REVIEW

Syntheses and Applications of Sucrose-Based Esters

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ABSTRACT: This review describes chemical and enzymatic syntheses of nonionic, anionic, and amphoteric sugar-based surfactants with special focus on methods for the regioselective synthesis of these surfactants.

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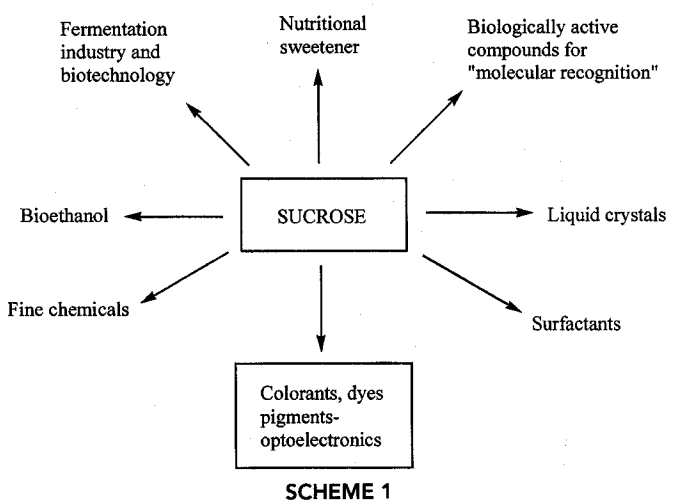
KEY WORDS: Fatty acid sucrose esters, review, sucrose, sucrose sulfates, surfactants.

Sucrose is one of the world's most abundantly produced organic compounds. It is available at a very high level of purity and at very low cost. Sucrose is synthesized by almost every green plant and is assimilated by most organisms. It is an early product of photosynthesis, and in plants such as sugarcane and beet, it serves as the major storage of saccharides. In other plants, it is converted to starch, inulin, or levan for carbohydrate storage. In many plants, the transport of oligo- and polysaccharides from one part of the plant to another proceeds through conversion to sucrose, translocation, and resynthesis. Large-volume markets such as surfactants, plastics, and polymers represent an obvious target for sucrose. In addition to its advantages of relatively low cost and high purity, sucrose is a readily available material with few storage or transportation problems. Compared to the competing feedstock, petroleum, sucrose has the advantage of being a renewable resource with a reduced adverse environmental impact.

Sucrose is a major international agriculture product. Its principal use is in the beverage and food industries, but it also finds some application in the chemical and processing industries. An industrial chemical process based on sucrose must convert sucrose into conventional feedstocks, such as ethanol and ethylene, or else develop new technology and products that utilize the particular properties of the sucrose molecule. The utilization of sucrose in food and nonfood industries is shown in Scheme 1.

The synthesis of long-chain fatty acid sucrose monoesters was one of the first major achievements of the Sugar Research Foundation (1). These esters were quickly approved in Japan for use as food additives in 1959 and subsequently found worldwide approval for application as nonionic surfactants (2–7) and emulsifiers in food products (8–15). The major advantage of these compounds lies in their total metabolism and biodegradability. In addition, sugar monoesters such as monolaurate have obvious advantages in the food and beverage industries since they inhibit the growth of *Escherichia coli* and other bacteria (16,17).

Sucrose monoesters are compatible with skin. They elicit little or no irritation, suggesting applications in cosmetics (18,19) including skin preparations (20), hair treatments (21,22), eyelash products (23), cosmetic oil gels (24, 25), and deodorant formulations (26). Sucrose monoesters have been used as plasticizers and as antistatic agents in plastics. The monoesters exhibit excellent fruit-preservative



SCHEME 1

This manuscript is dedicated to Professor Gérard Descotes on the occasion of his retirement in 2001.

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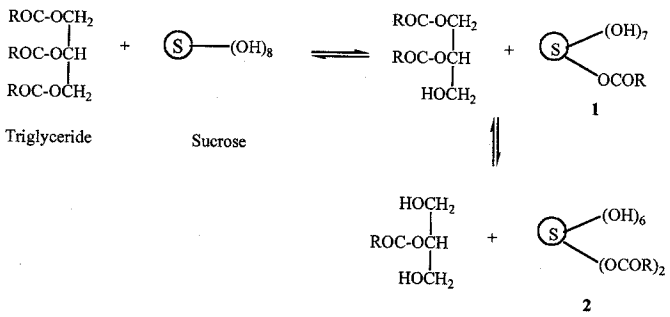

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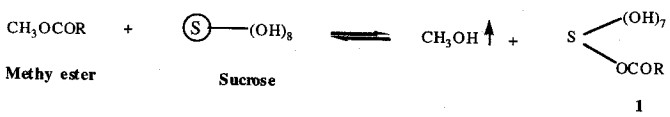


SCHEME 3

properties (27). They also have utility in drug formulation and delivery in the pharmaceutical industry (28–30).

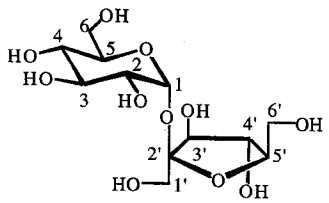
There are several commercial routes to fatty acid monoesters. The first involves transesterification of a fat or oil triglyceride with sucrose using a basic catalyst at 90°C in dimethylformamide (DMF) as solvent. DMF has subsequently been replaced by dimethyl sulfoxide (DMSO), a safer and less expensive solvent (31,32) (Scheme 2). The product contains >50% monoesters, >10% di- and higher esters, unreacted sucrose, and triglycerides. When fatty acid methyl esters are transesterified with sucrose, methanol is formed and can be removed by distillation. This drives the equilibrium in favor of the sucrose ester and improves the yield of desired product (Scheme 3). A solventless process has also been developed using a melt or slurry of sucrose, triglyceride (or methyl ester), and a basic catalyst (potassium carbonate or potassium soap) at 130°C (33). The crude product formed in the process finds some use in detergent formulations.

Sucrose monoesters including the stearate, behenate, oleate, palmitate, and myristate are manufactured in Japan and usually contain 70% monoester and 30% di-, tri-, and higher esters.

REGIOSELECTIVE CHEMICAL SYNTHESIS OF FATTY ACID SUCROSE ESTERS

Sucrose is a nonreducing disaccharide of unique structure (**3**) containing nine chiral centers. The eight hydroxyl groups, numbered as shown in Scheme 4, include three primary hydroxyls (at carbons 6, 1′, and 6′) and five secondary hydroxyls (at carbons 2, 3, 4, 3′, and 4′). Sucrose hydrolyzes with extreme ease under acidic conditions, but it is reasonably stable in the presence of strong bases. Thus, the preparation of sucrose derivatives is largely restricted to neutral or basic media.

Partially substituted sucrose derivatives are very difficult to isolate in pure form because of the formation of mixed products resulting from the multiplicity of hydroxyl groups present. In theory, esterification with an equimolar quantity of reagent could give rise to eight possible sucrose monoesters. However, the reactivities of the different primary and secondary hydroxyl groups vary slightly. In practice, the primary hydroxyls react preferentially. Of the three primary hydroxyls, those at carbons 6 and 6′ are generally more reactive than the primary hydroxyl at carbon 1′. The products of an equimolar derivatization reaction are always contaminated with small amounts of other monoesters as well as di- and trisubstituted esters, the composition of which varies according to reaction conditions and the reactants (12,34,35). To take full advantage of sucrose as a feedstock, it would be optimal to make selective modifications leading to a single product, having a single desirable physical, chemical, or biological property. Thus, in modifying sucrose for the preparation of sucrose esters, great care and attention must be focused on methods that afford the regioselective acylation of sucrose.



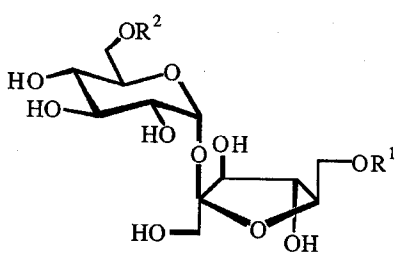
SCHEME 4

Selective acylation of sucrose with 3-acyl-5-methyl-1,3,4-thiadiazole-2(3H)-thiones in DMF reportedly gives predominantly 6′-acyl sucrose. Best results are obtained with 1,4-diazobicyclo-[2.2.2] octane (DABCO) as initiator and at low-temperature reaction conditions (36) (Scheme 5).

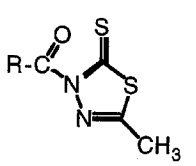
Similarly, with 3-acyl-thiazoledine-2-thione as acylating agent in the presence of triethylamine or DABCO at room temperature, acylation occurs readily, and 2-*O*-acyl sucrose is isolated in 41–46% yields. The yield can be improved to 70% when NaH is added to the reaction mixture as an initiator (37) (Scheme 6).

When 2-*O*-acyl sucrose is subjected to *in situ* intramolecular isomerization, using 1,8-diazobicyclo [5.4.0] undec-7-ene (DBU) or an aqueous solution of triethylamine, 6-*O*-acyl sucrose is formed in 60% yield (38) (Scheme 7).

In a dibutylstannylene-based approach to the synthesis of 6-*O*-acyl sucrose (Scheme 8), sucrose was first converted to a dibutylstannylene acetal by refluxing in methanol. The resulting acetal was isolated and reacted with fatty acid

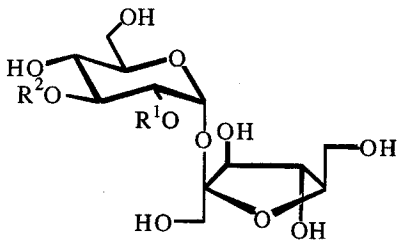


3. $R^1 = R^2 = R^3 = H$
4. R^1 = CO-R $R^2 = R^3 = H$
5. R^2 = CO-R $R^1 = R^3 = H$
6. R^3 = CO-R $R^1 = R^2 = H$



R = $(CH_2)_6$-CH_3
$(CH_2)_{10}$-CH_3
$(CH_2)_{16}$-CH_3

SCHEME 5



3. $R^1 = R^2 = H$
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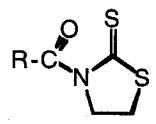
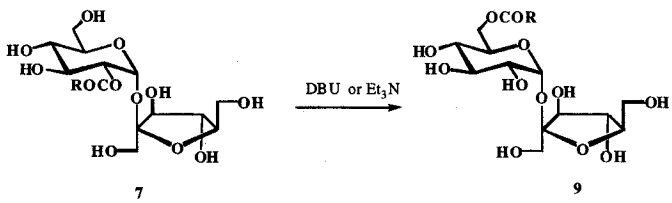
8. $R^1 = H$ $R^2 = CO\text{-}R$



$R = (CH_2)_6\text{-}CH_3$
$(CH_2)_{10}\text{-}CH_3$
$(CH_2)_{16}\text{-}CH_3$

SCHEME 6



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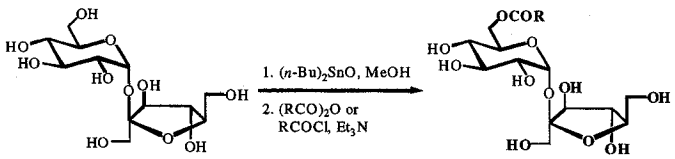
SCHEME 7



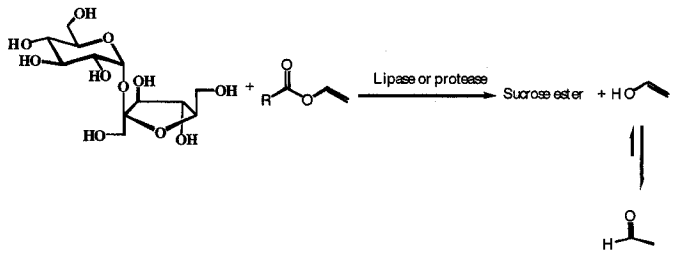
SCHEME 8

anhydrides in DMF at room temperature. In all cases, a single product, 6-*O*-acyl sucrose, was obtained. The high regioselectivity suggested that sucrose acted like a six-membered stannylene acetal. The anhydride-derived acyl species resulted in an electrophilic substitution at the activated primary C-6 position in the six-membered stannylene intermediate (39).

REGIOSELECTIVE ENZYMATIC SYNTHESIS OF FATTY ACID SUCROSE ESTERS

An alternative approach to the regioselective synthesis of carbohydrate esters makes use of enzymes in organic solvents. Enzymatic esterification of fatty acids with sugars in *tert*-butyl alcohol catalyzed by lipase from *Byssochlamys fulva* NTG9 has been studied. With different fatty acids, sucrose gave approximately 40% esterification (40). Using *Candida antarctica* lipase at elevated temperatures of 40–80°C gave a similar conversion of sucrose after a prolonged reaction time (7 d) (41). With lipase from *Mucor miehei* as catalyst in a solvent-free system, a 25% yield of predominantly 6-*O*-acyl sucrose was obtained. The yield could be increased markedly by direct addition of a suitable pair of solid hydrates to the reaction mixture to control the water activity (42).

The yield of lipase-catalyzed sucrose esterifications could also be improved significantly by using vinyl esters to drive the reaction through the tautomerization of the enol product (Scheme 9). Thus, 6-*O*-acyl sucrose was obtained by enzymatic esterification of sucrose with corresponding vinyl esters in a two-solvent medium consisting of 2-methyl-2-butanol (*tert*-amyl alcohol) and <20% of DMSO. Among the lipases tested, one from *Humicola lanuginosa* gave the best results. Both 6-*O*-lauryl sucrose and 6-*O*-palmityl sucrose were obtained in 70–80% yields (43). An enzymatic procedure for the acylation of a less reactive secondary hydroxyl group in sucrose also has been reported using a lipase from a filamentous fungus (44).



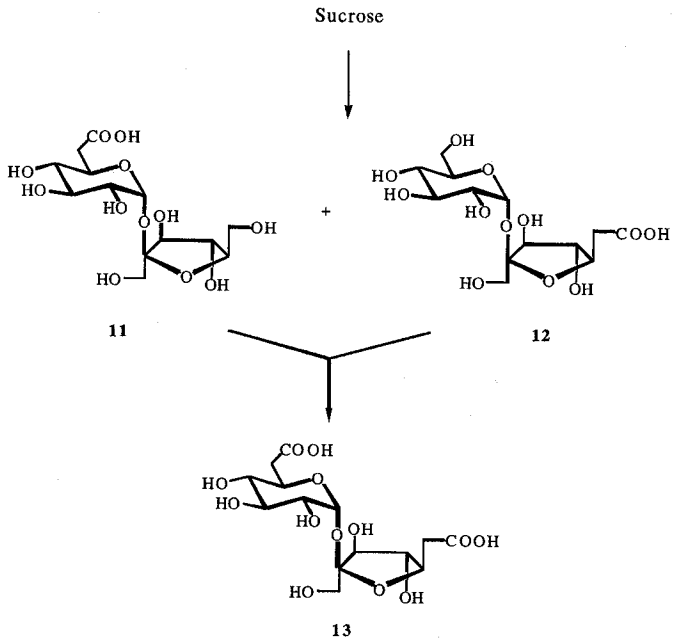
SCHEME 9

Proteases can also catalyze the transesterification of sugars. Thus, 1′-*O*-butyl ester of sucrose was prepared from sucrose and trichloroethyl butyrate with the protease subtilisin in anhydrous DMF (45). This approach has been extended to include subtilisin BPN and subtilisin Carlsberg in a variety of organic solvents for the preparation of monoesters starting from a vinyl ester (46). While some regioselectivity was observed, both 1′- and 6-*O*-acyl derivatives of sucrose were obtained. A commercially available, insoluble cross-linked form of subtilisin, called ChiroCLEC-BL (Altus Biologics Inc., Cambridge, MA), has also been used to catalyze the formation of acyl sucrose. When sucrose reacted with fatty acid vinyl esters in the presence of this enzyme, 1-*O*-acyl sucrose exclusively was isolated in 60% yield (47).

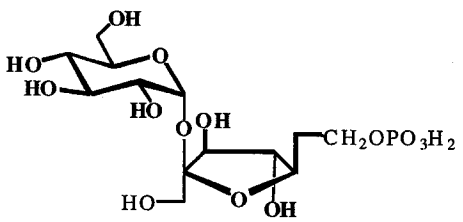
ANIONIC SUCROSE DERIVATIVES

Oxidation of the primary hydroxyl groups of sucrose to carboxylic acids has been studied extensively using oxygen with a platinum or palladium catalyst at pH 7–9 as the oxidant. Oxidation with platinum (10% Pt on carbon maintained at pH 7) takes place predominantly at the C-6 and C-6′ positions, yielding a mixture of the 6-monocarboxy, 6′-monocarboxy, and 6,6′-dicarboxy derivatives (Scheme 10). These sucronic acid derivatives are competitive inhibitors of invertase, and the 6-carboxy derivative can be hydrolyzed to yield fructose and glucoronic acid (48). The 6,1′,6′-tricarboxylic acid sucrose also has been prepared by catalytic oxidation of sucrose and found to be a useful complexing reagent in washing-agent formulations (49).

Sucrose 6′-phosphate, the monophosphate ester of sucrose, is an intermediate in the biosynthesis of sucrose. Synthesis of sucrose 6′-phosphate by an enzymatic method using uridine 5′-(-D-glucopyranosyl diphosphate) and D-fructose-6-phosphate has been reported (50). Chemical synthesis of sucrose-6′-phosphate has also been achieved by an unambiguous route. Thus, 2,3,4,6,1′,3′,4′-hepta-*O*-acetylsu-



SCHEME 10



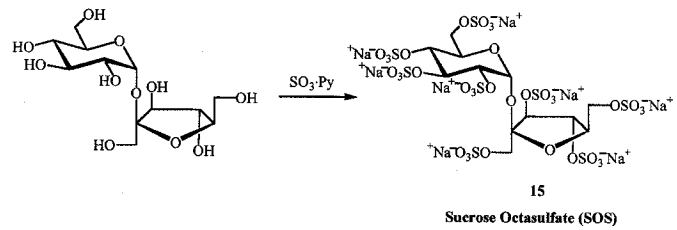
SCHEME 11

crose, prepared in five synthesis steps, can be reacted with cyanoethyl phosphate in pyridine to yield a crude product, from which pure sucrose-6′-phosphate is isolated as a barium salt (51) (Scheme 11).

Much attention also has been focused on the physiological properties of sulfated sugars, particularly on their enhanced anti-ulcerogenic activity (52,53). The aluminum salt of persulfated sucrose [Sucralfate; Hoechst-Marion-Roussell (HMR), Kansas City, MO], for example, is a popular drug with antipeptic ulcer activity (54). The many approaches to the synthesis of sucrose octasulfate (55,56) typically use a pyridine/sulfur trioxide complex (Pyr·SO_3) (57). The greatest difficulty in the preparation of sucrose octasulfate is its isolation, purification, and characterization. In the commercial process, the reaction mixture is usually neutralized with barium hydroxide, barium sulfate is separated, and the aqueous solution is concentrated to yield the sulfated sucrose as the barium salt (Scheme 12).

ANIONIC SUCROSE ESTERS

Long-chain fatty acid sucrose esters have shown promise as surfactants and compare well in overall detergency and emulsification performance with other surface-active compounds. The commercial use of these esters has been limited though, partly because of the presence of some residual solvent (usually DMF), which renders the product unsuitable as a food emulsifier. With long-chain fatty acid (carbon number >14) sucrose esters, water solubility can become a problem (Table 1). In one approach toward enhancing the aqueous solubility of sucrose esters, a polar group, such as a sulfo group, is introduced. The resulting acylsulfo sucrose derivatives are water-soluble and show much better surface-active properties (Table 1). Introduction of a sulfo group is preferred over a phospho group, since biodegradation leads to inorganic sulfate with a less-adverse environmental impact than inorganic phosphate, which is known to lead to eutrophication of lakes and rivers.



SCHEME 12

Sulfation of sucrose esters involves two different strategies. The first is the regioselective sulfation of fatty acid sucrose

TABLE 1
CMC Values of Sucrose Esters and Sulfated Sucrose Esters[a]

Surfactants	CMC (mol/L)
Sulfonation of 1′-*O*-acylsucrose	
1′-*O*-Lauroyl-6′-sulfosucrose	6.5×10^{-5}
1′-*O*-Lauroyl-6-sulfosucrose	7.1×10^{-5}
1′-*O*-Myristoyl-6′-sulfosucrose	4.8×10^{-5}
1′-*O*-Myristoyl-6-sulfosucrose	5.2×10^{-5}
1′-*O*-Stearoyl-6′-sulfosucrose	4.7×10^{-6}
1′-*O*-Stearoyl-6-sulfosucrose	5.6×10^{-6}
Sulfonation of 6-*O*-acylsucrose	
6-*O*-Myristoyl-4′-sulfosucrose	5.3×10^{-5}
6-*O*-Myristoyl-1′-sulfosucrose	5.9×10^{-5}
6-*O*-Stearoyl-4′-sulfosucrose	3.3×10^{-6}
6-*O*-Stearoyl-1′-sulfosucrose	3.8×10^{-6}
Displacement of sucrose 4,6-cyclic sulfate	
6-*O*-Palmitoyl-4-sulfosucrose	4.8×10^{-5}
6-*O*-Stearoyl-4-sulfosucrose	1.1×10^{-5}
6-*O*-Eicosanoyl-4-sulfosucrose	NS
6-*O*-Hexadecylamino-4-sulfosucrose	1.5×10^{-5}
6-*O*-Octadecylamino-4-sulfosucrose	NS
Acyl sucrose	
1′-*O*-Lauroylsucrose	1.5×10^{-4}
1′-*O*-Myristoylsucrose	9.1×10^{-5}
1′-*O*-Stearoylsucrose	NS
6-*O*-Lauroylsucrose	4.0×10^{-4}
6-*O*-Myristoylsucrose	1.3×10^{-4}
6-*O*-Stearoylsucrose	NS
Commercially available surfactant	
$C_{11}H_{23}SO_3Na$	1.2×10^{-3}
$C_{11}H_{23}SO_3Na$	2.5×10^{-3}
$C_{11}H_{23}SO_3Na$	8.6×10^{-3}
$C_{11}H_{23}SO_3Na$	2.1×10^{-3}

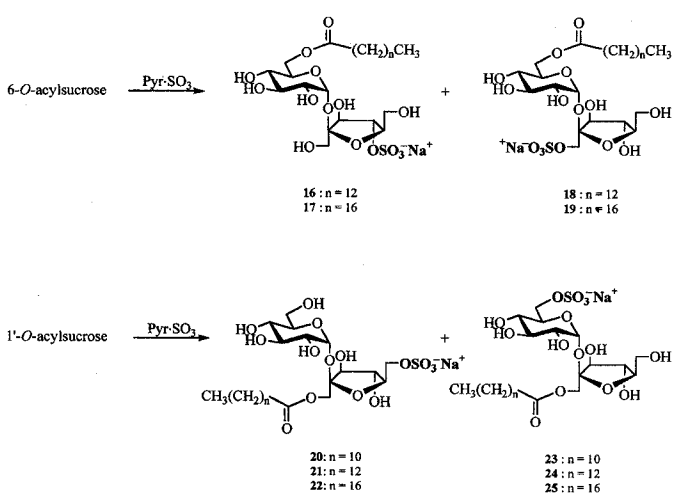
[a]NS, not soluble in water; CMC, critical micelle concentration.

esters. The second introduces the sulfo group through a nucleophilic displacement in a sucrose cyclic sulfo ester.

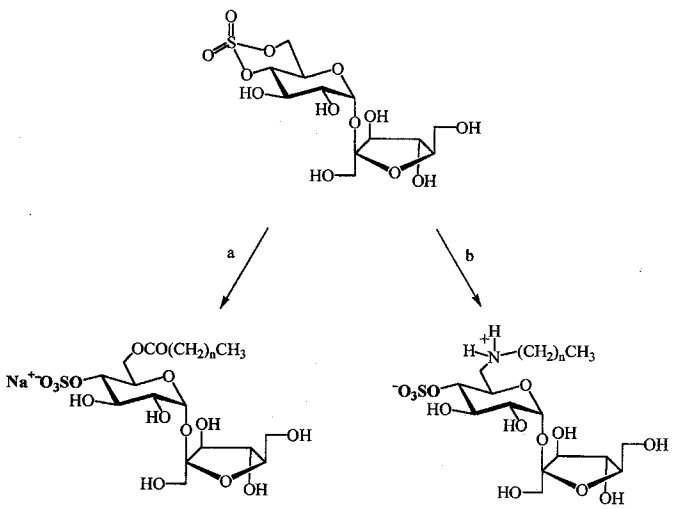
Sulfation of 6-*O*-acyl sucrose and 1′-*O*-acyl sucrose derivatives, using the Pyr·SO_3 complex, has been studied under a variety of different reaction conditions. Sulfation of 6-*O*-acyl-sucrose in pyridine in the presence of excess Pyr·SO_3 complex affords the 6-*O*-acyl-4′-sulfo-sucrose and 6-*O*-acyl-1′-sulfo-sucrose in 25 and 2% yield, respectively. Optimization of this reaction leads to the same 6-*O*-acyl-sucrose derivatives in 70 and 10% yield, respectively. Sulfonation of 1′-*O*-acyl-sucrose derivatives using Pyr·SO_3 under optimized reaction conditions leads to the formation of 1′-*O*-acyl-6′-sulfo-sucrose and 1′-*O*-acyl-6-sulfo-sucrose as major and minor products, respectively, with yields and regioselectivity ratios similar to those reported for the sulfation of 6-*O*-acylsucrose derivatives (58) (Scheme 13).

These results demonstrate that the presence of a long acyl chain can induce regioselectivity during the sulfation of acyl sucrose. As expected, sulfation of 1′-*O*-acyl sucrose derivatives occurred at the primary C6′ and C6 hydroxyls. However, sulfonation of 6-*O*-acyl-sucrose derivatives occurred primarily at the secondary C4′ hydroxyl and at the primary C1′ hydroxyl. The difference in regioselectivity observed during the sulfation of 6-*O*-benzoyl and 6-*O*-fatty acyl sucrose is apparently due to conformational and steric hindrance effects.

A second strategy for the sulfation of sucrose involves the use of sucrose cyclic sulfate intermediate. This intermediate is readily obtained in a two-step procedure involving the reaction of sucrose with thionyl chloride followed by the catalytic oxidation of the cyclic sulfite. The resulting sucrose cyclic sulfate can be opened using *O*-nucleophiles (palmitic, stearic, and eicosanoic acids) and *N*-nucleophiles (hexadecylamine and octadecylamine). On heating sucrose cyclic sulfate in DMF containing a slight excess (1.2 eq) of fatty acid and potassium bicarbonate, the 6-*O*-acyl-4-sulfate-sucrose is obtained regiospecifically in 75% yield. Reaction of sucrose cyclic sulfate with a slight excess of hexadecylamine or octadecylamine in DMF led to the corresponding amphoteric 6-deoxy-6-hexadecylammonio-4-sulfate-sucrose



SCHEME 13



(a) $CH_3(CH_2)_nCO_2H$ (1.2 eq), K_2CO_3 (1.2 eq), DMF, 80°C, 2 h
(b) $CH_3(CH_2)_nNH_2$, DMF, 80°C, 20 h

SCHEME 14

and 6-deoxy-6-octadecylammonio-4-sulfate-sucrose in 76 and 60% yields, respectively (58) (Scheme 14).

SURFACTANT PROPERTIES OF SUCROSE ESTERS

Sucrose esters of fatty acids having 12 or more carbon atoms are expected to display surface-active properties. The amphiphilic behavior of sucrose-based surfactants results from the presence of the hydrophilic free hydroxyl groups and hydrophobic alkyl chain.

At a specific concentration, called the critical micelle concentration (CMC), surfactant molecules aggregate to form micellar particles. This value is of practical importance since it represents the concentration of surfactant required to solubilize hydrophobic molecules in water. A calorimetric method for determining CMC (59) has recently been used to determine the CMC values of over 20 sucrose-based surfactants (39,47,58). The CMC values of sucrose esters and sulfated sucrose esters are given in Table 1. They are one to two orders of magnitude lower than those of other commercially available surfactants. As expected, the CMC value decreases with increasing acyl chain length. The 6-*O*-stearoyl and 1′-*O*-stearoyl sucrose derivatives with more than 14 carbon acyl chains were expected to be the most efficient surfactants, but these compounds were often water-insoluble. The water solubility of these fatty acid sucrose esters was increased by introducing a polar sulfo group. The resulting acylsulfo sucrose derivatives showed enhanced surface-active properties with exceptionally low CMC values. An amphoteric surfactant, 6-*O*-hexadecylammonio-4-sulfosucrose, was prepared that also displayed very good surface activity. All of these new anionic and amphoteric sulfosucrose-based surfactants display exceptional surface activity, are renewable materials, should be biodegradable and environmentally safe, and may thus have potential commercial value (60).

FUTURE TRENDS

This review has described the utilization of sucrose for the preparation of surfactants. Initial studies exploited sucrose simply as a polar headgroup to prepare mixtures of sucrose esters. Unlike the sugar ethers that are produced commercially in significant volumes, the sugar ester mixtures have found limited utility in the food and detergent industries, and product manufacturers have failed to develop other important applications in the cosmetic and pharmaceutical industries that often require pure compounds. Advances in regioselective chemical synthesis now make it possible to prepare such pure sucrose esters. The physical, chemical, and biological properties of these pure derivatives still need to be evaluated. Chemical engineering principles also need to be applied to scaleup and purification problems associated with their manufacture.

Use of lipases and proteases for the regioselective preparation of sucrose esters has been described. The application of biotechnology to protein engineering of these catalysts may further improve the regioselectivity and yield of the reactions they catalyze. The application of novel approaches including glycosyl transferases, acyl transferases, or sulfotransferases as catalysts in the synthesis of sucrose esters may also afford novel surfactant structures. Finally, biotransformation of sucrose to sucrose esters using whole-cell fermentation approaches may also provide a new approach in the manufacture of sucrose-based surfactants.

The biological evaluation of pure sucrose-based surfactants prepared by highly regioselective or regiospecific chemical, enzymatic, or fermentation-based methods might lead to valuable new insights.

Sucrose is a highly chiral molecule available in bulk quantities and at a relatively low cost. The regiospecific acylation of sucrose affords similarly highly chiral surfactants. These surfactants are capable of very specific interactions with other chiral molecules such as proteins, nucleic acids, and polysaccharides. Exploitation of the chiral specificity of sucrose-based surfactants may have importance in disciplines ranging from separation sciences to the pharmaceutical sciences.

REFERENCES

1. Kollinitsch, V., *Sucrose Chemicals,* The International Sugar Research Foundation, Washington, DC, 1970.
2. Paik, Y.H., and G. Swift, Polysaccharides as Raw-Materials for the Detergent Industry, *Chemistry & Industry* 2:55 (1995).
3. Husband, F.A., D.B. Sarney, M.J. Barnard, and P.J. Wilde, Comparison of Foaming and Interfacial Properties of Pure Sucrose Monolaurates, Dilaurate and Commercial Preparations, *Food Hydrocolloids 12*:237 (1998).
4. Hill, K., and O. Rhode, Sucrose-Based Surfactants for Consumer Products and Technical Applications, *Fett-Lipid 101*:25 (1999).
5. Torii, K., Sucrose Fatty Acid Ester-Based Cleaning Compositions for Rigid Surfaces, Japanese Patent 2,001,011,500 (2001).
6. Giles, C.C.D., F.A. Ellis, A.M. Murray, M.L. Pearce, and P.E. Red, Shampoo Compositions Containing Conditioning Agents and Surfactants, PCT Int. Appl. WO 0,045,779 (2000).
7. Keipert, S., and G. Schulz, Microemulsions with Sucrose Fatty Ester Surfactants. Part 1. *In Vitro* Characterization, *Pharmazie 49*:195 (1994).
8. Garti, N., A. Aserin, and M. Fanun, Non-ionic Sucrose Esters Microemulsions for Food Applications. Part 1. Water Solubilization, *Colloids Surf. A 164*:27 (2000).
9. Garti, N., V. Clement, M. Fanun, and M.E. Leser, Some Characteristics of Sugar Ester Nonionic Microemulsions in View of Possible Food Applications, *J. Agric. Food Chem. 48*:3945 (2000).
10. Katayama, T., and K. Fujii, Antimicrobial Sucrose Fatty Acid Esters Dispersed in Beverages, Japanese Patent 2,000,300,226 (2000).
11. Wittorff, J.H., L. Jorsal, and B.J. Stahl, Sucrose Fatty Acid Esters for Use as Increased Release of Active Ingredients, PCT Int. Appl. WO 0,025,598 (2000).
12. Megahed, M.G., Preparation of Sucrose Fatty Acid Esters as Food Emulsifiers and Evaluation of Their Surface Active and Emulsification Properties, *Grasas Aceites 50*:280 (1999).
13. Nakamura, S., Application of Sucrose Fatty Acid Esters as Food Emulsifiers, *Spec. Publ.–R. Soc. Chem. 230*:73 (1999).
14. Nakamura, S., O. Kawaguchi, and C. Wada, Improvement of Wheat Flour Products with Sucrose Fatty Acid Esters, Japanese Patent 11,243,842 (1999).
15. Koike, M., and H. Yokomichi, Fat and Oil Compositions Containing Sucrose Fatty Acid Esters for Frying of Frozen Foods and Foods Fried with Them, Japanese Patent 08,298,928 (1996).
16. Avela, E., Selective Substitution of Carbohydrate Hydroxyl Groups *via* Metal Chelates, *La Sucrerie Belge 92*:337 (1973).
17. Tomita, M., Sucrose Fatty Acid Esters as Anti-Bacterial Agents for Preparation of Beverage, Japanese Patent 10,070,971 (1998).
18. Watanabe, M., and T. Tagawa, Cosmetics, Japanese Patent 11,071,261 (1999).
19. Adachi, A., Cosmetic Emulsion Compositions, Japanese Patent 11,302,123 (1999).
20. Tanaka, N., Skin Preparations Containing Sucrose Fatty Acid Esters, Japanese Patent 2,001,106,640 (2001).
21. Nishikawa, Y., K. Fujii, and K. Kanayama, Acidic Hair Dyes Containing Sucrose Fatty Acid Esters, Japanese Patent 2,000,128,749 (2000).
22. Iida, I., Hair Treatment Aerosol Compositions Containing Sucrose Fatty Acid Esters, Nonionic Surfactants, and Lower Alcohols, Japanese Patent 11,222,417 (1999).
23. Takada, H., Y. Takashima, A. Yokotsuka, and Y. Soyama, Eyelash Cosmetic Composition Containing Sucrose Fatty Acid Esters, U.S. Patent 6,024,950 (2000).
24. Seto, M., Cosmetic Oil Gels Containing Sucrose Fatty Acid Esters and Surfactants, Japanese Patent 11,349,441 (1999).
25. Sakuyama, H., Cosmetic Gels Containing Monoglycerides and Sucrose Fatty Acid Esters for Massage, Japanese Patent 06,072,841 (1994).
26. Meyer, P.D., G.M. Vianen, and H.C.I. Baal, Sucrose Fatty Acid Esters in Deodorant Formulations, *Aerosol Spray Rep. 37(1/2)*:18 (1998).
27. Magae, Y., and Y. Itoh, Effect of Sucrose Ester of Fatty Acids on Fruit Body Formation of *Pleurotus ostreatus, Nippon Nogei Kagaku Kaishi 72*:631 (1998).
28. Vermeire, A., C. deMuynck, G. Vandenbossche, W. Eehaute, M.L. Geerts, and J.P. Remon, Sucrose Laurate Gels as a Percutaneous Delivery System for Oestradiol in Rabbits, *J. Pharm. Pharmacol. 48*:463 (1996).
29. Masutomi, N., S. Nakamura, and Y. Muratsubaki, Sucrose Fatty Acid Esters as Lubricants for Pharmaceutical and Confectionary Tablets, Japanese Patent 10,139,688 (1998).
30. Oda, K., and S. Chihara, Dental Alginate Impressions, Japanese Patent 10,139,616 (1998).
31. Hickson, J.L., Sucrochemistry, *American Chemical Society*

Symposium Series No. 41, American Chemical Society, Washington, DC, 1977, p. 341.
32. Hass, H.B., F.D. Snell, and W.I.C. York, Sugar Esters, U.S. Patent 2,893,990 (1959).
33. Parker, W.J., R.A. Khan, and K.S. Mufti, Surface-Active Products, Great Britain Patent 1,399,053 (1973).
34. Kasori, Y., and T. Yamazaki, Solventless Process for Preparing Sucrose Fatty Acid Esters, Great Britain Patent 2,256,869 (1992).
35. Komya, S., Method for Preparation and Isolation as Sucrose Fatty Acid Esters as Nonionic Surfactants, Japanese Patent 07,118,285 (1995).
36. Chauvin, C., and D. Plusquellec, A New Chemoenzymatic Synthesis of 6′-*O*-Acylsucroses, *Tetrahedron Lett. 32*:3495 (1991).
37. Chauvin, C., K. Baczko, and D. Plusquellec, New Highly Regioselective Reactions of Unprotected Sucrose. Synthesis of 2-*O*-Acylsucrose and 2-*O*-(*N*-alkylcarbamonyl)Sucrose, *J. Org. Chem. 58*:2291 (1993).
38. Baczko, K., C. Chauvin, J. Banoub, P. Thibault, and D. Plusquellec, A New Synthesis of 6-*O*-Acylsucrose and Mixed 6,6′-Di-*O*-acylsucroses, *Carbohydr. Res. 269*:79 (1995).
39. Vhalov, I.R., P.I. Vhalova, and R.J. Linhardt, Regioselective Synthesis of Sucrose Monoesters as Surfactants, *J. Carbohydr. Chem. 16*:1 (1997).
40. Ku, M.A., and Y.D. Hang, Enzymatic Synthesis of Esters in Organic Medium with Lipase from *Byssochlamys fulva, Biotechnol. Lett. 17*:1081 (1995).
41. Woundenberg van Oosterom, M., F. van Rantwijk, and R.A. Sheldon, Regioselective Acylation of Disaccharides in *tert*-Butyl Alcohol Catalyzed by *Candida antarctica* Lipase, *Biotechnol. Bioeng. 49*:328 (1996).
42. Kim, J.E., J.J. Han, J.H. Yoon, and J.S. Rhee, Effect of Salt Hydrate Pair on Lipase-Catalyzed Regioselective Monoacylation of Sucrose, *Biotechnol. Bioengin. 57*:121 (1998).
43. Ferrer, M., M.A. Cruces, M. Bernabe, A. Ballesteros, and F.J. Plou, Lipase-Catalyzed Regioselective Acylation of Sucrose in Two-Solvent Mixtures, *Biotechnol. Bioeng. 65*:10 (1999).
44. Plou Gasca, F.J., E. Pastor Martinez, M.A. Cruces Villalobos, M. Ferrer Martinez, and A. Ballesteros, Specific Enzymatic Acylation of a Secondary Hydroxyl of Sucrose, Spanish Patent 2,141,670 (2000).
45. Riva, S., J. Chopineau, A.P.G. Kieboom, and A.M. Klibanov, Protease-Catalyzed Regioselective Esterification of Sugars and Related Compounds in Anhydrous Dimethylformamide, *J. Am. Chem. Soc. 110*:584 (1988).
46. Rich, J.O., B.A. Bedell, and J.S. Dordick, Controlling Enzyme-Catalyzed Regioselectivity in Sugar Ester Synthesis, *Biotechnol. Bioeng. 45*:426 (1995).
47. Polat, T., H.G. Bazin, and R.J. Linhardt, Enzyme-Catalyzed Regioselective Synthesis of Sucrose Fatty Acid Ester Surfactants, *J. Carbohydr. Chem. 16*:1319 (1997).
48. Parpot, P., K.B. Kokoh, E.M. Belgsir, J.M. Leger, B. Beden, and C. Lamy, Electrocatalytic Oxidation of Sucrose: Analysis of the Reaction Products, *J. Appl. Electrochem. 27*:25 (1997).
49. Fritschela, W., E. Leupold, and M. Schilingman, Preparation of Sucrose Tricarboxylic Acid, Spanish Patent 218,150 (1987) and German Patent 35,355,720 (1987).
50. Hatch, M.D., Sugar Accumulation by Sugarcane Storage Tissue; the Role of Sucrose Phosphate, *Biochem. J. 93*:521 (1964).
51. Buchanan, J.G., D.A. Cummerson, and D.M. Turner, The Synthesis of Sucrose 6′-Phosphate, *Carbohydr. Res. 21*:283 (1972).
52. Levey, S., and S. Sheifield, Inhibition of the Proteolytic Action of Pepsin by Sulfate Containing Polysaccharides, *Gastroenterology 27*:625 (1954).
53. Anderson, W., and J. Watt, Carageenin Inhibition of Peptic Activity and Combination with Gastric Mucin, *J. Pharm. Pharmacol. 11*:318 (1959).
54. Marks, I.N., I.M. Samloff, I.M. Aarimaa, M. Aarimaa, and M. Siurala (eds.), Sucralfate: New Aspects in Therapy of Ulcers and Lesions, in *Second International Sucralfate Symposium Together with the World Congress of Gastroenterology in Stockholm*, Federal Republic of Germany, Germany, 1983, p. 112.
55. Ochi, K., Y. Watanabe, K. Okui, and M. Shindi, Crystalline Salts of Sucrose Octasulfate, *Chem. Pharm. Bull. 28*:638 (1980).
56. Chugai Pharmaceutical Co., Disaccharide Aluminum Polysulfates, French Patent 1,500,571 (1967).
57. Duff, R.B., Carbohydrates Sulphuric Esters. Demonstration of Walden Inversion on Hydrolysis of Barium 1,6-Anhydro-D-galactose-2-sulfate, *J. Chem. Soc.*:1597 (1949).
58. Bazin, H.G., T. Polat, and R.J. Linhardt, Synthesis of Sucrose-based Surfactants Through Regioselective Sulfonation of Acylsucrose and the Nucleophilic Opening of a Sucrose Cyclic Sulfate, *Carbohydr. Res. 309*:189 (1998).
59. Vulliez-Le Normand, B., and J.L. Eisele, Determination of Detergent Critical Micellar Concentration by Solubilization of a Colored Dye, *Anal. Biochem. 208*:241 (1993).
60. Linhardt, R.J., H.G. Bazin, and T. Polat, Sucrose Based Surfactants and Methods Thereof, U.S. Patent 6,184,196 (2001).

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