25, 0.27, 0.27, 0.29 (4 s, $SiCH_3$), 0.80–1.88 (signals from unit I), 1.03, 1.05 (2 s, $SiC(CH_3)_3$), 1.96–2.13 ($COCH_3$- and $C(CH_3)_2CCl_3$ signals), 3.777, 3.779, 3.785 (2 s, $COOCH_3$), 3.64–4.02 (m, 2×5^E-H, 1^I-H, 1^I-H'), 4.14–4.25 (m, 2×2^F-H), 4.38–4.52 (m, 2×2^E-H, 2×6^E-H, 2^H-H), 4.61–4.73 (m, 2×6^E-H', 4^F-H, 3^H-H, 3^H-H'), 4.75 (dd, 4^F-H, $^3J_{3F,4F}$ = 9.6 Hz), 4.97 (d, 5^F-H, $^3J_{4F,5F}$ = 10.1 Hz), 5.03 (d, 5^F-H, $^3J_{4F,5F}$ = 9.7 Hz), 5.41 (dd, 4^E-H, $^3J_{3E,4E}$ = 9.4 Hz, $^3J_{4E,5E}$ = 9.9 Hz), 5.42 (dd, 4^E-H, $^3J_{3E,4E}$ = 9.4 Hz, $^3J_{4E,5E}$ = 9.9 Hz), 5.47 (dd, 1^E-H, $^3J_{1E,2E}$ = 8.6 Hz, $^4J_{1E,3E}$ = 1.9 Hz), 5.60 (d, 1^E-H, $^3J_{1E,2E}$ = 8.6 Hz), 5.73 (ddd, 3^E-H, $^3J_{2E,3E}$ = 10.3 Hz), 5.75–5.86 (m, 3^E-H, 2×3^F-H), 6.10 (dd, 1^F-H, $^3J_{1F,2F}$ = 3.4 Hz, $^3J_{1F,P}$ = 4.3 Hz), 6.17 (dd, 1^F-H, $^3J_{1F,2F}$ = 3.5 Hz, $^3J_{1F,P}$ = 5.6 Hz), 8.32, 8.50 (2×br. s, CONH), 8.60 (d, NHAc, $^3J_{NH,2E}$ = 8.2 Hz), 8.64 (d, NHAc, $^3J_{NH,2E}$ = 7.5 Hz), 8.69 (br. s, CONH). – ^{13}C NMR (^{13}C,^{1}H COSY, 50.3 MHz, [D_5]pyridine): δ –5.12, –4.80 ($SiCH_3$), 18.08, 18.12 ($Si\underline{C}(CH_3)_3$), 19.40–42.13 (CH-, CH_2- and CH_3 signals), 52.04, 52.10 ($COO\underline{C}H_3$), 55.38, 55.41 (C-2^E), 62.42 (C-6^E), 68.56 (br., C-3^H), 69.30, 69.39 (C-4^E), 69.79, 69.74 (C-1^I), 71.33 (br., C-2^F), 72.13, 72.31 (C-5^E), 72.91, 73.06 (C-3^E), 74.06 (C-5^F), 74.41 (C-3^F), 78.07, 78.33 (C-4^F, C-2^H), 90.56 [$\underline{C}(CH_3)_2CCl_3$], 97.59, 98.16 (C-$1^F$), 101.69, 102.07 (C-$1^E$), 106.08 ($CCl_3$), 156.93 ($OCONH_2$), 169.72–171.59 (C=O). – ^{31}P NMR (81.0 MHz, [D_5]pyridine): δ –5.4, –6.8 (integral ratio 1.2:1). – $C_{60}H_{107}Cl_3N_3O_{21}PSi$ (1371.93, 1369.60), FAB-MS: *m/z* (%): 1392.7 $[M+Na]^+$, 684.3 $[f+Na–H]^+$, 662.3 $[f]^+$, 330.1 $[e]^+$, 272.1, 254.1.

tert-Butyldimethylsilyl-4-O-(2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-3-O-carbamoyl-2-O-{[(R)-2-methoxycarbonyl-2-(3,8,8,11,14,18-hexamethylnonadecyloxy)-ethoxy]-(2,2,2-trichloro-1,1-dimethylethyloxy)-phosphoryl}-α-D-glucopyranosiduronamide (**15**), mixture of diastereomers (isomeric at P)

R_f = 0.18 ($CHCl_3$-MeOH 15:1). – ^{1}H NMR (^{1}H,^{1}H COSY, 400 MHz, [D_5]pyridine): δ 0.306, 0.312, 0.34 (3×s, $SiCH_3$) [60], 0.82–1.90 [$SiC(CH_3)_3$ and signals from unit I], 1.95–2.24 ($COCH_3$ and $C(CH_3)_2CCl_3$ signals), 3.64–3.87 (m, 1^I-H, 1^I-H'), 3.71 (br. s, $COOCH_3$), 3.90 (m, 5^E-H, **15a**), 4.08–4.14 (m, 2^F-H, $^3J_{2F,3F}$ = 7.0 Hz, **15a**, 5^E-H, $^3J_{5E,6E}$ = 2.5 Hz, $^3J_{5E,6'E}$ = 4.5 Hz, **15b**), 4.36–4.45 (m, 2^E-H, 6^E-H, **15a**, 6^E-H, **15b**), 4.51 (br. dd, 2^H-H, $^3J_{2H,3H}$ = 5.5 Hz, $^3J_{2H,3'H}$ = 9.5 Hz), 4.58 (dd, 2^H-H, $^3J_{2H,3H}$ = 5.1 Hz, $^3J_{2H,3'H}$ = 5.3 Hz), 4.62 (dd, 6^E-H', $^2J_{6E,6'E}$ = 12.4 Hz, **15b**), 4.66–4.87 (m, 6^E-H', 4^F-H, 5^F-H, 3^H-H, 3^H-H', **15a**, 2^E-H, 2^F-H, 3^H-H, 3^H-H', **15b**), 5.13 (m, 4^F-H, $w_{1/2}$ ≈ 7.5 Hz, **15b**), 5.37 (dd, 4^E-H, $^3J_{3E,4E}$ = 9.6 Hz, $^3J_{4E,5E}$ = 9.9 Hz, **15a**), 5.47 (2×d, 1^E-H, $^3J_{1E,2E}$ = 8.4 Hz and $^3J_{1E,2E}$ = 8.5 Hz, **15a**), 5.52 (dd, 4^E-H, $^3J_{3E,4E}$ = 9.6 Hz, $^3J_{4E,5E}$ = 9.9 Hz, **15b**), 5.56 (br. dd, 3^F-H, $^3J_{3F,4F}$ = 7.4 Hz, **15a**), 5.71–5.74 (m, 1^F-H, **15a**, 5^F-H, **15b**), 5.78 (dd, 3^E-H, $^3J_{3E,4E}$ = 9.4 Hz, **15a**), 5.83 (dd, 3^E-H, $^3J_{2E,3E}$ = 10.1 Hz, $^3J_{3E,4E}$ = 9.6 Hz, **15b**), 5.84 (d, 1^E-H, $^3J_{1E,2E}$ = 8.2 Hz, **15b**), 5.91 (br. dd, 3^F-H, ^3J ≈ 2.0 and 3.5 Hz, **15b**), 7.85 (d, 1^F-H, $^3J_{1F,2F}$ = 2.6 Hz, **15b**), 8.02 (br. s, CONH, **15b**), 8.65 (br. s, CONH, **15a**), 8.76–8.78 (m, CONH, NHAc, **15a**), 9.85 (d, NHAc, $^3J_{NH,2E}$ = 9.1 Hz, **15b**), 10.10 (br. s, CONH, **15b**). – ^{13}C NMR (APT, 100.6 MHz, [D_5]pyridine) of **15a** [65]: δ –4.16, –3.55 (–, $SiCH_3$), 18.67 (+, $Si\underline{C}(CH_3)_3$), 20.06–42.72 (CH-, CH_2- and CH_3 signals), 52.59 (–, $COO\underline{C}H_3$), 55.92 (–, C-2^E), 62.42 (+, C-6^E), 68.94, 69.10 (+, C-3^H), 70.01 (–, C-4^E), 70.23 (+, C-1^I), 72.69, 74.12, 74.50, 76.11, 76.39 (–, C-3^E, C-5^E, C-2^F, C-3^F, C-5^F), 78.56 (C-4^F), 78.81 (br., C-2^H), 91.30 [+, $\underline{C}(CH_3)_2CCl_3$], 99.86, 100.14 (–, C-$1^F$), 102.20 (–, C-$1^E$), 106.89 (br., CCl_3), 157.48 (+, $OCONH_2$), 170.23, 171.00, 171.08, 171.25 (+, C=O) [60]. – ^{13}C NMR (^{13}C,^{1}H COSY, 50.3 MHz, [D_5]pyridine) of **15b** [65]: δ 18.67 ($Si\underline{C}(CH_3)_3$), 19.65–42.43 (CH, CH_2 and CH_3 signals), 51.92 ($COO\underline{C}H_3$), 54.70 (C-2^E), 62.72 (C-6^E), 68.86 (C-2^F), 69.61 (C-4^E, C-1^I), 71.49 (C-3^F), 72.25 (C-5^E), 74.90 (C-3^E), 78.31 (C-5^F), 78.62 (C-4^F), 86.21 (d, $\underline{C}(CH_3)_2CCl_3$, $^3J_{C,P}$ = 5 Hz), 90.69 (C-1^F), 104.38 (C-1^E), 109.56 (br., CCl_3), 156.37 ($OCONH_2$), 170.09, 170.63, 170.74, 170.86, 171.03, 171.90 (C=O). – ^{31}P NMR (81.0 MHz, [D_5]pyridine) of **15a**: δ –5.9, –6.1. – ^{31}P NMR (161.9 MHz, [D_5]pyridine), mixture of **15a** and **15b**: δ –6.1, –9.2, –9.7. – $C_{60}H_{107}Cl_3N_3O_{21}PSi$ (1371.93, 1369.60). – FAB-MS (linked scan, B/E mode): *m/z* (%): 1408.6 $[M+K]^+$, 1392.6 $[M+Na]^+$, 684.2 $[M+Na–GHI–H]^+$, 662 $[M+Na–GHI]^+$, 601.7, 330.1 $[e]^+$, 272.1, 254.1.

4-O-(2-Acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-2-O-tert-butyldimethylsilyl-3-O-carbamoyl-1-O-{[(R)-2-methoxycarbonyl-2-(3,8,8,11,14,18-hexamethylnonadecyloxy)-ethoxy]-hydroxyphosphoryl}-β-D-glucopyranuronamide (**14b**)

In a light-protected vial to **14a** (49.5 mg, 36 µmol) and zinc-copper couple (48.4 mg), 2,4-pentanedione (60 µl, 0.58 mmol) and pyridine (2.7 ml) were added and the suspension was stirred at 20 °C for 1 h. After filtration the residue was repeatedly washed with ethanol. From the combined filtrates solvents were removed, the residue dried at 10 Pa, then taken up in 1:8 ethanol–water (15 ml). Dowex 50 W X2 (H^+, 2.0 g) was added and the mixture stirred for 30 min. After filtration the resin was carefully washed with 1:8 ethanol-water. The combined filtrates were concentrated at a rotavapor, the remaining aqueous solution was lyophilized. Repeated FC (silica gel 63–

100 µm; first toluene–$CHCl_3$–MeOH 1:1:0.3 → 1:1:0.5, then $CHCl_3$–MeOH-H_2O 20:10:0.5) furnished **14b** (26.9 mg, 61%) in addition to **14c** (3.6 mg, 8%).

R_f = 0.63 ($CHCl_3$–MeOH-H_2O 20:10:0.5). – ^1H NMR (^1H,^1H COSY, 400 MHz, CD_3OD): δ 0.15, 0.17 (2 s, $SiCH_3$), 0.86–1.63 [$SiC(CH_3)_3$ and signals from unit I], 1.92, 1.97, 2.01 (3 s, 3×3 H, $OCOCH_3$), 2.10 (s, 3 H, $NHCOC\underline{H}_3$), 3.52–3.71 (m, 4 H, 1^I-H, 1^I-H'), 3.74–3.82 (m, 3 H, 2^E-H, 5^E-H, 2^F-H), 3.76 (s, 3 H, $COOCH_3$), 3.91 (dd, 1 H, 4^F-H), 4.07–4.20 (m, 3 H, 2^H-H, 3^H-H, 3^H-H'), 4.12 (dd, 1 H, 6^E-H), 4.45 (d, 1 H, 5^F-H), 4.48 (dd, 1 H, 6^E-H'), 4.78 (d, 1 H, 1^E-H), 4.95 (dd, 1 H, 4^E-H), 5.15 (dd, 1 H, 3^F-H), 5.19 (dd, 1 H, 3^E-H), 5.53 (br. dd, 1 H, 1^F-H), $^3J_{1E,2E}$ = 8.7 Hz, $^3J_{2E,3E}$ = 10.3 Hz, $^3J_{3E,4E}$ = 9.4 Hz, $^3J_{4E,5E}$ = 9.9 Hz, $^3J_{5E,6E}$ = 2.6 Hz, $^3J_{5E,6'E}$ = 5.1 Hz, $^2J_{6E,6'E}$ = 12.3 Hz, $^3J_{1F,2F}$ = 3.5 Hz, $^3J_{2F,3F}$ = 8.7 Hz, $^3J_{3F,4F}$ = 9.4 Hz, $^3J_{4F,5F}$ = 9.6 Hz, $^3J_{1F,P}$ = 6.1 Hz. – ^{13}C NMR (50.3 MHz, CD_3OD): δ –5.81, –5.26 ($SiCH_3$), 17.98 ($Si\underline{C}(CH_3)_3$), 18.92–42.01 (CH-, CH_2- and CH_3 signals), 51.58 ($COO\underline{C}H_3$), 54.61 (C-2^E), 62.27 (C-6^E), 65.97 (br. d, C-3^H, $^2J_{3H,P}$ = 5 Hz), 69.23, 69.49 (C-4^E, C-1^I), 70.92, 72.05, 73.45, 73.57 (C-3^E, C-5^E, C-3^F, C-5^F), 71.72 (d, C-2^F, $^3J_{2F,P}$ = 10 Hz), 77.92 (C-4^F), 79.05 (d, C-2^H, $^3J_{2H,P}$ = 9 Hz), 95.61 (d, C-1^F, $^2J_{1F,P}$ = 6 Hz), 101.11 (C-1^E), 158.12 ($OCONH_2$), 170.48, 171.02, 171.79, 171.87, 172.49, 172.58 (C=O). – ^{31}P NMR (81.0 MHz, CD_3OD): δ –1.2. – $C_{56}H_{102}N_3O_{21}PSi$ (1212.49, 1211.65). – FAB-MS: *m/z* (%): 1256.3 $[M+2\times Na-H]^+$, 1234.3 $[M+Na]^+$, 662 $[f]^+$.

4-O-(2-Acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-3-O-carbamoyl-1-O-{[(R)-2-methoxycarbonyl-2-(3,8,8,11,14,18-hexamethylnonadecyloxy)-ethoxy]-hydroxyphosphoryl}-β-D-glucopyranuronamide (**14c**)

14b (23.0 mg, 19 µmol) was dissolved in 3:1:1 acetic acid-THF-water (5.0 ml) and the mixture was stirred at 20 °C for 44 h, then water was added. The solution was concentrated at a rotavapor, the remaining solution was freeze-dried. FC (silica gel 63–100 µm; $CHCl_3$–MeOH–H_2O 20:10:0.5) furnished **14c** (16.0 mg, 79%). 4.5 mg of **14b** were recovered.

R_f = 0.31 ($CHCl_3$–MeOH-H_2O 20:10:0.5). – ^1H NMR (300 MHz, CD_3OD): δ 0.83–1.70 (signals from unit I), 1.91, 1.95, 1.98 (3 s, 3×3 H, $OCOCH_3$), 2.07 (s, 3 H, $NHCOC\underline{H}_3$), 3.49–3.81 (m, 4 H, 2^E-H, 5^E-H, 2^F-H), 3.74 (s, 3 H, $COOCH_3$), 3.92 (dd, 1 H, 4^F-H), 4.07–4.18 (m, 3 H, 6^E-H, 2^H-H, 3^H-H, 3^H-H'), 4.35 (d, 1 H, 5^F-H), 4.42 (dd, 1 H, 6^E-H'), 4.76 (d, 1 H, 1^E-H), 4.96 (dd, 1 H, 4^E-H), 5.03 (dd, 1 H, 3^F-H), 5.16 (dd, 1 H, 3^E-H), 5.53 (br. dd, 1 H, 1^F-H), $^3J_{1E,2E}$ = 8.8 Hz, $^3J_{2E,3E}$ = 10.4 Hz, $^3J_{3E,4E}$ = 9.6 Hz, $^3J_{4E,5E}$ = 9.9 Hz, $^3J_{5E,6'E}$ = 4.1 Hz, $^2J_{6E,6'E}$ = 12.1 Hz, $^3J_{1F,2F}$ = 4.1 Hz, $^3J_{2F,3F}$ = 8.8 Hz, $^3J_{3F,4F}$ = 9.3 Hz, $^3J_{4F,5F}$ = 9.9 Hz, $^3J_{1F,P}$ = 7.1 Hz. – ^{13}C NMR (75.5 MHz, CD_3OD, [61]): δ 20.02–43.05 (CH-, CH_2- and CH_3 signals), 52.69 ($COO\underline{C}H_3$), 55.65 (C-2^E), 63.19 (C-6^E), 67.00 (br. d, C-3^H, $^2J_{3H,P}$ = 5 Hz), 70.08, 70.68 (C-4^E, C-1^I), 71.76 (d, C-2^F, $^3J_{2F,P}$ = 9 Hz), 72.19, 73.01, 74.58, 74.94 (C-3^E, C-5^E, C-3^F, C-5^F), 78.66 (C-4^F), 79.87 (d, C-2^H, $^3J_{2H,P}$ = 9 Hz), 96.69 (d, C-1^F, $^2J_{1F,P}$ = 6 Hz), 102.08 (C-1^E), 159.44 ($OCONH_2$), 171.30, 171.89, 172.63, 172.72, 173.00, 173.47 (C=O). – ^{31}P NMR (121.5 MHz, CD_3OD): δ –1.1. – $C_{50}H_{88}N_3O_{21}P$ (1098.23, 1097.56). – FAB-MS: *m/z* (%): 1142.4 $[M+2\,Na-H]^+$, 1120.5 $[M+Na]^+$, 595.3 $[M+2\,Na-f]^+$, 570.1 $[f+Na-H]^+$.

Hydrolysis of 14c

14c (17.0 mg, 15 µmol) was dissolved in 2:1 methanol-water (2.2 ml). The solution was degassed (stream of argon, sonication) and cooled to 0 °C. 1 mol l^{-1} aqueous lithium hydroxide (degassed, 100 µl, 100 µmol) was added and the reaction mixture was stirred at 0 °C for 30 min and then at 20 °C for 45 min. The reaction was stopped by addition of Dowex 50 W X2 (H^+ form, 0.5 g). Stirring was continued for 30 min. After filtration the resin was washed with 2:1 methanol–water, then with water. The combined filtrates were concentrated at a rotavapor, the remaining solution was lyophilized. FC (silica gel 63–100 µm; $CHCl_3$–MeOH–H_2O 18:11:1) furnished **2** (2.2 mg, 13%) and methyl ester **14d** (8.6 mg, 60%).

Hydrolysis of 14d

To a degassed solution (*vide supra*) of **14d** (15.3 mg, 16 µmol) in 2:1 methanol–water (2.0 ml) at 0 °C a degassed aqueous lithium hydroxide solution (1 mol l^{-1}, 16 µl, 16 µmol) was added. The mixture was stirred for 30 min at 0 °C, then at 20 °C. After 2 h, 3h, 5 h and 6 h further 16 µl portions of the lithium hydroxide solution were added (altogether 64 µmol). Quenching of the reaction and work-up were performed as described above. FC (silica gel 63–100 µm; $CHCl_3$–MeOH-H_2O 18:11:1 → 18:11:2.7) provided **2** (7.0 mg, 44%). 6.6 mg of **14d** were recovered.

4-O-(2-Acetamido-2-deoxy-β-D-glucopyranosyl)-3-O-carbamoyl-1-O-{[(R)-2-methoxycarbonyl-2-(3,8,8,11,14,18-hexamethylnonadecyloxy)-ethoxy]-hydroxyphosphoryl}-β-D-glucopyranuronamide (**14d**)

R_f = 0.27 ($CHCl_3$–MeOH–H_2O 18:11:2.7). – ^1H NMR (400 MHz, 18 mmol l^{-1} in $CDCl_3$–CD_3OD–D_2O 18:13:2.7, TMS): δ 0.81–1.70 (signals from unit I), 2.00 (s, 3 H, $NHCOC\underline{H}_3$), 3.30–3.46 (m, 3 H, 5^E-H, 2^F-H, 4^F-H), 3.52–3.73 (m, 5 H, 2^E-H, 6^E-H, 6^E-H', 1^I-H, 1^I-H'), 3.77 (s, 3 H, $COOCH_3$), 3.89–3.96 (m, 2 H, 4^E-H, 5^F-H), 4.11–4.14 (m, 3 H, 2^H-H, 3^H-H, 3^H-H'), 4.33 (dd, 1 H, 3^E-H, partly hidden by a solvent signal), 4.51 (d, 1 H, 1^E-H), 4.98 (dd, 1 H, 3^F-H), 5.50 (br. dd, 1 H, 1^F-H), $^3J_{1E,2E}$ = 8.4 Hz, $^3J_{2E,3E}$ = 10.1 Hz, $^3J_{1F,2F}$ = 3.4 Hz, $^3J_{2F,3F}$ = 9.2 Hz, $^3J_{3F,4F}$ = 9.7 Hz, $^3J_{1F,P}$ = 6.5 Hz. – ^{13}C NMR (100.6 MHz, ^{13}C,^1H COSY, 18 mmol l^{-1} in $CDCl_3$–CD_3OD–D_2O 18:13:2.7, TMS): δ 19.65–42.44 (CH, CH_2 and CH_3 signals), 52.62 ($COO\underline{C}H_3$), 56.59 (C-2^E), 61.39 (C-6^E), 66.08 (br., C-3^H), 70.31, 70.42, 70.63, 71.17 (C-3^E, C-4^E, C-2^F, C-1^I), 74.13 (C-3^F), 75.30 (C-4^F), 76.50 (C-5^E), 77.53 (C-5^F, partly hidden by a solvent signal, identified by ^{13}C,^1H COSY), 79.04 (br., C-2^H), 95.39 (br., C-1^F), 101.73 (C-1^E), 159.22 ($OCONH_2$), 172.24, 172.36, 174.16 (C=O). – ^{31}P NMR (161.9 MHz, 18 mmol l^{-1} in $CDCl_3$-CD_3OD-D_2O 18:13:2.7, TMS): δ –2.8. $C_{44}H_{82}N_3O_{18}P$ (972.12, 971.53). – FAB-MS: *m/z* 1016.5 $[M+2\times Na-H]^+$, 994.5 $[M+Na]^+$, 595.3 $[M+2\times Na-f]^+$, 573.4 $[M+H+Na-f]^+$, 444.1 $[f+Na-H]^+$, 204.1 $[e]^+$.

4-O-(2-Acetamido-2-deoxy-β-D-glucopyranosyl)-3-O-carbamoyl-1-O-{[(R)-2-carboxy-2-(3,8,8,11,14,18-hexamethylnonadecyloxy)-ethoxy]-hydroxyphosphoryl}-β-D-glucopyranuronamide (**2**)

R_f = 0.19 ($CHCl_3$–MeOH–H_2O 18:11:2.7). – ^1H NMR (400 MHz, 7 mmol l^{-1} in $CDCl_3$–CD_3OD–D_2O 18:13:2.7, TMS, characteristic signals): δ 0.82–1.60 (signals from unit I), 2.02 (s, 3 H, $NHCOC\underline{H}_3$), 4.15 (unresolved m, 3 H, 2^{H}-H, 3^{H}-H, 3^{H}-H'), 4.50 (d, 1 H, 1^{E}-H, $^{3}J_{1E,2E} = 7.7$ Hz), 5.00 (dd, 1 H, 3^{F}-H, J = 9.7 and 9.9 Hz), 5.55 (br. s, 1 H, 1^{F}-H). – ^{13}C NMR (100.6 MHz, 7 mmol l^{-1} in $CDCl_3$–CD_3OD–D_2O 18:13:2.7, TMS): δ 19.66–42.49 (CH, CH_2, and CH_3 signals), 56.47 (C-2^{E}), 62.27 (C-6^{E}), 67.04 (br., C-3^{H}), 70.26 (br., C-2^{F}), 70.60, 71.15, 72.65 (C-3^{E}, C-4^{E}, C-1^{I}), 73.91 (C-3^{F}), 74.95 (C-4^{F}), 76.50 (C-5^{E}), 81.04 (br., C-2^{H}), 95.59 (br., C-1^{F}), 101.79 (C-1^{E}), 159.27 ($OCONH_2$), 172.19, 174.19 (C=O) [60]. – ^{31}P NMR (161.9 MHz, 7 mmol l^{-1} in $CDCl_3$–CD_3OD–D_2O 18:13:2.7, TMS): δ –2.9. – $C_{43}H_{80}N_3O_{18}P$ (958.09, 957.52). – FAB-MS: *m/z* (%): 1002.5 $[M+2\times Na-H]^+$, 980.5 $[M+Na]^+$, 581.3 $[M+2\times Na-f]^+$, 559.4 $[M+H+Na-f]^+$, 444.1 $[f+Na-H]^+$, 204.1 $[e]^+$.

Allyl 3,4-di-O-(2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-2-O-tert-butyldimethylsilyl-β-D-glucopyranosiduronamide (**9b**)

9a (423 mg, 0.35 mmol) was dechlorinated as described for the conversion **8a**→**11a**. FC (petroleum ether → petroleum ether-$CHCl_3$-ethanol 5:2:1) furnished **9b** (301 mg, 86%). *M.p.* 130–132 °C (ethyl acetate-petroleum ether). – $R_f = 0.32$ (petroleum ether–$CHCl_3$–ethanol 5:2:2). IR ($CHCl_3$): $\tilde{\nu}$ = 1749, 1685, 1533, 1520 cm^{-1}. – ^{1}H NMR (^{1}H,^{1}H COSY, 400 MHz, [D_5]pyridine): δ 0.27, 0.32 (2 s, 2×3 H, $SiCH_3$), 1.05 [s, 9 H, $SiC(CH_3)_3$], 1.99, 2.00, 2.02, 2.03, 2.10, 2.12, 2.14, 2.17 (8 s, 8×3 H, $COCH_3$), 4.03–4.07 (m, 2 H, 5^{E}-H, $5^{E'}$-H), 4.14 (ddt, 1 H, allyl-1-H), 4.27 (dd, 1 H, 2^{F}-H), 4.41 (dd, 1 H, 6^{E}-H), 4.45–4.54 (m, 4 H, 2^{E}-H, 6^{E}-H', $6^{E'}$-H, allyl-1-H'), 4.58 (dd, 1 H, 3^{F}-H), 4.61 (ddd, 1 H, $2^{E'}$-H), 4.71 (dd, 1 H, $6^{E'}$-H'), 4.74 (d, 1 H, 5^{F}-H), 4.90 (d, 1 H, 1^{F}-H), 4.96 (dd, 1 H, 4^{F}-H), 5.18 (dq, 1 H, allyl-3-H_{trans}), 5.36 (dq, 1 H, allyl-3-H_{cis}), 5.44 (dd, 1 H, 4^{E}-H), 5.46 (d, 1 H, $1^{E'}$-H), 5.49 (d, 1 H, 1^{E}-H), 5.49 (t, 1 H, $4^{E'}$-H), 5.75 (dd, 1 H, $3^{E'}$-H), 5.83 (dd, 1 H, 3^{E}-H), 5.99–6.08 (m, 1 H, allyl-2-H), 7.95, 8.52 (2×br. s, 2×1 H, CONH), 8.90 (d, 1 H, $NHAc^{E}$), 9.20 (d, 1 H, $NHAc^{E'}$), $^{3}J_{1E,2E} = 8.9$ Hz, $^{3}J_{2E,3E} = 10.3$ Hz, $^{3}J_{3E,4E} = 9.6$ Hz, $^{3}J_{4E,5E} = 9.7$ Hz, $^{3}J_{5E,6E} = 2.5$ Hz, $^{2}J_{6E,6'E} = 12.2$ Hz, $^{3}J_{1E',2E'} = 9.2$ Hz, $^{3}J_{2E',3E'} = 10.4$ Hz, $^{3}J_{3E',4E'} = 9.4$ Hz, $^{3}J_{4E',5E'} = 9.7$ Hz, $^{3}J_{5E',6'E'} = 3.9$ Hz, $^{2}J_{6E',6'E'} = 12.5$ Hz, $^{3}J_{1F,2F} = 6.3$ Hz, $^{3}J_{2F,3F} = 3.5$ Hz, $^{3}J_{3F,4F} = 5.1$ Hz, $^{3}J_{4F,5F} = 4.1$ Hz, $^{3}J_{NH,2E} = 8.9$ Hz, $^{3}J_{NH,2E'} = 8.9$ Hz. – ^{13}C NMR (^{13}C,^{1}H-LRHC, 100.6 MHz, ^{13}C,^{1}H COSY, APT, 50.3 MHz, [D_5]pyridine): δ –3.94, –3.86 (–, $SiCH_3$), 18.78 (+, $Si\underline{C}(CH_3)_3$), 20.92, 20.97, 21.04, 21.18, 21.33 (–, $OCO\underline{C}H_3$) [60], 23.66, 23.73 (–, $NHCO\underline{C}H_3$), 26.54 (–, $SiC(\underline{C}H_3)_3$), 55.20 (–, C-2^{E}), 55.39 (–, C-$2^{E'}$), 62.69 (+, C-6^{E}, C-$6^{E'}$), 69.62 (–, C-$4^{E'}$), 70.00 (–, C-4^{E}), 71.00 (+, allyl-C-1), 72.70, 73.05 (–, C-5^{E}, C-$5^{E'}$), 74.01 (–, C-3^{E}), 74.50 (–, C-$3^{E'}$), 75.13 (–, C-2^{F}), 77.58 (–, C-4^{F}), 79.49 (–, C-5^{F}), 80.88 (–, C-3^{F}), 99.79 (–, C-1^{E}), 102.12 (–, C-$1^{E'}$), 103.78 (–, C-1^{F}), 117.56 (+, allyl-C-3), 135.24 (–, allyl-C-2), 170.26, 170.87, 171.03, 171.09, 171.26 (+, $\underline{C}OCH_3$) [60], 173.20 (+, $CONH_2$). – $C_{43}H_{67}N_3O_{22}Si$ (1006.10, 1005.40), FAB-MS: *m/z* (%): 1028.7 $[M+Na]^+$, 1006.7 $[M+H]^+$, 948.6 $[f]^+$, 677.5 $[M+2\times H-e]^+$, 330.2 $[e]^+$.

Removal of the allyl group from 9b

(i) With palladium(II) chloride: **9b** (59.6 mg, 59 µmol) was dissolved in a 0.1 mol l^{-1} solution of sodium acetate in 20:1 acetic acid–water (1.2 ml). Palladium(II) chloride (15.7 mg, 89 µmol) was added and the mixture was stirred at 20 °C. After 24 h another portion of palladium(II) chloride (15.0 mg, 85 µmol) was added. Stirring was continued for 24 h. Water (10 ml) was added. Lyophilization and FC ($CHCl_3$–MeOH 10:1) furnished **16a** (25.7 mg, 46%), 6.5 mg of **9b** were recovered.

(ii) With palladium(II) acetate: To **9b** (61.7 mg, 61 µmol) and palladium(II) acetate (98 per cent, 15.2 mg, 66 µmol) 20:1 acetic acid–water (0.35 ml) was added. The mixture was stirred at 20 °C. After 24 h a further portion of palladium(II) acetate (28.2 mg, 123 µmol) was added. After altogether 103 h solvents were evaporated. FC ($CHCl_3$–MeOH 24:1 → 14:1) furnished **16a** (31.3 mg, 52%). 4.4 mg of **9b** were recovered.

(iii) With tetrakis(triphenylphosphine)palladium(0): In a light-protected vial **9b** (64.8 mg, 64 µmol), commercial tetrakis (triphenylphosphine)palladium(0) (75.5 mg, 65 µmol), and degassed acetic acid (2.3 ml) were stirred at 20 °C for 4 h. Ethyl acetate was added. Solvents were evaporated. Repeated FC ($CHCl_3$–MeOH 20:1 → 10:1, then $CHCl_3$–MeOH 15:1) furnished **16a** (52.2 mg, 84%).

Whilst at the end of the reactions mainly one compound could be detected by TLC ($CHCl_3$–MeOH 10:1) in the course of the FC separation a second product was formed which could be separated. In the [D_5]pyridine solution prepared for the NMR experiments from both compounds an equilibrium mixture was formed with the newly formed compound **16b** prevailing (ratio of α/β-**16a** and **16b**: 1.3:1:8.9 (determined from the ^{1}H NMR $SiC(CH_3)_3$ signals).

3,4-Di-O-(2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-2-O-tert-butyldimethylsilyl-D-glucopyranuronamide (**16a**) and *tert-Butyldimethylsilyl-3,4-di-O-(2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-α-D-glucopyranosiduronamide* (**16b**), 1.3:1:8.9 mixture of α-**16a** – β-**16a** – **16b** (calculated from the *tert*-butyl signal integrals)

R_f = 0.19 and 0.23 ($CHCl_3$–MeOH 10:1). – ^{1}H NMR (^{1}H,^{1}H COSY, 400 MHz, [D_5]pyridine) [62, 66]:
16a: δ 0.29, 0.33, 0.39, 0.40 (4 s, $SiCH_3$), 1.03, 1.09 (2 s, $SiC(CH_3)_3$), 1.96, 1.99, 2.01, 2.01, 2.03, 2.06, 2.09, 2.12 (8 s, $OCOCH_3$), 2.16, 2.18, 2.25, 2.26 (4 s, $NHCOC\underline{H}_3$), 5.12 (d, 1^{E}-H or $1^{E'}$-H, $^{3}J_{1E,2E} = 8.7$ Hz), 5.35 (d, 1^{F}-H, $^{3}J_{1F,2F} = 6.2$ Hz, β-**16a**), 5.82 (dd, 3^{E}-H or $3^{E'}$-H, $^{3}J_{2E,3E} = 10.4$ Hz, $^{3}J_{3E,4E} = 9.4$ Hz), 5.88 (dd, 3^{E}-H or $3^{E'}$-H, $^{3}J_{2E,3E} = 10.4$ Hz, $^{3}J_{3E,4E} = 9.4$ Hz), 8.12, 8.36, 8.51, 8.54 (4×br. s, CONH), 8.77 (d, NHAc, $^{3}J_{NH,2E} = 9.2$ Hz), 8.80 (d, NHAc, $^{3}J_{NH,2E} = 7.9$ Hz), 9.09 (d, NHAc, $^{3}J_{NH,2E} = 8.7$ Hz.
16b: δ0.15, 0.16 (2 s, 2×3 H, $SiCH_3$), 0.92 (s, 9 H, $SiC(CH_3)_3$), 1.95, 1.98, 2.00, 2.02, 2.03, 2.04 (6 s, 6×3 H, $OCOCH_3$), 2.38, 2.41 (2 s, 2×3 H, $NHCOC\underline{H}_3$), 3.73 (ddd, 1 H, $5^{E'}$-H), 4.00 (ddd, 1 H, 5^{E}-H), 4.09 (dd, 1 H, 2^{F}-H), 4.31 (dd, 1 H, $6^{E'}$-H), 4.57 (dd, 1 H, 4^{F}-H), 4.65–4.72 (m, 3 H, 2^{E}-H, $2^{E'}$-H, 6^{E}-H), 4.67 (dd, 1 H, 3^{F}-H), 4.73 (dd, 1 H, $6^{E'}$-H'), 4.86 (d, 1 H, 5^{F}-H), 4.93 (dd, 1 H, 6^{E}-H'), 5.42 (d, 1 H, $1^{E'}$-H), 5.44 (d, 1 H, 1^{F}-H), 5.57 (dd, 1 H, $4^{E'}$-H), 5.62 (d, 1 H, 1^{E}-H), 5.64 (dd, 1 H, 4^{E}-H), 5.67 (dd, 1 H, 3^{E}-H), 5.69 (dd, 1 H, $3^{E'}$-H), 8.42 (br. d, 1 H, CONH), 8.58 (br. s, 1 H, CONH), 8.62 (d, 1 H,

NHAc$^{E'}$), 9.02 (d, 1 H, NHAc^{E}), $^{3}J_{1E,2E}$ = 8.4 Hz, $^{3}J_{2E,3E}$ = 10.4 Hz, $^{3}J_{3E,4E}$ = 9.4 Hz, $^{3}J_{4E,5E}$ = 9.4 Hz, $^{3}J_{5E,6E}$ = 2.9 Hz, $^{3}J_{5E,6'E}$ = 3.4 Hz, $^{2}J_{6E,6'E}$ = 12.3 Hz, $^{3}J_{1E',2E'}$ = 8.7 Hz, $^{3}J_{2E',3E'}$ = 10.1 Hz, $^{3}J_{3E',4E'}$ = 9.6 Hz, $^{3}J_{4E',5E'}$ = 9.7 Hz, $^{3}J_{5E',6E'}$ = 2.2 Hz, $^{3}J_{5E',6'E'}$ = 3.9 Hz, $^{2}J_{6E',6'E'}$ = 12.3 Hz, $^{3}J_{1F,2F}$ = 3.4 Hz, $^{3}J_{2F,3F}$ = 9.4 Hz, $^{3}J_{3F,4F}$ = 8.8 Hz, $^{3}J_{4F,5F}$ = 9.7 Hz, $^{3}J_{NH,2E}$ = 8.0 Hz, $^{3}J_{NH,2E'}$ = 9.2 Hz, $^{2}J_{CONH,CONH}$ = 1.7 Hz. – ^{13}C NMR (^{13}C,^{1}H COSY, APT, 50.3 MHz, [D_5]pyridine) [62]: δ –6.12, –5.92 (–, $SiCH_3$), 17.25 (+, $Si\underline{C}(CH_3)_3$), 19.25, 19.29, 19.38, 19.47, 19.81, 19.88 (–, $OCO\underline{C}H_3$), 21.96, 22.07 (–, $NHCO\underline{C}H_3$), 24.62 (–, $SiC(\underline{C}H_3)_3$), 53.84, 53.94 (–, C-2^{E}, C-2$^{E'}$), 60.88 (+, C-6^{E}, C-6$^{E'}$) [60], 67.75 (–, C-4^{E}), 68.03 (–, C-4$^{E'}$), 70.73 (–, C-5$^{E'}$, C-5^{F}), 71.19 (–, C-5^{E}), 72.06 (–, C-2^{F}), 73.02 (–, C-3$^{E'}$), 73.76 (–, C-3^{E}), 76.65 (–, C-4^{F}), 76.73 (–, C-3^{F}), 93.41 (–, C-1^{F}), 99.48 (–, C-1$^{E'}$), 100.10 (–, C-1^{E}), 168.43, 168.48, 169.30 (possibly superposition of two signals), 169.38, 169.79 (+, $\underline{C}OCH_3$), 171.85 (+, $CONH_2$). – IR ($CHCl_3$) of the mixture: $\tilde{\nu}$ =1684, 1539, 1368, 1229, 1226, 1206, 1045 cm^{-1}. $C_{40}H_{63}N_3O_{22}Si$ (966.03, 965.37), FAB-MS (of the mixture): *m/z* (%): 966.2 [M+H]$^{+}$, 637.1 [M+2×H–e]$^{+}$, 330.0 [e]$^{+}$.

tert-Butyldimethylsilyl-3,4-di-O-(2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-2-O-{[(R)-2-methoxycarbonyl-2-(3,8,8,11,14,18-hexamethylnonadecyloxy)-ethoxy]-(2,2,2-trichloro-1,1-dimethylethyloxy)-phosphoryl}-α-D-glucopyranosiduronamide (**16c**), mixture of diastereomers (isomeric at P)

The mixture of **16a/16b** (118.8 mg, 123 µmol) was phosphorylated as described for the phosphorylation of **11e/12**. FC ($CHCl_3$–MeOH 30:1) followed by a FC separation of fractions containing impure **16c** (elution with $CHCl_3$–MeOH 24:1) furnished pure **16c** (97.5 mg, 48%).
R_f = 0.12 ($CHCl_3$–MeOH 20:1). – ^{1}H NMR (^{1}H,^{1}H COSY, 400 MHz, [D_5]pyridine) [62]: δ 0.28, 0.31 (2 s, 2×3 H, $SiCH_3$), 0.85–1.85 ($SiC(CH_3)_3$ and signals from unit I), 1.95–2.17 (24 H, $COCH_3$ signals), 2.57, 2.63 [2 s, 2×3 H, $C(CH_3)_2CCl_3$], 3.60–3.94 (m, 4 H, 5^{E}-H, 5$^{E'}$-H, 1^{I}-H, 1^{I}-H'), 3.87 (s, 3 H, $COOCH_3$), 4.28 (br. dd, 1 H, 6^{E}-H), 4.48–5.06 (m, 2^{E}-H, 6^{E}-H', 2$^{E'}$-H, 6$^{E'}$-H, 6$^{E'}$-H', 2^{F}-H, 3^{F}-H, 4^{F}-H, 5^{F}-H, 2^{H}-H, 3^{H}-H, 3^{H}-H'), 5.20 (d, 1 H, 1^{E}-H), 5.34 (d, 1 H, 1$^{E'}$-H), 5.55 (dd, 1 H, 3^{E}-H), 5.60 (dd, 1 H, 3$^{E'}$-H), 5.68 (2×dd, 2 H, 4^{E}-H, 4$^{E'}$-H), 5.75 (d, 1 H, 1^{F}-H), 8.13 (d, 1 H, NHAc^{E}), 8.40 (d, 1 H, NHAc$^{E'}$), 8.43 (br. s, 1 H, CONH), 8.68 (s, 1 H, CONH), $^{3}J_{1E,2E}$ = 8.4 Hz, $^{3}J_{2E,3E}$ = 10.1 Hz, $^{3}J_{3E,4E}$ = 9.7 Hz, $^{3}J_{1E',2E'}$ = 8.8 Hz, $^{3}J_{2E',3E'}$ = 9.9 Hz, $^{3}J_{3E',4E'}$ = 9.7 Hz, $^{3}J_{1F,2F}$ = 3.5 Hz, $^{3}J_{NH,2E}$ = 8.8 Hz, $^{3}J_{NH,2E'}$ = 8.2 Hz. – ^{13}C NMR (50.3 MHz, [D_5]pyridine): δ –5.35, –4.95 ($SiCH_3$), 17.92 [$Si\underline{C}(CH_3)_3$], 19.23–41.91 (CH, CH_2, and CH_3 signals), 52.04 ($COO\underline{C}H_3$), 54.13, 54.80 (C-2^{E}, C-2$^{E'}$), 61.16, 61.55 (C-6^{E}, C-6$^{E'}$), 68.19, 68.54 (C-4^{E}, C-4$^{E'}$), 68.78 (br., presumably C-3^{H}), 69.53 (br.), 70.95, 71.95, 72.02, 74.61, 74.72, 74.98, 76.91 (C-3^{E}, C-3$^{E'}$, C-5^{E}, C-5$^{E'}$, C-2^{F}, C-3^{F}, C-4^{F}, C-5^{F}, C-2^{H}, C-1^{I}), 77.81, 78.23 (2×d, C-2^{H}, $^{3}J_{2H,P}$ = 10 Hz and 6 Hz), 90.50 (d, $C(CH_3)_2CCl_3$, $^{3}J_{C,P}$ = 5 Hz), 91.58 (C-1^{F}), 100.00, 100.86 (C-1^{E}, C-1$^{E'}$), 105.69, 106.08 (CCl_3), 169.35-172.13 (C=O). ^{31}P NMR (81.0 MHz, [D_5]pyridine): δ –5.3, –4.8 (integral ratio 2.1:1). – $C_{73}H_{125}Cl_3N_3O_{28}PSi$ (1658.22, 1655.70). – FAB-MS: *m/z* (%): 1678 [M+Na]$^{+}$, 1656 [M+H]$^{+}$, 948.1 [M+H–GHI]$^{+}$, 330.0 [e]$^{+}$.

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[61] Slightly impure sample, see ref. [16]

[62] The E and E' assignments possibly have to be interchanged.

[63] The 2^F-H and 3^F-H signals could not be identified.

[64] The spectrum displayed small signals of triphenylphosphine or triphenylphosphine oxide.

[65] First, the ^{13}C NMR and APT spectra were recorded and displayed mainly signals of **14a**. Later on, the equilibrium between **14a** and **14b** was established as seen in a ^{13}C NMR and a $^{13}C,^{1}H$ COSY spectrum.

[66] A number of spectra have been recorded. Only in one instance a 2^F-OH signal at δ 6.30 (d, $^3J_{OH,2F} = 5.6$ Hz) could be detected.

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