Trends In Carbohydrate Research, Vol.13, No.2 (2021) 50-77 0975-0304/09

Trends in Carbohydrate Research

website: www.trendscarbo.com

Carbohydrate-Based Surfactants: Promises, Challenges and Future Prospective

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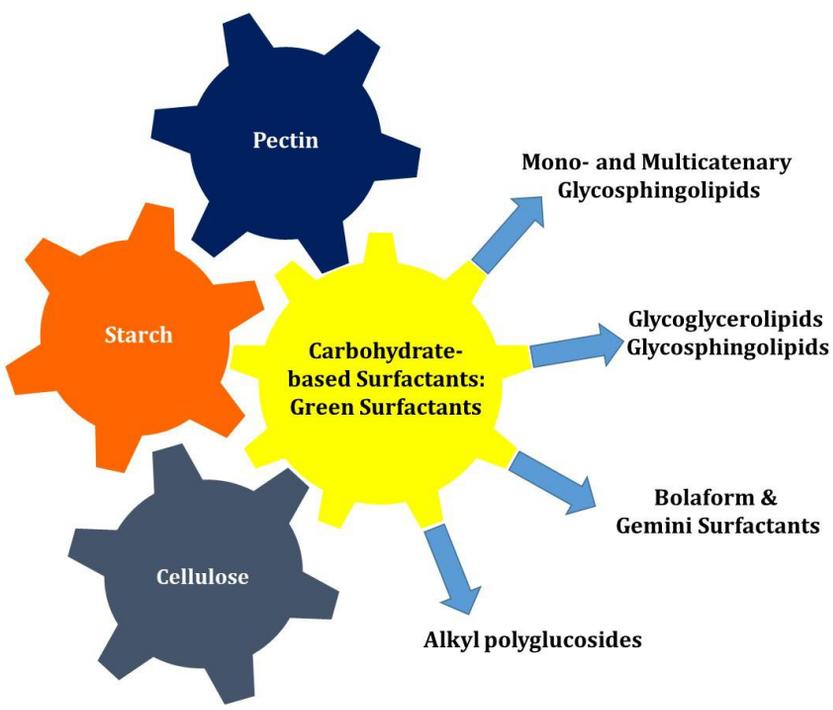
Received: May 11, 2021; Revised: June 13, 2021; Accepted: June 14, 2021

Graphical Abstract



Abstract

Carbohydrate-based surfactants (CBS) are an important class of amphiphilic compounds containing both hydrophilic and lipophilic moieties. These natural surfactants are biosynthesized within living cells and also easily can be prepared synthetically from the most abundant carbohydrate-rich renewable vegetable raw materials such as cellulose, pectin, hemicellulose, starch, etc. and fatty materials by sequential reactions. Extensive exploitation of non-renewable fossil fuels such as coal, petroleum; natural gas etc. damages the human and ecological health with significant contribution in overall pollution, thus the quest for novel methods and strategies has been accelerated to replace the conventional non-renewable fossil fuel sources with renewable, biodegradable, as well as sustainable sources for surfactant production. In this scenario, carbohydrate surfactants are of great interest because they are naturally abundant, biocompatible, highly biodegradable, and not noxious for the environment, which makes them an excellent alternative to surfactants from petrochemical sources.

Keywords: Surfactants; Amphiphiles; Glycosylation; Liposomes; Micelles

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Dedication: This paper is dedicated Prof. M. S. Wadia, Department of Chemistry, Savitribai Phule Pune University, Pune

1. Introduction

Carbohydrates are major building block in biological system and involved in a number of important biological processes including viral and bacterial adhesions, protein folding, cell growth and proliferation, cell–cell communication, as well as immune response and also used to generate diversity in nature due to inter and intracellular molecular interactions.[1-3] Moreover, carbohydrates are utilised in storage of energy (e.g., starch and glycogen) to acting as structural components (e.g., cellulose in plants and chitin in arthropods). Due to large number of reactive hydroxyl groups with geometrical and structural diversity, carbohydrates easily participates in hydrogen bonding in the aqueous environment. Furthermore, presence of diverge functional groups such as an aldehyde (an aldose) or a ketone, amino, carboxyl, phospho and sulfo group increases the hydrophilicity of the carbohydrate residue. Owing to this inherent nature, carbohydrate molecules possess excellent amphiphilic properties in solvent medium. Surfactants are amphiphilic molecules containing both a hydrophilic and a lipophilic moiety. Carbohydrate-based surfactants (CBS) are the most important class of amphiphilic compounds known as glycolipids.[4,5] These compounds are combination of a carbohydrate hydrophilic part, which can be a mono- or oligosaccharide, and a hydrophobic unit, usually derived from a fatty acid. This dual functionality exhibits unique physico-chemical properties to form stable emulsions and micelles or liposomes i.e. formation of small or large self-assembled aggregates at the dipolar interface, either at the air/water, oil/water or solid/water.[6] Carbohydrate surfactants are naturally biosynthesized within living cells so considered as natural surfactants,[7,8] or can be easily synthesized from the most abundant carbohydrate sources viz. (cellulose, pectin, hemicellulose, starch, etc.) and fatty materials by utilizing high-yielding established sequential reactions.[9,10] Essentially, CBS may be classified on the basis of presence of polar head group and a non-polar tail (amphiphilic structure) and the linkers between these two group. Using these three structural parameters, CBS/ glycolipids are classified in **Table 1**.[11]

Table 1. Classification of Carbohydrate surfactant/ glycolipids based on the amphiphilic structure and geometry[11]

Carbohydrate surfactant/ glycolipids	Hydrophilic group	Hydrophobic group	Linkers
Monocatenary Bicatenary	One head group	One tail	Ester, thioester, Ether, amine, amide
Multicatenary		Two tail	
		Multi tail	
Glycoglycerolipids		Acylglycerol	
Glycosphingolipids		Sphingoides	
Bolaforms	Two head groups	One spacer	
Geminis		One spacer/two tails	
Alkylpolyglucosides	Multi-head groups	One or multi-tails	

Due to numerous reactive hydroxyl groups, sugar molecules are excellent molecular architecture to study the surfactant mechanisms in modifying interfacial tension or viscosity properties. This controls the formation and the stability of colloidal systems such as micelles, vesicles, foams, emulsions, and suspensions. Therefore, carbohydrate derived surfactant has wide applications in different industries such as pharmaceutical, paints, pesticides, polymers, textiles, cosmetics, foods, cleaning detergents, oil, gas and mining etc. Moreover, these properties found useful in biology,[12] particularly for the extraction and purification of membranes proteins,[13] molecular recognition in glycobiology,[14] and immunology.[15] Moreover, carbohydrates are widely used bio-based moieties in formulation of surfactants, solvents, polymers etc. in the fields of synthesis, catalysis, biotechnology and analytical chemistry.[16-18] In continuation of our research interest in synthesis and applications of carbohydrate and their hybrid molecules,[19] this review highlights recent developments on carbohydrate-based surfactant (CBS) including the synthesis of simple *N*-glycoside, *O*-glycoside, sugar amines, and oligosaccharide based-surfactants that provide insight into their physicochemical aspects and applications.

2. Classification and Synthesis of Carbohydrate Based Surfactants

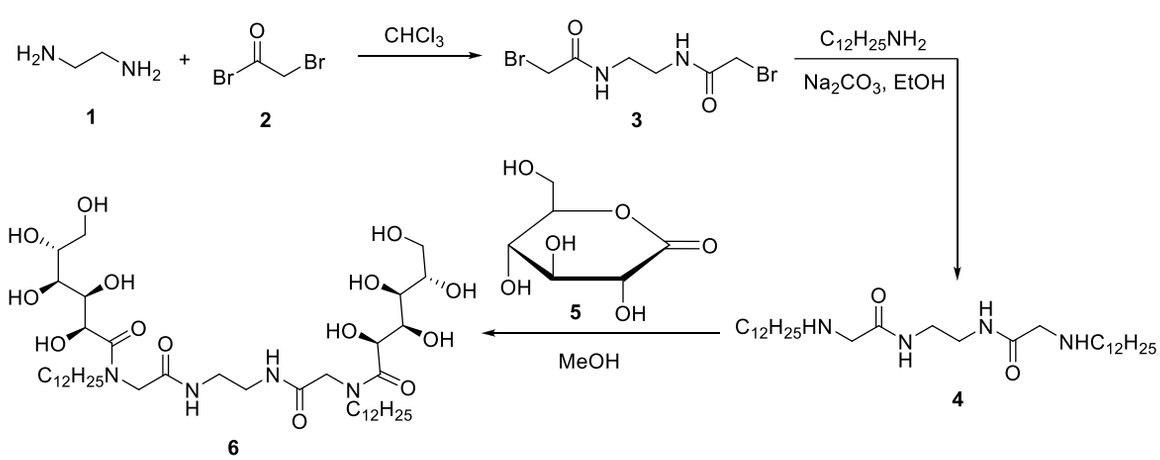
With the paradigm shift of industrial processes towards sustainability, investment on sustainable and safer chemicals like bio-based surfactants has been stressed upon by both the scientific community and authorities to minimize the hazards and risks. The factors that can be accounted for the use of bio-resources for surfactant preparation includes, (i) the natural amphiphilicity of certain biomolecules like carbohydrates and lipids, which is required to design a surfactant; and (ii) there's an economic advantage to use low-value agricultural wastes. A rigorous search for alternative to synthetic surfactants which is environmentally and industrially sustainable at the same time has ended with 'biosurfactants' produced from cheaper renewable feed stocks that is potentially endowed with all the physicochemical properties of its synthetic counterpart. Several families of biosurfactants such as alkyl polyglycosides (APG) or carbohydrate fatty acid esters are considered as "historical" ones due to the fact that they have been in use since time immemorial. Most of the industries manufacture surfactants based on polar moieties derived from polyethoxylated units (sodium lauryl ether sulphate, polyethoxylated fatty alcohols, ethoxylated sorbitan esters), ignoring the safety and toxicity concerns as well as their fossil origin. Thus, finding an alternative for hydrophilic moiety leads to carbohydrate based surfactants (CBS) extracted from renewable feedstock. Carbohydrates with their polyhydroxylated structure in combination with abundantly available fats (from renewable resources) suit to be an ideal replacement for their synthetic counterparts and a direct route for bio-based surfactant synthesis.[20-22] Carbohydrate-based-surfactants are of great interest because of they are naturally abundant, biocompatible, highly biodegradable, and not noxious for the environment, this makes them an excellent alternative to unmodified surfactants from petrochemical sources.[23-24]

3. Nitrogen-Containing Sugar Surfactants

3.1 Acyl hydrazones

Wang and co-worker demonstrated the protocol for the synthesis of novel sugar-based Gemini surfactant containing *N*, *N*' (*N*-dodecyl-2-D-Glucosaminyl acetyl) ethylenediamine (Glu(12)-(AA)-Glu(12)) spacer.[25] The first intermediate *N*,*N*'-*bis* (2-bromoacetyl) ethylenediamine **3** was synthesized from ethylenediamine **1** and bromoacetyl bromide **2** in chloroform. The intermediate **3** on treatment with dodecylaminein presence of Na_2CO_3 in ethanol afforded second intermediate *N*,*N*'-*bis* (2-dodecanoacetyl) ethylenediamine **4** then to the final product *N*, *N*' (*N*-dodecyl-2-D-glucosaminyl acetyl) ethylenediamine (Glu(12)-(AA)-Glu(12) compound **6** by refluxing it with D-(+)-Glucono-1, 5-lactone **5** in methanol (**Scheme 1**). The Critical micelle concentration (CMC)values of Glu(12)-(AA)-Glu (12) in surface tension determination at *p*H 4.0, 7.0 and 10.0 was at the 10^{-5}mol/L concentration level. In comparison with other Gemini surfactant containing similar hydrophilic spacers and same hydrophobic carbon chain length, this *N*, *N*' (*N*-dodecyl-2-D-glucosaminyl acetyl) ethylenediamine (Glu(12)-(AA)-Glu(12)) spacer exhibited higher surface activity. The protonation of tertiary amino groups in hydrophilic head group resulted in slight decrease in CMC value with decrease in *p*H of solution.

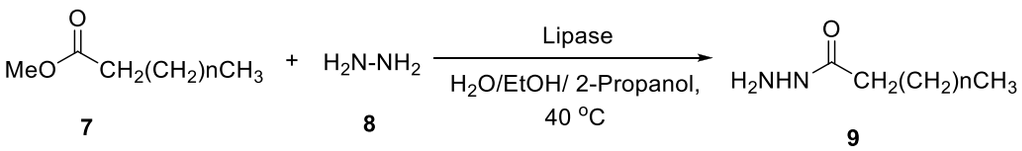
New series of sugar glycoside hydrazones were



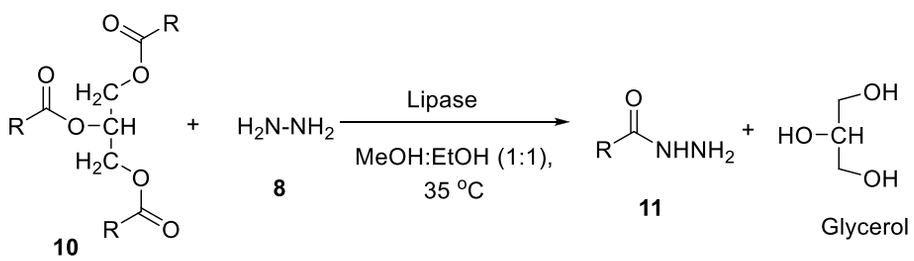
Scheme 1. Synthesis of novel Glu(12)-(AA)-Glu(12) Gemini surfactant

synthesized from commercially available fatty acid esters and vegetable oil by Carpenter and co-workers.[26] Initially, the acyl hydrazides **9** and **11** synthesized from fatty acid methyl ester **7** and vegetable oil triacylglycerides **10** respectively by using hydrazine and lipase enzyme (**Scheme 2a** and **2b**). The different sugar molecule **12** treated with acetylacetone **13** in presence of aq. $NaHCO_3$ as base afforded the intermediate C-glycoside ketone **14**. Finally, mono and polyunsaturated fatty acid hydrazides **16**(**a-j**) were synthesized successfully by utilizing this method via reacting intermediate **14** and acylhydrazine **15** by heating at 50 °C in 1:1 (MeOH: EtOH) (**Scheme 3**).[26]

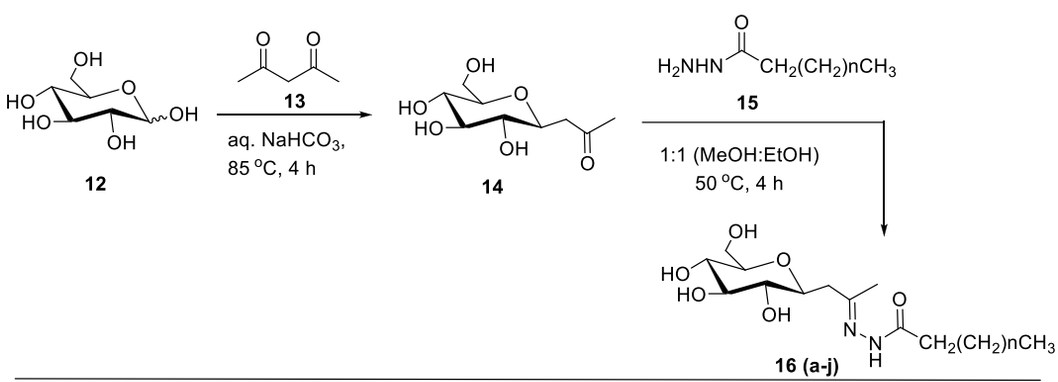
Xavier and co-worker reported the synthesis of



Scheme 2a. Synthesis of acylhydrazides from fatty acid methyl esters.[26]



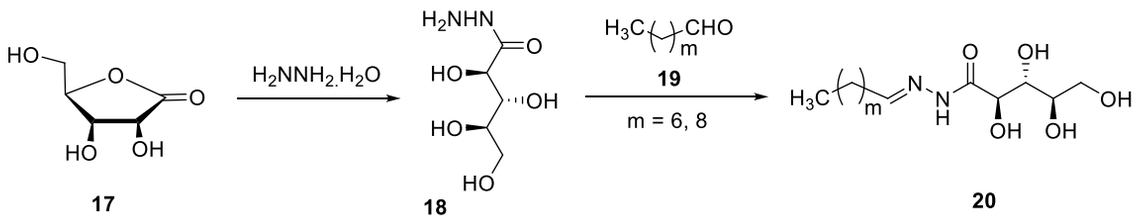
Scheme 2b. Synthesis of acylhydrazides from vegetable oil triacylglycerides.[26]



Carbohydrate (**12**)	Starting hydrazides(**15**)	Hydrazone products (**16 a-j**)
Glucose	Caprylic hydrazide	a) Glucose-C-glycoside caprylichydrazone
Xylose	Lauric hydrazide	b) Glucose-C-glycoside laurichydrazone
Rhamnose	Palmitic hydrazide	c) Glucose-C-glycoside palmitic hydrazone
Galacturonic acid	Stearic hydrazide	d) Glucose-C-glycoside stearic hydrazone
Lactose	Oleic hydrazide	e) Glucose-C-glycoside oleic hydrazone
		f) Glucose-C-glycoside linoleic hydrazone
		g) Xylose-C-glycoside laurichydrazone
		h) Rhamnose-C-glycoside laurichydrazone
		i) Galacturonic acid-C-glycoside laurichydrazone
		j) Lactose-C-glycoside laurichydrazone

Scheme 3. Synthesis of long chain *C*-glycoside ketohydrazones and fatty acid hydrazides.[26]

amphiphilic acylhydrazone surfactant **20** from D-ribono-1,4-lactone **17**.[27] First, hydrazine hydrate treatment with D-ribono-1,4-lactone **17** afforded the intermediate ribonohydrazide **18**, then treatment with octanal or decanal provided the desired amphiphilic acylhydrazone surfactant product **20** (**Scheme 4)**.

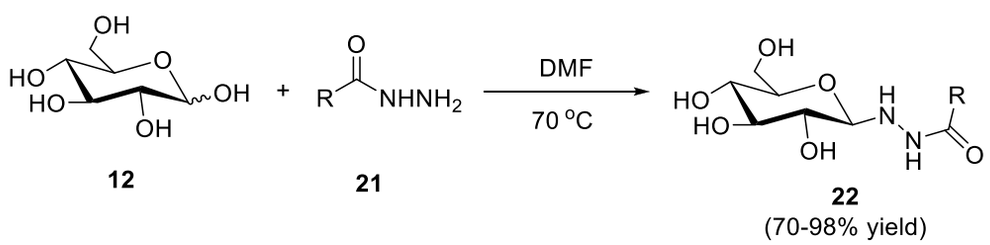


Scheme 4. Amphiphilic acylhydrazone synthesis via ring-opening of aldonolactones.[27]

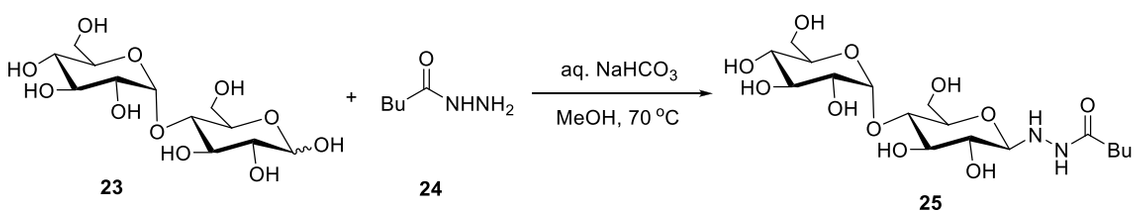
The synthesis of different amphiphilic 1-glycosyl-2-acylhydrazines series from readily available reducing sugar and hydrazides demonstrated by Auge and co-workers.[28] In present work, a series of glucosylhydrazide **22** synthesized from mono-saccharide sugar **12** and acylhydrazine **21** in DMF at 70°C without chromatographic step with good-to-excellent yield (**Scheme 5**).

Similarly, the reaction used for the synthesis of 1-(β-maltosyl)-2-octanoylhydrazine **25** by reacting maltose and octanoylhydrazine using basic aqueous $NaHCO_3$ (**Scheme 6)**. Synthesis of 1-maltosyl-2-octanoylhydrazine **25** is a typical disaccharide based surfactant with critical micellar concentration (CMC) range of 0.37 to 440 mM.[28]

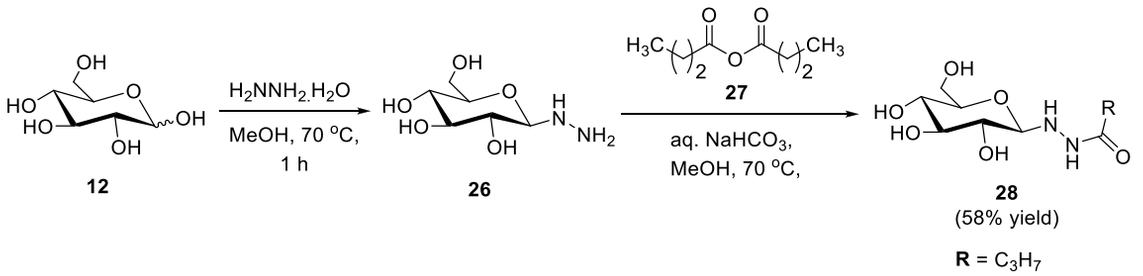
By using similar strategy, the product 1-(β-glucosyl)-2-butanoylhydrazine **28** (58% yield) obtained from intermediate glycosylhydrazine **26** and butyryl anhydride **27** by using aq. $NaHCO_3$ as base. The intermediate glycosylhydrazine **26** synthesized by the reaction of monosaccharide **12** and hydrazine hydrate in methanol at 70 °C (**Scheme 7**).



Scheme 5. Glucosyl hydrazide synthesis from monosaccharide sugar.[28]

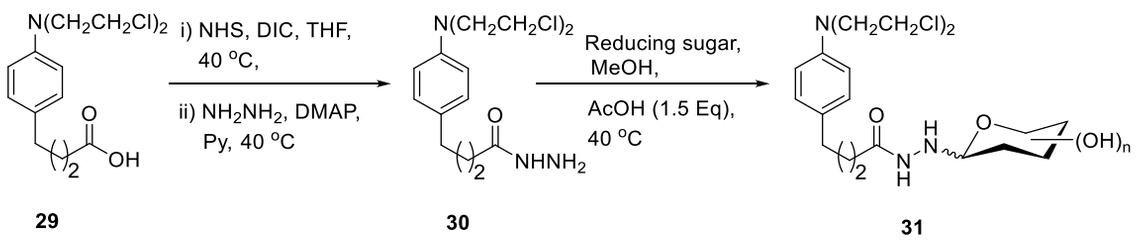


Scheme 6. Synthesis of 1-(β-maltosyl)-2- butanoyl hydrazine using maltose and butanoyl hydrazide.[28]

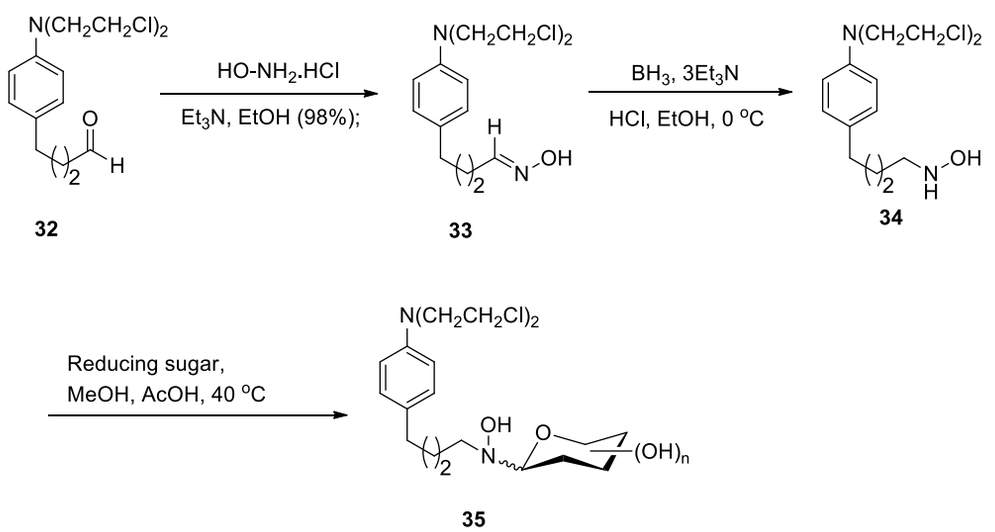


Scheme 7. Synthesis of 1-(β-glucosyl)-2-butanoylhydrazine from glycosylhydrazine **26** and butyryl anhydride **27**.[28]

Goff and co-workers synthesized new chlorambucil *N*-acylhydrazine-based compound **31** by chemoselective Neoglycosylation method.[29] First, the intermediate 4-(4-*N*', *N*'-bis(2-chloroethyl)amino)phenyl butanoic hydrazide **30** prepared from chlorambucil **29** by treatment of *N*-hydroxysuccinimide and DIC in THF at 40 °C for 6 h and then treatment with hydrazine, pyridine and DMAP led to the formation of the intermediate 4-(4-*N*', *N*'-bis(2-chloroethyl)amino)phenyl butanoic hydrazide **30**. Further, in a dram vial, aglycon compound **30** reacted with reducing sugar in presence of acetic acid in methanol furnished the crude neoglycosides **31** (**Scheme 8**).



Scheme 8.Chemoselectivesynthesis of neoglycosidesfromchlorambucil

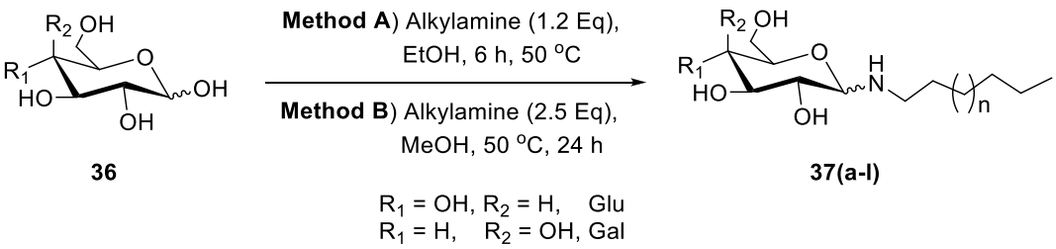


Scheme 9. Synthesis of *N*-glycosylamine compound **35**

3.2 Glycosylamines

Goff and co-workers synthesized new *N*-glycosylamine compound **35** using aldehyde **32** (**Scheme 9**).[29] Initially, intermediate oxime derivative **33** obtained by refluxing aldehyde **32** and hydroxylamine hydrochloride in ethanol using triethylamine base. Further, reduction of the intermediate oxime **33** with $BH_3.Et_3N$ and HCl in ethanol afforded the second intermediate **34**. Finally, the *N*-glycosylamine product **35** obtained from the intermediate **34** by treating with reducing sugar in ethanol using catalytic acetic acid (**Scheme 9**).

Neto *et al.*, synthesized series of *N*-alkylglucosamines and *N*-alkylgalactosamines **37** (**a-l**) using different alkylamines *via* **method A** and **method B** (**Scheme 10**).[30] Interestingly, reaction was completed with 1.5 equivalents of alkylamine in 6 hrs in ethanol (**method A**) and with 2.5 equivalents of alkylamine in 24 hrs in methanol (**method B**), respectively.

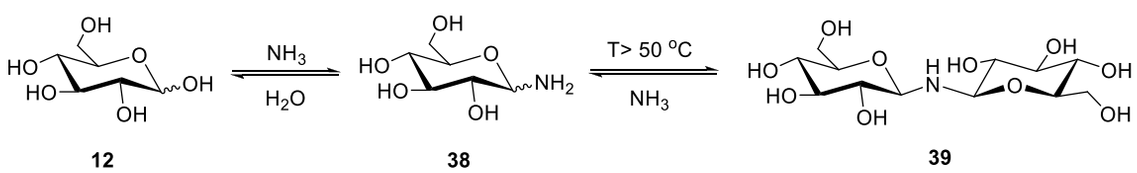


Scheme 10. Synthesis of *N*-alkylglucosamines and *N*-alkylgalactosamines

Table 2. Synthesis of *N*-alkylglucosamines and *N*-alkylgalactosamines by **Method A** or **B**

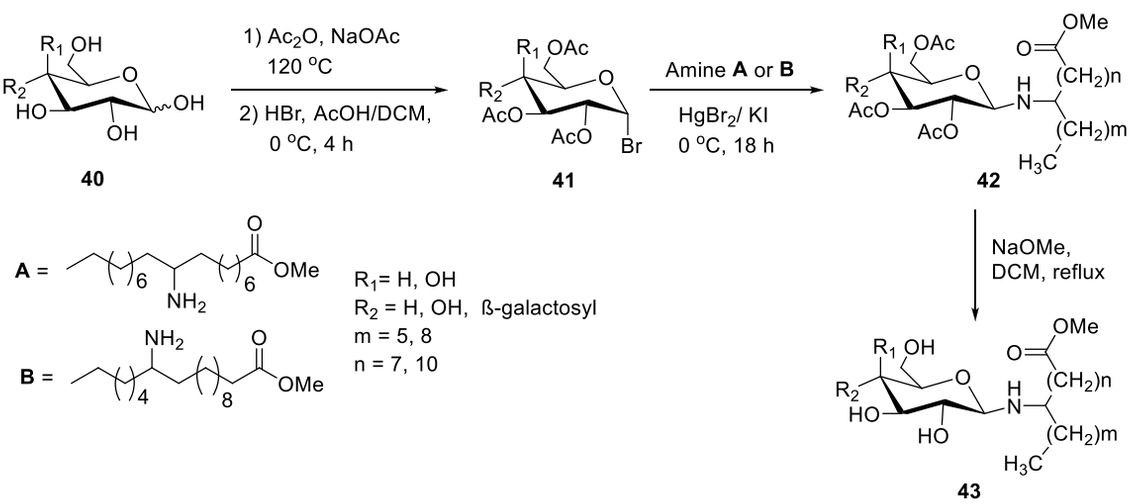
Alkyl amines	*N*-alkylglucosamines	%Yield (Method)	*N*-alkylgalactosamines	%Yield (Method)
Hexyl	C_6Glu (a)	86 (B)	C_6Gal (g)	76 (B)
Octyl	C_8Glu (b)	60 (B)	C_8Gal (h)	48 (B)
Decyl	C_{10}Glu (c)	83 (B)	C_{10}Gal (i)	83 (B)
Dodecyl	C_{12}Glu (d)	86 (A)	C_{12}Gal (j)	77 (A)
Hexadecyl	C_{16}Glu (e)	72 (B)	C_{16}Gal (k)	76 (B)
Octadecyl	C_{18}Glu (f)	96 (B)	C_{18}Gal (l)	92 (B)

Similar synthetic strategies were used to synthesize *N*-alkylglycosylamines with long chain amines in ethanol and water at room temperature by Lockhoff and co-workers in 1998[31] and El-Ghoul and co-workers in 1996.[32] However, the completion time varies from 24 hrs to several days. Lubineau and co-workers demonstrated another protocol in which glycosylamines **39** were synthesized by thetreatment of carbohydrates **12** with aqueous ammonia or primary amines (**Scheme 11**).[33]



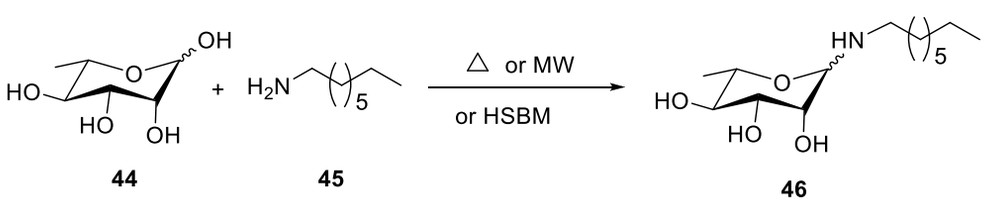
Scheme 11. Synthesis of glycosylamines **39** by using aqueous ammonia

Synthesis of methyl 12-glucosylamino octadecanoate **43** from different sugars like galactose, glucose, lactose and maltose and methyl 9-(**A**) or methyl 12-aminooctadecanoate (**B**) reported by Bogaert and co-workers.[34] The first intermediate **41** was obtained from by reacting sugar **40** with Ac_2O in the presence of NaOAc and followed by selective bromination by HBr in acetic acid.Subsequently, the intermediate **41** treated with amine **A** and **B** with $HgBr_2$ and KI gave the glucosylamino product **42**. Finally, the desired product 12-glucosylamino octadecanoate **43** was obtained by hydrolysis using NaOMe in DCM (**Scheme 12**). The physicochemical properties of these surfactants were found to depend on the alkyl chain length.



Scheme 12. Synthesis of methyl 12-glucosylaminooctadecanoate by multi-step process

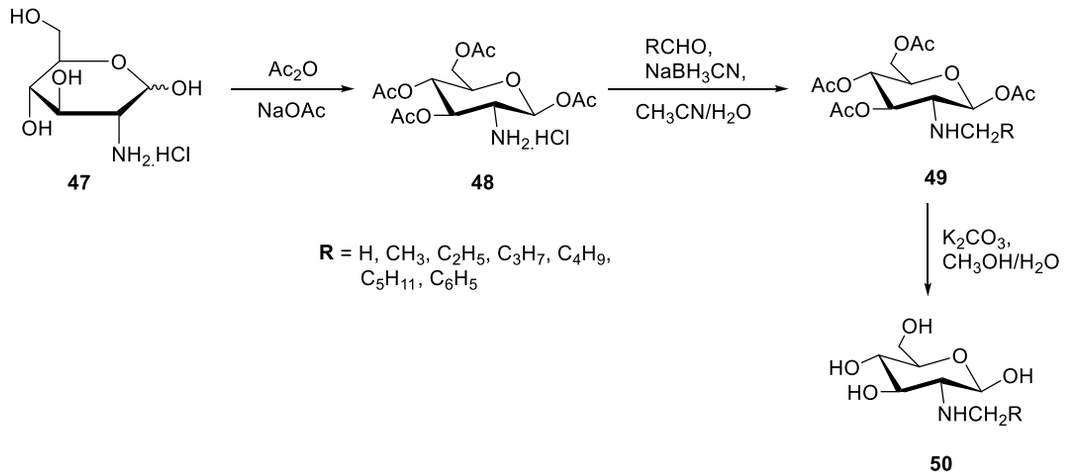
Further, Lingome and co-workers first put forward the synthesis of octylrhamnosyl-amine **46** from rhamnose **44** and octylamine **45** by green approach under solvent-free and mechanical milling assisted conditions (**Scheme 13**).[35]



Scheme 13. Mechanical milling assisted solventless synthesis of octylrhamnosyl-amine

3.3 Glucosamines

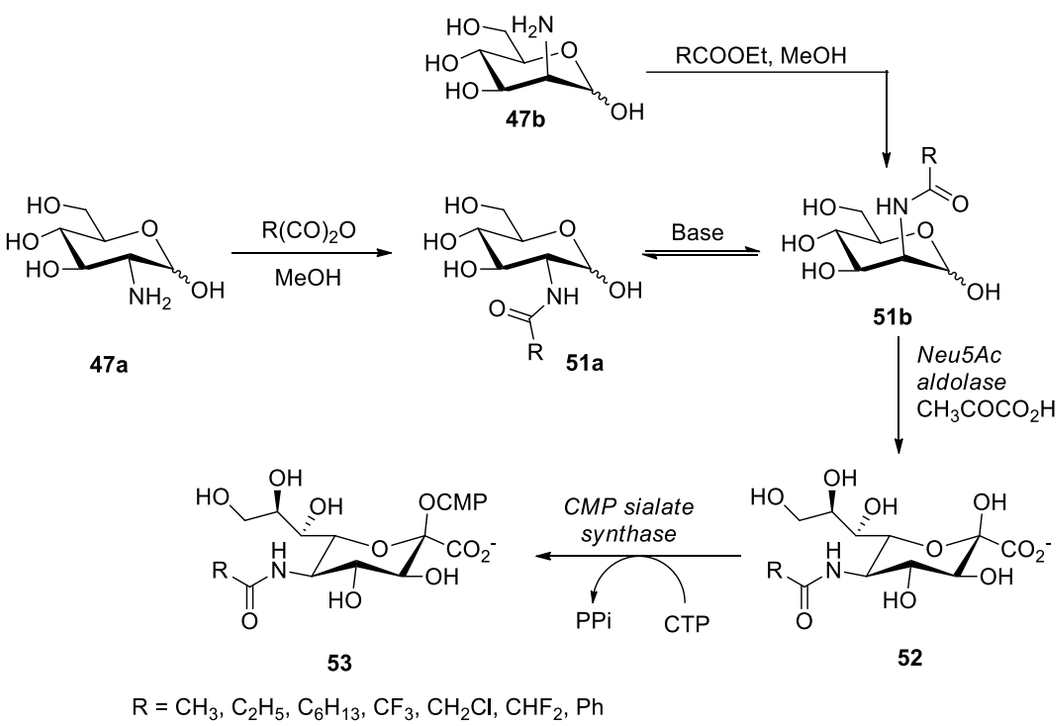
The reductive alkylation of per-*O*-acetyl-D-glucosamine to mono and di-*N*-alkylated derivatives of 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-β-D-glucose **50** demonstrated by Liberek and co-workers.[36] The acetylation of 2-amino-2-deoxy-D-glucose hydrochloride **47** with Ac_2O/ NaOAc afforded the 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-D-glucose hydrochloride **48**. The reductive alkylation using excess of $NaCNBH_3$ and appropriate aldehyde led to formation of the product **49**. By this method, mixtures of mono and di alkylated products obtained except valeric and benzaldehyde which afforded only mono-alkylated glucosamino products.Further, hydrolysis using K_2CO_3 in methanol/water furnished1,3,4,6-tetra-O-acetyl-2-amino-2-deoxy-β-D-glucose **50 (Scheme 14**).[36]



Scheme 14. Synthesis of *N*-Alkyl derivatives of 2-amino-2-deoxy-D-glucose

Humphrey and co-workers achieved the synthesis of *N*-acyl and *N*-haloacetylneuraminic acids by using D-glucosamine **47a** or D-mannosamine **47b** and immobilised sialic acid aldolase (**Scheme 14**).[37] A supersaturated solution of free base and appropriate anhydride was used for the acylation of D-glucosamine **47a** to afford the intermediate **51a**. It was observed that in alkaline condition *N*-acyl-glucosamines **51a** epimerised into *N*-acylmannosamine **51b**. Further, *N*-acyl-D-neuraminic acid **52** was obtained from *N*-acylmannosamine **51b** by treatment with *Neu5Ac aldolase*enzyme in the presence of 2-oxopropanoic acid. Subsequently, reaction of *N*-acyl-D-neuraminic acid **52** with *CMP sialate synthase* enzyme afforded the final product CMP-*N*-acyl-D-neuraminic acid **53** (**Scheme 15**).[37]

Acylation of glucosamines **47** with acyl chloride **54** in methanol afforded the *N*-acyl glucosamine surfactant

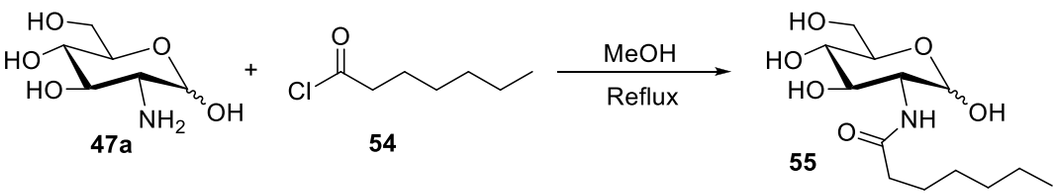


Scheme 15. Chemo-enzymatic method for the synthesis of *N*-acyl-D-neuraminic acid **52** and CMP-*N*-acyl-D-neuraminic acid **53**.

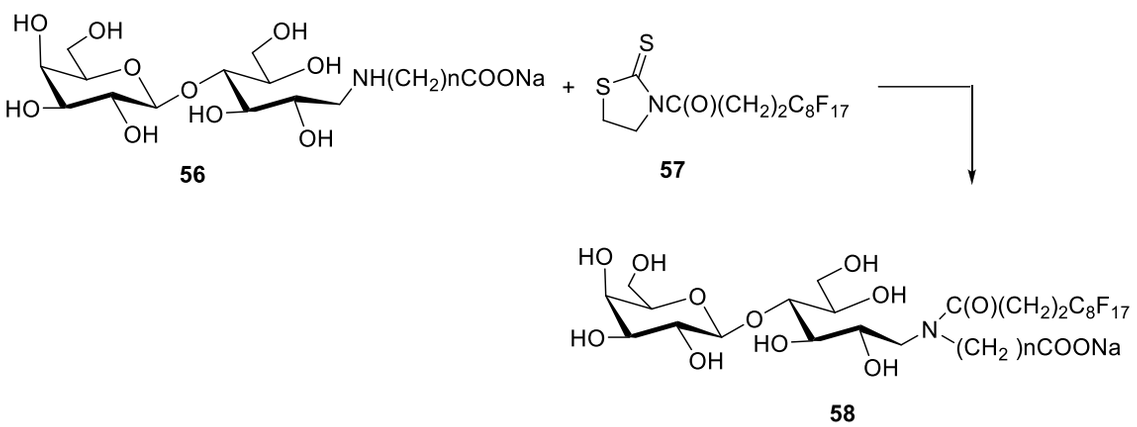
product **55** (**Scheme 16**).[37,38]

3.4 N- (Fluorinated Alkyl)-Surfactants

In recent years, investigation of carbohydrate based fluorosurfactant (class of one or more perfluoroalkylated hydrophobic chain) has gained much more interest.[39] In this, Zarif and co-worker synthesized the fluorinated compound **58** by the treatment of 1-amino-



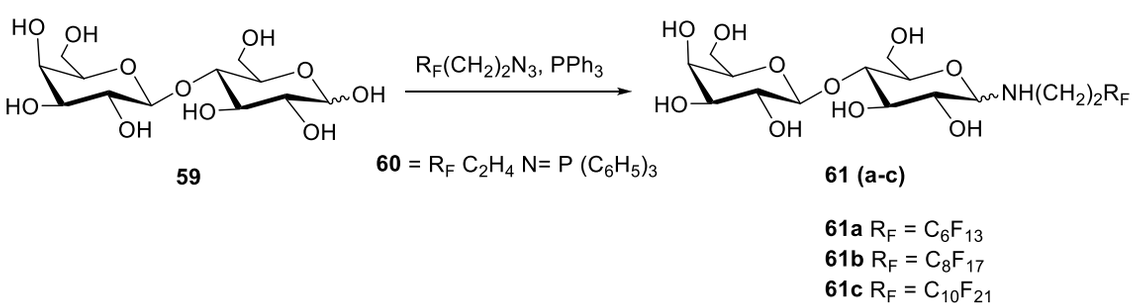
Scheme 16. Synthesis of*N*-heptanoyl glucosamine using acyl chloride**54**.



Scheme 17. Fluorination of 1-amino-1-deoxy-lactitol **56** by fluorinating agent **57**.

1-deoxy-lactitol **56** with the fluorinating agent **57** with moderate yield (**Scheme 17**).[40]

El-Ghoul and co-workers demonstrated the synthesis of *N*-[*Z*-(F-alkyl)ethyl]-lactosylamines **61(a-c)** by using iminophosphorane intermediate **60** [$R_FC_2H_4N{=}P(C_6H_5)_3$] as fluorinating agent which was generated by reaction of the fluoroalkylazide with triphenyl phosphine.[41,42] Lactose sugar **59** on treatment with iminophosphoranefetched different *N*-[*Z*-(F-alkyl)ethyl]-lactosylamines **61(a-c)** with significant



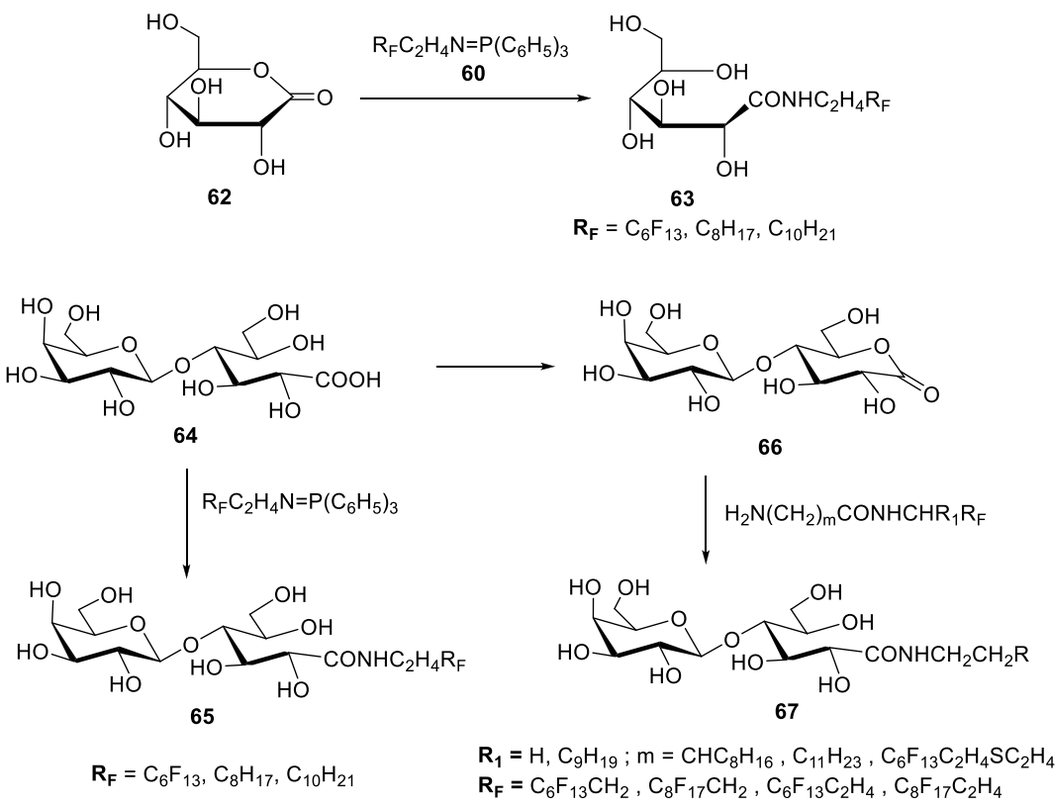
Scheme 18. Synthesis of *N*-[*Z*-(F-alkyl)ethyl]-lactosylamines.

yield (**Scheme 18)**.

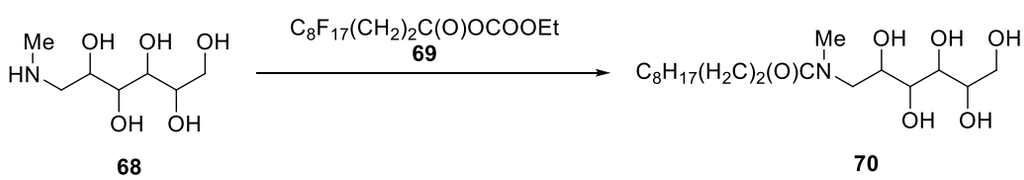
In continuation of this, Rico-Lattes and co-worker explored the applications of iminophosphorane intermediate **60** [$R_FC_2H_4N{=}P(C_6H_5)_3$] for the synthesis of*N*-[2-(F-alkyl)ethyl]-lactosylamines **63** as well as *N*-[2-(F-alkyl)ethyl]-lactobionamides **65** and **67** by using different fluorinating agents.[28,29] The easily available aza-Wittig product **61** [$R_FC_2H_4N{=}P(C_6H_5)_3$] on treatment with D-gluconolactone **62** afforded the product F-alkyl-D-gluconamides **63**. Lactobionic acid **64** on aza-Wittig reaction led to formation of F-alkyl-D-lactobionamide **65**product.Further,reaction of 1,5-bionolactone derivative **66** with amine under basic condition generated the product F-alkyl-D-lactobionamide **67** as sole product **(Scheme 19)**. The surface tension of Lactobionic derivatives at CMC value (~0.1 mM) was not good candidate for surfactants.[43]

Reiss and co-worker demonstrated another protocol in which new acyl fluorinating agent **69** used to synthesize *N*-[3-(F-octyl)propanoyl]-*N*-methyl-D-glucamide **70** from *N*-methyl-D-glucamine **68** (**Scheme 20)**.[44]

Trabelsi and co-workers attempted the synthesis of F-alkylated sugar carbamates **73** from monosaccharide D-Glucose **71** and fluorinated isocyanate **72** using DABCO catalyst. In this protocol, another fluorinated

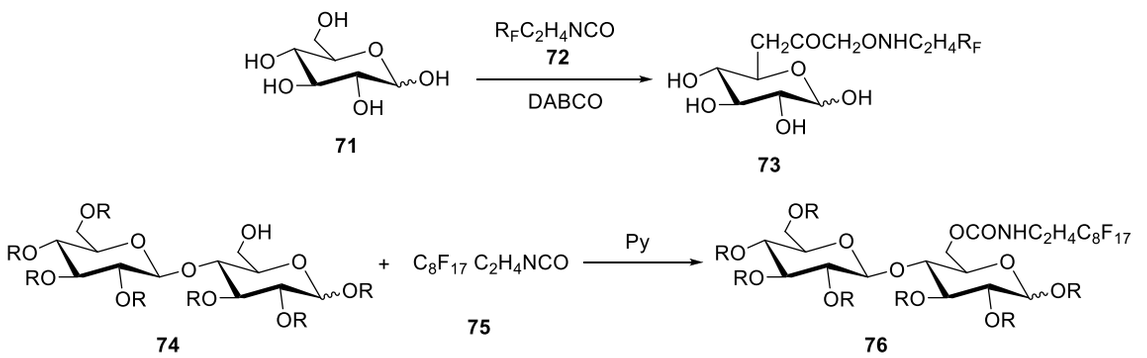


Scheme 19. Synthesis of variousF-alkyl amide derivatives.



Scheme 20. Synthesis of *N*-[3-(F-octyl)propanoyl]-*N*-methyl-D-glucamide**70** by usingacyl fluorinating agent **69**

isocyanate **75** used to synthesize fluorinated disaccharide **76** from disaccharide **74** in pyridine (**Scheme 21**).[45]

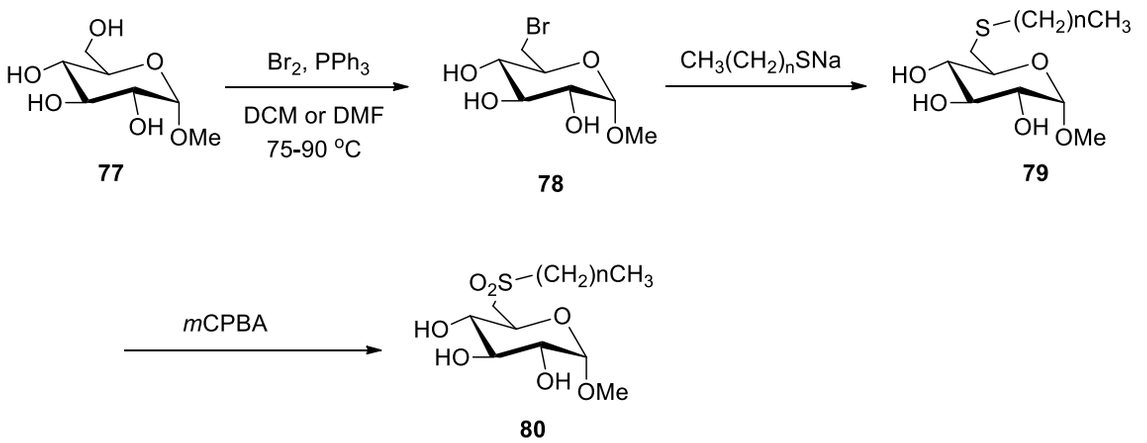


Scheme 21. Applications of fluorinated isocyanates for fluorination reaction.

3.5 Ethers

3.5.1 Thioethers

Synthesis of 6-alkylsulfonyl-6-deoxy glycoside **80** demonstrated by Lubineau and co-workers.[46] Reaction of methyl α-D-glycoside with Br_2/PPh_3 in dichloromethane furnished the intermediate sugar **78**, which on treatment with sodium thioxide gave the 6-alkylthio- glycoside **79**. Finally, oxidation with *m*CPBA afforded the desired product **80** without protection of the secondary hydroxyl groups (**Scheme 22**).

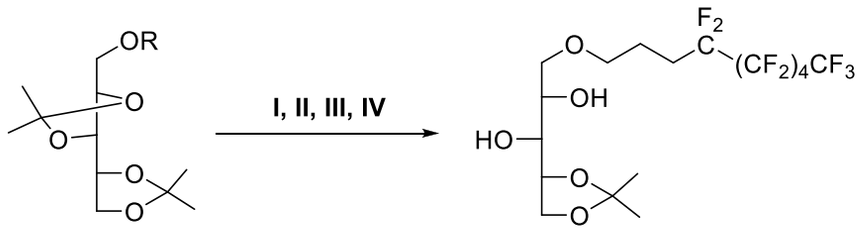


Scheme 22. Synthesis of 6-alkylthio- glycoside **79** and 6-alkylsulfonyl-6-deoxy glycoside **80**.

3.5.2 Fluorinated *O*-alkyl glycosides

Two main strategies are generally used for the synthesis of various fluoro-compounds. First, linear synthesis, in which glycosides synthesized from hydrocarbon chain containing a double bond with F-alkyl chain. Second, convergent synthesis, which involve F-alkyl chain preparation as initial step and glycosylation as final step. A spacer needed in between fluorinated alkyl chain and sugar head of F-alkyl glycosides for its stability.[47] Linear syntheses were demonstrated in various reports.[48-50]

The linear synthesis also well demonstrated by Paleta and co-worker in which synthesis of 1-*O*-(4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluorononyl)xylitol **82 (a-d)** derivatives from diacetonexylitol **81** mentioned (**Scheme 23**).[51] Initially, treatment of diacetone xylitol **81** with NaH in toluene and followed addition of allyl bromide under cool condition afford intermediate 1-*O*-allylxylitol as colourless liquid with 69% yield. This intermediate 1-*O*-allylxylitol on radical addition with perfluorohexyl iodide and AIBN afford the second intermediate 2,3:4,5-Di-*O*-isopropylidene-1-*O*-(4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluorononyl)xylitol. Reduction of third intermediate with Zinc/Ni(II) chloride hexahydrate under inert atmosphere condition and THF solvent gives third intermediate 2,3:4,5-di-*O*-isopropylidene-1-*O*-(4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluorononyl)-xylitol. The final product 1-*O*-(4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluorononyl)-xylitol

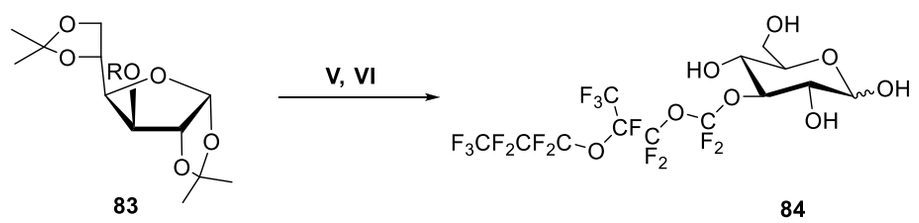


81 (a-d) **82 (a-d)**

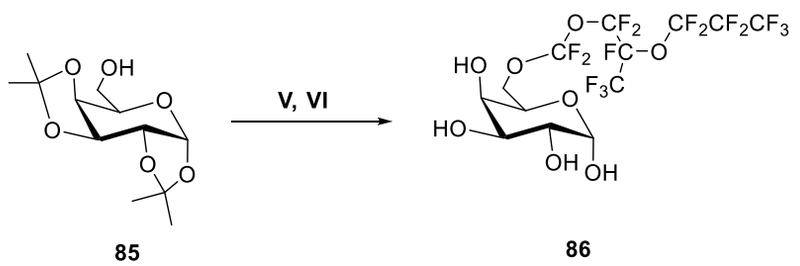
I = i) NaH, toluene, 100 °C, 3 h,
ii) CH_2=CH-CH_2Br, toluene, reflux, 18 h;
II = $C_6F_{13}I$, AIBN, 100 °C, 3 h;
III = Zn–$NiCl_2 \cdot 6H_2O$, THF–H_2O, r.t., 24 h;
IV = Conc.HCl, methanol, r.t., 1 h

82a R = H,
82b R = $CH_2CH{=}CH_2$,
82c R = $CH_2CHICH_2C_6H_{13}$,
82d R = $CH_2CH_2CH_2C_6F_{13}$

Scheme 23. Stepwise synthesis of 1-*O*-(4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluorononyl)-xylitol



83 **84**



85 **86**

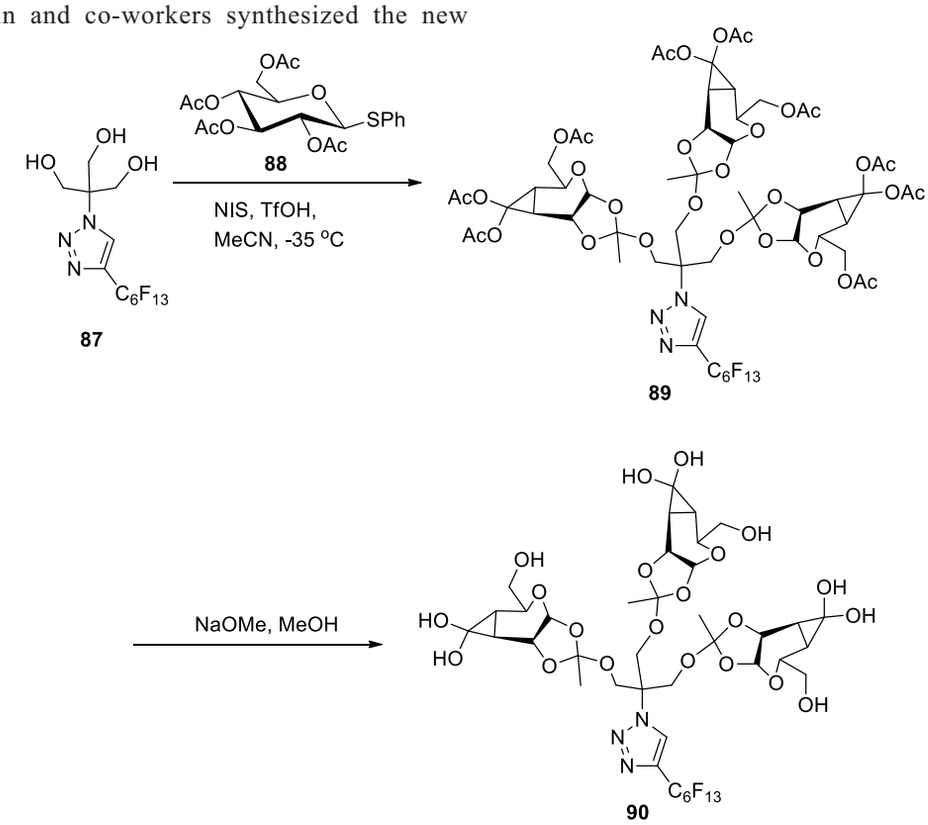
V = i) BuLi, THF, -78 °C, ii) THF, -78 °C, 2 h,
iii) r.t., 96 h
VI = CF_3COOH–H_2O (9:1), 30 min

Scheme 24. Synthesis of 3-*O*-(1,1,2,4,4,5,7,7,8,8,9,9,9-tridecafluoro-5-trifluoromethyl-3,6-dioxanon-1-yl)-D-glucopyranose **84** and 6-*O*-(1,1,2,4,4,5,7,7,8,8,9,9,9-tridecafluoro-5-trifluoromethyl-3,6-dioxanon-1-yl)-D-galactopyranose **86**

82(a-d) obtained from third intermediate by treating it with conc. HCl in methanol (**Scheme 23**).

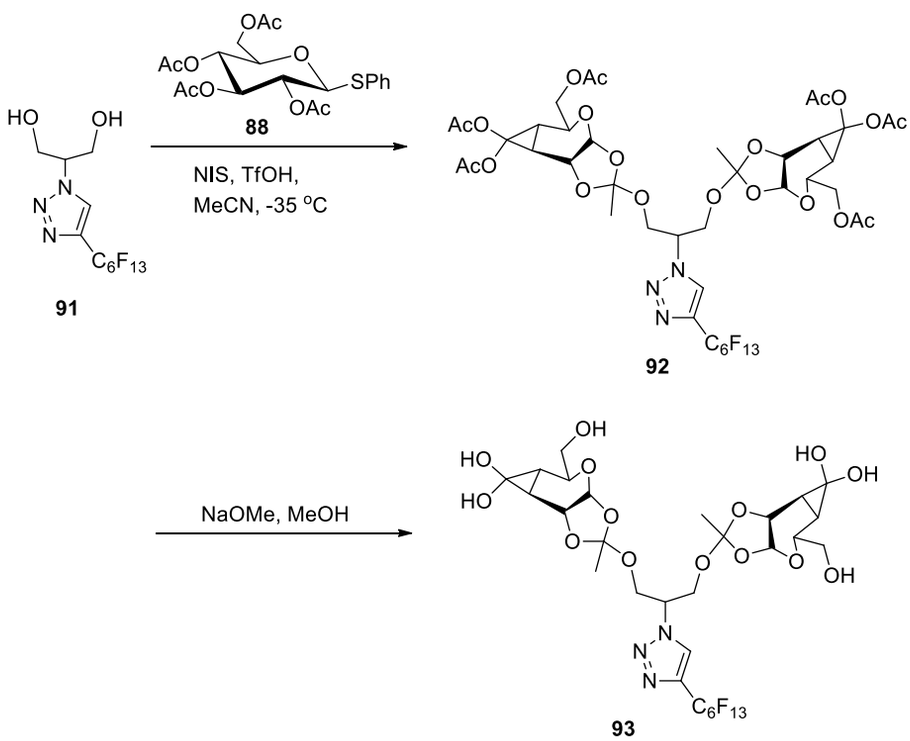
The synthesis of 3-*O*-(1,1,2,4,4,5,7,7,8,8,9,9,9-tridecafluoro-5-trifluoromethyl-3,6-dioxanon-1-yl)-D-glucopyranose **84** and 6-*O*-(1,1,2,4,4,5,7,7,8,8,9,9,9-tridecafluoro-5-trifluoromethyl-3,6-dioxanon-1-yl)-D-galactopyranose **86** from fluoroalkylatedglucofuranose **83** and fluoroalkylated-D-galactopyranose **85** respectively were also explored in the present protocol (**Scheme 24**). The treatment of compound 1,2:5,6-di-*O*-isopropylidene-D-glucofuranose **83** with butyl-lithium under nitrogen atmosphere and in dry THF condition gives intermediate product at room temperature. This intermediate on stirring with trifluoroacetic acid for 30 min. at room temperature afforded the product **84**. In similar way, the product **86** obtained from compound **85** (**Scheme 24**).[51]

Razgulin and co-workers synthesized the new surfactants containing two and three monosaccharide-based heads with a perfluoroalkyl tail.[52]The treatment of *N*-iodosuccinimide, triflic acid and thiophenol-2,3,4,6-tetra-*O*-acetyl-β-D-glucoside **88** with 2-(hydroxymethyl)-2-(4-(perfluorohexyl)-1*H*-1,2,3-triazol-1-yl)propane-1,3-diol **87** affords the tri-orthoglycosylated compound {1-[1,3-bis (3,4,6-tri-*O*-acetyl-D-glucopyranos-1,2-*O*-(1-ethyliden-1-yloxy)-2-((3,4,6-tri-*O*-acetyl-D-glucopyranos-1,2-*O*-(1-ethyliden-1-yloxy)methyl)propan-2-yl]-4-perfluorohexyl-1*H*-1,2,3-triazole} **89**. This tri-orthoglycosyl compound **89** gets deprotected under NaOMe/MeOH condition and affording product 1-[1,3-bis(D-glucopyranos-1,2-*O*-(1-ethyliden-1-yloxy)-2-((3,4,6-tri-*O*-acetyl-D-glucopyranos-1,2-*O*-(1-ethyliden-1-yloxy)methyl)propan-2-yl]-4-perfluorohexyl-1H-1,2,3-triazole **90** (**Scheme 25**).[52]



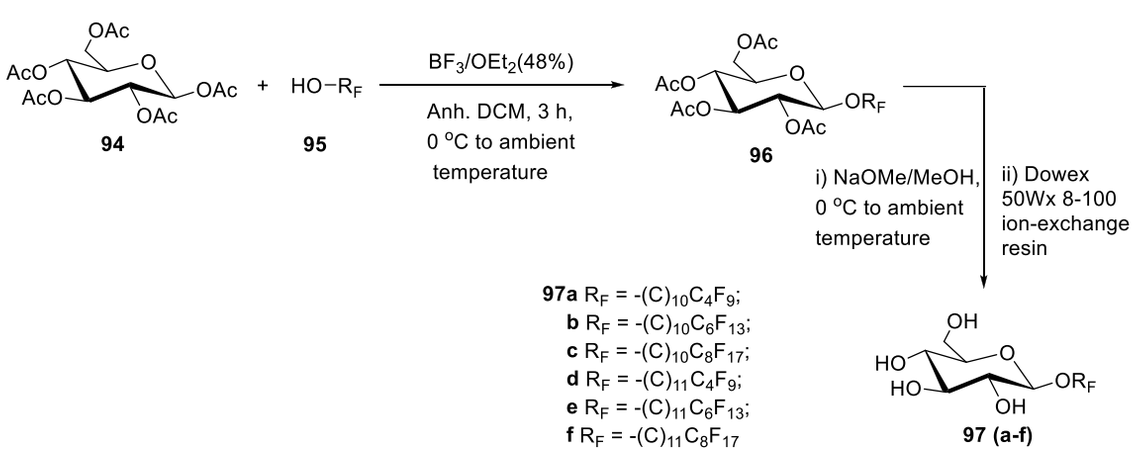
Scheme 25. Synthesis of three monosaccharide-based head and a perfluoroalkyl tail.

In similar approach, fluoroalkyl diol **91** fetch the product 1-(1,3-bis[D-glucopyranos-1,2-*O*-(1-ethyliden-1-yloxy)]propan-2-yl)-4-perfluorohexyl-1*H*-1,2,3-triazole **92** (**Scheme 26**) via sequential glycosylation followed by deprotection reaction like **Scheme 25**.[52]



Scheme 26. Synthesis of compound **93** containing two monosaccharide-based head and a perfluoroalkyl tail

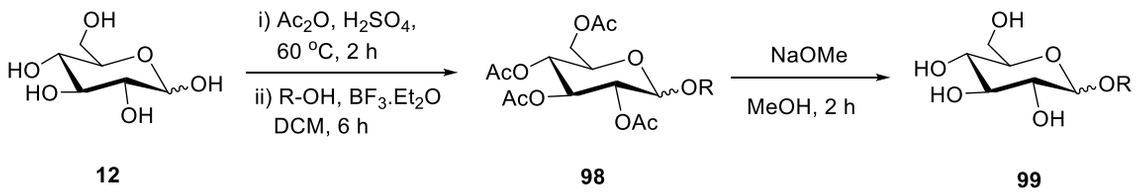
Li and co-workers reported the synthesis of new series of fluorinated glucopyranosides **97** (**a-f**) with 92 to 98% yield.[53] The treatment of fluorinated alcohol **95** with peracetylated-β-D-glucopyranose **94** in presence of Lewis acid BF_3/Et_2O or $ZnCl_2$ in anhydrous DCM at ambient temperature afford (fluoro)alkylated per-acetylated glucopyranoside **96** with 40-55% yield. Deacetylation of **96** using NaOMe in methanol and followed neutralization with Dowex 50W×8-100 ion exchange resin afford fluorinated glucopyranose **97** (**a-f**) (**Scheme 27**).



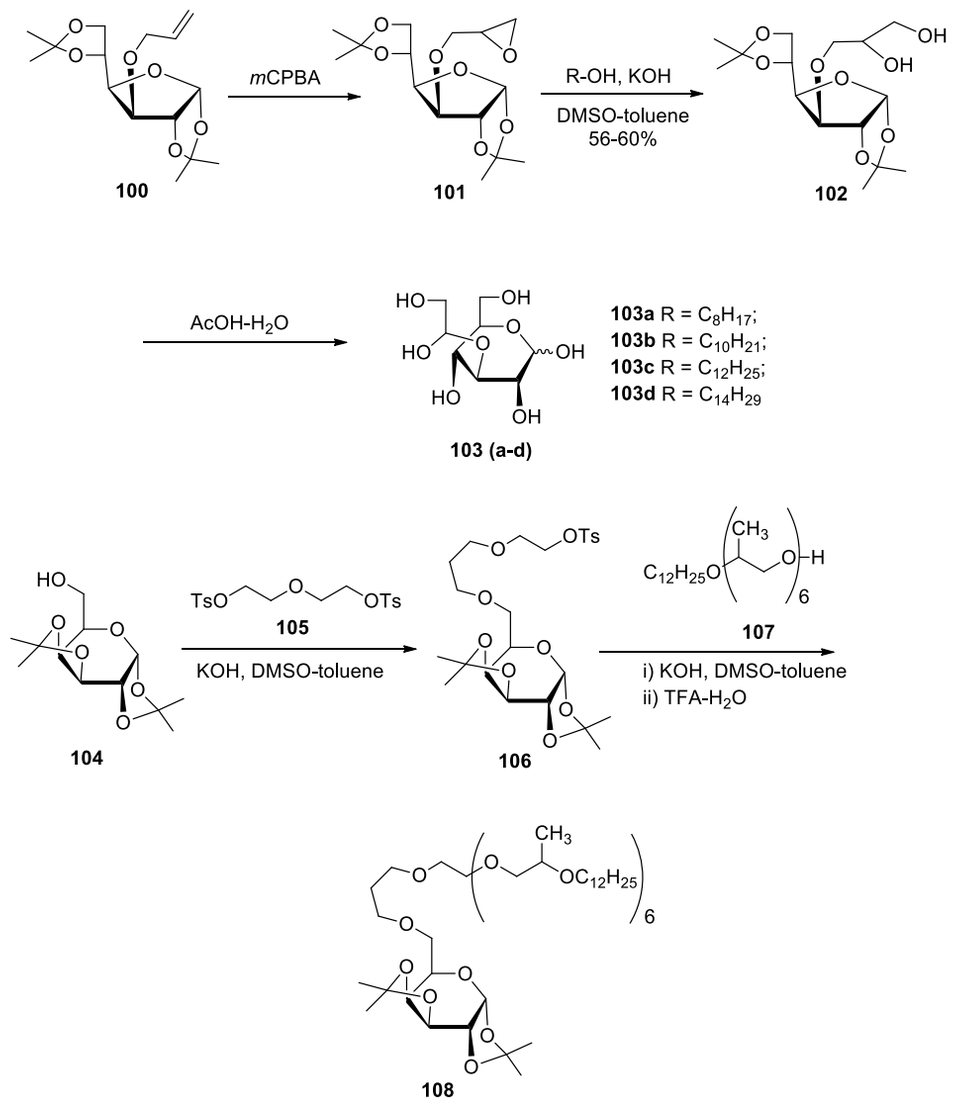
Scheme 27. Synthesis of perfluoroalkyl-β-D-glucopyranosides.

3.6 *O*-Alkyl glycosides

In 1893, Fischer first time reported the preparation of non-ionic alkyl glycoside surfactant β-hexadecyl-D-glycoside.[54]The first step involves protection of D-Glucose by using Ac_2O/H_2SO_4 which subsequently converted to peracetylated-β-D-glucopyranoside **98** with the help of Lewis acid BF_3/Et_2O in anhydrous DCM. The deprotection of **98** using NaOMe/MeOH leads to *O*-alkyl glucopyranoside **99** (**Scheme 28**).[55-57]



Scheme 28. Synthesis of *O*-alkyl glucopyranoside **99** via protection and deprotection method

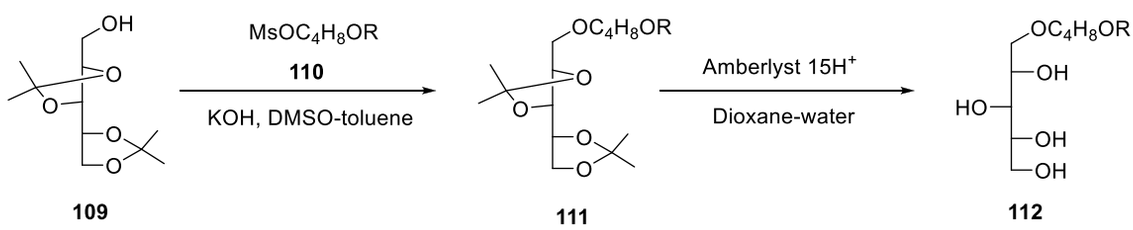


Scheme 29. Synthesis of glucidoamphiphile compounds from D-glucose and D-galactose

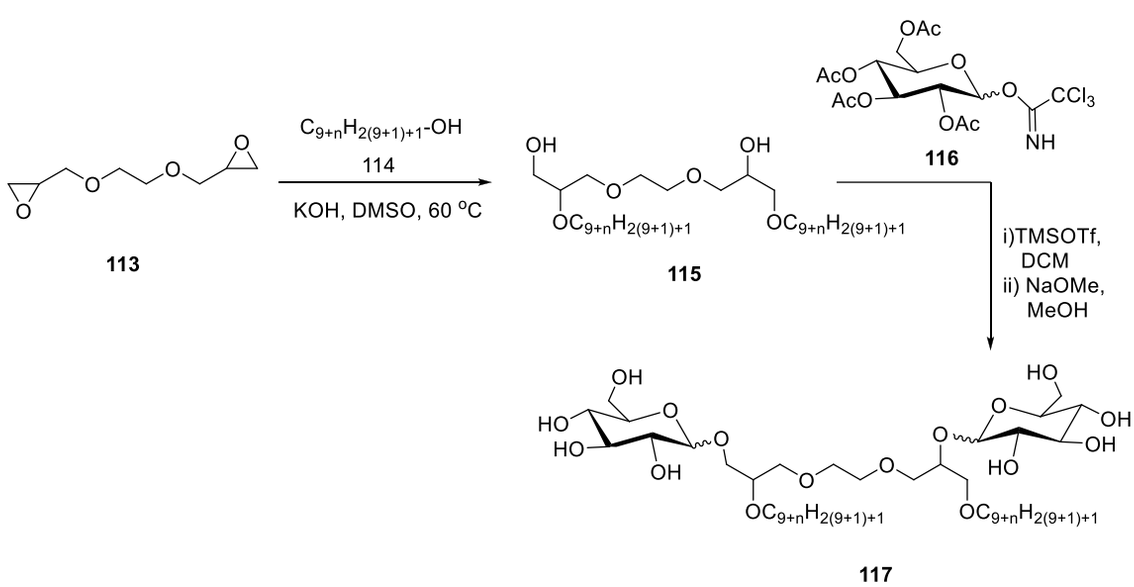
New glucidoamphiphile compound containing hydrophobic chain, glucidic moiety and spacer arm between them was reported by Goethals and co-worker.[58] To prepare these compounds, D-glucose, D-galactose and xylitol were used as starting materials. Epoxidation on allyl compound **100** affords the product **101** which on treatment with alcohol and KOH leads to the intermediate product **102**. Deprotectionof intermediate **102** with AcOH-H_2O gives derivatives **103** (**a-d**) (**Scheme 29)**. The protected D-galactose **104** on treatment with KOH and oxybis(ethane-2,1-diyl)bis(4-methylbenzenesulfonate) **105** in DMSO afford the intermediate **106**. The product 6-*O*-[2-*O*-n-dodecylpoly-(α-propyleneglycol)-diethylenglycol]-α-D-galactopyranose **108** obtained from intermediate **106** by condensation with 2-(dodecyloxy)propan-1-ol in presence of KOH base and DMSO-toluene solvent followed deprotection by trifluoroacetic acid in water (**Scheme 29**).

The third glucidoamphiphile compound (1-*O*-(4-*O*-Alkyl-butyleneglycol-1-yl)- D, L-xylitol) **112** was prepared from starting protected xylitol **109** (**Scheme 30**). In this compound **109**, xylitol moiety and alkyl chain are separated by butylene glycol spacer arm.The monoalkylatedbusulfan **110** on condensation with 2,3:4,5-di-*O*-isopropylidene-D,L-xylitol **109** in KOH base and DMSO-toluene solvent afford the intermediate **111** with 65% yield. The deprotection of intermediate **111** with Amberlyst resin $15H^+$ in dioxane-water gives product **112**.[58]

Liu and co-worker developed a novel, highly effective gemini alkyl *O*-glucosides **117** (**Scheme 31)**.[59] Regioselective ring opening of ethylene glycol epoxide by alkyl alcohols leads to the formation of gemini alkyl chain compound **115**. The compound (2*R*,3*R*,4*S*,5*R*)-2-(acetoxymethyl)-6-(2,2,2-trichloro-1-iminoethoxy)tetrahydro-2*H*-pyran-3,4,5-triyl triacetate **116** on glycosylation with gemini alkyl chain **115** under



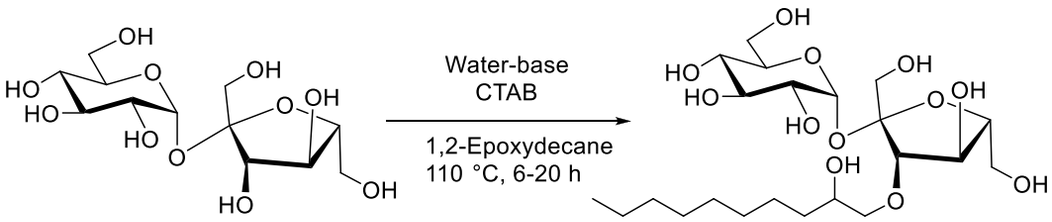
Scheme 30. Synthesis of 1-*O*-(4-*O*-Alkyl-butyleneglycol-1-yl)-D,L-xylitol from 2,3:4,5-di-*O*-isopropylidene-D,L-xylitol



Scheme 31. Synthesis of novel gemini alkyl *O*-glucoside surfactant **117**

TMSOTf and DCM afford the second intermediate which on deprotectionbyNaOMe/MeOH afford product gemini alkyl *O*-glucoside surfactant **117** (**Scheme 31**). Significantly better surface activity was shown by these new gemini alkyl *O*-glucosides than known results.[59]

Synthesis of amphiphilic sucrose hydroxyalkyl ether **119** from unprotected sugar **118** reported by Gagnaire and co-workers.[60] The sugar **118** on treatment with 1,2-epoxydecane in presence of cotyltrimethylammonium bromide (CTAB) as base and water afford amphiphilic sucrose hydroxyalkyl ether **119 (Scheme 32**).

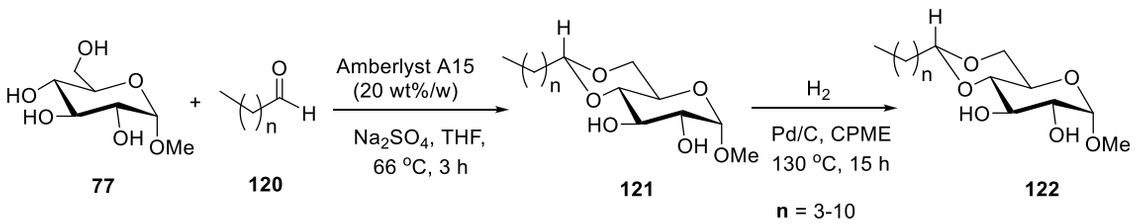


118 **119**

Scheme 32. Synthesis of amphiphilic hydroxyalkyl sucrose ether from unprotected sucrose

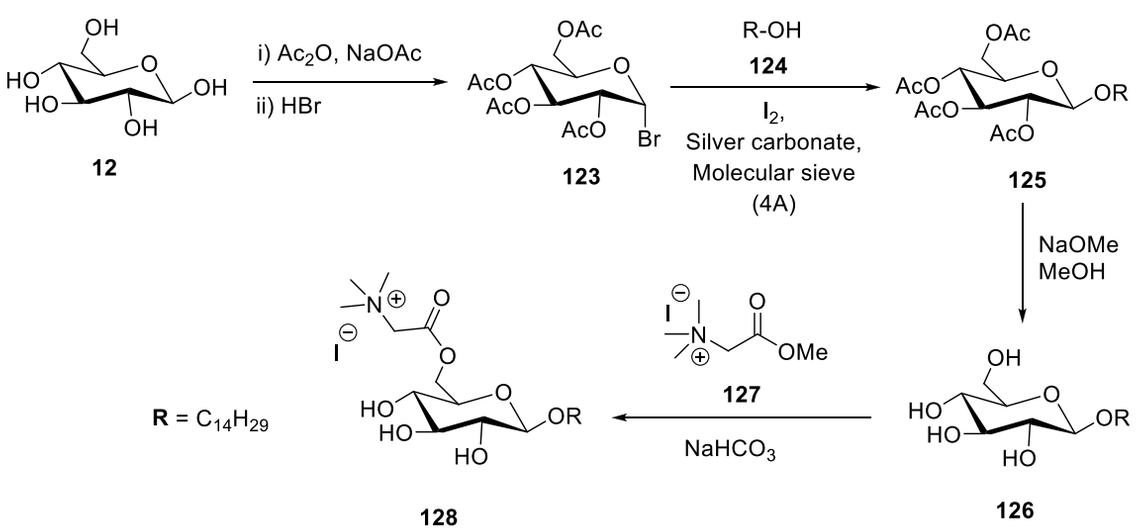
Belmessieri and co-workers developed a new series of methyl glycopyranoside ether **122** from methyl α-D-glucopyranoside **77**.[61] When methyl α-D-glucopyranoside **77**, aliphatic aldehyde **120** and Amberlyst A15 (20 wt%/w) were refluxed in dry THF under argon, an intermediate methyl pyranosideacetal **121** was obtained. The reductive cleavage of methyl pyranosideacetal **121** by using Pd/C in cyclopentyl methyl ether (CPME) afford the product methyl glycopyranoside ether **122** (**Scheme 33**).

In aqueous media, an ionic sugar-amino acid based surfactant (*N*,*N*,*N*-trimethyl-2-oxo-2-(((*2R*,*3S*,*4S*,*5R*)-3,4,5-trihydroxy-6-(tetradecyloxy)tetrahydro-2*H*-pyran-2-yl)methoxy)ethan-1-aminium iodide) **128** was synthesized by Esmaeilian and co-workers.[62] Koenigs-Knorr reaction used for the synthesis of 2,3,4,6-Tetra-



77 **120** **121** **122**

Scheme 33. Synthesis of methyl glycopyranoside ether from methyl α-D-glucopyranoside

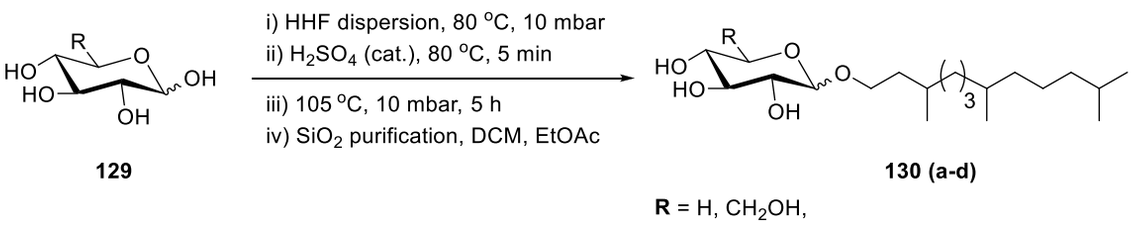


12 **123** **125** **126** **128**

Scheme 34. Synthesis of an ionic sugar-amino acid based surfactant

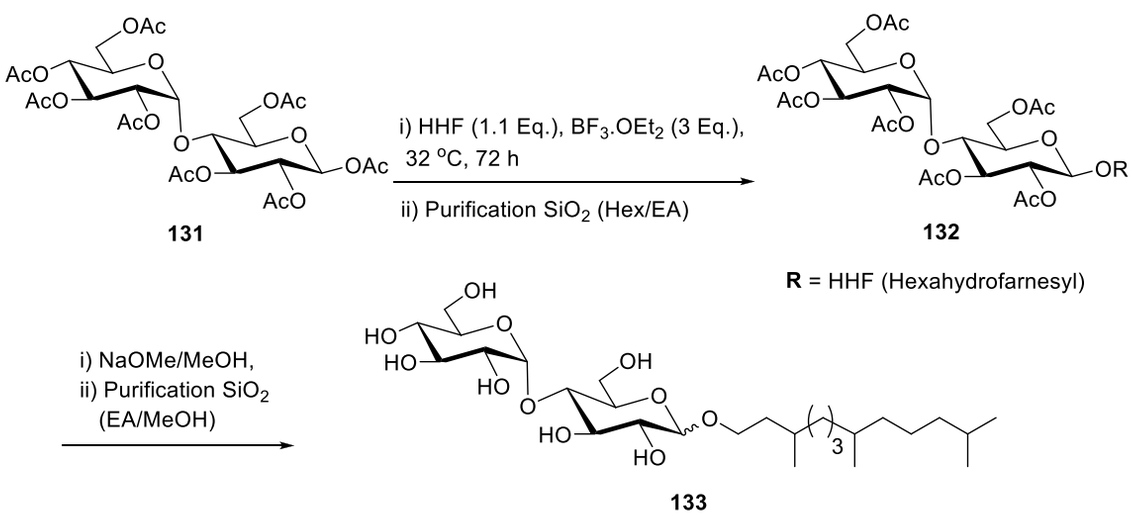
O-acetyl-alpha-D-glucopyranosyl bromide **123** from D-glucose[62] which involves protection by Ac_2O/NaOMe followed treatment with HBr. The treatment of tetradecanol **124** with **123** in presence of $I_2/AgCO_3$ (as catalyst), molecular sieves (water absorbent) and DCM solvent leads to intermediate **125**. Deprotection of **125** using NaOMe/MeOH afford the second intermediate **126**. Trans-esterification of compound **126** and 2-methoxy-*N*,*N*,*N*-trimethyl-2-oxoethan-1-aminium iodide **127** in DMF and catalytic $NaHCO_3$ afford the final product **128** (**Scheme 34**).[62]

Lemahieu and collaborator developed a new series of bio-based surfactants by coupling of hexahydrofarnesol with mono and disaccharides.[63] The commercial sugar**129** (such as arabinose, xylose, glucose and mannose) dispersed in excess of hexahydrofarnesol (HHF) with catalytic H_2SO_4 (2 mol%) at 105°C and 10 mbar vacuum led to the formation of products **130a-d** hexa-hydrofarnesyl mono glycosides (HHFA, HHFX, HHFG, and HHFMan) after purification with silica gel chromatography (**Scheme 35**).



Scheme 35. Synthesis of hexahydrofarnesyl mono glycosides (HHFA, HHFX, HHFG and HHFMan).

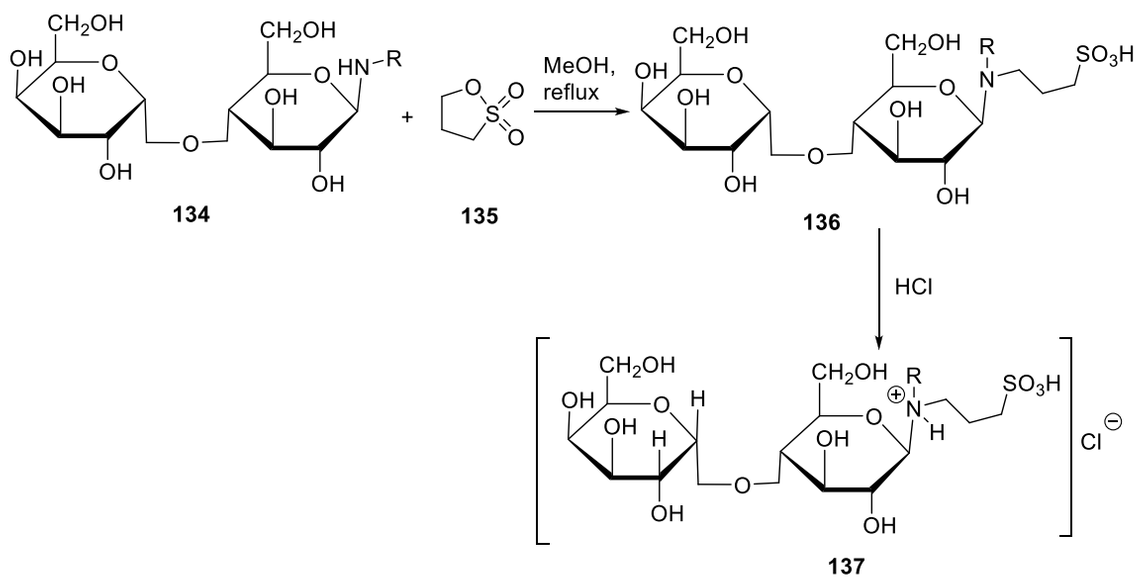
In this protocol, the synthesis of hexahydrofarnesylmaltosideHHFMalt**133** was also explored. The reagent $BF_3.OEt_2$ activates the anomeric position of peracetylated maltose **131** for glycosylation and gives intermediate **132** after purification with silica gel chromatography. The deprotection of **132** by NaOMe/MeOH following further purification with silica gel chromatography(elution with ethyl acetate and methanol) leads to the product hexahydrofarnesylmaltoside HHF Malt **133** (**Scheme 36**). The CMCs (Critical micellar concentration) and surface tensions values (by drop shape tensiometry) of synthesized surfactants was determined and summarised in **Table 3**. The results reveal that HHFMalt is the most hydrophilic surfactant in this series. The CMC values for branched C_{15}HHFMalt lies within the ones described for theC_{14} and C_{16}derivatives.[63]



Scheme 36. Synthesis of hexahydrofarnesylmaltosideHHFMalt **133**

Table 3. Summarised data for CMCs and corresponding surface tension for different hexahydrofarnesyl monoglycosides and diglycosides

		CMC		
Surfactant	**Polar head**	**mmol/L**	**ppm**	**υ_{CMC}, mN/m**
HHFA	Arabinose (C_5)	0.0037-0.0060	1.34-2.15	27.3
HHFX	Xylose (C_5)	0.0101-0.0304	3.65-10.98	28.6
HHFG	Glucose (C_6)	0.0092-0.0336	3.58-13.11	27.1
HHFMan	Mannose (C_6)	0.0041-0.0196	1.61-7.68	27.2
HHFMalt	Maltose (C_6-C_6)	0.0298	16.49	28.3



Scheme 37. Synthesis of lactose-based surfactants from *N*-alkyl-lactosylamines

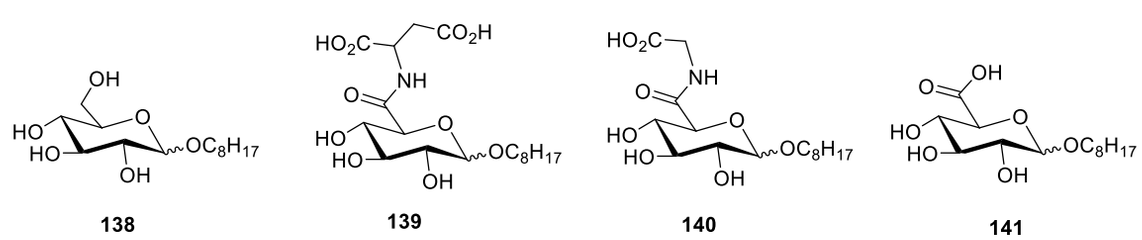


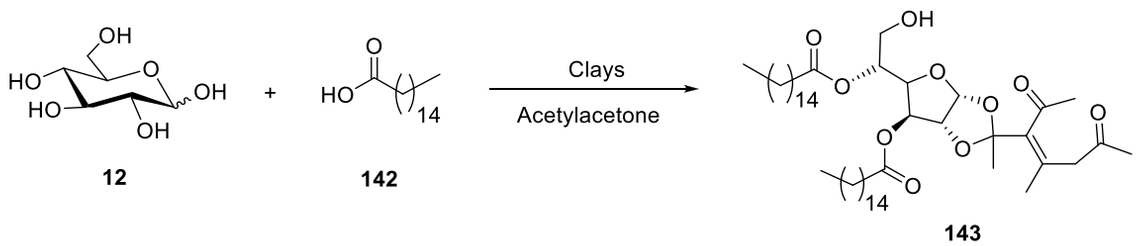
Fig. 1. Different octyl D-glucopyranoside-based surfactants

New lactose-based surfactant *O*-β-D-Galactopyranosyl-(1→4)-*N*-alkyl-(3-sulfopropyl)-D-glucosamine hydrochloride **137** synthesis was demonstrated by Michocka and co-workers.[64] By refluxing the *N*-alkyl-lactosylamine **134** with 1,3-propanesultone **135** in methanol afforded the intermediate **136** which was water insoluble. Hence, the aqueous suspension of **136** was treated with HCl which gave the final product **137** (**Scheme 37**). The evaluation of CMC result reveals that synthesized compound has low CMC values but significantly reduces the surface tension. These synthesized surfactants exhibit good wetting properties, excellent foaming ability as well as good durability of foam production.

Zdarta and co-workers performed the study on octyl D-glucopyranoside**138** and its derivatives [viz-*N*-(octylD-7-glucopyranosiduronyl)aspartic acid **139**, *N*-(octyl D-glucopyranosiduronyl)glycine **140** and octyl D-8-glucopyranosiduronic acid **141** for six different physicochemical properties with respect to natural environment (**Fig. 1**).[65] The study revealed that, octyl D-glucopyranosides were completely biodegradable by environmental microbial strains and exhibits efficient emulsifying property and effectively reduces the surface tension at surfactant/air interface at room temperature. As compared to surfactants synthesized from fossil raw resources, sugar-based surfactants were advantageous with respect to their renewable source and environment friendly nature.

3.7 Esters

Pappalardo and co-workers developed a new clay catalysed method for the synthesis of sugar-based ester surfactant **143** from D-glucose **12**.[66] The reaction between **12** and palmitic acid **142** at 100 °C gave the product (1*R*)-2-hydroxy-1-((3a*R*,6*S*,6a*R*)-2-methyl-2-((*E*)-4-methyl-2,6-dioxohept-3-en-3-yl)-6-(propionyloxy)tetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl)ethyl propionate **143** (**Scheme 38**).



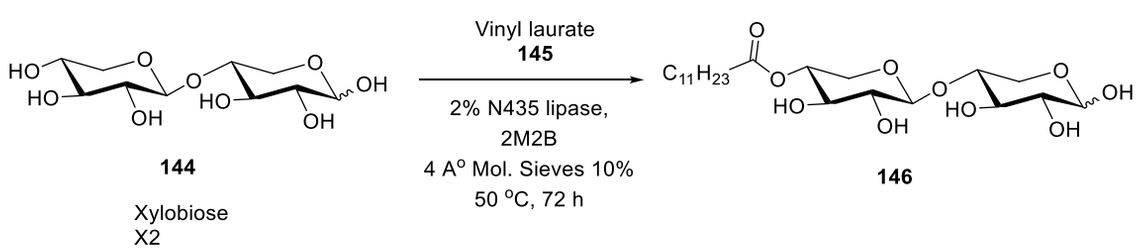
Scheme 38. Clay-catalysed synthesis of sugar-based ester surfactant **143**

The optimized reaction parameters are solvent, temperature and catalyst. Solvents such as toluene, cyclopentyl methyl ether and a biphasic mixture isododecane/water were found ineffective.It was observed that higher temperature (100 °C) provided better yield than lower temperature (80 °C). In addition, different clay catalysts like KSF, K10, K30 and Fe^{III}-K10 were tested for reaction optimization and the results of palmitic acid conversion with respect to catalyst summarised in **Table 4**. Among tested catalyst, montmorillonites exhibited significant palmitic acid conversion (43% at 100 °C). Fe^{III}-K10 montmorillonite is a reusable and environmentally benign catalyst, it makes more interest in this synthetic method.[66]

New xylo-oligosaccharide laurate ester surfactant **146** was synthesized by Gérard and co-workers *via* enzyme catalysed reaction (**Scheme 39**).[67]The reaction between xylobiose**144** and vinyl laurate **145** in the presence of 2-methylbutan-2-ol (2M2B), commercially available 2% polymer-supported lipase N435 (Novozymes) and 10% 4A° molecular sieves at 50°C produced the product **146** within 72 h.

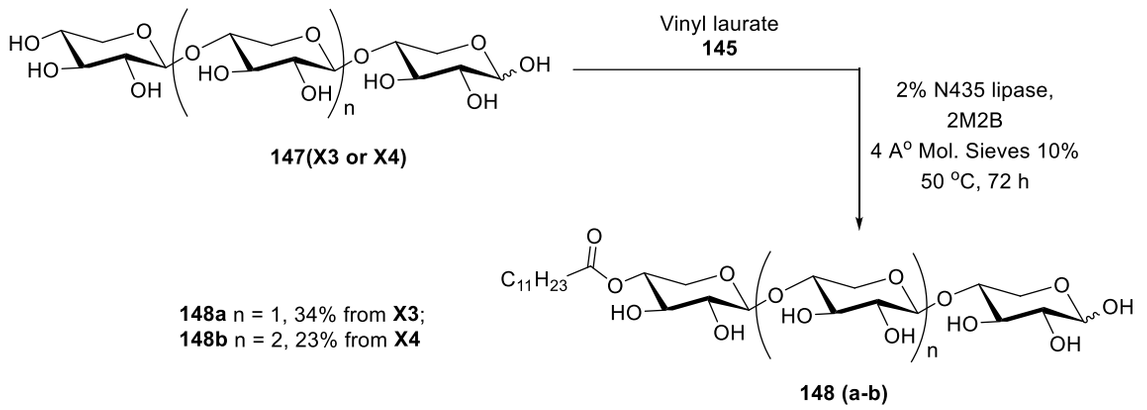
Table 4. Esterification of palmitic acid with d-glucose in the presence of different clays.

	Conversion%	
Catalyst	**80 °C**	**100 °C**
KSF	20	23
K10	22	32
K30	22	37
Fe^{III}-K10	trace	43



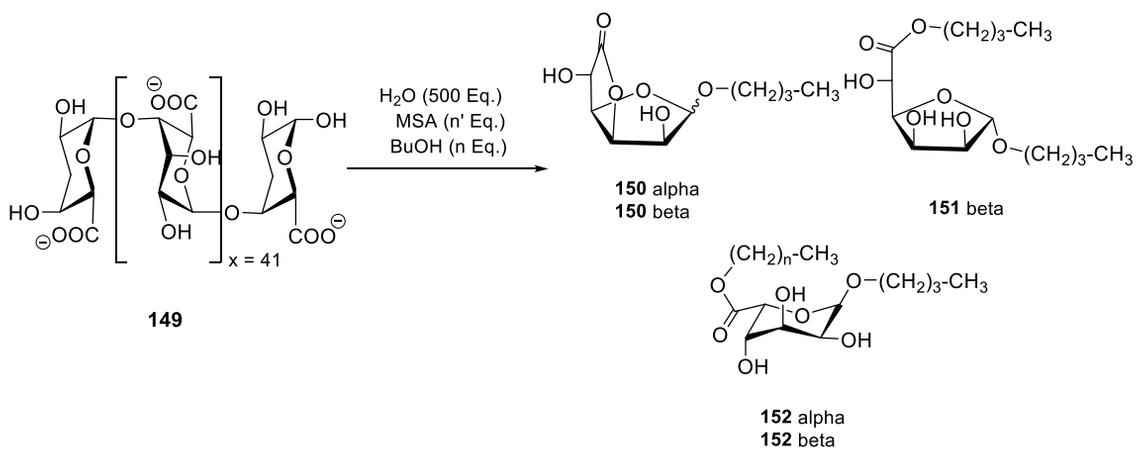
Scheme 39. Enzyme-catalysed synthesis of xylo-oligosaccharide laurate ester surfactant

In the same protocol, similar method wasused to synthesize 4''-*O*-laurylxylotriose **148a** and 4'''-*O*-laurylxylotetraose **148b**from xylotriose**147(X3)** and xylotetraose**147(X4)** respectively (**Scheme 40**).[67]



Scheme 40. Enzyme-catalysed synthesis of 4''-*O*-laurylxylotriose and 4'''-*O*-laurylxylotetraose

Sari-Chmayssem and co-workers reported the synthesis of alkyl-L-guluronamide-based surfactant **152** from polyguluronates and alginates.[68]The treatment of butanol (as nucleophilic solvent) with sodium polyguluronate **149** in presence of MSA (methane sulfonic acid) and water afforded three *n*-butyl L-guluronate monosaccharide derivatives which areanomeric mixtures viz- *n*-butyl α,β-L-gulofuranosidurono-6,3-lactone (**150** α,β), (*n*-butyl) *n*-butyl β-L-gulofuranosiduronate(**151**β) and (*n*-butyl) *n*-butyl α,β-L-gulopyranosiduronate (**152**α,β) (**Scheme 41**).

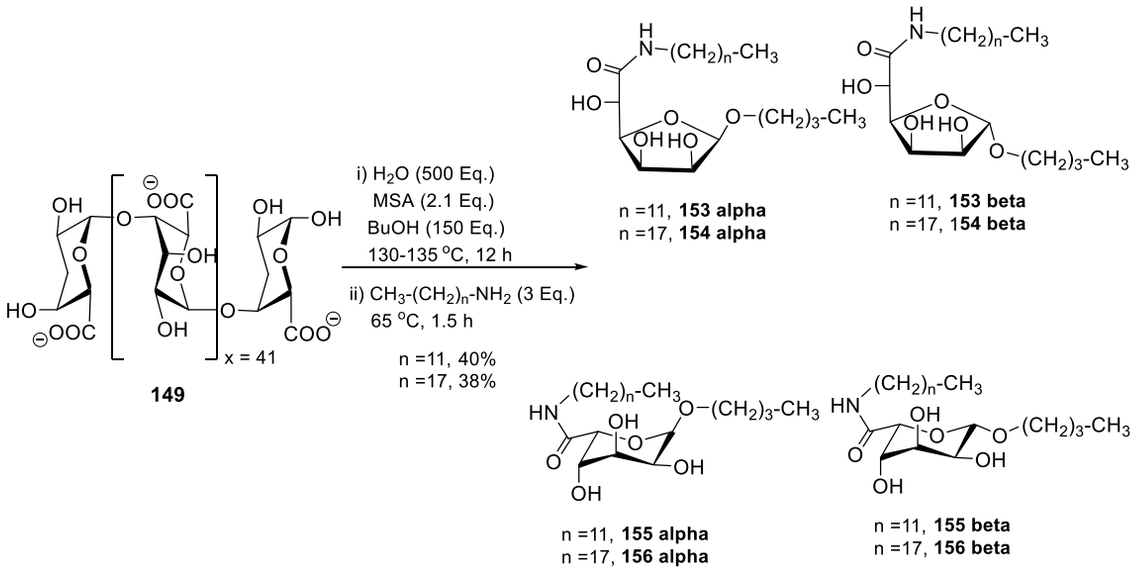


Scheme 41. Synthesis of *n*-butyl L-guluronate monosaccharide surfactant from L-polyguluronate

Further, the reaction mixture containing n-butyl L-guluronate monosaccharide **150-152** was subjected directly to excess of dodecyl or octadecyl amine (fatty amines) for the aminolysis reaction. The amine shows nucleophilic addition and also neutralizes the MSA. The reaction completed at 65 °C using 6 mbar pressure resulted in the products *N*-(*n*-alkyl)-*n*-butyl α,β-L-gulofuranosiduronamides (**153** α,β or **154** α,β) and *N*-(*n*-alkyl)-*n*-butyl α,β-L-gulopyrano-siduronamides (**155** α,β or **156** α,β) after purification by column chromatography (**Scheme 42**).[68]

Using similar strategy, six isomeric forms including two α,β-furanose forms (**153** α,β or **154** α,β) and two α,β-pyranose forms (**155** α,β or **156** α,β) for *N*-(*n*-alkyl)-*n*-butyl L-guluronamides; one α-furanose form **158** α or **159** α and its α-pyranose isomer **160**α or **161** α for *N*-(*n*-alkyl)-*n*-butyl D-mannuronamide synthesized from alginate **157** (**Scheme 43**).[68]

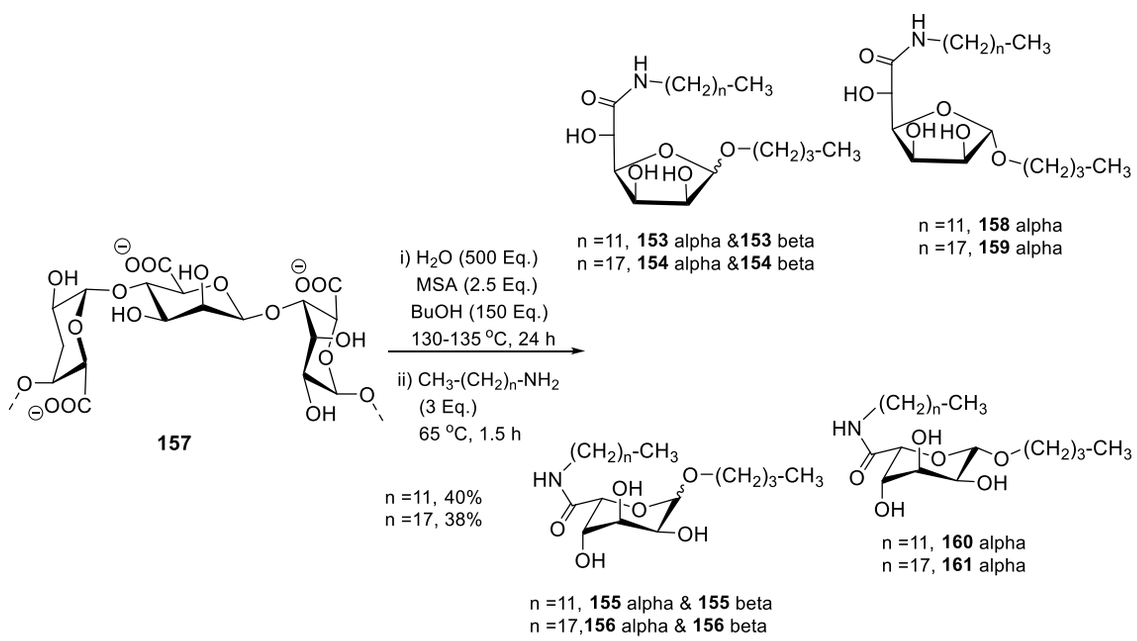
Enzyme Novozym 435 catalysed synthesis of 1-*O*-lauryl-D-mannitol **164** reported by Pinna and co-



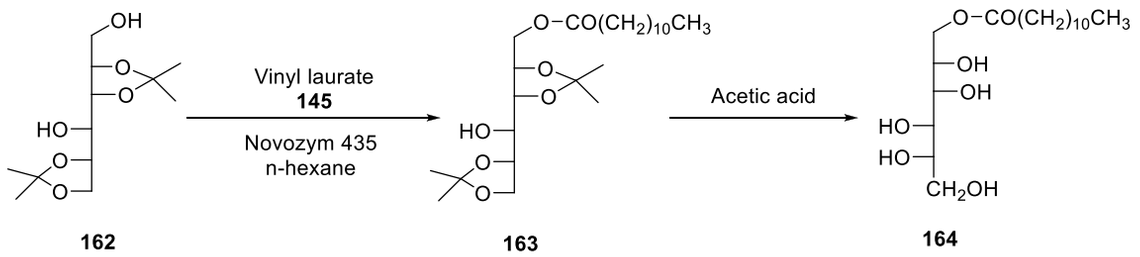
Scheme 42. Synthesis of *N*-(*n*-alkyl)-*n*-butyl α,β-L-gulofuranosiduronamides and *N*-(*n*-alkyl)-*n*-butyl α,β-L-gulofuranosiduronamides.

workers.[69]The compound 1,2:4,5-di-*O*-isopropylidene-D-mannitol **162**on treatment with vinyl laurate**145** using catalytic amount of immobilized *Candidaantarctica* lipase B (Novozym 435) produced the intermediate **163** which on deprotection by acetic acid led to the final product **164** (**Scheme 44**).

Drummond and co-workers developed a new protocol for the synthesis of sucrose and glucose-based surfactants.[70] In the first series, the reaction between lactose **59** and acyl chloride **165** in the presence of 1-

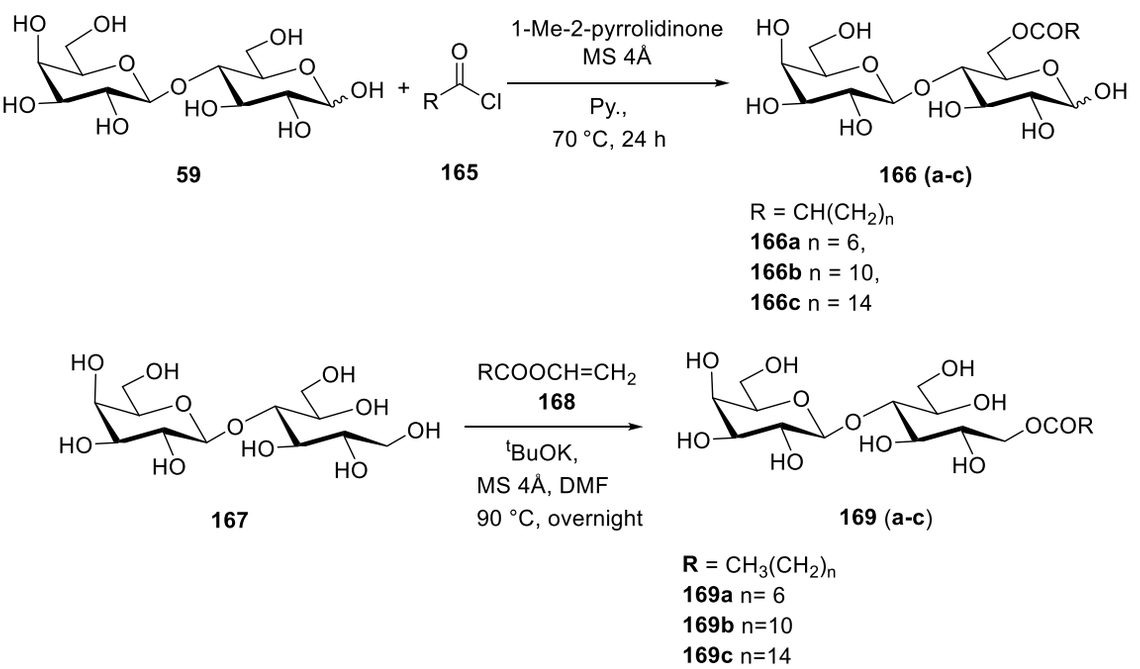


Scheme 43. Synthesis of L-guluronamide and D-mannuronamide surfactants from alginate



Scheme 44. Synthesis of 1-*O*-lauryl-D-mannitol surfactant

Me-2-pyrrolidinone and 4A°molecular sieve at 70 °C afforded the sucrose-based surfactants **166a-c**. Next, treatment of vinyl ester **168** with lactitol **167** using ^{t}BuOK as base and 4A° molecular sieves at 90 °C afforded the fatty acid mono-esters of lactitol **169a-c** in good to excellent yield (**Scheme 45**).



Scheme 45. Synthesis of fatty acid mono-esters of lactose **59** and lactitol**167**.

4. Conclusions and Future Perspectives

Carbohydrate based surfactant (CBS) brings an inclination towards sustainable cleaning agents owing to their surface active nature and numerous advantages. Ongoing research on harnessing the low-cost wastes as starting material promises the enormous potential of CBS. However, there is always a demand for further research to develop novel production processes with significant yield synchronous with the overall production cost. Use of cheap agricultural crops, wastes etc adds extra value towards safer, cleaner and greener processes to architect economically viable CBS. Apart from economic viewpoint, sustainability is another dominant parameter that provides impetus to CBS production over conventional surfactants. Application of green chemistry approaches is the need of the hour while designing novel methods to enhance the quality and yield of the product; and minimizing the cost of production with cheaper and renewable resources. Wastes from food processing, animal fats, and dairy industrial sectors have tremendous scope in biosurfactant production. The focus should be on development of production-consumption-disposal

stages and their impacts such as carbon footprint, toxicity, and resource depletion. Nevertheless, the versatility of carbohydrate moiety cannot be underestimated, and research must emphasise on developing appropriate processes,separation and purification of products to avail the complete benefits of carbohydrate chemistry. The success of CBS will also depend on the development of suitable polar solvents and specific catalysts for the effective conversion to obtain the desire products. The polyfunctional bio-surfactants with surface active properties are sufficient enough to capture the attention and can replace their synthetic counterpart that will offer sustainable future to research and innovation.

Authors Biographies

Raju R. Kale, born in Maharashtra, India in 1981. He completed MSc (Organic Chemistry) in 2004 at Department of Chemistry, Savitribai Phule Pune University, then completed his Ph.D. on "Synthesis of Carbohydrate based biologically important molecules" at Department of Chemistry, Banaras Hindu University, Varanasi, India (Mentor: Prof. Vinod K. Tiwari) in 2011. He worked as Post-doctoral fellow on 'Design and synthesis of carbohydrate based vaccines for Cancer and HIV therapy' (Mentor: Prof. C. Y. Wu) at Genomics Research Centre, Academia Sinica, Taiwan. After this, worked as Institute Post-doctoral fellow on "Synthesis and applications of novel nucleosides and MBH-adducts" at Indian Institute of Technology Bombay, Powai, Mumbai (Mentor: Prof. I. N. N. Namboothiri). Presently, he is working as Assistant professor at Department of Chemistry, KTHM College, Nashik, Affiliated to SavitribaiPhule Pune University, Pune. Dr. Kale has published several peer-reviewed research papers/book chapters in high repute journals and in addition filed four patents. His current research involves the synthesis of carbohydrate hybrid molecules, green chemistry/ catalyst based new synthetic methodologies for medicinally important molecules and medicinal chemistry. Currently, three Ph.D. students are working in his group.

Nitin Jadhav was born in Maharashtra (India) in 1986. He received his B.Sc. Chemistry in 2007 and M.Sc. Organic Chemistry in 2009 from SavitribaiPhule Pune University, Pune. At present, he is pursuing a Ph.D. under the supervision of Dr. V. B. Gaikwad and Dr. Raju R. Kale at Department of Chemistry, K. R. T. Arts, B. H. Commerce and A. M. Science (K. T. H. M.) College, Nashik affiliated to SavitribaiPhule Pune University, Pune, India. His research interest focuses on synthesis of biologically active coumarin-pyrazole derivatives.

Sanchayita Rajkhowa, is currently working as Assistant Professor (Department of Chemistry, Jorhat Institute of Science & Technology, Jorhat, Assam, India). She has graduated from Miranda House, DU and earned her master degree from University of Delhi and then doctorate degree from North Eastern Hill University (NEHU), Shillong, India in the year 2017. Her research is focused on surface chemistry, surfactants, carbohydrate chemistry, ionic liquids and their impact on drug discovery and development. Dr. Rajkhowa has published several research papers in journals of both international and national repute. She has been awarded Young Scientist Award by CONIAPS XXIV on Innovations in Physical Sciences in the year2019. She has also authored several book chapters on chemistry, environment and ecology with international publishers. Her latest edited book is on "MANAGEMENT OF CONTAMINANTS OF EMERGING CONCERN (CEC) IN ENVIRONMENT" with Elsevier.

Bhausaheb B. Muntode was born in Maharashtra (India) in 1989. He received his B.Sc. Chemistry in 2010 and M.Sc. Organic Chemistry in 2013 from SavitribaiPhule Pune University, Pune.At present, he is pursuing a Ph.D. under the supervision of Dr.Raju R. Kale and Dr. V. B. Gaikwad at Department of Chemistry, K. R. T. Arts, B. H. Commerce and A. M. Science (K. T. H. M.) College, Nashik affiliated to SavitribaiPhule Pune University, Pune, India. His research interest includes Multi component reactions, organic synthesis, green chemistry and catalysis.

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JyotirmoySarma received the M.Sc. degree in Chemistry from the department of Chemistry, Gauhati University, India, in 2007 and a Ph.D. degree in Chemistry jointly from CSIR- NEIST, Jorhat and Gauhati University, India, in 2014. He currently works as assistant professor at the Department of Chemistry, The Assam Kaziranga University, Jorhat, Assam, India. His current research interests include the area of adsorption of surfactants, surface chemistry, waste management and energy sector.

Acknowledgements

The author thanks Council of Scientific and Industrial Research (CSIR), New Delhi for the funding. The authors are also thankful to Prof. Vinod. K. Tiwari, Department of Chemistry, Banaras Hindu University, Varanasi, India for valuable suggestions and encouragement and Principal, KTHM College, Nashik for the providing necessary infrastructure and valuable support. *JS* expresses his gratitude to Kajiranga University, Jorhat for the support.

Conflict of Interest

The authors declare no conflict of interest.

References

1. (a) Rudd, P. M.; Elliott, T.; Cresswell, P.; Wilson, I. A.; Dwek, R. A. Glycosylation and the immune system. *Science.* **2001**, *291*, 2370-2376; (b) Bertozzi, C. R.; Kiessling, L. L. Chemical glycobiology. *Science,* **2001**, *291*, 2357-2364.
2. Tiwari, V. K. (*ed*.). Carbohydrates in Drug Discovery and Development, *Elsevier Publication*, **2020**. ISBN: 9780128166758.
3. (a) Tiwari, V. K.; Mishra, B. B.; Mishra, K. B.; Mishra, N.; Singh, A. S.; Chen, X. Cu(I)-Catalyzed Click Reaction in Carbohydrate Chemistry. *Chem. Rev*., **2016**, *116*, 3086-3240; (b) Agrahari, A. K.; Bose, P.; Jaiswal, M. K.; Rajkhowa, S.; Singh, A. S.; Hotha, S.; Mishra, N.; Tiwari, V. K. Cu(I)-Catalyzed Click Reaction in Carbohydrate Chemistry. *Chem. Rev*., **2021**, *121*, DOI: https://doi.org/10.1021/acs.chemrev.0c00920
4. Dembitsky V. M. Chemistry and Biodiversity of the Biologically Active Natural Glycosides. *Chem. Biodivers.* **2004**, *1*, 673-781.
5. Queneau, Y.; Jarosz, S.; Lewandowski, B.; Fitremann, J. Sucrose Chemistry and Applications of Sucrochemicals. *Adv. Carbohydr. Chem. Biochem*.**2008**, *61*, 217-292.
6. Sorrenti, A.; Illa, O.; Ortuño, R. M. Amphiphiles in aqueous solution: well beyond a soap bubble.*Chem. Soc. Rev*. **2013**, *42*, 8200–8219.
7. Chortyk, O.T.; Kays, S.J.; Teng, Q. J. Characterization of Insecticidal Sugar Esters of *Petunia. Agric. Food Chem*.. **1997**, *45*, 270-275.
8. Arendale, R. F.; Severson, R. F.; Sisson, V. A.; Costello, C. E.; Leary, J. A.; Himmelsbach, D. S.; van Halbeck, J. Characterization of the sucrose ester fraction from Nicotianaglutinosa. *J. Agric. Food Chem.* **1990**, *38*, 75–85.
9. Steber, J.; Guhl, W.; Stelter, N.; Schroeder, F. R. Alkyl polyglycocides-ecological evaluation of new generation of nonionic surfactants. *TensideSurfact. Deterg*., **1995**, *32*, 512-515.
10. Warwel, S.; Bruse, F.; Demes, C.; Kunz, M.; Klass, M. Polymers and surfactants on the basis of renewable resources. *Chemosphere,* **2001**, *43*, 39-48.
11. Chester, A. Nomenclature of glycolipides. *Pure and Applied Chemistry*, **1997**, *69*, 2475-2487.
12. Uchegbu, I. F.; Vyas, S. P. Erratum to "Non-ionic surfactant-based vesicles (niosomes) in drug delivery". *Int. J. Pharm*.**1998**, *172*, 33-70.
13. Baroon, C.; Thompson, T. E. Solubilization of bacterial membrane proteins using alkyl glucosides and dioctanoyl phosphatidylcholine. *Biochem. Biophys. Acta*., **1975**, *382*, 276-285.
14. Plusquellec, D.; Chevalier, G.; Talibart R., Wroblewski, H. Synthesis and characterization of 6-*O*-(*N*-heptylcarbamoyl)-methyl-α-D-glucopyranoside, a new surfactant for membrane studies.*Anal. Biochem*. **1989**, *179*, 145-153.
15. Varki, A. Biological roles of oligosaccharides: all of the theories are correct. *Glycobiology*. **1993**, *3*, 97-130.
16. Besson, M.; Gallezot, P.; Pinel, C. Conversion of biomass into chemicals over metal catalysts. *Chem. Rev*., **2014**, *114*, 1827–1870.

17. Corma, A.; Iborra, S.; Velty, A. Chemical routes for the transformation of biomass into chemicals. *Chem. Rev*., **2007**, *107*, 2411–2502.
18. Queneau, Y.; Jarosz, S.; Lewandowski, B.; Fitremann, J. Sucrose chemistry and applications of sucrochemicals. *Adv. Carbohydr. ChemBiochem,***2007**, *61*, 217-292.
19. (a) Hosamani, B.; Kale, R. R.; Wachtel, E.; Kesselman, E.; Danino, D.; Friedman, N.; Sheves, M.; Nambothiri, I. N. N.; Patchornik, G. Membrane protein crystallization in micelles conjugated by nucleoside base-pairing: A different concept. *J. Struct. Bio.,* **2016**, *3*, 379-386.; (b) Dhandapani, G.; Nair, D. K.; Kale, R. R.; Wachtel, E.; Nambothiri, I. N. N.; Patchornik, G. Role of amphiphilic [metal:chelator] complexes in a non-chromatographic antibody purification platform. *J. Chromat. B*., **2019**, *1133*, 121830.; (c) Jadhav, N. K.; Kale, B. R.;Alam, M. S.; Gaikwad, V. B.; Prasad, V.; Kale, R. R. Synthesis and Functionalization of Coumarin-Pyrazole Scaffold: Recent Development, Challenges and Opportunities. *Curr. Org. Syn.,* **2021**, *18*, https://doi.org/10.2174/1570179418666210301122322
20. Holmberg, K. Natural surfactants. *Curr. Opin. Colloid Interface Sci*. **2001**, *6*, 148-159.
21. Jessop, P. G.;Ahmadpour, F.;Buczynski, M. A.; Burns, T. J.; Green, N. B.; Korwin, R.; Long, D.;Massad, S. K.; Manley, J. B.;Omidbakhsh, N.; Pearl, R.; Pereira, S.;Predale, R. A.;Sliva, P. G.; Van der Bilt, H.; Weller, S.; Wolf, M. H. Opportunities for greener alternatives in chemical formulations. *Green Chem*., **2015**, *17*, 2664–2678.
22. Almeida, M. V. D.;Hyaric, M. L. Carbohydrate derived surfactants. *Mini-Rev. Org. Chem*. **2005**, *2*, 283–297.
23. Besson, M.;Gallezot, P.;Pinel, C. Conversion of biomass into chemicals over metal catalysts. *Chem. Rev*. **2014**, *114*, 1827–1870.
24. Corma, A.; Iborra, S.; Velty, A. Chemical routes for the transformation of biomass into chemicals. *Chem. Rev*. **2007**, *107*, 2411–2502.
25. Wang, R.; Wan-Yan, R.; Yang, S.; Wang, D.; Yin, Z. Synthesis and Aggregation of Novel Sugar-Based Gemini Surfactant with a *N*, *N*'-Acetylethylenediamine Spacer in Aqueous Solution. *J. Surfact. Deterg*. **2020**, *23*, 697-703.
26. Carpenter, C. A.; Kenarb, J. A.; Price, N. P. J. Preparation of saturated and unsaturated fatty acid hydrazides and long chain *C*-glycoside ketohydrazones. *Green Chem*., **2010**, *12*, 2012–2018.
27. Xavier, N. M.; Rauter, A. P.; Queneau, Y. Carbohydrate-Based Lactones: Synthesis and Applications. *Top Curr. Chem*.**2010**, *295*, 19-62.
28. Augé, J.; Lubin-Germain, N. Glycosylhydrazides, a new class of sugar surfactant. Preparation and amphiphilic properties of 1-Glycosyl-2-acylhydrazines. *J. Carbohydr. Chem.,* **2008**, *19*, 379-392.
29. Goff, R. D.; Thorson, J. S. Assessment of ChemoselectiveNeoglycosylation Methods Using Chlorambucil as a Model. *J. Med. Chem*. **2010**, *53*, 8129–8139.
30. Neto, V.; Voisin, A.; Heroguez, V.; Grelier, S.; Coma, V. Influence of the Variation of the Alkyl Chain Length of *N*-Alkyl β-D-glycosylamine Derivatives on Antifungal Properties. *J. Agric. Food Chem*. **2012**, *60*, 10516-10522.
31. Lockhoff, O.; Stadler, P. Syntheses of glycosylamides as glycolipid analogs. *Carbohydr. Res.,* **1998**, *314*, 13-24.
32. El-Ghoul, M.; Latge, P.; Rico, I.; Lattes, A.; Godefroy, L. *N*-alkyl, n-acetylglycosylamines. **1996**, *US Patent 5539091A*.
33. Lubineau, A.; Augé, J.; Drouillat, B. Improved synthesis of glycosylamines and a straightforward preparation of *N*-acylglycosylamines as carbohydrate-based detergents. *Carbohydr. Res.,* **1995**, *266*, 211-219.
34. Bogaert, P. M. P.; Langezaal, W. P. C.;Haveren, J. V.; Slaghek, T. M.; Meeren, P. van der. Non-reductive coupling of branched amino fatty acid esters with mono and disaccharides: synthesis of a new class of alkyl glycosylamines. *Fett/Lipid*. **1999**, *101*, 64-70.
35. Lingome, C. E.; Pourceau, G.; Gobert-Deveauxb, V.; Wadouachi, A. Efficient synthesis of glycosylamines in solventless conditions promoted by mechanical milling. *RSC Adv*., **2014**, *4*, 36350-36356.
36. Liberek, B.; Melcer, A.; Osuch, A.; Wakiec´, R.; Milewskib, S.; Wisniewski, A. *N*-Alkyl derivatives of 2-amino-2-deoxy-D-glucose. *Carbohydr. Res.,* **2005**, *340*, 1876-1884.
37. Humphrey, A. J.; Fremann, C.; Critchley, P.; Malykh, Y.; Schauerc, R.; Bugg, T. D. H. Biological Properties of *N*-Acyl and *N*-HaloacetylNeuraminic Acids: Processing by Enzymes of Sialic Acid Metabolism, and Interaction with Influenza Virus. *Bioorg. Med. Chem.,* **2002**, *10*, 3175-3185.
38. Inouye, Y.; Onodera, K.; Kitaoka, S.; Hirano, S. Some Fatty Acid Derivatives of D-Glucosamine. *J. Am. Chem. Soc.,* **1956**, *78*, 4722–4724.
39. Riess, J. G.; Greiner, J. G. Carbohydrate and related polyol-derived fluorosurfactants: an update. *Carbohydr. Res*., **2000**, *327*, 147-168.
40. Zarif, L.; Riess, J. G.; Pucci, B.; Guedj, C.; Pavia, A. A. Double-tailed perfluoroalkylated glycolipids as components for drug delivery and targeting systems. Preliminary biocampatibilty results. *Art. Cells, Blood Subst.Immob. Biotech*., **1994**, *22*, 1485.
41. El-Ghoul, M.; Escoula, B.; Rico, I.; Lattes, A. Synthesis of new fluorinated non-ionic surfactants derived from lactose: the *N*-[*Z*-(F-alkyl)ethyl]-lactosylamines and lactobionamides. *J. Fluorine Chem*., **1992**, *59*, 107-112.
42. Rico-Lattes, I.; Lattes, A. Synthesis of new sugar-based surfactants having biological applications: key role of their self-association. *Colloids Surf. A: Physicochem. Eng. Aspects*., **1997**, *123*, 37-48.
43. Rico-Lattes, I.; Guidetti, B.; Lattes, A. Molecular organized systems with fluorinated compounds: from synthesis to biological applications. *J. Fluorine Chem*., **2001**, *107*, 355-361.
44. Riess, J. G.; Greiner, J. *Carbohydrates as Organic Raw Materials*, G. Descotes (Ed.), VCH, Weimheim, **1993**, 209.
45. Trabelsi, M.; Jouani, M. A.; Szonyi, F.; Cambon, A. Synthèse de glycosides et de nucléosides *F*-alkylés. *J. Fluorine Chem*., **1992**, *56*, 105-107.
46. Lubineau, A.; Augé, J.; Drouillat, B. Improved synthesis of glycosylamines and a straightforward preparation of *N*-acylglycosylamines as carbohydrate-based detergents. *Carbohydr. Res*., **1995**, *266*, 211-219.
47. Hein, M.; Mietchen, R. A new group of liquid crystals based on perfluoroalkylated carbohydrates. *Tetrahedron Lett*., **1998**, *39*, 6679-6682
48. Dolbier, W.R. Structure, Reactivity, and Chemistry of Fluoroalkyl Radicals. *Chem. Rev*., **1996**, *96*, 1557-1584.
49. Huang, W.Y. Perfluoroalkylation initiated with sodium dithionite and related reagent systems. *J. Fluorine Chem*., **1992**, *58*, 1-8.
50. Leon-Ruaud, P.; Plusquellec, D. Synthese de nouveaux tensioactifsglycosidiques par l'intermediaire de sucreshalogenes. Thioethers et sulfones derives de l'α-d-glucoside et l'α-d-mannoside de methyle. *Tetrahedron,* **199**1, *47*, 5185-5192.
51. Paleta, O.; Dlouha, I.; Kaplanek, R.; Kefurt, K.; Kodicek, M. Novel amphiphilic fluoroalkylated derivatives of xylitol, D-glucose and D-galactose for medical applications: hemocompatibility and co-emulsifying properties. *Carbohydr. Res*., **2002**, *337*, 2411–2418.
52. Razgulin, A. V.; Mecozzi, S. Synthesis, emulsification and self-assembly properties of sugar-containing semifluorinated amphiphiles. *Carbohydr. Res*., **2015**, *406*, 10-18.
53. Li, X.; Turanek, J.; Knotigova, P.; Kudla´c˘kova, H.; Masek, J.;

Pennington, D. B.; Rankin, S. E.; Knutson, B. L.; Lehmler. H. -J. Synthesis and biocompatibility evaluation of fluorinated, single-tailed glucopyranoside surfactants. *New J. Chem*., **2008**, *32*, 2169-2179.

54. Fischer, E. *Ueber die Gluooside der Alkohole. Berichte Der Deutschen Chemischen Gesellschaft*., **1893**, *26*, 2400-2412.
55. Bocker, T.; Thiem, J.; Fisher, F. Studies on liquid-crystalline glycosides. *Liq. Cryst.,* **1989**, *6*, 349-356.
56. Adasch, V.; Hofmann, B.; Milius, W.; Platz, G.; Voss, G. Preparation of alkyl α- and β-D-glucopyranosides, thermotropic properties and X-ray analysis. *Carbohydr. Res*., **1998**, *314*, 177-187.
57. Minden, H.M.; Brandenburg, K.; Seydel, U.; Koch, M. H. J.; Garamus, V.; Willumeit, R.; Vill, V. Thermotropic and lyotropic properties of long chain alkyl glycopyranosides. Part II. Disaccharide headgroups. *Chem. Physics Lipids*. **2000**, *106*, 157-179.
58. Goethals, G.; Fernandez, A.; Martin, P.; Miñana-Pérez, M.; Scorza, C.; Villa, P.; Godé, P. Spacer arm influence on glucidoamphiphile compound properties. *Carbohydr*. *Polymers.,* **2001**, *45*, 147-154.
59. Liu, S.; Sang, R.; Hong, S.; Cai, Y.; Wang, H. A Novel Type of Highly Effective Nonionic Gemini Alkyl *O*-Glucoside Surfactants: A Versatile Strategy of Design.*Langmuir,* **2013**, *29*, 8511-8516.
60. Gagnaire, J.; Toraman, G.; Descotes, G.; Bouchu, A.; Queneau, Y. Synthesis in water of amphiphilic sucrose hydroxyalkylethers. *Tetrahedron Lett.,* **1999**, *40*, 2757-2760.
61. Belmessieri, D.; Gozlan, C.; Duclos, M.-C.; Molinier, V.; Aubry, J. -M.; Dumitrescu, O.; Lina, G.; Redl, A.; Duguet, N.; Lemaire, M. Synthesis, surfactant properties and antimicrobial activities of methyl glycopyranoside ethers. *Eur. J. Med. Chem*., **2017**, *128*, 98-106.
62. Esmaeilian, N.; Dabir, B.; Malek, R. M. A.; Arami, M.; Mazaheri, F. M. Synthesis of an ionic sugar-amino acid based surfactant in aqueous media.*J. Mol. Liq.,* **2020**, *318*, 114269.
63. Lemahieu, G.; Aguilhon, J.; Strub, H.; Molinier, V.; Ontiveros, J. F.; Aubry, J. -M. Hexahydrofarnesyl as an original bio-sourced alkyl chain for the preparation of glycosides surfactants with enhanced physicochemical properties.*RSC Adv*., **2020**, *10*, 16377–16389.
64. Michocka, K.; Staszak, K.; Gwiazdowska, D.; Wieczorek, D. Synthesis, Surface and Antimicrobial Activity of New Lactose-Based Surfactants. *Molecules,* **2019**, *24*, 4010.
65. Zdarta, A.; Pacholak, A.; Smułek, W.; Zgoła-Grześkowiak, A.; Ferlin, N.; Bil, A.; Kovensky, J.; Grand, E.; Kaczorek, E. Biological impact of octyl D-glucopyranoside based surfactants. *Chemosphere,* **2018**, *217*, 567-575.
66. Pappalardo, V. M.; Cavuoto, D.; Sangiorgio, S.; Speranza, G.; Cappelletti, G.; Ravasio, N.; Zaccheria. F. Clays as Effective Solid Acid Catalysts for the Preparation of Sugar Esters with Surfactant Properties. *Chem.Sel.,* **2020**, *5*, 8009 –8014.
67. Gérard, D.; Méline, T.; Muzard, M.; Deleu, M.; Plantier-Royon, R.; Rémond, C. Enzymatically-synthesized xylo-oligosaccharides laurate esters as surfactants of interest. *Carbohydr. Res*., **2020**, *495*, 108090.
68. Sari-Chmayssem, S.; Pessel F.; Guégan, J. P.; Taha, S.; Mawlawic H.; Benvegnu, T. Direct and one-pot conversion of polyguluronates and alginates into alkyl-L-guluronamide-based surfactant compositions. *Green Chem.,* **2016**, *18,* 6573-6585.
69. Pinna, M. C.; Salis, A.; Monduzzi, M. Novel mannitol based non-ionic surfactants from biocatalysis: Part two: improved synthesis. *J. Mol. Cat. B: Enzymatic.* **2004**, *27*, 233-236.
70. Drummond, C. J.; Wells, D. Nonionic lactose and lactitol based surfactants: comparison of some physico-chemical properties. *Colloids and surfaces A: Physicochemical and Engineering Aspects*. **1998**, *141*, 131-142.