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PAPER

Efficient solvent-free cationization of AlkylPolyglycoside based surfactant compositions using natural glycine betaine

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

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We describe here a new strategy for the preparation of 100% bio-based sugar based cationic surfactants using glycine betaine butyl ester as the cationizing agent. We first studied $NaHCO_3$-catalyzed transesterification reactions of pure fatty alcohols and equimolar mixtures of alkyl glucosides or xylosides and fatty alcohols. Using solvent-free processes, moderate to high levels of cationization (48-90%) concerning both fatty alcohols and carbohydrates, were obtained with a certain regioselectivity toward C6 and/or C3 positions in the D-glucose and D-xylose series. This synthetic approach can be also extended to commercial AlkylPolyGlycosides containing large proportions of fatty alcohols (90-96%) to provide original cationized glycoside compositions, as (co-)emulsifiers.

Introduction

Although they represent only 10% of the overall surfactant market (280,000 metric tons), cationic surfactants are an important class of amphiphilic compounds with regard to their performance. Indeed, thanks to their positively charged head group, these surface-active molecules are used in many industrial applications as fabric softeners, conditioning agents in cosmetics, asphalt additives, desinfectants and biocides, corrosion inhibitors and organophilic clays.[1]

Current cationic surfactants include several chemical classes such as amines, alkylimidazolines, alkoxylated amines, and quaternized ammonium compounds (or Quats). By far the most significant cationic surfactants used in cosmetics are Quats. The positive charge makes them electrostatically attracted to the negative damaged sites on hair and skin protein which makes them resist rinse-off.

However, most cationic surfactants were found to have an acute aquatic toxicity and they are generally poorly biodegradable. Another disadvantage is the origin of the raw materials used for their manufacture, mostly derived from petrochemicals that could have adverse effects on our health and environment. As an example, cetyltrimethylammonium bromide (CETAB) that is widely used as topic antiseptics and in many household products such as shampoos, hair conditioning product and cosmetics,[2] has a correct biodegradability, but it is very toxic to the aquatic environment. It is also irritating and dangerous to handle. These toxicological and eco-toxicological data are representative of the behaviour of cationic surfactants that are obtained by quaternization of fatty amine using halogenated agents. These characteristics highlight the opportunity of developing cationic surfactants with an improved environmental profile through the use of vegetable resources as starting materials.

Another challenging problem to be solved with cationics is their low compatibility with anionic surfactants, thus forming insoluble aggregates in aqueous media. One possible strategy to improve the compatibility of cationic surfactants with the anionics, is to insert polar groups such as sugar moieties into the hydrophilic cationic headgroup.[3]

Unfortunately, sugar based cationic surfactants have not been investigated extensively. Typical examples are alkyl polyglycosides (APG) functionalized as *O*-(2-hydroxy-3-trimethylammonium)propyl ethers[4] by alkali catalyzed addition of 2,3-epoxypropyl-trimethylammonium chloride (QUAB 151) with an order of reactivity OH (4) > OH(6) > OH(2) > OH(3), and alkyl 6-trimethylammonio-6-deoxy or 6-dialkylammonio-6-deoxy D-glucopyranoside chlorides[5,6]. Other cationic sugar derivatives incorporated the positively charged moiety at the anomeric position of the carbohydrate residue (pyridinium-type)[7] or within the aglycone part (quaternary ammonium-type)[8]. All these structures are supposed to improve the biodegradability level compared to the cationic surfactants found on the market. Nevertheless, the chemical syntheses to produce them are not generally eco-friendly (use of hazardous reagents and solvents, production of pollutants) which minimizes the benefit of these novel cationic surfactants for sustainable development.

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†Electronic Supplementary Information (ESI) available: Supplementary data include ^{1}H NMR, 1D TOCSY, 2D HMQC, 2D HSQC spectra of cationized *O*-tetradecyl glucoside and myristic alcohol mixtures. See DOI: 10.1039/x0xx00000x

In this context, for several years, our work was focused on the use of glycine betaine (GB) as a natural substance for the preparation of cationic surfactants entirely derived from vegetable raw materials.[9] Naturally present in many fruits, cereals and beet, GB accounts for 27% in weight of molasses of sugar beet and it is obtained industrially after extraction of saccharose. This compound possesses a quaternary trimethylalkylammonium moiety and thus it allows to transfer, under appropriate conditions, its cationic character in the structure to which it is chemically linked. In our hands, GB was selected as an natural starting material for the production of biodegradable cationic emulsifiers for road-making applications or for uses in cosmetics.[10]

In this paper, the synthetic approaches for the preparation of original cationic glycosidic surfactants are described involving a transesterification reaction between a butyl ester derivative of GB and sugar-based non-ionic surfactants, namely glucose and xylose. The most challenging issue of this work was to propose an efficient cationization method that could be used to a wide range of AlkylPolyGlycoside (APG)-containing surfactant compositions, including mixtures based on a large excess of fatty alcohols. Environmental friendly solvent free processes were developed and were readily transferred to a 2 L reactor scale. Preliminary formulation studies of these cationic sugar surfactant compositions clearly revealed their interest as emulsion stabilizers for applications in cosmetics.

Results and discussion

Activation of glycine betaine

Because of its chemical inertness, GB cannot be used directly in its native form as a reagent. The preparation of derivatives to improve GB reactivity towards nucleophiles, such as alcohols or amines, has been the subject of intensive work within our laboratory. In particular, GB butyl ester **1** was found to be an efficient activated form to provide amide-type surfactants through its reaction with fatty amines.[9] As a consequence, this GB-based derivative **1** was selected as a cationizing reagent for the introduction of cationic moieties into glycosidic surfactants.

Esterification reaction of GB with *n*-butanol (2 equiv.) was carried out at 130-140°C**,** in the presence of methane sulfonic acid (MSA) as a biodegradable catalyst[11] and under reduced pressure (500 mbar) for 3 h (Fig.1): the solvent was distilled out during heating and the water formed during the reaction was eliminated through the use of a Dean-Stark apparatus. The reaction mixture was diluted with ethyl acetate/*n*-butanol 4/1 (v/v) and then washed with an aq. saturated $NaHCO_3$ solution. The extracted organic phase was dried and concentrated under reduced pressure to provide GB butyl ester **1** as a hydroscopic white powder (55% yield). The modest yield resulted from a partial hydrolysis of butyl ester **1** during the treatment of the organic phase with the basic aqueous solution. Indeed, GB esters are known to be sensitive to hydrolysis for pH values higher than 5.5-6.[9]

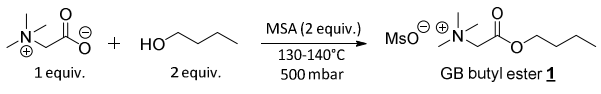

Fig.1 Synthetic scheme used to produce GB butyl ester **1**.

Transesterification reaction of GB butyl ester 1

Studies of the transesterification reaction with several substrates were necessary to provide an efficient general method for cationizing commercial sugar-based surfactants composed of alkylpolyglycoside and fatty alcohol mixtures. The reactions of GB butyl ester **1** were first investigated with pure myristic alcohol **2** and pure *O*-tetradecyl glucoside **3** and next with a controlled mixture of myristic alcohol/*O*-tetradecyl glucoside with the aim of studying the comparative reactivities of these two nucleophiles. Finally, our attention was focused on the application of the transesterification reaction to the crude reaction mixture resulting from the synthesis of GB butyl ester **1** and commercial APG surfactant compositions.

*Use of pure myristic alcohol **2***

Transesterification reaction involving GB butyl ester **1** and myristic alcohol **2** (3 equiv.) was achieved with or without the presence of acid (MSA) or base ($NaHCO_3$) catalyst (Fig. 2). It was decided to perform the reaction at 80-85°C to obtain a liquid and homogenous mixture and under reduced pressure (5-10 mbar) to facilitate the elimination of *n*-butanol formed all through the reaction. The composition of the reaction mixtures was estimated from the ^1H NMR spectra in $CDCl_3/CD_3OD$ (1/1, v/v). Then, using the integration values of the methylene groups of the butyl and myristic chains directly linked to glycine betaine, GB butyl ester **1** and GB myristic ester **4** were quantified. ^1H NMR signal corresponding to the terminal CH_3 of the fatty chains was used as an internal reference.

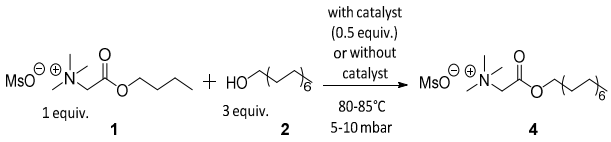

Fig.2 Synthetic scheme used to produce GB myristic ester **4**.

At 3 hours reaction time, it appeared that the use if $NaHCO_3$ catalyst furnished the best conditions for the transesterification reaction (Table 1). Indeed, as already described for vegetable oils, the base-catalyzed transesterification reaction proceeded faster than the acid-catalyzed reaction.[12,13] Moreover, due to this reason, together with the fact that the alkaline catalysts are less corrosive than acidic compounds, industrial processes usually favour base catalysts, such as sodium or potassium carbonates.[13]

Table 1. Compositions in GB esters **1** and **4** after 3 hours of reaction.

Esters in the reaction mixture	With catalyst (0.5 equiv.)		Without catalyst
	MSA	$NaHCO_3$	
GB Myristic ester **4**	36%	100%	0%
GB butyl ester **1**	64%	0%	100%

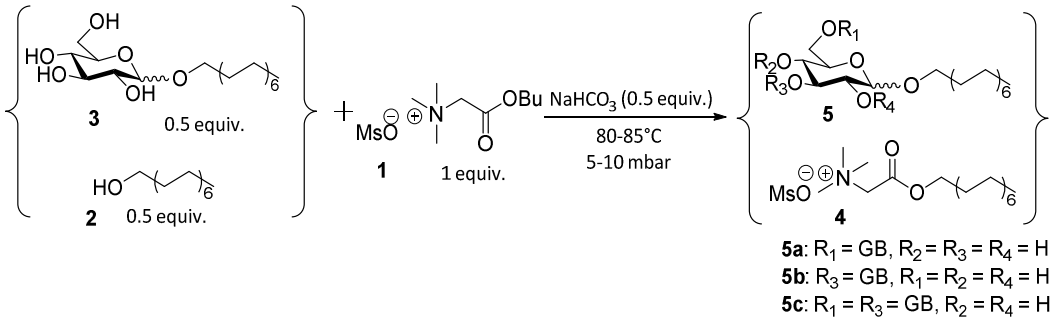

Fig. 3 Conditions used for the transesterification reaction with *O*-tetradecyl glucoside **3** in the presence of myristic alcohol **2**.

Use of pure O*-tetradecyl glucoside **3** or an equimolar mixture of myristic alcohol **2** and* O*-tetradecyl glucoside **3***

The use of identical reaction conditions with 3 equivalents of pure *O*-tetradecyl glucoside **3** (α/β=0.71/0.29)[15] instead of myristic alcohol **2**, was unsuccessful. Despite the heating at 80-85°C, the mixture remained highly viscous, thus inhibiting the stirring and the homogenization of the reaction mixture. Next, in order to ensure a sufficient fluidity at 80-85°C and under 5-10 mbar, it was envisaged to perform the reaction of the *O*-tetradecyl glucoside **3** (0.5 equiv.) in the presence of an equimolar amount of myristic alcohol **2** (0.5 equiv.) (Fig.3). Furthermore, the presence of fatty alcohol in the reaction mixture could mimic the compositions found in commercial APG surfactants.

After 3 hours of reaction, the mixture became so viscous that the stirring stopped. ^{1}H NMR analysis of this mixture in $CDCl_3/CD_3OD$/MSA[16] (1/1/0.01, v/v/v) showed the presence of new signals (doublets) near the main signal (doublet) at 4.78 ppm corresponding to the α-anomeric proton of the starting *O*-tetradecyl glucoside **3** (Fig.4).

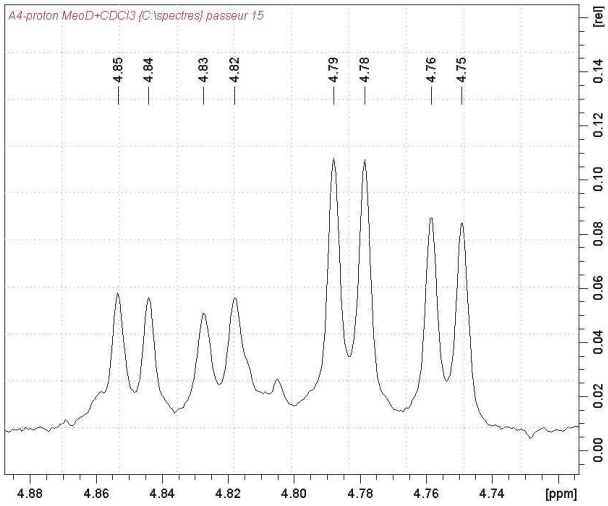

Fig. 4 ^{1}H NMR signals observed around the signal of the α-anomeric proton of glucoside **3** after 3 hours of reaction.

A series of additional NMR experiments (1D-TOCSY, COSY, HMBC) was achieved from this crude reaction mixture that allowed to identify the signal at 4.75 ppm as the α-anomeric proton of the *O*-tetradecyl glucoside **3** after cationization by GB at position 6 (compound **5a**, Fig. 3).

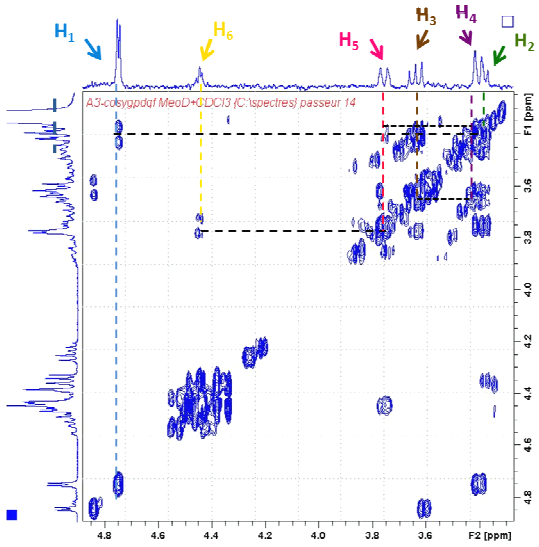

Fig. 5 Projection of a 1D TOCSY sub-spectrum on one axis of a 2D-COSY spectrum leading to the assignment of the signals relative to the carbohydrate moiety of the targeted molecule (including the signal at 4.74 ppm).

A 1D TOCSY (TOtal Correlation SpectroscopY) experiment was first investigated based on the selective preservation of the spin excitation of the proton at 4.75 ppm (spin-lock). This 1D selective TOCSY experiment provided the spin excitation of the nearby protons by polarization transfer within the same molecule. As a consequence, only the relaxation of the excited spins were observed. In this way, a sub-spectrum was obtained that revealed exclusively the signals relative to the molecule including the signal at 4.75 ppm (see ESI, Fig. 1). Furthermore, in order to identify the protons corresponding to the signals observed in the TOCSY spectrum, the 1D TOCSY sub-spectrum was used in projection on one axis of a 2D-COSY (Correlation SpectroscopY) spectrum (Fig. 5). This experiment allowed to determine the correlations within a

same cycle and thus to assign the signals relative to the carbohydrate moiety of the targeted molecule (including the signal at 4.75 ppm).

In parallel, a 2D-HMBC (Heteronuclear Multiple Bond Correlation) experiment correlated chemical shifts of the protons with the carbons separated with two bonds (see ESI, Fig. 2). This study allowed to highlight the chemical groups bound to GB. Finally, the projection of the 1D TOCSY sub-spectrum on HMBC spectrum clearly proved that the chemical linkage between GB and glucoside **3** operated at the position 6 of the carbohydrate residue (see ESI, Fig. 3).

In a second step, the reaction mixture was purified by silica gel chromatography with AcOEt-AcOH-H_2O as the eluent (the volume ratio was gradually changed from 8:1.5:0.5 to 6:2:2) to yield a sample composed of exclusive cationized versions of glucoside **3**. ^{1}H NMR analysis showed the presence of two major (2 doublets at 4.75 ppm and 4.84 ppm) and two minor (2 doublets at 4.81 ppm and 4.79 ppm) products corresponding to cationized forms of the α isomer of glucoside **3** (see ESI, Fig 4). 1D-TOCSY, COSY, HMBC experiments applied to this sample allowed the assignment of the signal at 4.84 ppm to the α-glucoside cationized at position 3 (compound **5b**, Fig. 3). The minor signals at 4.81 ppm and 4.79 ppm were not identified through NMR analysis but we hypothesized the presence of two additional glucosides possessing a GB moiety at either position 2 or position 4. In this way, the total cationization level of the α-isomer was estimated to be 65%.

With the aim of characterizing the minor signals, it was decided to change the transesterification reaction conditions by using GB butyl ester **1** in excess (3 equiv. instead of 1 equiv.) in order to favour the formation of these minor cationized products. It is noteworthy that the excess of butyl ester **1** avoided caking as reaction continued to 18 hours. ^{1}H NMR showed the predominance of the signal at 4.81 ppm (Fig. 6) that was ascribed from additional 1D (TOCSY, see ESI, Fig. 5) and 2D (COSY, HSQC, HMBC) NMR analyses, to the α anomer of glucoside cationized at both positions 3 and 6 (compound **5c**, Fig. 3). In these novel reaction conditions, the conversion level of the α anomer of glucoside **3** into cationized glucoside derivatives was estimated to be 85%.

As for β-isomer of *O*-tetradecyl glucoside **3**, the same approach was not applied because the signals of the GB fatty ester **4** resulting from the transesterification reaction of GB butyl ester **1** with myristic alcohol **2**, overlapped those of the anomeric proton of β-isomers (see ESI, Fig. 6), However, from the sample isolated after purification by silica gel chromatography it was found that this β-isomer was also transformed into cationized derivatives but the use of 2D NMR experiments did not provide any information about their structures (see ESI, Fig.7).

Finally, the conversion of myristic alcohol **2** into GB myristic ester **4** was quantified by evaluating from ^{1}H NMR spectra, the difference of alcohol **2** amounts present in the reaction mixture between the beginning and the end of the reaction. The estimated conversion level was found to be 60-70% and 80-90 % using the first (alcohol **2**/glucoside **3**/GB butyl ester **1** = 0.5/0.5/1) and the second (alcohol **2**/glucoside **3**/GB butyl ester **1** = 0.5/0.5/3) reaction conditions, respectively. Remarkably, the same level of cationization of glucoside **3** (65% and 85%, respectively for the α-isomer) as for myristic alcohol **2** was observed, thus highlighting similar reactivities of these two polyol and alcohol nucleophiles towards the $NaHCO_3$-catalyzed transesterification process.

*Use of an equimolar mixture of myristic alcohol **2** and O-tetradecyl xyloside **6***

Pentose-based surfactants (Alkyl PolyPentosides, APP) are another class of bio-based surfactants derived from agriculture waste products (L-arabinose and D-xylose).[17] Structurally, they differ from standard APG by the absence of primary alcohol function. Therefore, these non-ionic surfactants represented attractive substrates to study the efficiency of the transesterification reaction toward glycosides bearing only secondary hydroxyl groups.

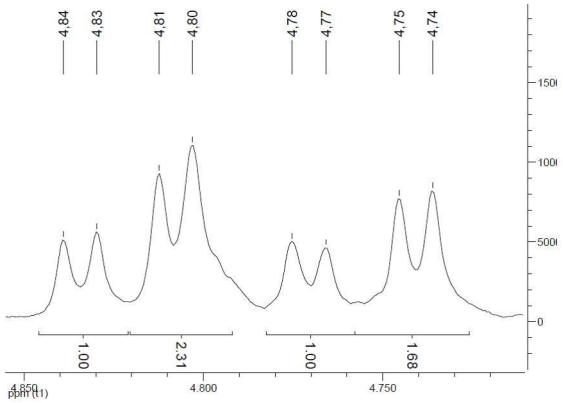

Fig. 6 ^{1}H NMR signals observed around the signal of the α-anomeric proton of glucoside **3** when using 3 equiv. of GB butyl ester **1** at 18 hours reaction time.

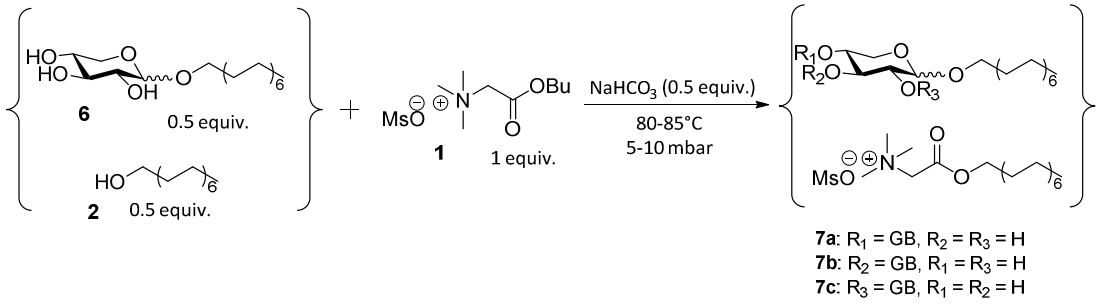

Fig. 7 Conditions used for the transesterification reaction with *O*-tetradecyl xyloside **6** in the presence of myristic alcohol **2.**

Thus, the reaction was performed with *O*-tetradecyl xyloside **6** (α/β=0.56/0.44)[18] reproducing the conditions used with glucoside **3** (Fig. 7). After 3 hours of reaction, ^{1}H NMR analysis of the mixture in $CDCl_3/CD_3OD$/MSA[16] (1/1/0.01, v/v/v) showed the presence of new signals (doublets) near the main signal (doublet) at 4.72 ppm

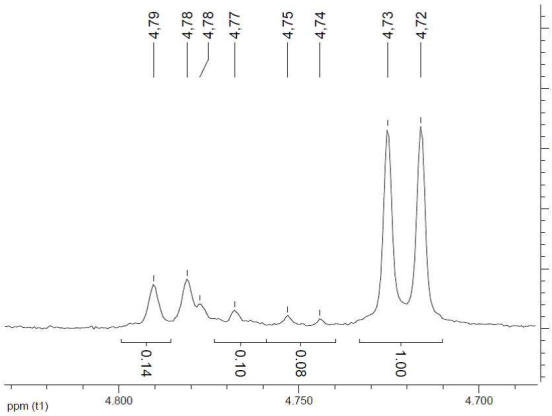

Fig. 8 ^{1}H NMR signals observed around the signal of the α-anomeric proton of xyloside **3** after 3 hours of reaction.

corresponding to the α-anomeric proton of the starting *O*-tetradecyl xyloside **6** (Fig. 8). Further 1D TOCSY and 2D COSY, HSQC, HMBC NMR experiments established the presence of a product (doublet at 4.78 ppm) resulting from the cationization of α-xyloside **6** at position 3 (compound **7b**, Fig. 7). The structure of minor α-xylosides characterized by the two doublets at 4.77 ppm and 4.74 ppm were ascribed to xylosides possessing a GB moiety grafted at position 2 or 4 (compounds **7a** and **7c**, Fig. 7). The conversion level of α-xylosides into cationized products was evaluated to be 23%. Next, seeing that the mixture remained fluid after 3 hours, the reaction conditions were maintained during 24 hours. An increased conversion level (48%) was then observed in these conditions.

Direct cationization process using GB butyl ester as a crude reaction mixture and commercial APG surfactants

Our next goal was to find the more appropriate conditions for the efficient grafting of GB on alkyl glucosides as commercial surfactant compositions, that is in the presence of a large excess of fatty alcohol, and by using GB butyl ester **1** as a non-purified crude reaction mixture. In this way, the absence of any purification step should make the process more profitable and more economically feasible. For that purpose, we first selected a product sold under the name "Montanov® 14" by the company Seppic which essentially consists of the combination of approximately 90 % in mole of myristic alcohol and about 10 % in mole of myristyl glucosides as a mixture of α/β isomeric compounds (α/β = 0.71/0.29; mol/mol) with one to four glucose units. This surfactant composition is generally used as a co-emulsifying agent that gives consistency to O/W emulsions.

Our attention was directed toward the quantities of GB butyl ester **1** and $NaHCO_3$ catalyst required for the cationization of Montanov® 14. The reactions were achieved using cationizing reagent **1** as a mixture resulting from the esterification of GB (n equiv.) with *n*-butanol (2n equiv.) in the presence of MSA (1.5n equiv.) at 130-140°C and 500 mbar for 4 hours, without any further treatment. For each transesterification reaction tested (entries 1-8, Table 2), a prior neutralization of the solution composed of GB butyl ester **1** (n equiv.), *n*-butanol (n equiv.) and residual MSA (0.5n equiv.) was performed with $NaHCO_3$ (0.5n equiv.). Next, Montanov® 14 (APG = 0.1 equiv.; myristic alcohol = 0.9 equiv.) and $NaHCO_3$ (n' equiv.) were added and the mixture was stirred at 80°C and under 5-10 mbar (Fig. 9). The level of cationization was determined exclusively for the α isomers (Table 2) through ^{1}H NMR experiments.

The increase in GB butyl ester **1** used (0.1 to 1 equiv.) clearly improved the level of conversion of the α isomers into the corresponding cationized products (entries 1-4). An analysis by mass spectrometry of the mixture also revealed the presence of monocationic di- and triglucosides which were not observed in NMR spectra. Conversely, the use of low amounts of $NaHCO_3$ (0.7 to 0.3, entries 4-6, Table 2) afforded cationized Montanov® 14 with a

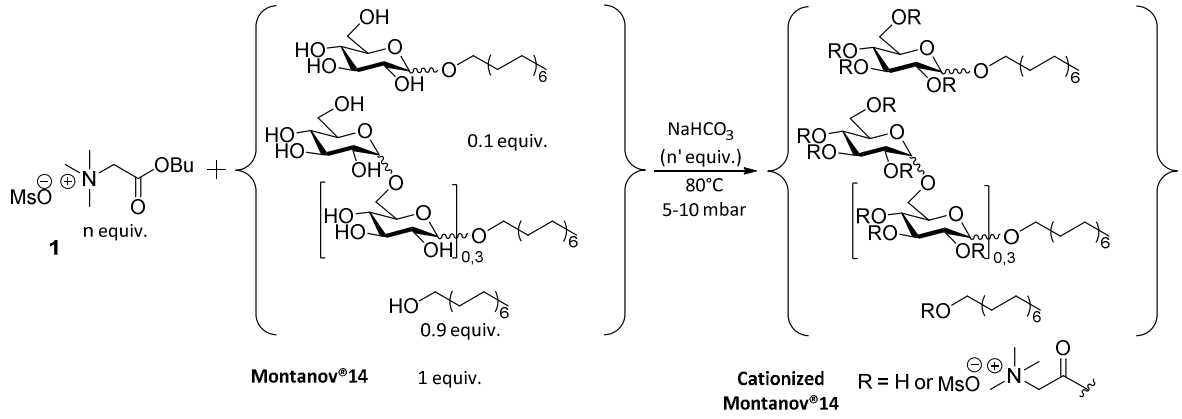

Fig. 9 Conditions used for the cationization reaction of Montanov® 14.

high degree of GB grafting. As previously obtained when using an equimolar ratio of myristic alcohol and *O*-tetradecyl glucoside, the transformation of myristic alcohol into GB myristic ester proceeded quite efficiently (66% of conversion for entry 6).

Table 2. Evaluation of the conversion level of Montanov ®14 into cationized product, depending on GB butyl ester **1** and $NaHCO_3$ quantities used.

Entries	GB butyl ester **1** (n equiv.)	$NaHCO_3$ (n' equiv.)	t (h)	Conversion* (%)
1	0.1	0.07	30	0
2	0.2	0.14	30	0
3	0.3	0.21	30	12
4	1	0.7	3.5	75
5	1	0.5	4	73
6	1	0.3	3	71
7	1	0.1	3	64

** the conversion was estimated exclusively for the α isomers.*

In order to prevent the cleavage of the GB ester linkages due to the presence of residual $NaHCO_3$, an additional neutralization step of the final mixtures was envisaged. The procedure involved the dissolution of the hot reaction mixture in an ethanol solution containing 2n' equivalents of MSA, then two successive hot and cold filtrations (to remove both sodium methane sulfonate salts and residual GB) and finally the concentration of the filtrate under reduced pressure.

The solvent-free process was next extended to the cationization of two additional APG compositions, namely Montanov® 68 and Montanov® 202 composed of cetearyl alcohol ($C_{16\text{-}C18}$) & cetearyl glucosides (APG/$C_{16\text{-}18}$ = 0.08/0.92, α/β = 0.81/0.19; mol/mol), and arachidyl alcohol (C_{20}) & behenyl alcohol (C_{22}) & arachidyl/behenyl glucosides (APG/$C_{20\text{-}22}$ = 0.04/0.96, α/β = 0.73/0.27; mol/mol), respectively (Fig.10). These commercial surfactants are employed as O/W emulsifiers in formulations. Despite the low proportion of APG compared to fatty alcohols, high levels of cationization (66-69%) of the α isomers were obtained with the two compositions (Table 3), demonstrating the general applicability of this new cationization approach using GB-derived reagent. Similar conversion rates of fatty alcohols into GB fatty esters as for Montanov® 14 were also observed. Finally, the scale up of the syntheses was successfully achieved using a 2 L reactor for the production of cationized versions of Montanov® 14, 68 and 202 at a Kg scale.

Evaluation of the emulsifying properties of cationized Montanov® 202[19]

Emulsifying ability of Montanov® 202 and its cationized version was comparatively studied in two systems. A first series of O/W emulsions was prepared by mixing the emulsifier (Montanov® 202 or its cationized version) (3% in weight), triglycerides (10% in weight), a preservative agent (1% in weight) and a pH 5.5 buffer solution (up to 100% in weight). A demixtion phenomenon occurred after 1 day using Montanov® 202 whereas emulsions based on cationized Montanov® 202 remained stable for at least one week. The second type of emulsions was formulated using a thickening natural gum (Solagum™ TARA, 0.5% in weight) in addition to the emulsifier (Montanov® 202 or its cationized version) (3% in weight), triglycerides (10% and 20% in weight), the preservative agent (1% in weight) and the pH 5.5 buffer solution (up to 100% in weight). In this second case, the stability of all emulsions was observed after one week at room temperature or at 45°C. These preliminary results suggested that cationized APG compositions are promising emulsifiers compared to commercial Montanov® products. Further experiments are in progress to evaluate the behaviour of these new cationic surfactant compositions in formulations used in cosmetics.

Table 3. Evaluation of the conversion level of Montanov® 68 and Montanov® 202 into cationized products.

Commercial APG	Composition (equiv.)	GB butyl ester **1** (equiv.)	$NaHCO_3$ (equiv.)	t (h)	Conversion* (%)
Montanov® 68	APG: 0.08 $C_{16\text{-}18}$: 0.92	1	0.3	3	69
Montanov® 202	APG: 0.04 $C_{20\text{-}22}$: 0.96	1	0.3	3	66

** the conversion was estimated exclusively for the α isomers.*

Conclusions

In this study, a versatile and efficient method for the cationization of fatty alcohols and carbohydrate-based surfactants was developed through base-catalyzed transesterification reactions using a 'green' glycine betaine butyl ester reagent. This environmentally benign solvent free synthetic approach was successfully applied to mixtures of fatty alcohols and hexose- or pentose-based surfactants, leading to high levels of conversion of these non-ionic substrates into cationized forms. It is noteworthy

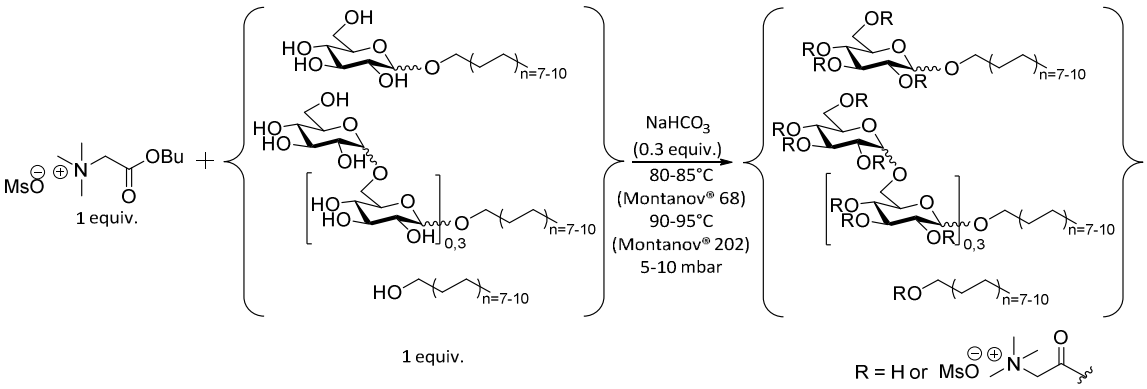

Fig. 10 Conditions used for the cationization reaction of Montanov® 68 and Montanov® 202.

that the grafting of the GB residue into alkyl glycosides operated with high efficiencies even in the presence of a large excess of fatty alcohols. Novel cationic GB-containing APG versions were produced from commercial compositions at a Kg scale and exhibited promising emulsifying properties. The study of their application in cosmetic formulations is currently underway.

Experimental section

General

All commercially available chemicals were used without further purification. Analytical TLC was performed on Merck 60 F254 silica gel nonactivated plates. A solution of 5% H_2SO_4 in EtOH was used to develop the plates. Merck 60 H (5-40µm) silica gel and semi-automated systems such as CombiFlash Teledyne Isco or the Büchi ensemble Pump C-601 and Controller C-610 with GraceResolv silica cartridges (from 4 to 80g) were used for column chromatography. Electropositive electrospray (ESI+) mass spectra were acquired on MS/MS TOF and the Shimadzu ensemble LCMS-2020 mass spectrometers. NMR spectra were recorded on a Bruker Avance III 400 spectrometer operating at 400.13 MHz for ^{1}H, equipped with a BBFO probe with a Z-gradient coil and a GREAT 1/10 gradient unit. The zg30 Bruker pulse program was used for 1D ^{1}H NMR, with a TD of 64k, a relaxation delay d1 = 2s. 2D COSY experiments were acquired using the cosygpdqf pulse program. Matrices consisting of 256 (t1)×2048 (t2) complex data points were recorded with a 1.5 s recovery delay (d1) and an AQ time of 0.25s. 1D TOCSY experiments were acquired using the selmlgp pulse program with a mixing time of 200ms in major cases. ^{13}C NMR spectra were recorded at 100.61 MHz. Sequences as jmod,zgpg30 were used with a TD is 64k and a relaxation delay of 2s for a spectral width of 220 ppm was used. Fourier transform was performed after apodization with an exponential function using a LB of 0.6 Hz to 2Hz. 2D HSQC (^{1}H-^{13}C) experiments were acquired using the hsqcetgpsisp.2 pulse program for high sensitivity with an AQ=0.25s , d1=1.5s, ns=2 to 24 depending of the concentration. Generally 256 experiences are acquired (t1). Fourier transform was performed in both dimensions with a SINE function (SSB=3). 2D HMBC (^{1}H-^{13}C) experiments were performed with either the hmbcplrndqf or the impact-hmbc pulse program. D1 was set to 0.3s to 1.5s, delay d6 for the evolution of long range coupling was set to 65 ms, NS is depending on the concentration and the number of series was generally 256 (t1). All the data were processed with a SINE function in both dimensions (SSB=3).

Synthesis of GB butylester mesylate 1. Methanesulfonic acid (MSA) (35.71 g, 371.6 mmol, 2.0 equiv.) was added to a suspension of glycine betaine (21.8 g, 185.8 mmol, 1.0 equiv.) in *n*-butanol (27.53 g, 371.6 mmol, 2.0 equiv.). The reaction mixture was gradually heated to 130-140°C under reduced pressure (500 mbar). The heteroazeotropic solution water/*n*-butanol distillated during the reaction was removed with a Dean-Stark apparatus. After 4 h, the reaction mixture was allowed to cool down to room temperature and to come back to atmospheric pressure. A solution of ethyl acetate/*n*-butanol (4:1 v:v) (150 mL) was then added to the reaction mixture and a solution of saturated $NaHCO_3$ was used to neutralize MSA. The organic layer was isolated and concentrated to afford **1** (27.53 g, 102.2 mmol, 55%) as a very hygroscopic white solid. δ_H (400 MHz, $CDCl_3$/CD_3OD: 1:1) 0.93 (3H, t, *J* 7.4, CH_3), 1.38 (2H, m, CH_2), 1.65 (2H, m, CH_2CH$_2$O), 2.71 (3H, s, $CH_3SO_3^-$), 3.32 (9H, s, $(CH_3)_3N^+$),4.24 (2H, t, *J* 6.7, CH_2O), 4.34 (2H, s, CH_2CO); δ_C (100 MHz, $CDCl_3$/CD_3OD: 1:1) 14.3 (CH_3), 19.4 (*C*H$_2$CH$_3$), 30.9 (*C*H$_2$CH$_2$O), 39.5 ($CH_3SO_3^-$),54.2 ($(CH_3)_3N^+$),63.5 (CH_2N^+),67.0 (CH_2O), 165.3 (CO); *m/z* (ESI+) 174.1494 ([M-MsO$^-$]$^+$ requires $C_9H_{20}NO_2$ 174.1494).

Synthesis of GB myristyl ester mesylate 4.

General synthesis. To a solid mixture of GB butyl ester **1** (1.0 g, 3.72 mmol, 1 equiv.) and myristic alcohol **2** (2.39 g, 11.16 mmol, 3 equiv.) was added or no a catalyst (acidic or basic). The media was then heated to 80-85°C under reduced pressure (5-10 mbar). The reaction was followed by 1H NMR analysis with the deuterated mixture $CDCl_3$/CD_3OD (1:1) used as solvent.

Synthesis without catalyst. After 24 h, the heat was stopped and the pressure was allowed to come back to atmospheric pressure. ^{1}H NMR analysis had shown that no transesterification product was present in the crude reaction media.

Synthesis with an acidic catalyst. The acidic catalyst, methanesulfonic acid (178 mg, 1.86 mmol, 0.5 equiv.), was added to the solid mixture. After 3 h, the heat was stopped and the crude reaction mixture was allowed to cool down to room temperature and to come back to atmospheric pressure. ^{1}H NMR analysis was used to determine the following molar ratio: **4**/**1**/GB = 36/64/0. δ_H (400 MHz, $CDCl_3$/CD_3OD: 1:1) 0.85 (t, *J* 6.7, CH_3 **4** and **2**), 0.93 (t, *J* 7.4, CH_3 **1**), 1.24 (m, $(CH_2)_{10}$, **4** and **2**), 1.38 (m, C*H*$_2$CH$_3$ **1**), 1,52 (m, OCH$_2$CH$_2$C*H*$_2$ **4** and **2**), 1.65 (m, C*H*$_2$CH$_2$O **4** and **1**), 2.71 (s, CH_3SO_3 **4**, **1** and MSA), 3.32 (s, $(CH_3)_3N^+$, **4** and **1**), 4.24 (t, *J* 6.7, CH_2O **4** and **1**), 4.34 (s, CH_2CO **4** and **1**).

Synthesis with a basic catalyst. The basic catalyst, sodium bicarbonate (156 mg, 1.86 mmol, 0.5 equiv.), was added to the solid mixture. After 3 h, the heat was stopped and the crude reaction mixture was allowed to cool down to room temperature and to come back to atmospheric pressure. ^{1}H NMR analysis was used to determine the following molar ratio: **4**/**1**/GB = 99/0/1. δ_H (400 MHz, $CDCl_3$/CD_3OD: 1:1) 0.85 (t, *J* 6.7, CH_3 **4** and **2**), 1.52 (m, OCH$_2$CH$_2$C*H*$_2$ **4** and **2**), 1.65 (m, C*H*$_2$CH$_2$O **4**), 2.71 (s, CH_3SO_3 **4** and sodium mesylate), 3.26 (s, $(CH_3)_3N^+$ GB), 3.32 (s, $(CH_3)_3N^+$ **4**), 3.75 (s, CH_2CO GB), 4.24 (t, *J* 6.7, CH_2O **4**), 4.34 (s, CH_2CO **4**).

***O*-tetradecyl-D-glucoside 3: Purification of Montanov® 14.** Montanov® 14 (composed of 2 g of **3** and 8 g of **4**) was dissolved in a CH_2Cl_2/MeOH (1:1 v/v) mixture (100mL). To ease the dissolution, the mixture obtained was heated to 40°C and then silica (30g) was added in order to make a solid deposit. A purification by flash chromatography on silica gel (CH_2Cl_2/MeOH: 9:1) of this solid deposit allowed to obtain an α/β (71/29) mixture of **3** as a white solid (1.86 g, 4.94 mmol, 93%). *Rf* 0.35 (CH_2Cl_2/MeOH: 9:1); δ_H (400 MHz, $CDCl_3/CD_3OD$: 1:1) α isomer: 0.85 (3H, t, *J* 6.6, CH_3), 1.24 (22H, m, $(CH_2)_{11}$), 1.60 (2H, m, C*H*$_2$CH$_2$O), 3.35 (1H, dd, *J* 8.6, 10.0, 4-H), 3.40 (1H, dd, *J* 3.7, 9.8, 2-H), 3.43 (1H, m, CH$_2$C*H*$_{2a\ or\ b}$O), 3.56 (1H, m, 5-H), 3.65 (1H, ap. t, *J* 9.4, 3-H), 3.69 (1H, m, CH$_2$C*H*$_{2a\ or\ b}$O), 3.75 (2H, ddd, *J* 2.5, 11.8, 14.1, H_6), 4.78 (1H, d, *J* 3.8, 1-H); β isomer: 0.85 (3H, t, *J* 6.6, CH_3), 1.24 (22H, m, $(CH_2)_{11}$), 1.60 (2H, m, C*H*$_2$CH$_2$O), 3.21 (1H, dd, *J* 7.8, 8.8, 2-H), 3.26 (1H, m, 4-H), 3.36 (1H, ap. t, *J* 7.7, 3-H), 3.53 (1H, m, CH$_2$C*H*$_{2a\ or\ b}$O), 3.71 (1H, dd, *J* 5.6, 12.1 Hz, 5-H), 3.86 (2H, dd, *J* 3.0, 12.1, 6-H), 3.87 (1H, m, CH$_2$C*H*$_{2a\ ou\ b}$O), 4.25 (1H, d, *J* 7.8, 1-H); δ_C (100 MHz, $CDCl_3/CD_3OD$: 1:1) α isomer: 14.3 (CH_3), 22.4, 28.7, 29.9, 30.2, 31.4, 32.3 ($(CH_2)_{12}$), 61.3 (6-C), 68.1 (CH$_2$*C*H$_2$O), 70.2 (4-C), 71.8 (5-C), 73.9 (3-C), 76.7 (2-C), 98.5 (1-C); β isomer: 14.3 (CH_3), 22.4, 28.7, 29.9, 30.2, 31.4, 32.3 ($(CH_2)_{12}$), 61.6 (6-C) , 70.1 (CH$_2$*C*H$_2$O), 70.2 (3-C), 71.8 (5-C), 76.1 (4-C), 76.5 (2-C), 102.9 (1-C); *m/z* (ESI+) 399.2723 ($[M+Na]^+$ requires $C_{20}H_{40}O_6Na$ 399.2723).

Synthesis of GB cationized *O*-tetradecyl-D-glucoside 5. To a solid mixture composed of butyl ester **1** (1 g, 3.72 mmol, 1.0 equiv.), glucoside **3** (699 mg, 1.86 mmol, 0.5 equiv.) and myristic alcohol **2** (398 mg, 1.86 mmol, 0.5 equiv.) was added $NaHCO_3$ (156 mg, 1.86 mmol, 0.5 equiv.). This mixture was then put under reduced pressure (5-10 mbar) and was heated to 80-85°C. After 3 h, the reaction media was allowed to cool down to room temperature and to come back to atmospheric pressure. This mixture was thus dissolved in a CH_2Cl_2/MeOH (1:1) mixture acidified beforehand by MSA (178 mg, 1.86 mmol, 0.5 equiv.) in order to make a silica solid deposit. This deposit was purified by chromatography on silica gel (AcOEt/AcOH/H_2O 8:1.5:0.5 to 6:2:2) to afford different isomers of **5** (626 mg, 1.12 mmol, 60%) as a white powder. *Rf* 0.40-0.20 (AcOEt/AcOH/H_2O 7:2:1); δ_H (400 MHz, $CDCl_3/CD_3OD$: 1:1) α isomer only: **5a**: 0.85 (3H, t, *J* 7.3, CH_3), 1.43-1.24 (22H, m, $(CH_2)_{11}$), 1.51 (2H, m, C*H*$_2$CH$_2$O), 1.99 (0.8H, s, CH_3, $CH_3CO_2^-$), 2.73 (2.2H, s, $CH_3SO_3^-$), 3.32 (9H, s, $(CH_3)_3N^+$), 3.36-3.41 (2H, m, 2-H and 4-H), 3.53 (1H, m, CH$_2$C*H*$_2$O), 3.64 (1H, ap. t, *J* 9.9, 3-H), 3.69 (1H, m, CH$_2$C*H*$_2$O), 3.75 (1H,m, 5-H), 4.31 (2H, s, $(CH_3)_3N^+$C*H*$_2$), 4.45 (2H, m, 6-H), 4.75 (1H, d, *J* 3.6, 1-H), **5b**: 0.85 (3H, t, *J* 7.3, CH_3), 1.43-1.24 (22H, m, $(CH_2)_{11}$), 1.51 (2H, m, C*H*$_2$CH$_2$O), 1.99 (0.8H, s, CH_3, $CH_3CO_2^-$), 2.73 (2.2H, s, $CH_3SO_3^-$), 3.32 (9H, s, $(CH_3)_3N^+$), 3.53 (1H, m, CH$_2$C*H*$_2$O), 3.58-3.64 (3H, m, 2-H, 4-H and 5-H), 3.69 (1H, m, CH$_2$C*H*$_2$O), 3.78 (1H, m, 6-H), 4.31 (2H, s, $(CH_3)_3N^+$C*H*$_2$) 4.84 (1H, d, *J* 3.6, 1-H), 5.27 (1H, dd, *J* 8.2, 10.2, 3-H), **5c**: 0.85 (3H, t, *J* 7.3, CH_3), 1.43-1.24 (22H, m, $(CH_2)_{11}$), 1.51 (2H, m, C*H*$_2$CH$_2$O), 1.99 (0.8H, s, CH_3, $CH_3CO_2^-$), 2.73 (2.2H, s, $CH_3SO_3^-$), 3.32 (9H, s, $(CH_3)_3N^+$), 3.53 (1H, m, CH$_2$C*H*$_2$O), 3.61-3.68 (2H, m, 2-H and 4-H), 3.69 (1H, m, CH$_2$C*H*$_2$O), 3.84 (1H,m, 5-H), 4.31 (4H, s, $(CH_3)_3N^+$C*H*$_2$) 4.40 (1H, dd, *J* 2.3, 11.4, 6$_{a\ or\ b}$-H), 4.51 (1H, dd, *J* 3.8, 6$_{a\ or\ b}$-H), 4.81 (1H, d, *J* 3.6, 1-H), 5.24 (1H, ap. t, *J* 9.7, 3-H); δ_C (100 MHz, $CDCl_3/CD_3OD$: 1:1) α isomer only: 14.3 (CH_3), 22.4, 28.7, 29.9, 30.2, 31.4, 32.3 ($(CH_2)_{12}$), 39.5 ($CH_3SO_3^-$), 54.2 ($(CH_3)_3$), 60.8 (6-C **5b**), 63.5 (CH_2N^+), 64.7 (6-C **5c**), 64.8 (6-C **5a**), 67.3 (*C*H$_2$CO), 67.7 (4-C **5c**), 69.3 (5-C **5c**), 69.4 (4-C **5a**), 69.7 (4-C **5b**), 70.0 (2-C **5c**), 70.1 (CH$_2$*C*H$_2$O), 71.6 (5-C **5b**), 71.8 (5-C **5a**), 73.5 (3-C **5a**), 76.5 (2-C **5a**), 78.1 (3-C **5b**), 78.5 (3-C **5c**), 98.4 (1-C **5b**), 98.8 (1-C **5a**), 99.0 (1-C **5c**), 165.2 (CH$_2$*C*O), 175.1 (CH_3CO); *m/z* (ESI+) 476.3584 ($[M\text{-}MsO^-]^+$ and $[M\text{-}AcO^-]^+$requires $C_{25}H_{50}NO_7^+$ 476.3582).

***O*-tetradecyl-D-xyloside 6: Purification of 2637JG.** The purification of 34 g of 2637JG was done according to the protocol to obtain *O*-tetradecyl-D-glucoside **3**. The solvent mixture CH_2Cl_2/MeOH (9.5:0.5 then 9:1) was used to afford an α/β (56/44) mixture of **6** (8.20 g, 23.7 mmol, 28%) as a white powder. *Rf* 0.35 (CH_2Cl_2/MeOH 9:1); δ_H (400 MHz, $CDCl_3/CD_3OD$: 1:1) α isomer: 0.85 (3H, t, *J* 6,7, CH_3), 1.24 (22H, m, $(CH_2)_{11}$), 1.61 (2H, m, C*H*$_2$CH$_2$O), 3.38 (1H, dd, *J* 3.7, 9.4, 2-H), 3.42 (1H, m, CH$_2$C*H*$_{2a\ or\ b}$O), 3.56-3.48 (3H, m, 4-H, 5$_{a\text{-}b}$-H), 3.59 (1H, m, 3-H), 3.66 (1H, m, CH$_2$C*H*$_{2a\ or\ b}$O), 4.73 (1H, d, *J* 3.8, 1-H), β isomer: 0.85 (3H, t, *J* 6.7, CH_3), 1.24 (22H, m, $(CH_2)_{11}$), 1.61 (2H, m, C*H*$_2$CH$_2$O), 3.20 (1H, ap. T, *J* 10.0, 5$_{a\ or\ b}$-H), 3.22 (1H, dd, *J* 7.3, 8.9, 2-H), 3.34 (1H, t, *J* 9.1, 3-H), 3.53 (1H, m, 4-H), 3.90 (1H, dd, *J* 5.2, 11.9, 5$_{a\ or\ b}$-H), 4.20 (1H, d, *J* 7.3 Hz, 1-H); δ_C (100 MHz, $CDCl_3/CD_3OD$: 1:1) α isomer: 14.3 (CH_3), 22.4, 28.7, 29.9, 30.2, 31.4, 32.3 ($(CH_2)_{12}$), 61.6 (5-C), 68.2 (CH$_2$*C*H$_2$O), 69.7 (4-C), 72.1 (2-C), 72.1 (3-C), 98.6 (1-C), β isomer: 14.3 (CH_3), 22.4, 28.7, 29.9, 30.2, 31.4, 32.3 ($(CH_2)_{12}$), 61.6 (5-C), 69.6 (4-C), 69.9 (CH$_2$*C*H$_2$O), 73.1 (2-C), 76.1 (3-C), 103.4 (1-C).

Synthesis of GB cationized *O*-tetradecyl-D-xyloside 7. To a solid mixture composed of butyl ester **1** (1 g, 3.72 mmol, 1.0 equiv.), xyloside **6** (637 mg, 1.86 mmol, 0.5 equiv.) and myristic alcohol **2** (398 mg, 1.86 mmol, 0.5 equiv.) was added $NaHCO_3$ (156 mg, 1.86 mmol, 0.5 equiv.). This mixture was then put under reduced pressure (5-10 mbar) and was heated to 80-85°C. After 24 h, the reaction media was allowed to cool down to room temperature and to come back to atmospheric pressure. ^{1}H NMR analysis was used in order to evaluate the conversion of α isomer of **6** into α isomer of **7** (48%). δ_H (400 MHz, $CDCl_3/CD_3OD$: 1:1) 0.85 (t, *J* 7.3, CH_3 **2**, **4**, **6, 7**), 0.93 (t, *J* 7.4, CH_3 **1**), 1.24 (m, $(CH_2)_{11}$ **2**, **4**, **6**, **7**), 1.38 (m, OCH$_2$C*H*$_2$ **1**), 1.51 (m, C*H*$_2$CH$_2$O **2**, **4**, **6**, **7**), 1.65 (m, C*H*$_2$CH$_2$O **1, 4**), 2.73 (s, $CH_3SO_3^-$, **1**, **4**, **7**), 3.33 (s, $(CH_3)_3N^+$ GB, **1**, **4**, **7**), 3.43-3.38 (m, 2-H **7bα**, 4-H **7bα**, CH$_2$C*H*$_{2a\ ou\ b}$O **6**, **7**), 3.66-3.62 (m, 5-H **7bα**, CH$_2$C*H*$_{2a\ or\ b}$O **6**, **7**), 4.24 (t, *J* 6.7, CH$_2$O **1, 4**), 4.28 (s, CH_2N^+ GB), 4.25-4.18 (m, $(CH_3)_3N^+$C*H*$_2$ **7**), 4.34 (s, CH$_2$CO **1**, **4**), 4.73 (1H, d, *J* 3.8, 1-H, **6α**), 4.78 (1H, d, *J* 3.8, 1-H, **7bα**), 5.18 (1H, m, 3-H **7bα**); δ_C (100 MHz, $CDCl_3/CD_3OD$: 1:1) 14.3 (CH_3), 19.4, 22.4, 28.7, 29.9, 30.2, 31.4, 32.3 (aliphatic CH_2), 39.5 ($CH_3SO_3^-$), 54.2 ($(CH_3)_3$ N^+), 63.5 (CH_2N^+), 70.1 (CH$_2$*C*H$_2$O), 67.3 (*C*H$_2$CO), 98.6 (1-C **7bα**), 77.3 (3-C **7bα**), 72.5 (2-C **7bα**), 165.2 (CO); *m/z* (ESI+) 446.50 ($[M\text{-}MsO^-]^+$ requires $C_{24}H_{48}NO_6^+$ 446.35).

Synthesis of GB cationized *O*-alkyl-D-glucosides starting from crude materials

Crude butyl ester 1. The synthesis of the crude butyl ester **1** was performed with the protocol set forth before, excluding the purification step. For this reaction glycine betaine (8.71 g, 74.3 mmol, 1.0 equiv.), *n*-butanol (11.00 g, 148.6 mmol, 2.0 equiv.) and MSA (9.27 g, 96.6 mmol, 1.5 equiv.) were used to afford a yellow liquid. ^{1}H NMR analysis was used to follow the reaction between GB and *n*-butanol to give **1b** mixture and to determine the following molar ratio: **1**/MSA/*n*-BuOH: 39/21/40.

GB cationized *O*-alkyl-D-glucosides. The excess of methanesulfonic acid (343 mg, 3.57 mmol, 0.5 equiv.) in crude **1** (1.92 g, 7.13 mmol, 1.0 equiv.) was neutralized with $NaHCO_3$ (299 mg, 3.57 mmol, 0.5 equiv.). The mixture obtained was stirred under reduced pressure (20 mbar) in order to remove the water produced during neutralization. Once the bubbling finished, the media was allowed to come back to atmospheric pressure and after Montanov® and $NaHCO_3$ (280 mg, 2.14 mmol, 0.3 equiv.) were added. The mixture obtained was then put under reduced pressure once more (20 mbar) and was heated to 80-85°C for Montanov® 14 and 68 and to 90-95°C for Montanov® 202. Once the mixture was become too viscous to allow stirring, the heat was stopped. At 50°C, the mixture was allowed to come back to atmospheric pressure and a solution of EtOH acidified with MSA (441 mg, 4.28 mmol, 0.6 equiv.) was added. Once the mixture was totally dispersed in acidified EtOH, the hot solution was then filtered and the filtrate was allowed to cool down to room temperature. GB then crystallized were removed by a second filtration. Solvent of the second filtrate was removed under vacuum pressure to afford a yellow paste. ^{1}H NMR analysis was used to evaluate the conversion of *O*-alkyl-D-glucoside α isomers into cationized *O*-alkyl-D-glucoside α isomers (Montanov® 14: 66%; Montanov® 68: 69%, Montanov® 202: 65%).

Evaluation of the emulsifying properties of cationized Montanov® 202. The fat phase composed of emulsifier (Montanov® 202 or its cationized version) (3% weight) and triglycerides (10-20% weight) and the aqueous phase (pH 5.5 buffer solution QS 100% weight) were heated to 90°C (water bath) for 30 min. Once the two phases were removed from the bath, the aqueous one was added to the fat one. The mixture obtained was emulsified with a Silverson® mixer (4000 rpm) for 4 min. The mixture, still under stirring (150 rpm), was allowed to cool down for 20 min. After 10 min of stirring, the cooling was accelerated with a cold water bath and then the preservative (Sepicide HB®) was added.

Acknowledgments

This work was supported by the company SEPPIC. The authors thank Dr. Loïc Lemiègre for helpful discussions during the first part of the work (ENSCR) and Mrs. Virginie Barthe for her contribution to the production of cationic APG (SEPPIC) at a 2L reactor scale.

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Solvent-free transformation of AlkylPolyglycosides into 100% bio-based cationic sugar surfactants proceeded efficiently using a natural glycine betaine-derived cationizing agent