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Synthesis and surface-active properties of some alkyl 2-amino-2-deoxy-β-D-glucopyranosides

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Abstract

Several alkyl 2-acetamido-2-deoxy-β-D-glucopyranosides were synthesized using either the oxazoline or the *N*-allyloxycarbonyl procedure. The latter procedure gave better yields with fatty alcohols and cholesterol. The derivatives thus prepared were partly or fully deprotected and their surface-active properties assessed.

Keywords: 2-Amino-2-deoxy-D-glucose; Amphiphiles; Surfactant; ^{14}C-labelled

1. Introduction

A series of alkyl 2-acetamido-2-deoxy-β-D-glucopyranosides has been prepared in order to evaluate their propensity to incorporate into the phospholipidic bilayer membranes of small unilamellar vesicules [1].

A recent report on the surface activities, biodegradabilities, and antimicrobial properties of a few members of the same family has been published [2] which prompted us to report on our own results in this field.

We have chosen 2-amino-2-deoxy-D-glucose as the hydrophilic head of amphiphilic molecules because it meets a number of requirements: (*i*) it is both readily available and often found in compounds involved in biological recognition such as bacterial antigens

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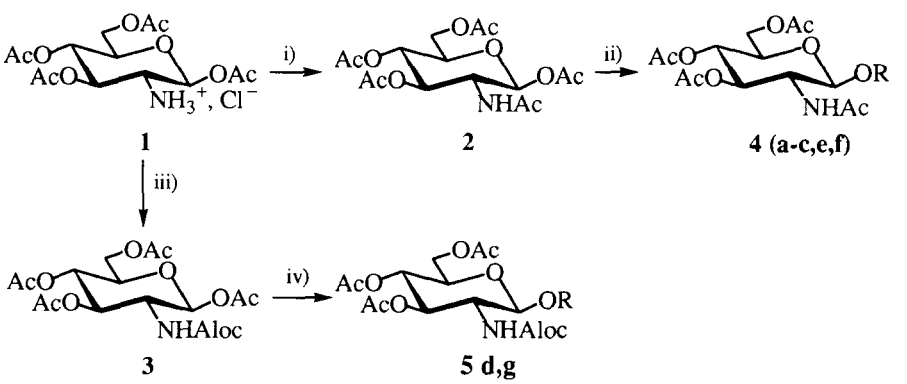
[3], blood group determinants [4], molecules responsible for cell–cell adhesion [5]; (*ii*) several highly stereoselective methods are available for the syntheses of 2-amino-2-deoxyglycosides [6]; (*iii*) the amino functionality allows chemiospecific transformations such as radioactive labelling.

This work is part of a larger programme pertinent to the role of high molecular weight assemblies of carbohydrates in biological recognition (polymers [7], liposomes [1], or amphiphilic molecules that form supramolecular arrangements [8]).

2. Results and discussion

Of the methods described in the literature, only a few afford 2-acetamido-2-deoxy-β-D-glycosides with a high degree of stereoselectivity. The Koenigs–Knorr [9] methodology is restricted to strongly reactive acceptor alcohols and therefore is not applicable to fatty alcohols. Although the "phthalimido procedure" [10] can be used for fatty alcohols, it requires alkaline deprotection of the amino phthaloyl protective group which does not allow convenient access to partly protected *O*- or *N*-acetyl derivatives. The improved oxazoline method [11,12] does not exhibit the aforementioned drawbacks and has the advantage that no deprotection of the amino group after the glycosylation step is necessary; however, poor yields and stereoselectivities are often observed. The allyloxycarbonyl methodology developed in our laboratory [13] conveniently gives *O*-acetyl 2-amino-2-deoxy sugar derivatives; its stereoselectivity is high although a re-*N*-acetylation step is required, as in the phthalimido procedure.

Because of the constraints imposed by the preparation of both acetamido and amino derivatives, we decided to use either the Kiso and Anderson procedure [12] or, where glycosylation was found to be slow, the allyloxycarbonyl method [13].



Scheme 1. i) $(CH_3CO)_2O$, pyr; ii) ROH, $FeCl_3$; iii) ClCOOAll, Na_2CO_3; iv) ROH, TMSOTf. **a**, R = *n*-C_8H_{17}, **b**, R = *n*-C_9H_{19}, **c**, R = *n*-$C_{11}H_{23}$, **d**, R = *n*-$C_{12}H_{25}$, **e**, R = *n*-$C_{14}H_{29}$, **f**, R = *n*-$C_{18}H_{37}$, **g**, R = β-cholesteryl. Abbreviations used: All, CH_2=CH-CH_2–; Aloc, AllOCO–; pyr., pyridine; Me_3SiOTf, trimethylsilyl trifluoromethanesulfonate.

Table 1
^{13}C NMR (δ, ppm) of fully protected glycosides [a]

	C-1	C-2	C-3	C-4	C-5	C-6	NHAc
4a [b]	100.7	54.7	72.6	69.0	71.6	62.4	23.2
4b [b]	100.7	54.8	72.4	68.8	71.7	62.3	23.3
4c [b]	99.7	53.7	71.6	68.0	70.6	61.4	22.2
4e [b]	99.8	53.7	71.6	68.0	70.7	61.4	22.2
4f [b]	100.7	54.9	72.4	68.8	71.7	62.2	23.3
	C-1	C-2	C-3	C-4	C-5	C-6	NHAloc
5d [b]	100.9	56.0	72.2	68.8	71.5	62.1	132.6, 117.4, 65.6
5g [c]	99.6	56.1 [d]	72.1	69.0	71.6	62.3	132.7, 117.7, 65.7

[a] Spectra recorded in $CDCl_3$, with Me_4Si as internal standard. All compounds contained additional signals corresponding to OAc (19.8–20.7).
[b] The spectra contained signals corresponding to the alkyl chains: OCH_2 70.0 ± 0.9; $(CH_2)_n$ 22.2 + 0.5, 25.3 ± 0.4, 28.6–29.2, and 31.4 ± 0.5; CH_3 13.7 ± 0.4.
[c] The spectrum contained signals corresponding to the cholesterol moiety: $CH{=}C$ 122.0, 140.4; quaternary C 36.7, 42.3; CH 28.0, 31.8, 35.8, 50.1, 56.4 [d], 56.7 [d], 79.9; CH_2 20.8, 23.8, 24.3, 28.2, 29.4, 31.9, 36.2, 37.2, 38.8, 39.5, 39.7; CH_3 11.9, 18.7, 19.3, 22.6, 22.8.
[d] Attributions could be reversed between C-2 and CH [d] of the aglycon.

The synthesis of both donors **2** and **3** was achieved starting from the easily available 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranose hydrochloride **1** [14], as reported in the literature [15].

Six aliphatic alcohols ($C_nH_{2n+1}OH$, $8 \leq n \leq 18$), as well as cholesterol, were treated according to the glycosylation procedures outlined in Scheme 1. Starting from donor **2**, the yields of β-glycosides (after chromatographic purification) ranged from 60 to 70% (less than 30% with cholesterol). It is notable that when donor **3** was employed, yields reached 90% with dodecanol and 71% with cholesterol, thus illustrating the effectiveness of this method with alcohols of low reactivity. Both glycosylation reactions were highly stereoselective with the acceptor alcohols chosen for this work. The structure of the derivatives **4** and **5** was determined by ^{13}C and ^{1}H NMR spectroscopy (Tables 1 and 2); assignments were confirmed by selective irradiation of H-2 and by 2D COSY (^{1}H–^{13}C) correlations.

In order to obtain compounds with more pronounced hydrophilic character (NH_2-free) and *N*-acetyl derivatives with unlabelled or a ^{14}C-labelled acetamido function, we achieved the complete and partial deprotection of the glycosides **4** and **5** (Scheme 2).

Derivatives **4 (a–c, e, f)** were either selectively de-*O*-acetylated by the Zemplén procedure [16] to produce the corresponding 2-acetamido derivatives **6 (a–c, e, f)** or fully deprotected by heating for 5 h in 4 M sodium hydroxide to afford compounds **8 (a–c, e, f)**. Yields were almost quantitative using either procedure. Fully deprotected glycosides **8 (d, g)** were obtained from **5 (d, g)** either in one step (heating for 5 h in 4 M sodium hydroxide) or two steps. The latter procedure was achieved by de-*N*-allyloxycarbonylation [13] to give the intermediates **9 (d, g)**, followed by Zemplén de-*O*-acetylation. This proved less successful because of the poor solubility of the amino derivatives **9 (d, g)** in the mixture THF–water. Compounds **8 (d, g)** could, in turn, be obtained from **9 (d, g)** either by *N*-acetylation followed by Zemplén de-*O*-acetylation or by Zemplén

Table 2
^{1}H NMR (δ, ppm; J, Hz) of fully protected glycosides [a]

	H-1	H-2	H-3	H-4	H-5	H-6	H-6′	NH	NHAc
	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6'}$	$J_{5,6}$	$J_{6,6'}$	$J_{2,NH}$	
4a [b]	4.73	3.87	5.34	5.07	3.77	4.28	4.13	6.37	2.09
	8.3	*10.0*	*9.8*	*9.5*	*2.0*	*4.8*	*12.0*	*8.7*	
4b [b]	4.70	3.82	5.33	5.07	3.73	4.27	4.13	5.89	2.09
	8.4	*10.1*	*9.5*	*10.0*	*2.4*	*4.8*	*12.2*	*8.8*	
4c [b]	4.73	3.87	5.35	5.07	3.77	4.28	4.13	6.42	2.09
	8.3	*10.3*	*9.5*	*9.6*	*1.8*	*4.8*	*12.1*	*8.5*	
4e [b]	4.73	3.88	5.34	5.07	3.77	4.28	4.13	6.33	2.08
	8.3	*10.2*	*9.6*	*9.6*	*1.8*	*4.7*	*12.2*	*8.7*	
4f [b]	4.67	3.82	5.30	5.05	3.69	4.23	4.11	5.70	2.09
	8.3	*10.2*	*9.5*	*9.9*	*2.1*	*4.8*	*12.3*	*8.6*	
	H-1	H-2	H-3	H-4	H-5	H-6	H-6′	NH	NHAloc
	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6'}$	$J_{5,6}$	$J_{6,6'}$	$J_{2,NH}$	
5d [b]	4.56	3.63	5.21	5.05	3.72	4.28	4.13	5.12	5.89, 5.25, 4.65
	5.1		*9.6*	*9.6*	*2.3*	*4.9*	*12.2*	*8.7*	
5g [c]	4.82	3.51	5.34	5.04	3.69	4.27	4.11	4.82	5.90, 5.21, 4.47
			9.5	*9.7*	*2.3*	*4.9*	*12.1*		

[a] Spectra recorded in $CDCl_3$, with Me_4Si as internal standard; all compounds contained additional signals corresponding to OAc (1.94 ± 0.01 to 2.05 ± 0.03).
[b] Spectra contained signals corresponding to the alkyl chains: OCH_2 3.47 ± 0.02 and 3.84 ± 0.02; CH_2 1.55 ± 0.03; $(CH_2)_n$ $1.26 \pm 0;02$; CH_3 0.88 ± 0.3).
[c] Spectra contained signals corresponding to the cholesterol moiety: CH=C 5.34; CH and CH_2 3.51, 0.88–2.26; CH_3 0.67, 0.85, 0.88, 0.99.

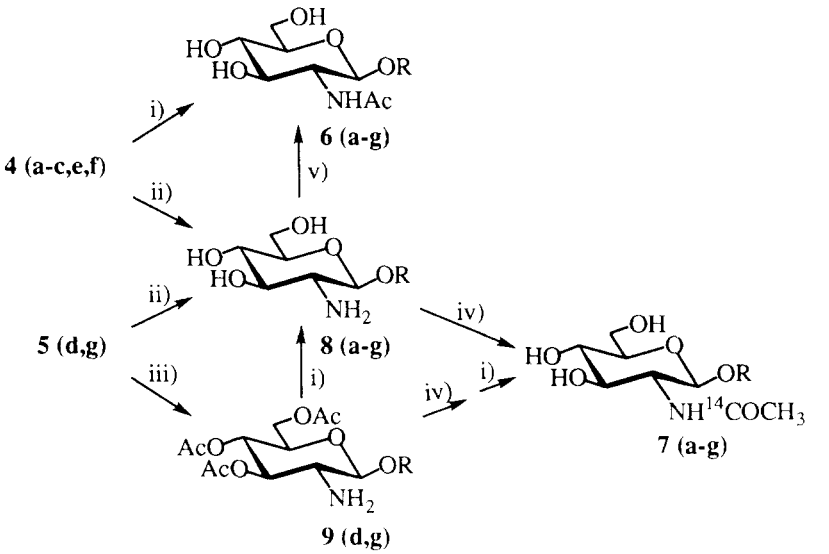
de-*O*-acetylation followed by *N*-acetylation. Both pathways afforded almost quantitative yields.

The ^{14}C-labelled compounds **7 (a–g)** were obtained in the same manner using ^{14}C-labelled acetic anhydride and a slightly different work-up in order to minimize the handling of radioactive effluents.

Partly and fully deprotected derivatives were recovered as crystals that in many cases contained water of hydration, which was difficult to remove completely by heating under vacuum. It is notable that their melting points seem to be very dependent on the amount of hydrated water and therefore often do not correspond with those reported in the literature (e.g. **6a** and **6d**). This observation is in contrast with that found for their fully acetylated derivatives. The amount of hydrated water was determined by the Karl Fischer titration.

The ^{13}C and ^{1}H NMR parameters of the partly and fully deprotected derivatives, in organic solvents and/or water, are reported in Tables 3 and 4, respectively. Assignments were ascertained by 2D COSY (^{1}H–^{13}C) and HMQCGR (heteronuclear multiquantum coherence gradient) and HMBCGR (heteronuclear multibond coupling gradient) correlations.

Krafft temperatures of the above derivatives were determined by slow heating of aqueous mixtures containing 0.01 M, 0.1 M, and 1 M of the amphiphilic compounds, respectively. Surface tensions (γ) and critical micellar concentrations (cmc) were



Scheme 2. i) MeONa, MeOH; ii) 4 M NaOH, 90°C; iii) $Pd(PPh_3)_4$, $CH_2(COOMe)_2$; iv) $(CH_3^{14}CO)_2O$, MeOH; v) $(CH_3CO)_2O$, MeOH. Abbreviations, as in Scheme 1.

determined above this temperature by the ring method of Lecomte du Nouÿ [17]. Results reported in Table 5 show that: (*i*) only the short chains (C_8–C_{10})-NH_2-free derivatives display a Krafft temperature below 25°C; (*ii*) 2-acetamido derivatives are much less hydrophilic than their 2-OH counterparts, as might be anticipated; their water solubility and cmc are lower (e.g. octyl β-D-glucopyranoside is soluble in water at room temperature with a cmc of 17 mM [18]); (*iii*) the solubility of the 2-NH_2 compounds is similar to their 2-OH analogues (e.g. cmc of **8a** is 23 mM versus 17 mM for octyl β-D-glucopyranoside); (iv) the cmc values seem to be relatively unaffected by salt formation (e.g. 23 mM for **8a** and 30 mM for its hydrochloride [2]).

Due to their low cmc values and low solubilities in water, the 2-acetamido derivatives **6 (a–g)** and their ^{14}C-labelled analogues **7 (a–g)** are highly suitable for incorporation into the bilayers of liposomes [1] and for the formation of mixed monolayers. The ability of such amphiphiles to form supramolecular assemblies are under investigation.

3. Experimental

General methods.—Melting points were determined on a Büchi apparatus and are uncorrected. TLC analyses were performed on aluminium 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 min. 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 on a Bruker AC-200 or AM-300 spectrometer

Table 3
^{13}C NMR (δ, ppm) of partly and fully deprotected glycosides [a]

	C-1	C-2	C-3	C-4	C-5	C-6	NHAc
6a [b,f]	102.4	57.5	76.4	72.4	78.4	62.7	23.6
6b [b,f]	102.4	57.6	76.5	72.4	78.5	62.7	23.6
6c [b,f]	102.3	57.5	76.4	72.4	78.4	62.7	23.5
6d [b,f]	102.3	57.6	76.5	72.3	78.4	62.7	23.5
9d [c,f]	104.4	58.1	71.8	69.0	75.5	62.4	—
6e [b,f]	102.4	57.6	76.6	72.5	78.6	62.8	23.6
6g [c,g,h]	99.7	56.3 [i]	74.5 [j]	70.8	75.8 [j]	61.7	23.0
8a [d,f]	103.4	58.1	76.6	71.7	78.0	62.5	—
8b [d,f]	104.4	58.1	77.4	71.6	77.9	62.5	—
8c [d,f]	104.1	58.1	77.1	71.6	77.9	62.6	—
8d [d,f]	103.4	58.1	76.6	71.8	78.2	62.6	—
8e [d,f]	104.0	57.7	76.9	71.4	77.5	62.4	—
8f [e,f]	103.5	56.8	76.1 [j]	70.8	75.8 [j]	62.0	—
8g [e,h]	101.6	56.1 [i]	76.1 [j]	70.6	75.7 [j]	61.8	—

[a] Spectra recorded with Me_4Si as internal standard in: [b] C_5D_5N, [c] $CDCl_3$, [d] CD_3OD, [e] CD_3OD–$CDCl_3$ (1:1), 53°C. [f] Additional signals corresponding to the alkyl chain: OCH_2 70.0 ± 0.8; $(CH_2)_n$ 23.0 ± 0.7, 26.5 ± 0.6, 29.1–30.7 and 32.4 ± 0.7; CH_3 14.0 ± 0.4. [g] Additional signals corresponding to OAc 20.7, 20.8. [h] Additional signals corresponding to the cholesterol moiety: $CH{=}C$ 122.0 ± 0.2, 136.8 ± 3.5; quaternary C 36.1 ± 0.4, 42.3 ± 0.2; CH 27.9 ± 0.2, 31.8 ± 0.1, 35.7 ± 0.2, 50.2 ± 0.1, 56.6 [i], 56.8 ± 0.2 [i], 79.5; CH_2 21.0 ± 0.2, 23.7 ± 0.2, 24.2 ± 0.2, 28.0 ± 0.1, 29.5 ± 0.1, 31.9 ± 0.2, 36.2 ± 0.2, 37.2 ± 0.2, 38.8 ± 0.2, 39.5 ± 0.2 39.8 ± 0.2; CH_3 11.1 ± 0.2, 18.5 ± 0.2, 19.3 ± 0.3, 22.3 ± 0.3, 22.9. [i] Attributions could be reversed between C-2 and CH of the aglycon. [j] Attributions could be reversed between C-3 and C-5.

working at 200 or 300 MHz and 50 or 75.5 MHz respectively, with Me_4Si as the internal chemical shift reference. Elemental analyses were performed 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.

[1,1′-^{14}C]Acetic anhydride was purchased from Sigma (14.3 mCi mmol^{-1}). This compound was adjusted to 0.35 mCi mmol^{-1} by addition of unlabelled acetic anhydride. Dichloromethane was washed twice with water, dried with $CaCl_2$, and distilled from P_2O_5. THF was distilled from a sodium–benzophenone mixture under Ar. CH_2Cl_2 and THF were stored over 4 Å molecular sieves.

Glycosylation reactions.—Procedure A. The glycosylation donor **2** [15] (2.5 g, 6.4 mmol), the acceptor alcohol (8.3 mmol, 1.3 equiv), anhyd ferric chloride (1.35 g, 8.3 mmol), and 4 Å molecular sieves (3.0 g) were dried together under reduced pressure at room temperature. Dry, alcohol-free CH_2Cl_2 (25 mL) was added, the mixture was refluxed for 10 h, and stirred overnight at room temperature. The mixture was filtered through Celite, concentrated, and chromatographed on a silica gel column eluted as further indicated.

Procedure B. A mixture of the glycosylation donor **3** [15] (1.5 g, 3.5 mmol) and the acceptor alcohol (3.5 mmol, 1.0 equiv) was dissolved in dry alcohol-free CH_2Cl_2 (40 mL). The solution was flushed with Ar for 15 min and the temperature was then lowered to −20°C. Trimethylsilyl trifluoromethanesulfonate (635 μL, 3.5 mmol, 1.0 equiv) was introduced through a syringe and the mixture was left stirring under Ar at −20°C for 18

Table 4
^{1}H NMR (δ, ppm; J, Hz) of partly and fully deprotected glycosides [a]

	H-1 $J_{1,2}$	H-2 $J_{2,3}$	H-3 $J_{3,4}$	H-4 $J_{4,5}$	H-5 $J_{5,6'}$	H-6 $J_{5,6}$	H-6′ $J_{6,6'}$	NH $J_{2,NH}$	OH-3 $J_{3,OH}$	OH-4 $J_{4,OH}$	OH-6 $J_{6,OH}$	NHAc
6a [b]	5.02	4.52	4.39	4.17	3.92	4.35	4.53	8.94	7.19	7.27	6.54	2.13
	8.1		*9.2*	*8.5*				*8.4*				
6b [b]	5.00	4.50	4.36	4.16	3.90	4.32	4.51	8.87	7.14	7.31	6.47	2.09
	8.4	*8.4*	*9.5*	*9.6*	*2.4*	*5.7*	*9.5*	*8.5*	*5.2*	*4.5*	*6.3*	
6c [b]	5.02	4.51	4.36	4.17	3.93	4.26	4.51	8.93	7.16	7.26	6.51	2.14
								8.4				
6d [b]	5.03	4.51	4.38	4.17	3.91	4.29	4.51	8.90	7.15	7.32	6.49	2.10
								8.3				
6e [b]	5.04	4.53	4.38	4.19	3.92	4.34	4.53	8.93	7.18	7.36	6.51	2.14
								8.5				
6g [c]	4.57		3.31–3.91 (unresolved)									2.02
	7.1											
8a [d]	4.31	2.65	3.32	3.36	3.30	3.71	3.85	—	—	—	—	—
	8.1	*9.4*			*1.9*	*4.9*	*12.0*					
8b [d]	4.33	2.66	3.34	3.38	3.31	3.71	3.87	—	—	—	—	—
	8.1	*9.3*			*1.4*	*4.7*	*11.9*					
8c [d]	4.24	2.62	3.30	3.31	3.29	3.71	3.89	—	—	—	—	—
	7.9	*9.1*			*1.5*	*4.7*	*11.8*					
8d [d]	4.29	2.63	3.31	3.33	3.30	3.68	3.90	—	—	—	—	—
	8.0	*9.2*			*1.6*	*4.4*	*11.9*					
8e [d]	4.23	2.64	3.28–3.34 (m)			3.72	3.88	—	—	—	—	—
	8.0	*9.2*				*4.6*	*11.8*					
8f [e]	4.15	2.60	3.26	3.26	3.34	3.80	3.75	—	—	—	—	—
	7.9	*8.6*			*1.4*	*4.4*	*11.9*					
8g [e]	4.34	2.63	3.26–3.43 (m)			3.84	3.75	—	—	—	—	—
	8.0	*9.6*			*3.2*	*4.7*	*11.9*					
9d [e,f]	4.44	2.93	5.02	4.98	3.68	4.29	4.11		—	—	—	—
	8.1	*8.3*	*8.3*	*9.5*	*2.4*	*4.8*	*12.2*	*5.5*				

[a] Spectra recorded with Me_4Si as internal standard: the spectra contained signals corresponding to: OCH_2 3.55 ± 0.05, 3.90 ± 0.1; CH_2 1.60 ± 0.04; $(CH_2)_n$ 1.23 ± 0.07; CH_3 0.85 ± 0.05. The spectra were recorded in: [b] C_5D_5N, [c] CD_3OD–$CDCl_3$ (1:1), 53°C, [d] CD_3OD, [e] $CDCl_3$. [f] The spectrum contained additional signals corresponding to OAc 2.01–2.07.

Note. Compound **6f** was of very low solubility in all solvents including Me_2SO and the spectrum could not be recorded.

h. Triethylamine (1 mL, 7.2 mmol) was then added and the mixture allowed to reach room temperature. After evaporation to dryness, the mixture was chromatographed on silica gel.

For de-*O*-acetylation, the 2-acetamido-2-deoxyglucoside **4** (1.0 g) was dissolved in dry MeOH (50 mL) and treated with a catalytic amount of NaOMe in MeOH [16]. After 16 h at room temperature, the mixture was neutralized with Amberlite IR 120 (H^+ form), filtered, and evaporated. Compound **6** was obtained pure in almost quantitative yield and did not require any purification.

For complete deprotection, the fully protected compound (**4** or **6**) or the per-*O*-acetylated derivative **9** (1.0 g) was refluxed with 4 M aq NaOH (30 mL) for 5 h. After

Table 5
Surface-active properties of alkyl 2-amino-2-deoxy-β-D-glucosides [a]

	Krafft temp. (°C)	cmc (mM)	γ [b] (mN m^{-1})	cmc [c] [2] (mM)	γ [b,c] [2] (mN m^{-1})
6a	82–83	1.5 [d]	—		
6b	92–94	—	—		
6c–g	> 100	—	—		
8a	< 20	23	32.5	30	32
8b	< 20	7.0	30.2		
8d	54–55	0.23 [e]	26.9 [e]	2	31
8e–g	> 100	—	—		

[a] Determined by means of surface pressure measurements in pure water at room temperature unless otherwise stated.
[b] Surface pressure at the cmc.
[c] Results reported in the literature [2] for the NH_2, HCl analogues at room temperature.
[d] Determination performed by colorimetric measurement [19], approximate value.
[e] Measurements realized at 60°C.

stirring overnight at room temperature, the mixture was partly neutralized to pH 8–8.5 by addition of concd aq HCl and exhaustively extracted with diethyl ether. Compound **8** was either recovered as an analytically pure material or required purification by column chromatography on silica gel.

For *N*-acetylation with acetic anhydride, **8** (1.0 g) was dissolved in 1:1 MeOH–$CHCl_3$ (60 mL) and treated with a slight excess (1.5–1.8 equiv) of acetic anhydride at room temperature for 12 to 72 h depending on the substrate. Water (5 equiv) was added and the mixture was evaporated to dryness. Purification of compound **6** was achieved by recrystallization from MeOH–$CHCl_3$.

For *N*-acetylation with [1,1'-^{14}C]acetic anhydride, **8** (100 mg) was dissolved in 1:1 MeOH–$CHCl_3$ (6 mL) and treated with a 1.6 equiv of the labelled reagent (0.35 mCi mmol^{-1}) at room temperature for 12 to 72 h depending on the substrate. The solvent and the excess of reagent were then removed under a stream of N_2 at room temperature. The product was then washed by vortexing three times in water (1 mL). Removal of water was effected in the same manner until the supernatant was no longer radioactive. Labelled compounds **7** were shown to be pure by TLC and were dried and used without further purification.

n-*Octyl 2-acetamido-3,4,6-tri*-O-*acetyl-2-deoxy*-β-D-*glucopyranoside* (**4a**).—Procedure A was applied followed by column chromatography (3:1 EtOAc–hexane), 1.74 g (59%). Mp 127°C; $[\alpha]_D$ −10.0° (*c* 2.7, $CHCl_3$); ^{13}C and ^{1}H NMR, Tables 1 and 2. Anal. Calcd for $C_{22}H_{37}NO_9$: C, 57.50; H, 8.12; N, 3.05. Found: C, 57.34; H, 8.43; N, 3.13.

n-*Nonyl 2-acetamido-3,4,6-tri*-O-*acetyl-2-deoxy*-β-D-*glucopyranoside* (**4b**).—Procedure A was applied followed by column chromatography (3:1 EtOAc–hexane), 2.09 g (69%). Mp 119°C; $[\alpha]_D$ −12.8° (*c* 2.6, $CHCl_3$); ^{13}C and ^{1}H NMR, Tables 1 and 2. Anal. Calcd for $C_{23}H_{39}NO_9$: C, 58.33; H, 8.30; N, 2.96. Found: C, 58.26; H, 8.30; N, 2.91.

n-*Undecyl 2-acetamido-3,4,6-tri*-O-*acetyl-2-deoxy-β*-D-*glucopyranoside* (**4c**).—Procedure A was applied followed by column chromatography (3:1 EtOAc–hexane), 1.99 g (62%). Mp 123°C; $[\alpha]_D$ −11.4° (*c* 2.6, $CHCl_3$); ^{13}C and ^1H NMR, Tables 1 and 2. Anal. Calcd for $C_{25}H_{43}NO_9$: C, 59.86; H, 8.64; N, 2.79. Found: C, 59.53; H, 8.63; N, 2.65.

n-*Tetradecyl 2-acetamido-3,4,6-tri*-O-*acetyl-2-deoxy-β*-D-*glucopyranoside* (**4e**).—Procedure A was applied followed by column chromatography (3:1 EtOAc–hexane), 2.16 g (62%). Mp 126°C; $[\alpha]_D$ −10.5° (*c* 2.5, $CHCl_3$); ^{13}C and ^1H NMR, Tables 1 and 2. Anal. Calcd for $C_{28}H_{49}NO_9$: C, 61.86; H, 9.08; N, 2.58. Found: C, 61.55; H, 9.02; N, 2.56.

n-*Octadecyl 2-acetamido-3,4,6-tri*-O-*acetyl-2-deoxy-β*-D-*glucopyranoside* (**4f**).—Procedure A was applied followed by column chromatography (30:1 $CHCl_3$–MeOH) and three recrystallizations from MeOH, 2.03 g (53%). Mp 127–128°C; $[\alpha]_D$ −10.5° (*c* 1.9, $CHCl_3$); ^{13}C and ^1H NMR, Tables 1 and 2. Anal. Calcd for $C_{32}H_{57}NO_9$: C, 64.08; H, 9.58; N, 2.34. Found: C, 64.17; H, 9.19; N, 2.33.

n-*Dodecyl 3,4,6-tri*-O-*acetyl-2-allyloxycarbonylamino-2-deoxy-β*-D-*glucopyranoside* (**5d**).—Procedure B was applied followed by column chromatography (2:1 EtOAc–hexane), 1.76 g (90%). Syrup; $[\alpha]_D$ −0.2° (*c* 2.6, $CHCl_3$); ^{13}C and ^1H NMR, Tables 1 and 2. Anal. Calcd for $C_{28}H_{47}NO_{10}$: C, 60.30; H, 8.50; N, 2.51. Found: C, 60.47; H, 8.56; N, 2.55.

β-Cholesteryl 3,4,6-tri-O-*acetyl-2-allyloxycarbonylamino-2-deoxy-β*-D-*glucopyranoside* (**5g**).—Procedure B was applied followed by column chromatography (30:1 $CHCl_3$–MeOH), 1.88 g (71%). Mp 223–224°C; $[\alpha]_D$ −8.2° (*c* 1.9, $CHCl_3$); ^{13}C and ^1H NMR, Tables 1 and 2. Anal. Calcd for $C_{43}H_{67}NO_{10}$: C, 68.14; H, 8.91; N, 1.85. Found: C, 67.99; H, 8.77; N, 1.70.

n-*Octyl 2-acetamido-2-deoxy-β*-D-*glucopyranoside* (**6a**).—Obtained from **4a** by the de-*O*-acetylation procedure described above, 0.70 g (94%). Mp 131°C (dec.; lit. [2], 175–177°C); $[\alpha]_D$ −19.4° (*c* 2.8, pyridine; lit. [2], −11.0°, *c* 1, MeOH); ^{13}C and ^1H NMR, Tables 3 and 4. Anal. Calcd for $C_{16}H_{31}NO_6 \cdot 0.5\ H_2O$: C, 56.12; H, 9.41; N, 4.09. Found: C, 56.35; H, 9.19; N, 3.98.

n-*Nonyl 2-acetamido-2-deoxy-β*-D-*glucopyranoside* (**6b**).—Obtained from **4b** by the de-*O*-acetylation procedure described above, 0.72 g (98%). Mp 170°C; $[\alpha]_D$ −14.8° (*c* 2.5, pyridine); ^{13}C and ^1H NMR, Tables 3 and 4. Anal. Calcd for $C_{17}H_{33}NO_6$: C, 58.77; H, 9.57; N, 4.03. Found: C, 58.84; H, 9.50; N, 3.90.

n-*Undecyl 2-acetamido-2-deoxy-β*-D-*glucopyranoside* (**6c**).—Obtained from **4c** by the de-*O*-acetylation procedure described above, 0.75 g (98%). Mp 175°C; $[\alpha]_D$ −19.1° (*c* 2.6, pyridine); ^{13}C and ^1H NMR, Tables 3 and 4. Anal. Calcd for $C_{19}H_{37}NO_6 \cdot 0.5\ H_2O$: C, 59.35; H, 9.96; N, 3.64. Found: C, 59.22; H, 9.74; N, 4.03.

n-*Dodecyl 2-acetamido-2-deoxy-β*-D-*glucopyranoside* (**6d**).—Obtained from **8d** by *N*-acetylation as described above, 1.01 g (88%). Mp 161°C (dec.); $[\alpha]_D$ −16.7° (*c* 1.5, pyridine); ^{13}C and ^1H NMR, Tables 3 and 4. Anal. Calcd for $C_{20}H_{39}NO_6 \cdot 0.5\ H_2O$: C, 60.28; H, 10.12; N, 3.51. Found: C, 60.43; H, 10.27; N, 3.82.

n-*Tetradecyl 2-acetamido-2-deoxy-β*-D-*glucopyranoside* (**6e**).—Obtained from **4e** by the de-*O*-acetylation procedure described above, 0.77 g (98%). Mp 150°C (dec.); $[\alpha]_D$ −17.6° (*c* 2.5, pyridine); ^{13}C and ^1H NMR, Tables 3 and 4. Anal. Calcd for $C_{22}H_{43}NO_6 \cdot 0.5\ H_2O$: C, 61.94; H, 10.40; N, 3.28. Found: C, 61.95; H, 10.36; N, 3.33.

n-*Octadecyl 2-acetamido-2-deoxy-β-*D*-glucopyranoside* (**6f**).—Obtained from **4f** by the de-*O*-acetylation procedure described above, 0.76 g (94%). Mp 177–180°C (dec.); $[\alpha]_D$ −18.3° (*c* 0.1, 1:1 $CHCl_3$–MeOH); due to the poor solubility of this derivative in all solvents, no satisfying NMR spectrum could be recorded. Anal. Calcd for $C_{26}H_{51}NO_6 \cdot 0.5\ H_2O$: C, 64.70; H, 10.86; N, 2.90. Found: C, 64.98; H, 11.05; N, 2.54.

*β-Cholesteryl 2-acetamido-2-deoxy-β-*D*-glucopyranoside* (**6g**).—Obtained from **8g** by *N*-acetylation as described above, 0.90 g (88%). Mp 190–195°C (dec.); $[\alpha]_D$ −37.8° (*c* 0.1, $CHCl_3$); ^{13}C and ^1H NMR, Tables 3 and 4. Anal. Calcd for $C_{35}H_{59}NO_6 \cdot H_2O$: C, 69.16; H, 10.11; N, 2.30. Found: C, 69.43; H, 10.27; N, 2.11.

n-*Octyl 2-amino-2-deoxy-β-*D*-glucopyranoside* (**8a**).—Obtained from **4a** by the complete deprotection procedure described above, 0.64 g (98%). Mp 132°C; $[\alpha]_D$ −33.6° (*c* 1.7, MeOH); ^{13}C and ^1H NMR, Tables 3 and 4. Anal. Calcd for $C_{14}H_{29}NO_5 \cdot 0.5\ H_2O$: C, 55.98; H, 10.07; N, 4.66. Found: C, 55.35; H, 9.89; N, 5.09.

n-*Nonyl 2-amino-2-deoxy-β-*D*-glucopyranoside* (**8b**).—Obtained from **4b** by the complete deprotection procedure described above, 0.61 g (89%). Mp 153°C (dec.); $[\alpha]_D$ −32.8° (*c* 1.6, MeOH); ^{13}C and ^1H NMR, Tables 3 and 4. Anal. Calcd for $C_{15}H_{31}NO_5 \cdot H_2O$: C, 55.70; H, 10.28; N, 4.33. Found: C, 55.31; H, 10.00; N, 4.38.

n-*Undecyl 2-amino-2-deoxy-β-*D*-glucopyranoside* (**8c**).—Obtained from **4c** by the complete deprotection procedure described above, 0.63 g (95%). Mp 108–110°C; $[\alpha]_D$ −31.6° (*c* 1.0, MeOH); ^{13}C and ^1H NMR, Tables 3 and 4. Anal. Calcd for $C_{17}H_{35}NO_5$: C, 61.23; H, 10.58; N, 4.20. Found: C, 60.79; H, 10.40; N, 4.12.

n-*Dodecyl 2-amino-2-deoxy-β-*D*-glucopyranoside* (**8d**).—Obtained from **5d** by the complete deprotection procedure described above, 0.51 g (82%). Mp 130°C; $[\alpha]_D$ −29.8° (*c* 2.5, $CHCl_3$); ^{13}C and ^1H NMR, Tables 3 and 4. Anal. Calcd for $C_{18}H_{37}NO_5$: C, 62.22; H, 10.73; N, 4.03. Found: C, 61.71; H, 10.50; N, 4.06.

n-*Tetradecyl 2-amino-2-deoxy-β-*D*-glucopyranoside* (**8e**).—Obtained from **4e** by the complete deprotection procedure described above, 0.60 g (87%). Mp 165–170°C (dec.); $[\alpha]_D$ −22.6° (*c* 0.2, MeOH); ^{13}C and ^1H NMR, Tables 3 and 4. Anal. Calcd for $C_{20}H_{41}NO_5$: C, 63.97; H, 11.00; N, 3.73. Found: C, 63.88; H, 11.06; N, 3.88.

n-*Octadecyl 2-amino-2-deoxy-β-*D*-glucopyranoside* (**8f**).—Obtained from **4f** by the complete deprotection procedure described above, 0.66 g (90%). Mp 119–120°C; $[\alpha]_D$ −25.3° (*c* 0.9, 1:1 $CHCl_3$–MeOH); ^{13}C and ^1H NMR, Tables 3 and 4. Anal. Calcd for $C_{24}H_{49}NO_5 \cdot 0.5\ H_2O$: C, 65.42; H, 11.44; N, 3.18. Found: C, 65.35; H, 10.96; N, 2.90.

*β-Cholesteryl 2-amino-2-deoxy-β-*D*-glucopyranoside* (**8g**).—Obtained from **5g** by the complete deprotection procedure described above, 0.76 g (97%). Mp 216–220°C (dec.); $[\alpha]_D$ −49.2° (*c* 0.9, 1:1 $CHCl_3$–MeOH); ^{13}C and ^1H NMR, Tables 3 and 4. Anal. Calcd for $C_{33}H_{57}NO_5 \cdot 2.5\ H_2O$: C, 66.86; H, 10.54; N, 2.36. Found: C, 66.79; H, 10.12; N, 2.51.

n-*Dodecyl 3,4,6-tri-*O*-acetyl-2-amino-2-deoxy-β-*D*-glucopyranoside* (**9d**).—Triphenylphosphine (142 mg, 0.54 mmol) and palladium bis(dibenzylidene acetone) (54.6 mg, 0.095 mmol) were reacted under Ar in oxygen-free THF (10 mL) for 15 min. The *N*-allyloxycarbonyl glucoside **5d** (1.5 g, 2.7 mmol) and dimethyl malonate (1.8 mL) dissolved in oxygen-free THF (10 mL) were then added and the mixture was left stirring under Ar, at room temperature, for 24 h. After evaporation to dryness, the mixture was chromatographed on silica gel (2:1 EtOAc–hexane), 1.1 g (85%). Syrup; $[\alpha]_D$ +2.5° (*c*

2.5, $CHCl_3$); ^{13}C and ^1H NMR, Tables 3 and 4. Anal. Calcd for $C_{24}H_{43}NO_8$: C, 60.87; H, 9.15; N, 2.97. Found: C, 60.62; H, 9.13; N, 2.86.

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