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# Direct Conversion of Alginate Oligo- and Polysaccharides into Biodegradable and Non-Ecotoxic Anionic Furanic Surfactants – An Experimental and Mechanistic Study

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**Abstract:** A series of novel anionic furanic surfactants characterized by the presence of a couple of lipophilic chains acetal-linked to a sodium 2-furoate head group, were prepared by the conversion of oligo-alginates or alginate to butyl 5-(dibutoxymethyl)-2-furoate, followed by the introduction of fatty alkyl chains containing 7 to 18 carbon atoms and the release of the carboxylate function. A plausible mechanism for the unexpected formation of butyl 5-(dibutoxymethyl)-2-furoate was proposed through a study based on both experimental results and density functional calculations. One-pot processes involving hydrolysis, butanolysis, dehydration, transesterification, transacetalization and saponification reactions, were successfully developed to provide furan-type surfactants under conditions that respect the principles of green chemistry. The surface activities of these products in a pure form or as a mixture were evaluated and quite low values of superficial tensions ( $<25 \text{ mN m}^{-1}$ ) and foaming properties were obtained depending of the alkyl chain length. In addition, a readily biodegradability and an absence of aquatic ecotoxicity were evidenced for a surfactant composition based on sodium 5-(diocetylloxymethyl)-2-furoate.

## Introduction

Bio-based furanic synthons such as furfural and 5-hydroxymethylfurfural (HMF), are referred to as "platform" molecules, i.e. simple and small molecules derivable from biomass that could be used as building blocks for higher-value chemicals and materials.<sup>[1,2]</sup> In the context of climate change and limitation of fossil resources, their wide application in consumer products drives a growing demand for their sustainable production. These compounds can be produced by acid-catalyzed dehydration of pentoses (xylose) and hexoses (glucose, fructose), respectively. These sugars are present in natural polysaccharides such as xylan (a xylose polysaccharide), starch (a polyglucan), inulin (a polyfructan), or in disaccharides such as sucrose (a disaccharide of glucose and fructose) and cellobiose (a glucose dimer). HMF and related structures have been listed as "Top 10+4" bio-based chemicals by the U.S. Department of Energy (DOE).<sup>[3,4]</sup> For instance, HMF can be converted into 2,5-

dimethylfuran (DMF)<sup>[5]</sup> to provide an alternative biofuel of ethanol or 2,5-furan dicarboxylic acid (FDCA)<sup>[6]</sup> to substitute terephthalic acid for the production of bio-based polyesters (polyethylene furoates).

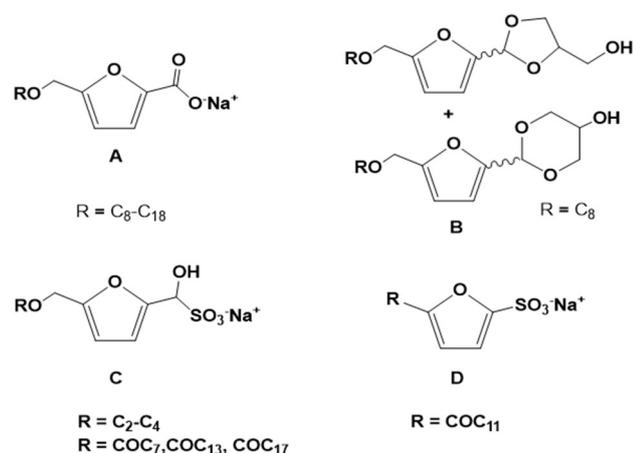
Another class of bioderived furanic chemicals from HMF are biodegradable surfactants. Surfactants are one of the most representative chemical commodities, not only in terms of quantity but also in view of the great variety of applications in household industry and agriculture areas. These surface active agents are included in more than 50% of manufactured goods such as laundry detergents, dishwashing detergents, cleaning products, cosmetic hair-care and personal care products, agricultural chemicals, oilfield chemicals and others. The global surfactants market accounted for \$31.29 billion in 2017 and is expected to reach \$58.85 billion by 2026 growing at a compound annual growth rate (CAGR) of 7.3% during the forecast period.<sup>[7]</sup>

Anionic surfactants (sulfonates, carboxylates, phosphonates, and sulfates) and non-ionic surfactants (ethoxylates and carbohydrates) dominate the market by representing almost 90% of the total surfactant production. The majority of surfactants are produced from petrochemical raw materials that are non-renewable sources. These petroleum-based products are facing a significant increase in the stringent regulations worldwide, due to their poor biodegradability and questionable toxicity profile. Therefore, alternatives made from renewable biomass feedstocks are being developed for use as biodegradable and safer substitutes in chemical, pharmaceutical, cosmetic, and environment industries.<sup>[8,9]</sup>

Over the past 10 years, the synthesis of bio-based surfactants from HMF or furfural derivatives has been investigated to furnish a new class of anionic or non-ionic surfactants characterized by the presence of a difunctionalized 2,5-furan moiety. These structures include 5-alkoxymethylfuran-2-carboxylate sodium salts (A),<sup>[10]</sup> 5-alkoxymethylfurfural glycerol acetals (B),<sup>[11]</sup> 5-alkoxy- and 5 acyloxy-methylfuran-2- $\alpha$ -hydroxymethanesulfonic acid sodium salts (C),<sup>[12]</sup> and oleo-furansulfonates (D)<sup>[13]</sup> (Figure 1). The synthetic routes of furan carboxylates (A) and furfural glycerol acetals (B) involved the selective etherification of HMF with fatty alcohols using heterogeneous solid acid, followed by an oxidation with a gold catalyst or an acetalization with glycerol. Furanmethane sulfonate ethers and esters (C) were prepared through a sulfonation of 5-alkoxymethylfuran-2-aldehydes or 5-alkoxymethylfuran-2-aldehydes employing sodium bisulfite.

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Oleofuran surfactants (D) were produced by furan Friedel-Crafts acylation within single layer (SPP) zeolite catalyst followed by



**Figure 1.** Structure of surfactants derived from HMF or furfural.

sulfonation.

To date, only the surface activities of the oleo-furan-sulfonates (D) have been reported in the literature.<sup>[13]</sup> These acylfurans are high-performing surfactants in low concentration and temperature, and more importantly, enhance hard water stability that permits a broad range of applications in hard water. For acyloxymethylfuran sulfonates (C), a reversion to aldehydes was observed in aqueous solutions at pH values higher than 8, thus confirming the instability of the sulfonated products under basic conditions.<sup>[12]</sup>

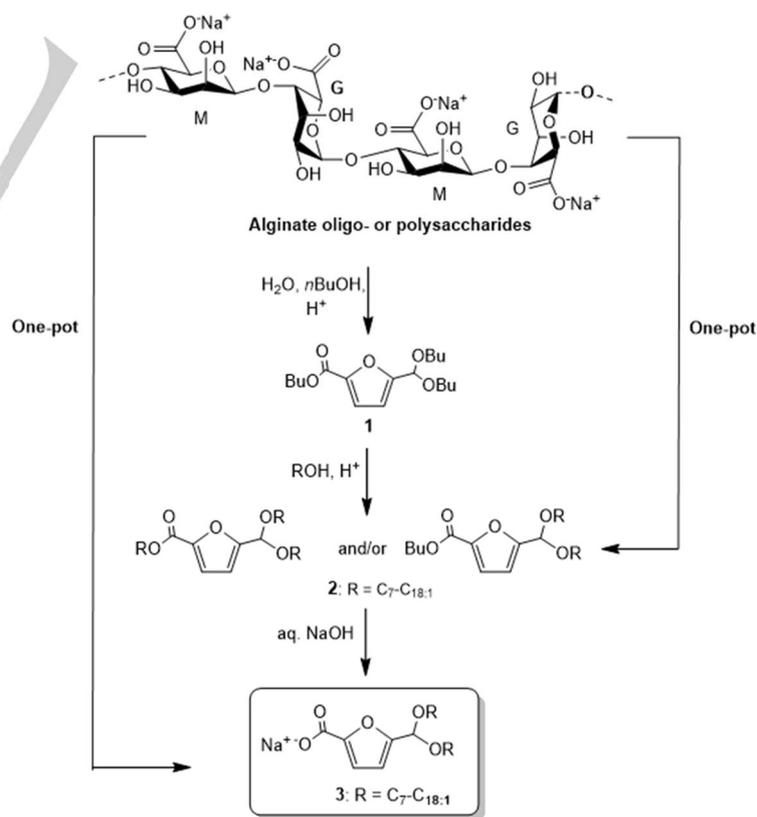
In this context, we investigated the synthesis and physico-chemical evaluation of sodium 5-(dialkoxymethyl)-2-furoates **3** (FurCO<sub>2</sub>Na-C<sub>n</sub>C<sub>n</sub>) as a novel family of anionic furan-based surfactants (Scheme 1). Owing to the presence of a couple of lipophilic chains acetal-linked to a furan-2-carboxylate unit, these amphiphilic molecules are expected to exhibit improved performance and/or original surface properties compared to their single-tailed counterparts. Precursor molecules of these double-tailed furan surfactants were prepared by reacting HMF and fatty alcohols in the presence of beta zeolite catalyst but the synthetic pathway led to the formation of by-products resulting from etherification reactions.<sup>[14]</sup> Furthermore, the subsequent oxidation step of the 5-(dialkoxymethyl)-2-hydroxymethylfurans, required to give the corresponding carboxylate surfactants, has not been reported.

Therefore, there is a real need for a new synthetic method to produce furan-type surfactants which overcomes the defects, disadvantages of the prior art, especially for a process allowing the direct conversion of oligo-, polysaccharides into sodium 2-furoates without using HMF or other furanic derivatives as starting materials. Indeed, furanics, and especially HMF, exhibit physicochemical behaviors that are obstacles to their commercialization, mainly due to their high miscibility in aqueous media and/or chemical instabilities. In considering a more satisfactory solution, our approach (Scheme 1) was based upon the direct transformation of uronates found in natural alginate or oligo-alginates into alkyl 5-(dialkoxymethyl)-2-furoates **2** (FurCO<sub>2</sub>C<sub>n</sub>-C<sub>n</sub>C<sub>n</sub>) followed by a saponification step to give anionic sodium 5-(dialkoxymethyl)-2-furoates **3** (FurCO<sub>2</sub>Na-C<sub>n</sub>C<sub>n</sub>). This alternative means is more effective than strategies based on HMF transformations because it not only avoids the oxidation step as the starting carbohydrates possess the carboxylate functionality, but also authorizes the use of uronate polysaccharides under both homopolymeric and heteropolymeric forms.

A procedure to synthesize alkyl 5-(dialkoxymethyl)-2-furoates **2** was recently described<sup>[15]</sup> via a dehydration reaction of gluconic acid derivatives which can be dehydro-gluconic acid (DHG), 2 keto-gluconic acid (2KGA) or 5 keto-gluconic acid (5KGA). The synthesis requires the prior preparation of the precursors DHG,

2KGA and 5KGA employing a three-step process based on (1) enzymatic oxidation or enzymatic dehydrogenation of glucose to 1,5-gluconolactone; (2) hydrolysis of 1,5-gluconolactone to gluconate; and (3) enzymatic conversion of gluconate to DHG, 2KGA or 5KGA. When the dehydration of these gluconic acid derivatives is performed in an alcohol (e.g. MeOH, EtOH, *n*BuOH), the furan acetal ester **2** can be formed but this molecule is in equilibrium with the corresponding aldehyde. Consequently, the production of alkyl 5-(dialkoxymethyl)-2-furoates **2** through a convenient and direct transformation of natural carbohydrate resources remains a challenge.

Herein we report a new process for the production of furan acetal esters **2** and original furan acetal carboxylates **3**, starting from alginate, oligomannuronates (oligo[M]) and oligoguluronate (oligo[G]). Alginate, a major carbohydrate compound contained in brown seaweeds, is composed of the two kinds of hexuronic acids, such as  $\beta$ -D-mannuronic acid and  $\alpha$ -L-guluronic acid, via 1,4-glycosidic linkage, that are arranged in homopolymeric and heteropolymeric blocks.<sup>[16]</sup> Furanic derivatives **2-3** are obtained through a series of environmentally friendly chemical transformations of oligo-alginates or alginate based on: (i) hydrolysis and/or glycosidation, esterification, dehydration reactions with *n*BuOH leading to the formation of butyl 5-(dibutoxymethyl)-2-furoate intermediate **1**; (ii) transesterification, transacetalization reactions in fatty alcohol media (from heptyl to oleyl alcohols) to give furan acetal esters **2** and; (iii) saponification reaction to give access to the anionic furanic surfactants **3** (Scheme 1). In addition, one-pot processes have been developed to furnish the ester and carboxylate compounds without any separation and purification of intermediates. The reaction mechanism for the formation of the key butyl 5-(dibutoxymethyl)-2-furoate intermediate **1** has been investigated using density functional theory (DFT). Finally, physicochemical studies of the sodium 5-(dialkoxymethyl)-2-furoate surfactants **3** have been achieved and clearly highlight the potential for these original materials as surface-active agents and foaming products.



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**Scheme 1.** Strategies for the synthesis of alkyl 5-(dialkoxyethyl)-2-furoates **2** (FurCO<sub>2</sub>C<sub>n</sub>-C<sub>n</sub>C<sub>n</sub>) and sodium 5-(dialkoxyethyl)-2-furoates **3** (FurCO<sub>2</sub>Na-C<sub>n</sub>C<sub>n</sub>) from alginate oligo- or polysaccharides.

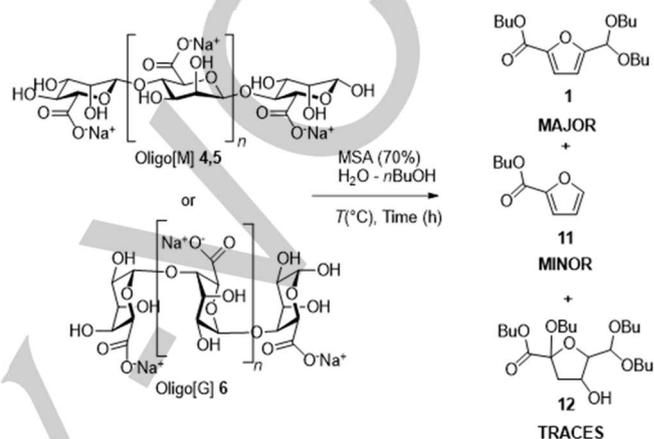
## Results and Discussion

## Chemical transformation of alginate oligo- and polysaccharides into butyl 5-(dibutoxymethyl)-2-furoate

In the first stage of the work, the reactivity of oligo-alginates and alginate was investigated towards acid-promoted hydrolysis and/or butanolysis and dehydration reactions to provide monomeric butyl 5-(dibutoxymethyl)-2-furoate **1**. Oligomannuronates (Oligo[M]) **4**, **5** and Oligogulonate (Oligo[G]) **6** characterized by different mannuronate/gulonate (M/G) ratios and a degree of polymerization ranging from 4 to 30 (Scheme 2), were produced by a controlled acid hydrolysis of alginates.<sup>[17,18]</sup> These oligo-alginates were first selected to identify the reaction conditions required to transform the uronate units into furanic derivative **1**. Acid treatment of Oligo[M] and Oligo[G] was performed with readily biodegradable methanesulfonic acid (MSA, 70% aq. solution) in the presence of water and *n*BuOH used as both nucleophilic reagent and solvent. The solvent was heated at reflux and the water, initially added in the reaction mixture and formed during the reaction, was eliminated by using a Dean-Stark apparatus. After the work-up and purification by silica gel column chromatography, a mixture of non-polar products composed of major butyl 5-(dibutoxymethyl)-2-furoate **1** and minor butyl 2-furoate **11** was isolated (wt ratio % for **1/11** ≥ 9). The more volatile-by-product **11** was easily removed under vacuum to give pure 2,5-disubstituted furan **1**. In addition to these furanic products, trace amounts of 4-hydroxy-tetrahydrofuran compound **12** disubstituted at the C-2 position by butoxy and butoxycarbonyl groups (wt ratio % for **12/1** ≤ 0.05), were isolated and characterized by a series of NMR experiments (<sup>1</sup>H, <sup>13</sup>C Jmod, COSY, HSQC, HMBC) and high resolution mass spectrometry (see ESI).

A variety of reaction conditions, in terms of H<sub>2</sub>O, *n*BuOH and MSA quantities used, temperature and reaction time, were envisaged as summarized in Table 1. The number of equivalent of the reagents as well as the yields were determined relative to one sugar unit of the oligomers (see ESI). Initial conditions based on the use of 1.7 eq. of MSA in the presence of 26 eq. of H<sub>2</sub>O and 151 eq. of *n*BuOH at 140 °C for 24 h (Table 1, entry 1) were applied to Oligo[M] **4** and led to the formation of a small amount of furanic compound **1** (5% molar yield, 9% mass yield). A significant improvement in yield was observed by increasing both the quantity of MSA used and temperature while reducing

reaction time (Table 1, entries 2,3). A halving of the quantities of H<sub>2</sub>O and *n*BuOH used, preserved the level of transformation of Oligo[M] into butyl 5-(dibutoxymethyl)-2-furoate **1** (Table 1, entry 4). Finally, a decrease in the amount of MSA up to 4.45 eq. (Table 1, entry 5) provided the best reaction conditions to produce furoate derivative **1** with a reproducible molar yield of 33% (mass yield = 60%). This moderate yield is probably due to the formation of *humins* which are byproducts of any acid catalyzed reaction of carbohydrates at high temperatures. Recent studies showed that *humins* are chemical networks mainly composed of furan moieties with different functional groups.<sup>[19]</sup>



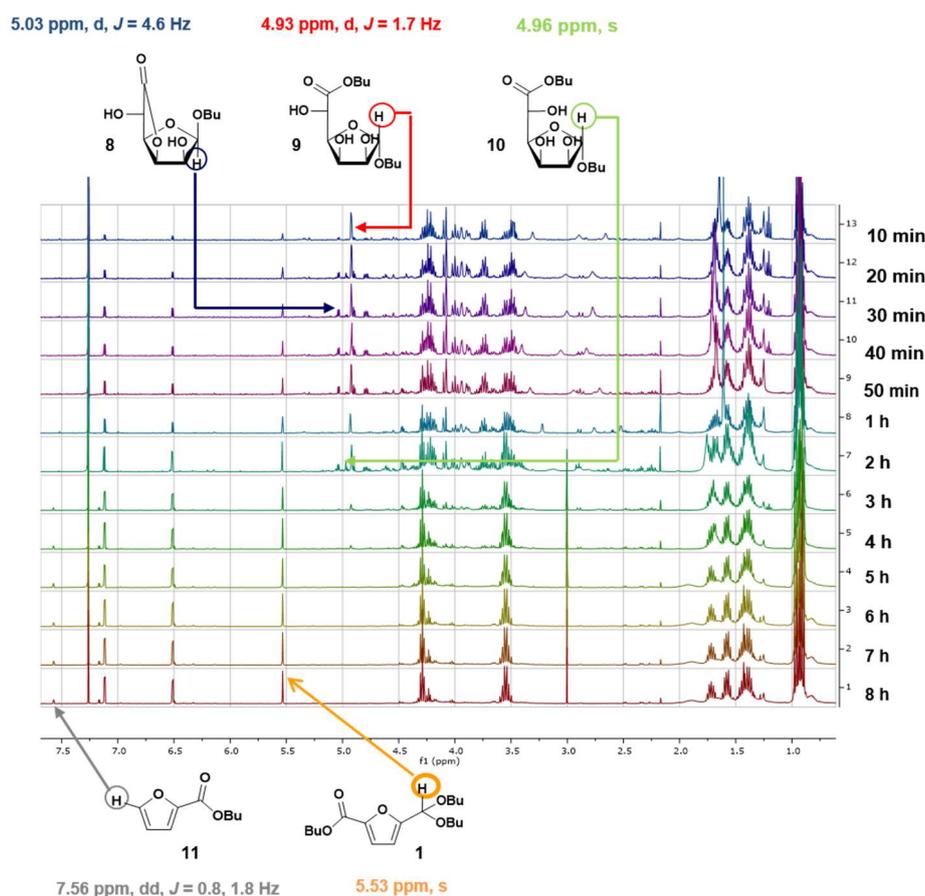
**Scheme 2.** Transformation of Oligo[M] **4,5** or Oligo[G] **6** into butyl 5-(dibutoxymethyl)-2-furoate **1**. **4**: M/G = 2.7, DP = 4 (*n* = 2), M = 718.48 g mol<sup>-1</sup>; **5**: M/G = 6.3, DP = 22 (*n* = 20), M = 3853.13 g mol<sup>-1</sup>; **6**: M/G = 0.04, DP = 30 (*n* = 28), M = 5271.6 g mol<sup>-1</sup>.

To explore how the conversion of oligo [M] **4** into butyl 5-(dibutoxymethyl)-2-furoate **1** proceeded, a kinetic study was investigated through <sup>1</sup>H NMR experiments (Figure 2) carried out from the reaction mixture corresponding to entry 5 (Table 1). The NMR study showed the formation of butyl 5-(dibutoxymethyl)-2-furoate **1** (5.53 ppm for the acetal proton) from the first minutes of the reaction and the quantity produced increased with reaction time. In addition, the presence of a butylated uronate evidenced by a doublet at 4.93 ppm with a coupling constant of 1.7 Hz for the anomeric proton, was observed after 10 minutes of reaction. This is (*n*-butyl)-*n*-butyl α-D-mannofuranosiduronate **9** previously characterized in our laboratory as the kinetic product of the glycosidation reaction (Figure 2);<sup>[20]</sup> this mannuronate compound is no longer detected by <sup>1</sup>H NMR after 6 h of reaction. Two additional products were identified during this period. The first one has a characteristic doublet signal at 5.03 ppm with a coupling

**Table 1.** Yields for the synthesis of butyl 5-(dibutoxymethyl)-2-furoate **1** from Oligo[M] **4,5** and Oligo[G] **6**, depending on H<sub>2</sub>O, *n*BuOH and MSA (70%) quantities used, temperature and reaction time.<sup>[a]</sup>

Entry	Oligomers	H <sub>2</sub> O [eq.]	<i>n</i> BuOH [eq.]	MSA [eq.]	T [°C]	Time [h]	Molar yield [%]	Mass yield [%]
1	<b>4</b>	26	151	1.7	140	24	5	9
2	<b>4</b>	26	151	6	150	9.5	21	38
3	<b>4</b>	26	151	6	160	8	26	46
4	<b>4</b>	13	76	6	160	6	28	51
5	<b>4</b>	13	76	4.45	160	6	33	60
6	<b>5</b>	13	76	4.45	160	6	20	36
7	<b>6</b>	13	76	4.45	160	6	16	29

[a] Yields are calculated after isolation of pure compound **1** by silica gel column chromatography.



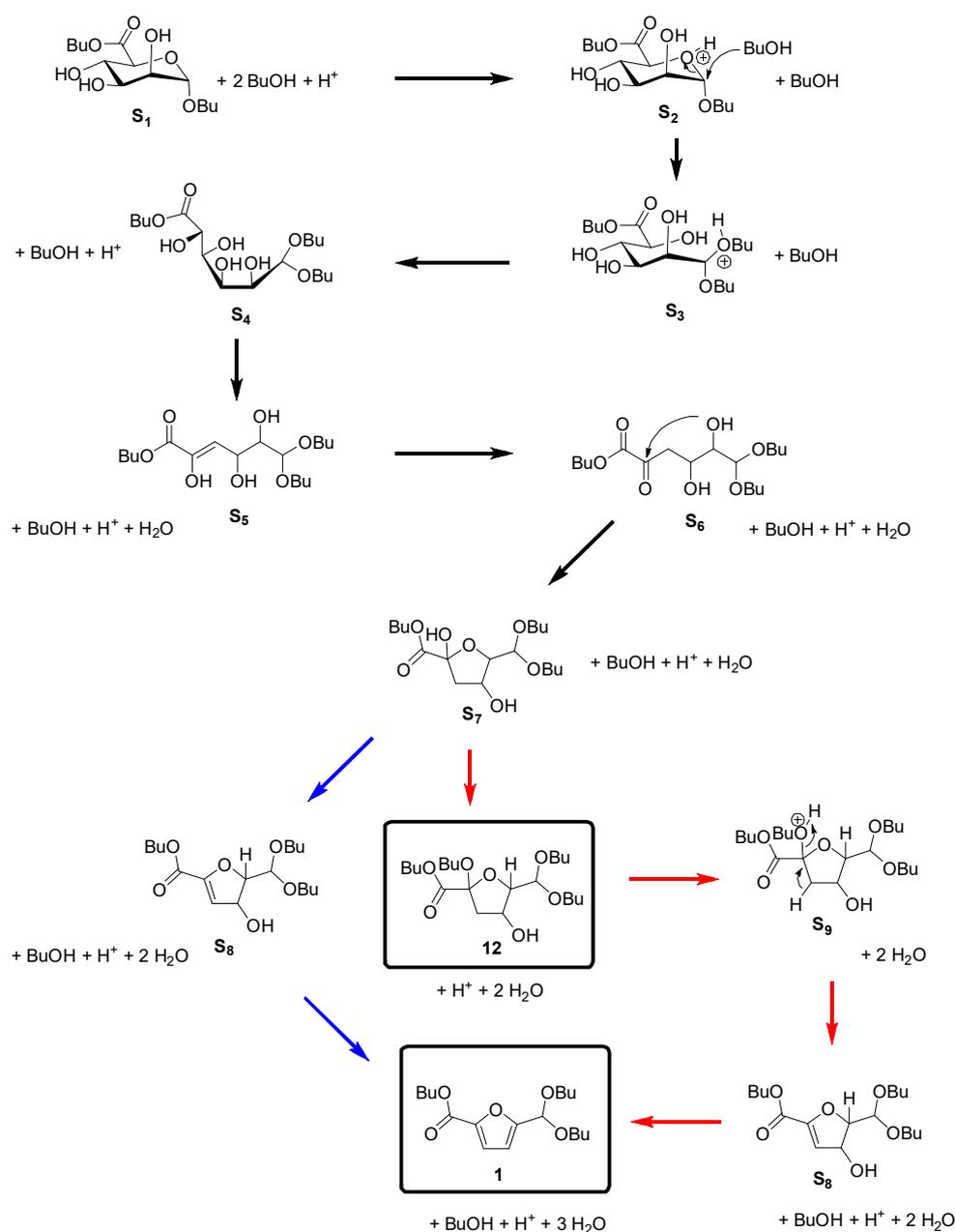
**Figure 2.**  $^1\text{H}$  NMR analysis ( $\text{CDCl}_3$ , pre-treated on basic alumina) of the reaction mixture with time during the transformation of Oligo[M] **4** into butyl 5-(dibutoxymethyl)-2-furoate **1**. Identification of by-products **8-11**.

constant of 4.6 Hz. This product corresponds to *n*-butyl  $\beta$ -D-mannofuranosiduronono-6,3-lactone **8**, no longer present after 6 h of reaction. The second product is characterized by a singlet at 4.96 ppm that is assigned to the anomeric proton of (*n*-butyl)-*n*-butyl- $\beta$ -L-gulofuranosiduronate **10** which disappeared after 3 h of reaction. This by-product results from the transformation of the minor guluronate fraction found in Oligo[M] **4**. As illustrated in Figure 2, the presence of butyl 2-furoate **11** was observed after 3 h of reaction and its proportion did not increase over time. Similarly, all butyl uronates seem to have disappeared after 6 h of reaction to afford butyl 5-(dibutoxymethyl)-2-furoate **1**. It is noteworthy that no butyl mannuronate in a pyranoside conformation was detected in the reaction medium over the entire study period.

To go further in the elucidation of the reaction mechanism for the unexpected transformation of oligo [M] **4** into butyl 5-dibutylacetal-2-furoate **1**, a study using density functional theory (DFT) was carried out by calculating the energy of transition states, free energies of reaction and activation at 160 °C (433K). Based on experimental observations, i.e. no detection of the thermodynamic product (*n*-butyl)-*n*-butyl  $\alpha$ -D-mannopyranosiduronate **S1** and isolation of 4-hydroxy-tetrahydrofuran compound **12**, a plausible mechanism for the formation of butyl 5-dibutylacetal-2-furoate **1** is given (Scheme 3). As soon as (*n*-butyl)-*n*-butyl  $\alpha$ -D-mannopyranosiduronate **S1** is produced, its conversion into 2-furoate product **1** occurs through (i) the formation of 4-hydroxy-tetrahydrofuran **S7** containing both hydroxy and butoxycarbonyl groups at the C-2 position and (ii) either successive dehydration reactions of intermediate **S7** (blue pathway, Scheme 3) or through the prior formation of the isolated 4-hydroxy-tetrahydrofuran **12** followed by a couple of *n*BuOH and  $\text{H}_2\text{O}$  elimination reactions (red pathway, Scheme 3).

**Transformation of (*n*-butyl)-*n*-butyl  $\alpha$ -D-mannopyranosiduronate **S1** into 4-hydroxy-tetrahydrofuran **S7**:** Conversion of butyl mannuronate **S1** into tetrasubstituted tetrahydrofuran **S7** is catalyzed by MSA, symbolized by  $\text{H}^+$  in Scheme 3. The pathway is divided into four steps: (i) ring opening of mannopyranosiduronate **S1** through a *n*BuOH nucleophilic attack at the anomeric position to give an open acetal **S3** which is then deprotonated to produce **S4**, (ii) dehydration reaction to yield butyl  $\alpha$ -enol ester **S5**, (iii) keto-enol tautomerism to provide butyl  $\alpha$ -keto ester **S6** and (iv) cyclisation of **S6** to afford tetrasubstituted tetrahydrofuran **S7**. This reaction mechanism is advanced following a study using DFT (see computational details in the experimental section). Based on DFT calculations (with the B3LYP functional), we propose the reaction path energetic profile of Figure 3. The reaction pathway between **S1** and **S7** looks thermodynamically favorable since **S7** appears 10 kcal mol $^{-1}$  more stable than **S1** with a maximal reaction barrier of around 40 kcal mol $^{-1}$ .

**Dehydration reactions of 4-hydroxy-tetrahydrofuran **S7** to butyl 5-dibutylacetal-2-furoate **1**:** Two pathways involving either one (blue path) or three (red path) intermediates were envisaged to transform tetrasubstituted tetrahydrofuran **S7** into butyl 5-(dibutoxymethyl)-2-furoate **1**, as described in Scheme 3. From the calculated energy profile (Figure 3), one could conclude that the path **S7-S8-1** (in blue in Scheme 3) is thermodynamically more favorable than the second **S7-12-S9-S8-1** path (in red in Scheme 3). Indeed, this second path exhibits a strong reaction barrier of 70 kcal mol $^{-1}$  between **S7** and **12**. On the opposite, the **S7-S8-1** path (blue path in Scheme 3) exhibits only a 13 kcal mol $^{-1}$  barrier (between **S7** and **S8**). The reaction path between **S8** and **1** shows that the hydroxyl group at the C-4 position is combined with the hydrogen atom at the C-5 position and the formed water molecule seems to stick to the methanesulfonic acid through hydrogen



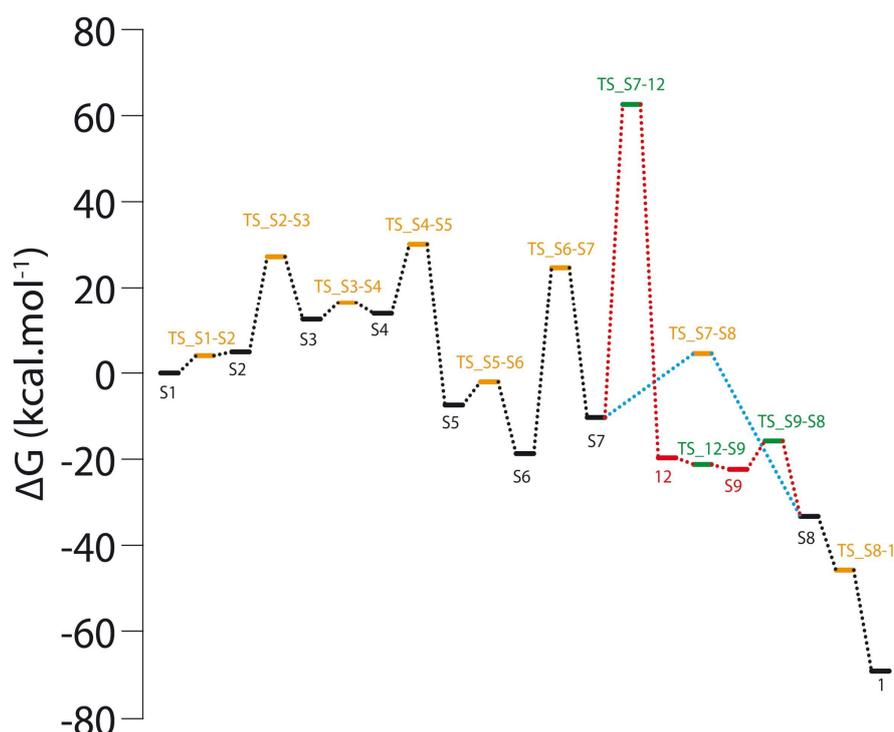
**Scheme 3.** Mechanism details for the formation of butyl 5-(dibutoxymethyl)-2-furoate **1**.

bounding (see the transition state between **S8** and **1** in ESI). From these DFT results, one can also observe that the transition state between **S8** and **1** seems to be more stable than **S8** ( $\Delta G^{\text{S8}} = -35 \text{ kcal mol}^{-1}$  and  $\Delta G^{\text{TS}_{\text{S8-1}}} = -45 \text{ kcal mol}^{-1}$ ). DFT calculations using the M06 functional have been performed and confirm this energy ordering. At this stage, there is no clear explanation for such behavior.

The best reaction conditions applied to oligo [M] **4** were extended to oligo [M] **5** and oligo[G] **6** possessing a higher degree of polymerization and different M/G ratios (Table 1, entries 6,7). The molecular weight of these oligo-alginates was found to have an impact on the level of conversion to furanic product **1**, with a lower yield observed when increasing the degree of polymerization of the substrates. Furthermore, a similar reactivity towards dehydration reactions was demonstrated for M and G uronate entities, thus making direct use of alginate as a raw material possible. At this stage, the optimization of the reaction

conditions was envisaged from polymers rather than oligomers **5** and **6** using a sodium alginate extracted from *Laminaria digitata*, a brown algae species, characterized by a degree of polymerization of 362 and M/G ratio of 0.6.

A one-pot two-step procedure was investigated from sodium alginate **7** (M/G = 0.6, DP = 362, M = 63411.4 g mol<sup>-1</sup>) under conditions that favored both the depolymerization reaction and the formation of the furan moiety. The first step of the synthesis involved the hydrolysis and butanolysis of the polysaccharide in a hydroalcoholic acid solution to promote the production of monomer D-mannuronic acid and L-guluronic acid derivatives. Alginate **7** was dispersed into a solution of 172 eq. of *n*BuOH and 100 eq. of H<sub>2</sub>O in the presence of 4.45 or 6 eq. of MSA (Table 2). The reaction mixture was then heated to 110 or 160°C for 8.5 h. During this first stage, the presence of butyl 5-(dibutoxymethyl)-2-furoate **1** was not detected, regardless of the temperature. This result indicates that the removal of water is essential to achieve the cyclodehydration reaction.



**Figure 3.** Proposed reactions pathways **S1** and **1** based on B3LYP DFT calculations at 433K. The blue and red pathways are consistent with the colors used in scheme 3.

The second step involves the cyclodehydration of butyl monuronates at high temperature (160°C) by removing water by

**Table 2.** Yields for the synthesis of butyl 5-(dibutoxymethyl)-2-furoate **1** from sodium alginate **7**, depending on MSA (70%) quantities used and temperature.<sup>[a]</sup>

Entry	T [°C]		MSA [eq.]	Molar yield [%]	Mass yield [%]
	1 <sup>st</sup> step	2 <sup>nd</sup> step			
1	110	160	4.45	22	41
2	160	160	4.45	24	45
3	110	160	6.0	30	51
4	160	160	6.0	28	48

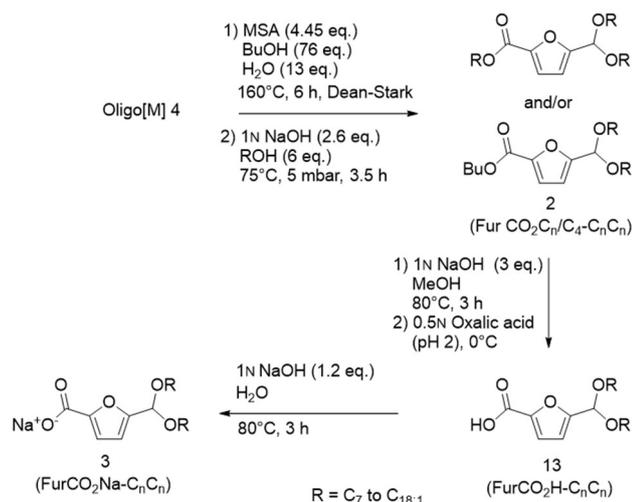
[a] Yields are calculated after isolation of pure compound **1** by silica gel column chromatography. 1<sup>st</sup> step: *n*BuOH (172 eq.), H<sub>2</sub>O (100 eq.), 8.5 h; 2<sup>nd</sup> step: 15 h, Dean-Stark.

azeotropic distillation via a Dean-Stark apparatus. The same work-up as for oligo-alginate transformation was followed to furnish the desired furanic monomer **1** in molar yields of 22–30% (mass yields = 41–51%). An increase of temperature during the first stage of the process did not give any significant improvement of the overall yield. Conversely, it was found that the MSA amount had a real impact, especially when the first step was carried out at 110°C (Table 2, entries 1,3). Remarkably, the production of butyl 5-(dibutoxymethyl)-2-furoate **1** from alginate (Table 2, entry 3) was made nearly as effective as the procedure developed from oligo-alginates (Table 1, entry 5). This approach advantageously eliminates the requirement for a preliminary step of alginate depolymerization to afford oligomeric guluronate or mannuronate blocks as starting materials for the synthesis of the furanic intermediate **1**.

### Conversion of oligomannuronates to sodium 5-(dialkoxyethyl)-2-furoates

In order to bring a more lipophilic character to the furanic molecules, longer hydrophobic alkyl chains derived from heptanol to oleyl alcohol were introduced onto butyl 5-(dibutoxymethyl)-2-furoate **1**. Oligo[M] **4** was used as the raw material to produce the desired alkyl 5-(dialkoxyethyl)-2-furoates **2** derived from fatty alcohols but alginate **7** could also have been used. We first investigated the transesterification/transacetalization conditions previously developed in our laboratory for the synthesis of alkyl  $\alpha$ -mannopyranosiduronate surfactants.<sup>[20]</sup> From the reaction mixture resulting from the optimized conversion of oligo[M] **4** to furanic intermediate **1** (Table 1, entry 5), simultaneous transesterification and transacetalization were performed in dodecanol (6 eq.) at 70°C and under reduced pressure (5 mbar) in order to eliminate the butanol formed in the reaction. Under these conditions, the furanic derivative **1** completely degraded due to the presence of excess MSA and no transesterification and/or transacetalization products were isolated. Further experiments were then performed from butyl 5-dibutylacetal-2-furoate **1** in a pure form and using dodecyl alcohol (6 eq.), in order to determine the appropriate amount of MSA required to furnish the transesterification/transacetalization products while avoiding the degradation of furan intermediate **1**. After optimization, a catalytic amount of MSA (0.3 eq.) was found to provide in a quite satisfactory yield (~75%), a mixture of two furanic didodecyl acetals composed largely of butyl ester FurCO<sub>2</sub>C<sub>4</sub>-C<sub>12</sub>C<sub>12</sub> (no transesterification reaction has occurred) and a small quantity of dodecyl ester FurCO<sub>2</sub>C<sub>12</sub>-C<sub>12</sub>C<sub>12</sub> resulting from both transesterification and transacetalization reactions.

Taking into account the good results provided by the use of 0.3 eq. of MSA to transform pure butyl 5-dibutylacetal-2-



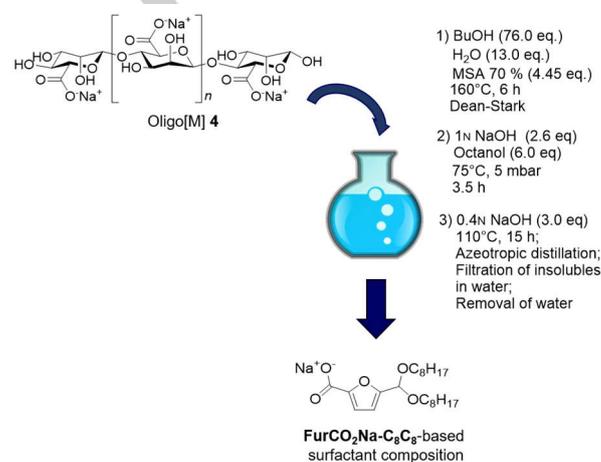
**Scheme 4.** Synthetic pathway for the production of sodium 5-(dialkoxymethyl)-2-furoates **3** (FurCO<sub>2</sub>Na·C<sub>n</sub>C<sub>n</sub>) from oligo[M] **4**.

furoate **1** into transacetalization products, a novel one-pot process was developed based on two steps reaction with conversion of oligo[M] **4** to butyl 5-(dialkoxymethyl)-2-furoate **1** followed by *in situ* partial MSA neutralization with a 1N aqueous NaOH solution and transesterification, transacetalization reactions with fatty alcohols at 75°C and under reduced pressure (Scheme 4). Addition of 2.6 eq. of 1N aq. NaOH solution was required to maintain 0.3 eq. of MSA in the reaction mixture. This synthetic process was successfully applied to various fatty alcohols, from heptyl (C<sub>7</sub>-OH) to oleyl (C<sub>18:1</sub>-OH) alcohols and the corresponding reaction products which possess two lipophilic chains acetal-linked to the furan unit and an alkyl ester, were isolated in 26–34% molar yields (C<sub>7</sub>-OH: 26% FurCO<sub>2</sub>C<sub>4</sub>-C<sub>7</sub>C<sub>7</sub> yield; C<sub>8</sub>-OH: 29% FurCO<sub>2</sub>C<sub>4</sub>-C<sub>8</sub>C<sub>8</sub>, FurCO<sub>2</sub>C<sub>8</sub>-C<sub>8</sub>C<sub>8</sub> yield; C<sub>12</sub>-OH: 32% FurCO<sub>2</sub>C<sub>4</sub>-C<sub>12</sub>C<sub>12</sub>, FurCO<sub>2</sub>C<sub>12</sub>-C<sub>12</sub>C<sub>12</sub> yield; C<sub>18:1</sub>-OH: 34% FurCO<sub>2</sub>C<sub>4</sub>-C<sub>18:1</sub>C<sub>18:1</sub> yield). It is noteworthy that the transformation efficiency was improved with increasing fatty alcohol chain lengths. Since the use of fatty alcohols with increased molecular weights decreases the concentration of butyl/alkyl 5-(dialkoxymethyl)-2-furoates **2** (FurCO<sub>2</sub>C<sub>n</sub>/C<sub>4</sub>-C<sub>n</sub>C<sub>n</sub>) in the reaction medium, it is probably easier to inhibit furan degradation (production of *humins*) using more dilute conditions based on C<sub>12</sub>-C<sub>18:1</sub> fatty alcohols.

The last step aimed at converting alkyl esters **2** into 5-(dialkoxymethyl)-2-furoic acids **13** and their corresponding sodium salt forms **3**. Compounds **2** were then saponified (1N aq. NaOH solution, 3 eq.) in methanol for 3 h at 80°C to yield sodium carboxylates (Scheme 4). Protonation of these carboxylates was achieved by an acid treatment (0.5N aq. oxalic acid) at 0°C until pH 2 to give the corresponding furoic acids **13** in 48–79% yields (C<sub>7</sub>: 79% FurCO<sub>2</sub>H·C<sub>7</sub>C<sub>7</sub> yield; C<sub>8</sub>: 59% FurCO<sub>2</sub>H·C<sub>8</sub>C<sub>8</sub> yield; C<sub>12</sub>: 48% FurCO<sub>2</sub>H·C<sub>12</sub>C<sub>12</sub> yield; C<sub>18:1</sub>: 58% FurCO<sub>2</sub>H·C<sub>18:1</sub>C<sub>18:1</sub> yield) after liquid-liquid extraction with ethyl acetate and silica gel column chromatography. The use of oxalic acid (pK<sub>a</sub> 1.2) instead of HCl was found to be more appropriate to preserve the acetal function in a more efficient way. As an example the acidification with a 0.5N aq. HCl solution carried out for FurCO<sub>2</sub>H·C<sub>8</sub>C<sub>8</sub>, dramatically decreased the yield (36%). Finally, a treatment of purified furoic acids **13** with 1N aq. NaOH (1.2 eq.) at 80°C for 3 h followed by freeze-drying of the reaction mixture afforded the desired sodium 5-(dialkoxymethyl)-2-furoates **3** in quasi-quantitative yields (98–100%).

### Development of one-pot processes for the synthesis of sodium 5-(dioctyloxymethyl)-2-furoate-based surfactant compositions.

The next challenge was to develop one-pot processes, more easily transferable to an industrial scale, while using reaction conditions in line with the principles of green chemistry. The study was conducted using *n*-octanol as the fatty alcohol for physico-chemical reasons, which will be explained in the next section. A first process consisted in reproducing the synthetic pathway previously described (Scheme 4), but following a one-pot mode, which eliminates the isolation and purification step of the transesterification, transacetalization products **2**. Saponification was carried out directly in the reaction mixture without isolating butyl/octyl 5-(dioctyloxymethyl)-2-furoates **2**. Removal of excess octanol was performed during the isolation of pure 5-(dioctyloxymethyl)-2-furoic acid **13** by silica gel column chromatography. As previously described, a final 1N aq. NaOH treatment at 80°C provided the expected sodium 5-



**Scheme 5.** One-pot, cascade procedure to produce sodium 5-(dioctyloxymethyl)-2-furoate **3** (FurCO<sub>2</sub>Na·C<sub>8</sub>C<sub>8</sub>) from oligo[M] **4**.

(dioctyloxymethyl)-2-furoate **3** quasi-quantitatively. This synthetic route, which included a single purification step, provided the desired pure furanic carboxylate surfactant **3** in an overall molar yield of 27%.

An alternative process was investigated to provide a more efficient way of manufacturing anionic furanic surfactants without requiring the steps of acidification, liquid-liquid extraction, column chromatography purification and transformation of furoic acid into sodium 2-furoate (Scheme 5). Octanol was efficiently removed in the final step of the process by azeotropic distillation with water. The resulting mixture that consisted in solid particles, was treated with water and the insolubles (containing *humins*) were eliminated by filtration. Then, the filtrate was concentrated and freeze-dried to afford a surfactant composition that represented 2.5 times the mass of the starting oligomers. This mixture is comprised of 2.66 mass % of water, 4.42 mass % of octanol, 42.61 mass % of organic substances (composed of sodium 5-(dioctyloxymethyl)-2-furoate, FurCO<sub>2</sub>Na·C<sub>8</sub>C<sub>8</sub>) and 50.31 mass % of salts as shown by thermogravimetric analysis (TGA) and LC-MS (see ESI). This one-pot, cascade procedure clearly represents a more convenient synthetic route to furan-based anionic surfactant compositions.

At this stage, the aim of the study was to calculate the main green chemistry metrics (Atom Economy, Mass Intensity and E-Factor)<sup>[21]</sup> to measure the environmental impact of the one-pot procedure carried out from 1 g of oligo[M] **4** (for full calculation data, see ESI). The total mass

of the sodium 5-(dioctyloxymethyl)-2-furoate-based surfactant composition was considered for the calculation since this surface-active mixture will be evaluated as such in physico-chemical characterizations. *n*BuOH, unreacted *n*-octanol and water were regarded as recycled materials through distillation. We started by investigating the Atom Economy (AE) which measures the ratio of the mass of the final product to the sum of all the masses of all starting materials, expressed as a percentage. The value obtained (AE 51) showed a moderate amount of reagents that are incorporated into the surfactant due to the use of *n*BuOH which is not present in the final molecule. The green character of the cascade process was illustrated by the calculation of Mass Intensity (MI) and Environmental Factor (E-Factor) metrics. MI considers the yield, stoichiometry, the solvent, and the reagent used in the reaction mixture, and expresses this on a weight/weight basis rather than a percentage. E-Factor draws attention to the quantity of waste that is produced for a given mass of product. Low values were obtained concerning both MI (2.09) and E-Factor (1.09), thus giving evidence of a satisfactory environmental impact of this one-step synthetic pathway.

### Physicochemical properties of sodium 5-dialkylacetal-2-furoates

Krafft temperatures, surface activities at the air-water interface and foaming properties were investigated for **FurCO<sub>2</sub>Na-C<sub>7</sub>C<sub>7</sub>**, **FurCO<sub>2</sub>Na-C<sub>8</sub>C<sub>8</sub>**, **FurCO<sub>2</sub>Na-C<sub>12</sub>C<sub>12</sub>**, **FurCO<sub>2</sub>Na-C<sub>8:12</sub>C<sub>18:1</sub>**, and **FurCO<sub>2</sub>Na-C<sub>8</sub>C<sub>8</sub>**-based composition resulting from the one-pot cascade procedure. Furthermore, biodegradability and aquatic ecotoxicity were evaluated for the **FurCO<sub>2</sub>Na-C<sub>8</sub>C<sub>8</sub>**-based surfactant composition.

**Krafft temperature.** The solubility of ionic surfactants in water is highly temperature-dependent. The Krafft point or Krafft temperature,  $T_k$ , is defined as the intersection of the solubility and CMC curves, i.e. it is the temperature at which the solubility of the monomeric surfactant is equivalent to its CMC at the same temperature. Knowledge of the Krafft temperature is crucial in many applications since below  $T_k$  the surfactant will not perform efficiently. Despite different alkyl chain lengths, **FurCO<sub>2</sub>Na C<sub>7</sub>C<sub>7</sub>** and **FurCO<sub>2</sub>Na C<sub>8</sub>C<sub>8</sub>** have identical  $T_k$  equal to 25°C (Table 3) as for industrial sodium lauryl ether sulfate (SLES). Compounds **FurCO<sub>2</sub>NaC<sub>12</sub>C<sub>12</sub>** and **FurCO<sub>2</sub>Na C<sub>8:12</sub>C<sub>18:1</sub>** possessing a couple of dodecyl or oleyl chains have a slightly higher  $T_k$  (28°C).

**Air-water interfacial behavior.** Table 3 shows the CMC values obtained for sodium 5-(dialkoxymethyl)-2-furoates **3**. The data also include values obtained with sodium laureth sulfate (SLES) in order to carry out a comparison. Indeed, SLES is an anionic surfactant which is widely used in rinse off products as a primary surfactant. In addition to excellent detergency (also referred as cleansing), it also has attractive foamability. Similar to conventional ionic single chain surfactants, the CMC values decrease with increasing double chain length from C<sub>7</sub> to C<sub>8</sub>. This is attributed to the increasing hydrophobicity of surfactant molecules which increases the mutual repulsion between polar water molecules and nonpolar hydrophobic chains. However, this tendency does not occur with chain length from C<sub>12</sub> to C<sub>18:1</sub> since the CMC value increases when the length of the two hydrophobic chains attached to the sodium 2-furoate moiety grows. This result could be explained by the insufficient water solubility of these compounds at the temperature used for the CMC measurement (25°C) which is lower than their  $T_k$  values. The lowest CMC was determined for **FurCO<sub>2</sub>Na-C<sub>8</sub>C<sub>8</sub>** (0.69 mmol L<sup>-1</sup>) and it represents twice that of SLES. Surprisingly, the CMC of **FurCO<sub>2</sub>Na-C<sub>8</sub>C<sub>8</sub>**-based surfactant

composition comprised of a large quantity of salts, is at the same level as pure **FurCO<sub>2</sub>Na-C<sub>8</sub>C<sub>8</sub>**.

Surface tensions are also influenced by the alkyl chain length and the geometry of the double-tailed structure. As shown in Table 3, surface tension at the CMC ( $\gamma_{CMC}$ ) slightly decreases from 26.4 to 23.9 mN m<sup>-1</sup> as chain length grows from C<sub>7</sub> to C<sub>12</sub>. However, higher  $\gamma_{CMC}$  of **FurCO<sub>2</sub>Na-C<sub>18:12</sub>C<sub>18:1</sub>** is observed. All these surface tensions compare favorably with the approximate value of 32 mN m<sup>-1</sup> obtained with SLES. Remarkably, **FurCO<sub>2</sub>Na-**

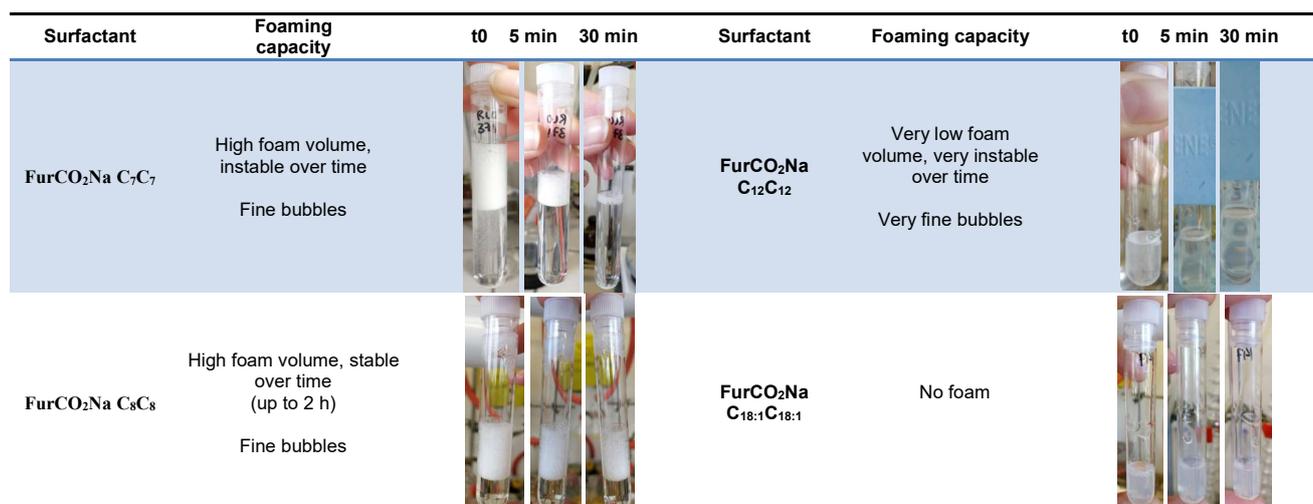
**Table 3.** CMC and  $\gamma_{CMC}$  values of sodium 5-(dialkoxymethyl)-2-furoates (FurCO<sub>2</sub>Na-C<sub>7</sub>C<sub>7</sub>) and SLES reference at 25°C.

Product	$T_k$ (°C)	CMC [g L <sup>-1</sup> ]	CMC [mmol L <sup>-1</sup> ]	$\gamma_{CMC}$ [mN m <sup>-1</sup> ]
<b>FurCO<sub>2</sub>Na-C<sub>7</sub>C<sub>7</sub></b>	25	1.1	2.92	26.4
<b>FurCO<sub>2</sub>Na-C<sub>8</sub>C<sub>8</sub></b>	25	0.28	0.69	24.6
<b>FurCO<sub>2</sub>Na-C<sub>12</sub>C<sub>12</sub></b>	28	0.58	1.12	23.9
<b>FurCO<sub>2</sub>Na-C<sub>18:12</sub>C<sub>18:1</sub></b>	28	2.30	3.38	28.6
<b>FurCO<sub>2</sub>Na-C<sub>8</sub>C<sub>8</sub></b> -based composition	n.d.	0.31	n.d.	31.7 <sup>[a]</sup>
<b>SLES</b>	25	0.14	0.33	31.8

**C<sub>8</sub>C<sub>8</sub>**-based surfactant composition resulting from one-pot procedure and SLES exhibit similar  $\gamma_{CMC}$ , but  $\gamma$  further reduces dramatically at higher concentrations to a minimum value of 24.1 mN m<sup>-1</sup> when **FurCO<sub>2</sub>Na-C<sub>8</sub>C<sub>8</sub>**-based mixture is used. These results could be related to the double-tailed furanic structure, which could exhibit various arrangements at the air-water interface depending on alkyl chain length and concentration. The  $\gamma_{CMC}$  values of surfactants **3** are largely below 30 mN m<sup>-1</sup> and are much smaller than that of SLES. They may be caused by closer packing of **FurCO<sub>2</sub>Na-C<sub>n</sub>C<sub>n</sub>** resulting from more favorable arrangements at the interface which could be optimized, even above CMC for **FurCO<sub>2</sub>Na-C<sub>8</sub>C<sub>8</sub>**-based surfactant composition.

In summary, **FurCO<sub>2</sub>Na-C<sub>8</sub>C<sub>8</sub>**, in a pure form or as a mixture, represents the most attractive molecule in terms of CMC and  $\gamma$  values, and this original anionic furanic surfactant is competitive with conventional SLES.

**Foaming properties.** The foam was created by three vigorous shakings by hand of a closed glass tube (1 cm diameter) containing 5 mL of 0.1% wt surfactant solution. The foams produced were characterized by their volume and the bubble sizes whereas their stabilities were evaluated through the study of foam volume decrease over time. For this purpose, photographs were taken when the shaking was stopped ( $t_0$ ), and 5 min and 30 min after that moment (Figure 4). The obtained results clearly showed the influence of the alkyl chain length on the surfactant foaming properties. The highest foamability was observed with **FurCO<sub>2</sub>Na-C<sub>7</sub>C<sub>7</sub>** and **FurCO<sub>2</sub>Na-C<sub>8</sub>C<sub>8</sub>** that led to high foam volumes composed of fine bubbles. By extending the length of the double chain to 12 and 18 carbon atoms, the foam capacity was dramatically reduced. In the case of **FurCO<sub>2</sub>Na-C<sub>8</sub>C<sub>8</sub>**, the foam is very stable over time – it is still present after 2 h – even if the foam starts to collapse after 30 min (Figure 3). In contrast, the collapse of foam generated by **FurCO<sub>2</sub>Na-C<sub>7</sub>C<sub>7</sub>** begins quickly, starting at 5 min, and the foam has virtually disappeared after 30 min. Thus, **FurCO<sub>2</sub>Na-C<sub>8</sub>C<sub>8</sub>** exhibits the most efficient foaming properties while having the best surface activity, namely low CMC (0.69 mmol L<sup>-1</sup>) and surface tension (24.6 mN m<sup>-1</sup>) values. More interestingly, the **FurCO<sub>2</sub>Na-C<sub>8</sub>C<sub>8</sub>**-based surfactant composition resulting from the one-pot procedure showed a foaming capability in terms of volume and stability, comparable to pure product



**Figure 4.** Foaming properties of sodium 5-(dialkoxymethyl)-2-furoates **3** ( $\text{FurCO}_2\text{Na-C}_n\text{C}_n$ ).

(data not shown). In this regard, the sodium 5-(dioctyloxymethyl)-2-furoate derivative represents a potential cosmetic ingredient for shower gels and cleansers.

**Aquatic ecotoxicity and biodegradability studies.** A series of aquatic ecotoxicity and biodegradation tests have been performed with the surfactant composition based on sodium 5-(dioctyloxymethyl)-2-furoate. *Daphnia* toxicity was determined using the OECD 202 method.<sup>[22]</sup> The principle consisted in exposing *Daphnia* to the test substance at a range of concentrations (1, 3.5, 10, 35 and 100 mg L<sup>-1</sup>) for a period of 48 h. Immobilization was recorded at 24 h and 48 h and compared with control values. The results were analyzed in order to calculate the EC<sub>50</sub>, i.e. the concentration estimated to immobilize 50 % of the *Daphnia* within the stated exposure period, at 48 h. The optional determination of the EC<sub>50</sub> at 24 h was also performed. Since EC<sub>50</sub> values at 24 h and 48 h exceeded 100 mg L<sup>-1</sup>, sodium 5-(dioctyloxymethyl)-2-furoate composition was considered non-toxic to these microcrustaceans. In addition, toxicity towards algae was evaluated according to the OECD 201 method.<sup>[23]</sup> The purpose of this test is to determine the effects of a substance on the growth of freshwater microalgae (green algae, *Pseudokirchneriella subcapitata*). Exponentially growing test organisms are exposed to the test substance in batch cultures over a period of normally 72 h. Despite the relatively brief test duration, effects over several generations can be assessed. The test endpoint is inhibition of growth, expressed as the logarithmic increase in biomass (average specific growth rate) during the exposure period. From the average specific growth rates recorded in a series of test solutions, the concentration bringing about x% inhibition of growth rate (e.g. 50%) is determined and expressed as the E<sub>r</sub>C<sub>x</sub> (e.g. E<sub>r</sub>C<sub>50</sub>). In addition, the No Observed Effect Concentration (NOEC) can be determined. E<sub>r</sub>C<sub>50</sub>, E<sub>r</sub>C<sub>20</sub> and E<sub>r</sub>C<sub>10</sub> values at 72 h and NOEC were found to be higher than 100 mg L<sup>-1</sup>. As a result, **FurCO<sub>2</sub>Na-C<sub>8</sub>C<sub>8</sub>**-based surfactant composition was considered to be non-toxic to these green algae.

Aerobic ready biodegradability of the furanic surfactant composition was finally studied using the OECD 301 A method<sup>[24]</sup> based on dissolved organic carbon (DOC) measurements. The inoculum was prepared from activated sludge of the Maxéville (France) wastewater treatment plant, which treats predominantly domestic sewage (98%). A measured volume of inoculated mineral medium, containing a known concentration of the test substance (15 mg L<sup>-1</sup> of DOC) as the nominal sole source of organic carbon, is aerated at 22 ± 2°C. Degradation is followed by DOC analysis at frequent intervals (t<sub>0</sub>, 1 day, 4 days, 7 days, 11

days, 14 days, 18 days, 20 days, 25 days and 28 days) over a 28-day period. The degree of biodegradation is calculated by expressing the concentration of DOC removed (corrected for that in the blank inoculum control) as a percentage of the concentration initially present. As the limit value of 70% biodegradation was reached within 10 days (9 days were required), sodium 5-dioctylacetal-2-furoate-containing composition was described as 'readily biodegradable'. Furthermore, a high level of biodegradation (96%) was obtained over the 28-day period.

## Conclusions

In this study, the synthesis of a new family of anionic surfactants possessing a couple of lipophilic chains linked by an acetal function to a furan-2 carboxylate head group have been developed using natural oligo-, polyuronate derivatives as starting materials. It has been demonstrated for the first time that the production of anionic furanic surfactants can be performed following one-pot processes, without having to isolate and purify any reaction intermediates and through the limitation of the waste production. More importantly, this method bypasses the use of unstable HMF as the furan moiety is formed *in situ* by cyclodehydration of *n*-butyl (*n*-butyl glycoside uronate) intermediates. DFT calculations suggest that the thermodynamically more favorable pathway should be the direct double dehydration reaction of the 4-hydroxy-tetrahydrofuran intermediate **S7** containing both hydroxy and butoxycarbonyl groups at the C-2 position without involving the formation of the isolated butoxylated derivative **12**. These 100% bio-based sodium 5-(dialkoxymethyl)-2-furoates showed considerable ability for surface tension reduction, even as a mixture composed of a large quantity of salts. In addition, a high foamability was observed with sodium 5-(dioctyloxymethyl)-2-furoate, as a pure form or as a mixture with salts, with the production of high volumes of stable foam. Finally, these surfactants are expected to be eco-friendly molecules as shown with the surfactant composition based on sodium 5-(dioctyloxymethyl)-2-furoate which exhibited both readily biodegradability and absence of aquatic ecotoxicity. In view of their remarkable surface active properties and environmental profile, these compounds could represent bio-sourced alternatives to the alkyl ether sulfates (notably sodium lauryl ether sulfate, SLES) that are based on petroleum-derived ethylene oxides. Further studies based on the use of monomeric D-glucuronic acid and D-glucurono-3,6-lactone are now under investigation with a view to improving the yield for the synthesis of these original furanic surfactants.

## Experimental Section

**Procedure for the synthesis of butyl 5-(dibutoxymethyl)-2-furoate (1) from oligomannuronates (4):** To a suspension of oligomannuronates **4** (1.0 g, 3.62 mmol, 1.0 eq.) in *n*BuOH (25.4 mL, 275.12 mmol, 76 eq.) was added a methanesulfonic acid 70% aqueous solution (2.21 g, 16.11 mmol, 4.45 eq.). The reaction mixture was heated at atmospheric pressure to 120°C. Starting from this temperature threshold, water (0.85 mL, 47.06 mmol, 13.0 eq.) was slowly added to the reaction mixture. Then, in the presence of a Dean-Stark apparatus filled with *n*BuOH, the temperature was increased to reach 160°C and the reaction mixture was stirred for 6 h. After neutralization with a 1N aqueous solution of NaOH (10.2 mL, 10.2 mmol, 2.82 eq.), the reaction mixture was concentrated under reduced pressure. The residue was taken up with Et<sub>2</sub>O. The resulted suspension was strongly stirred for 1 h, filtered through a Büchner funnel precoated with celite and rinsed several times with Et<sub>2</sub>O. The filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography using cyclohexane + 1 % Et<sub>3</sub>N as the eluent to give butyl 5-(dibutoxymethyl)-2-furoate **1** (389 mg, 1.19 mmol, 33%) as a yellow oil after removal of butyl 2-furoate **11** under vacuum (6.8 10<sup>-2</sup> bar). Using CH<sub>2</sub>Cl<sub>2</sub>/MeOH (98/2, v/v) as the eluent, trace amounts of 4-hydroxy-tetrahydrofuran compound **12** (13 mg, 0.031 mmol, 1%) were additionally isolated.

**Procedure for the synthesis of butyl 5-(dibutoxymethyl)-2-furoate (1) from sodium alginate (7):** To a solution of sodium alginate **7** (1.0 g, 3.38 mmol, 1.0 eq.) in *n*BuOH (53.2 mL, 581.36 mmol, 172 eq.) and water (6.1 mL, 338.0 mmol, 100 eq.) was a methanesulfonic acid 70% aqueous solution (2.78 g, 20.28 mmol, 6.0 eq.). The reaction mixture was heated at atmospheric pressure to 110°C during the day. After 8 h of reaction, water was eliminated with the help of a Dean-Stark apparatus filled with *n*BuOH via a butanol/water azeotrope; the reaction mixture was heated to 160°C overnight (16 h). After neutralization with a 1N aqueous solution of NaOH (15.0 mL, 15.0 mmol, 4.44 eq.), the reaction mixture was concentrated under reduced pressure. The residue was taken up with Et<sub>2</sub>O. The resulted suspension was strongly stirred for 1 h, filtered through a Büchner funnel precoated with celite and then rinsed several times with Et<sub>2</sub>O. The filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography using cyclohexane + 1 % Et<sub>3</sub>N as the eluent to give butyl 5-(dibutoxymethyl)-2-furoate **1** (332 mg, 1.018 mmol, 30%) as a yellow oil after removal of butyl 2-furoate **11** under vacuum (6.8.10<sup>-2</sup> bar).

**Procedure for the synthesis of alkyl 5-(dialkoxymethyl)-2-furoates (2) from oligomannuronates (4):** To a suspension of oligomannuronates **4** (1.0 g, 3.62 mmol, 1.0 eq.) in *n*BuOH (25.4 mL, 275.12 mmol, 76 eq.) was added a methanesulfonic acid 70% aqueous solution (2.21 g, 16.11 mmol, 4.45 eq.). The reaction mixture was heated at atmospheric pressure to 120°C. Starting from this temperature threshold, water (0.85 mL, 47.06 mmol, 13.0 eq.) was slowly added to the reaction mixture. Then, in the presence of a Dean-Stark apparatus filled with *n*BuOH, the temperature was increased to reach 160°C and the reaction mixture was stirred for 6 h. After partial neutralization with a 1N aqueous solution of NaOH (2.6 eq.), fatty alcohol (6 eq.) was added. The mixture was then heated to 75°C and the pressure was progressively reduced to 5 mbar to azeotropically remove water and *n*BuOH. Under these conditions, the reaction mixture was stirred for 4 h. The mixture was then neutralized with a 1N NaOH solution and extracted with EtOAc and water. The aqueous phase was extracted 3 times with EtOAc and the combined organic

phases were washed with water. The organic phase was dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, concentrated and purified on silica gel column chromatography using cyclohexane/AcOEt (98/3, v/v) as the eluent.

**Procedure for the synthesis of 5-(dialkoxymethyl)-2-furoic acids (13) from alkyl 5-(dialkoxymethyl)-2-furoates (2):** To alkyl 5-(dialkoxymethyl)-2-furoates **2** (1.0 equiv.) was added a 1N aqueous solution of NaOH (3.0 eq.) and the mixture was solubilized in MeOH (0.1 M). The resulting solution was heated at 80°C for 3 h. The reaction mixture was then acidified with a 0.5N oxalic acid solution until pH 2 and extracted with EtOAc. The aqueous phase was extracted 3 times with EtOAc and the combined organic phases were washed with water until neutral pH of the aqueous phase. The organic phase was dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated. The residue was purified by silica gel column chromatography using cyclohexane/EtOAc (90/10, v/v) as the eluent to isolate the fatty alcohol and cyclohexane/EtOAc (30/70, v/v) as the eluent to give 5-(dialkoxymethyl)-2-furoic acids.

**Procedure for the synthesis of 5-(dialkoxymethyl)-2-furoic acids (13) from oligomannuronates (4):** To a suspension of oligomannuronates **4** (1.0 g, 3.62 mmol, 1.0 eq.) in *n*BuOH (25.4 mL, 275.0 mmol, 76 eq.) was added a methanesulfonic acid 70% aqueous solution (2.21 g, 16.11 mmol, 4.45 eq.). The reaction mixture was heated at atmospheric pressure to 120°C. Starting from this temperature threshold, water (0.85 mL, 47.06 mmol, 13.0 eq.) was slowly added to the reaction mixture. Then, in the presence of a Dean-Stark apparatus filled with *n*BuOH, the temperature was increased to reach 160°C and the reaction mixture was stirred for 6 h. After partial neutralization with a 1N aqueous solution of NaOH (2.6 eq.), fatty alcohol (6 eq.) was added. The mixture was then heated to 75°C and the pressure was progressively reduced to 5 mbar to azeotropically remove water and *n*BuOH. Under these conditions, the reaction mixture was stirred for 4 h. At room temperature and under atmospheric pressure, a 0.4N aqueous solution of NaOH (3 eq.) was added and the reaction mixture was heated to 110°C overnight (16 h). The reaction mixture was then acidified with a 0.5N oxalic acid solution until pH 2 and extracted with EtOAc. The aqueous phase was extracted 3 times with EtOAc and the combined organic phases were washed with water until neutral pH of the aqueous phase. The organic phase was dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated. The residue was purified by silica gel column chromatography using cyclohexane/EtOAc (90/10, v/v) as the eluent to isolate the fatty alcohol and cyclohexane/EtOAc (30/70, v/v) as the eluent to give 5-(dialkoxymethyl)-2-furoic acids.

**Procedure for the synthesis of sodium 5-(dialkoxymethyl)-2-furoates (3) from 5-(dialkoxymethyl)-2-furoic acids (13):** To 5-(dialkoxymethyl)-2-furoic acids **13** (1.0 eq.) was added a 1N aqueous solution of NaOH (1.2 eq.) and the mixture was solubilized in water ([**13**] = 0.1 mol/L). The resulting solution was heated at 80°C for 3 h. The pH value (around 12) was indicative of the carboxylate function. The reaction mixture was allowed to cool at room temperature and was then freeze-dried to obtain a powder.

**One-pot procedure for the synthesis of a surfactant composition based on sodium 5-(dioctyloxymethyl)-2-furoate (FurCO<sub>2</sub>Na-C<sub>8</sub>C<sub>8</sub>):** To a suspension of oligomannuronates **4** (1.0 g, 3.62 mmol, 1.0 eq.) in *n*BuOH (25.4 mL, 275.0 mmol, 76 eq.) was added a methanesulfonic acid 70% aqueous solution (2.21 g, 16.11 mmol, 4.45 eq.). The reaction mixture was heated at atmospheric pressure to 120°C. Starting from this temperature threshold, water (0.85 mL, 47.06 mmol, 13.0 eq.) was slowly added to the reaction mixture. Then, in the presence of a Dean-Stark apparatus filled with *n*BuOH, the temperature was increased to reach 160°C and the reaction mixture was stirred for 6 h. After

partial neutralization with a 1N aqueous solution of NaOH (9.41 mL, 2.6 eq.), octanol (2.83 g, 21.72 mmol, 6 eq.) was added. The mixture was then heated to 75°C and the pressure was progressively reduced to 5 mbar to azeotropically remove water and *n*BuOH. Under these conditions, the reaction mixture was stirred for 4 h. At room temperature and under atmospheric pressure, a 0.4N aqueous solution of NaOH (3 eq.) was added and the reaction mixture was heated to 110°C overnight (16 h). Then octanol was eliminated by successive azeotropic distillation with water. The resulting mixture which consisted in solid particles was treated with water and the insoluble impurities were eliminated by filtration. Then, the filtrate was concentrated and freeze-dried to afford a surfactant composition (2.48 g) as a fine powder which contains 2.66 mass % of water, 4.42 mass % of octanol, 42.61 mass % of organic substances (composed of sodium 5-(dioctyloxymethyl)-2-furoate, **FurCO<sub>2</sub>Na-C<sub>8</sub>C<sub>8</sub>**) and 50.31 mass % of salts.

**Krafft temperature measurements:** Clear 1% wt solutions of surfactants were prepared and left to cool at -18°C in the freezer overnight to ensure complete precipitation of the compounds in the form of hydrated crystals. Krafft point was measured by the naked eye as the temperature at which the 1% wt dispersion solutions become clear on gradual heating.

**Air-water interfacial properties:** Surface tension was determined with a *Du Noüy* ring tensiometer (K100-Krüss, Germany) equipped with platinum ring having a radius of 9.544 mm and wire diameter of 0.37 mm at 25°C and run by Lab Desktop-Software. The surface tension ( $\gamma$ ) was measured at different concentrations by adding a subsequent volume of ultrapure water to a sodium 5-(dialkoxymethyl)-2-furoate **2** solution (initial concentration: 15 g L<sup>-1</sup>) with a 765 Dosimat (Metrohm) which was connected with system programmed by LabDesktop-Software to a crystallizing dish. The concentration and the surface tension were automatically determined by the software. For each concentration, the solution was stirred for 60 s and equilibrated for 60 s, and the average of five readings was taken. The critical micelle concentration (CMC) was obtained from the break point of the plot of  $\gamma$  versus log C.

**DFT-based study:** In order to characterize the reaction path, DFT calculations were performed using the B3LYP<sup>[25]</sup> and M06<sup>[26]</sup> functionals and the 6-31+G\* basis set<sup>[25c]</sup> for all the atoms with the Gaussian 16.A03 software<sup>[27]</sup>. Grimme dispersions are also taken into account using the Grimme D3 damping function<sup>[28]</sup> and the calculations were performed using the Polarizable Continuum model (PCM)<sup>[29]</sup> with methanol as solvent. Frequency calculations were performed in order to ensure the nature (intermediates or transition states) of each of the studied compounds and the Gibbs free energies were calculated at 433K. Coordinates of all intermediates and transitions states are given in Supporting Information.

## Supporting Information Summary

General procedures for the synthesis of 2,5-disubstituted furans **1**, **2**, **13**, **3** and **FurCO<sub>2</sub>Na-C<sub>8</sub>C<sub>8</sub>**-based surfactant composition, <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra of compounds **3**, **12** and **13**, green chemistry metrics of the one-pot procedure for the synthesis of **FurCO<sub>2</sub>Na-C<sub>8</sub>C<sub>8</sub>**-based surfactant composition, mass spectrum of **FurCO<sub>2</sub>Na-C<sub>8</sub>C<sub>8</sub>**, thermogravimetric analysis of **FurCO<sub>2</sub>Na-C<sub>8</sub>C<sub>8</sub>**-based surfactant composition, cartesian coordinates of the intermediates and transitions states calculated at the DFT/B3LYP level, representation of the transition state between **S8** and **1**,

example of surface tension curve and CMC for **FurCO<sub>2</sub>Na-C<sub>8</sub>C<sub>8</sub>** are available in Supporting Information.

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## Conflict of Interest

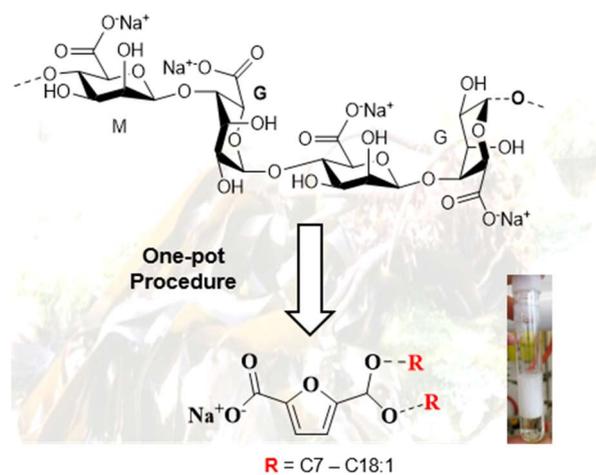
The authors declare no conflict of interest.

**Keywords:** alginate oligo- and polysaccharides • density functional calculations • furanics • green chemistry • surfactants

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## Entry for the Table of Contents



Direct transformation of natural alginate oligo- and polysaccharides into sodium 5-(dialkoxymethyl)-2-furoates proceeded efficiently through hydrolysis, alcoholysis, dehydration, transesterification, transacetalization and saponification reactions to provide 100% bio-based anionic furanic surfactants. In particular, sodium 5-(dioctyloxymethyl)-2-furoate, as a pure form or as a mixture resulting from a green one-pot procedure, exhibited both attractive surface active properties, readily biodegradability and absence of aquatic ecotoxicity.