ELSEVIER

www.elsevier.nl/locate/carres

Carbohydrate Research 324 (2000) 97–106

CARBOHYDRATE RESEARCH

Syntheses of amphiphilic glycosylamides from glycosyl azides without transient reduction to glycosylamines☆

Paul Boullanger *, Valérie Maunier, Dominique Lafont

Laboratoire de Chimie Organique II, Unité Mixte de Recherche CNRS 5622, Université de Lyon 1, Chimie Physique Electronique de Lyon, 43 bd du 11 Novembre 1918, F-69622 Villeurbanne, France

Received 28 July 1999; accepted 22 October 1999

Abstract

Protected glycosyl azides react with acyl chlorides in the presence of triphenylphosphine to afford glycosylamides in high yields, at room temperature. Starting from the β-glycosyl azides, the reaction is highly stereoselective and occurs with retention of configuration, whereas the α-azido anomers display a lower stereoselectivity giving rise to α/β mixtures of glycosylamides. The reaction was applied to several monosaccharidic azides and to lactosyl azide with various acyl chlorides; it was shown to be of general use for preparing 1,2-trans β-glycosylamides.

Keywords: Glycosyl azides; Glycosylamides; Triphenylphosphine; Acyl chlorides; Staudinger reaction

1. Introduction

Amphiphilic glycosylamides constitute a valuable class of non-ionic biosurfactants. Several methods for preparation of such derivatives have already been described in the literature. All of them involve the acylation of low-stability glycosylamine intermediates [2–7]. The latter can hydrolyse, anomerize or dimerize very easily; they can also undergo several degradative rearrangements [5,8]. Furthermore, their condensations with acylating agents exhibit somewhat contradictory results, depending on the reaction conditions. Thus, for example, β-D-glucopyranosylamine in the presence of lauroyl chloride was reported either to deglycosylate and afford dodecanoylamide quantitatively [4] or to react to give *N*-lauroyl-β-D-glucopyranosylamine in 51% yield [5].

In a search for a new route to 6-amido-6-deoxy carbohydrates, we have recently used a modified Staudinger reaction between 6-azido-6-deoxy carbohydrates and fatty acid chlorides [9]. This paper deals with the extension of the above procedure to the anomeric position, starting from protected glycosyl azides.

2. Results and discussion

As recently reviewed [10], peracetylated glycopyranosyl azides are easily prepared from glycopyranosyl halides or glycopyranose peracetates by nucleophilic displacement. They can be reduced with various reagents [10] to per-O-acetylated glycopyranosylamines, but the latter are endowed with the same inconve-

☆ For a preliminary communication, see Ref. [1].

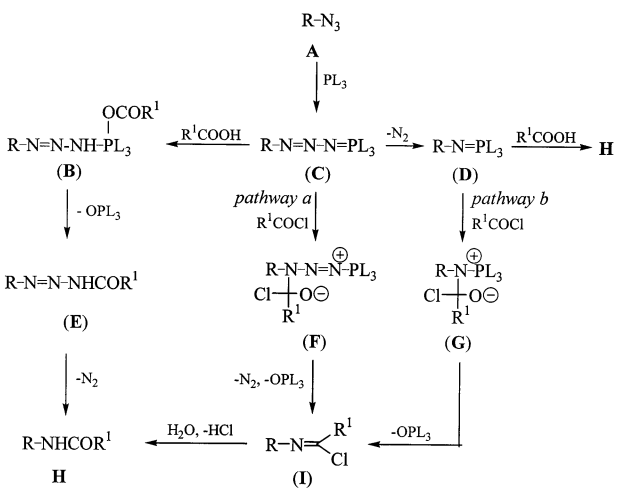
* Corresponding author. Tel.: +33-4-7243-1162; fax: +33-4-7889-8914.

E-mail address: paul.boullanger@univ-lyonl.fr (P. Boullanger)

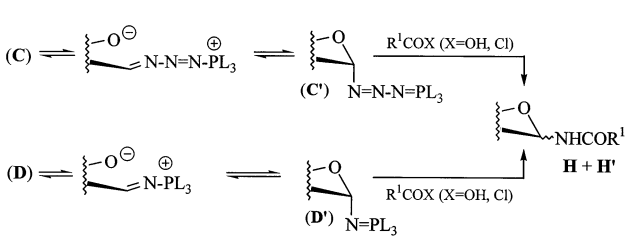
0008-6215/00/$ - see front matter
PII: S0008-6215(99)00284-0

niences as their unprotected counterparts, to which one must add the possibilities of O → N acetyl migrations. The Staudinger reaction [11,12] could allow the direct reaction of carboxylic acids or their halides, anhydrides or esters with glycosyl azides without transient reduction [12–15]. In addition to our preliminary communication [1], the only examples reported to date for the synthesis of glycosylamides from glycosyl azides involved the reaction of carboxylic acids [16] or anhydrides [17]. This paper will attempt to rationalize our results in the light of recent reports devoted, on one hand to the reactions of acyl chlorides with aliphatic phosphazenes [18,19] and, on the other hand, to the reactions of glycosyl azides with carboxylic acids [16].

A simplified mechanism [19] for the reaction of alkyl azides **A** (RN_3) with carboxylic acid derivatives (R^1COX) in the presence of trialkylphosphines (PL_3) is summarized in Scheme 1. Triazaphosphadiene [**C**] can afford phosphazene [**D**] by loss of a nitrogen (Staudinger reaction) and also the intermediates [**B**] (or [**F**], pathway a) by addition of a carboxylic acid (or acyl chloride) in a non-Staudinger process. Both intermediates [**B**] and [**F**] finally give rise to amide **H** either via adduct [**E**] or chloroimine [**I**]. Phosphazene [**D**] can follow a similar pathway (b) to afford amide **H**.



Scheme 1.



Scheme 2.

In the case of glycosyl azides, this mechanism is further complicated by the anomeric effect [20]. Due to the ylid character of phosphazenes [**C**] and [**D**], anomerization can occur via open-chain intermediates [**C′**] and [**D′**] leading to anomeric mixtures of compounds **H** and **H′** (Scheme 2).

Results reported in the literature are somewhat contradictory with regard to yields and stereochemistry. Glycosyl azides do not seem to react with a carboxylic acid and triphenylphosphine, unlike alkyl azides [21]; more nucleophilic phosphines are required providing that the acid is added to the azide before the phosphine [16]. A lower reaction temperature was also shown to slow down the formation of phosphazene [**D**] from [**C**] and to increase the yield of the reaction [16]. It is worth mentioning that these conditions (low temperature and addition of the phosphine in the last stage of the reaction) were shown to favor the non-Staudinger process via the adduct [**B**]. Anomerization was not observed in such processes and yields were generally good [16].

The main aim of this work was to find the optimum conditions in which triphenylphosphine could be used to afford glycosylamides. Despite its lower reactivity [22], it is stable to oxidation and hydrolysis and easier to handle than non-aromatic phosphines.

Glycosyl azides **1**–**4** were prepared as described in the literature [10,23,24] as well as **6** [25], **7** [26] and **8** [27]. Compound **5** was synthesized from 1,3,4,6-tetra-*O*-acetyl-2-allyloxycarbonylamino-2-deoxy-β-D-glucopyranose [28] and trimethylsilyl azide as for the *N*-acetyl derivative [29].

In order to check the feasibility of the Staudinger reaction, compound **1** was first reacted with octanoic acid in the presence of triphenylphosphine. As already described in the literature [16], no condensation occurred with a wide variety of conditions. Nevertheless, with octanoyl chloride compound **9** was obtained in good yield in 15 min at room

Table 1
Condensation of glycosyl azides with acid chlorides in the presence of PPh_3 [a]

Azido sugar	Acid chloride	CH_2Cl_2	Yield (%) C_6H_6	Toluene	Product
1	$C_7H_{15}COCl$ [b]	90	84	95	**9**
1	$C_{17}H_{35}COCl$	75			**15**
1	**27**			73	**16**
2	$C_7H_{15}COCl$	90	72	94	**10**
3	$C_7H_{15}COCl$	60	80	85	**11**
4	$C_7H_{15}COCl$	60	67	56	**12**
4	**27**	83			**17**
5	$C_7H_{15}COCl$	52	80	83	**13**
6	$C_7H_{15}COCl$ [c]	63			**14**
7	$C_7H_{15}COCl$ [c]	83 (α/β, 9:1)			**18**
8(β)	$C_7H_{15}COCl$ [d]		37		**19**(β)
8(α)	$C_7H_{15}COCl$ [d]		28 (α/β, 3:1)	30 (α/β, 1:1)	**19**(α+β)

[a] Reactions in 0.2 M solution for 15 min at room temperature with 1.3 equivalents of PPh_3 and 2 equivalents of acyl chloride, unless otherwise stated.
[b] 73% yield in dioxane.
[c] Overnight at room temperature.
[d] 2 h at room temperature

temperature, using 2 equiv of the acyl chloride and 1.3 equiv of triphenylphosphine. The yield was mostly dependent on the solvent: in 0.2 M solutions, it ranged from 73% in dioxane to 95% in toluene (Table 1).

Other experiments were run varying the order of addition of the reagents. They were realized in chloroform-*d* and checked by ^{31}P and ^{13}C NMR spectroscopy. When triphenylphosphine (1.05 equiv) was added to a $CDCl_3$ solution of azide **1**, nitrogen release was immediate and the ^{31}P NMR spectrum displayed the formation of a β-phosphazene [**D**] (δ 17.15 ppm). The signal corresponding to a triazaphosphadiene intermediate [**C**] (expected around 25 ppm [19]) was not seen. In the absence of any acylating agent, anomerization to the α-phosphazene was observed (δ 13.73 ppm); a 1:1 α/β mixture was obtained after 8 h at room temperature and the equilibrium (1:4, β/α) was reached after 24 h.

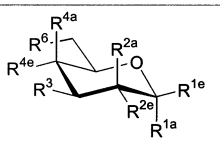
If octanoyl chloride was immediately added after the evolution of nitrogen had ceased (15 min, pathway b), the signal corresponding to the β-phosphazene rapidly disappeared (1 h) with concomitant appearance of the signal for triphenylphosphine oxide (δ 29.53 ppm). During this stage of the reaction, the β-chloroimine [**I**] was detected as the main product by ^{13}C NMR spectroscopy (δ C-1 89.38 ppm, δ quaternary C 152.33 ppm). After 3 h, the latter decreased with the signal enhancements for the β-glucopyranosylamide **9** (δ C-1 78.14 ppm) and triphenylphosphine oxide hydrochloride (δ ^{31}P 41.38 ppm), which means that triphenylphosphine oxide can act as an acid scavenger in the hydrolysis of [**I**] to **H**. No anomerization occurred, but the yield of the reaction, after separation of **9**, remained low (58%).

When octanoyl chloride was added to the azide **1**, before the addition of triphenylphosphine, no triazaphosphadiene [**C**] nor phosphazene [**D**] could be detected by ^{31}P NMR spectroscopy. The reaction appeared to be immediate, as indicated by the instantaneous evolution of nitrogen gas and the concomitant appearance of triphenylphosphine oxide. The absence of a signal for phosphazene [**D**] in ^{31}P NMR spectroscopy would agree with a reaction following pathway a.

The reaction was then extended to other acyl chlorides and other β-glycosyl azides (Table 1). The yields and β-stereoselectivities remained high, even with acyl chlorides of low reactivity (e.g. **27**). A noticeable exception was that observed for the conversion of β-mannopyranosyl azide **8**(β) into **19**(β) in 37% yield, solely in benzene (Table 2).

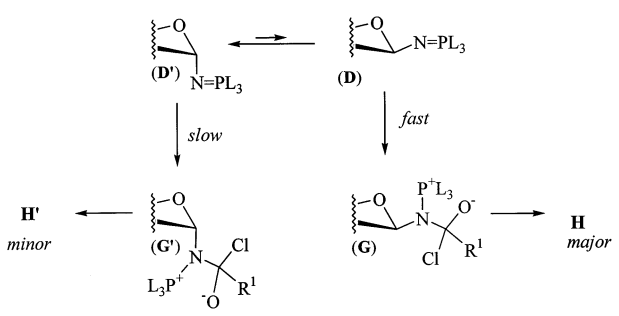
Reactions starting from α-glycosylpyranosyl azides were found to be slower (several hours at room temperature) and retention of anomeric configuration was not observed. Thus, compound **7** afforded a 9:1 α/β mixture of glycosylamide **18** in 83% yield in CH_2Cl_2,

Table 2
Structures of glycosylazides and glycosylamides employed



	R^{1a}	R^{1e}	R^{2a}	R^{2e}	R^3	R^{4a}	R^{4e}	R^6
1	H	N_3	H	OAc	OAc	H	OAc	OAc
2	H	N_3	H	OAc	OAc	OAc	H	OAc
3	H	N_3	H	OAc	OAc	H	OAc_4-β-D-Gal	OAc
4	H	N_3	H	NHAc	OAc	H	OAc	OAc
5	H	N_3	H	NHAloc	OAc	H	OAc	OAc
6	H	N_3	H	OBn	OBn	H	OBn	OBn
7	N_3	H	H	OAc	OAc	H	OAc	OAc
8α	N_3	H	OAc	H	OAc	H	OAc	OAc
8β	H	N_3	OAc	H	OAc	H	OAc	OAc
9	H	$NHCOC_7H_{15}$	H	OAc	OAc	H	OAc	OAc
10	H	$NHCOC_7H_{15}$	H	OAc	OAc	OAc	H	OAc
11	H	$NHCOC_7H_{15}$	H	OAc	OAc	H	OAc_4-β-D-Gal	OAc
12	H	$NHCOC_7H_{15}$	H	NHAc	OAc	H	OAc	OAc
13	H	$NHCOC_7H_{15}$	H	NHAloc	OAc	H	OAc	OAc
14	H	$NHCOC_7H_{15}$	H	OBn	OBn	H	OBn	OBn
15	H	$NHCOC_{17}H_{35}$	H	OAc	OAc	H	OAc	OAc
16	H	NHCOZ	H	OAc	OAc	H	OAc	OAc
17	H	NHCOZ	H	NHAc	OAc	H	OAc	OAc
18	$NHCOC_7H_{15}$	H	H	OAc	OAc	H	OAc	OAc
19α	$NHCOC_7H_{15}$	H	OAc	H	OAc	H	OAc	OAc
19β	H	$NHCOC_7H_{15}$	OAc	H	OAc	H	OAc	OAc
20	H	$NHCOC_7H_{15}$	H	OH	OH	H	OH	OH
21	H	$NHCOC_{17}H_{35}$	H	OH	OH	H	OH	OH
22	H	$NHCOC_7H_{15}$	H	OH	OH	OH	H	OH
23	H	$NHCOC_7H_{15}$	H	OH	OH	H	β-D-Gal	OH
24	H	$NHCOC_7H_{15}$	H	NHAc	OH	H	OH	OH
25	H	NHCOZ	H	NHAc	OH	H	OH	OH
26	H	$NHCOC_7H_{15}$	H	NH_2	OH	H	OH	OH

27 = ZCOCl $Z=CH_2OCH_2CHC_{14}H_{29}$ (with $C_{12}H_{25}$)



Scheme 3.

whereas **8**(α) afforded an anomeric mixture of **19** in proportions varying with the solvent (Table 1). In such cases, the reaction times were long enough to allow anomerization of the phosphazene intermediates [**D**], before the addition of the acyl chloride. A tentative explanation for the preference of the amido anomeric group for occupation of the β-equatorial position could lie in the higher steric hindrance of the axial α-anomeric group in intermediate [**G**], as compared with the β anomer. Although the α-phosphazene [**D′**] is the favored anomer, a faster addition of acyl chloride on the β-phosphazene [**D**] could explain the stereoselectivity of the reaction (Scheme 3).

In conclusion, the reaction of acyl chlorides on 1,2-trans β-glycosyl azides, in the presence of triphenylphosphine at room temperature, was shown to afford glycosylamides in very good yields and high anomeric equatorial stereoselectivity. The same reaction, performed on α-glycosyl azides, led to anomeric mixtures of glycosylamides. The choice of solvent was essential for the best results. The late addition of triphenylphosphine to the reaction led to the best yields and fastest reactions, possibly due to the formation of a triazaphosphadiene intermediate. This modified Staudinger procedure constitutes, in our opinion, a high-yielding and highly stereoselective method for the synthesis of 1,2-trans β-D-glycopyranosylamides. Also, it avoids most of the drawbacks encountered in the previously reported methods (using glycopyranosylamine intermediates) and seems to be well suited to the synthesis of neoglycolipids and surface-active derivatives.

3. Experimental

General methods.—Tetrahydrofuran (THF) was distilled from a sodium–benzophenone mixture under an argon atmosphere. Dichloromethane was washed once with H_2SO_4, twice with water and dried with $CaCl_2$ before distillation. Methanol was refluxed with NaOMe before distillation. Dichloromethane and THF were stored over 4 Å molecular sieves and MeOH over 3 Å molec-

ular sieves. Melting points were determined on a Büchi apparatus and were uncorrected. Thin-layer chromatography (TLC) was performed on aluminum sheets coated with Silica Gel 60 F_{254} (E. Merck). Compounds were visualized by spraying the TLC plates with dilute 15% aq H_2SO_4, followed by charring at 150 °C for a few minutes. Column chromatography was performed on Silica Gel Geduran Si 60 (E. Merck). Optical rotations were recorded on a Perkin–Elmer 241 polarimeter in a 1 dm cell at 21 °C. ^1H and ^{13}C NMR spectra were recorded with a Bruker AC-200 or AM-300 spectrometers operating at 200 (or 300 MHz) or 50 MHz (or 75.5 MHz), respectively, with Me_4Si as the internal standard, ^{31}P NMR spectra were recorded with a Bruker AC-200 operating at 81 MHz. In the NMR spectra of *N*-octanoyl and *N*-octadecanoyl glycopyranosylamines (except **9**), the signals corresponding to the alkyl chains are not repeated since ^1H and ^{13}C chemical shifts are closely related to those found for **9** (± 0.3 and ± 2 ppm, respectively). In the case of *O*-acetyl derivatives, the additional signals corresponding to $OCOCH_3$ (^1H, 2.0 ± 0.1 ppm; ^{13}C 170.5 ± 1.5 and 20.0 ± 0.5 ppm) are not reported. Elemental analyses were carried out by the Laboratoire Central d'Analyses du CNRS (Vernaison, France). The amount of water present in some of the derivatives was determined by Karl–Fischer titration.

General procedure for the Staudinger reaction.—To a mixture of glycosyl azide (1.0 mmol) and acyl chloride (2.0 mmol, except when otherwise stated), dissolved in the appropriate solvent (4 mL), was added dropwise a solution of triphenylphosphine (1.3 mmol) in the same solvent (1 mL) at room temperature (rt). The reaction was monitored by TLC immediately after the evolution of nitrogen had ceased and was worked up usually after 15 min, unless otherwise stated. Thus, the mixture was diluted with $CHCl_3$ (20 mL), washed once with a satd aq soln of $NaHCO_3$ (5 mL) and then with water until neutral pH was achieved. After drying over Na_2SO_4, the solution was filtered, evaporated to dryness and then purified by column chromatography on silica gel.

*3,4,6-Tri-*O*-acetyl-2-allyloxycarbonylamino-2-deoxy-β-*D*-glucopyranosyl azide* (**5**).—To a solution of 1,3,4,6-tetra-*O*-acetyl-2-allyloxycarbonylamino-2-deoxy-β-D-glucopyranose [28] (1.90 g, 4.40 mmol) in dry CH_2Cl_2 (20 mL) were added successively trimethylsilyl azide (1.16 mL, 8.8 mmol) and Me_3SiOTf (128 μL, 0.65 mmol). After 48 h at rt, the mixture was neutralized with $NaHCO_3$ and washed with a satd aq soln of $NaHCO_3$ and water to neutrality. After drying over Na_2SO_4 and evaporation, the mixture was chromatographed on silica gel (1:2 EtOAc–petroleum ether). Compound **5** was obtained as a crystalline solid after concentration of its solution: 1.32 g (72%); mp 115–116 °C; $[\alpha]_D$ −23.5° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 5.91 (m, 1 H, C*H*=), 5.34–5.21 (m, 4 H, N*H*, H-3, CH_2=), 5.09 (dd, 1 H, $J_{3,4}$ 9.5 Hz, $J_{4,5}$ 9.7 Hz, H-4), 4.80 (d, 1 H, $J_{1,2}$ 8.4 Hz, H-1), 4.59 (d, 2 H, allyl CH_2), 4.29 (dd, 1 H, $J_{5,6a}$ 4.8 Hz, $J_{6a,6b}$ 12.4 Hz, H-6a), 4.16 (dd, 1 H, $J_{5,6b}$ 2.2 Hz, H-6b), 3.80 (ddd, 1 H, H-5), 3.80 (ddd, 1 H, $J_{2,3}$ 10.0 Hz, $J_{2,NH}$ 10.2 Hz, H-2); ^{13}C NMR ($CDCl_3$): δ 156.40 (NH*C*O), 133.09 (*C*H=), 118.52 (CH_2=), 89.33 (C-1), 74.46 (C-3), 72.75 (C-5), 69.01 (C-4), 66.70 (allyl CH_2), 62.61 (C-6), 56.26 (C-2). Anal. Calcd for $C_{16}H_{22}N_4O_9$ (414.36): C, 46.37; H, 5.35; N, 13.52. Found: C, 46.13; H, 5.23; N, 13.48.

*2,3,4,6-Tetra-*O*-acetyl-*N*-octanoyl-β-*D*-glucopyranosylamine* (**9**).—Prepared from **1** [23,24] (0.205 g, 0.55 mmol) and octanoyl chloride (0.179 g) in toluene (2 mL) by the general procedure. Column chromatography purification (1:1 EtOAc–petroleum ether) yielded a crystalline solid, 0.252 g (95%); mp 76 °C; $[\alpha]_D$ +11.0° (*c* 1.0, $CHCl_3$); ^1H NMR (Me_2CO-d_6): δ 7.66 (d, 1 H, $J_{1,NH}$ 9.5 Hz, CON*H*), 5.40 (dd, 1 H, $J_{1,2}$ 9.5 Hz, H-1), 5.34 (dd, 1 H, $J_{2,3}$ 9.5 Hz, $J_{3,4}$ 9.9 Hz, H-3), 5.00 (dd, 1 H, $J_{4,5}$ 10.0 Hz, H-4), 4.88 (dd, 1 H, H-2), 4.25 (dd, 1 H, $J_{5,6a}$ 4.7 Hz, $J_{6a,6b}$ 12.5 Hz, H-6a), 4.05 (dd, 1 H, $J_{5,6b}$ 2.3 Hz, H-6b), 4.00 (ddd, 1 H, H-5), 2.19, 1.56, 1.28, 0.86 (4 m, 15 H, C_7H_{15}); ^{13}C NMR (Me_2CO-d_6): δ 172.53 (NH*C*O), 77.33 (C-1), 72.96, 70.51, 68.56 (C-2, C-3, C-4, C-5), 61.70 (C-6) 35.56, 31.37, 28.70, 28.68, 25.03, 22.20, 13.28 (C_7H_{15}). Anal. Calcd for $C_{22}H_{35}NO_{10}$ (473.51): C, 55.80; H, 7.45; N, 2.96. Found: C, 55.48; H, 7.43; N, 2.55.

2,3,4,6-Tetra-O-*acetyl*-N-*octanoyl*-β-D-*galactopyranosylamine* (**10**).—Prepared from **2** [23,24] (0.399 g, 1.07 mmol) and octanoyl chloride (0.348 g) in toluene (4 mL) by the general procedure. Purification by column chromatography (1:1 EtOAc–petroleum ether) yielded a colorless oily material: 0.478 g (94%); $[\alpha]_D$ +23.0° (*c* 1.0, $CHCl_3$); ^{1}H NMR (Me_2CO-d_6): δ 7.63 (d, 1 H, $J_{1,NH}$ 9.9 Hz, CON*H*), 5.42 (dd, 1 H, $J_{3,4}$ 3.5 Hz, $J_{4,5}$ 1.2 Hz, H-4), 5.39 (dd, 1 H, $J_{1,2}$ 9.3 Hz, H-1), 5.24 (dd, 1 H, $J_{2,3}$ 10.2 Hz, H-3), 5.08 (dd, 1 H, H-2), 4.27 (ddd, 1 H, $J_{5,6a}$ 7.1 Hz, $J_{5,6b}$ 6.5 Hz, H-5), 4.11 (dd, 1 H, $J_{6a,6b}$ 11.2 Hz, H-6b), 4.04 (ddd, 1 H, H-6a); ^{13}C NMR (Me_2CO-d_6): δ 173.53 (NH*C*O), 78.44 (C-1), 72.31, 70.89, 68.41, 67.24 (C-2, C-3, C-4, C-5), 61.14 (C-6). Anal. Calcd for $C_{22}H_{35}NO_{10}$ (473.51): C, 55.80; H, 7.45; N, 2.96. Found: C, 55.71; H, 7.21; N, 2.55.

2,3,6-Tri-O-*acetyl*-*4*-O-*(2,3,4,6-tetra*-O-*acetyl*-β-D-*galactopyranosyl)*-N-*octanoyl*-β-D-*glucopyranosylamine* (**11**).—Prepared from **3** [10,23,24] (0.396 g, 0.60 mmol) and octanoyl chloride (0.195 g) in toluene (2.5 mL) by the general procedure. Purification by column chromatography (1:1 EtOAc–petroleum ether) resulted in a crystalline solid: 0.388 g (85%); mp 71 °C; $[\alpha]_D$ +3.0° (*c* 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 6.08 (d, 1 H, $J_{1,NH}$ 9.4 Hz, CON*H*), 5.34 (dd, 1 H, H-4′), 5.29 (dd, 1 H, $J_{2,3}$ 9.4 Hz, $J_{3,4}$ 9.1 Hz, H-3), 5.20 (dd, 1 H, $J_{1,2}$ 9.4 Hz, H-1), 5.10 (dd, 1 H, $J_{1',2'}$ 7.8 Hz, $J_{2',3'}$ 10.4 Hz, H-2′), 4.93 (dd, 1 H, $J_{3',4'}$ 3.4 Hz, H-3′), 4.81 (dd, 1 H, H-2), 4.43 (d, 1 H, H-1′), 4.39 (m, 1 H, H-6′b), 4.10 (m, 3 H, H-6′a, H-6a, H-6b), 3.85 (m, 1 H, H-5′), 3.74 (m, 2 H, H-4, H-5); ^{13}C NMR (Me_2CO-d_6): δ 173.51 (NH*C*O), 101.43 (C-1′), 78.27 (C-1), 77.03, 75.11, 74.04, 71.96, 71.74, 71.30, 69.90, 67.98 (C-2, C-3, C-4, C-5, C-2′, C-3′, C-4′, C-5′), 63.19, 61.78 (C-6, C-6′). Anal. Calcd for $C_{34}H_{51}NO_{18}$ (761.77): C, 53.61; H, 6.75; N, 1.84. Found: C, 53.67; H, 7.08; N, 1.81.

2-Acetamido-3,4,6-tri-O-*acetyl*-*2-deoxy*-*1*-N-*octanoyl*-β-D-*glucopyranosylamine* (**12**).—Prepared from **4** [23,24] (0.191 g, 0.51 mmol) and octanoyl chloride (0.166 g) in C_6H_6 (2 mL) by the general procedure. Purification by column chromatography (EtOAc) resulted in a crystalline solid: 0.161 g (67%); mp 180 °C; $[\alpha]_D$ −1.0° (*c* 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 6.92 (d, 1 H, $J_{1,NH}$ 8.5 Hz, CON*H*), 6.15 (d, 1 H, $J_{2,NH}$ 8.2 Hz, AcN*H*), 5.11 (dd, 1 H, $J_{3,4}$ 9.5 Hz, $J_{4,5}$ 10.4 Hz, H-4), 5.08 (dd, 1 H, $J_{1,2}$ 9.2 Hz, H-1), 5.04 (dd, 1 H, $J_{2,3}$ 10.0 Hz, H-3), 4.29 (dd, 1 H, $J_{5,6a}$ 4.3 Hz, $J_{6a,6b}$ 12.4 Hz, H-6a), 4.14 (ddd, 1 H, H-2), 4.06 (dd, 1 H, $J_{5,6b}$ 2.1 Hz, H-6b), 3.76 (ddd, 1 H, H-5), 1.93 (s, 3 H, NHCOCH_3); ^{13}C NMR ($CDCl_3$): δ 174.06 (NH*C*O), 79.70 (C-1), 73.39, 73.08, 68.24 (C-3, C-4, C-5), 61.91 (C-6), 53.04 (C-2). Anal. Calcd for $C_{22}H_{36}N_2O_9$ (472.53): C, 55.92; H, 7.68; N, 5.93. Found: C, 55.89; H, 7.61; N, 5.89.

3,4,6-Tri-O-*acetyl*-*2*-*allyloxycarbonylamino*-*2-deoxy*-*1*-N-*octanoyl*-β-D-*glucopyranosylamine* (**13**).—Prepared from **5** (0.360 g, 0.87 mmol) and octanoyl chloride (0.283 g) in toluene (4 mL) by the general procedure. Purification by column chromatography (1:1 EtOAc–petroleum ether) resulted in a crystalline solid: 0.369 g (83%); mp 159 °C; $[\alpha]_D$ +11.0° (*c* 1.0, $CHCl_3$); ^{1}H NMR (Me_2CO-d_6): δ 7.59 (d, 1 H, $J_{1,NH}$ 9.3 Hz, CON*H*), 6.50 (d, 1 H, $J_{2,NH}$ 9.7 Hz, AlocN*H*), 5.88 (m, 1 H, C*H*=CH$_2$), 5.31 (dd, 1 H, $J_{1,2}$ 9.8 Hz, H-1), 5.27 (dd, 1 H, $J_{2,3}$ 9.9 Hz, $J_{3,4}$ 9.9 Hz, H-3), 5.23 and 5.13 (2 dd, 2 H, CH=CH_2), 4.96 (dd, 1 H, $J_{4,5}$ 9.7 Hz, H-4), 4.50 (m, 2 H, CH_2–CH=CH$_2$), 4.25 (dd, 1 H, $J_{5,6a}$ 4.6 Hz, $J_{6a,6b}$ 12.3 Hz, H-6a), 4.02 (dd, 1 H, $J_{5,6b}$ 2.3 Hz, H-6b), 3.82 (ddd, 1 H, H-5), 3.73 (ddd, 1 H, H-2); ^{13}C NMR (Me_2CO-d_6): δ 173.66 (NH*C*O), 157.14 (NH*C*OOAll), 134.30 (*C*H=CH$_2$), 116.97 (CH=*C*H$_2$), 79.67 (C-1), 74.34, 74.04, 69.66 (C-3, C-4, C-5), 65.72 (*C*H$_2$–CH=CH$_2$), 62.91 (C-6), 55.87 (C-2). Anal. Calcd for $C_{24}H_{38}N_2O_{10}$ (514.57): C, 56.02; H, 7.44; N, 5.44. Found: C, 56.27; H, 7.51; N, 5.39.

2,3,4,6-Tetra-O-*benzyl*-N-*octanoyl*-β-D-*glucopyranosylamine* (**14**).—Obtained from **6** [25] (0.200 g, 0.35 mmol) and octanoyl chloride (0.114 g) in CH_2Cl_2 (1.5 mL) for 18 h at rt by the general procedure. Purification by column chromatography (1:2.5 EtOAc–petroleum ether) resulted in a crystalline solid: 0.145 g (63%); mp 127–128 °C (EtOH); $[\alpha]_D$ −12.9° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.32–7.09 (m, 20 H, C_6H_5), 5.46 (d, 1 H, $J_{1,NH}$ 9.3

Hz, CON*H*), 5.08 (dd, 1 H, $J_{1,2}$ 9.1 Hz, H-1), 4.89 and 4.69–4.40 (s and m, 8 H, CH_2Ph), 3.77–3.64 (m, 4 H, H-3, H-4, H-6a, H-6b), 3.52 (m, 1 H, H-5), 3.33 (dd, 1 H, H-2); ^{13}C NMR ($CDCl_3$): δ 173.24 (NH*C*O), 138.47, 138.21, 138.12, 137.91, 128.66–127.81 (C_6H_5), 86.22, 80.08 (C-2, C-3), 78.87, 77.72, 76.34 (C-1, C-4, C-5), 75.84, 75.00, 74.60, 73.62 (CH_2–Ph), 68.19 (C-6). Anal. Calcd for $C_{42}H_{51}NO_6$ (665.84): C, 75.76; H, 7.72; N, 2.10. Found: C, 75.54; H, 7.84; N, 2.14.

2,3,4,6-Tetra-O-*acetyl*-N-*octadecanoyl-β*-D-*glucopyranosylamine* (**15**).—Prepared from **1** [23,24] (1.00 g, 2.68 mmol) and stearoyl chloride (1.06 g, 3.46 mmol) in CH_2Cl_2 (12 mL) for 1 h at rt by the general procedure. Purification by column chromatography (1:1 EtOAc–petroleum ether) resulted in a crystalline solid: 1.23 g (75%); mp 102 °C; $[\alpha]_D$ +8.0° (*c* 1.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 6.16 (d, 1 H, $J_{1,NH}$ 9.4 Hz, CON*H*), 5.31 (dd, 1 H, $J_{2,3}$ 9.5 Hz, $J_{3,4}$ 9.5 Hz, H-3), 5.25 (dd, 1 H, $J_{1,2}$ 8.0 Hz, H-1), 5.06 (dd, 1 H, $J_{4,5}$ 9.9 Hz, H-4), 4.91 (dd, 1 H, H-2), 4.32 (dd, 1 H, $J_{5,6a}$ 4.3 Hz, $J_{6a,6b}$ 12.5 Hz, H-6a), 4.06 (dd, 1 H, $J_{5,6b}$ 1.9 Hz, H-6b), 3.82 (ddd, 1 H, H-5); ^{13}C NMR ($CDCl_3$): δ 173.44 (NH*C*O), 78.14 (C-1), 73.57 (C-5), 72.75 (C-3), 70.65 (C-2), 68.21 (C-4), 61.69 (C-6). Anal. Calcd for $C_{32}H_{55}NO_{10}$ (613.78): C, 62.62; H, 9.03; N, 2.28. Found: C, 62.77; H, 9.16; N, 2.17.

2,3,4,6-Tetra-O-*acetyl*-N-*(5-dodecyl-3-oxanonadecanoyl)-β*-D-*glucopyranosylamine* (**16**).—Prepared from **1** [23,24] (0.146 g, 0.39 mmol) and **27** (0.148 g, 0.30 mmol) in toluene (2.5 mL) for 4 h by the general procedure. Purification by column chromatography (1:2 EtOAc–petroleum ether) resulted in an amorphous solid: 0.177 g (73%); ^{1}H NMR ($CDCl_3$): δ 7.29 (d, 1 H, $J_{1,NH}$ 9.9 Hz, CON*H*), 5.36 (dd, 1 H, $J_{2,3}$ 9.4 Hz, $J_{3,4}$ 9.4 Hz, H-3), 5.25 (dd, 1 H, $J_{1,2}$ 9.6 Hz, H-1), 5.08 (dd, 1 H, $J_{4,5}$ 9.9 Hz, H-4), 5.00 (dd, 1 H, H-2), 4.31 (dd, 1 H, $J_{5,6a}$ 4.4 Hz, $J_{6a,6b}$ 12.5 Hz, H-6a), 4.08 (dd, 1 H, $J_{5,6b}$ 1.9 Hz, H-6b), 3.90 (d, 2 H, NHCOCH_2), 3.82 (m, 1 H, H-5), 3.33 (d, 2 H, CH_2OCH_2CH); ^{13}C NMR ($CDCl_3$): δ 77.70 (C-1), 74.93 (NHCO*C*H_2), 73.68 (C-5), 72.82 (C-3), 70.22 (C-2), 68.18 (C-4), 70.19 (O*C*H_2CH), 61.68 (C-6), 38.10 (OCH$_2$*C*H). Anal. Calcd for $C_{44}H_{79}NO_{11}$ (798.10): C, 66.22; H, 9.98; N, 1.75. Found: C, 66.39; H, 10.16; N, 1.77.

2-Acetamido-3,4,6-tri-O-*acetyl-2-deoxy-1*-N-*(5-dodecyl-3-oxanonadecanoyl)-β*-D-*glucopyranosylamine* (**17**).—Prepared from **4** [23,24] (0.55 g, 1.47 mmol) and **27** (0.412 g, 0.84 mmol) in CH_2Cl_2 (6 mL) for 4 h by the general procedure. Purification by column chromatography (1:1 EtOAc–petroleum ether) resulted in an amorphous solid: 0.545 g (83%); ^{1}H NMR ($CDCl_3$): δ 7.65 (d, 1 H, $J_{1,NH}$ 8.8 Hz, CON*H*), 5.75 (d, 1 H, $J_{2,NH}$ 8.7 Hz, AcN*H*), 5.14 (dd, 1 H, $J_{3,4}$ 9.4 Hz, $J_{4,5}$ 10.2 Hz, H-4), 5.08 (dd, 1 H, $J_{1,2}$ 9.6 Hz, H-1), 5.04 (dd, 1 H, $J_{2,3}$ 9.6 Hz, H-3), 4.29 (dd, 1 H, $J_{5,6a}$ 4.3 Hz, $J_{6a,6b}$ 12.4 Hz, H-6a), 4.22 (ddd, 1 H, H-2), 4.08 (dd, 1 H, $J_{5,6b}$ 2.0 Hz, H-6b), 3.90 (d, 2 H, NHCOCH_2), 3.77 (m, 1 H, H-5), 3.33 (d, 2 H, CH_2OCH_2CH), 1.91 (s, 3 H, NHCOCH_3); ^{13}C NMR ($CDCl_3$): δ 79.85 (C-1), 75.08 (NHCO*C*H_2), 73.71, 73.10, 67.93 (C-3, C-4, C-5), 70.25 (O*C*H_2CH), 61.86 (C-6), 52.92 (C-2), 38.02 (OCH$_2$*C*H), 22.99 (NHCO*C*H_3). Anal. Calcd for $C_{44}H_{80}N_2O_{10}$ (797.12): C, 66.30; H, 10.12; N, 3.51. Found: C, 66.00; H, 10.11; N, 3.53.

2,3,4,6-Tetra-O-*acetyl*-N-*octanoyl-α*-D-*glucopyranosylamine* (**18**).—Prepared from **7** [26] (0.203 g, 0.54 mmol) and octanoyl chloride (0.176 g) in CH_2Cl_2 (2.5 mL) for 16 h by the general procedure. Purification by column chromatography (1:1 EtOAc–petroleum ether) resulted in a 9:1 α/β mixture (0.210 g, 83%) from which the pure α anomer was separated by a second column chromatography (ether) and obtained as a crystalline solid: 0.175 g (70%); mp 124–125 °C (hexane); $[\alpha]_D$ +86.6° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 6.31 (d, 1 H, $J_{1,NH}$ 7.2 Hz, CON*H*), 5.87 (dd, 1 H, $J_{1,2}$ 5.1 Hz, H-1), 5.34 (dd, 1 H, $J_{2,3}$ 9.7 Hz, $J_{3,4}$ 9.4 Hz, H-3), 5.18 (dd, 1 H, H-2), 5.06 (dd, 1 H, $J_{4,5}$ 9.6 Hz, H-4), 4.30 (dd, 1 H, $J_{5,6a}$ 4.7 Hz, $J_{6a,6b}$ 12.3 Hz, H-6a), 4.06 (dd, 1 H, $J_{5,6b}$ 2.3 Hz, H-6b), 3.90 (ddd, 1 H, H-5); ^{13}C NMR ($CDCl_3$): δ 174.25 (NH*C*O), 74.12 (C-1), 70.32, 68.49, 67.98 (C-2, C-3, C-4, C-5), 61.86 (C-6). Anal. Calcd for $C_{22}H_{35}NO_{10}$ (473.51): C, 55.80; H, 7.45; N, 2.96. Found: C, 55.66; H, 7.49; N, 2.99.

2,3,4,6-Tetra-O-*acetyl*-N-*octanoyl-α*-D-*mannopyranosylamine* (**19**(α)).—Prepared

from **8**(α) [27] (0.148 g, 0.40 mmol) and octanoyl chloride (0.130 g) in C_6H_6 (2 mL) for 2 h by the general procedure. Purification by column chromatography (1:1 EtOAc–petroleum ether) resulted in an unseparated 3:1 α/β mixture from which the ^1H and ^{13}C NMR spectra of both anomers could be analyzed separately: 0.052 g (28%); ^1H NMR ($CDCl_3$): δ 6.32 (d, 1 H, $J_{1,NH}$ 8.6 Hz, CON*H*), 5.66 (dd, 1 H, $J_{1,2}$ 4.6 Hz, H-1), 5.26 (dd, 1 H, $J_{2,3}$ 3.4 Hz, $J_{3,4}$ 7.3 Hz, H-3), 5.21 (dd, 1 H, H-2), 5.14 (dd, 1 H, $J_{4,5}$ 6.9 Hz, H-4), 4.40 (dd, 1 H, $J_{5,6a}$ 6.0 Hz, $J_{6a,6b}$ 12.0 Hz, H-6a), 4.24 (dd, 1 H, $J_{5,6b}$ 3.9 Hz, H-6b), 3.98 (m, 1 H, H-5); ^{13}C NMR ($CDCl_3$): δ 172.62 (NH*C*O), 74.67 (C-1), 71.45 (C-5), 69.10 (C-3), 68.40 (C-2), 67.00 (C-4), 61.78 (C-6).

*2,3,4,6-Tetra-*O*-acetyl-*N*-octanoyl-β-*D*-mannopyranosylamine* (**19**β).—Prepared from **8**(β) [27] (0.101 g, 0.27 mmol) and octanoyl chloride (0.088 g) in C_6H_6 (1.5 mL) for 2 h by the general procedure. Purification by column chromatography (1:1 EtOAc–petroleum ether) resulted in an amorphous solid: 0.048 g (37%); ^1H NMR ($CDCl_3$): δ 6.11 (d, 1 H, $J_{1,NH}$ 9.5 Hz, CON*H*), 5.57 (dd, 1 H, $J_{1,2}$ 1.3 Hz, H-1), 5.36 (dd, 1 H, $J_{2,3}$ 3.2 Hz, H-2), 5.23 (dd, 1 H, $J_{3,4}$ 10.0 Hz, $J_{4,5}$ 10.0 Hz, H-4), 5.11 (dd, 1 H, H-3), 4.32 (dd, 1 H, $J_{5,6a}$ 5.0 Hz, $J_{6a,6b}$ 12.5 Hz, H-6a), 4.07 (dd, 1 H, $J_{5,6b}$ 2.0 Hz, H-6b), 3.78 (m, 1 H, H-5); ^{13}C NMR ($CDCl_3$): δ 172.62 (NH*C*O), 75.95 (C-1), 74.30 (C-5), 71.70 (C-3), 70.30 (C-2), 65.20 (C-4), 62.25 (C-6). Anal. Calcd for $C_{22}H_{35}NO_{10}$ (473.51): C, 55.80; H, 7.45; N, 2.96. Found: C, 55.63; H, 7.28; N, 2.91.

N-*Octanoyl*-β-D-*glucopyranosylamine* (**20**).—Compound **9** (0.428 g, 0.90 mmol) dissolved in dry MeOH (20 mL) was treated for 16 h at rt with a catalytic amount of MeONa. The mixture was then neutralized with IR 120 (H^+ form), filtered and evaporated to dryness and compound **20** was obtained as a crystalline solid: 0.248 g (90%); physical properties identical to those reported in the literature [4].

N-*Octadecanoyl*-β-D-*glucopyranosylamine* (**21**).—Obtained from **15** (1.105 g, 1.80 mmol) as described above, as a crystalline solid: 0.698 g (87%); mp 179 °C; $[\alpha]_D$ +8.0° (*c* 1.2, Me_2SO); ^1H NMR (C_5D_5N): δ 9.05 (d, 1 H, $J_{1,NH}$ 8.9 Hz, CON*H*), 5.84 (dd, 1 H, $J_{1,2}$ 9.2 Hz, H-1), 4.38 (dd, 1 H, $J_{6a,6b}$ 11.5 Hz, H-6a), 4.26–4.04 (m, 4 H, H-2, H-3, H-4, H-6b), 3.99 (m, 1 H, H-5); ^{13}C NMR (C_5D_5N): δ 173.97 (NH*C*O), 81.51 (C-1), 79.95, 79.82, 74.82, 72.18 (C-2, C-3, C-4, C-5), 63.06 (C-6). Anal. Calcd for $C_{24}H_{47}NO_6$ (445.63): C, 64.69; H, 10.65; N, 3.14. Found: C, 64.45; H, 10.65; N, 3.09.

N-*Octanoyl*-β-D-*galactopyranosylamine* (**22**).—Obtained from **10** (0.478 g, 1.01 mmol) as described above, as a crystalline solid: 0.283 g (90%); physical properties identical to those reported in the literature [4].

*4-*O*-(β-D-Galactopyranosyl)-*N*-octanoyl-β-D-glucopyranosylamine* (**23**).—Obtained from **11** (0.378 g, 0.50 mmol) as described above, as a crystalline solid: 0.216 g (92%); mp 185 °C (dec); $[\alpha]_D$ +16.0° (*c* 0.5, DMF); ^1H NMR (Me_2SO-d_6): δ 8.00 (d, 1 H, $J_{1,NH}$ 8.9 Hz, CON*H*), 4.70. (dd, 1 H, $J_{1,2}$ 9.2 Hz, H-1), 4.20–3.08 (m, 13 H, lactose ring protons); ^{13}C NMR (C_5D_5N): δ 173.31 (*C*ONH), 107.04 (C-1′), 83.32 (C-1), 82.16, 79.14, 78.90, 78.36, 76.28, 75.17, 73.57, 71.20 (C-2, C-3, C-4, C-5, C-2′, C-3′, C-4′, C-5′), 63.17, 63.10 (C-6, C-6′). Anal. Calcd for $C_{20}H_{37}NO_{11}$ (467.51): C, 51.38; H, 7.98; N, 2.99. Found: C, 51.60; H, 7.95; N, 2.34.

*2-Acetamido-2-deoxy-1-*N*-octanoyl-β-D-glucopyranosylamine* (**24**).—Obtained from **12** (0.288 g, 0.60 mmol) as described above, as a crystalline solid: 0.174 g (82%); mp 165 °C (dec); $[\alpha]_D$ +12.0° (*c* 0.5, DMF); ^1H NMR (C_5D_5N): δ 9.31 (d, 1 H, $J_{2,NH}$ 8.7 Hz, AcN*H*), 9.20 (d, 1 H, $J_{1,NH}$ 8.8 Hz, CON*H*), 5.84. (dd, 1 H, $J_{1,2}$ 9.7 Hz, H-1), 4.71 (dd, 1 H, $J_{2,3}$ 10.0, $J_{3,4}$ 10.0 Hz, H-3), 4.45 (dd, 1 H, $J_{5,6b}$ 2.2, $J_{6a,6b}$ 11.9 Hz, H-6b), 4.34 (dd, 1 H, $J_{4,5}$ 9.4 Hz, H-4), 4.25 (dd, 1 H, $J_{5,6a}$ 5.4 Hz, H-6a), 4.16 (ddd, 1 H, H-2), 3.99 (ddd, 1 H, H-5), 2.16 (s, 3 H, NHCOCH_3); ^{13}C NMR (C_5D_5N): δ 172.54 (NH*C*O), 80.67 (C-1), 80.01, 76.25, 72.02 (C-3, C-4, C-5), 62.46 (C-6), 56.10 (C-2), 23.23 (NHCO*C*H_3). Anal. Calcd for $C_{16}H_{30}N_2O_6$, 0.75 H_2O (359.52): C, 53.39; H, 8.82; N, 7.78. Found: C, 53.88; H, 8.50; N, 7.28.

*2-Acetamido-2-deoxy-1-*N*-(5-dodecyl-3-oxanonadecanoyl)-β-D-glucopyranosylamine* (**25**).—Obtained from **17** (0.438 g, 0.56 mmol) as described above, as an amorphous solid: 0.329 g (90%); ^1H NMR (C_5D_5N, 50 °C): δ

9.33 (d, 1 H, $J_{1,NH}$ 8.2 Hz, CON*H*), 8.90 (d, 1 H, $J_{2,NH}$ 8.4 Hz, AcN*H*), 5.69 (dd, 1 H, $J_{1,2}$ 9.7 Hz, H-1), 4.61 (dd, 1 H, $J_{2,3}$ 10.0 Hz, H-2), 4.40 (dd, 1 H, $J_{5,6b}$ 2.5 Hz, $J_{6a,6b}$ 11.9 Hz, H-6b), 4.29 (dd, 1 H, $J_{3,4}$ 9.3 Hz, H-3), 4.21 (m, 2 H, NHCOCH_2), 4.20 (dd, 1 H, $J_{5,6a}$ 5.4 Hz, H-6a), 4.07 (dd, 1 H, $J_{4,5}$ 9.7, H-4), 3.97 (m, 1 H, H-5), 3.54 (m, 2 H, CH_2OCH_2CH), 2.10 (s, 3 H, NHCOCH_3); ^{13}C NMR (C_5D_5N, 50 °C): δ 171.79, 171.23 (NH*C*O), 81.12 (C-1), 80.25 (C-5), 76.15 (C-3), 75.28 (OCH_2CH), 72.38 (C-4), 71.33 (NHCOCH_2), 62.55 (C-6), 55.79 (C-2), 38.58 (OCH_2CH), 23.19 (NHCOCH_3). Anal. Calcd for $C_{38}H_{74}N_2O_7$, 1.75 H_2O (702.52): C, 64.96; H, 11.11; N, 3.98. Found: C, 65.05; H, 10.66; N, 4.01.

*2-Amino-2-deoxy-1-*N*-octanoyl-β-*D*-glucopyranosylamine* (**26**).—Compound **13** (0.495 g, 0.96 mmol) was O-deacetylated as described above, and the crude solid obtained was redissolved in dry THF (10 mL). N-Deallyloxycarbonylation was then ensured as follows: triphenylphosphine (0.050 g, 0.19 mmol) was added under argon to a soln of $Pd_2(dba)_3$ (0.016 g, 0.017 mmol) in dry THF. After 20 min at rt, the resulting yellow solution was added to the above mixture to which was added dimethylmalonate (0.8 mL, 9.2 mmol). After 16 h at rt, the mixture was evaporated to dryness. Purification by column chromatography (6:3:1 EtOAc–EtOH–water) resulted in a crystalline solid: 0.151 g (52%), mp 150 °C (dec); $[\alpha]_D$ +2.0° (*c* 0.5, DMF); ^{1}H NMR (C_5D_5N): δ 9.47 (d, 1 H, $J_{1,NH}$ 9.0 Hz, CON*H*), 5.83 (dd, 1 H, $J_{1,2}$ 9.2 Hz, H-1), 4.46 (dd, 1 H, $J_{5,6b}$ 2.5 Hz, $J_{6a,6b}$ 11.8 Hz, H-6b), 4.36 (dd, 1 H, $J_{5,6a}$ 4.4 Hz, H-6a), 4.22 (dd, 1 H, $J_{2,3}$ 9.1 Hz, $J_{3,4}$ 8.9 Hz, H-3), 4.04 (m, 2 H, H-4, H-5), 3.34 (m, 1 H, H-2); ^{13}C NMR (C_5D_5N): δ 173.60 (NH*C*O), 81.26 (C-1), 79.60, 78.56, 71.16 (C-3, C-4, C-5), 62.02 (C-6), 57.50 (C-2). Anal. Calcd for $C_{14}H_{28}N_2O_5$, 0.25 H_2O (308.88): C, 54.43; H, 9.29; N, 9.06. Found: C, 54.58; H, 9.31; N, 8.78.

5-Dodecyl-3-oxanonadecanoyl chloride (**27**).—A mixture of 2-dodecyl hexadecanol (2.012 g, 4.90 mmol) and ethyl diazoacetate (555 μL, 5.28 mmol) in CH_2Cl_2 (25 mL) was treated at −20 °C for 3 h with $BF_3{\cdot}Et_2O$ (60 μL, 0.47 mmol). The mixture was then left to reach 0 °C and was extracted with a satd aq soln of $NaHCO_3$, then washed with water. After evaporation to dryness, the mixture was purified by column chromatography (1:20 EtOAc–petroleum ether); ethyl 5-dodecyl-3-oxanonadecanoate (1.24 g, yield 51%) was obtained as a syrup. Anal. Calcd for $C_{32}H_{64}O_3$ (496.82): C, 77.35; H, 12.98. Found: C, 77.12; H, 12.93.

The above material (1.20 g, 2.42 mmol) was treated at 50 °C with a mixture of KOH (1.2 g, 21.4 mmol) and EtOH (10 mL) for 5 h. After evaporation of the solvent, the mixture was redissolved in water (50 mL), extracted with ether (3 × 60 mL) and the organic solution was evaporated to dryness. The mixture was then treated with 1 N aq HCl (20 mL), diluted with water (30 mL) and then re-extracted with ether (3 × 60 mL). After evaporation, the organic solution was purified by column chromatography (EtOAc); 5-dodecyl-3-oxanonadecanoic acid was obtained as a crystalline solid: 1.03 g (91%), mp 38–40 °C. ^{1}H NMR ($CDCl_3$): δ 4.08 (s, 2 H, OCH_2COOH), 3.45 (d, 2 H, OCH_2), 1.61 (m, 2 H, CH_2CH_2O), 1.26 (m, 48 H, CH_2), 0.88 (t, 6 H, CH_3). Anal. Calcd for $C_{30}H_{60}O_3$ (468.78): C, 76.86; H, 12.90. Found: C, 76.93; H, 13.16.

The above derivative (0.882 g, 1.88 mmol) was treated overnight at rt with $SOCl_2$ (1.2 mL, 16.45 mmol). After evaporation to dryness, the crude compound **27** was obtained in quantitative yield and was used as such without further purification.

Acknowledgements

The authors are indebted to Condea Chemie GmbH for a generous gift of 2-dodecylhexadecanol and to Professor G. MacKenzie (University of Hull, UK) for fruitful discussions.

References

[1] V. Maunier, P. Boullanger, D. Lafont, *J. Carbohydr. Chem.*, 16 (1997) 231–235.
[2] E. Brown, R. Joyau, M. Paterne, *Tetrahedron Lett.*, 30 (1977) 2575–2578.
[3] P. Léon-Ruaud, M. Allaimat, D. Plusquellec, *Tetrahedron Lett.*, 32 (1991) 1557–1560.

[4] D. Plusquellec, C. Brenner-Henaff, P. Léon-Ruaud, S. Duquenoy, M. Lefeuvre, H. Wroblewski, *J. Carbohydr. Chem.*, 13 (1994) 737–751.
[5] A. Lubineau, J. Augé, B. Drouillat, *Carbohydr. Res.*, 266 (1995) 211–219.
[6] M. Shiozaki, M. Arai, W.M. Macindoe, T. Mochizuki, T. Wakabayashi, S.I. Kurabata, T. Tatsuta, H. Marda, M. Nishijima, *Bull. Chem. Soc. Jpn.*, 70 (1997) 1149–1161.
[7] M. Masuda, T. Shimizu, *J. Carbohydr. Chem.*, 17 (1998) 405–416.
[8] K. Linek, J. Alföldi, M. Durindova, *Chem. Pap. Chem. Zvesti*, 47 (1993) 247–250.
[9] V. Maunier, P. Boullanger, D. Lafont, Y. Chevalier, *Carbohydr. Res.*, 299 (1997) 49–57.
[10] Z. Györgydeak, L. Szilagyi, H. Paulsen, *J. Carbohydr. Chem.*, 12 (1993) 139–153.
[11] H. Staudinger, J. Meyer, *Helv. Chim. Acta*, 2 (1919) 635–646.
[12] Y.G. Gololobov, L.F. Kasukhin, *Tetrahedron*, 48 (1992) 1353–1406.
[13] J. Barluenga, F. Palacios, *Org. Prep. Proc. Int.*, 23 (1991) 1–65.
[14] E. Zbiral, E. Bauer, *Phosphorus*, 2 (1972) 35–39.
[15] (a) M.D. Bachi, J. Vaya, *J. Org. Chem.*, 44 (1979) 4393–4396. (b) M.D. Bachi, J. Klein, *J. Chem. Soc., Perkin Trans. 1*, (1983) 1925–1928.
[16] (a). T. Inazu, K. Kobayashi, *Synlett*, (1993) 869–870. (b) M. Mizuno, I. Muramoto, K. Kobayashi, H. Yaginuma, T. Inazu, *Synthesis*, (1999) 162–165.
[17] J.J. Garcia-Lopez, F. Santoyo-Gonzalez, A. Vargas-Berengel, *Synlett*, (1997) 265–266.
[18] I. Bosch, A. Gonzalez, F. Urpi, J. Vilarrasa, *J. Org. Chem.*, 61 (1996) 5638–5643.
[19] D.E. Shalev, S.M. Chiacchiera, A.E. Radkovski, E.M. Kosower, *J. Org. Chem.*, 61 (1996) 1689–1701.
[20] H. Paulsen, Z. Györgydeak, M. Friedmann, *Chem. Ber.*, 107 (1974) 1590–1613.
[21] J. Garcia, F. Urpi, J. Vilarrasa, *Tetrahedron Lett.*, 25 (1984) 4841–4844.
[22] F. Urpi, J. Vilarrasa, *Tetrahedron Lett.*, 27 (1986) 4623–4624.
[23] F.D. Tropper, F.O. Andersson, S. Braun, R. Roy, *Synthesis*, (1992) 618–620.
[24] C. Petö, G. Batta, Z. Györgydeak, F. Sztariczskai, *Liebigs Ann. Chem.*, (1991) 505–507.
[25] T. Ogawa, S. Nakabayashi, S. Shibata, *Agric. Biol. Chem.*, 47 (1983) 281–286.
[26] Z. Györgydeak, L. Szilagyi, *Liebigs Ann. Chem.*, (1987) 235–241.
[27] Z. Györgydeak, H. Paulsen, *Liebigs Ann. Chem.*, (1977) 1987–1991.
[28] P. Boullanger, J. Banoub, G. Descotes, *Can. J. Chem.*, 65 (1987) 1343–1348.
[29] L. Szilagyi, Z. Györgydeak, *Carbohydr. Res.*, 143 (1985) 21–41.