Carbohydrate Research 412 (2015) 28–33

Contents lists available at ScienceDirect

Carbohydrate Research

journal homepage: www.elsevier.com/locate/carres

Rapid communication

Alkyl-imidazolium glycosides: non-ionic—cationic hybrid surfactants from renewable resources

Abbas Abdulameer Salman*, Mojtaba Tabandeh, Thorsten Heidelberg*, Rusnah Syahila Duali Hussen, Hapipah Mohd Ali

Chemistry Department, Faculty of Science, University of Malaya, 50603 Kuala Lumpur, Malaysia

ARTICLE INFO

Article history:
Received 3 April 2015
Accepted 26 April 2015
Available online 5 May 2015

Keywords:
Emulsion
Cationic surfactant
Hexagonal phase
Self-assembly
Surface tension

ABSTRACT

A series of surfactants combining carbohydrate and imidazolium head groups were prepared and investigated on their assembly behavior. The presence of the imidazolium group dominated the interactions of the surfactants, leading to high CMCs and large molecular surface areas, reflected in curved rather than lamellar surfactant assemblies. The carbohydrate, on the other hand, stabilized molecular assemblies slightly and reduced the surface tension of surfactant solutions considerably. A comparative emulsion study discourages the use of pure alkyl imidazolium glycosides owing to reduced assembly stabilities compared with APGs. However, the surfactants are believed to have potential as component in carbohydrate based surfactant mixtures.

1. Introduction

Over the last decades sugar based surfactants[1–7] have gained both scientific and economic interest owing to increasing concerns in biocompatibility[8] and sustainable resources.[9,10] Application fields include emulsifiers[11,12], detergents[2] as well as medical delivery systems.[13,14] Most investigations focus on non-ionic surfactants, which utilize the polyhydroxy-character of carbohydrates as hydrophilic surfactant antipode. While non-ionic surfactants provide advantages with respect to an enhanced assembly stability, e.g. towards pH-changes or electrolytes,[15] this insensitivity restricts the application of certain formulation methods, which utilize medium induced phase changes, like the pH-mediated transition of fatty acid micelles into liposomes.[16] Unfortunately, carbohydrate surfactants involving ionic charges have not been investigated extensively. Typical examples are anionic alkyl glycuronates, i.e. salts of oxidized glycosides with a carboxylic acid,[17–19] on the one hand, and cationic N-alkylated amino-derivatives of sugars on the other. Chemical instability[20,21] limits the application of glycosylamines[22] and their subsequent ammonium ions,[23] which resemble the potentially most easily accessible sugar based cationic surfactants. Instead acylated products[24,25] and derivatives of the corresponding reduced glycamines, or amino-polyols,[26–28] have gained more interest.

Both cationic and anionic surfactants are principally susceptible for medium triggered assembly changes. However, the presence of a carbohydrate in the surfactant head group should reduce the impact of the latter. Therefore ionic carbohydrate surfactants are expected to exhibit reasonable assembly stability despite their susceptibility for medium-induced changes. This makes them potentially interesting candidates for medical delivery systems. In view of excess negative charges on biological cell membranes[29,30] cationic surfactants are likely mediating better interactions of a carrier with a cellular target; hence they are favored over anionic surfactants. The introduction of a positive charge, referring to an amino- or ammonium group, on a carbohydrate can be achieved in various ways. Constraints, however, arise from economic considerations. While glycamines provide the most direct access, the resulting open chain structure does not match nature-typical carbohydrate patterns. This has implications on molecular interactions based on the hydrogen bonding network in sugar-based surfactant assemblies and potentially affects the bio-recognition of a drug carrier, thus disfavoring the approach. The preparation of a glycolipid[19] and subsequent introduction of an amino-group,[31,32] on the other hand, requires a multi-step synthesis, which renders it non-economic. In order to reduce the number of required chemical transformations and optimize the production efficiency, an

* Corresponding authors.
E-mail addresses: abbass@um.edu.my (A.A. Salman), heidelberg@um.edu.my (T. Heidelberg).

http://dx.doi.org/10.1016/j.carres.2015.04.022
0008-6215/

approach comprising of glycosylation and subsequent amination was targeted, where the latter not only introduces the cation to the sugar but the hydrophobic domain as well. This approach reflects the previously reported strategy for the synthesis of alkyl triazole glycosides (ATG).[33]

2. Results and discussion

2.1. Synthesis

The surfactants were synthesized in a 3-stage process, involving glycosylation of bromoethanol,[34] its subsequent use for the alkylation[35] of mono-N-alkylated imidazoles[36] and a final deprotection step.[37] The synthetic scheme is displayed in Fig. 1.

Alkyl-imidazolium glycoside surfactants (AIGs) with C_8 (**6a**), C_{12} (**6b**) and C_{16} (**6c**) hydrocarbon chains were obtained in practically identical high yields, as shown in Table 1. This indicates high efficiency and suggests a wide application range for the surfactant synthesis. The overall yield, however, was limited by the carbohydrate precursor **4**,[34] which's preparation was not yield optimized. The use of xylene as solvent instead of the more common toluene[35] enabled a higher reaction temperature and considerably sped up the conversion of **4** into the surfactant precursor **5**. Despite the short reaction time the conversion was not affected by the chain length.

2.2. Physical properties

In order to rationalize the physical behavior of AIGs their surfactant properties were compared with those of the corresponding alkyl glycosides, **7** (resembling APG surfactants), as well as their methyl-imidazolium counterparts, **8**. The structures of the surfactants are displayed in Fig. 2, while their behavior is summarized in Table 2.

Table 1
Synthesis of glycosyl imidazolium surfactants

Compd	Alkyl chain	Yield (basis: **4**)
6a	C_8H_{17}	91%
6b	$C_{12}H_{25}$	91%
6c	$C_{16}H_{33}$	92%

The investigation on Krafft and cloud points indicated no temperature limitations for the use of the surfactants **6**; none of the compound exhibited clouding behavior at high temperature, while all enabled the formation of micelles below room temperature. This behavior is in agreement with the corresponding methyl-imidazolium chlorides,[38] which were referred to in lieu of published data for the corresponding bromides **8**. However, similar behavior of quaternary ammonium surfactants with chloride and bromide ions[40] justifies this reference. In contrast, APG models **8** with alkyl chains above 10 carbon atoms exhibit Krafft points above room temperature, which moreover, increase upon extension of the alkyl chain.[39] The lower Krafft temperatures for **6** indicate increasing water solubility upon introduction of the imidazolium ion. The latter is also reflected in significantly increased CMC values for the surfactants **6** with respect to the APG-analogs **7**.[40,41] However, the water solubility of AIGs remains far below that of the imidazolium surfactants **8**,[42,43] thus proposing dominance of the sugar over the cation with respect to interactions with water. This dominance is mirrored in the surface tension of solutions above the CMC, which resemble those of the APG-models[42,44] rather than the imidazolium surfactants.[44,45] A similar behavior has previously been reported for ester-linked cationic carbohydrate surfactants involving a head group comprising of a sugar and an ammonium salt.[45]

Contact penetration experiments with water, an example is shown in Fig. 3, only indicated the presence of a hexagonal phase for compounds **6**. It was assumed to be the normal H_I phase. The exclusive formation of this phase is in contrast to the previous reports on the behavior of alkyl glycosides, for, which a diversity of phases was found in case of the C_8 surfactant **7a**,[46–48] while only lamellar lyotropic phases were reported for the higher homolog **7b**.[49] In order to understand the different lyotropic phase behavior of **6** and **7**, the molecular surface area of compound **6b** was determined based on the slope for the concentration depending region of the surface tension plot displayed in Fig. 4.

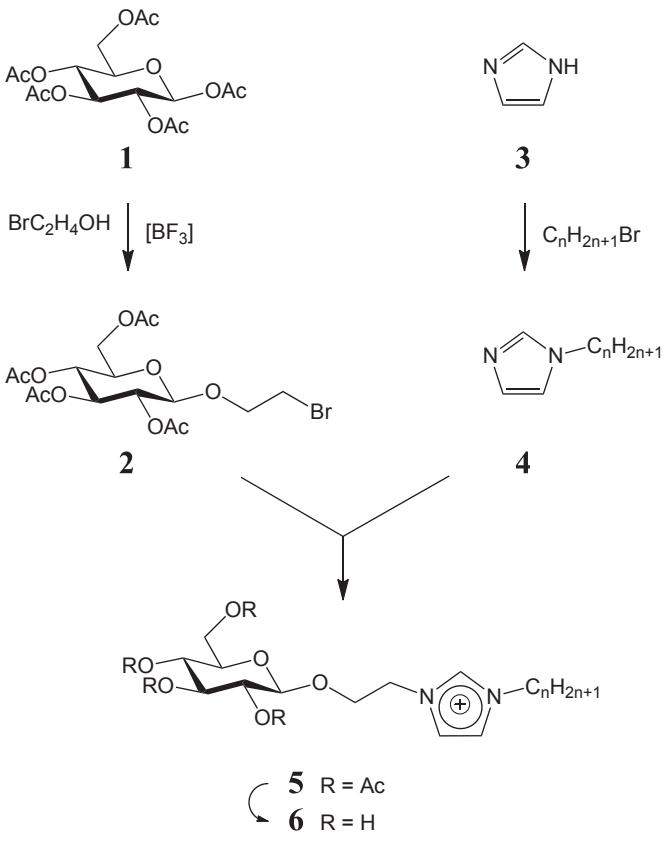

Fig. 1. Synthetic scheme for glycosyl imidazolium surfactants.

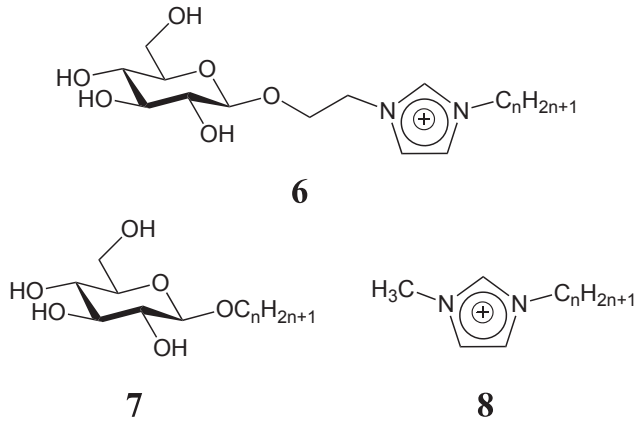

Fig. 2. Structure comparison of surfactants.

Table 2
Surfactant properties in comparison

Compd	Alkyl chain	T_K [°C]	T_C [°C]	CMC [mmol L^{-1}]	γ_{CMC} [mN m^{-1}]	Ref.
6a	C_8H_{17}	<10	>90	16	24.8	
6b	$C_{12}H_{25}$	<10	>90	1.5	25.5	
6c	$C_{16}H_{33}$	<10	>90	0.31	39.8	
7a	C_8H_{17}	N/A	>80	6.5	30.0	[39,40]
7b	$C_{12}H_{25}$	37.5	>80	0.19	~30.5	[39,41,42]
8a	C_8H_{17}	—	—	170/121	41.3	[42]
8b	$C_{12}H_{25}$	—	—	9.0/4.3	37.2	[42,43]
8c	$C_{16}H_{33}$	—	—	0.8	41	[43]

Form the Gibbs adsorption isotherm the surface excess concentration can be calculated according to Eq. 1,[50]

$$\Gamma_{max} = -\frac{10^{-3}}{2.303nRT}\left(\frac{\partial\gamma}{\partial \log C}\right)_{max T}, \quad (1)$$

where $[\partial\gamma/\partial \log c]$ is the surface tension slope, T is the absolute temperature, R is the universal gas constant (8.314 J mol^{-1} K^{-1}), and n is the number of surfactant species at the interface (here n=1). The minimum area per surfactant molecule A_{min} is obtained by applying Eq. 2,

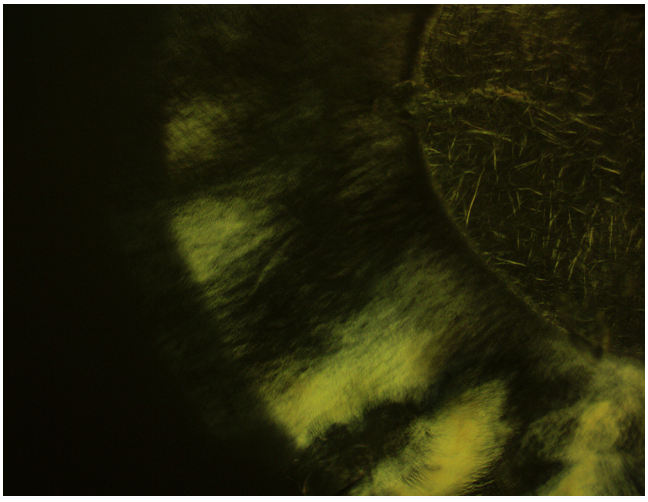

Fig. 3. OPM image for water penetration of **6c** showing the hexagonal H_I phase.

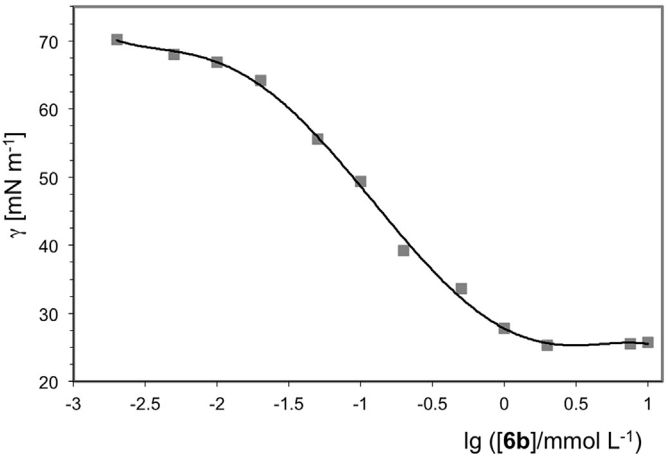

Fig. 4. Surface tension behavior of AIG **6b**.

$$A_{min} = \frac{10^{20}}{N\Gamma_{max}}, \quad (2)$$

where N is Avogadro's number (6.022×10^{23} mol^{-1}). The application of Eqs. 1 and 2 on the graph displayed in Fig. 4 led to a molecular surface area of 53 $Å^2$ for compound **6b**. This substantially exceeds a value of below 40 $Å^2$, reported for APG analog **7b** and its homologs.[51,52] In fact, the value gets near the 63 $Å^2$, found for octyl β-glucoside in a hexagonal lyotropic phase,[53] and is in line with the exclusive formation of curved assembly structures for sugar-based Y-shape surfactants, for, which similar molecular surface areas were reported.[54] It is assumed that the expansion of the hydrophilic domain by the hydrated imidazolium ion and repulsive charge interactions are responsible for the increased surface area and the related disappearance of the lamellar phase for the AIGs **6**.

Surface tensions of micellar solutions below 30 mN m^{-1} characterize AIGs with chain lengths of up to 12 carbon atoms as good surface active surfactants, thus suggesting their application as emulsifier. In order to evaluate the emulsifying abilities of **6**, oil-in-water emulsions were prepared and the stability of the latter was compared to formulations based on structurally related surfactants **7** and **8**. Due to accessibility constraints, surfactants with different alkyl chain length were applied as reference, i.e. **7b** and **8c**. However, the investigation of a wide range of chain lengths for **6** enables a differentiation of head group and chain effects. The results are summarized in Table 3.

AIGs are less effective emulsifiers for W/O systems than APGs, as indicated by the relative emulsion stabilities of **6b** and **7b**. The emulsion stability depends strongly on a balance of the surfactant antipodes, i.e. the hydrophilic chain and the hydrophobic combined sugar-imidazolium head group. Among the investigated AIGs the C_{12}-surfactant **6b** was most effective. This is in line with previous reports on the behavior of non-ionic surfactants, indicating enhanced emulsion stability upon increasing the alkyl chain length from C_7 to C_{10},[55] but reduced interfacial activity upon further increase from C_{12} to C_{18}.[56] Both longer and shorter alkyl chain lengths led to a significant drop of the emulsion stability. The C_8-surfactant **6a** was particularly instable, as indicated by complete phase separation within a single day. The emulsion behavior of **6c** and **8c** were almost identical. However, a comparison of the turbidity of the water phase after 4 days revealed a slightly higher separation for the pure imidazolium surfactant **8c**. The observations suggest dominance of ionic interactions for the surfactant at the water-oil

Table 3
Emulsion stability (W/O)

Compd	Visible phase separation	Full phase separation
6a	3 h	<1 d
6b	2–3 d	>14 d
6c	1–2 d	> 4 d
7b	>14 d	>30 d
8c	1–2 d	> 4 d

interface with only minor impact of the carbohydrate. It is believed that repulsive charge interactions of surfactant head groups destabilize assemblies at the water-oil interface, thus giving rise to a phase separation. Unfortunately, this discourages the use of pure AIGs as W/O-emulsifier.

3. Conclusion

Alkyl imidazolium glycosides are easily accessible cationic-nonionic hybrid surfactants. Although the applied synthetic scheme suffers of high production costs owing to the number of reaction steps, the latter may be substantially reduced by application of a Fischer glycosylation approach similar to previously reported ATG surfactants.[33] The cationic imidazolium ion dominates the surfactants, assembly behavior, both in presence and absence of an oil phase. However, the presence of the carbohydrate enables a significant reduction of the surface tension. While charge dominated surfactant interactions discourage the application of pure AIGs for both delivery systems and emulsions, a stabilizing effect of the sugar on the assembly behavior suggests potential for combinations with non-ionic or anionic sugar based surfactants.

4. Experimental

4.1. General methods

Starting materials and reagents of synthesis grade and solvents of AR grade were obtained from various commercial sources and used without prior treatment. Purification of the surfactants and their precursors applied extraction, crystallization and distillation but avoided chromatography. All surfactants were NMR spectroscopically analyzed (^{1}H and ^{13}C, recorded on 400 MHz spectrometers) in both acetylated and deprotected form, and their identities were confirmed by high-resolution mass spectrometry based on electrospray ionization. The ^{1}H NMR spectra indicated high chemical and diastereomeric purity of the surfactants. Physical investigation applied distilled water with a conductivity of 1.1±0.1 μS cm^{-1}.

Cloud points (T_C) were determined by heating clear surfactant solutions (20 mmol L^{-1} for C_8, 7.5 mmol L^{-1} for C_{12} and 1 mmol L^{-1} for C_{16}) slowly up to 100 °C while monitoring for visible changes. Krafft points (T_K) were estimated based on the behavior of these solutions to cooling (4 °C) for several days. The lyotropic phase behavior of the surfactant was investigated by optical polarizing microscopy using the contact penetration technique.[57,58] Systematic surface tension measurements based on the Du Nouy ring method were applied to study the surfactants, aggregation and surface behavior. CMCs were determined from a logarithmic display of the surface tension against the surfactant concentration as intersection of linear regressions for the concentration depending region and the plateau at high surfactant concentration.

Emulsions, containing 3.8 g water and 0.2 g methyl laurate, were prepared based on a surfactant content of 0.5% m/m. Samples were homogenized with an IKA T10 basic mixer for 2 min at maximum speed (~14,000 rpm) in 5 mL vials and subsequently stored at room temperature and monitored on phase separation over a period of a few weeks.

4.1.1. Synthesis of base-glycoside[34]

β-Glucose pentaacetate **1** (6.00 g, 15 mmol) and bromoethanol (2.1 g, 17 mmol) were dissolved in CH_2Cl_2 (50 mL) and treated with $BF_3\times OEt_2$ (3.3 g, 23 mmol). The reaction was stirred at rt for 3 h and then washed with a satd $NaHCO_3$ (aq) and water. The organic layer was dried over $MgSO_4$ and concentrated. The product was crystallized from ethanol to give **2** as colorless crystals (3.85 g, 55%).

4.1.2. Synthesis of alkylated imidazoles[36]

A solution of imidazole **3** (30 mmol) in THF (60 mL) was treated with NaOH (25 mL, 40% aq) and the alkyl bromide (30 mmol), and the reaction was refluxed overnight. The solvent was evaporated and the crude reaction mixture was extracted with CH_2Cl_2 against water. The organic layer was washed with water, dried over $MgSO_4$ and concentrated. The final product was distilled under vacuum (~5 mbar) to provide **4** as yellow oily liquid in 80–85% yield.

4.1.3. Synthesis of alkyl-imidazolium glycoside

A solution of 2-bromoethyl glucoside **2** (1.1 mmol) and the alkylated imidazole **4** (3.3 mmol) in xylene (2 mL) was heated to 125 °C for 1 h. The solvent was evaporated and the crude product was taken up in MeCN (10 mL) and extracted 4 times with hexane (60 mL) to remove remaining imidazole **4**. The acetonitrile phase was concentrated under reducing pressure to provide the desired product **5** as a pale yellow syrup in ~95% yield.

4.1.4. Deacetylation of surfactant precursors

The surfactant precursor **5** (0.5 mmol) was dissolved in methanol (30 mL) and treated with a catalytic amount of sodium methoxide to obtain a basic medium (pH~9). The mixture was stirred for overnight at room temperature and subsequently neutralized with Amberlite IR 120 (H^+). Evaporation of the solvent furnished the final surfactant **6** in ~95% yield.

4.2. 1-(2-β-D-Glucopyranosyloxyethyl)-3-octyl-imidazolium bromide (*6a*)

4.2.1. 1-Octyl–3-[2-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyloxy)-ethyl]-imidazolium bromide (*5a*)

Compound **2** (0.50 g, 1.1 mmol) and **4a** (0.60 g, 3.3 mmol) were reacted in xylene (2 mL) according to general procedure 4.1.3 to provide **5a** (0.66 g, 95%) as pale yellow syrup. $[\alpha]_D^{25}$ −25 (*c* 0.1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.17 (s, N=*CH*–N), 7.57 (s, CH=N–*CH*), 7.20 (s, CH–*CH*–N), 5.18 (dd~t, H-3), 5.00 (dd~t, H-4), 4.92 (dd, H-2), 4.80–4.65 (m, 2H, CH_2N), 4.60 (d, H-1), 4.27–4.20 (m, 4H, H-6a, CH_2O-a, α-CH_2), 4.12 (dd~bd, H-6b), 4.07 (ddd~dt, CH_2O-b), 3.77 (ddd, H-5), 2.07, 2.00, 1.97 (3 s, 3+6+3H, Ac), 1.90 (m_c, 2H, β), 1.37–1.20 (m, 10H, bulk-CH_2), 0.85 (t, 3H, CH_3); $^3J_{1,2}$=8.0, $^3J_{2,3}$=9.5, $^3J_{3,4}$=9.5, $^3J_{4,5}$=10.0, $^3J_{5,6a}$=5.0, $^3J_{5,6b}$=1.5, $^2J_6$=12.0 Hz. ^{13}C NMR (100 MHz, $CDCl_3$): 170.51, 169.85, 169.65, 169.46 (CO), 137.17 (N=*CH*–N), 123.83 (CH=N–*CH*), 120.64 (CH–*CH*–N), 100.49 (C-1), 72.28 (C-3), 72.01 (C-5), 71.16 (C-4), 68.14 (C-2), 68.11 (CH_2O), 61.66 (C-6), 50.17 (α-CH_2), 49.87 (CH_2N), 31.56 (ω-2), 30.05, 28.91, 28.80 (bulk-CH_2), 26.21 (γ), 22.47 (ω-1), 20.79, 20.76, 20.49, 20.47 (Ac) 13.96 (ω).

4.2.2. 1-(2-β-D-Glucopyranosyloxyethyl)-3-octyl-imidazolium bromide (*6a*)

Compound **5a** (0.35 g, 0.55 mmol) was dissolved in methanol (30 mL) and treated with a catalytic amount of sodium methoxide according to general prodecure 4.1.4 to furnish **6a** (0.29 g, 96%) as pale yellow syrup. $[\alpha]_D^{25}$ +18 (*c* 0.1, MeOH). ^{1}H NMR (400 MHz, CD_3OD): δ 7.72 (d~bs, CH=N–*CH*), 7.66 (d~bs, CH–*CH*–N), 4.56–4.43 (m, 2H, CH_2N), 4.37 (d, H-1), 4.25 (t, 2H, α-CH_2), 4.20 (ddd~dt, CH_2O-a), 4.04 (ddd, CH_2O-b), 3.91 (dd, H-6a), 3.67 (dd, H-6b), 3.40 (dd~t, H-3), 3.36–3.30 (m, H-5), 3.28 (dd~t, H-4), 3.20 (dd~t, H-2), 1.91 (p, 2H, β-CH_2), 1.44–1.26 (m, 10H, bulk-CH_2), 0.92 (t, 3H, CH_3); $^3J_{1,2}$=8.0, $^3J_{2,3}$=9.0, $^3J_{3,4}$=9.0, $^3J_{4,5}$=9.5, $^3J_{5,6a}$=1.5, $^3J_{5,6b}$=5.5, $^2J_{6,6'}$=12.0 Hz. ^{13}C NMR (100 MHz, CD_3OD): δ 138.2 (N–*C*=N), 122.84 (CH=N–*CH*), 121.94 (CH–*CH*–N), 103.11 (C-1), 76.70, 76.59 (C-3, C-5), 73.54 (C-2), 70.15 (C-4), 67.33 (CH_2O), 61.23 (C-6), 49.61, 49.51 (α,CH_2N), 31.67 (ω-2), 29.72 (β), 28.82, 28.67 (bulk-CH_2), 25.91 (γ), 22.26 (ω-1), 13.02 (ω). HRMS: Calcd for

$C_{19}H_{35}N_2O_6$ 387.2495, 388.2529 (21%); found 387.2485, 388.2514 (21%).

4.3. 1-(2-β-D-Glucopyranosyloxyethyl)-3-dodecyl-imidazolium bromide (**6b**)

4.3.1. 1-Dodecyl−3-[2-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyloxy)-ethyl]-imidazolium bromide (**5b**)

Compound **2** (0.5 g, 1.1 mmol) and **4b** (0.8 g, 3.3 mmol) were reacted in xylene (2 mL) according to general procedure 4.1.3 to provide **5b** (0.73 g, 96%)as pale yellow syrup. $[\alpha]_D^{25}$ −13 (*c* 0.1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.17 (s, N═*CH*–N), 7.59 (s, CH═N–*CH*), 7.21 (s, CH–*CH*–N), 5.20 (dd~t, H-3), 5.02 (dd~t, H-4), 4.94 (dd, H-2), 4.84–4.68 (m, 2H, CH_2N), 4.63 (d, H-1), 4.30–4.20 (m, 4H, H-6a, CH_2O-a, α-CH_2), 4.16 (dd~bd, H-6b), 4.10 (ddd~bdt, CH_2O-b), 3.80 (ddd, H-5), 2.08, 2.02, 1.99 (3 s, 3+6+3H, Ac), 1.92 (p, 2H, β-CH_2), 1.40–1.20 (m, 18H, bulk-CH_2), 0.87 (t, 3H, CH_3);$^3J_{1,2}$=8.0, $^3J_{2,3}$=9.0, $^3J_{3,4}$=9.5, $^3J_{4,5}$=9.5, $^3J_{5,6a}$=5.0, $^3J_{5,6b}$=1.5, $^2J_6$=12.0 Hz. ^{13}C NMR (100 MHz, $CDCl_3$): 170.57, 169.91, 169.71, 169.53 (CO), 137.23 (N═*CH*–N), 123.89 (CH═N–*CH*), 120.69 (CH–*CH*–N), 100.55 (C-1), 72.35 (C-3), 72.07 (C-5), 71.22 (C-4), 68.20 (C-2, CH_2O), 61.72 (C-6), 50.23 (α), 49.94 (CH_2N), 31.62 (ω-2), 30.11, 29.55 (2×), 29.45, 29.34, 29.29, 28.93 (bulk-CH_2), 26.29 (γ), 22.65 (ω-1), 20.85, 20.82, 20.55, 20.53 (Ac) 14.0 (ω).

4.3.2. 1-(2-β-D-Glucopyranosyloxyethyl)-3-dodecyl-imidazolium bromide (**6b**)

Compound **5b** (0.37 g, 0.53 mmol) was dissolved in methanol (30 mL) and treated with a catalytic amount of sodium methoxide according to general procedure 4.1.4 to furnish **6b** (0.26 g, 95%) as pale yellow syrup. $[\alpha]_D^{25}$ +20 (*c* 0.1, MeOH). ^{1}H NMR (400 MHz, CD_3OD): δ 7.74 (d, CH═N–*CH*), 7.68 (d, CH–*CH*–N), 4.58–4.45 (m, 2H, CH_2N), 4.38 (d, H-1), 4.26 (t, 2H, α-CH_2), 4.25–4.19 (m, CH_2O-a), 4.05 (ddd, CH_2O-b), 3.90 (dd~bd, H-6a), 3.67 (dd, H-6b), 3.39 (dd~t, H-3), 3.37–3.31 (m, H-5), 3.28 (dd~t, H-4), 3.20 (dd~t, H-2), 1.92 (p, 2H, β-CH_2), 1.38 (m_c, 2H, γ-CH_2), 1.30 (m_c, 16H, bulk-CH_2), 0.91 (t, 3H, CH_3); $^3J_{1,2}$=8.0, $^3J_{2,3}$=9.0, $^3J_{3,4}$=9.0, $^3J_{4,5}$=9.0, $^3J_{5,6a}$=1.5, $^3J_{5,6b}$=5.5, $^2J_6$=12.0, $^3J_{imidazole}$=1.5 Hz. ^{13}C NMR (100 MHz, CD_3OD): δ 138 (N–*C*═N), 124.25 (CH═N–*CH*), 123.34 (CH–*CH*–N), 104.46 (C-1), 78.05, 77.96 (C-3, C-5), 74.93 (C-2), 71.55 (C-4), 68.74 (CH_2O), 62.62 (C-6), 51.01, 50.91 (α,CH_2N), 33.05 (ω-2), 31.15 (β), 30.74 (2×), 30.67, 30.56, 30.45, 30.13 (bulk-CH_2), 27.32 (γ), 23.72 (ω-1), 14.48 (ω). HRMS: Calcd for $C_{23}H_{43}N_2O_6$ 443.3121, 444.3155 (26%); found 443.3123, 444.3149 (25%).

4.4. 1-(2-β-D-Glucopyranosyloxyethyl)-3-hexadecyl-imidazolium bromide (**6c**)

4.4.1. 1-Hexadecyl−3-[2-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyloxy)-ethyl]-imidazolium bromide (**5c**)

Compound **2** (0.20 g, 0.40 mmol) and **4c** (0.40 g, 1.2 mmol) were reacted in xylene (2 mL) according to general procedure 4.1.3 to provide **5c** (0.32 g, 96%)as pale yellow syrup. $[\alpha]_D^{25}$ −33 (*c* 0.1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.16 (s, N═*CH*–N), 7.51 (s, CH═N–*CH*), 7.12 (s, CH–*CH*–N), 5.14 (dd~t, H-3), 4.96 (dd~t, H-4), 4.88 (dd, H-2), 4.80–4.63 (m, 2H, CH_2N), 4.56 (d, H-1), 4.24–4.13 (m, 4H, H-6a, CH_2O-a, α-CH_2), 4.09 (dd~bd, H-6b), 4.04 (ddd~dt, CH_2O-b), 3.73 (ddd, H-5), 2.02, 1.96, 1.93 (3 s, 3+6+3H, Ac), 1.85 (p, 2H, β-CH_2),1.34–1.13 (m, 26H, bulk-CH_2), 0.80 (t, 3H, CH_3); $^3J_{1,2}$=8.0, $^3J_{2,3}$=9.0, $^3J_{3,4}$=9.5, $^3J_{4,5}$=9.5, $^3J_{5,6a}$=5.0, $^3J_{5,6b}$=1.5, $^2J_6$=12.0 Hz. ^{13}C NMR (100 MHz, $CDCl_3$): 170.54, 169.91, 169.73, 169.53 (CO), 137.30 (N═*CH*–N), 123.90 (CH═N–*CH*), 120.62 (CH–*CH*–N), 100.57 (C-1), 72.35 (C-3), 72.09 (C-5), 71.23 (C-4), 68.21 (C-2, CH_2O), 61.73 (C-6), 50.25 (α), 49.95 (CH_2N), 31.90 (ω-2), 30.14, 29.66 (3×), 29.63 (2×), 29.57, 29.48, 29.35, 29.33, 28.94 (bulk-CH_2), 26.31 (γ), 22.66 (ω-1), 20.85, 20.83, 20.56, 20.53 (Ac) 14.0 (ω).

4.4.2. 1-(2-β-D-Glucopyranosyloxyethyl)-3-hexadecyl-imidazolium bromide (**6c**)

Compound **5c** (0.20 g, 0.27 mmol) was dissolved in methanol (20 mL) and treated with a catalytic amount of sodium methoxide according to general procedure 4.1.4 to furnish **6c** (0.15 g, 96%) as pale yellow syrup. $[\alpha]_D^{25}$ +12 (*c* 0.1, MeOH). ^{1}H NMR (400 MHz, CD_3OD): δ 7.74 (d, CH═N–*CH*), 7.68 (d, CH–*CH*–N), 4.55–4.42 (m, 2H, CH_2N), 4.36 (d, H-1), 4.24 (t, 2H, α-CH_2), 4.20 (ddd~dt, CH_2O-a), 4.04 (ddd, CH_2O-b), 3.92 (dd, H-6a), 3.67 (dd, H-6b), 3.37 (dd~t, H-3), 3.36–3.30(m, H-5), 3.27 (dd~t, H-4), 3.19 (dd, H-2), 1.92 (p, 2H, β-CH_2), 1.45–1.21 (m, 24H, bulk-CH_2), 0.91 (t, 3H, CH_3); $^3J_{1,2}$=8.0, $^3J_{2,3}$=9.0, $^3J_{3,4}$=9.0, $^3J_{4,5}$=9.5, $^3J_{5,6a}$=1.5, $^3J_{5,6b}$=5.5, $^2J_6$=12.0, $^3J_{imidazole}$~2 Hz. ^{13}C NMR (100 MHz, CD_3OD): δ 138.1 (N–*C*═N), 122.82 (CH═N–*CH*), 121.92 (CH–*CH*–N), 103.11 (C-1), 76.72, 76.60 (C-3, C-5), 73.52 (C-2), 70.14 (C-4), 67.30 (CH_2O), 61.23 (C-6), 49.60, 49.50 (α, CH_2N), 31.66 (ω-2), 29.72 (β-CH_2), 29.37 (3×), 29.34 (2×), 29.33, 29.27, 29.16, 29.06, 28.72 (bulk-CH_2), 25.92 (γ), 22.32 (ω-1), 13.03 (ω). HRMS: Calcd for $C_{27}H_{51}N_2O_6$ 499.3747, 500.3781 (30%); found 499.3744, 500.3773 (29%).

Acknowledgments

Financial support for the investigation by the University of Malaya under research grant UM.C/625/1/HIR/MOHE/SC/09 and by the Malaysian Ministry of Education under FRGS grant FP032-2013B is gratefully acknowledged.

Supplementary data

Supplementary data (Details of the synthetic procedures as well as characteristic data for the intermediates are provided in the Supplementary data that can be obtained from the journal web-page. The material also contains images of NMR spectra, enabling the evaluation of the surfactant purity.) related to this article can be found at http://dx.doi.org/10.1016/j.carres.2015.04.022.

References

1. Holmberg K. *Curr Opin Colloid Interface Sci* 2001;**6**:148–59.
2. Hill K, Rhode O. *Fett/Lipid* 1999;**101**:25–33.
3. Polat T, Linhardt RJ. *J Surf Det* 2001;**4**:415–21.
4. Allen DK, Tao BY. *J Surf Det* 1999;**2**:383–90.
5. Sarney DB, Vulfson EN. *Trends Biotech* 1995;**13**:164–72.
6. Getha D, Tyagi R. *Tenside Surfact Deterg* 2012;**46**:417–27.
7. Rybinski WV, Hill K. *Angew Chem Int Ed Engl* 1998;**37**:1328–45.
8. Pletnev MY. *SOFW J* 2006;**132**:2–8. 10–12.
9. Hill K, Kjellin M, Johansson I. *From surfactants from renewable resources*. 1st ed. Chichester, UK: John Wiley & Sons Ltd.; 2010. p. 65–84.
10. Biermann U, Friedt W, Lang S, Lühs W, Machmüller G, Metzger JO, et al. *Angew Chem Int Ed Engl* 2000;**39**:2206–24.
11. Ducret A, Giroux A, Trani M, Lortie R. *J Am Oil Chem Soc* 1996;**73**:109–13.
12. Akoh CC. *J Am Oil Chem Soc* 1992;**69**:9–13.
13. Szuts A, Szabo-Revesz P. *Int J Pharm* 2012;**433**:1–9.
14. Savic S, Tamburic S, Savic MM. *Expert Opin Drug Deliv* 2010;**7**:353–69.
15. Hepworth P. *Chem Tech Surfactants* 2006:133–52.
16. Fukuda H, Goto A, Yoshioka H, Goto R, Morigaki K, Walde P. *Langmuir* 2001;**17**:4223–31.
17. Roussel M, Benvegnu T, Lognoné V, Le Deit H, Soutrel I, Laurent I, et al. *Eur J Org Chem* 2005:3085–94.
18. Milkereit G, Morr M, Thiem J, Vill V. *Chem Phys Lipids* 2004;**127**:47–63.
19. Vill V, Böcker T, Thiem J, Fischer F. *Liq Cryst* 1989;**6**:349–56.
20. Campa C, Donati I, Vetere A, Gamini A, Paoletti S. *J Carbohydr Chem* 2001;**20**:263–71.
21. Isbell HS, Frush JJ. *J Org Chem* 1958;**23**:1309–19.
22. Muhizi T, Coma V, Grelier S. *Carbohydr Res* 2008;**343**:2369–75.
23. Li YM, Zhang XH, Li Y, Li C, Guo X. *Colloid Surf A: Physicochem Eng Aspects* 2014;**443**:224–32.
24. Lockhoff O, Stadler P. *Carbohydr Res* 1998;**314**:13–24.
25. Lubineau A, Augén J, Douillat B. *Carbohydr Res* 1995;**266**:211–9.

26. Li H, Wei J, Huang H, Xiao S, Yu C, Hu Y, et al. *Adv Mat Res* 2012:518–23.
27. (a) Warwel S, Ruesch Klaas M, Schier H, Bruse F, Wiege B. *Tenside, Surfactants, Deterg* 2001;**38**:7–14;
(b) Warwel S, Bruese F, Wiege B. *Tenside, Surfactants, Deterg* 2003;**40**:327–31.
28. Vill V, Kelkenberg H. *Thiem J Liq Cryst* 1992;**11**:459–67.
29. Epand RM, Epand RF. *Biochim Biophys Acta* 2009;**1788**:289–94.
30. Anderson KL. *Biotech Histochem* 1998;**73**:278–88.
31. Weingarten S. *Thiem J Synlett* 2003:1052–4.
32. Hanessian S, Ducharme D, Masse R, Capmau ML. *Carbohydr Res* 1978;**63**:265–9.
33. Sani FA, Heidelberg T, Hashim R. *Farhanulla Colloid Surf B: Biointerfaces* 2012;**97**:196–200.
34. Dahmén F, Frejd T, Grönberg G, Lave T, Magnusson G, Noori G. *Carbohydr Res* 1983;**116**:303–7.
35. Hemmert C, Fabié A, Fabre A, Vical FB, Gornitzka H. *Eur J Med Chem* 2013;**60**:64–75.
36. Lee M, Choi UH, Wi S, Slebodnick C, Colby RH, Gibson HW. *J Mater Chem* 2011;**21**:12280–7.
37. Zemplén G, Gerecs A, Hadácsy I. *Chem Ber* 1936;**69**:1827–9.
38. Luczak J, Jungnickel C, Joskowska M, Thöming J, Hupka J. *J Colloids Interface Sci* 2009;**336**:111–6.
39. Ryan LD, Kaler EW. *Langmuir* 1997;**13**:5222–8.
40. Cornellas A, Perez L, Comelles F, Ribosa I, Manresa A, Garcia MT. *J Colloid Interface Sci* 2011;**355**:164–71.
41. Viscardi G, Quagliotto P, Barolo C, Savarino P, Barni E, Fisicaro E. *J Org Chem* 2000;**65**:8197–203.
42. Persson CM, Claesson PM. *Langmuir* 2000;**16**:10227–35.
43. Baltazar QQ, Chandawalla J, Sawyer K, Anderson JL. *Colloids Surf A: Physicochem Eng Asp* 2007;**302**:150–6.
44. Ricardo NMPS, Gleninning A, Price C. *Polym Eng Sci* 1996;**36**:182–7.
45. Gan C, Wang H, Zhao Z, Yin B. *J Surfact Deterg* 2014;**17**:465–70.
46. Sakya P, Seddon JM, Vill V. *Liq Cryst* 1997;**23**:409–24.
47. Häntzschel D, Schulte J, Enders S, Quitzsch K. *Phys Chem Chem Phys* 1999;**1**:895–904.
48. Misran O, Timimi BA, Heidelberg T, Sugimura A, Hashim R. *J Phys Chem B* 2013;**117**:7335–44.
49. Boyd BJ, Drummond CJ, Krodkiewska I, Grieser F. *Langmuir* 2000;**16**:7359–67.
50. Rosen MJ. *Surfactants and interfacial phenomena*. New York: Wiley-Interscience; 1978.
51. Shinoda K, Yamaguchy T, Hori R. *Bull Chem Soc Jpn* 1961;**34**:237–41.
52. Aveyard R, Binks BP, Chen J, Esquena J, Fletcher PDI, Buscall R, et al. *Langmuir* 1998;**14**:4699–709.
53. Nguan HS, Heidelberg T, Hashim R, Tiddy GJT. *Liq Cryst* 2010;**37**:1205–13.
54. Ali TH, Hussen RSD. *Heidelb T Colloids Surf B: Biointerfaces* 2014;**123**:981–5.
55. Niraula B, King TC, Chun TK, Misran M. *Colloid Surf A: physiochem Eng Asp* 2004;**251**:117–32.
56. Szelag H, Sadecka E, Pawlowicz R, Kusiemska A. *Pol J Chem Tech* 2013;**15**:128–35.
57. Rendall K, Tiddy GJT, Trevathan MA. *J Chem Soc Faraday Trans* 1983;**79**:637–49.
58. Laughlin RG. *Adv Colloid Interface Sci* 1992;**41**:57–79.