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Solvent-free esterification process for the synthesis of glucose bolaform surfactants

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ABSTRACT

Glucose bolaform esters or surfactants have been synthesized by esterification reaction in the absence of organic solvent using short chain acid dichlorides as linkers (spacers). The glucose was first reacted with formic acid to produce glucose formate, followed acylation with acid dichloride to produce glucose bolaform esters. No organic solvent was used in the reaction but access acid dichloride behaved like a medium for the reaction. A stream of nitrogen gas was used to eliminate the acid vapor produced during the reaction. Several structures of glucose bolaform compounds containing C_3 to C_9 hydrocarbon chain linkers were and characterized. The physical properties and the effects of the different spacers/linkers on surfactant properties were also evaluated. The yields of glucose bolaform esters obtained at optimum reaction condition (45°C reaction temperature, 2:1 molar ratio of glucose/acid dichloride and 50 min. reaction time) were 71.06%, 64.39%, 57.73%, 49.60% of 1,3-propanedioate-bis-glucopyranoside, 1,6-hexanedioate-bis-glucopyranoside, 1,8-octanedioate-bis-glucopyranoside, 1,9-nonanedioate-bis-glucopyranoside respectively. It was noticed that short chain acid dichlorides were easier to react to form glucose bolaform esters than long chain acid dichlorides. The products obtained were lighter in colour indicating less caramelization of reactants during reaction. Surface tension and HLB values of the bolaform esters were ranged from 13 to 17, and 32.8 to 39.8 mN/m respectively. Based on the HLB values the products are potential emulsifiers for oil in water emulsion.

Key words: Synthesis, bolaform ester, solventless method, glucose.

INTRODUCTION

Bolaform surfactants or bolaamphiphiles are amphiphilic molecules that have two hydrophilic head groups linked together through a hydrophobic hydrocarbon chain or 'spacer'[1,2]. These types of surfactant have received much attention in recent years due their interesting surfactant properties, notably better solubility in water and show lower critical micelle concentration which means a decrease in aggregation number in micelle formation[3]. Various attempts to synthesis bolaform surfactant have been reported. Jolanda *et. al*[4] had reported the synthesis of nonionic bolaamphiphiles from glucose and α,ω-diaminoalkane by catalytic hydrogenation at elevated pressure (40bar). The synthesis of novel nonionic bolaform amphihiles with nonidentical alditylhead groups involving 1,6-diaminohexane and aldohexoses was described by Boelo *et. al*[5]. Herwig *et al*[6] used a novel enzymatic method to synthesize disaccharide based bolaamphiphiles. However, most of the reported works involved the use of toxic solvents, such as N,N-dimethylformamide (DMF), dimethylacetamide (DMA), dimethylsulfoxide (DMSO), chloroform, benzene and toluene[7]. This is mainly due to lack of mutual solvent to dissolve both of glucose and the hydrocarbon spacer used. Toxic solvent residues in the products are difficult to remove and thus, hindered their uses in food and pharmaceutical products.

This paper reported the synthesis of glucose bolaform esters using short chain acid dichlorides as linkers in a solventless system, thus avoided using toxic solvent. The optimum reaction condition and the yield were determined. The physical properties of the products were also evaluated.

MATERIAL AND METHODS

Materials

Malony dichloride (C_3), adipoyl chloride (C_6), suberoyl chloride (C_8), azelaoyl chloride (C_9), D-glucose (99%) and formic acid (98%) were purchased from Sigma Aldrich. Ethanol (95%) was obtained from Merck Company. All chemicals used were of high purity.

Synthesis of glucose bolaform esters

Glucose was first formated with formic acid to form a reactive glucose formate before reacted with acid dichloride according to the method described by Aburto *et al.* [8]. The formylation was carried out by reacting the glucose (2.7g, 15 mmol)) with formic acid (6 ml) with constant stirring at room temperature in a three-necked flask equipped with a magnetic bar and a nitrogen tubing until the glucose was completely dissolved. The reaction mixture was then heated to the desired temperature and the required amount of acid dichloride was added drop wise with constant stirring. The temperature was maintained until the reaction was completed, then cooled down to room temperature and ethanol (20 ml) was added to precipitate the product. The solvent was then evaporated at 40°C and the product was washed several times with ethanol (95%) to remove traces of HCL liberated during the reaction and acid dichloride. The product was characterized by FTIR (Perkin Elmer spectrometers) and NMR (JEOL JNM ECA-400 spectrometer). The esterification was confirmed by ^1H and ^{13}C NMR spectroscopies. Similar procedure was repeated to study the effects reaction temperature, reaction time, molar ratio of glucose to acid dichloride (from 2:1 to 6:1) and spacer chain length on the yield and on the surfactant properties of the products.

Physical Properties Study

Physical Appearance

The physical appearance of the glucose bolaform esters was determined by visual observation. In general, the compound will be either solid or liquid. Solubility test was done by adding a small amount of sample in distilled water and the solubility was observed visually.

Hydrophilic-Lipophilic Balance (HLB) And Surface Tension Measurements

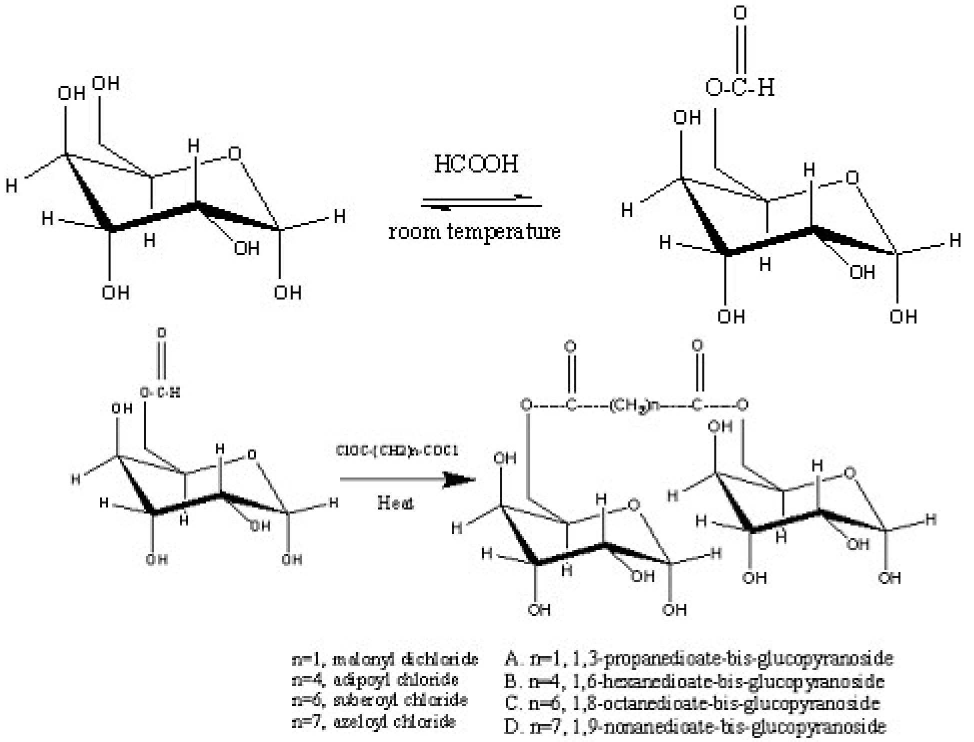
HLB values of the products were determined according to the method described by Griffin (9). The method was based on the "hydrophilic group numbers" assigned to the various hydrophilic and lipophilic moieties appearing in the surfactant as given by the following formula,

$$HLB = 20 * Mh / M$$

where Mh is the molecular mass of the hydrophilic portion of the molecule and M is the molecular mass of the whole molecule. Surface tension was measured using the KRÜSS tensiometers. Glucose bolaform solution (1% w/v) was prepared in distilled water.

RESULTS AND DISCUSSION

Glucose bolaform esters of different linker chain length were synthesized by reacting glucose with aliphatic acid dichlorides (malonyl dichloride, adipoyl chloride, suberoyl chloride, azelaoyl chloride). The reaction was carried out in the absence of an organic solvent but the reactant (acid dichloride) acted as a medium for the reaction. The esterification reaction was carried out under nitrogen atmosphere and the liberated acid vapor was eliminated by a stream of nitrogen gas. In the absence of formic acid, the esterification reaction was very slow and required high temperature that led to caramelization of glucose and products. With formic acid, the highly reactive formated glucose produced stimulated the reaction between glucose and acid dichloride through transesterification reaction resulted in high yield of product. The reaction proceeded at low temperature thus, avoided caramelization. Scheme 1 shows the pathway for the synthesis reaction.



Scheme 1: Reaction scheme for the synthesis of glucose bolaform esters: product A (n=1), B(n=4), C(n=6) and D(n=7). OH and OH' reprent hydroxyl groups (OH) on the first glucoce (left) and second glucose (right) of the product respectively

Product identified from reaction of glucose with malonyl dichloride (n=1) was 1,3-propanedioate-bis-glucopyranoside (**A**): ^{1}H NMR (methanol-d4): δ 4.3781(OH-1 and OH-1'), 4.6533 (OH-2 and OH-2'), 3.6773 (OH-3 and OH-3'), 3.9147 (OH-4 and OH-4'), 4.0179 (OH-5 andOH-5'), 5.0088 (OH-6 and OH-6'). ^{13}C NMR: δ 168.2937 (C–1 and C–1'), 93.8588 (C–2 and C–2'), 71.7628 (C–3 and C– '), 73.8270 (C–4 and C–4'), 78.0702 (C–5 and C–5'), 98.1710 (C–6 and C–6'). IR ν_{max} (cm^{-1}): 3300 (OH), 2854-2922 (CH$_2$), 1735 (C=O), 1175 (C-O-C), 1100 (C-O).

Product identified from reaction of glucose with adipoyl chloride (n=4) was 1,6-hexanedioate-bis-glucopyranoside (**B**). ^{1}H NMR (methanol-d4): δ 4.4993 (OH-1 and OH-1'), 4.7659 (OH-2 and OH-2'), 3.7080 (OH-3 and OH-3'), 3.7794 (OH-4 and OH-4'), 3.8445 (OH-5 and OH-5'), 5.1817 (OH-6 and OH-6'); ^{13}C NMR: δ 163.6619 (C–1 and C–1'), 93.8737 (C–2 and C–2'), 71.7528 (C–3 and C–3'), 73.7332 (C–4 and C–4'), 77.9693 (C–5 and C–5'), 98.0562 (C–6 and C–6'); IR ν_{max} (cm^{-1}): 3300 (OH), 2854-2922 (CH$_2$), 1735 (C=O), 1175 (C-O-C), 1100 (C-O).

Product identified from reaction of glucose with suberoyl chloride (n=6) was 1,8-octanedioate-bis-glucopyranoside (**C**). ^{1}H NMR (methanol-d4): δ 4.4983 (OH-1 and OH-1'), 4.7575 (OH-2 and OH-2'), 3.7033 (OH-3 and OH-3'), 3.7692 (OH-4 and OH-4'), 3.8343 (OH-5 and OH-5'), 5.1284 (OH-6 and OH-6'); ^{13}C NMR: δ 163.4021 (C–1 and C–1'), 93.8047 (C–2 and C–2'), 71.6991 (C–3 and C–3'), 73.6643 (C–4 and C–4'), 77.9003 (C–5 and C–5'), 97.9796 (C–6 and C–6'); IR ν_{max} (cm^{-1}): 3300 (OH), 2854-2922 (CH$_2$), 1735 (C=O), 1175 (C-O-C), 1100 (C-O).

Product identified from reaction of glucose with azelaoyl chloride (n=7) was 1,9-nonanedioate-bis-glucopyranoside (**D**). ^{1}H NMR (methanol-d4): δ 4.4960 (OH-1 and OH-1'), 4.5162 (OH-2 and OH-2'), 3.6836 (OH-3 and OH-3'), 3.7743 (OH-4 and

OH-4'), 4.0885 (OH-5 and OH-5'), 5.1280 (OH-6 and OH-6'); ^{13}C NMR: δ 164.8166 (C–1 and C–1'), 93.8585 (C–2 and C–2'), 71.5847 (C–3 and C–3'), 73.7104 (C–4 and C–4'), 77.9465 (C–5 and C–5'), 98.0411 (C–6 and C–6'); IR ν_{max} (cm^{-1}): 3300 (OH), 2854-2922 (CH_2), 1735 (C=O), 1175 (C-O-C), 1100 (C-O).

All compounds showed broad peak at 3300 cm^{-1} that are characteristic of the OH stretching from glucose, along with the 2854-2922cm^{-1} band (CH_2 stretching), 1735cm^{-1} band (C=O stretching for glucose bolaform esters), 1175cm^{-1} band (C-O-C stretching in glucose bolaform esters) and 1100 cm^{-1} band (C-O stretching in glucose bolaform esters). The band at 2854-2922cm^{-1} is characteristic of C-H stretches. This confirms that the acid dichloride was grafted onto glucose. The esterification is evidences by the presence of the ester carbonyl group (C=O) stretching at 1735 cm^{-1}.

^1H NMR analysis showed that there is a great change on the chemical shift for hydroxyl group in position 1 (OH-1) for all bolaform compounds compared to glucose. A shift of about 0.9-1.1 was observed. The large chemical shift change of OH–1 is due to the deshielding effect of the electronegative oxygen atom. That means there is an influence from an external group to cause the change. When looking at the reactivity of the hydroxyl groups, it is obvious that only the primary hydroxyl groups at position 1 of the glucose unit is being the most reactive sites. The chemical shift value for the other hydroxyl group does not show much change due to the steric effects of the glucose ring. In addition, formation of diesters was less favorable due to high activation energies of esterification of secondary hydroxyl groups (10). In general, there is only small different in chemical shift (about 0.06-0.2) for other hydroxyl groups relative to glucose. This indicated that only single acylated product was obtained.

^1H NMR analysis has indicated that the products contain two glucose head groups. This was evident when considering the integration number of proton in the glucose ring. The peak at ä 4.3781 – 4.7659 ppm has an integration number twice of the original glucose ring, an indication of resonance from two different hydrogens. This means that two glucoses were grafted onto the acid dichloride producing a bolaform compound.

Table 1: Percentage yield and appearance of glucose bolaform esters obtained by esterification at optimum reaction conditions

Glucose bolaform ester	Yield (wt %)	Appearance
1,3-propanedioate-bis-glucopyranoside	71.1	Brown sticky liquid
1,6-hexanedioate-bis-glucopyranoside	64.4	White sticky paste
1,8-octanedioate-bis-glucopyranoside	57.7	White sticky paste
1,9-nonanedioate-bis-glucopyranoside	49.6	White sticky paste

Table 2: Typical yields of 1,3-propanedioate-bis-glucopyranoside at various molar ratios of glucose to malonyl dichloride (C_3)

Mole ratioglucose: acid dichloride	Yield(%)
2:1	71.1
3:1	66.4
4:1	60.1
5:1	54.6
6:1	40.9

Yield of glucose bolaform esters

Table 1 shows the percentage yield of glucose bolaform esters (compared to the initial weight of glucose used) obtained at optimum reaction condition. Results showed that the maximun yields were steadily decreased from 1,3-propanedioate-bis-glucopyranoside (C_3, 71.1%) to 1,9-nonanedioate-bis-glucopyranoside (C_9, 49.6%). This suggests that short chain acid dichlorides are easier to react with glucose to formed glucose bolaform ester than the long chain acid dichlorides. The decrease is associated with a more steric hindrance in a longer fatty acid chain.

The reaction time is very significant in the synthesis of glucose bolaform ester. The best reaction time was 50 minutes. Above 50 minutes, yield was decreased and the caramel started to form. With longer reaction times the product was probably hydrolyzed both by acid dichloride medium and the liberated HCl that led to decrease in yield. On the other hand, the optimum molar ratio of glucose to acid dichloride was found at about 2:1 for all bolaform products where the highest yield was obtained (Table 1). The conversion was gradually decreased when the molar ratio exceeded 2:1 (Table 2).

At lower reaction temperature (40ºC), only small amount of glucose bolaform esters was formed. At slightly higher temperature (about 45ºC), there was a good dispersion of formated glucose in the acid dichloride medium resulted in higher reactivity and yield. At 50ºC, the reaction was more reactive as indicated by a rapid liberation of hydrochloric acid vapor from the reaction. At above 50ºC, glucose bolaform esters started to caramelize and some probably hydrolyzed by acid dichloride medium. This could be seen as the yield begun to decrease. From the above results, the best reaction conditions for synthesizing glucose bolaform esters

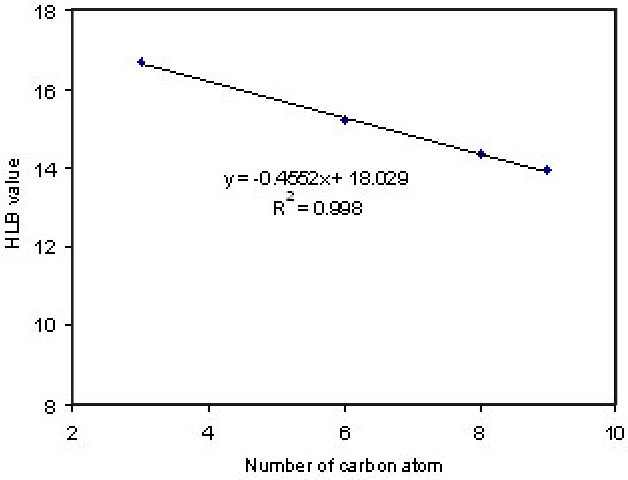


Fig. 1: HLB values of glucose bolaform surfactants with increasing hydrocarbon chain length of acid dichlorides from C_3 to C_9

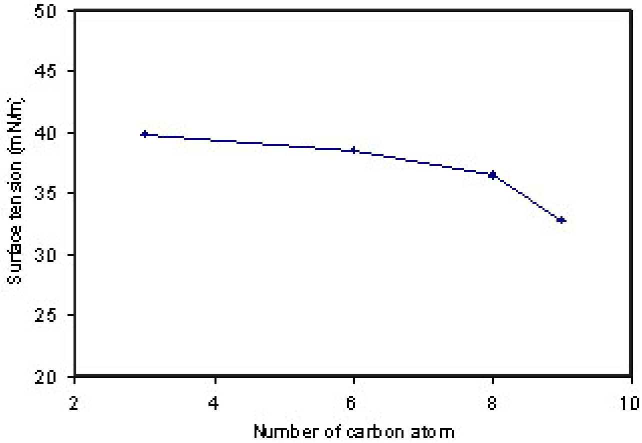


Fig. 2: Surface tensions of 1% glucose bolaform solution with increasing hydrocarbon chain length of acid dichlorides from C_3 to C_9

were 45ºC reaction temperature, 50 minutes reaction time and mole ratio of glucose to acid dichloride of 2:1.

The appearance of glucose bolaform esters, after purification, was changed from that of a non-sticky rigid powder of glucose to a sticky liquid of glucose bolaform ester. As the chain length of the acid dichloride increased from C_3 to C_9, the appearances of the products were changed from sticky liquid to sticky paste and similarly, the color changed from light brown to white sticky paste.

Surfactant Properties

HLB values of the glucose bolaform esters obtained in this study ranged from 14-17. Based on Griffin's classification (surfactants with HLB values range from 8 to 18 are commonly used as oil in water emulsions), the products are potential surfactants for oil-in-water emulsion. However, the HLB values decreased linearly with the increasing of acid dichloride chain length (Figure 1).

On the other hand, surface tension measurements of glucose bolaform esters indicated that the products are better surfactants as the carbon chain length of the linker or spacer increased (become longer). At 1% surfactant concentration, the surface tension of water (72.5 mN/m at 25ºC) was reduced singnificantly to 40 mN/m in C_3 and to 32 in C_9. These surface tensions are comparerable to those of commercial surfactants such as sorbitol polyoleate and sucrose polyoleate where the surface tention are in the range of 43.8-46.6 mN/m (11)Akoh, 1992). This is shown by the reduction of surface tension from 40 mN/m in C_3 to 33 mN/m in C_9 acid dichlorides (Figure 2).

When the chain length of the surfactant is increased, its solubility in water will be decreased due to increase in hydrophobility of the molecule and thus, enhance the adsorption of the molecule onto the surface. This phenomenon will reduce the surface tension of the system as seen in Figure 2. As conclusion, glucose bolaform esters with different spacer chain lengths have been successfully synthesized in a solvent-less system. The reaction proceeded at moderate reaction temperature thus, avoided caramelization of reactant and products. Spectroscopy analysis using FT-IR and NMR confirmed the glucose was grafted onto acid dichloride linker to produce a single diglucose ester product. Based on HLB and surface tension values, the bolaform esters are potential surfactants for oil-in-water emulsion.

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