Synthesis Of Decyl Mannoside

Muhamad Baihakhi Bin Shamsudin, Dr Nurul Fadhilah Binti Kamalul Aripin,

Faculty of Chemical Engineering, Universiti Teknologi Mara

***Abstract*—A new mixtures of mannose and decanol was synthesis. This synthesis main objective was to produce synthetic glycosides as one of the alternative for natural mannoside which consist of single alkyl chain with mannose head group. Three major procedures involved in the synthesis of decyl mannoside which are peracetylation, glycosylation and followed by deacetylation procedure. NMR analysis was used to determine the structure of the product and to analyze the product purity. The product which is decyl mannoside has purity of 67% due to some error might occur during synthesis procedure. Overall, the experiment was succesfull since the product was produced. .**

Keywords— Glycolipid, mannose, synthetic glycoside, decyl mannoside

I. INTRODUCTION

Glycolipids are amphililic compounds that demonstrating the properties of liquid crystal because of the tendency of de-mixing tendency of the polar part of the molecule as well as the non-polar part [1]. Alkyl Poly-Glycosides (APGs) which is known its characteristics such as biodegradable, non-ionic surfactants, have given several importance in industrial research. There is difference in structure form among these technical glycolipids which is they only comprise of one alkyl chain also natural compounds which is they typically contain a double alkyl tail. These differences contributes to exhibit different phase behavior, thus it will restrict the use of APGs in the field of membrane related research. Only a smectic mesophase in pure condition can formed due to the single chain glycolipids. For natural, double chain glycolipids, though, columnar phases have been reported [2]. Major issue towards research in biological studies due to the differences in phase structures.

Glycolipids are tremendously remarkable amphiphilic molecules that comprise of a monosaccharide or oligosaccharide which act as hydrophilic headgroup as well as hydrophobic hydrocarbon chains [3]. Glycolipids plays important part in material science as well as in life science. They have somewhat diverse of their biological functions, which consist of formation of cell membrane, function in biomembrane, element of membrane domains or as mediators of cell-cell identification routes. Glycolipids commonly known that it is broadly applied in the field for the products of consumer also as an applications for biochemical such as food additives, cleaners, foundations, medicines, and protein science. In addition, biochemistry owed to their outstanding properties which comprising of low toxic content, outstanding surface activity. Glycolipids also have ability of decontamination quiet efficient, biocompatible property and readily biodegradable property. Besides, they are very potential to be used in drug delivery also in the process of membrane proteins crystallization, etc [4].

In fact, regarding to our living systems, glycolipids are one of the resources that rich of liquid crystals. Mostly glycolipids are amphotropic liquid crystal, which have ability to form thermotropic liquid crystal under heated state as well as lyotropic liquid crystal in state of aqueous solutions. Large amount of thermotropic mesophases of alkyl glycosides might be perceived to have bilayer liquid crystal textures which are relying on its stereo- chemistry. This means it's rely on their length of alkyl chain, category of headgroup as well as anomeric configuration also includes temperature. It is found that the mesophases can be formed through segregation process microphase segregation among the hydrogen-bonded networks of sugar ring also the van der Waals interaction in aliphatic chains of hydrophobic. The behaviour of thermotropic phase of glycolipids can show two kinds of endothermic peaks through heating process [5]. First kind of transition temperature (T_{lc}) is a transition which comes from its solid crystal into the liquid crystal mesophase. For the second one is the higher transition temperature (T_{iso}) which is started with liquid crystal mesophase to the isotropic states. The thermotropic liquid crystal mesophase ought to ascribe to the hydrogen-bonding networks of temperature-sensitive intermolecular in the sugar headgroups [6].

Mannose quite similar with glucose is categorized as a simple sugar which comes from collection of aldohexose in the family of carbohydrate [7]. Mannose usually discovered into a wide variety of fruit (together with cranberries). Dextro mannose (D-mannose) is believed to forestall bacteria beyond enduring at the urinary tract's walls. This act is to avoid and deal with urinary tract infections. Since mannose and glucose are epimers for the C2 position, it can be said that they are distinctive out of each other. Surprisingly, they are mainly different in physical behaviours. Additionally, stereoisomers at the C1 position can be found with two possibilities and orientations of the hydroxyl group also might be found with two possibilities (axial/equatorial). Therefore, following from stereoisomers and orientations, two anomers are formed which are, α-D-mannose together with β-D-mannose. When in the form of ring, mannose will have chiral structure, but it will have achiral structure when in the linear form.

α-D-mannose have physical characteristic which is commonly known as sugar that have sweet taste, whereas β-D-mannose slightly different from it which is have bitter taste. However, when time passing by, the sweetness of a pure solution α-D-mannose will loss. As monosaccharides dissolve in water, it will experience reactions which is known as reversible ring-opening. This will cause the existence of the ring forms in equilibrium together with the linear forms. Afterwards, the C1 is allow to rotate (mutarotation), and once it structure turn back into the ring form, then it will form β-D-mannose. As soon as equilibrium is reach, the amounts of β-isomer will be greater than the α-isomer. This issue due to the hydroxyl on the C1 in the β-isomer have more stable (equatorial) position [8].

In this research, with concern regarding the natural mannoside which simple structure that comprise of single alkyl chain with mannose head group, production of synthetic glycoside will be done as alternative for the natural mannoside.

.

II. METHODOLOGY

A. Materials

D-mannose was obtained from Merck.Chemicals, acetic anhydride, catalyst which is boron trifluoride bought from Sigma Aldrich (USA), sulphuric acid, ethyl acetate, anhydrous magnesium sulphate ($MGSO_4$), sodium methoxide decanol, dichloromethane, sodium bicarbonate (NA_2CO_3), acetonitrile, hexane, methanol, butanol all were purchased from Merck.Chemicals

B. Synthesis procedures and sample analysis

General Peracetylation Procedure: D-mannose (30g, 27.8mmol) in acetic anhydride (150ml, 286mmol) was prepared in a round bottom flask and stirred in the ice bath for 15 minutes.The solution then was catalyzed by concentrated sulphuric acid which was added 2 drops and it was further stirred on an ice bath for 10 minutes. Then, the mixture was allowed to warm under room temperature with ongoing stirring for 45 minutes. Later, the mixture was transferred into a separating funnel and 100 ml of ice water was used to dilute it and followed with extraction with 100 ml of ethyl acetate. The extraction process was done 3 times by washing the mixture with ice water. Then, the organic layer that appeared was quenched 2 times with saturated hydrogen carbonate solution. Later, the extracted product was dried with anhydrous magnesium sulphate ($MgSO_4$) followed with filtered and then evaporated.

General Glycosylation procedure: The mannose solution (11.703 g) and decanol (2.7 g) were dissolved in 60 ml dichloromethane and were stirred in a round bottom flask at room temperature. Boron Trifluoride (1.23 g) which is the catalyst was injected into the solution and the reaction was left for 24 hours. Later, the solution was poured into saturated sodium bicarbonate (Na_2CO_3) and the organic layer that appeared was washed two times with water. Then, evaporation was done to evaporate the dichloromethane and followed with an acetonitrile-hexane extraction to remove unreacted alcohol. The acetonitrile layer was collected and evaporated to get the product

General deacetylation procedure: The solution were dissolved in 150 ml methanol and sodium hydroxide was added to induce a basic medium. The solution then was stirred for 12 hours. After the reaction completed, methanol in the solution was evaporated and the product was separated by an extraction with n-butanol and distilled water. Diluted sulphuric acid in a small amount was added to neutralize the excess sodium methoxide. Later, the organic layer was collected and the solvent was evaporated to obtain the product and the product was dried in a vacuum oven at 50ºC for 48 hours.

The decyl mannose was analyzed in deutro-chloroform and the measurements were conducted at room temperature. All proton spectra were measured on a Bruker NMR spectrometer at 400 MHz.

III. RESULTS AND DISCUSSION

A. NMR analysis on the product of the analysis

Analyses of NMR spectra allow for evaluate the product quality in experiment. The evaluation can be done by comparing the integral of the α-anomer and the β-anomer of the peak. Figure 1.1 shows the NMR spectrum of a decyl mannoside with main peaks to verify the characteristic of the product. Figure 1.2 shows the integration of the peak of decyl mannoside. Figure 1.3 and Figure 1.5 shows the NMR spectrum for mannose and decanol respectively. While Figure 1.4 and 1.6 shows the structure and chemical shift of mannose and decanol respectively.

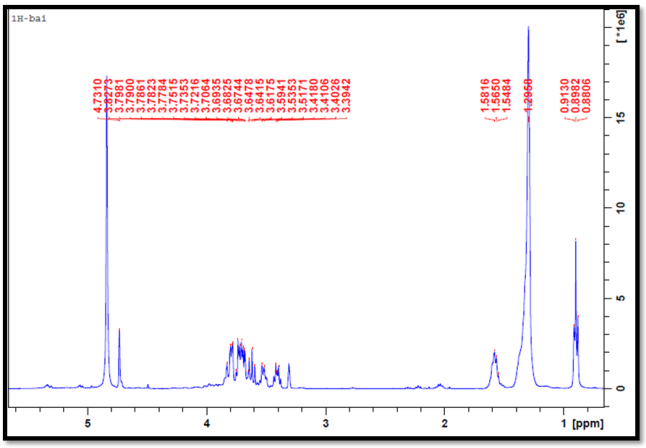

Figure 1.1: ^{1}H-NMR spectrum of decyl manoside

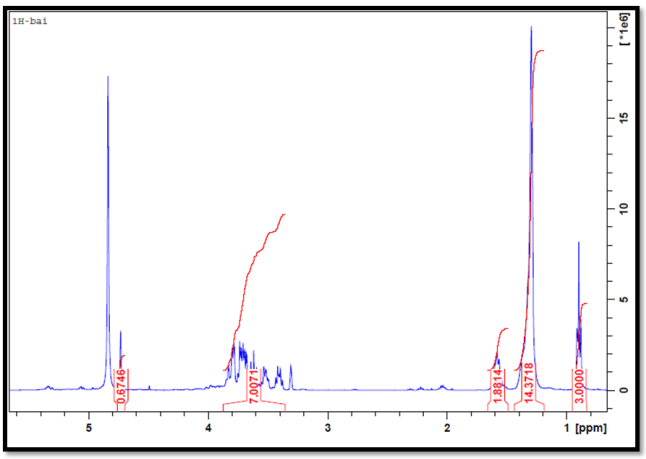

Figure 1.2: Integration peak of decyl mannoside

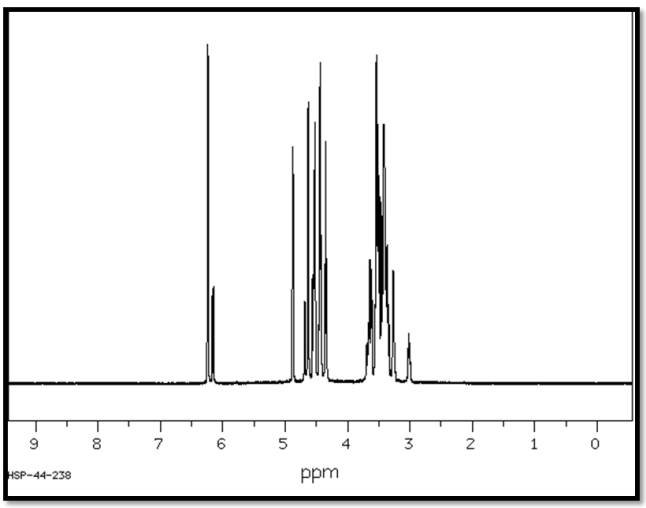

Figure 1.3: ^{1}H-NMR spectrum of mannose (Retrieved from http://sdbs.db.aist.go.jp/sdbs/cgi-bin/direct_frame_top.cgi)

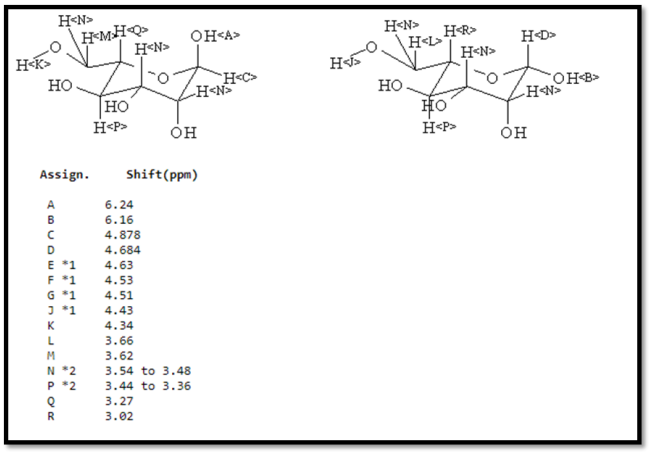

Figure 1.4: Mannose structure and chemical shift

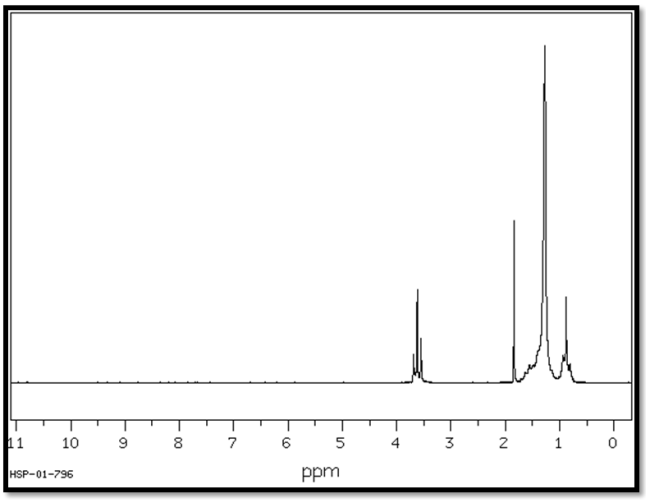

Figure 1.5: ^{1}H-NMR spectrum of decanol (Retrieved from http://sdbs.db.aist.go.jp/sdbs/cgi-bin/direct_frame_top.cgi)

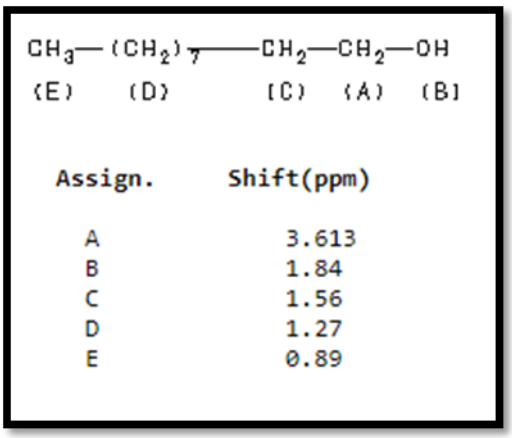

Figure 1.6: 1-decanol structure and chemical shift

From the Figure 1.1, at peak ~0.9 ppm indicates the presence of CH_3. This proved by the integration of the value from Figure 1.2 which is 3 which means 3H. At peak ~1.29 ppm indicates that the presence of $(CH_2)_7$ chain and can be confirmed with the integration values which is roughly 14. As for peak at ~1.58, it give the information about the (CH_2CH_2-OH) structure. This, prove the presence of decanol in the product formed. Next is to determine the content of another starting material which is mannose in the product. By referring the product spectrum and mannose spectrum, it seems that almost similar peak from mannose spectrum (Figure 1.3) appeared indicates that the presence of mannose in the product. This can be proven by the integration of the peak from Figure 1.2 which is 7 indicates the present of 7H in the mannose structure. The highest peak appeared in the Figure 1.1 which is ~4.7 ppm indicates that alpha link between mannose and the chain. By referring the integration value corresponding to the peak, the value is 0.67 which means only 67% product formed from the synthesis.

The purity of the product quite low based on the result. There are some error may contribute to this result. The reaction may need for longer period time during first part of glycosylation procedure. This means during reaction involved mannose solution with dichloromethane and catalysed by boron trifluoride, the reaction should left more than 24 hours in order to get product with greater yield. In the synthesis of decyl mannoside, alcohol which is decanol is used and then extraction has been done to remove it. Nevertheless inappropriate extraction will cause the decanol did not remove completely. This lead to decanol remains in the product. In addition, NMR spectrum cannot detect unreacted alcohol due to the the signals of the alcohol CH_2 overlap with sugar signals [9]. The alkyl chains average length in the products can be determined from their peak integrals.

IV. Conclusion

This experiment was considered successfully since the presence of product after all of the synthesis has been done even though the purity of the product did not achieve 100% which is 67%. NMR analysis was done to determine the content on the product and it shown alpha linkage occurs which means the interaction occurs between mannose and decanol for the formation of the synthetic glycosides. More precaution in the glycosylation procedure especially in the evaporation process of the solvent will give more purity toward the product.

Acknowledgment

Assalamualaikum W.B.T. I would like to express my gratitude to all those who gave me the possibility to complete this thesis. I am very grateful to have supervisor like Dr. Nurul Fadhilah Kamalul Aripin whose help, stimulating suggestion, motivation, and encouragement that helped me to complete this study in time and writing of the thesis. I want to thank the staff of Faculty of Chemical Engineering, Universiti Teknologi MARA for giving me permission to use and commence this research in the first instance and to do the necessary experiment work. I would also like to give special thanks to my parents Mr. Shamsudin Bin Ab Kadir and Mrs. Zainab Binti Wan Omar because they always give moral support for me during my research. Thank you

References

[1] R. Hashim, H. H. A. Hashim, N. Z. M. Rodzi, R. S. D. Hussen, and T. Heidelberg, “Branched chain glycosides: Enhanced diversity for phase behavior of easily accessible synthetic glycolipids,” *Thin Solid Films*, vol. 509, no. 1–2, pp. 27–35, 2006.

[2] H. M. Von Minden *et al.*, “Thermotropic and lyotropic properties of long chain alkyl glycopyranosides. Part II. Disaccharide headgroups,” *Chem. Phys. Lipids*, vol. 106, no. 2, pp. 157–179, 2000.

[3] Y. Zhang, L. Chen, and X. Wu, “Thermotropic liquid crystalline and surface-active properties of n-alkyl α-D-mannopyranosides,” *J. Mol. Liq.*, pp. 2–10, 2018.

[4] V. Vill and R. Hashim, “Carbohydrate liquid crystals: Structure - Property relationship of thermotropic and lyotropic glycolipids,” *Curr. Opin. Colloid Interface Sci.*, vol. 7, no. 5–6, pp. 395–409, 2002.

[5] S. Ogawa, K. Asakura, and S. Osanai, “Thermotropic and glass transition behaviors of n-alkyl β-d-glucosides,” *RSC Adv.*, vol. 3, no. 44, p. 21439, 2013.

[6] G. Liao *et al.*, “Thermotropic liquid crystalline properties of amphiphilic branched chain glycolipids,” *Liq. Cryst.*, vol. 33, no. 3, pp. 361–366, 2006.

[7] Z. Mosapour Kotena, R. Behjatmanesh-Ardakani, and R. Hashim,

"AIM and NBO analyses on hydrogen bonds formation in sugar-based surfactants (α/β-d-mannose and n-octyl-α/β-d-mannopyranoside): a density functional theory study," *Liq. Cryst.*, vol. 41, no. 6, pp. 784–792, 2014.

[8] M. L. T. Cossio *et al.*, *Advances in Carbohydrate Chemistry and Biochemistry*, vol. XXXIII, no. 2. 2012.

[9] N. F. K. Aripin, "Synthesis and Characterisation of Maltosides and Lactosides Based on Alcohol Mixtures Obtained From Palm Oil and Palm Kernel Oil . Nurul Fadhilah Binti Kamalul Aripin Dissertation Submitted in Fulfilment of the Requirements for Degree of Master of Science," no. June, 2009.