CLICK CHEMISTRY DERIVED SUGAR-BASED SURFACTANTS WITH VARIOUS SHAPES: SYNTHESIS AND PHYSICAL STUDIES

TAMMAR HUSSEIN ALI

FACULTY OF SCIENCE
UNIVERSITY OF MALAYA
KUALA LUMPUR

2015

CLICK CHEMISTRY DERIVED SUGAR-BASED SURFACTANTS WITH VARIOUS SHAPES: SYNTHESIS AND PHYSICAL STUDIES

TAMMAR HUSSEIN ALI

THESIS SUBMITTED IN FULFILMENT OF THE REQUIRMENTS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY

CHEMISTRY DEPARTMENT
FACULTY OF SCIENCE
UNIVERSITY OF MALAYA
KUALA LUMPUR

2015

UNIVERSITY OF MALAYA

ORGINAL LITEARY WORK DECLARATION

Name of Candidate: **Tammar Hussein Ali**

Registration / Metric No. : **SHC 110057**

Name of Degree: Doctor of philosophy

Title of project paper / research report / dissertation / thesis

"**Click chemistry derived sugar-based surfactants with various shapes: synthesis and physical studies**".

Field of Study: Organic Synthesis

I do solemnly and sincerely declare that:

(1) I am the sole author / writer of this work
(2) This work is original
(3) Any use of any work in which copyright exists was done by way of fair dealing and for permitted purpose and any excerpt or extract from, or reference to or reproduction of any copyright work has been disclosed expressly and sufficiently and the title of the work and its authorship have been acknowledged in this work.
(4) I do not have any actual knowledge nor ought I reasonably to know that the making of this work constitutes an infringement of any copyright work.
(5) I hereby assign all and every right in the copyright to this work to the University of Malaya (" UM") , who henceforth shall be the owner of the copyright in this work and that any reproduction or use in any form or by any means whatsoever is prohibited without the written consent of UM have been first had and obtained .
(6) I am fully aware that if in the course of making this work I have infringed any copyright whether intentionally or otherwise, I may be subject to legal action or any other action as may be determined by UM.

Candidate's Signature Date: 24-02-2015

Subscribed and solemnly declared before,

Witness's Signature

Name: Date

Designation:

Click chemistry derived sugar-based surfactants with various shapes: synthesis and physical studies

Abstract:

Surfactants are important bulk chemicals with diverse applications in various fields, ranging from food over detergents to industrial products like lubricants. Growing environmental awareness and limitation of petrochemical resources have shifted the focus towards the utilization of renewable resources. Good candidates are sugar based surfactants. A series of new surfactants were prepared by click chemistry using functionalized glucosides as the hydrophilic domain. Variations of the molecular structure led to three different shapes, i.e. Y-shape, X-shape and reverse Y-shape, referring to the geometric arrangements of the hydrophobic and hydrophilic domains, respectively. Since the shape of a surfactant affects its molecular assembly behaviour, each surfactant type gives rise for specific applications. Despite the application of multi-step syntheses, reasonable overall conversions yields, ranging from 20 to 55%, were obtained. The surfactants were characterized by NMR spectroscopy (^{1}H as well as ^{13}C) and mass spectrometry, and their physical behaviour was investigated by optical polarizing microscopy and systematic surface tension measurements of aqueous solutions to determine the CMC. Except for one hydrophobic dominant reverse-Y-shape compound all surfactants exhibited very low Krafft temperatures, indicating good molecular solubility in water. The surface dominance of the hydrophilic domain, especially for X and Y-shape surfactants, led to preferred spherical aggregation in water, suggesting good emulsifying properties for oil in water. In fact, some of the surfactants led to metastable O/W-emulsions in absence of a polymeric stabilizer and required several days to separate. The surfactants may find technical applications particularly for water based emulsion systems, like e.g. oil recovery or pharmaceutics.

Surfaktan berasaskan gula terbitan dari kimia klik dengan bentuk yang pelbagai: Sintesis dan kajian fizikal

Abstrak:

Surfaktan adalah bahan kimia pukal penting yang mempunyai pelbagai kegunaan dalam banyak bidang, merangkumi makanan, bahan cuci dan produk industri seperti minyak pelincir. Peningkatan dalam kesedaran terhadap persekitaran dan kekurangan sumber petrokimia telah megalihkan tumpuan terhadap penggunaan sumber boleh diperbaharui. Calon yang baik adalah surfaktan berasaskan gula. Suatu siri baru surfaktan telah disediakan melalui kimia klik menggunakan glukosida yang difungsikan seperti domain hidrofilik. Kepelbagaian dalam struktur molekul telah menjurus kepada penghasilan tiga jenis bentuk, iaitu, bentuk-Y, bentuk-X dan bentuk-Y terbalik, merujuk kepada susunan geometrik domain hidrofobik dan hidrofilik masing-masing. Memandangkan bentuk surfaktan mempengaruhi kelakuan penghimpunan molekul, maka setiap surfaktan menjurus kepada aplikasi yang khusus. Walaupun sintensis melibatkan beberapa langkah, tetapi, hasil keseluruhan adalah munasabah, antara 20 ke 55%, telah diperolehi. Surfaktan telah dicirikan menggunakan spektroskopi NMR (^{1}H dan juga ^{13}C) dan spektrometri jisim, serta sifat fizikal telah disiasat menggunakan mikroskop polarisasi optik dan ukuran ketegangan permukaan yang sistematik bagi larutan akueus untuk menentukan CMC. Semua bahan surfaktan kecuali yang mempunyai domain hidrofobik bentuk-Y terbalik mempamerkan suhu Krafft yang amat rendah, menunjukkan kelarutan yang baik dalam air. Penguasaan permukaan oleh domain hidrofilik terutamanya bagi surfaktan berbentuk-X dan Y menjurus kepada penghasilan aggregat berbentuk sfera di dalam air, mencadangkan ciri pengemulsian yang baik bagi minyak dalam air. Malah, beberapa surfaktan menjurus kepada penghasilan metastabil emulsi minyak-dalam-air tanpa ketiadaan polimer penstabil dan memerlukan beberapa hari untuk terasing. Surfaktan boleh digunakan untuk aplikasi

teknikal khususnya untuk sistem emulsi berasaskan air, seperti pemulihan minyak atau farmaseutikal.

ACKNOWLEDGEMENTS

Praise belongs to God,

The First, without a first before Him, the Last, without a last behind Him.

Beholders' eyes fall short of seeing Him,

Describers' imaginations are unable to depict Him.

He originated the creatures through His power with an origination;

He devised them in accordance with His will with a devising.

He made them walk on the path of His desire,

He sent them out on the way of His love.

Nothing can go against God's willing.

He assigned from His provision to every human

A spirit nourishment known and apportioned.

No decrease decreases those whom He increases;

No increaser increases those of them whom He decreases.

Each spirit He strikes a fixed term in life, for each He sets up a determined end;

When I walk through the days of life and research embracing the reckoning of time,

God seizes me the abundant reward,

His Grace, His Mercy and His Greatest Love.

Worth of Praise above all!

I would like to dedicate my heartfelt gratitude to my supervisor Assoc. Prof. Dr. Thorsten Heidelberg, Dr. Rusnah Syahila Duali Hussen and Dr. Hairul Anuar Bin Tajuddin for their excellent guidance throughout the entire course of this work. I would like to express my earnest appreciation for their valuable advices and motivation ever since my PhD. days in University of Malaya. They have always believed in my abilities and trusted me with several projects. Although they have been very challenging, they served as stepping-stones for intellectual and professional advancement.

Next, I dedicate my gratefulness and respect without limits to my beloved family members my father, mother, brothers, sisters and uncle for their unconditional support and encouragement throughout the period of my research. Their companionship from afar during the difficulty times I faced is indeed a cherishing moment for me.

Apart from that, I am also thankful to all of my friend, my PhD. Colleagues in the Department of Chemistry and my entire friend throughout my life for support and cooperation during the period of this endeavor. Furthermore, I relish the blessings and encouragement for those people, who are their names may not appear here, their efforts and help will be still in mind forever.

Last for but no least, my gratitude also goes to NMR staff and the staffs in Department of Chemistry in University of Malaya for their help in the necessary equipment's and things.

In short, sincere acknowledgement is conveyed again for all of above for assisting me to achieve my research goal.

Table of Contents

List of Figures

List of Schemes

List of Tables

List of Abbreviation

˚C	Degree Celsius
2D	Two-dimensional
Å	Angstrom
Ac	Acetate group
APGs	Alkylpolyglycosides
ATGs	Alkyltriazoleglycosides
$BF_3.Et_2O$	Borontrifluride-diethylether compex
CD_3OD	Deuterated methanol
$CDCl_3$	Deuterated chloroform
CH_3Cl	Chloroform
CMC	Critical Micelle Concentration
CuAAC	Copper-catalyzed azide–alkyne cycloaddition
d	Doublet
dd	Double doublet
dd~t	Double doublet about triplet
ddd	Double double doublet
dt	Double triplet
D	dimensional
DCM	Dichloromethan
DDAB	Di-dodecyldimethyl ammonium bromide
DEPT	Distortion-less Enhancement by Polarization Transfer
DMAP	Dimethylaminopyridine
DMF	Dimethylformamide
DMSO-d	Deuterated dimethylsulfoxide
DOC	Sodium deoxycholate
DOPE	Di-oleoylphosphatidylethanolamine
DOTAP	1,2-dioleoyl-3- trimethylammonium propane
eq.	Equivalent
Eq.	Equation
EWG	Electron with drawing group
g	Gram
Glc	Glucose
hrs	Hours
H_1	Hexagonal phase
HMQC	Heteronuclear Multi-Quantum Correlation
HPLC	High-performance liquid chromatography
HRMS	High resolution mass spectrometry
Hz	Hertz
J	Coupling constant
kJ	Kilo joule
L	Gel phase
L_1	Micellar solution
La	Lamellar
m	Multiple
m_c	Center of multiple
mg	Milligram
mL	Milliliter
mmol	Millimole
mol	Mole

N	Normality
NaOH	Sodium hydroxide
NaOMe	Sodium methoxide
NCS	N-Chlorosuccinimide
NMR	Nuclear magnetic resonance
O/W	oil-in-water emulsion
O/W/O	oil-in-water-in-oil emulsion
OPM	Optical polarizing microscopy
PENDANT	Polarizing enhancement nurtured during attached nucleus testing
PPh_3	Triphenylphosphine
s	Singlet
SDBS	Sodium dodecylbenzesulfate
SDS	Sodium dodecyl sulfate
t	Triplet
tert-	Tertiary
TDOC	Sodium taurodeoxycholate
THF	Tetrahydrofuran
TLC	Thin layer chromatography
TsCl	Tosyl chloride
TsOH	4-Toluene sulfonic acid momohydrate
W/O	Water-in-oil emulsion
W/O/W	Water-in-oil-in-water emulsion
W/S/O	Water-surfactant-oil

Chapter 1 : Introduction

1.1 Introduction

Synthetic surfactants have become a necessary commodity after their introduction in the early 20th century because of their vital functions as cleaning, dispersing, emulsifying, and antifoaming agents. Surfactant synthesis involves the combination of hydrophilic and hydrophobic molecular regions. The first synthetic material used specifically for its surface-active properties was sulfated oil, which was introduced in the 19th century as a dyeing aid. This material was obtained by treating castor oil with sulfuric acid. In the past century the surfactant synthesis steadily moved towards inexpensive and renewable starting materials. (Shinoda, Carlsson, & Lindman, 1996). To date, the development of surfactants has no limitations. The availability of new chemical processes and raw material has resulted in the development of an extensive range of new surface-active compounds. Ecologists demand the increase of these compounds because of population growth, and surfactant technology is geared toward the use of new raw material resources. Environmental issues and surfactant shortage, which is expected to escalate, cause a continuous shift in chemical developments to utilization of renewable biological resources to ensure sustainable raw materials. Surfactants are broadly used in chemical processes, technical lubricant applications, pharmaceutical formulations, household products, agricultural chemicals, and food, among others. Non-ionic surfactants, which among others provide advantages in terms of skin compatibility, are most commonly based on ethylene oxides, due to cost effects. However, the slow biodegradation of ethers is a considerable disadvantage, particular for large scale household products. A better biocompatibility is expected for surfactants that utilize carbohydrates as resources instead. Besides reduced environmental impacts, carbohydrates ensure sustainable raw

materials as well.

Glycolipids combine a fatty acid-derived hydrophobic domain with a sugar-based hydrophilic head group. These compounds originate entirely form renewable resources and are important both scientifically and technically (Hato *et al*. 1999). The origin of the surfactant behaviour is the intrinsic duality of two molecular antipodes, *i.e.* the hydrophobic hydrocarbon chain and the hydrophilic sugars, leading to an intra-molecular separation that gives rise to supra-molecular assemblies and, hence, surface and interphase activity. The biological origin makes sugar-based surfactants less harmful to the environment compared with other synthetic surfactants. Besides environmental advantages, physicochemical properties of sugar-based surfactants makes them interesting for a wide range of applications (Shinoda *et al*., 1996). However, higher economic costs limit the application potential.

Given the increasing interest in sugar-based surfactants, the main challenge remains in their synthesis, especially the connection of the hydrophilic (sugar) to the hydrophobic tail. In addition to solubility issues and selectivity, the synthesis of these surfactants is complex, because of the formation of isomeric mixtures, resulting in a variety of configurations in the carbohydrate domain (Hato *et al*., 1999). Click chemistry is a promising approach to a modular synthesis of sugar-based surfactants, because it enables the efficient combination of the two surfactant-antipodes (hydrophilic and hydrophobic domains). Sharpless *et al*. have introduced both the concept as well as suitable reactions conditions (Kolb *et al.* 2001; Rostovtsev *et al.* 2002). Among these the copper-catalyzed azide–alkyne cycloaddition (CuAAC) is mostly utilized. It can be processed both in aqueous and organic solvents and uses inexpensive reagents and catalysts. It is versatile with respect to compatibility of functional groups and applies mild reaction conditions, while providing a selective stereo-chemical output in high

efficiency (Baier, Siebert, Landfester, & Musyanovych, 2012) (Xu, Yao, Fu, & Shen, 2009).

1.2 Outline of thesis

The motivation of this thesis is to synthesize new sugar-based surfactants and to study their behavior in W/S/O systems. The surfactants are referred to herein as Y-shape, reverse Y-shape and X-shape surfactants, based on the general chemical structure reflecting the antipodes of alkyl chains and sugar head groups. The different surfactant shapes give rise to specific applications, since the molecules' shape affects the assembly behaviour and the assembly geometry in closely related to applications.

The work in the thesis is organized into several chapters, reflecting different aspects. The first chapter gives an introduction on sugar-based surfactants, while the second chapter provides the theoretical and experimental background for understanding the subsequent chapters. This covers understanding of surfactants and their phase behaviour as well as special features of non-ionic surfactants, and an introduction to click chemistry. The third chapter is addressing the synthesis of Y-shape surfactants, followed by unexpected reaction outcomes observed in attempts to synthesize Y-shape surfactants. These involve a base-induced cyclization of di-propargylic system to *m*-substituted toluenes and an incomplete coupling (mono-click) of di-propargylic substrates. Subsequent following are chapters on reverse Y-shaped sugar-based surfactants and X-shaped sugar-based surfactants. Finally, the last chapter draws out conclusion of this work and provides recommendations for future research.

1.3 Objectives of thesis

The major objectives of this research work were:

1. To synthesise sugar-based surfactants with different shapes.
2. To produce surfactants with a variety of spacers by click chemistry.
3. To compare physical properties of different shaped surfactants.
4. To enhance the water-solubility of sugar-based surfactants (surfactants with low Krafft point).
5. To determine the effect of different linkers on the surfactant behavior.

Chapter 2 : Motivation and background

2.1 Surfactants (Surface Active Agent)

A surfactant (abbreviated form of surface-active agent) is an amphiphilic organic molecule. Surfactants contain both hydrophobic (tail) and hydrophilic (head) groups, and the presence of these two antipodes determines the physicochemical properties of surfactants in a solution (Figure 2-1) for both aqueous and non-aqueous media.

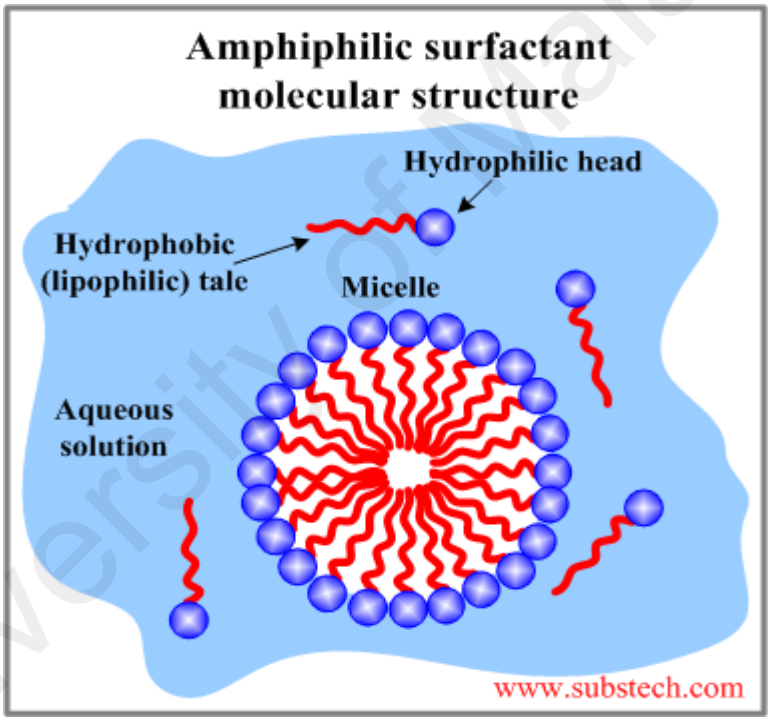


Figure 2-1. Surfactant molecule showing hydrophilic and hydrophobic components (Kopeliovich, 2013, http://www.substech.com/dokuwiki/doku.php?id=surfactants)

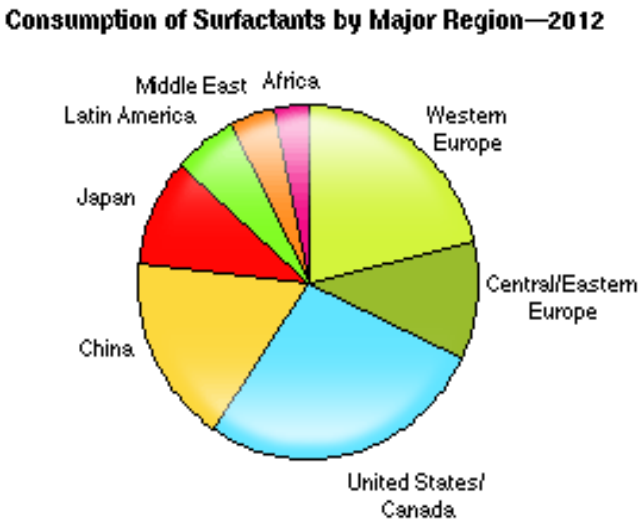


Figure 2-2: Worldwide consumption of surfactants (Janshekar, Inoguchi, Elvira O. Camara Greiner, & Ma, 2013)

The amphiphilic nature of non-ionic surfactants makes the hydrophilic heads of the surfactant molecules dissolve in the water phase, while the hydrophobic tails tend to aggregate at the interfaces. This way they modify the surface tension of an aqueous solution, reducing the surface or interfacial tension and stabilizing foam. In aqueous systems surfactant molecules tend to form a layer at the air–water interface until saturation is reached. Above the molecular solubility further addition of surfactants to the bulk liquid leads to the formation of aggregates (clusters), which are larger than the molecular dissolved surfactant. The surfactant self-organizes into micelles, which can effectively facilitate the microsolubilization or emulsification of an otherwise insoluble organic phase (Oss & Jan, 2008). The critical micelle concentration is the minimum surfactant concentration at which the surface or interfacial tension initially reaches the lowest value, indicating that the surfactant molecules self-aggregate in solution.

In recent years, surfactant products have considerably increased. Ceresana estimated that the global surfactant market will generate revenues of more than 41 billion US$ in 2018, assuming an average annual growth of 4.5%, which leads to roughly 37% share of the global chemical consumption. Figure 2-2 shows an overview of the regional distribution of surfactant market worldwide (Pianoforte, 2012).

Surfactants are increasingly distributed and developed for utilization in various industries such as detergents, emulsifiers, wetting agents and defoamers for example: fabric softeners, formulations and paints. They have emerged as product group with highest market volume in the chemical sector. In view of their tremendous consumption, the synthesis of surfactants should focus on producing environmental compatible materials. The use of renewable resources, such as sugars, provides good prospects for this.

2.2 Classification

Surfactant can be classified into two categories based on their source into chemical and biological surfactants. Biological surfactants are mostly produced by microorganisms during the process of microbial activities. They exhibit unique properties, such as mild production condition, low toxicity, high biodegradability and environmental compatibility (Desai & Banat, 1997) (Hamme, Singh, & Ward, 2003) (Kitamoto, Isoda, & Nakahara, 2002). On the other hand, chemical surfactants are more economic. There are numerous classifications for chemical surfactants. An important one emphasizes on the charge of the hydrophilic head group; surfactants are grouped into ionic (both cationic and anionic), non-ionic and zwitterionic surfactants, as shown in Figure 2-3 (Muthuprasanna *et al*., 2009).

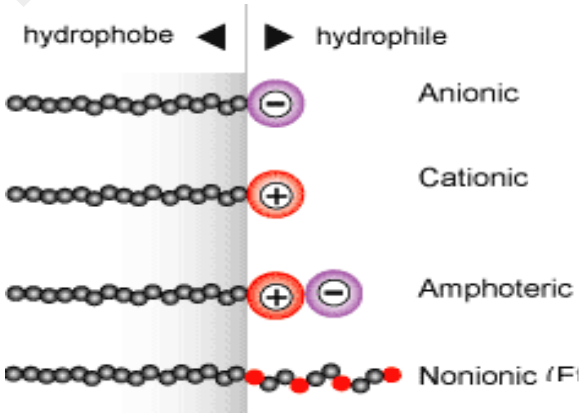
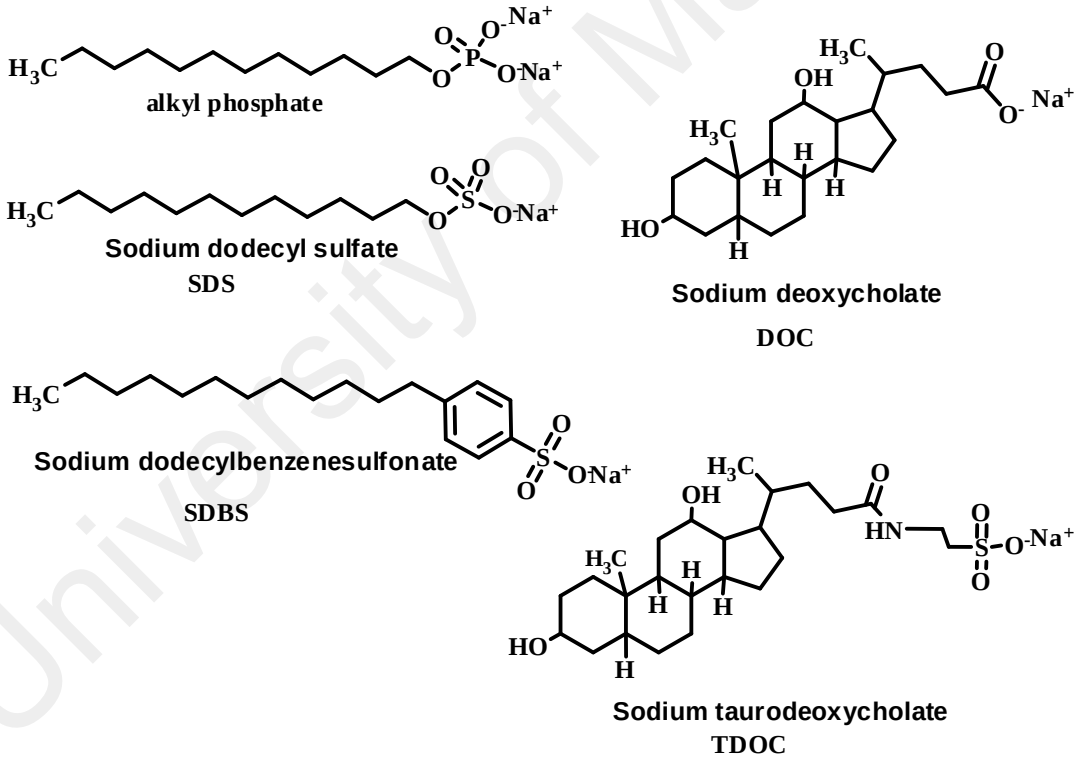


Figure 2-3: Schematic structure of surfactants types. (“How to disperse and stabilize pigments", http://www.inkline.gr/inkjet/newtech/tech/dispersion/)

The hydrophobic "tail" group of surfactant can range from simple hydrocarbon chains, which may be straight or branched, and either saturated or unsaturated, over complex aromatics and fluoro-carbon chains to siloxanes.

2.1.1 Anionic surfactants

The most common head groups of these surfactants are sulfate, carboxylate and sulfonate in combination with sodium or potassium counter ions. The behaviour of anionic surfactants is easily affected by the pH of the medium. The acid sensitivity decreases in the order carboxylate > phosphate > sulphate ~ sulfonate. Scheme 2-1 shows the most common types of anionic surfactants.

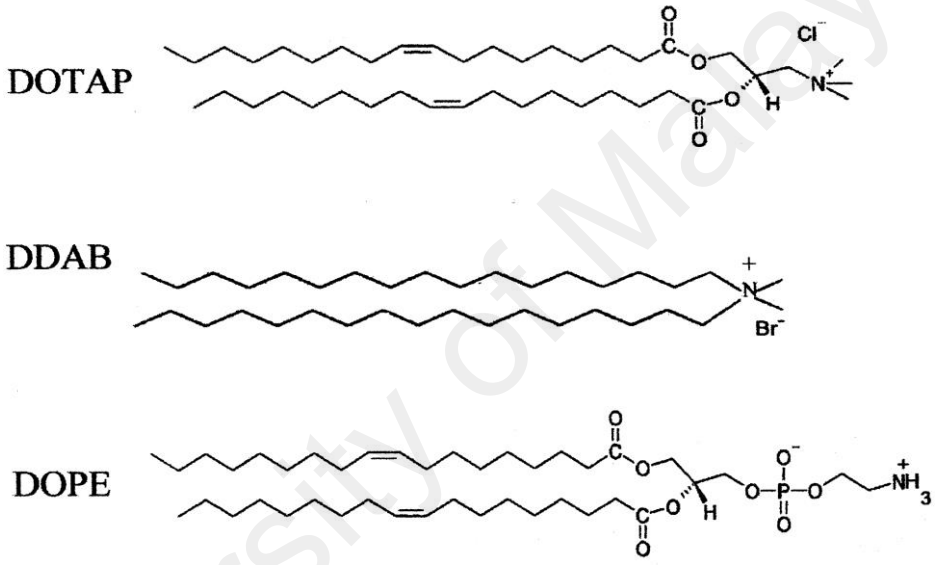


Scheme 2-1: Structure of the most common anionic surfactants.

2.1.2 Cationic surfactants

Cationic surfactants are commonly amines and ammonium salts. The vast majority of cationic surfactants are imidazolines, benzimidazol, ammonium salt and quaternary ammonium compounds (Bajpai & Tyagi, 2006; Kang *et al.* 2011). Usually

amine-based cationic surfactants are applied in protonated state, *i.e.* at acidic pH. Examples are shown in Scheme 2-2. Cationic surfactants find uses in industrial sectors such as bitumen emulsifiers, personal care formulations and as softeners and antistatic additives particularly for textiles. Owing to high hydrolytic stability their toxicity exceeds other surfactant classes (Holmberg, Jonsson, Kronberg, & Lindman, 2002) (Alkhatib, 2006). This disfavours their use for bulk products, like detergents.

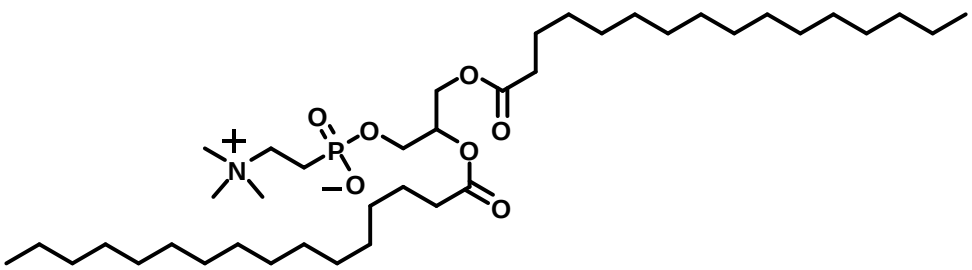


Scheme 2-2: Structure of the most common cationic surfactants (Alkhatib, 2006).

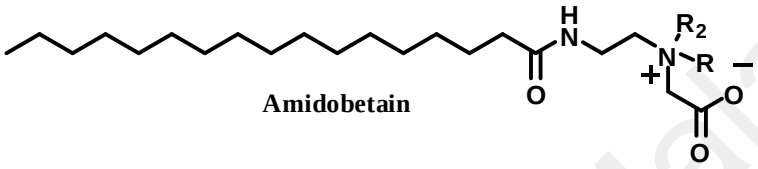
2.1.3 Zwitterionic surfactants

Zwitterionic or amphoteric surfactants consist of two oppositely charges in the head group. The positive charge almost invariably is an ammonium ion, while the negative charge mostly refers to carboxylates in synthetic surfactants, while phosphates are more common for biological analogs. Zwitterionic surfactants are least used owing to synthetic obstacles leading to high prices. The common types of this surfactant are depicted in Scheme 2-3. They are generally stable in a wide range of pH (acidic and baseic media) and exhibit low toxicity; therefore they are used partially in personal care

products and antibacterial agent, (Alargova *et al*., 2003) (FernLey, 1978) (Gawish, Hazzaa, Zourab, & El-Din Gebril, 1981) *etc*.



Dipalmitoylphosphatidylcholine



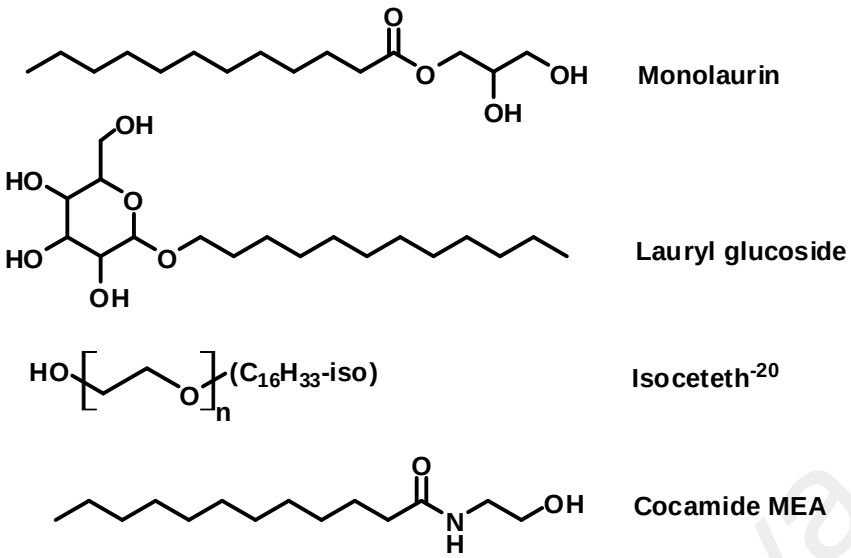
Amidobetain

Betain

Scheme 2-3: Structure of some zwitterionic surfactants, R_1 and R_2 different lengths of alkyl group (Holmberg *et al*., 2002) (Alkhatib, 2006).

2.1.4 Non-ionic surfactant

Non-ionic surfactants have a non-charged polar head group, which either comprises of a polyether or polyalcohol (for example sorbitan and sucrose esters, alkyl glycoside and, polyethylene glycol ethers). A variety of non-ionic surfactants are depicted in Scheme 2-4. Compared to other surfactant types, non-ionic surfactant have advantage, since they are less sensitive to electrolytes and much less strongly binding to biomolecules (like proteins) (Holmberg *et al*., 2002) (Alkhatib, 2006). Lower toxicity, compatible with other surfactant types and compatibility with high salinity media add on to the advantages. Because of that, they are the most common surfactants used in the wide field of scopes. Non-ionic surfactants can be divided into esters, ethers and amides based on the nature of the linkage between the hydrophilic and hydrophobic domain.



Scheme 2-4: Structure of the most common cationic surfactants.

2.2 Phase behavior

Surfactant molecules consist of hydrophilic and lipophilic domains. The presence of these incompatible regions makes them amphiphilic. When surfactants are dispersed in water, they adsorb at the air-water interface. The hydrophilic domain interacts with water, while the lipophilic (hydrophobic) domain points towards the air, *i.e.* away from the water. When the air-water interface is saturated with surfactants additional surfactant forms aggregates, which are termed 'micelles'. This aggregate formation is illustrated in Figure 2-4.

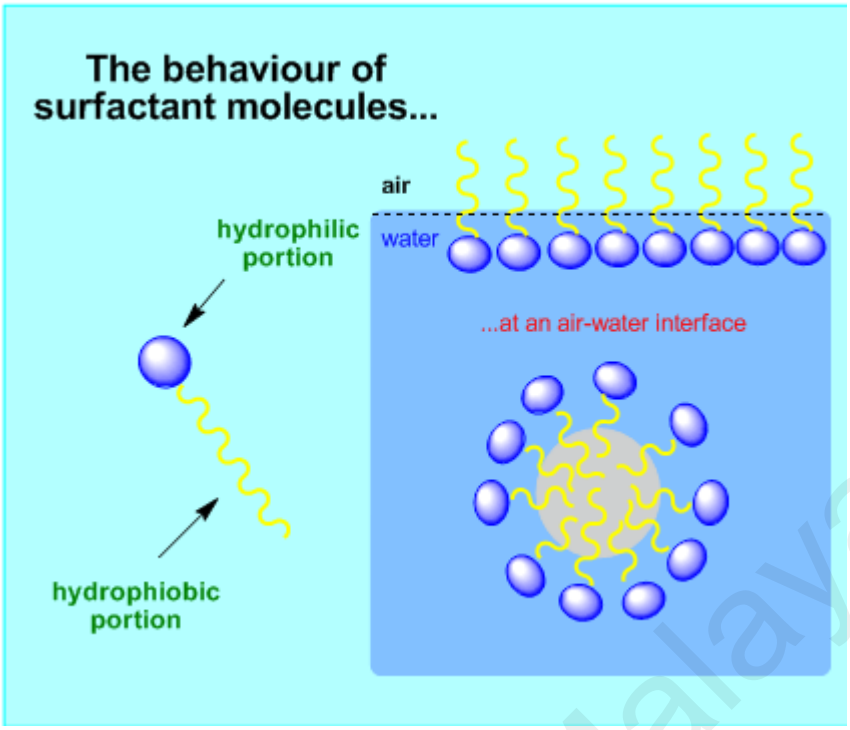


Figure 2-4: Behaviour of surfactant molecules in water. ("Greener Industry," http://greener-industry.org.uk/pages/protecting/protecting_3_pop_up.htm)

The self-assembly of surfactants in micelles occurs at short time scales (Aniansson & Wali, 1974; Jensen *et al.*, 2013).The hydrophobic domain of the surfactant forms the core of the micelles, while the hydrophilic domain ensures interaction of the aggregate with the aqueous environment, as depicted in Figure 2-5 (Aniansson & Wali, 1974; Jensen *et al.*, 2013). The aggregation is driven by hydrophobic effect, which can be understood thermodynamically as maintenance of the hydrogen-bonding network in water by avoiding disturbances due to the interaction of the hydrophobic domain with water molecules. At higher concentration, the self-assembly of surfactants turns into a macroscopic ordered structure, a liquid crystalline phase. Details on these are discussed in section 2.4.

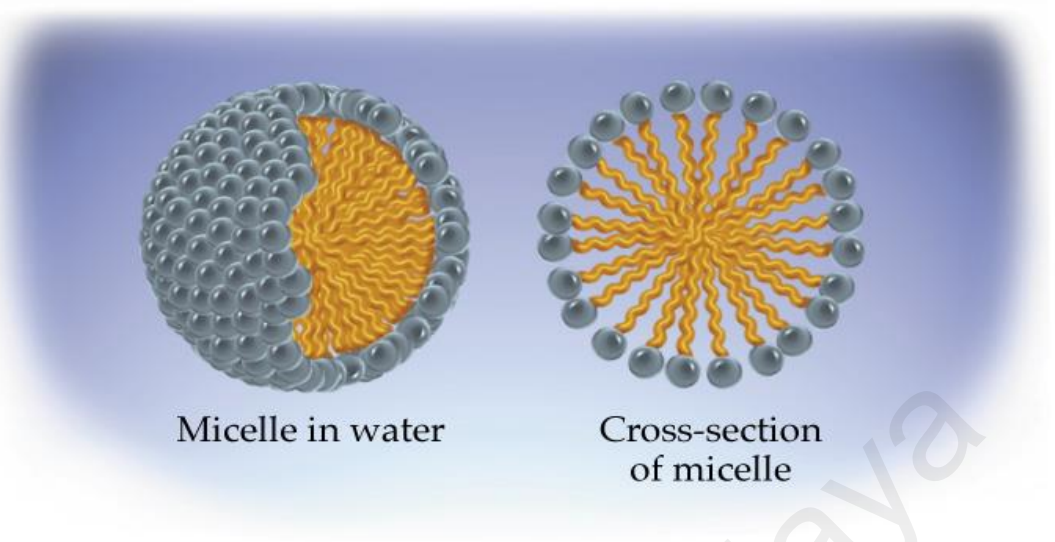


Figure 2-5: Self-assembly of surfactant molecules in micelles (Banerjee, 2012).

2.3 Surfactant molecular structure and related assemblies

2.3.1 The packing parameter

The simplest aggregate of surfactant molecules in water or oil is called a micelle, and surfactant solutions (water or oil) are commonly referred to as micellar solutions (Goyal & Aswal, 2001). Micelles are important in a wide range of fields, such as biochemistry, pharmacy, chemistry, and medicine. They are applied for augmenting and controlled solubilization, enhancing oil recovery and regulating chemical reaction rates. Their presence determines various properties of the surfactant solution, such as viscosity, capacity to solubilize water-insoluble materials and cloud point.

Micelles may appear in different shapes: (1) relatively small, spherical, and prevalent; (2) ellipsoidal, elongated cylindrical (rod-like) micelles with hemispherical ends; (3) large, flat lamellar micelles (dislike extend oblate spheroids (Figure 2-6) (Goyal & Aswal, 2001; Moulik, 1996; Nagarajan, 2002; Milton J Rosen, 2004). The shapes may change into each other, for example spherical micelles of sodium dodecyl sulfate (SDS) changing into a cylindrical configuration in a saline environment (Moulik,

1996; Hayashi & Ikeda, 1980). Parameters such as temperature, overall surfactant concentration, pH, ionic strength, surfactant composition and liquid phase additives affect both, the aggregation number and the shape of a micelle (Rosen, 2004; Winsor, Thornton, & Great, 1968). The calculation principles for the micellar packing shape are relatively straight forward. Aggregated structures have lower energy than isolated molecules in the solution (Fisher, 2000). However, the actual shape of the aggregate can be determined on the basis of the geometry constraints for various micelle shapes and the space occupied by the hydrophilic and hydrophobic groups of the related surfactant molecules. The packing parameter, whichcan be calculated according to Equation 2.1, is facilitated to determine the shape of the micelle (Figure 2-7) (Rosen, 2004):

$$V_H/L_c a_o, \qquad \text{Eq. 2.1}$$

where

V_H = volume of the hydrophobic groups in the micelle core.

a_o = optimal cross-section area occupied by the hydrophilic groups.

L_c = critical chain length (hydrophobic group) in the core.

Therefore, the packing parameter can be defined as a measure of the curvature of the molecular aggregate, that is, the ratio of the tail volume to the optimal head group area. A small packing parameter indicates a small tail area with a dominating head group, while a large packing parameter reflects either a larger tail area or a small head group. Thus, highly curved aggregates (e.g. spheres) in water are attributed to small packing parameters, whereas aggregates with less curvature (e.g. vesicles or macroscopic bilayers) are attributed to large packing parameters (Figure 2-6) (Fisher, 2000).

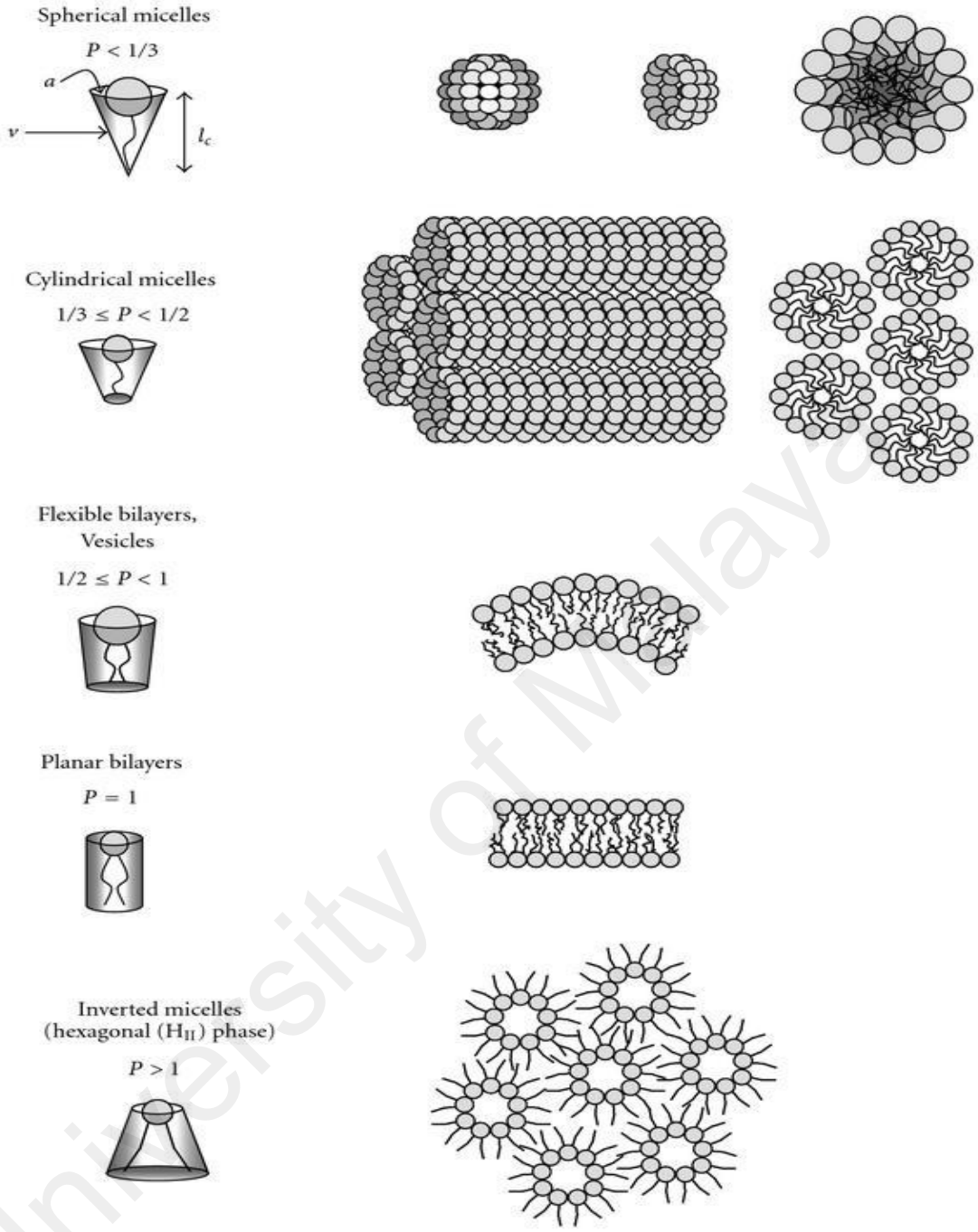


Figure 2-6: Packing parameter of a surfactant molecule and correlated assembly structures (Balazs & Godbey, 2011).

2.3.2 Liquid crystals

More than a century since the discovery of liquid crystal textures, analysis by polarizing microscopy has become a primary tool for the characterization and identification of different liquid crystalline phases. The molecules in a crystal are usually ordered in both position and orientation; this feature can be considered the main

difference between a crystal and a liquid, in which neither positional nor orientation restrictions apply. Liquid crystals do not exhibit positional order like a liquid. However, the orientation of molecules is not at random but reflects a more or less ordered system. The assembly of amphiphilic molecules in a solvent, e.g. surfactants in water, gives rise to liquid crystalline behaviour, if the assembly gets macroscopic, i.e. exceeds the size of a micelle (Rosen, 2004).

Lyotropic liquid crystals are frequently found in everyday life. For example, detergents are often formulated into liquid crystal phases to improve the washing performance (foam stabilization), butter for cooking often contain lyotropic liquid crystal phases; the outermost layer of the skin and the biological membrane contain liquid crystal phases. In conclusion, lyotropic liquid crystals are essential for everyday human activities.

Amphiphilic molecules in the aqueous solution start to assemble in micelles (L_1-phase), which geometric shape depends on the packing parameter of the individual surfactants. The viscosity of surfactant solutions increases because of the ordered molecular arrangement, particularly for larger assembly dimensions, which reflect the formation of liquid crystalline phases (Rosen, 2004). Spherical micelles can easily pack into a (discontinuous) cubic liquid crystal (I_1-phase). Hexagonal liquid crystals (H_1-phase) form upon close packing of cylindrical micelles, while disc-shaped micelles easily turn into lamellar liquid crystals (Lα-phase). The phases are displayed in Figure 2-7. In general, surfactants with bulky head groups prefer the hexagonal phase, whereas surfactants with two hydrophobic chains favour the lamellar phase. The increase of the surfactant concentration changes the shape of a surfactant assembly, from spherical over cylindrical to lamellar. Hexagonal phases are usually encountered at lower surfactant concentration than lamellar phases. Some cylindrical micelles become branched and

interconnected with increasing surfactant concentration, thus leading to a bicontinuous liquid crystalline phase (V_1-phase) (Milton J Rosen, 2004).

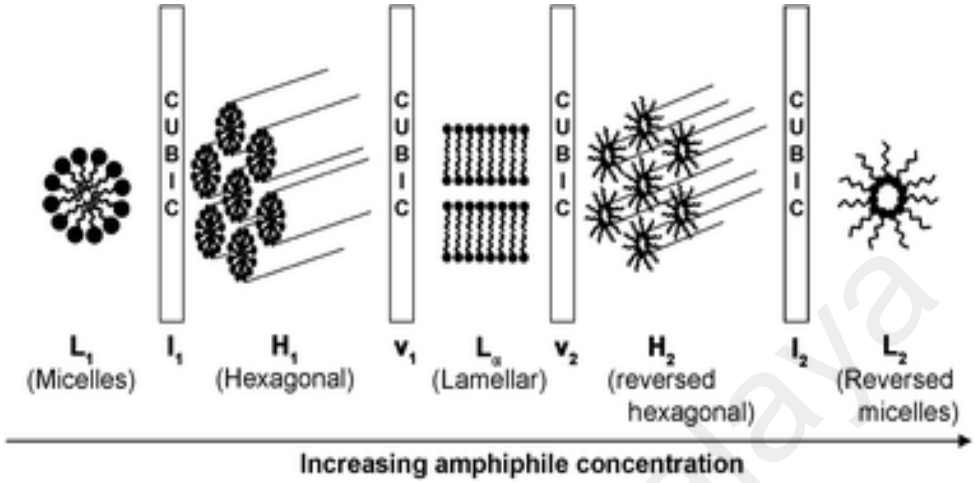


Figure 2-7: Assembly types of surfactants Micelles with cubic (l, V), hexagonal (H), and lamellar (Lα) liquid crystal structures (Kaasgaard & Drummond, 2006).

2.3.3 Emulsion

An emulsion is a ternary mixture of water, an organic liquid that is immiscible with water (typically oil) and an amphiphile (surfactant) that mediates miscibility. It is considered as a colloidal system. The mixture typically exhibits a turbid milky appearance, due to the microscopically separated fluids, giving rise to light scattering (Siwakunakorn, 2006). Emulsions are frequently found in everyday life and play an important role in a wide range of applications. Examples are mayonnaise, food creams, margarine and ice cream (Siwakunakorn, 2006). Applications involve oil recovery, liquid–liquid extraction, extraction from chemically contaminated soils, lubricants and cutting oils, pharmaceuticals and cosmetics, washing, impregnation, textile finishing, and chemical reactions in microemulsions (Schwuger & Stickdornt, 1995). According to the nature of the dispersed and continuous phases, emulsion can be classified into two categories. The first category contains simple emulsions, *i.e*. either water-in-oil (W/O) emulsion or oil-in-water (O/W) emulsion. In a W/O emulsion, oil is considered the continuous phase, while water forms droplets or a dispersed phase; in an O/W emulsion,

water is the continuous and oil the dispersed phase (Pichot, 2010; Jiao, 2002; Opawale, 1997; Dalgleish, 2006). The second category refers to multiple emulsions that can be water-in-oil-in-water (W/O/W) or oil-in-water-in-oil (O/W/O) emulsion. The W/O/W emulsion consist of water droplets dispersed in oil droplets dispersed in the aqueous continuous phase, whereas the O/W/O emulsion consists of oil droplets that are dispersed inside water droplets dispersed in an oil continuous phase (Siwakunakorn, 2006).

Emulsion stabilization is a major issue in basic research, industry, and life science applications. The conversion of a turbid milky emulsion into an optically transparent and thermodynamically more stable micro- or nano-emulsion enables a visual comparison of relative emulsion stabilities. However, any mixture of water and oil would results in an unstable phase, usually leading to quick separation. To enhance the emulsion stability, a third component (a surface active agent, "surfactant") must be added as an emulsifier to mediate the interaction of the immiscible fluids and hence stabilize the 'phase' (Gonzalez, 2009). Thermodynamically unstable emulsions are caused by the large increase in the interfacial area of the dispersed phase liquid compared with that of the continuous phase liquid. The increase in interfacial area is associated with excessive interfacial free energy (according to Equation 2.2) between the two immiscible liquids, thus leading to a thermodynamically unstable system that tends to revert back to the original two-phase system to minimize the interfacial area.

$$\Delta G = \gamma \Delta A \qquad \text{Eq. 2.2}$$

where ΔG is the interfacial free energy, γ is the interfacial tension, and ΔA is the total interfacial area of the dispersed phase.

A number of micro-emulsion phases structured into microscopic and macroscopic assemblies can be formed in the W/S/O system, as shown in Figure 2-6.

The phases can be divided into two main groups. The first group includes micelles that are built of limited or discrete size such as spherical, prolate, or cylindrical aggregates. These micelles are like drops of oil in water, whereas reverse micelles are like drops of water in oil (Figure 2-6) (Muthuprasanna *et al*., 2009) (Tadros, 2013). The second group includes complex, unlimited self-assemblies that present macroscopic structures, like the hexagonal phase as 1D continuity, the lamellar phase structures as 2D continuities, and the bicontinuous cubic phase and sponge phase as 3D continuity (Figure 2-8).

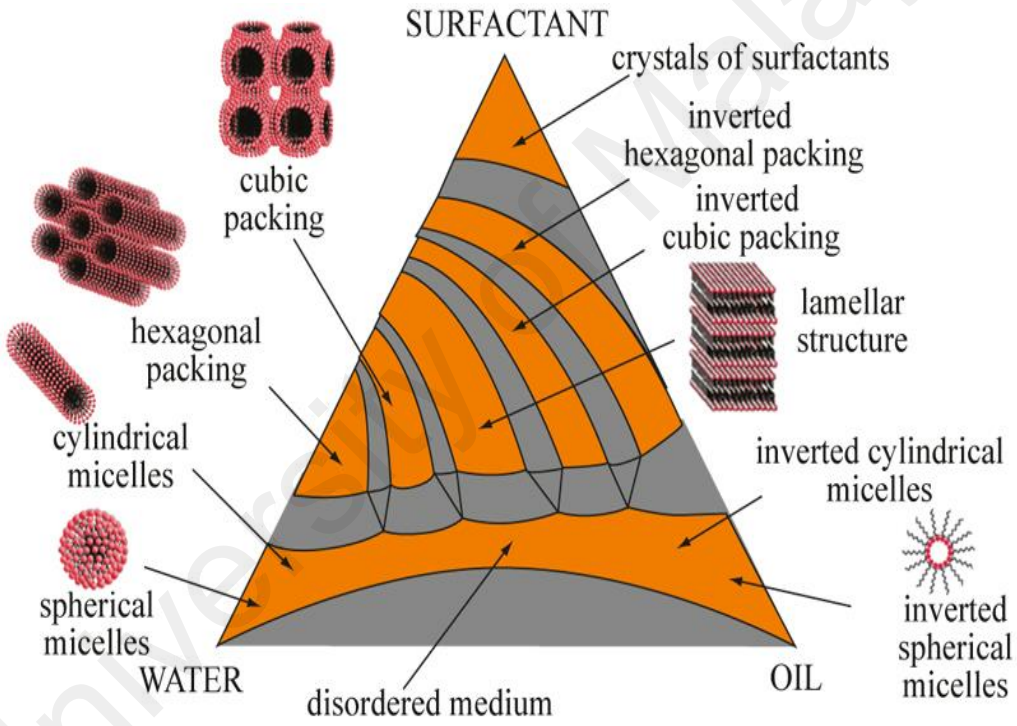


Figure 2-8: Micro emulsion phase structured in the W/S/O system and reverse micelle (Eremin , 2009).

2.4 Environmental effects and surfactant toxicity

Surfactants form the largest amount of synthetic chemicals worldwide. They are routinely deposited into the aqueous environment in diverse ways, either as part of an intended process or by various industrial applications and household wastes. Chemical and physicochemical processes are important sources of toxic substance emission into the marine environment (Emmanuel *et al*., 2005).

Surfactants are found in wastewater discharges, sewage treatment plant effluents, surface and ground water, and sediments worldwide (M.-H. Li, 2008) (Emmanuel *et al*., 2005). Cation surfactants are strongly sorbed by solid materials, particularly clay, whereas anionic surfactants are not appreciably sorbed by inorganic solid materials. Both anionic and nonionic surfactants have significant sorptions in activated sludge and organic sediments (Columbia, 1999). The toxicity of surfactants is indicated by the ability of the compounds to adsorb and penetrate the cell membrane of aquatic organisms (M.-H. Li, 2008) (M J Rosen, Li, Morrall, & Versteeg, 2001). The main reasons of surfactant toxicity on microorganisms are as follows. The interaction of the lipid component of the surfactant with microorganisms leads to the disruption of cellular membranes and loss of microbial contents to the exterior. Protein reaction with the surfactant molecule is crucial to the cell function of microorganisms (Zhang Xiaoxa, 2010) (Volkering, Breure, & Rulkens, 1998) (Laha & Luthy, 1991). In addition, surfactants that are not toxic by itself can cause toxicity owing to the emulsification of highly toxic organic contaminants (Zhang Xiaoxa, 2010) (Shin, Ahn, & Kim, 2005).

A dramatic example was demonstrated in the Deepwater Horizon oil spill in 2010, in which more than 200 million gallons of crude oil was released into the Gulf of Mexico (Figure 2-9) (Goldsmith *et al*., 2011) (Foley, 2012). In order to minimize the adverse effects associated with the oil spill, the application of surfactants was the optimum solution applied to emulsify the oil slick on top of water to help dissipate and degrade the oil (Judith Taylor, 2010). At the end of the acute crisis, 1.8 million gallons of co-dispersant surfactants (9500A di-octyl sodium and sulfosuccinate Doss) were transported to the deep-water oil plumes in the gulf. Although the flow of oil and gas was stopped, researchers continued to evaluate the use of surfactants in the cleanup and their long-term effects on the environment and human health (Reddy CM, Arey JS,

Seewald JS, Sylva SP, Lemkau KL, Nelson RK, Carmichael CA, McIntyre, CP. Fenwick J, Ventura GT, Van Mooy BA, 2011).

Figure 2-9. Deepwater Horizon. Dispersant was pumped directly into the deep-water blowout during the Gulf of Mexico disaster BP ("Dispersant use during the BP Deepwater Horizon oil spill," 2011)

2.5 Sugar based surfactants

At the end of 20th century, the synthesis of surfactants from petroleum-based raw materials gradually declined. A reason is limited resources of petroleum, which resulted in considerably high prices. Besides, growing environmental and health concerns, discouraged the use of phosphorous and highly branched alkenes, which cause eutrophication affect biodegradation processes (Ogawa & Osanai, 2012). The extensive surfactant use in various applications in household products, personal care, and enhance oil recovery enhancement has led to harmful effects because of their large-scale releases to the environment, resulting in toxicity to aquatic organisms (Beach & Wendy, 2011). Thus, new types of surfactants that emphasize on sustainable resources and biocompatibility are necessary. Utilizing biologically renewable resources, such as sugar-based surfactants, is recommended. Sugar surfactants can be classified into glycoside [example, polyglucoside (alkyl polyglucosides, APGs)], alkyl glucamides,

and sugar esters on the basis of the chemical linkage of the two components, *i.e*. sugar and lipid. These biodegradable surfactants exhibit surface-active properties and low human toxicity, which are attributed to their natural components and linkages. These surfactants are also derived from natural and renewable sources, adding to the benefits of a green chemical industry. Therefore, replacing traditional surfactants with more environmentally benign compounds is becoming a trend (Piispanen, 2002).

The main characteristics of sugar-based surfactants (Figure 2-10) are the hydrophilic groups in their polar moiety. Many possibilities for linkage (spacer) between the hydrophobic alkyl chain and hydrophilic sugar head group exist, which together provide unique physicochemical properties to the surfactants. This structural characteristic is becoming highly desirable for commodity surfactants and has been paid much attention by various researchers in surface and colloidal science from both fundamental and technological perspectives (Fukada, 2000).

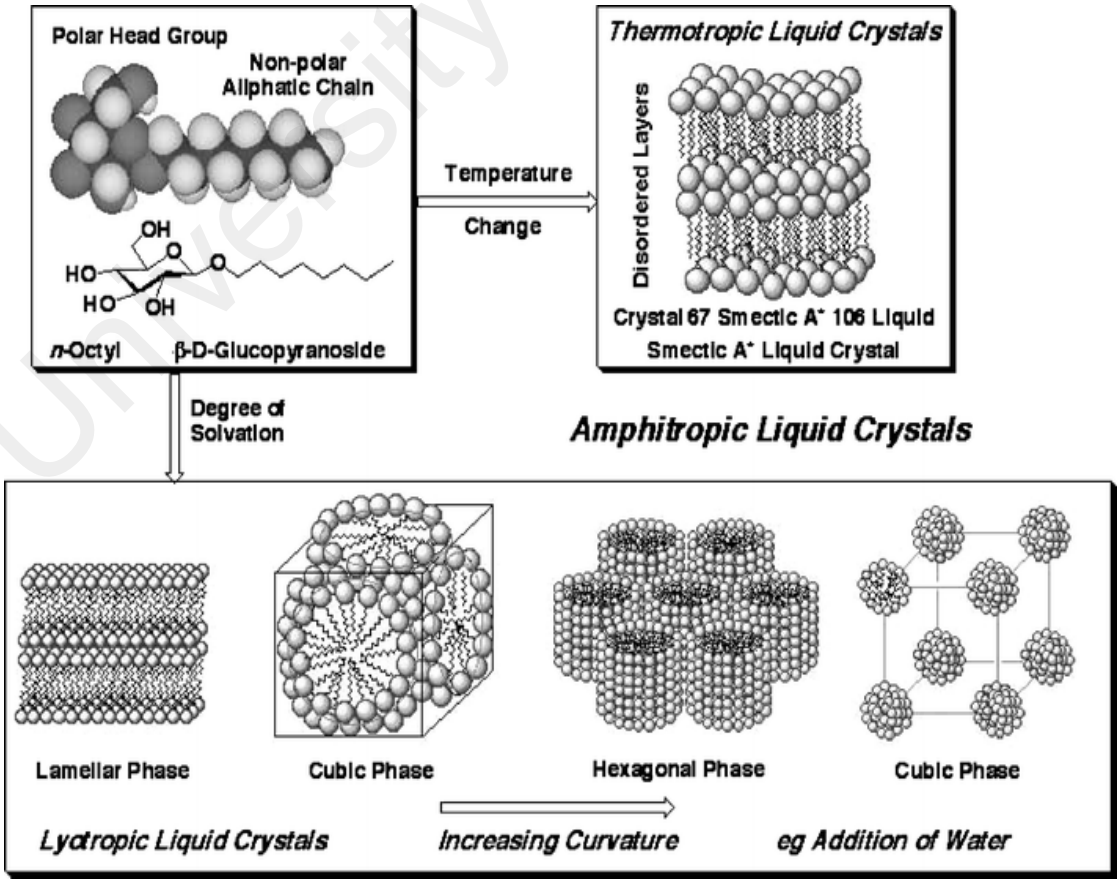


Figure 2-10: Sugar-based surfactants and their physicochemical properties (Goodby *et al*., 2007)

A new generation of bio-related surfactants has emerged. Besides enhanced biodegradability and sustainability of resources, their physicochemical properties provide additional advantages over classic surfactants. All specimens belong to the class of non-ionic surfactants, and include APGs, sorbitan esters and methyl ester glucosides. To enhance the variety, sugar-based surfactants can subsequently be chemically modified. However, surfactants made from glucose, which is widely found in nature, suffer form synthetic limitations (von Rybinski & Hill, 1998). The first challenge is selectivity, owing to the number of hydroxyl groups present in carbohydrates. Typically this demands for the application of protecting and activating groups and/or catalysts, including enzymes. Several studies have investigated this approach and found potential ways to form suitable linkages at different positions of the sugar to produce numerous products involving various carbohydrates (Rodrigues, Canac, & Lubineau, 2000) (Carpenter, Kenar, & Price, 2010) (Hersant *et al*., 2004) (Ranoux, Lemiègre, Benoit, Guégan, & Benvegnu, 2010) (Foley, Phimphachanh, Beach, Zimmerman, & Anastas, 2011). The different solubilities of fatty acid or alcohols, resembling the hydrophobic region, and carbohydrates, which form the basis for the hydrophilic head group, impede their reaction owing to limitations on the reaction medium that has to be equally suitable for both components. Another obstacle is the purification of surfactants, which particularly suffers from the same high interaction potential with various compounds that makes the surfactant highly useful in the first. However, the by far highest challenge is production costs, referring to not only cost-effective resources but an efficient and economic production method as well. Nonetheless, sugar-based surfactants have recently become the most promising surfactants because of their broad applications, multi-functionality, competitive price, high product safety, and environmental compatibility (Fukada, 2000).

2.6 Click chemistry introduction

2.6.1 Fundamentals of click chemistry

Recent developments in biological screening led to a paradigm shift in drug development. While previously biological activity tests resembled the rate-determining step, today automatized multi-sample assays enable an extreme fast screening. Due to this, the isolation or synthesis of potential active compounds is now limiting the screening of potential drugs. This led to the demand of a methodology that enables fast preparation and purification of small amounts of compounds with high structural diversity. Sharpless *et al*. recognized that typically applied methods in drug discovery could not cope with that demand. Instead of a wide array of chemical reactions, many of them requiring extensive treatments of reaction solvents, he suggested to focus on only a few but highly efficient and selective reactions. This led to the concept of click chemistry. (Kolb *et al*., 2001) (Weissleder, Ross, Rehemtulla, & Gambhir, 2010). Click chemistry refers to reactions that are modular and have a wide in scope, but provide high chemical yields, and only generate harmless by-products. Moreover, the process must be stereospecific and provide physiologically stable structures. Besides, the reaction should not be sensitive to oxygen or water, thus enabling the utilization of standard commercial solvents (Lewis *et al*., 2002) (Manetsch *et al*., 2004) (Akeroyd & Klumperman, 2011) (Such, Johnston, Liang, & Caruso, 2012). The concept was developed in parallel with synthetic libraries, aiming for the same target.

2.6.2 Azide–alkyne cycloaddition: the basics

Organic azides and alkynes are largely inert towards both biological molecules and aqueous environments. However, Huisgen *et al*. reported the 1,3-dipolar cycloaddition of these two functional groups, which is now commonly known as the Huisgen cycloaddition (Huisgen, Knorr, Möbius, & Szeimies, 1965). Unfortunately the reaction required elevated temperatures and often produced mixtures of the two

regioisomers when applying asymmetric alkynes. Various attempts to control the regioselectivity have been reported, but without much success (Tornøe, Christensen, & Meldal, 2002) (Appukkuttan, Dehaen, Fokin, & Eycken, 2004) (Rostovtsev *et al*., 2002). The reaction only gained a boost of interest after the discovery of a copper-catalyst by Meldal and coworkers (Tornøe *et al*., 2002) and Sharpless and coworkers (Rostovtsev *et al*., 2002), which exclusively yielded the 1,4-disubstituted 1,2,3-triazole.

2.6.3 Fundamental of organic azide

Azide is the anion with the formula N_3^-. It a linear anion that can be represent by several resonance structures, an important one being $N^-=N^+=N^-$ (Bräse, Gil, Knepper, & Zimmermann, 2005). The aliphatic azido group is also linear, with the N α in a sp^2 hybridization state carrying a lone electron pair while the other nitrogens can be considered as sp-hybridized (Cenini *et al*., 2006). There are several methods for the synthesis of organic azides, but most of these are prepared directly or indirectly from sodium azide (Turnbull & SCRIVEN, 1988).

2.6.4 Mechanistic aspects of the Copper-catalyzed azide–alkyne cycloaddition (CuAAC)

Since its discovery in the last decade by Sharpless and co-workers, the CuAAC, i.e. the coupling of terminal alkynes and organic azides catalyzed by a Cu(I)-catalyst, has become the most popular reaction for applications technique in chemistry, biology, and material science (Oyelere, Chen, Yao, & Boguslavsky, 2006). The dipolar character and the relative instability of the azido group enables nucleophiles to attack at the electrophilic terminal nitrogen, whereas the more electron-rich alkyl N can react with electrophiles and coordinate to transition metals, as indicated in Figure 2-11 (Hein & Fokin, 2010a).

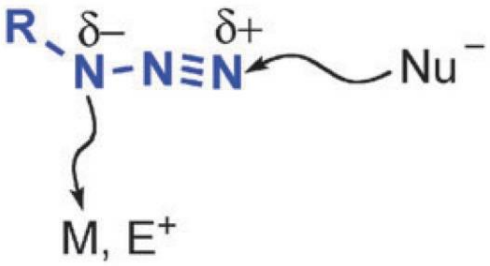
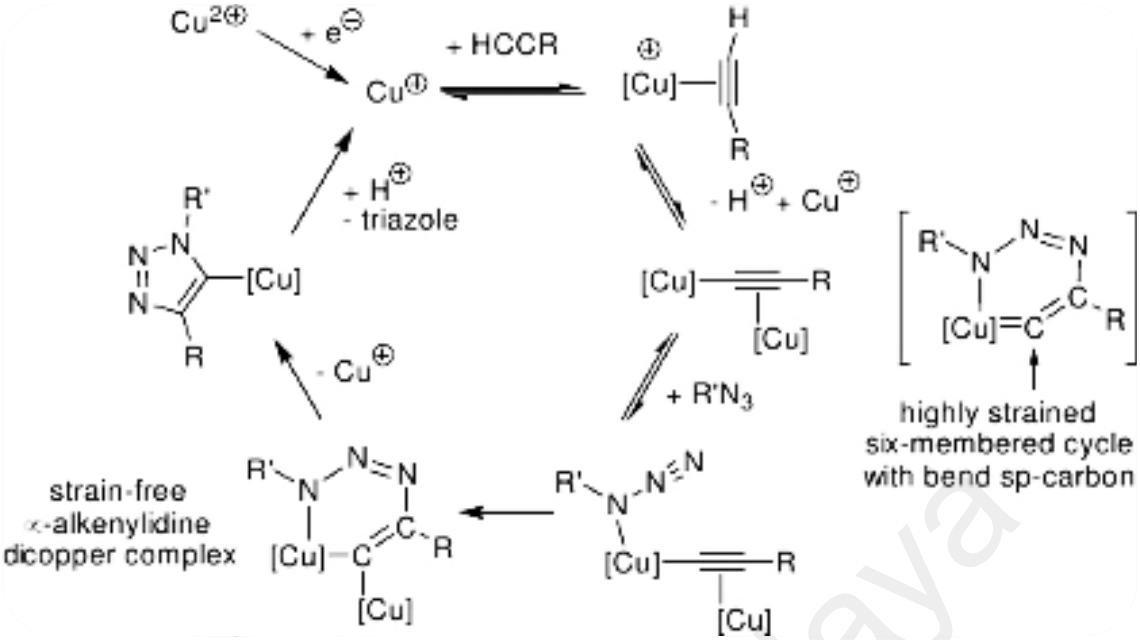


Figure 2-112: Common reactivity patterns of organic azides (Hein & Fokin, 2010a).

The copper-catalyzed (CuAAC) reaction mechanism is complex, and some aspects are still unclear, such as the form of the copper acetylide intermediate. However, the mechanism proceed in a stepwise manner starting with the generation of copper (I) acetylide. In the presence of a base, the terminal acetylene hydrogen, being the most acidic, is deprotonated first to give a Cu acetylide intermediate. The azide is then activated by coordination to copper forming another intermediate. In the next step, the nucleophilic carbon on the copper (I) acetylide reacts with the electrophilic terminal nitrogen on the azide and a strained copper metallacycle forms. This is followed by protonation; the source of proton is the hydrogen, which was pulled off from the terminal acetylene by the base. The metallocycle undergoes ring contraction and the triazole product is formed by dissociation, which regenerates the copper catalyst for further reaction cycles (Himo *et al*., 2005) (Akeroyd & Klumperman, 2011) (Hein & Fokin, 2010a). The process is depicted in Scheme 2-5.



Scheme 2-5: Proposed mechanistic pathways for the Cu(I)-catalyzed azide-alkyne cycloaddition (Straub, 2007).

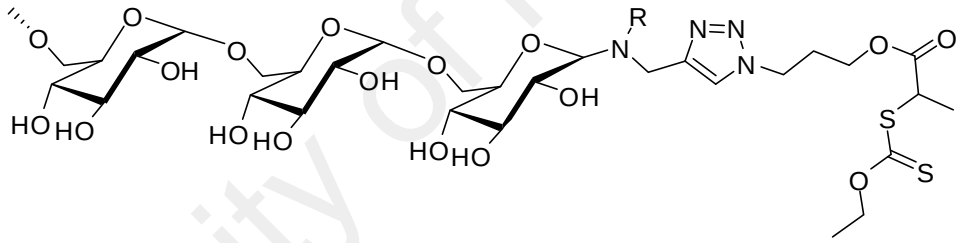
2.6.5 The effect of solvent on the reaction yield of CuAAC

In general, the copper-catalyzed azide-terminal alkyne cycloaddition (CuAAC) is well known as a mild reaction, which can be processed under a wide range of conditions. It is among the most useful tools for building new molecular architectures, because it is compatible with most common functional groups. A wide range of protic and aprotic solvents (such as THF, EtOH, DMSO and tert-butanol) including water, has been utilized for the CuAAC reaction since its discovery. Recently, Lee *et al.* (Lee, Park, Jeon, & Kim, 2006), have reported a two phase system involving dichloromethane and water for the CuAAC reaction, and found that the yield and the rate of reaction significantly increased compared to other organic solvent systems.

2.6.6 Click chemistry reaction in a wide range of synthesis application

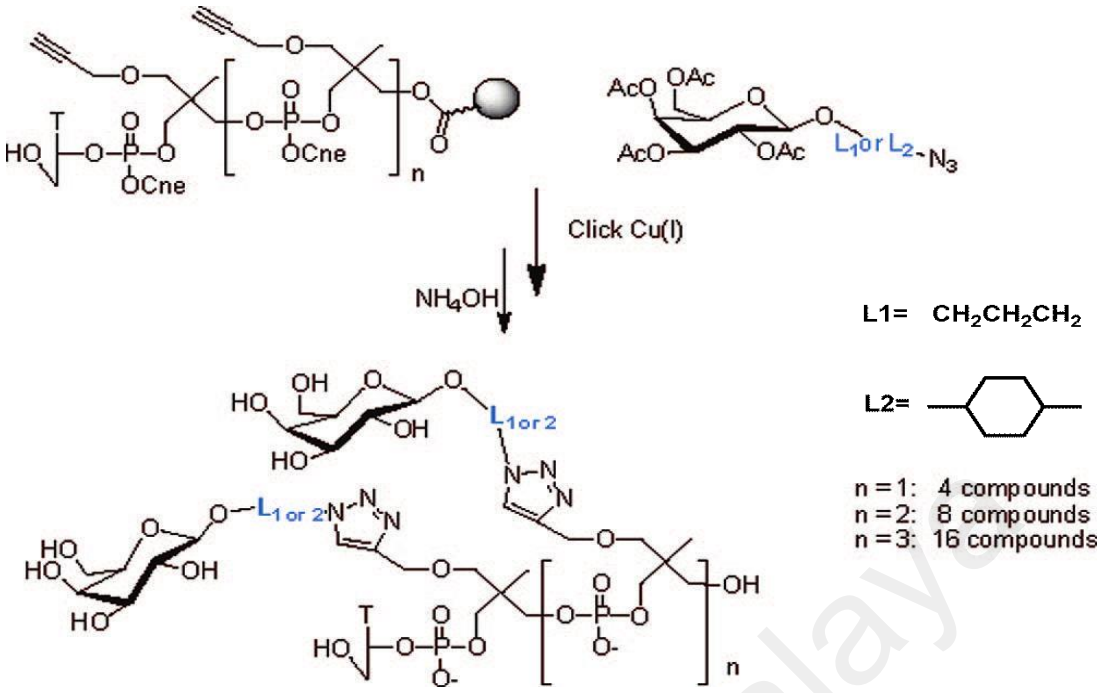
Click chemistry is a promising technique to engineer the architecture and function of materials (Dedola, Nepogodiev, & Field, 2007a; Lutz & Zarafshani, 2008; Meldal & Tornøe, 2008; Such *et al*., 2012) The synthesis of 1,2,3-triazole is attracting much attention because of its key characteristics, such as the reactants are easy to

introduce, highly specific and stabile (generally inert to severe hydrolytic, and oxidizing conditions, even at high temperature), while the reaction product is chemically and biologically stable (Hein & Fokin, 2010a) (Avti, Maysinger, & Kakkar, 2013) (Kwak, Moon, Choi, Murugan, & Park, 2013). Given the high efficiency of the Cu-catalyzed 1,2,3-triazole synthesis, numerous studies have applied click chemistry in diverse fields. Dedola *et al*. (2007) provided a survey that highlights the synthesis of simple glycoside and oligosaccharide mimetics, glyco-macrocycles, glycopeptides, glyco-clusters, and carbohydrate arrays. Akeroyd and Klumperman (2011) reviewed the application of click chemistry in conjunction with living radical polymerization (LRP) for the synthesis of advanced macromolecular architectures (Scheme 2-6).



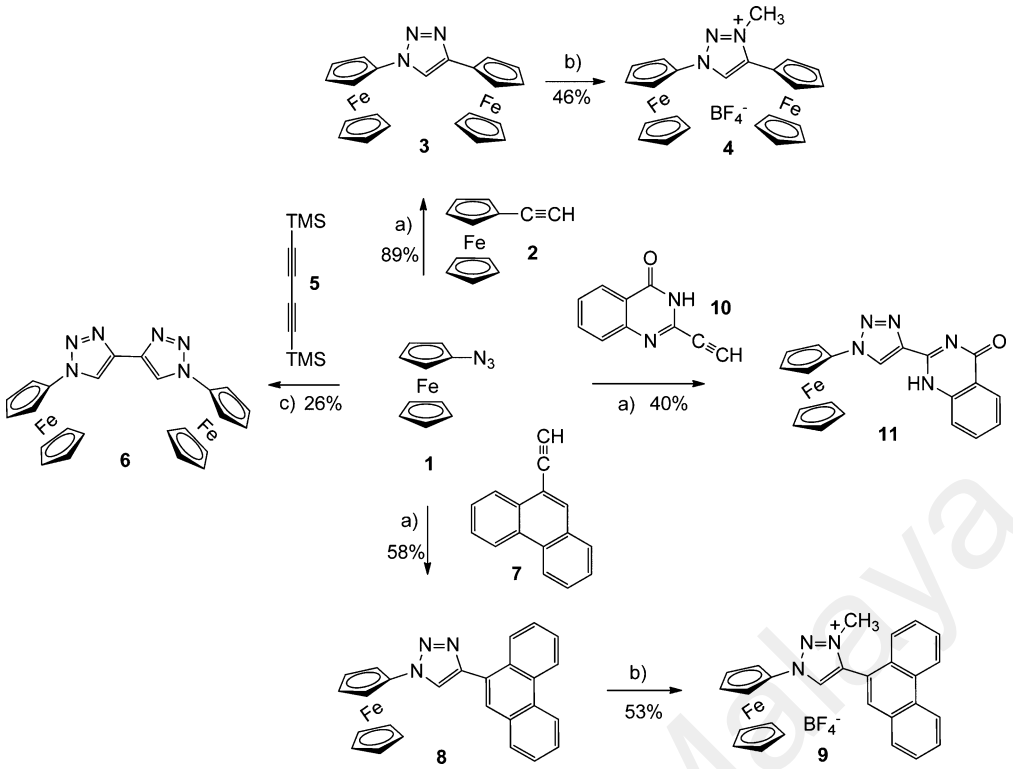
Scheme 2-6: Dextran RAFT agent prepared via click chemistry (adapted from Akeroyd & Klumperman, 2011).

Pourceau and co-workes (Pourceau, Meyer, Vasseur, & Morvan, 2008) have reported the synthesis of di-, tri-, and tetragalactosyl clusters bearing a phosphodiester linkage based on solid support involving a polyalkyne scaffold by that was coupled with an azidoalkyl galactoside in CuAAC fashion, as depict in Scheme 2-7.



Scheme 2-7: Di-, tri-, and tetragalactosyl clusters were synthesized using using CuAAC reaction (Pourceau *et al*., 2008).

Recently, the synthesis of symmetrical bis-triazole using copper-catalyzed azide-alkyne cycloaddition (CuAAC) has received considerable interest based on related coordination chemistry properties (Schuster, Yang, Raubenheimer, & Albrecht, 2009) (Albrecht, 2008) (Karthikeyan & Sankararaman, 2009) (Nakamura, Terashima, Ogata, & Fukuzawa, 2011) (Heckenroth, Kluser, Neels, & Albrecht, 2008), (Stefani, Canduzini, & Manarin, 2011). Many symmetrical and unsymmetrical bis-triazoles have published (Aizpurua *et al*., 2010) (Fiandanese, Bottalico, Marchese, Punzi, & Capuzzolo, 2009) (Doak, Scanlon, & Simpson, 2011) (Romero, Orenes, Tárraga, & Molina, 2013). Besides, a number of monosubstituted and di-substituted ferrocene-coupled triazoles have been prepared by using the copper-catalyzed click reaction, as shown in Scheme 2-8.



Scheme 2-8: Preparation of 1-Substituted Ferrocene-Triazoles : a conditions: (a) $CuSO_4 \cdot {}_5H_2O$, sodium ascorbate, THF/H_2O, room temperature; (b) CH_2Cl_2, $(MeO)_3BF_4$, room temperature; (c) BuNF (TBAF),$CuSO_4 \cdot {}_5H_2O$, sodium ascorbate, THF/H_2O, room temperature (Romero *et al*., 2013).

Chapter 3 : New Y-shaped surfactants from renewable resources

3.1 Introduction

The concept of sugar-based surfactants *via* a Fischer glycosylation leading to surfactants with high water solubility is very interesting from both ecological and industrial perspective (Salkar, Minamikawa, & Hato, 2004). Attractive features involve, the exclusive utilization of renewable resources, *i.e*. a carbohydrates and fatty acids, which constitute the most abundant groups of natural products, and the perspective of an environmentally friendly product (Korchowiec, Baba, Minamikawa, & Hato, 2001) (Nilsson, Soderman, & Johansson, 1998). Given the increasing interest in sugar-based surfactants, the main challenge remains in their synthesis (glycoside surfactants). This is attributed to the limited miscibility of the two components, i.e. the hydrophilic carbohydrate and the hydrophobic hydrocarbon chain. Only short chain alcohols can act as solvents for both reactants, but unfortunately give rise to non-surfactant impurities in alkyl poly glycosides (APGs). Moreover, the solubilization of reducing carbohydrates, like glucose, requires high temperature. In addition to solubility issues and selectivity, the synthesis of these surfactants is complex because of the formation of isomeric mixtures, resulting in a variety of conformations in the carbohydrate domain (Masakatsu Hato *et al*., 1999). Click chemistry is a promising approach to the modular synthesis of sugar-based surfactants because it enables the efficient combination of the two surfactant antipodes (hydrophilic and hydrophobic domains). These leads to alkyl triazole glycoside (ATG) surfactants (Sani, Heidelberg, Hashim, & Farhanullah, 2012), exhibiting similar surfactant behaviour than APGs, but they can be prepared at significantly lower temperature. However, our concept is to synthesize a new classes of non-ionic surfactants exhibiting a three-armed (Y) shape, combining two parallel carbohydrate molecules as hydrophilic head group with one hydrocarbon chain.

The linkage between the two units was employed click chemistry coupling (Sani *et al*., 2012). The surfactant type was expected to provide high solubility in water.

3.2 Materials and methods

3.2.1 Chemicals

Chemicals were purchased from commercial sources and were used without further purification. TLC was performed on precoated plates of silica gel 60 (GF254 by Merck), and developed by treatment with 15 % ethanolic sulfuric acid and subsequent heating. Column chromatography was performed by the flash technique on silica gel 35-60 mesh (Merck).

3.2.2 Characterization and determination of interfacial properties

Structural identities are based on NMR spectra (^{1}H and ^{13}C, recorded on a Bruker AVN-400 MHz spectrometer). Matrix-assisted laser desorption/ionization (MALDI) time of flight (TOF) mass spectra were recorded at the Mass Spectra Service Centre of the National University of Singapore on a Shimadzu/Kratos (Columbia, MD) AXIMA CFR mass spectrometer in reflectron mode. The samples were co-precipitated with 2,5-dihydroxy-benzoic acid (DHB, 5mg/100µl in MeOH/H_2O 1:1) and were irradiated by a N_2-laser at λ =335 nm. For an analysis of the physicochemical properties, all solutions were prepared by using distilled water. The surface tension was measured with a KSV Sigma 702 tensiometer,using the DuNouy ring method. Surface tension measurements of aqueous solutions of the surfactant product were recorded at 25±0.1°C under atmospheric pressure. The critical micelle concentration (CMC) value was assessed at the intersection of the linear portions of the plot of the surface tension against the logarithm of the surfactant concentration. The surface tension at this intersection point is called the surface tension at CMC. The experiments were repeated twice with high repeatability and the curves coincided.

The phase behaviour of the glycolipids was investigated lyotropically under the Optical Polarizing Microscope (OPM) (Olympus BH-2 OPM equipped with Mettler FF82 hot stage and Mettler FP80 Central Processor) using the contact penetration technique (Milkereit *et al*., 2005; von Minden *et al*., 2000). Two different solvents were applied at room temperature (around 27 ºC), one of which is polar (water), while the other one is non-polar (1-undecanol).

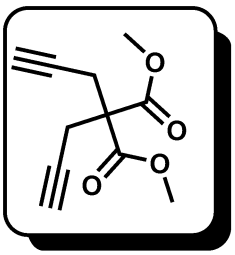
3.2.3 Krafft and cloud points

The measurement of the Krafft temperature, T_k, applied heating of an ice cooled surfactant solution, 1 % (m/m), on a hotplate stirrer with temperature controller at a rate of 5 °C min^{-1} over the range from 10 to 100 °C. The sample was optically monitored for changes of transparency. Similarly, surfactant solutions of 10 mM concentration were heated at same rate to determine the cloud point.

3.2.4 Preparation and Stability of the Emulsion

Emulsion was prepared based on a ratio of 19 parts water and 1 part oil. A surfactant concentration of 0.5% surfactant was applied and the mixtures were mixed with a homogenizer (T10 basic, IKA) for approximately 2 minutes at room temperature at a speed of 14,450 rpm. The emulsion samples were stored at room temperature and monitored on phase separation over a period of a few weeks.

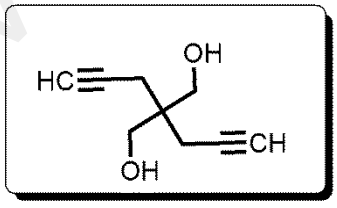
3.2.5 Experimental



Chemical Formula: $C_{11}H_{12}O_4$
Molecular Weight: 208.2106

3.2.5.1 Dimethyl 2,2-di(propynyl)malonate

A procedure similar to that reported in literature (Carney, Donoghue, Wuest, Wiest, & Helquist, 2008) was employed. Dimethyl malonate (6.0 mL, 52 mmole) was added dropwise to a suspension of sodium hydride (60 % wt in mineral oil, 4.22 g, 105.5 mmol) in dry THF (100 mL) which was stirring at 10°C. Then the reaction mixture was left stirring for 10min., and then propargyl bromide (80 % wt. In toluene, 12.0 mL, 107.7 mmol) was added dropwise. The reaction mixture was warmed to room temperature and stirred for overnight. The reaction mixture was extracted three times with water and Et_2O. The combine organic phases were washed with brine water, dried over $MgSO_4$, filtered and concentrated on a rotary evaporator leaving white solid. The solid was crystallized from ethyl acetate to give 9.44 g of a crystalline white solid (84 % yield).

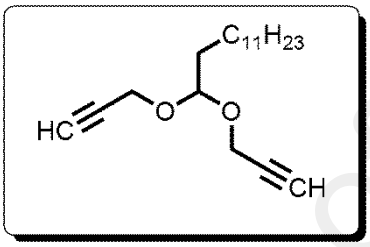


Chemical Formula: $C_9H_{12}O_2$
Molecular Weight: 152.1904

3.2.5.2 4,4-Di(hydroxymethyl)-1,6-heptadiyne (5)

Lithium aluminium hydride (1.2 g, 32.43 mmol) was added to stirred solution of the Dimethyl 2,2-di(propynyl)malonate (3.0 g, 14.42 mmol) in anhydrous THF at 10 ° C. The reaction mixture was allowed to warm to room temperature and stirred for overnight. 1.2 mL of water was added slowly to stop the reaction, an aq. 10 % NaOH

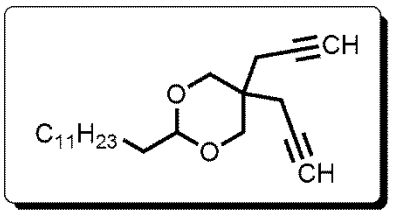
solution (1.2 mL), and then additional water (3.6 mL). Then the reaction mixture was left to stir for around 30 min. until the suspended solids become white. The reaction mixture was filtered and the solid rinsed with CH_2Cl_2, the filtrate dried over $MgSO_4$ and concentrated in a rotary evaporator to produce 2.0g colorless crystal (91% yield). ^{1}H NMR ($CDCl_3$) δ = 3.71 (s, 4H, 2x OC<u>H</u>$_2$); 2.35 (d, 4H, 2x CH_2 propargyl); 2.05 (t, 2H, 2x CH propargyl). ^{13}C NMR ($CDCl_3$) δ = 80.35 (2x <u>C</u> ≡CH); 71.19 (2x C≡ <u>C</u>H); 66.21 (2x <u>C</u>H_2OH); 42.00 (C quaternary); 21.80 (CH_2 propargyl). ^{13}C NMR ($CDCl_3$) δ =80.34 (2x <u>C</u> ≡CH); 71.22 (2x C≡ <u>C</u>H); 66.26 (2x <u>C</u>H_2OH); 42.08 (C quaternary); 21.65 (CH_2 propargyl).



Chemical Formula: $C_{19}H_{32}O_2$
Molecular Weight: 292.4562

3.2.5.3 Lauraldehyde dipropargyl acetal (6)

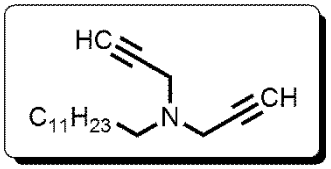
A mixture of lauraldehyde (4.6 g, 24.9 mmol), (3.5 mL, 62.3 mmol, 2.5 eq.) propargyl alcohol, (0.9 g, 4.7 mmol) p-toluenesulfonic acid monohydrate, (20mL) toluene, and 4 g of 4 Å molecular sieves was stirred at 60 °C for 4h in vacuum system. The mixture was quenched with triethylamine (5mL), washed with saturated $NaHCO_3$, 2N KOH and dried over $MgSO_4$. The solution was concentrated to give a pale yellow oil (5.35 g. yield 74 %). ^{1}H NMR (MeOD, *d4*) δ = 4.8 (t, 1H, C<u>H</u> $(OCH_2)_2$ acetal); J=5.66; 4.24 (2x m, 2H, 2x OC<u>H</u>$_2$CH); 2.42 (2x t, 1H, 2x C≡CH propargyl); J= 2.42; 1.65 (m, 2H, α-CH2); 1.38 (m, 2H, B-CH_2); 1.20-1.34 (m, 16H, bulk-CH_2); 0.88 (t, 3H, CH_3); J=6.76; ^{13}C NMR (MeOD, *d4*) δ = 103.0 (<u>C</u>H acetal); 80.9 (2x <u>C</u> ≡CH); 75.5 (2x C≡ <u>C</u>H); 54.2 (2x O<u>C</u>H_2), 34.4 (α-CH_2); 33.14 (B-CH_2); 30.83, 30.76, 30.74, 30.53 (bulk-CH_2); 25.54 (∞-1 CH2); 23.80 (∞-CH_2); 14.59 (CH_3).



Chemical Formula: $C_{22}H_{36}O_2$
Molecular Weight: 332.5200

3.2.5.4 5,5-Bis(2-propynyl)-2-undecyl-1,3-dioxane (7)

A mixture of lauraldehyde (1.92 mL, 8.68 mmol), (1.5 g, 9.85 mmol, 1.1 eq) 4,4-di(hydroxymethyl)-1,6-heptadiyne, (0.9 g, 4.7 mmol) p-toluenesulfonic acid monohydrate, (20 mL) toluene, and 4 g of 4 Å molecular sieves was stirred at 60 °C for 4h in vacuum system. The mixture was quenched with triethylamine (5 mL), washed with an aqueous solution of $NaHCO_3$, 2N KOH and dried over $MgSO_4$. The solution was concentrated to give a dark yellow oil (2.5 g. 80 % yield). ^{1}H NMR ($CDCl_3$) δ = 4.46 (t, 1H, CH-acetal); 3.98, 3.63 (2x d, 4H, 2x O$\underline{C}H_2$CH); 2.72, 2.19 (2x d, 2H ,2x $C\underline{C}H_2$ propargyl), J= 2.85; 2.05 (q, 2H, 2x CH propargyl), J=2.76; 1.62- 1.67 (m, 2H, CH$\underline{C}H_2$ chain); 1.47-1.22 (m, 20H, bulk-CH_2); 0.91 (t, 3H, CH_3). ^{13}C NMR ($CDCl_3$) δ = 102.75($\underline{C}$H acetal); 80.65 (2x $\underline{C}$ =CH); 78.56 (2x C= $\underline{C}$H); 71.56, 71.18 (2x O$\underline{C}H_2$), 35.16 (α-CH_2); 34.75 (C quaternary); 29.65, 29.63, 29.56, 29.54, 29.50, 29.35 (bulk-CH_2); 23.89 (CH_2 propargyl); 22.69 (B-CH_2); 22.54, 22.36 (∞, ∞° , CH_2); 14.12 (CH_3).

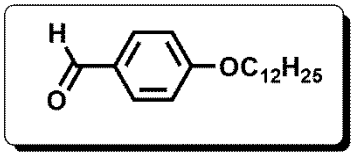


Chemical Formula: $C_{18}H_{31}N$
Molecular Weight: 261.4454

3.2.5.5 *N*,*N*-dipropargyl dodecylamine (10)

Dodecyl amine (2g, 10.7mmol) and K_2CO_3 (3.1 g, 22.6 mmol, 2.1 eq.) were suspended in acetonitrile. (2.5 mL, 22.6 mmol) propargyl bromide was added dropwise to the mixture and stirred at room temperature for 24h. The reaction mixture was filtered and the resulting solution was concentrated on a rotary evaporator yielding

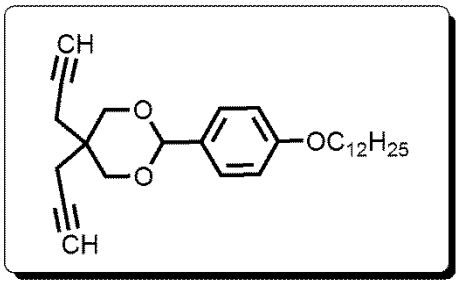
yellow oil. The crude oil was purified by flash chromatography on a silica gel column using chloroform as eluent, resulting in 2 g of clear oil (yield 71 %). ^{1}H NMR ($CDCl_3$) δ =3.43 (t, 4H, N[CH_2C]$_2$); 2.51 (t, 2H, CH_2N); J=7.60; 2.20 (quartet, 2H, 2x $\equiv$CH); 1.46 (m, 2H, α-CH_2); 1.34-1.19 (m, 18H, bulk-CH_2); 0.88 (t, 3H, CH_3); ^{13}C NMR ($CDCl_3$) δ =78.88 (2x $CH_2\underline{C}CH$); 72.74 (2x $CH_2C\underline{C}H$); 53.08 (α-$\underline{C}H_2N$); 42.14 (2x $N\underline{C}H_2C$); 31.88 (β-CH_2); 29.62, 29.59, 29.54, 29.47, 29.30 (bulk-CH_2); 27.44, 27.31 (ω-1,ω'-1); 22.64 (ω-CH_2); 14.04 (CH_3).



Chemical Formula: $C_{19}H_{30}O_2$
Molecular Weight: 290.4403

3.2.5.6 *p*-dodecanoxybenzaldehyde

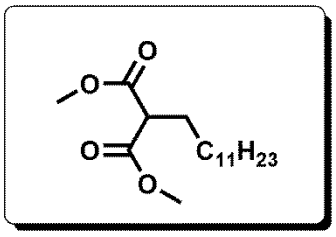
The compound was prepared similarly according to literature (Liu & Houghton, 2012). P-hydroxybenzaldehyde (5 g, 40.9 mmol) was dissolved in 50 mL DMF, (16.8 g, 122mmol) K_2CO_3 and (11.7 mL, 49.2 mmol) 1-bromododecane were added to the solution. The reaction mixture was stirred for 4h at 80 °C, then removed the DMF by rotary evaporator, added water and extracted ethyl acetate. The combine organic phases was washed with brine water, dried over $MgSO_4$ and concentrate in rotary evaporator. The product was purified by flash column chromatography using 20 % ethyl acetate in hexane as eluent to resulting 11.6 g as a brown liquid (98 % yield).



Chemical Formula: $C_{28}H_{40}O_3$
Molecular Weight: 424.6154

3.2.5.7 2-(4(dodecyloxy)phenyl)-5,5-bis(2-propynyl)-1,3-dioxane (11)

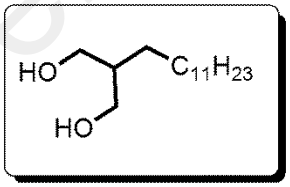
A mixture of p-dodecanoxybenzaldehyde (2.0 g, 6.88 mmol), (1.2 g, 7.89 mmol, 1.1 eq.) 4,4-di(hydroxymethyl)-1,6-heptadiyne, (0.9 g, 4.7 mmol) p-toluenesulfonic acid monohydrate, (20 mL) toluene, and 4 g of 4 Å molecular sieves was stirred at 60 °C for 4h in vacuum system. The mixture was quenched with triethylamine (5 mL), washed with an aqueous solution of $NaHCO_3$ and 2N KOH, dried over $MgSO_4$ and concentrated in rotary evaporator. The product was purified by flash column chromatography using hexane as eluent to resulting 2.1 g as a yellowish-white powder (72 % yield). ^{1}H NMR ($CDCl_3$) δ = 7.39, 6.89 (2x d, 4H, CH- benzene); 5.37 (s, 1H, (OC<u>H</u>)$_2$ acetal); 4.10, 3.86 (2x d, 4H, 2x OC<u>H</u>$_2$C); 3.94 (t, 2H, OCH$_2$-chain); 2.80, 2.24(2x d, 4H, OC<u>H</u>$_2$ propargyl), J=2.56; 2.08, 2.05 (2x t, 2H, 2x C<u>H</u> propargyl); 1.80- 1.71 (m, 2H, B-CH$_2$); 1.47-1.22 (m, 18H, bulk-CH$_2$); 0.88 (t, 3H, CH$_3$). ^{13}C NMR ($CDCl_3$) δ =159.69 ($C_{benzene\text{-}O\text{-}chain}$); 130.18 ($C_{benzene\text{-}acetal}$); 127.34, 114.31 (2x CH benzene); 101.95 (CH acetal); 80.55, 78.53 (2x <u>C</u> propargyl); 71.73, 71.29 (2x CH propargyl); 68.08 (OCH2 chain); 35.12 (<u>C</u> quaternary); 31.92 (B-CH$_2$); 29.65, 29.63, 29.59, 29.57, 29.39, 29.35, 29.21 (bulk-CH$_2$); 26.0 (∞-CH$_2$); 22.69, 22.66 (2x CH2 propargyl); 14.12 (CH$_3$).



Chemical Formula: $C_{17}H_{32}O_4$
Molecular Weight: 300.4336

3.2.5.8 Dimethyl-2-dodecylmalonate (12)

A procedure similar to (Matoba, Kajimoto, Nishide, & Node, 2006) that methyl 2-(2-propynyl)-4-pentynoate was employed in the synthesis. Dimethyl malonate (6.0 mL, 52 mmole) was added dropwise to a suspension of sodium hydride (60 % wt in mineral oil, 2.11 g, 52.75 mmol) in dry THF (100 mL) which was stirring at 10 °C. Then the reaction mixture was left stirring for 10min., and then 1-bromo dodecane (12.72 mL, 53 mmol) was added dropwise. The reaction mixture was warmed to room temperature and stirred for overnight. The reaction mixture was extracted three times with water and Et_2O. The combine organic phases were washed with brine water, dried over $MgSO_4$, filtered and concentrated on a rotary evaporator leaving white solid. The solid was crystallized from ethyl acetate to give 11.0 g of a crystalline white solid (93 % yield).

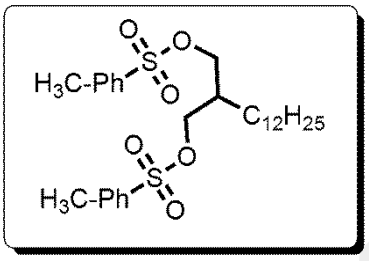


Chemical Formula: $C_{15}H_{32}O_2$
Molecular Weight: 244.4134

3.2.5.9 2-Dodecylpropane-1,3-diol (13)

The synthesis was similar method to 4,4-di(hydroxymethyl)-1,6-heptadiyne. Lithium aluminium hydride (1.2 g, 32.43 mmol) was added to stirred solution of the Dimethyl 2,2-di(propynyl)malonate (4.3 g, 14.42 mmol) in anhydrous THF at 10 ° C. The reaction mixture was allowed to warm to room temperature and stirred for overnight. 2 mL of water was added slowly to stop the reaction, an aq. 10 % NaOH solution (2 mL), and then additional water (3.2 mL). Then the reaction mixture was left

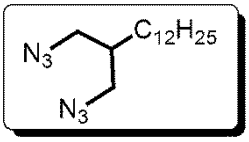
stirring for around 30 min. until the suspended solids became white. The reaction mixture was filtered and the solid rinsed with CH_2Cl_2, the filtrate dried over $MgSO_4$ and concentrate in rotary evaporator to produce 3.3 g colorless oil (94 % yield). ^{1}H NMR ($CDCl_3$) δ = 3.83- 3.60 (m, 4H, 2x CH_2OH); 1.87-1.70 (m, 1H, CH); 1.34- 1.17 (m, 20H, bulk-CH_2); 0.88 (t, 3H, CH_3). ^{13}C NMR ($CDCl_3$) δ = 66.37 (2x CH_2OH); 41.99 (CH); 29.84, 29.67, 29.64, 29.61, 29.53, 29.32 (bulk-CH_2); 27.75 (α-CH_2); 27.21 (B-CH_2); 22.65 (∞-CH_2); 14.22 (CH_3).



Chemical Formula: $C_{15}H_{30}O_6S_2$
Molecular Weight: 370.5251

3.2.5.10 2-Dodecylpropane-1,3-diyl bis(4-methylbenzenesulfate (14)

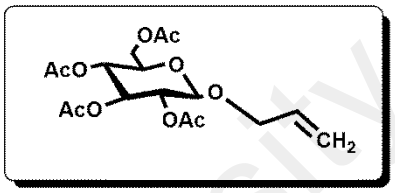
To a solution of 2-dodecylpropane-1,3-diol (1.6 g, 6.54 mmol) in 50 mL THF was added 10 mL of 40 % NaOH followed by 4-toluenesulfonyl chloride (3.74 g, 19.63 mmol, 3 eq) then the reaction mixture were stirred for overnight. The reaction mixture was poured into water and extracted with ethyl acetate. The combine organic phases was dried over $MgSO_4$ and concentrate in rotary evaporator to provide pure colorless crystal 3 g (83 % yield). ^{1}H NMR ($CDCl_3$) δ = 7.74, 7.35 (2x d, 4H, CH- benzene); 3.74-3.71 (m, 4H, 2x CH_2-Tosyl); 2.44 (s, 6H, 2x CH_3Tosyl); 2.00-1.93 (m, 1H, $CH(CH_2\text{-Tosyl})_2$); 1.26 (m, 20H, bulk-CH_2); 0.88 (t, 3H, CH_3). ^{13}C NMR ($CDCl_3$) δ = 144.8 ($\underline{C}SO_3$ tosyl); 132.6 ($\underline{C}CH_3$ tosyl); 130.0, 127.8 (4x CH tosyl); 68.79, 67.84 (2x CH_2-Tosyl); 37.97 (CH); 31.86 (α-CH_2); 29.64, 29.59, 29.58, 29.56, 29.47, 29.39, 29.30, 26.86, 26.26 (bulk-CH_2); 25.55 (B-CH_2); 22.62 (∞-CH_2); 21.53 (CH_3 tosyl); 14.01 (CH_3).



Chemical Formula: $C_{15}H_{30}N_6$
Molecular Weight: 294.4389

3.2.5.11 2-Dodecylpropane-1,3-diazido (15)

2-dodecylpropane-1,3-diyl bis(4-methylbenzenesulfate) (2 g, 3.61 mmol) and anhydrous NaN_3 (0.94 g, 14.47 mmol, 3 eq.) was added to a DMF and the mixture was stirred at 80 °C for overnight. Removed the solvent by evaporation in vacuo, washed the residue with water and DCM, separated the organic layer and dried over $MgSO_4$ and then concentrated to give 2.8 g (93 % yield). ^{1}H NMR ($CDCl_3$) δ = 3.34-3.23 (m, 4H, 2x CH_2N_3); 1.73-1.66 (m, 1H, $C(CH_2N_3)_2$); 1.18 (m, 20H, bulk-CH_2); 0.81 (t, 3H, CH_3). ^{13}C NMR ($CDCl_3$) δ = 52.68 (2x CH_2N_3); 38.65 (CH); 31.89 (∞-CH_2); 29.63, 29.61, 29.54, 29.32, 29.13 (bulk-CH_2); 26.67 (B-CH_2) ; 22.66 (α -CH_2); 14.08 (CH_3).

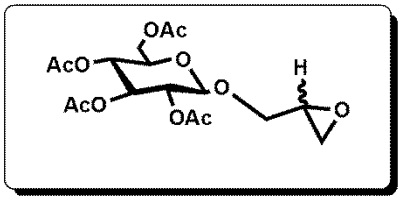


Chemical Formula: $C_{17}H_{24}O_{10}$
Molecular Weight: 388.3665

3.2.5.12 Allyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (1)

(10 g, 25.6 mmol) glucose pentaacetate and 1.9 mL (27.8 mmol, 1.1 eq.) allyl alcohol were dissolved in 120 mL dichloromethane and treated with 4.8 mL (38.2 mmol, 1.5 eq.) BF_3xEt_2O. The reaction was stirred at room temperature for 3 hour and then washed with an aqueous solution of $NaHCO_3$ and dried over $MgSO_4$. The solvent was concentrated and crystalized by ethanol to get (6.4 g) white crystal and the residue was purified by column chromatography using hexane: ethyl acetate (3:1) as eluent to obtain (2.3 g), total yield was 87 %. ^{1}H NMR ($CDCl_3$) δ = 5.80-5.65 (m, 1H, allylic CH=); 5.20-5.10 (m, 2H, allylic CH_2=); 5.08 (dd~t, 1H, H-3); J=9.5 Hz; 4.95 (dd~t, 1H, H-4); J=10.0 Hz; 4.8 (dd~t, 1H, H-2); J=9.5 Hz; 4.47 (d, 1H, H-1); J=8.0 Hz; 4.25-

4.09 (m, 2H, H-6); 4.06-3.91 (2m, 4H, H-6, OCH_2); 3.64 (ddd, 1H, H-5); J=4.5, 2.5 Hz; 1.97, 1.93, 1.91, 1.89 (4x s,3H, 4x Ac); ^{13}C NMR ($CDCl_3$) δ = 170.51, 170.11, 169.31,169.20 (4x $\underline{C}OCH_3$); 133.26 ($\underline{C}H=CH_2$); 117.46 ($CH=\underline{C}H_2$); 99.43 (B C1); 72.72 (C4); 71.62 (C2); 71.16 (OCH2); 69.88 (C6); 68.31 (C3); 61.82 (C5); 20.60, 20.53, 20.47 (4x OCH_3).

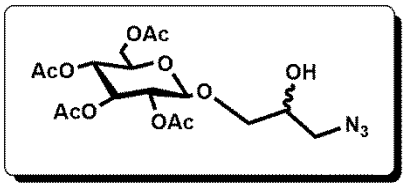


Chemical Formula: $C_{17}H_{24}O_{11}$
Molecular Weight: 404.3659

3.2.5.13 2,3-Epoxypropyl 2,3,4,6-Penta-*O*-acetyl-*β*-D-glucopyranoside (3)

Compound **1** (2 g, 5.15mmol) was dissolved in 100 mL dichloromethane, MCPBA (2.2 g, 12.8 mmol, 2.5 eq.) was added to the solution and the mixture left stirred overnight at room temperature. The reaction mixture washed with an aqueous solution of $NaHCO_3$ twice. The organic layer was dried over $MgSO_4$ and evaporatord in vacuum to concentrate. 20 mL of ethyl acetate was added to the mixture to crystalize to give pure compound 2 (1.0 g) white crystal and the residue was purified by flash chromatography over silica gel (3:1 hexane: ethyl acetate) to give (0.6 g) , total yield was 77 %. ^1H NMR ($CDCl_3$) δ = 5.12/5.05 (2 dd~t, 1H, H-3); J=9.50 Hz; 5.00/4.95 (2 dd~t, 1H, H-4); J=10.0, 4.91/4.89 (2 dd, 1H, H-2); J=9.5 Hz; 4.57/4.48 (2 d, 1H, H-1); J=8.0 Hz; 4.19/4.16 (dd, 1H, H-6a); J=12.0 Hz; 4.04 (dd~bd, 1H, H-6b); 3.91, 3.79 (2 dd, 1H, $OC\underline{H}_2$ I); J=3.0 Hz; 3.74, 3.64 (2 dd, 1H, OCH_2 II); J=6.5 Hz; 3.64 (m, 1H, H-5); 3.05 (m, 1H, $CH_2C\underline{H}OCH_2$); J=2.5 Hz; 2.69 (m, 1H, $CH_2CHOC\underline{H}_2$ I); 2.56/2.46 (m, 1H, CH2CHOC$\underline{H}_2$ II); 2.08, 2.07, 2.04, 2.01 (4x s, 3H, 4x $COCH_3$); ^{13}C NMR ($CDCl_3$) δ =170.96, 170.46, 170.05, 169.31 (4x $\underline{C}OCH_3$); 100.90, 100.39 (2 x C1); 72.69, 72.65 (2x C3); 71.79 (C5); 71.02 (C2); 70.43, 68.99 (OCH_2); 68.20, 68.19 (C4); 61.62 (C6);

50.41, 50.15 ($CH_2C\underline{H}OCH_2$); 43.97, 43.92 ($CH_2CHOC\underline{H}_2$); 20.57, 20.52, 20.45 (4x $CO\underline{C}H_3$).



Chemical Formula: $C_{17}H_{25}N_3O_{11}$
Molecular Weight: 447.3939

3.2.5.14 (2′-hydroxy-3′-azidopropyl)-2,3,4,6-Penta-*O*-acetyl-*β*-D-gluco pyranoside (4)

Anhydrous NaN_3 (0.8 g, 12.3 mmol, 2.5 eq.) was added to a DMF solution of compound **2** (2 g, 4.9 mmol, 1 eq.) and the solution was stirred at 80 °C for overnight. Removed the solvent by evaporation in vacuo, washed the residue with water and DCM, separated the organic layer and dried over $MgSO_4$ and then concentrated to give compound **3** as a syrup (2 g, yield 90 %). ^{1}H NMR ($CDCl_3$) δ = 5.22 (dd~t, 1H, H-3); J= 9.44; 5.10-5.03 (2 dd~t, 1H, H-4); J=10.0; 4.97 (2 dd, 1H, H-2); J=9.5; 4.55 (2 d, 1H, H-1); J=8.0; 4.25-4.15 (m, 2H, H-4, H-6); 3.99-3.69 (m, 4H, H-5, $OC\underline{H}_2CHOH$, $OCH_2C\underline{H}OH$); 3.40-3.27 (m, 2H, $CHOHC\underline{H}_2N_3$); 2.10, 2.06, 2.04, 2.01 (4x s, 3H, 4x Ac); ^{13}C NMR ($CDCl_3$) δ = 170.61, 170.14, 169.42, 169.38 (4x $\underline{C}OCH_3$); 101.40, 101.28 (C1); 72.72,72.57 (C3); 72.16 ($OCH_2\underline{C}HOH$); 71.95 ($O\underline{C}H_2$); 71.24, 71.22 (C2); 69.66, 69.53 (C5); 68.41, 68.35 (C4); 61.97, 61.95 (C6); 53.00, 52.98 ($CHOH\underline{C}H_2N_3$); 20.58, 20.29 ($CO\underline{C}H_3$).

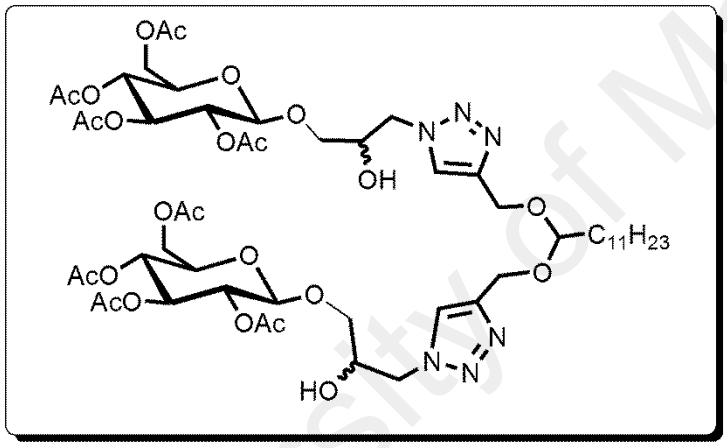
3.2.5.15 General Procedure for Click-Chemistry

A solution of the sugar azide (4 mmole) and the divalent hydrocarbon precursor (2 mmol) in methanol (50 mL) was treated with copper (II) salt ($Cu(OAc)_2$ or $CuSO_4$ 0.4 mmol, 15 % eq.) and sodium ascorbate (0.4 g, 2.0 mmol, 45 % eq.). The solution was stirred at room temperature for overnight. The reaction mixture was filtered and concentrated under reduced pressure, and the residue was purified by filtrating through

5 cm silica gel with 1:1 ethyl acetate: hexane as eluent to remove the remaining starting materials (sugar and alkyl chain), followed by methanol to collect the surfactant precursors.

3.2.5.16 General procedure II for surfactant de-protection

The acetylated surfactant was carried out using methanol as solvent and treated with a catalytic amount of NaOMe. TLC revealed complete conversion after 4 hours stirring at room temperature. The catalyst was neutralization by Amberlite IR120 (H^+) and then the solvent was evaporatord to give the final surfactant.

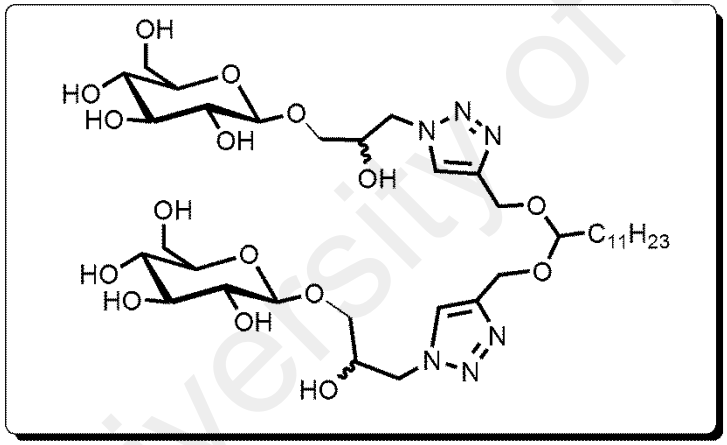


Chemical Formula: $C_{52}H_{80}N_6O_{24}$
Molecular Weight: 1173.2174

3.2.5.15.1 1,1-Bis{1-[2-hydroxy-3-(2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranosyloxy)-propyl]-(1,2,3-triazol-4-yl)-methyl}-dodecane (18).

Sugar azide **4** (2.0 g, 4.4 mmol) and dipropargyl acetal **6** (0.6 g, 2.2 mmol) were coupled with Cu(OAc) (80 mg, 0.4 mmol) and Na-ascorbate (0.4 g, 2 mmol) in MeOH according to the general procedure **I** to provide **18** (1.6 g, 64 %) as a brown syrup. In order to simplify the NMR analysis the compound was acetylated at the remaining hydroxyl group. ^{1}H NMR ($CDCl_3$) δ = 7.65/7.63 (2 s, 2H, 2x triazole); 5.32 (m, 2H, CHOH); 5.27/5.18 (2 dd~dt, 2H, 2x H-3); J = 9.5 Hz; 5.11/5.10 (2 dd~dt, 2H, H-4); *J* = 10.0 Hz; 5.05/5.01 (dd, 2H, H-2); J = 9.0 Hz; 4.78-4.48 (m, 11H, 2x H-1, CH-acetal, 2x CH_2-triazole, 2x triazole-$\underline{C}H_2OCH$); 4.28, 4.25 (2 dd~dt, 2H, 2x H-6a); 4.16- 4.07

(dd~bd, 2H, 2x H-6b); 3.98-3.89 (2dd, 2H, 2x OCH_2a); J = 4.5 Hz; 3.75 (ddd, 2H, 2x H-5); J = 4.5, 2.0 Hz; 3.67-3.59 (2dd, 2H, 2x OCH_2b); J = 6.0 Hz; 2.09- 2.01 (m, 30H, 10x CH_3–acetate); 1.74-1.68 (m, 2H, γ -CH_2); 1.40- 1.24 (m, 18H, CH_2-bulk); 0.87 (t, 3H, CH_3). ^{13}C NMR ($CDCl_3$) δ =170.49, 170.04, 169.8, 169.58, 169.36, 169.32, 169.29 (10x CH_3CO); 145.32, 145.22 (2x C-triazole); 123.66, 123.59 (2x CH-triazole); 102.67, 102.64 (2x C-1); 101.07, 100.64 (CH-acetal); 72.60, 72.51 (2x C-3); 72.00 (2x CHOH); 71.17, 71.09 (2x C-2); 70.41, 70.15 (2x C-5); 68.32, 68.28 (2x C-4); 67.39, 67.30 (2x OCH_2); 61.78, 61.74 (2x C-6); 58.71 (2x triazole-$\underline{C}H_2OCH$); 49.57, 49.46 (2x $CHOH\underline{C}H_2$-triazole); 33.13(β-CH_2); 31.82 (∞-2); 29.56, 29.52, 29.47, 29.39, 29.24 (bulk-CH_2); 24.56 (γ -CH_2); 22.58 (∞-1); 20.92, 20.70, 20.68, 20.62, 20.58, 20.47, 20.45 (10x CH_3CO); 14.01 (CH_3).

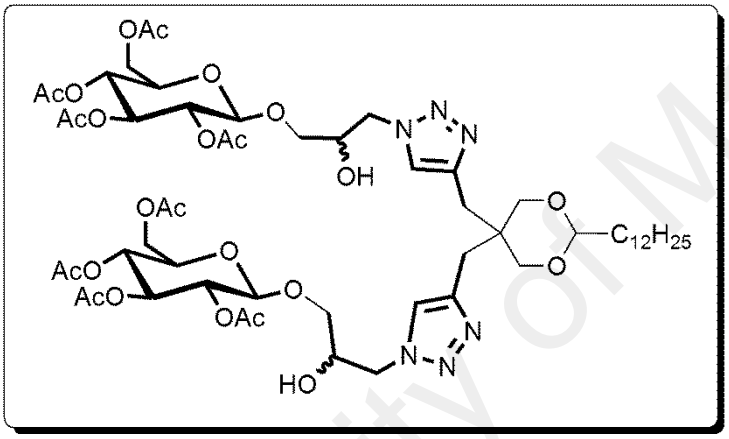


Chemical Formula: $C_{36}H_{64}N_6O_{16}$
Molecular Weight: 836.9240

3.2.5.15.2 1,1-Bis{1-[2-hydroxy-3-(*β*-D-*gluco*pyranosyloxy)-propyl]-(1,2,3-triazol-4yl)-methyl}dodecane (19).

18 (1.2 g, 1.0 mmol) was reacted according to general procedure **II** to produce **19** (0.73 g, 91 %) as brown syrup. ^{1}H NMR (CD_3OD) δ =8.05 (s, 2H, 2x triazole); 4.74 (t, 1H, CH-acetal); 4.70 (d, 2H, OCH_2a); 4.65 (d, 2H, CH_2b); J = 12.0 Hz; 4.63-4.48 (m,4H, 2x (triazole-$\underline{C}H_2OCH$); 4.33, 4.30 (2d~t, 2H, H-1); J = 8.0 Hz; 4.19- 4.12 (m, 4H, 2x $\underline{C}H_2$-triazole); 3.91 (dd~bd, 2H, H-6a); 3.68 (dd, 2H, 2x H-6b); J = 12.0 Hz; 3.60- 3.52 (m, 2H, 2x CHOH); 3.43 (2 dd, 2H, H-3); J = 9.0 Hz; 3.40-3.30 (m, 4H, H-

4, H-5); 3.28 (dd, 2H, H-2); J = 9.0 Hz; 1.69- 1.64 (m, 2H, β-CH_2); 1.33- 1.20 (m, 18H, CH_2-bulk); 0.87 (t, 3H, CH_3). ^{13}C NMR (CD_3OD) δ = 144.46 (2x C-triazole); 124.86 (2x CH-triazole); 103.29 (2x C1); 102.58(CH-acetal); 76.67 (2x C-3); 76.51 (2x C-5); 73.75, 73.69 (2x C-2); 70.78 (2x OCH_2); 70.63, 70.61 (2x C-4); 68.95 (2x CHOH); 61.28 (2x C-6); 58.27 (2x triazole-$\underline{C}H_2OCH$); 52.86, 52.65 (2x CHOH$\underline{C}H_2$-triazole); 32.97 (β-CH_2); 31.74 (∞-2); 29.46, 29.43, 29.40, 29.23, 29.15 (bulk-CH_2); 24.31 (γ -CH_2); 22.41 (∞-1); 13.14 (CH_3). HRMS (MALDI) calcd. for $C_{36}H_{64}N_6O_{16}$ [M+Na]: 859.4277, 860.4310 (1x ^{13}C, 40 %); found: 859.4294 (100%), 860.4 (32%).

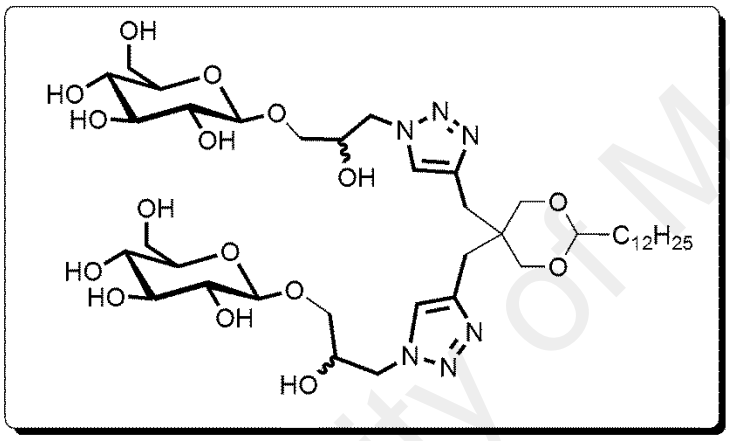


Chemical Formula: $C_{56}H_{86}N_6O_{24}$
Molecular Weight: 1227.3078

3.2.5.15.3 5,5-Bis{1-[(2-hydroxy-3-(2,3,4,6-tetra-*O*-acetyl-*β*-D-*gluco*pyranosyloxy)-propyl]-1,2,3-triazol-4-yl-methyl}-2-undecyl-1,3-dioxane (20).

Sugar azide **4** (2.0 g, 4.4 mmol) and dipropargyl acetal **7** (0.7 g, 2.2 mmol) were coupled with $Cu(OAc)_2$ (80 mg, 0.4 mmol) and Na ascorbate (0.4 g, 2 mmol) in MeOH according to the general procedure **I** to provide **20** (1.5 g, 56 %) as a brown syrup. ^{1}H NMR (DMSO, 80°C) δ = 7.84-7.76 (m, 2H, 2x triazole); 5.26 (dd~m, 2H, 2x H-3); J = 9.5 Hz; 4.91 (dd~t, 2H, 2x H-4); J = 9.5 Hz; 4.85-4.79 (m, 4H, 2x H-1, H-2), J = 8.0, 10.0 Hz; 4.43 (t, 1H, CH-acetal); 4.40-4.20 (m, 8H, 2x (CH_2OC, CHOH$C\underline{H}_2$-triazole); 4.18 (dd, 2H, H-6a); 4.08 (dd, 2H, H-6b); J = 12.0 Hz; 3.74-3.65 (m, 2H, 2x CHOH); 3.64 (bd, 2H, OCH_2a); 3.54 (bd, 2H, CH_2b); 3.48- 3.32 (m, 2H, H-5); J = 5.0, 2.0 Hz; 2.92, 2.40 (ds, 4H, triazole-CH_2); 2.01, 2.00, 1.99, 1.97, 1.95, 1.93 (s, 24H, 8x CH_3-

acetate); 1.58- 1.51 (m, 2H, β-CH_2); 1.40- 1.20 (m, 18H, bulk-CH_2); 0.85 (t, 3H, CH_3). ^{13}C NMR (DMSO, 80°C) δ = 170.27, 169.81, 169.56, 169.45 (8x CH_3CO); 141.72 (2x C-triazole); 125.20 (2x CH-triazole); 102.23 (CH acetal); 100.57, 100.43 (2x C-1); 73.23 (2x $\underline{C}H_2C$); 72.91, 72.86 (2x C-2); 71.71 (2x C-4); 71.45 (2x C-3); 71.29 (2x OCH_2); 69.14 (2x C-5); 68.72, 68.55 (2x CHOH); 62.41 (2x C-6); 53.00 (2x CH_2-triazole); 36.08 (C quaternary); 34.81 (β-CH_2); 31.64 (∞-2); 29.33; 29.01 (bulk-CH_2); 28.17, 27.41 (2x CCH_2-triazole); 23.76 (B-CH_2); 22.38 (∞-1); 20.76, 20.67, 20.59 (8x CH_3CO); 14.16 (CH_3).

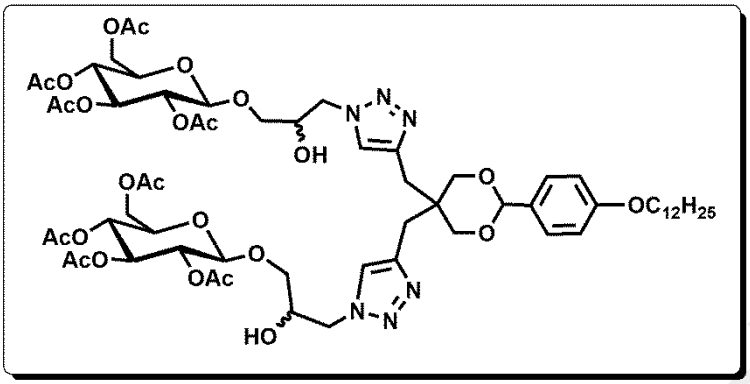


Chemical Formula: $C_{40}H_{70}N_6O_{16}$
Molecular Weight: 891.0144

3.2.5.15.4 5,5-Bis{1-[(2-hydroxy-3-(*β*-D-*gluco*pyranosyloxy)-propyl]-1,2,3-triazol-4-yl-methyl}-2undecyl-1,3-dioxane (21).

20 (1.0 g, 0.80 mmol) was reacted according to general procedure **II** to produce **21** (0.70 g, 96 %) as brown syrup. ^{1}H NMR (CD_3OD) δ = 7.99 (bs, 2H, triazole); 4.69-4.40 (m, 4H, 2x (H-1, OCH_2a)); 4.32 (t, 1H, CH-acetal); 3.96 (bs, 2H, 2x OCH_2b); 3.92-3.22 (m, 22H, 2x (H-6a,b, H-3, H-5, H-2, H-4, CHOH, CH_2-triazole, $CH\underline{C}H_2$-triazole); 1.65 (m, 2H, β-CH_2); 1.44 (m, 2H, γ-CH_2); 1.31 (m, 18H, bulk-CH_2); 0.91 (t, 3H, CH_3). ^{13}C NMR (CD_3OD) δ = 142.32 (2x C-triazole); 128.93 (2x CH-triazole); 104.75, 104.69 (2x C1); 104.05(CH-acetal); 78.03 (2x C-3); 77.90 (2x C-5); 75.13, 75.06 (2x C-2); 74.52 (2x $C\underline{C}H_2OCH$); 72.18, 72.06 (2x OCH_2); 71.56 (2x C-4); 70.29(2x CHOH); 62.67 (2x C-6); 54.47 (2x $CHOH\underline{C}H_2$-triazole); 35.90 (C); 33.07, 30.78, 30.75, 30.73,

30.67, 30.47 (bulk-CH_2); 25.03 (2x CCH_2-triazole); 23.74 (∞-1); 14.46 (CH_3). ^{13}C-peaks for glycerol-linker and CH_2N were broad and very weak due to diastereomeric effects, while triazole carbons could not be observed.

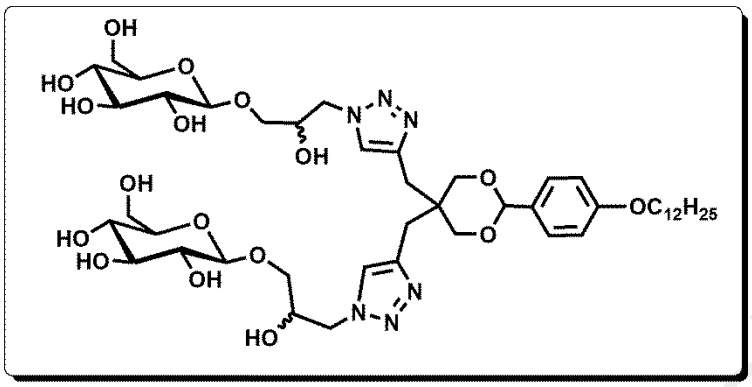


Chemical Formula: $C_{62}H_{90}N_6O_{25}$
Molecular Weight: 1319.4032

3.2.5.15.5 5,5-Bis{1-[(2-hydroxy-3-(2,3,4,6-tetra-*O*-acetyl-*β*-D-*gluco*pyranosyloxy)-propyl]-1,2,3-triazol-4-yl-methyl}-2-(4-dodecyloxy-phenyl)-1,3-dioxane (22).

Sugar azide **4** (2.0 g, 4.4 mmol) and dipropargyl acetal **11** (0.9 g, 2.2 mmol) were coupled with $Cu(OAc)_2$ (80 mg, 0.4 mmol) and Na-ascorbate (0.4 g, 2 mmol) in MeOH according to the general procedure **I** to provide **22** (1.7 g, 60 %) as a brown syrup. ^{1}H NMR ($CDCl_3$) δ = 7.94, 7.81, 7.60 (3x bs, 2H, triazole); 7.43, 6.89 (2x d, 4H, benzene); 5.44 (bs, 1H, CH-acetal); 5.26, 5.23, 5.21 (2 dd~td, 2H, 2x H-3), J= 9.4; 5.11-4.98 (m, 4H, 2x H-4, H-2); 4.63-3.45 (m, 24H, 2x H-1, H-5, H-6a, H-6b, OCH_2, CHOH, $CHCH_2$-triazole, CH_2O-acetal); 3.22- 3.0, 2.82- 2.73 (m, 4H, 2x triazole-CH_2); 2.07, 2.06, 2.04, 2.03, 2.01, 2.00 (s, 24H, 8x CH_3-acetate); 1.80- 1.73 (m, 2H, β-CH_2); 1.48-1.20 (m, 18H, bulk-CH_2); 0.88 (t, 3H, CH_3). ^{13}C NMR ($CDCl_3$) δ = 170.69, 170.19, 169.60, 169.42 (8x CH_3CO); 159.67 ($C_{benzene\text{-}O\text{-}chain}$); 142.21 (2x C-triazole); 130.47 ($C_{benzenel}$); 129.73 (2x CH-triazole); 127.42, 114.27(2x CH benzene); 102.08 (CH acetal); 101.33, 101.16 (2x C-1); 74.61, 74.47 (2x $\underline{C}H_2C$); 72.58, 72.54 (2x C-3); 72.01, 71.09 (2x C-5); 71.70 (2x OCH_2); 71.23, 71.20 (2x C-2); 69.19, 69.09 (2x CHOH); 68.35,

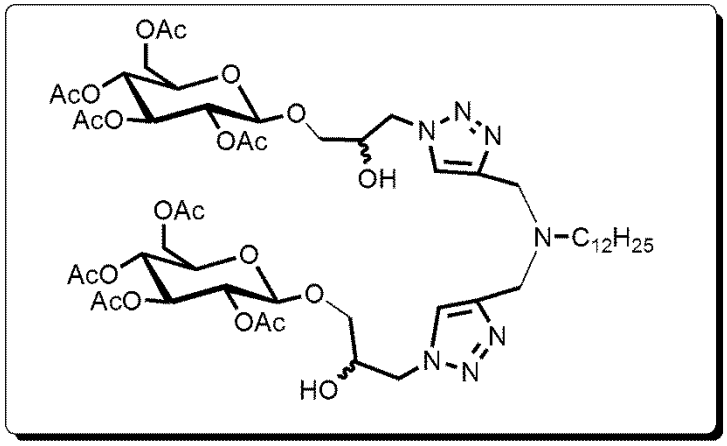
68.31 (2x C-4); 68.09 (OCH_2-chain); 61.85, 61.82 (2x C-6); 52.66, 52.55 (2x CH_2-triazole); 45.83 (C quaternary); 36.35 (β-CH_2); 31.90 (γ -CH_2); 29.64; 29.62, 29.59, 29.57, 29.39, 29.33, 29.22 (bulk-CH_2); 26.01 (2x CCH_2-triazole); 22.67 (∞-1); 20.78, 20.73, 20.71,20.57 (8x CH_3CO); 14.11 (CH_3).



Chemical Formula: $C_{46}H_{74}N_6O_{17}$
Molecular Weight: 983.1098

3.2.5.15.6 5,5-Bis{1-[(2-hydroxy-3-(*β*-D-*gluco*pyranosyloxy)-propyl]-1,2,3-triazole-4-yl-methyl}-2-(4dodecyloxy-phenyl)-1,3-dioxane (23).

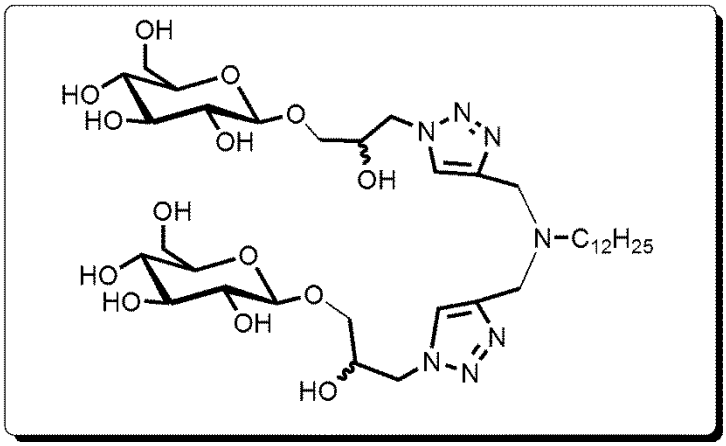
22 (1.3 g, 0.99 mmol) was reacted according to general procedure **II** to produce **23** (0.95 g, 98 %) as brown syrup. ^{1}H NMR (DMSO) δ = 7.99-7.94 (4 s, 2 H, triazole), 7.37, 6.90 (2 d, 2×2 H, C_6H_4), 5.37 (s, acetal), 4.70-2.95 (m, 30 H), 3.16 (s, 4 H, $CH_2C_{triazole}$), 1.69 (m, 2H, ß-CH_2), 1.39 (mc, 2 H, γ -CH_2), 1.24 (m, 16 H, bulk-CH_2), 0.85 (t, 3 H, CH_3). ^{13}C NMR (DMSO) δ = 158.77 (Ar-CO), 142.42 (triazole-C), 131.96 (Ar-C), 127.43 (Ar-CH), 124.08 (triazole-CH), 113.73 (Ar-CH), 103.45, 100.77 (dioxane-CH,C-1), 76.90, 76.39, 73.39 / 73.34 (C-2, C-3, C-5), 72.99 / 72.96 (CH_2O), 69.90, 68.35 / 68.26 (C-4,CHOH), 67.32 (CH_2O), 60.92 / 60.89 (C-6), 52.6 (bs, CH_2N) 25.42 (dioxane-C), 31.15 (ω -2),28.88, 28.86, 28.84, 28.62, 28.55, 28.52 (bulk-CH_2), 25.36 ($CH_2C_{triazole}$), 21.95 (ω -1), 13.81 (ω). HRMS (MALDI) calcd. for $C_{46}H_{74}N_6O_{17}$ [M+Na]: 1005.5008, 1006.5042 (1× ^{13}C, 51%),1007.5076 (2×^{13}C, 13%); found: 1005.4984 (100%), 1006.4970 (59%), 1007.4910 (18%).



Chemical Formula: $C_{52}H_{81}N_7O_{22}$
Molecular Weight: 1156.2332

3.2.5.15.7 *N*,*N*-Bis{1-[2-hydroxy-3-(2,3,4,6-tetra-*O*-acetyl-*β*-D-*gluco*pyranosyloxy) propyl]-(1,2,3-triazol-3-yl)-methyl]-dodecyl amine (16).

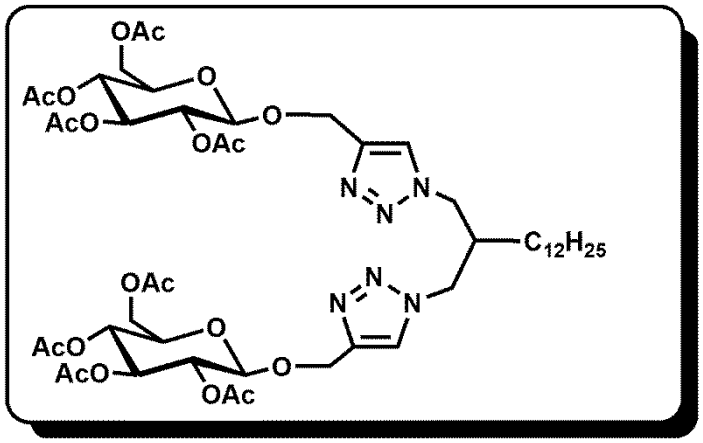
Sugar azide **4** (2.0 g, 4.4 mmol) and dipropargylated amine **10** (0.5 g, 2.2 mmol) were coupled with CuSO4x5 aq (0.1 g, 0.3 mmol) and Na-ascorbate (0.4 g, 2 mmol) in MeOH (12 mL) according to the general procedure **I**. Chromatographic purification applied pure EtOAc instead of the hexane-EtOAc mixture with respect to the higher polarity or the amine to provide **16** (1.4 g, 63 %) as a brown syrup. Application of $Cu(OAc)_2$ instead of $CuSO_4$ led to a lower coupling yield. ^{1}H NMR ($CDCl_3$) δ = 7.78 (s, 2H, 2x CH-triazole); 5.22 (dd~t, 2H, 2x H-3); J= 9.52; 5.06 (dd~t, 2H, 2x H-4); J=9.81; 5.00 (dd~t, 2H, 2x H-2); J= 9.52; 4.06 (d, 2H, 2x H-1); J= 8.0; 4.59-4.10 (m, 6H, 2x CHOH, C$\underline{H}_2$N); 4.28-4.07 (m, 4H, 2x H-6); 3.98-3.49 (m, 10H, 2x H-5, OC$\underline{H}_2$, CH_2C-triazole); 2.56 (m~bs, 2H, C$\underline{H}_2$N-chain) 2.06, 2.02, 2.00 (s, 3H, 4x $COCH_3$); 1.61 (bd, 2H, β-CH2); 1.26 (s, 18H, bulk-CH_2); 0.88 (t, 3H, CH_3); ^{13}C NMR ($CDCl_3$) δ =170.52, 170.01, 169.54, 169.33 (4x $\underline{C}OCH_3$); 123 (bs, CH-triazole); 101.26, 101.07 (2 x C1); 72.64 (C3); 72.05, 71.95 (C-2); 71.34 (C-5); 71.58 ($OCH_2\underline{C}HOH$); 68.8 (bs, O$\underline{C}H_2$); 68.64 (C4); 61.87 (C6); 53.10 (bs, C$\underline{H}_2$N-chain); 31.84 (∞-2); 29.61, 29.57, 29.26 (bulk-CH_2); (∞-1); 22.59 (CH_2); 20.65, 20.59, 20.45 ($CO\underline{C}H_3$); 14.04 (CH_3). ^{13}C-peaks for glycerol-linker and CH_2N were broad and very weak due to diastereomeric effects, while triazole carbons could not be observed.



Chemical Formula: $C_{36}H_{65}N_7O_{14}$
Molecular Weight: 819.9398

3.2.5.15.8 *N,N*-Bis{1-[2-hydroxy-3-(*β*-D-*gluco*pyranosyloxy)propyl]-(1,2,3-triazol-3-yl)-methyl]-dodecyl amine (17).

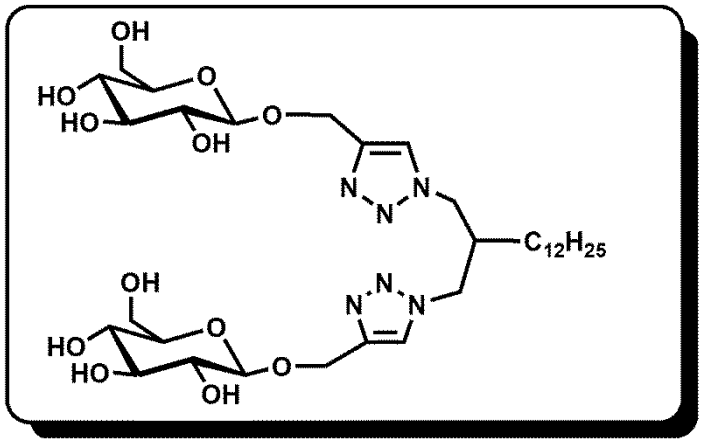
16 (1.0 g, 0.87 mmol) was reacted according to general procedure **II** to produce **17** (0.70 g, 99 %) as brown syrup. ^{1}H NMR (DMSO, 80°C) δ =7.87 (s, 2H, 2x CH triazole); 4.51 (d, 2H, 2x H-1); 4.37-4.26 (m, 2H, H-3); 4.20 (dd~t, 2H, H-2); 4.08-3.98 (bd, 2H, H-4); 3.77-3.61 (m, 8H, 2x [CH_2 triazole, H-5, H-6a]); 3.54-3.44 (bd, 4H,2x [CHOH, H-6b]); 3.26-3.00 (m, 8H, 2x [OCH_2, NCH_2]); 2.38 (bd, 2H, α-CH_2N chain); 1.46 (bd, 2H, B-CH_2); 1.24 (s, 18H, bulk-CH_2); .086 (t, 3H, CH_3); ^{13}C NMR (DMSO, 80°C) δ =144.13 (triazole-C); 124.85 (triazole-CH); 104.02, 103.88 (B-C1); 77.46, 77.23 (C3); 74.10,74.02 (C5); 71.35 (C2); 71.2 ($OCH_2\underline{C}HOH$); 70.91 ($O\underline{C}H_2$); 69.08, 69.02 (C4); 61.85 (C6); 53.21, 53.14 ($CHOH\underline{C}H_2$N triazole); 49.00 ($N\underline{C}H_2$N-triazole); 48.27 (α-CH_2N chain); 31.67 (∞-2); 29.41, 29.35, 29.03 (bulk-CH_2); 27.26, 27.21 (B-CH_2); 22.38 (∞-1); 14.17 (CH_3). HRMS (MALDI) calcd. for $C_{36}H_{65}N_7O_{14}$ [M+H]: 820.4668, 821.4701 (1x ^{13}C, 40 %); found: 820.4662 (100%), 821.4618 (48%).



Chemical Formula: $C_{49}H_{74}N_6O_{20}$
Molecular Weight: 1067.1401

3.2.5.15.9 Dodecyl-1,3-bis[4-(2,3,4,6-tetra-*O*-acetyl-*β*-D-*gluco*pyranosyloxymethyl) -1,2,3-triazol-1-yl]-propane (24).

Propargyl glucoside **2** (Allen & Tao, 1999) (2.0 g, 5.1 mmol) and diazide **15** (0.7 g, 2.5 mmol) were coupled with $Cu(OAc)_2$ (80 mg, 0.4 mmol) and Na-ascorbate (0.4 g, 2 mmol) in MeOH according to the general procedure **I** to provide **24** (1.3 g, 47 %) as a brown syrup. ^{1}H NMR ($CDCl_3$) δ = 7.72 (s, 2H, 2x triazole); 5.18 (2 dd~t, 2H, 2x H-3), J = 9.3; 5.1 (dd~t, 2H, 2x H-4);), J = 9.5; 4.98 (dd~t, 2H, 2x H-2);), J = 9.5; 4.94 (d, 2H, 2x OCH_2a);); 4.83 (d, 2H, 2x OCH_2b) , J = 12.5; 4.70 (d, 2H, 2x H-1); 4.33-4.23 (m, 6H, 2x H-6a, CH_2-triazole); 4.17 (dd~bd, 2H, H-6b), J = 12.0; 3.79 (ddd, 2H, 2x H-5), J = 4.5, 2.5; 2.60 (p, 1H, α-CH_2); 2.09, 2.07, 2.04, 2.03, 2.00 (4x s, 24H, 8x CH_3-acetate); 1.52- 1.20 (m, 22H, bulk-CH_2); 0.88 (t, 3H, CH_3). ^{13}C NMR ($CDCl_3$) δ =170.67, 170.20, 169.43, 169.41 (8x $CH_3\underline{C}O$); 144.01 (2x C-triazole); 124.39 (2x CH-triazole); 99.88 (2x C1); 72.73 (2x C3); 71.92 (2x C5); 71.22 (2x C2); 68.30 (2x C4); 62.77 (2x OCH_2); 61.78 (2x C6); 50.55 (2x CH_2-triazole); 40.17 (2x α-CH_2); 31.88 (∞-2); 29.71, 29.63, 29.59, 29.52, 29.50, 29.45, 29.31, 29.27 (2x bulk-CH_2); 26.66 (2x γ-CH_2); 22.65 (∞-1); 21.01, 20.86, 20.80, 20.74, 20.66, 20.56 (8x $\underline{C}H_3CO$); 14.09 (CH_3).



Chemical Formula: $C_{33}H_{62}N_6O_{12}$
Molecular Weight: 734.8784

3.2.5.15.10 2-Dodecyl-1,3-bis[4-(*β*-D-*gluco*pyranosyloxymethyl)-1,2,3-triazol-1-yl]-propane (25).

24 (1.0 g, 9.4 mmol) was reacted according to general procedure **II** to produce **25** (0.66 g, 97 %) as brown syrup. ^{1}H NMR (CD_3OD) δ = 8.06 (s, 2H, 2x triazole); 4.98 (d, 2H, OCH_2a); 4.81 (d, 2H, OCH_2b), J = 12.5 Hz, 4.49- 4.38 (m, 6H, 2x (H-1, $CH_{2\text{-triazole}}$)); 3.93 (dd, 2H, 2x H-6a); 3.68 (dd, 2H, 2x H-6b), J = 12.0 Hz; 3.41-3.28 (m, 6H, 2x (H-3, H-5, H-4)); 3.28 (dd≈t, 2H, 2x H-2), J = 9.0 Hz; 2.71- 2.61 (m, 1H, α-CH_2); 1.50-1.30 (m, 22H, bulk-CH_2); 0.92 (t, 3H, CH_3). ^{13}C NMR (CD_3OD) δ = 146.82 (2x C-triazole); 126.35 (2x CH-triazole); 103.69, 103.67 (2x C1); 78.08 (2x C-3); 78.00 (2x C-5); 75.04 (2x C-2); 71.66 (2x C-4); 63.07 (2x OCH_2); 62.82 (2x C-6); 52.45 (2x $CH\underline{C}H_2$-triazole); 41.46 (α-CH); 33.08 (∞-2); 30.78, 30.72, 30.55, 30.49, 30.43, 30.16 (bulk-CH_2); 27.79 (B-CH_2); 23.74 (∞-1); 14.46 (CH_3).

3.3 Results and discussion

The synthesis of the Y-shape surfactants applied a click-coupling concept based on the Huisgen 1,3-dipolar addition of azides to terminal acetylenes (Hein & Fokin, 2010b), as displayed in Figure 3.1. The respective building blocks were a monovalent carbohydrate derivative on the one hand, and a divalent hydrocarbon precursor on the other. Both reactants were coupled in a 2:1 ratio.

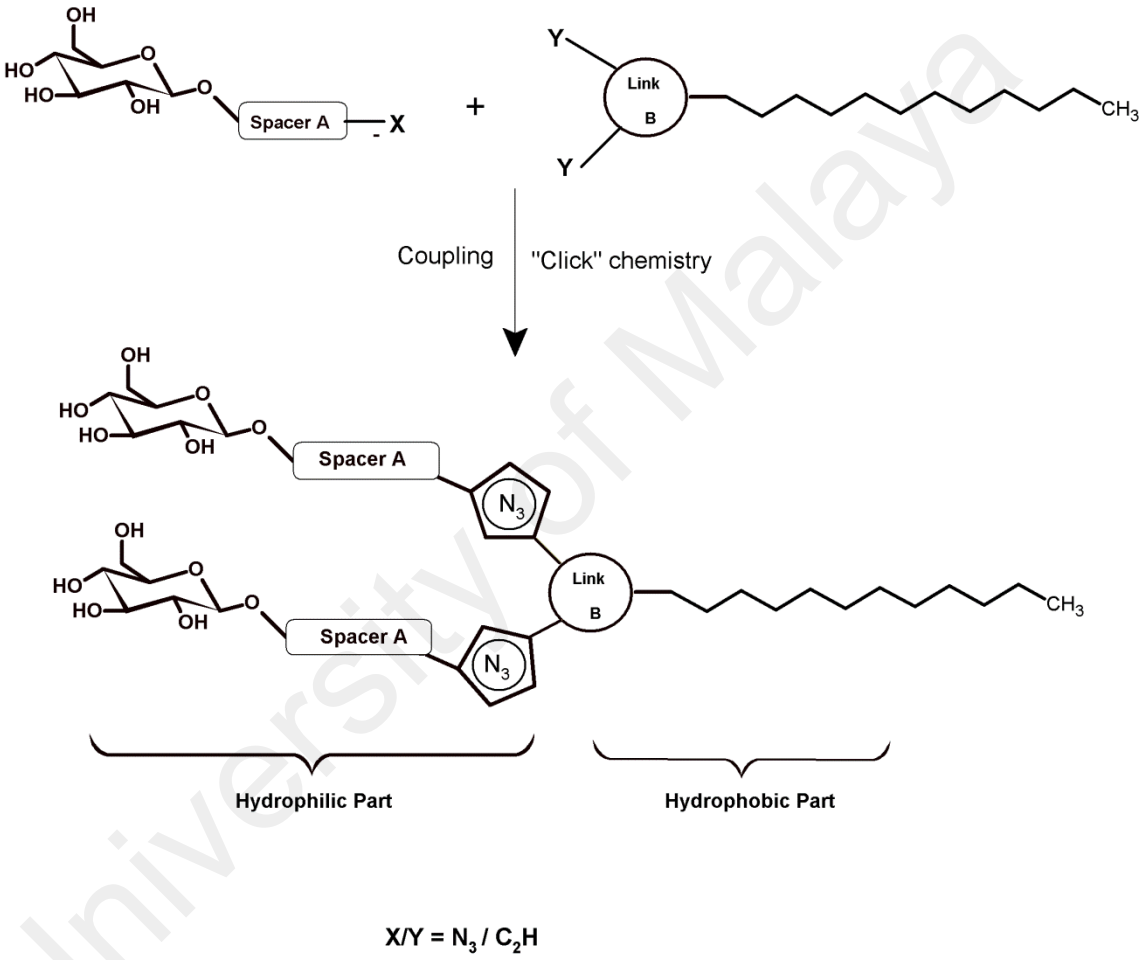
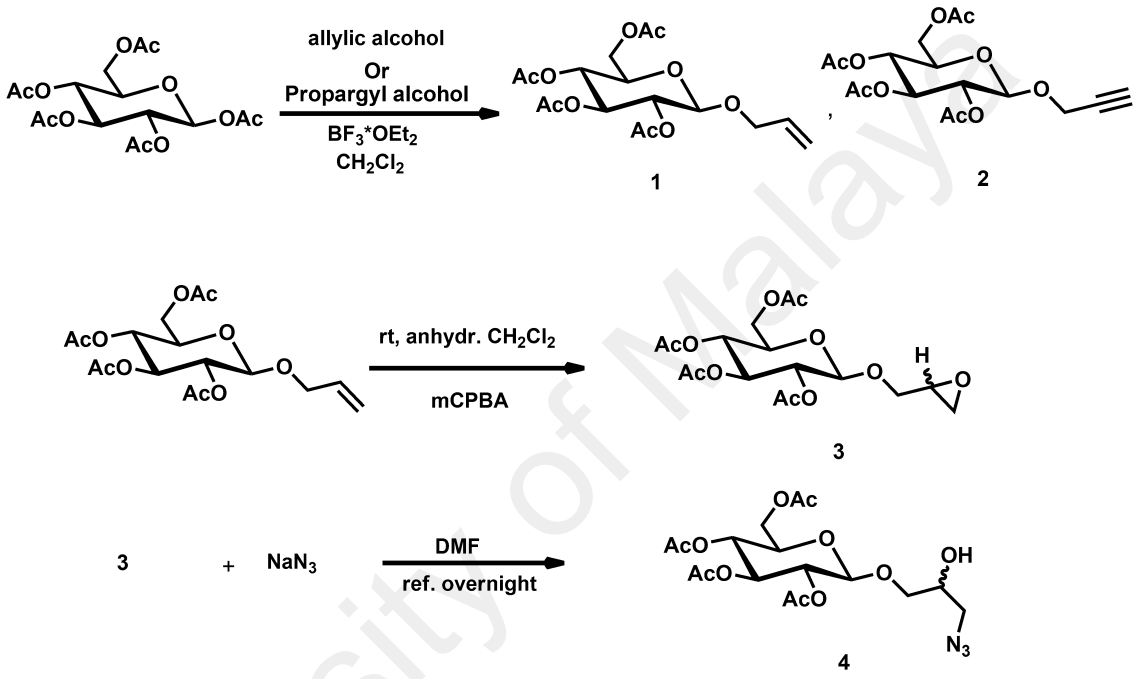


Figure 3-1: General surfactant design.

While propargyl glycosides have already been utilized for the preparation of ATGs (Sani *et al*., 2012), the current approach emphasized on a reverse strategy, which applied the carbohydrate as azide component. The azide was introduced to the carbohydrate by epoxidation of allyl glucoside, **1**, and subsequent nucleophilic ring opening (Tran, Kitov, Paszkiewicz, Sadowska, & Bundle, 2011). This approach is significantly more economic than the conversion of a fatty acid into an azide, as

previously applied for ATGs (Sani *et al*., 2012). A disadvantage, on the other hand, is the formation of diastereomeric mixtures due to missing stereo-selectivity for the epoxide **3** (Barnett & Ralph, 1971), which complicates the spectral analysis of the surfactants. The synthesis of all carbohydrate building blocks is summarized in Scheme 3.1.

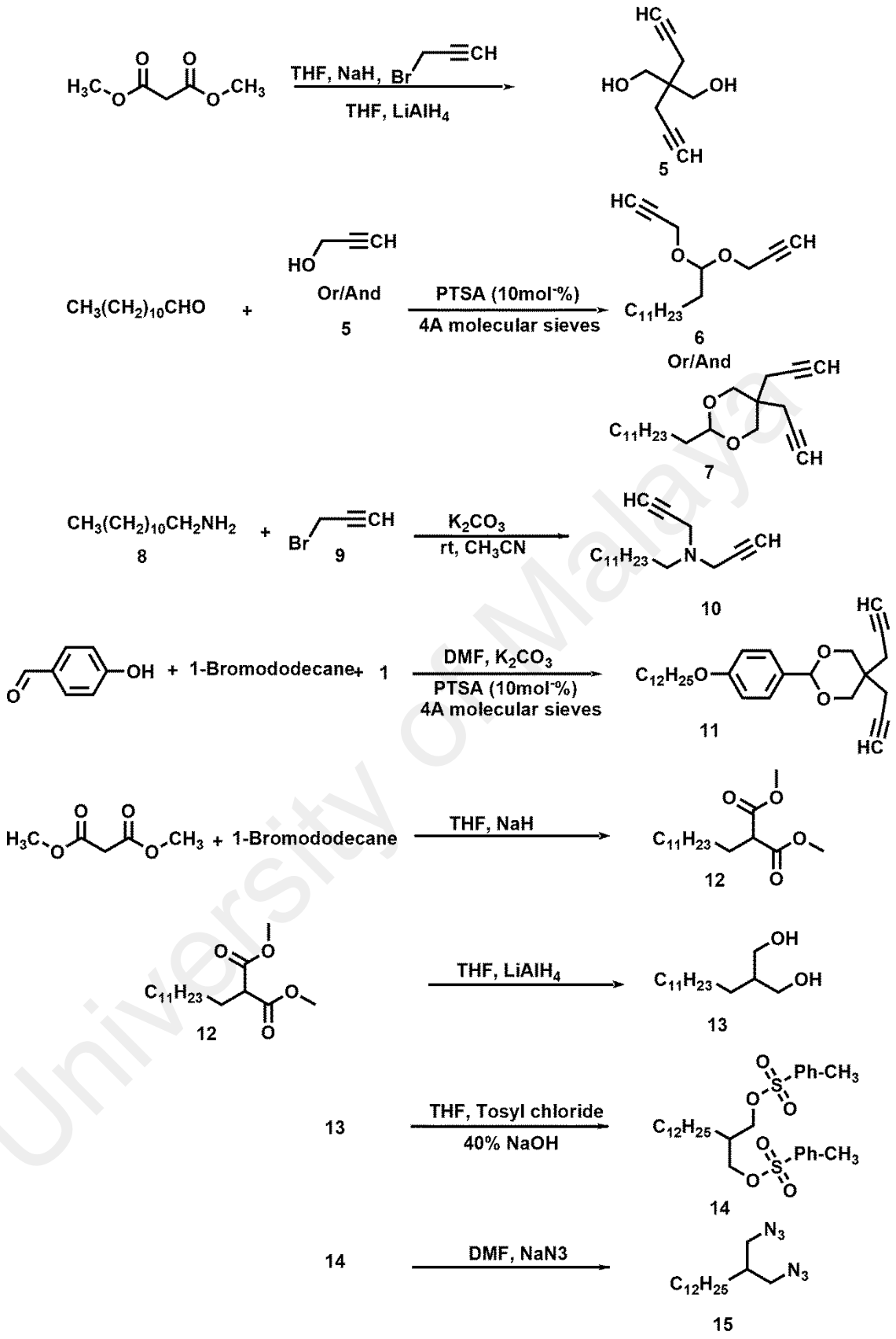


Scheme 3-1: Synthesis the hydrophilic parts of the surfactants.

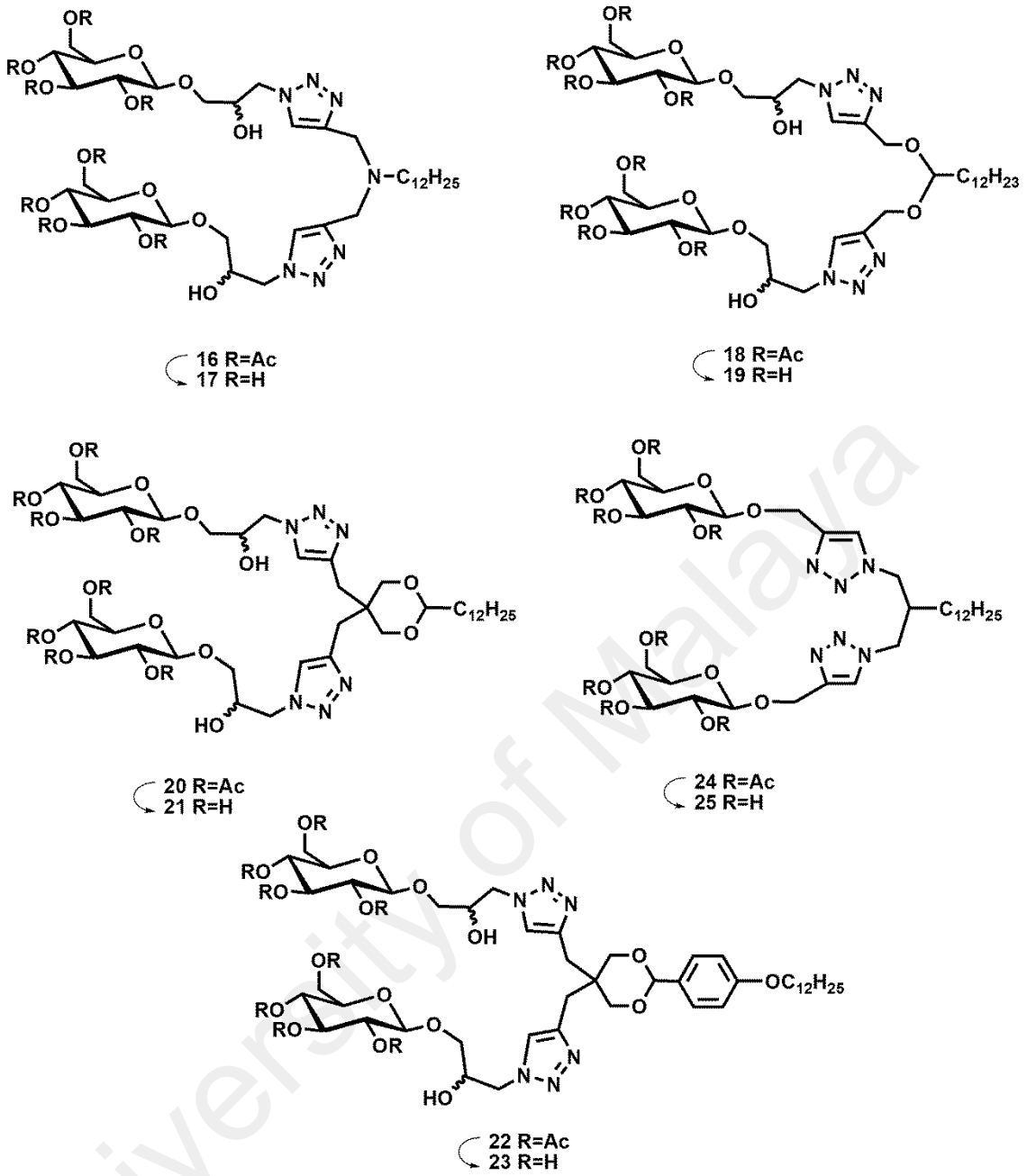
For the synthesis of the hydrocarbon precursor a variation of linkers, labeled B in Figure 3.1 was applied. Structures **6**, **7**, **10**, **11** and **15**, see Scheme 3.2. The formation of acetal system from an aldehyde and alcohol (contained alkyne system) component as shown in Scheme 3.2 were applied to synthesis the hydrophobic part which was proceeding through the nucleophilic attack of alcohol on the carbonyl group, this was conducted in connection with the hydrophilic part by click-chemistry. However, we believe the using of the acetal system is the best choice to provide two alkyne arms for further reaction, were chosen based on easy accessibility, higher yield and faster to form. The formation of water as a by-product is the main problem in acetal formation so to shift the equilibrium to the product side we used molecular sieves (A4) as scavengers

to remove the water from the reaction mixture. The big challenge was to form an aromatic Acetal system with alkyne alcohol since these types of compounds are not stable although to enhance the stabilization of this compound we use dihydroxy diyne system to form an aromatic cyclic Acetal system which was more stable and can be isolated and characterized. Besides, all structures were required to exhibit chemical stability at neutral and high pH. Sensitivity under acidic conditions, on the other side, was considered as potential benefit to enhance the biological degradation process in wastewater. The open chained acetal in **7** is particularly interesting, due to its easy hydrolysis under slightly acidic wastewater conditions, which effectively separates the hydrophilic and hydrophobic domains, thus avoiding surfactant-based biological hazards. Precursor **11** incorporates an aromatic moiety in the hydrocarbon domain. This was aimed for potential beneficial interaction with fossil oil.

Since the discovery of the CuAAC reaction a large number of different methods have been applied in the synthesis of 1,2,3-triazoles using various forms of Cu(I) catalyst (Tornøe *et al*., 2002). Coupling of the precursors applied the copper(I) catalyzed variant of the Huisgen cycloaddition (Lallana, Riguera, & Fernandez-Megia, 2011). Most surfactant precursors were obtained in ~60% yield. The structures of the coupling products and the final surfactants, obtained by subsequent deacetylation are displayed in Figure 3-3. Interestingly the efficiency for coupling a diazido-hydrocarbon precursor with the propargyl glycoside was with 50% below those obtained for the reverse coupling, applying a dipropargylated hydrocarbon and carbohydrate azide **4** instead.



Scheme 3-2: Synthesis of hydrophobic parts involving Y-shape linkage.



Scheme 3-3: Surfactant structures

3.4 Phase behavior

3.4.1 Liquid crystalline behaviour

Almost all surfactants showed high solubility in water at room temperature. Except for compound **25**, which exhibit a cubic lyotropic phase, displayed in Figure 3.2, only micellar solutions (L_1-phase) were observed. This behavior reflects the dominant surface area of the hydrophilic domain, owing to the side-by-side alignment of two carbohydrate head-groups as displayed Figure 3.3. This dominance leads to a curving of

surfactant assemblies towards the hydrophobic domain, resulting in micelles. This surfactant behavior is particularly beneficial for oil in water emulsification applications.

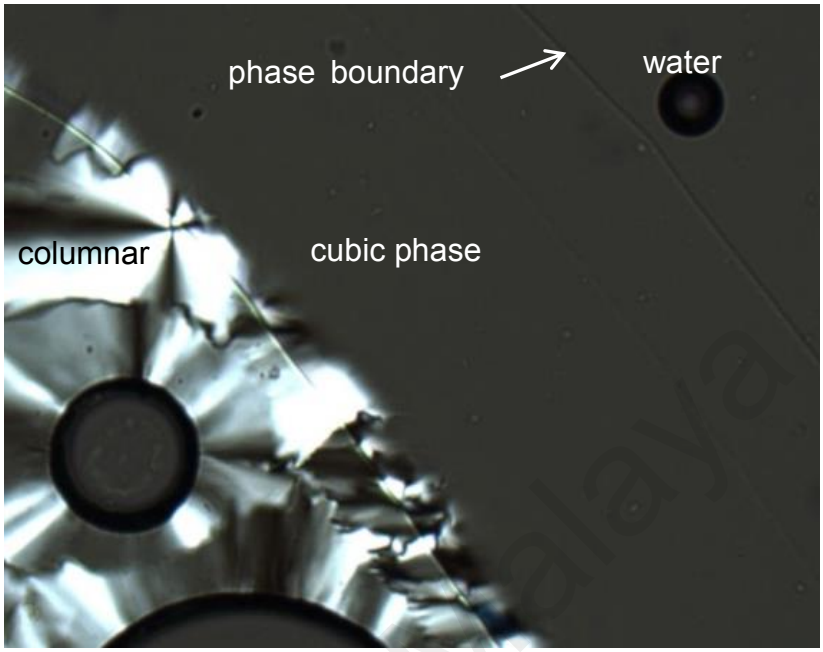
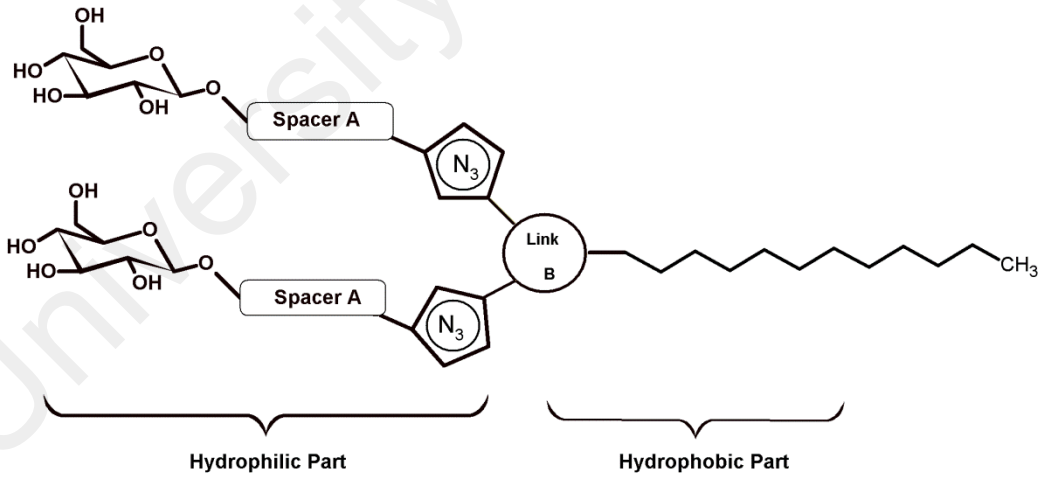


Figure 3-2: Contact penetration OPM for surfactant 25



(a)

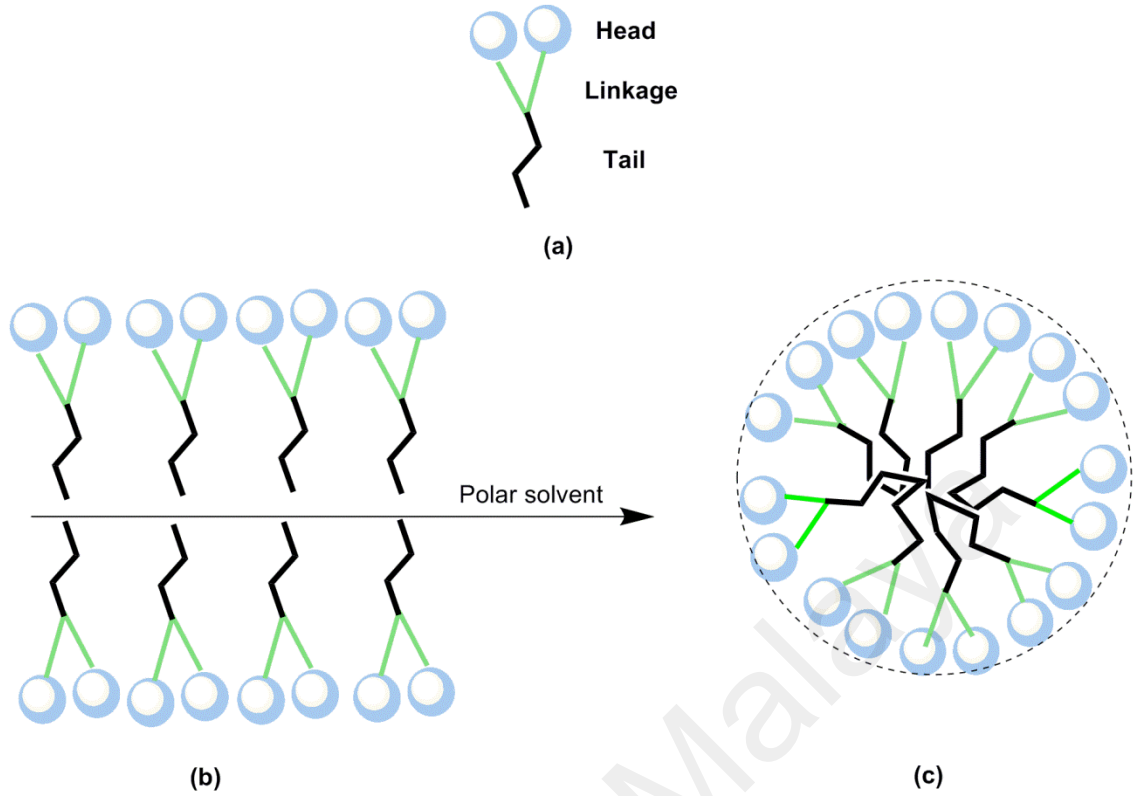


Figure 3-3: Structure diagram of surfactant assemble shows (a) single surfactant molecules (b) the surfactant molecules in low concentration solvent (c) the surfactant molecules arrangement in micelle solution.

3.4.2 Air-water interface behavior and emulsion stabilization

All surfactants exhibited Krafft points below 10 °C, while no clouding was observed upon heating. This renders the surfactants as promising candidates for emulsifier applications. Based on the Krafft temperature, the surface tension investigation was performed at room temperature. Besides the CMC and the related lowest surface tension for surfactant solutions, γCMC, the minimum molecular surface areas, A_{min}, as well as the Gibbs enthalpy for the micelle formation, ΔG°_{misc} were determined based on the Gibbs adsorption isotherm equation. The surface excess concentration, T_{max} ,can be calculated from the slope of the surface tension γ_{CMC} against the logarithmic surfactant concentration at the concentration depending region according to equation 3.1 (Milton J Rosen, 2004),

$$\Gamma_{\max} = -\frac{1}{2.303nRT}\left(\frac{\partial\gamma}{\partial \log C}\right)_{\max T} \qquad \text{eq. 3.1}$$

where, [$\partial \gamma / \partial \log c$] is the slope, T is the absolute temperature, R is the universal gas constant (8.314 J $mol^{-1}K^{-1}$), and n is the number of species whose concentration at the interface varies with the surfactant bulk phase concentration (in this case n = 1). The minimum area per surfactant molecule A_{min} is obtained by applying equation 3.2,

$$A_{\min} = \frac{10^{20}}{N_A \Gamma_{\max}} \qquad \text{eq. 3.2}$$

where, N is Avogadro's number ($6.022 \times 10^{23} mol^{-1}$).

The CMC measurement also provides access to the standard free energy of the aggregation, ΔG°_{Misc}, which can be obtained from equation 3.3 as

$$\Delta G_{mic} = RTLn(cmc/55.5) \qquad \text{eq.3.3}$$

The surface tension derived surfactant characteristics are summarized in Table 3.1. All surfactants exhibit similar CMCs, reflecting the size of the hydrocarbon chain. The higher CMC values for **19** and **21**, compared to **17**, **23** and **25**, probably originates from the incorporation of one carbon of the hydrocarbon chain into the linking unit of the surfactant (acetal), which reduces the hydrophobicity. The surface tension above the CMC fits with 35-50 mN m^{-1} into the previously reported range of values for double headed surfactants (Oskarsson, Frankenberg, Annerling, & Holmberg, 2007). The minimum surface area per surfactant exceeds with more than 50 $Å^2$ the typical value of single headed glycosides (~40 $Å^2$ (Nguan, Heidelberg, Hashim, & Tiddy, 2010)), by more than 20 %. The effect is significantly larger than that of an in-line-attachment of a second sugar molecule, which only leads to a slight growth in molecular surface area (maltoside < 45 $Å^2$) (Nguan *et al.*, 2010). It reflects an enhanced efficiency of the side-by-side alignment to induce a curved assembly. Based on these findings, the side-by-

side arrangement of two sugar head-groups is expected to potentially improve the emulsifying properties of a surfactant.

Table 3-1: CMC, surface tension at CMC, minimum area per surfactant molecule and standard free energy of micellization.

Compound	cmc (mM)	γ_{cmc} (mN/m)	A_{min} (Å^2)	ΔG_{mic} (KJ.mole^{-1})
17	**0.42**	**39.3**	**57**	**12**
19	**0.57**	**34.7**	**53**	**11**
21	**0.14**	**43.1**	**51**	**15**
23	**0.11**	**48.9**	**62**	**16**
25	**0.15**	**39.8**	**53**	**15**

Despite the different lyotropic behavior of propargyl glucoside-derived surfactant **25,** compared with those surfactants obtained from 3-azido-2-hydroxy-propyl glucoside, **4**, the molecular surface area for **17**, **19**, **21**, **23** and **25** is similar, thus suggesting the same assembly behavior according to the packing theory. This suggests that the cubic phase observed in Figure 3.2 is discontinuous, *i.e.* referring to a closest packing of micelles. The latter is expected to exhibit a dynamic motion of the phase border over a longer observation time. However, the phase border appeared to be rather static. An explanation may be found in conformational constraints of the carbohydrate head-group linkage to the hydrophobic domain bridging triazole, owing to the directly linked pyranose-ring, whereas all other surfactants consist of additional carbon atoms, giving rise to more flexibility. Conformational constraints could result in interdigitation of head-groups for neighbored micelles, thus limiting water accessibility leading to a kinetic barrier for the surfactant solubilization.

With exception of amine-linked surfactant **17** all Y-shape surfactants led to reasonably good emulsion stabilities, requiring several days for phase separation in absence of polymeric stabilizers. Details of the emulsion stability study are displayed in

Figure 3.4. The reason for the poor emulsifying property of surfactant **17** may be related to repulsive ionic interactions due to a partial protonation of the amine, which can destabilize the assembly. The slightly decreased stability for surfactant **23,** on the other hand, probably reflects reduced interaction efficiency due to the aromatic ring. The latter, however, is expected to increase the interaction for an oil phase involving aromatic hydrocarbon contents.

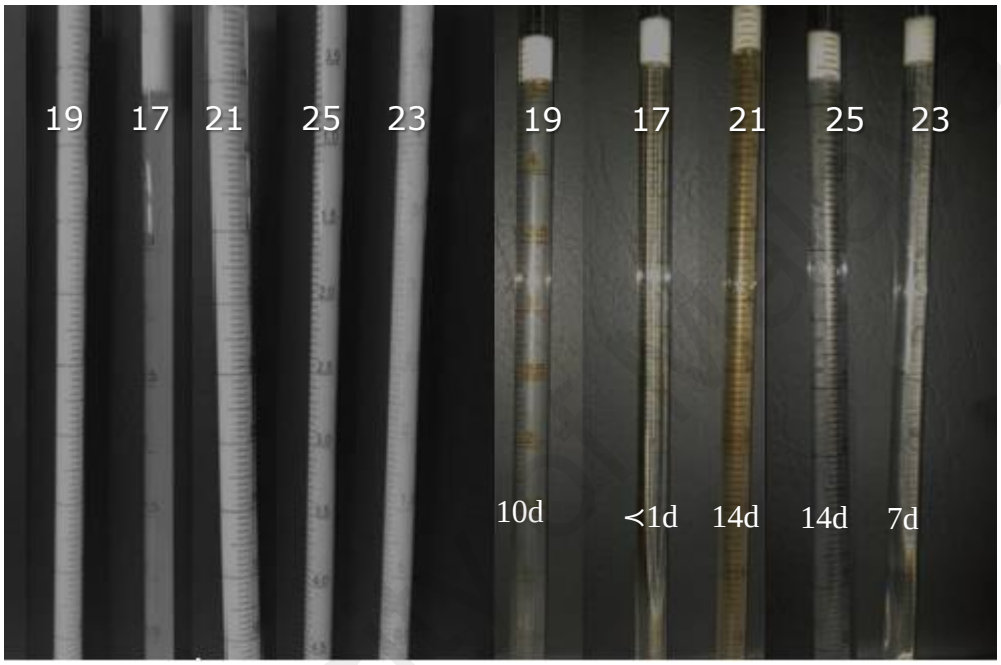


Figure 3-4: Emulsion stability (O/W).

3.5 Conclusions

Sugar based Y-shape surfactants can be easily prepared from renewable resources, in this case glucose. Their structural design favors the formation of miscellar assemblies and increases the solubility in water, thus enhancing the surfactant's emulsifier potential for oil in water formulations. Good linkers between the hydrocarbon chain and the sugar head-group involve acetalic structures, as these are easily cleaved under slightly acid waste-water conditions, thus avoiding surfactant based toxic effects, while an amine based linker led to poor emulsification efficiency, probably due to repulsive ionic interactions. While propargyl glucoside is an effective surfactant building block, azido-propyl glucoside, derived from allyl glucoside, is even more economic. Besides, the additional carbon atoms between the sugar ring and the triazole linkage enhance the kinetic water solubility of the surfactant, thus adding advantages for emulsifier applications.

Chapter 4 : Unusual base-induced cyclization of dipropargylic systems to *m*-substituted toluenes

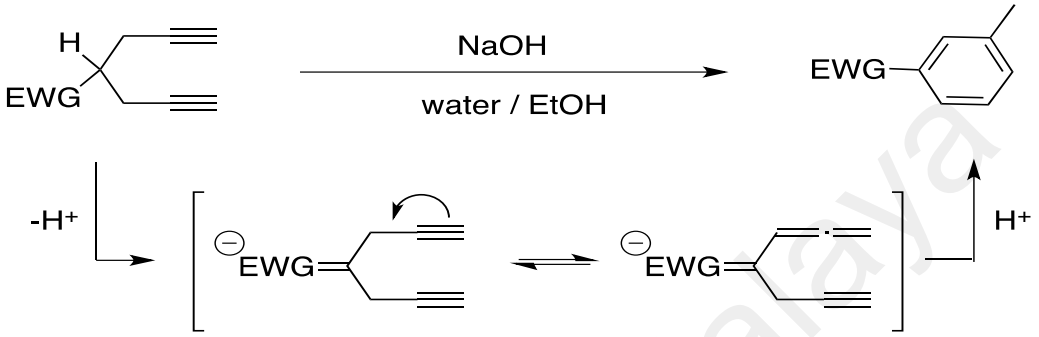


Figure 4-1: Initial alkyne-allene- isomerization

4.1 Introduction

The equilibrium of alkynes and allenes gave rise to various cyclizations, frequently involving aldol-type reactions. Many reactions are initiated by coordinating metals; this fits both intra- (Brummond, Davis, & Huang, 2009; Brummond, Lu, & Virginia, 1999; Lu, Jin, Bao, & Yamamoto, 2010; Trost & Rudd, 2002) and intermolecular reactions (Shibata, Noguchi, & Tanaka, 2010). However, initiation can also apply basic conditions, if resonance effects drive the reaction (Kitagaki, Teramoto, & Mukai, 2007).

Based on a targeted synthesis of dendrimers by exploitation of 'click'-chemistry, we synthesized various dipropargylic building blocks. The purification of some of these led to unexpected problems, due to the presence of aromatic compounds despite exclusive use of aliphatic reagents and solvents. This led to an investigation of the source of the aromatics, revealing an unexpected intrinsic reactivity for 1,5-hexadiynes with an EWG on the central carbon.

4.2 Experimental

4.2.1 General cyclization procedure

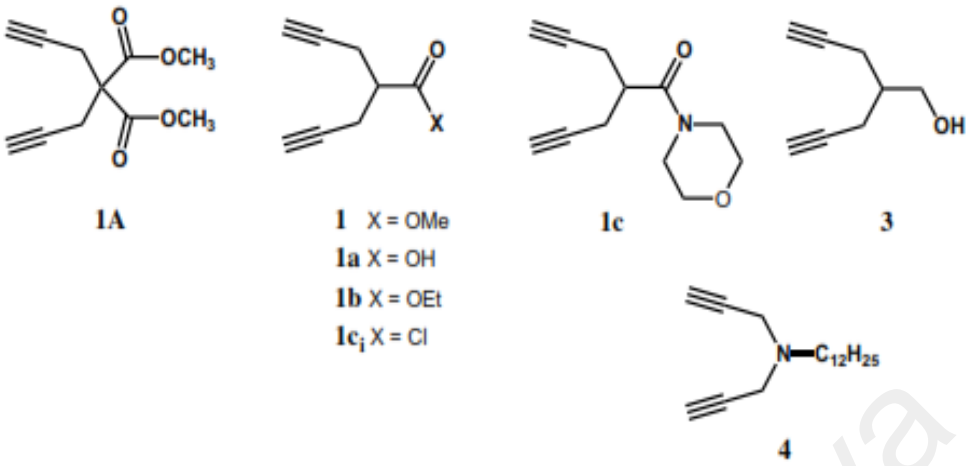
The dipropargylic substrate was dissolved in aqueous EtOH (24 mL, 75% v/v) and NaOH (12 eq.) was added, after which the reaction was heated to reflux overnight. The cooled reaction mixture was acidified with aqueous HCl and extracted three times with CH_2Cl_2. The combined organic layers were washed with brine, dried over $MgSO_4$, and the solvent was evaporatord in vacuum to leave the respective product (mass recovery 85 % and above). The conversion rate was determined based on relative ^{1}H-NMR integrations of the aromatic product and remaining starting material.

4.2.2 Product Identification

Purification of 3-methylbenzoic acid, **2**, applied chromatography followed by subsequent crystallization. **2**: ^{1}H NMR (400 MHz, $CDCl_3$) δ= 10.3 (bs, OH), 7.94 (s), 7.93 (d), 7.42 (d), 7.42 (d), 7.36 (t), 2.42 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ= 172.5, 138.3, 129.2, 134.6, 130.7, 128.4, 127.4, 21.2.

Purification of N-ethyl-3-methyl-benzamide applied column chromatography. IR (ATR) 3304 (NH), 2923, 2852 (CH), 1644 (C=O), 1550 cm^{-1}(C=C). ^{1}H NMR (400 MHz, $CDCl_3$) δ= 7.52 (s), 7.46 (t), 7.22 (m, 2H), 6.13 (bs, NH), 3.42/3.41 (2 q, 2 H, Et-CH_2), 2.31 (s, 3 H, CH_3), 1.17 (t, 3 H, Et-CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ= 167.7, 138.38, 134.5, 132.1, 128.4, 123.6, 34.9, 21.3, 14.9. MS: 163, 162, 119, 91 in accordance with (Tay, Rahman, & Abas, 2009).

4.2.3 Synthesis of di-propargyl system compounds



4.2.3.1 Synthesis of dimethyl 2,2-di(propynyl)malonate (1A):

A procedure similar to a literature reported process (Carney *et al*., 2008) was employed: Dimethyl malonate (6.0 mL, 52 mmol) was added dropwise to a stirred suspension of NaH (60 % wt in mineral oil, 4.22 g, 106 mmol) in dry THF (100 mL) at 10 °C. After 10 min propargyl bromide (80 % w/w in toluene, 12.0 mL, 108 mmol) was added dropwise. The reaction was allowed to warm to room temperature and stirred overnight. The reaction mixture was distributed between water and ether, and the aqueous phase was extracted twice with ether. The combine organic phases were washed with brine, dried over $MgSO_4$, filtered and concentrated on a rotary evaporator leaving white solid. The solid was crystallized from ethyl acetate to give 1A (9.44 g, 84%) as crystalline white solid.

4.2.3.2 Synthesis of methyl 2-(propynyl)-4-pentynoate (1)

The synthesis of **1** followed a literature reported method: (Carney *et al*., 2008) **1A** (4.70 g, 22.6 mmol) and LiCl (2.95 g, 69.7 mmol) were dissolved a mixture of DMSO (40 mL) and water (1 mL). The reaction was refluxed for 1 h and subsequently cooled to room temperature. The mixture distributed between $CHCl_3$ and water and the aqueous layer was extracted repeatedly with $CHCl_3$. The combined organic phases were

washed with brine, dried over MgSO4, filtered through silica gel and concentrate to provide a crude product, which was purified by flash chromatography column using 20% ethyl acetate in hexane to give **1** (3.0 g, 90 %) as pale yellow oil.

4.2.3.3 Synthesis of 2-(propynyl)-4-pentynoic acid (1a)

Methyl ester **1** (3.0 g, 20 mmol) was dissolved in aqueous ethanol (24 mL, 75 % v/v), before treatment with NaOH (10 g, 0.25 mol), and the mixture was refluxed overnight. After removal of the solvent the residue was acidified with diluted HCl and extracted with CH_2Cl_2. The organic phase was washed with brine, dried over $MgSO_4$ and concentrated. After chromatographic purification using hexane and ethyl acetate the product crystallized upon evaporation of the solvent to give **1a2** (1.7 g, 60 %). 1H NMR ($CDCl_3$) δ= 10.29 (bs, OH), 2.83 (mc, CH), 2.68 (mc, 4 H, CH2), 2.05 (t, 2 H, C≡CH). ^{13}C NMR ($CDCl_3$) δ= 178.5, 80.2, 70.8, 42.9, 19.6.

4.2.3.4 Synthesis of ethyl 2-(propynyl)-4-pentynoate (1b)

A solution of **1a** (0.70 g, 5 mmol) in EtOH (50 mL) was treated with H_2SO_4 (0.5 mL) and heated to reflux overnight. The solvent was carefully evaporatord and the residue treated with aqueous $NaHCO_3$. The product was isolated by triple-extractions with CH_2Cl_2, dried over $MgSO_4$ and concentrated to give **1b** (0.75 g, 88 %). ^{1}H NMR ($CDCl_3$) δ= 4.20 (q, 2H, Et-CH2), 2.76 (mc, CH), 2.66-2.61 (m, 4 H, CH2), 2.02 (t, 2 H, C≡CH), 1.28 (t, 3 H, Et-CH3).

4.2.3.5 Synthesis of 2-(propynyl)-4-pentynoic acid morpholide (1c)

A solution of 1a (2.0 g, 15 mmol) and $(COCl)_2$ (3.8 g, 30 mmol) in $CHCl_3$ (100 mL) was heated to reflux overnight. Excess reagent and solvent were evaporatord and the remaining acid chloride **1ci 3** (2.2 g, 98 %). The crude acid chloride **1ci** (0.60 g, 3.9 mmol) was re-dissolved in CH_2Cl_2 (50 mL) and treated with morpholine (0.40 g, 4.7 mmol) and triethylamine (5.4 mL, 39 mmol). The reaction was stirred overnight and

then washed with aqueous NaHCO3. The organic solution was dried over MgSO4 and concentrated. The crude product was purified by chromatography using hexane and ethyl acetate 6:1 to give **1c** as a white solid (0.47 g, 60 %). ^{1}H NMR ($CDCl_3$) δ= 3.71-3.65 (m, 6 H), 3.63-3.59 (m, 2 H), 3.10 (mc, CH), 2.49 (dd, 4 H, CH2), 2.01 (t, 2 H, C≡CH). ^{13}C NMR ($CDCl_3$) δ= 171.3, 81.2, 70.3, 67.0, 66.9, 46.5, 42.5, 39.3, 21.6.

4.2.3.6 Synthesis of 2-(propynyl)pent-4-yn-1-ol (3)

$LiAlH_4$ (0.27 g, 7.5 mmol) was added to stirred solution of **1** (1.1 g, 7.2 mmol) in anhydrous THF at 10 °C. The reaction mixture was allowed to warm to room temperature and stirred overnight. Water (1.2 mL) was added carefully to destroy excess reagent, followed by 10% NaOH aq (1.2 mL) and more water (3.6 mL). Precipitating aluminates were filtered off and rinsed with CH_2Cl_2. The aqueous phase was extracted with CH_2Cl_2 and the combined organic phases were dried over $MgSO_4$ and concentrate to leave **3** (0.8 g, 91 %) as colorless oil.

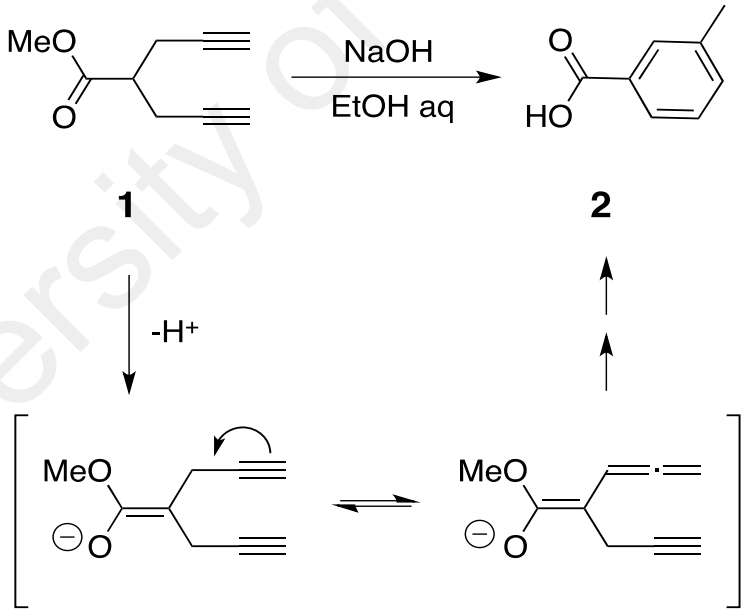
4.2.3.7 Synthesis of *N,N*-dipropargyl-dodecylamine (4)

Dodecyl amine (2.0 g, 11 mmol) and K_2CO_3 (3.1 g, 23 mmol, 2.1 eq.) were suspended in acetonitrile and propargyl bromide (2.5 mL, 23 mmol) was added dropwise to the mixture. The reaction was stirred at room temperature for 24h, then filtered and the resulting solution was concentrated on a rotary evaporator yielding a yellow oil. The crude oil was purified by flash chromatography on a silica gel using chloroform as eluent, providing a clear oil (2.0 g, 71%). ^{1}H NMR ($CDCl_3$) δ= 3.43 (t, 4 H), 2.51 (t, 2 H), 2.20 (q, 2 H), 1.46 (m, 2 H), 1.34-1.19 (m, 18 H), 0.88 (t, 3 H). ^{13}C NMR ($CDCl_3$) δ= 78.9, 72.7, 53.1, 42.1, 31.9, 29.62, 29.59, 29.54, 29.47, 29.3, 27.4, 27.3, 22.6, 14.0.

4.3 Results and discussion

Dipropargyl acetates, like **1**, formed 3-methyl-benzoate upon treatment with strong base in aqueous alcohol at elevated temperature. The reaction is depicted in Scheme 4-1. Despite the low reaction yield of below 40 % for the transformation of methyl 2,2-dipropargyl-acetate, **1**, to 3-methyl benzoic acid, **2**, the reaction is interesting because of the unexpected reaction product and related mechanistic implications.

It indicates an intrinsic reactivity of the 1,5-hexadiyne core for aromatic cylization under moderate reaction conditions. The reaction is believed to pass through an initial alkyne-allene- isomerization, as shown in Figure 4-1, probably driven by resonance stabilization of the enolate.

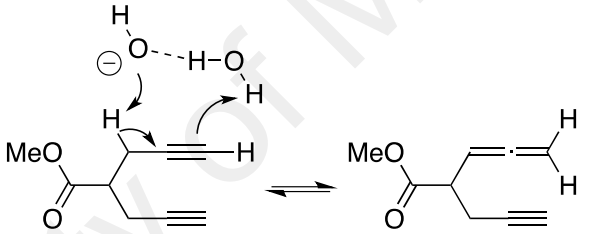


Scheme 4-1: Cyclization of methyl dipropargyl-acetate

Base induced isomerization of alkynes and allenes have been reported previously (Abrams & Shaw, 1987; Spence, Wyatt, Bender, Moss, & Nantz, 1996; Wotiz, barelski, & Koster, 1973). However, for these reactions stronger bases are normally applied (Kitagaki *et al*., 2007; Wotiz *et al*., 1973). Reaction mechanisms involving a cyclic proton transfer mediated by a deprotonated diamine (Abrams &

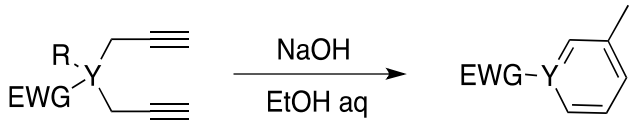
Shaw, 1987; Wotiz *et al*., 1973) or a alkali amide (Wotiz *et al*., 1973) have been proposed. Both mechanisms propose a push-pull concept. The same may apply in water.

Based on the distance of the carbons for the proton transfer, a transition state involving a hydrated hydroxide is favored over a isolated hydroxide ion. Scheme 4-2 displays the isomerization of dialkyne 1 into the corresponding alkynyl-allene. This reaction is likely driven by the conjugation of the enolate, as shown in Scheme 4-1. Subsequent reaction of the allene with the second triple bond provides the aromatic ring. Although the current reaction is new, the concept of isomerization of alkenes and allenes through enolates with subsequent cyclization has been reported previously (Kitagaki *et al*., 2007).



Scheme 4-2: Proposed mechanism for alkyne-allene isomerization

In order to investigate this unexpected reactivity a comparative study was performed, using a selection of structurally different dipropargylic starting materials. The structures of investigated starting materials are summarized in Scheme 4-3, while the reaction results are displayed in Table 4-1.



Scheme 4-3: Variation of substrates for attempted cyclization of 1,1-diprogargyls

Table 4-1: Attempted cyclization of 1,1-dipropargyls.

Compound No.	EWG	R	Y	Yield
1	CO_2Me	H	C	37 %
1a	CO_2H	H	C	30 %
1b	CO_2Et	H	C	25 %
1c	CON_4H_8O	H	C	>35 %*
1A	CO_2Me	CO_2Me	C	No reaction†
3	CH_2OH	H	C	Trace
4	N/A	$C_{12}H_{25}$	N	No rection

* No detection of leftover starting material, but diverse degradation products. Yield estimation based on complete integration of ^{1}H-NMR.

† no detection of aromatic compounds, but saponification of ester

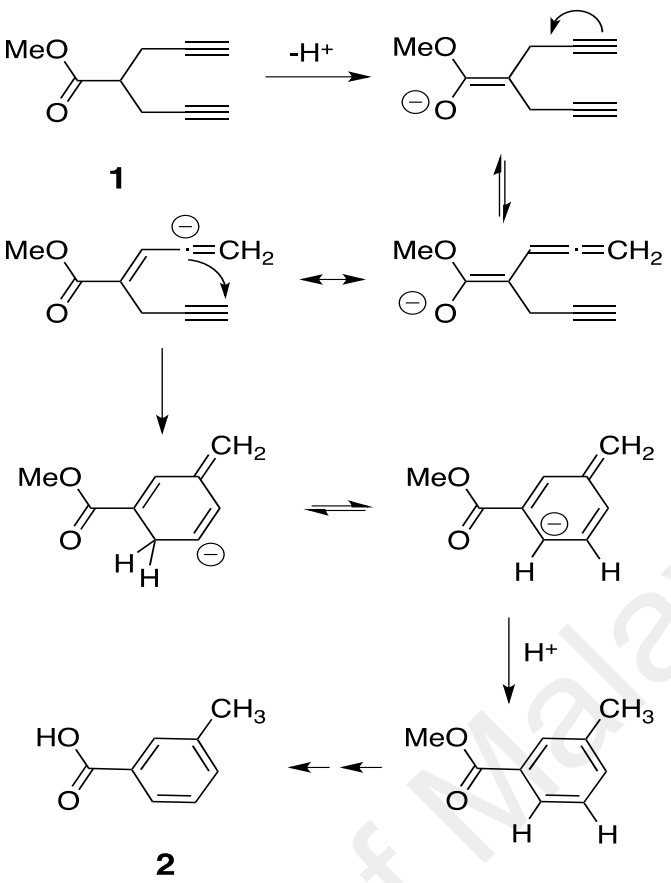
Table 4-1 illustrates the importance of a hydrogen atom at the central carbon of the starting material. Various dipropargyl-acetic acid derived substrates (**1, 1a-c**) provided aromatic products in accordance with Scheme 4-3, while in the absence of a central hydrogen atom, referring to entries **1A** and **4**, no aromatic products were detected. The application of morpholide **1c** led to the surprising isolation of N-ethyl-3-methyl-benzamide, instead of the expected morpholide. A rational for this conversion could not be found. The minor cyclization of alcohol 3, despite missing CH-acidity at the central carbon, is surprising. The NMR of the crude product indicated the presence of more than one aromatic product. It is assumed that an initial oxidation of the alcohol led to an aldehyde, which cyclized according to Scheme 4-1. Subsequent Cannizzaro reaction of the intermediate benzaldehyde gave rise to a mixture of aromatic compounds.

Besides the comparison of different dipropargylic starting materials, a variation of reaction conditions was investigated to provide more insights to the cyclization process. Substantial decrease of the base concentration failed to convert **1** into **2**, thus demonstrating the requirement for drastic basic conditions. Moreover, the reaction requires long exposure to high temperature (reflux), as both reduction of either reaction

time or temperature led to practically exclusive recovery of the starting material. It is therefore assumed that the isomerization bears high activation energy.

Previous reports describe the isomerization of dipropargyl acetic acid **1b** to meta-toluenic acid **2** upon either thermal exposure of an aqueous solution or treatment with acid without heating (Perkin & Simonsen, 1907). These findings appear to contradict the above statements regarding required reaction conditions. It is assumed that the rearrangement originates from the alkene-allene precursor shown in Figure 4-1. The formation of the allene is driven by conjugation based on enolization of the central carbonyl. This process, may be catalyzed either by acidic or basic conditions. The reported acid-induced isomerization of **1** under comparably mild conditions suggests a more effective acidic catalysis compared to the base-induced reaction.

Scheme 4-4 displays a proposal for the mechanism of the cyclization. The reaction can be described as an intramolecular nucleophilic addition of an allene-enolate to an alkyne. The reaction follows a 6-endo-dig route, which commonly is less favored compared to the competing 5-exo-dig cyclization (Gilmore & Alabugin, 2011). However, Vasilevsky *et al*. reported a similar 6-endo-dig cyclization for an alkyne without enhanced electrophilicity (Vasilevsky, Baranov, Mamatyuk, Gatilov, & Alabugin, 2009). Tautomeric rearrangement of the resulting vinyl anion through a formal 1,2-hydrogen shift provides a resonance stabilized anion, which upon protonation readily leads to the substituted toluene derivative.

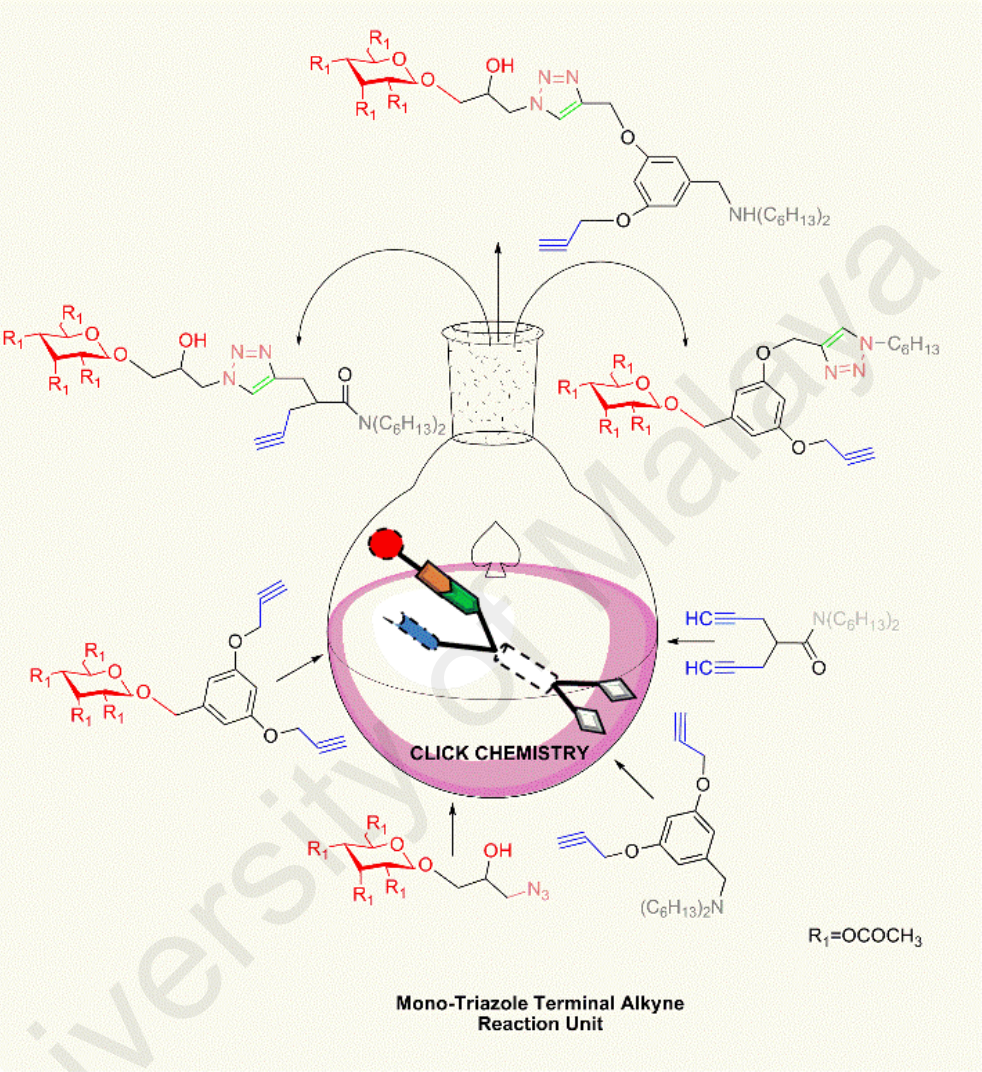


Scheme 4-4: Proposed cyclization mechanism

4.4 Conclusions

We have described a new route to simple aromatic compounds based on the cyclization of 1,6- hexadiynes. The reaction requires a minimum of one hydrogen atom at each sp3-hybridised carbon of the starting material. Although the presence of an electron-withdrawing group at the central carbon is required, initial air induced oxidation enables partial cyclization of 2-propynyl-3-butynol as well.

Chapter 5 : Unexpected mono-coupling "click chemistry'' of di-terminal alkyne



5.1 Introduction

The discovery of click chemistry by Sharpless and co-workers in 2001 is considered as the most straightforward synthesis of 1,3-dipolar cycloaddition of azide and terminal alkynes (Stefani *et al*., 2011) (Kolb *et al*., 2001). Although the concept of click chemistry was only introduced in the last decade, the copper-catalyzed azide-alkyne cycloaddition (CuAAC) has already become one of the most utilized reactions in various application fields (Meldal & Tornøe, 2008) (Such *et al*., 2012) (Dedola, Nepogodiev, & Field, 2007b). The CuAAC combines the advantages of simple reaction

conditions, regioselectivity (in contrast to the thermal process), high efficiency under mild conditions, minimal by products and practically no significant side reactions, while being compatible with most functional groups, thus enabling a wide application potential. It is frequently accessed in drug discovery, polymer and material science, the life science sector etc. (Dedola *et al*., 2007b) (Kolb & Sharpless, 2003) (Meldal & Tornøe, 2008). Recently, the synthesis of symmetrical and unsymmetrical bis-triazoles using the CuAAC has attractive considerable interest in the coordination chemistry (Schuster *et al*., 2009) (Albrecht, 2008) (Stefani *et al*., 2011) (Heckenroth *et al*., 2008) (Karthikeyan & Sankararaman, 2009) (Lalrempuia, McDaniel, Müller-Bunz, Bernhard, & Albrecht, 2010). Despite several successful reports on the synthesis of symmetrical and unsymmetrical bis-triazoles (Fiandanese *et al*., 2009) (Aizpurua *et al*., 2010), Bradley *et al*. (Doak *et al*., 2011) reported that the synthesis of a number of unsymmetrical bis- triazoles based on the reaction of TMS butadiyne with benzyl azide under standerd CuAAC condition only gave trace amounts (5%) of the symmetrical product (bis-triazole) but 53% of mono-triazole. The unusual output was attributed to the acidic nature of the substrate.

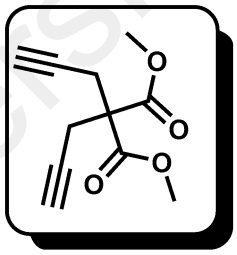
In the attempts to prepare new double-headed carbohydrate surfactants using the click chemistry concept, we experienced difficulties to drive the reaction of dipropargylic substrates to completion. Instead of the expected bis-triazoles the only mono-click products were obtained in surprisingly high yield.

5.2 Materials and methods

5.2.1 Material and Characterization

Starting materials and solvents of analytical grade were acquired from various commercial sites and used without further purifications. TLC analyses were performed on silica gel 60 (Merck F_{254}) and were visualized by UV, 15 % ethanolic sulfuric acid and subsequent heating or treatment with potassium permanganate. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ on a 400 and 600 MHz spectrometers at room temperature. Matrix-assisted laser desorption/ionization (MALDI) time of flight (TOF) mass spectra were recorded at the Mass Analytical Service Centre of the National University of Singapore on a Shimadzu/Kratos (Columbia, MD) AXIMA CFR mass spectrometer in reflection mode. The samples were co-precipitated with 2,5-dihydroxy-benzoic acid (DHB, 5 mg/100 µl in MeOH/H_2O 1:1) and were irradiated by a N_2-laser at λ=335 nm.

5.2.2 Experimental

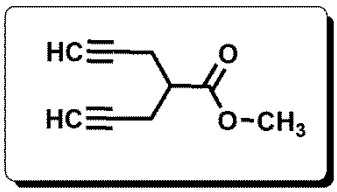


Chemical Formula: $C_{11}H_{12}O_4$
Molecular Weight: 208.2106

5.2.2.1 Dimethyl 2,2-di(propynyl)malonate (5)

A procedure similar to that reported in literature (Carney *et al*., 2008) was employed. Dimethyl malonate (6.0 mL, 52 mmole) was added dropwise to a suspension of sodium hydride (60 % wt in mineral oil, 4.22 g, 105.5 mmol) in dry THF (100 mL) which was stirring at 10°C. Then the reaction mixture was left stirring for 10min., and then propargyl bromide (80 % wt. In toluene, 12.0 mL, 107.7 mmol) was added dropwise. The reaction mixture was warmed to room temperature and stirred for

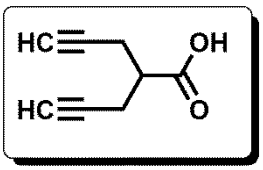
overnight. The reaction mixture was extracted three times with water and Et_2O. The combine organic phases were washed with brine water, dried over $MgSO_4$, filtered and concentrated on a rotary evaporator leaving white solid. The solid was crystallized from ethyl acetate to give 9.44 g of a crystalline white solid (84 % yield).



Chemical Formula: $C_9H_{10}O_2$
Molecular Weight: 150.1745

5.2.2.2 Methyl-2-bis (propynyl) acetate

The synthesis of methyl 2-(2-propynyl)-4-pentynoate was carried out according to the method reported in the literature (Carney *et al.*, 2008). Dimethyl 2,2-di(propynyl)malonate (4.70 g, 22.6 mmole) and lithium chloride (2.95 g, 69.70 mmole) were dissolved in a mixture of 1 mL water and 40 mL DMSO. The mixture was then reflux for 1h. After cooling, the mixture was extracted with $CHCl_3$ and H_2O. The combined organic phases were washed with brine water and dried over MgSO4, filtered through silica gel and concentrate in a rotary evaporator to give yellow oil. The crude oil was purified by flash chromatography column using 20 % ethyl acetate in hexane as the eluent to give 3.0 g of a pale yellow oil (90 % yield).

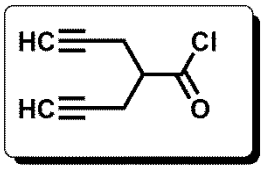


Chemical Formula: $C_8H_8O_2$
Molecular Weight: 136.1479

5.2.2.3 2-Bis (propynyl) acetic acid

Hydrolysis of methyl-2-bis (propynyl) acetate (3 g, 20.11 mmole) was done by additional of NaOH (10 g, 250 mmole) in aqueous ethanol (24 mL, 75 % v/v). The mixture was then reflux for overnight at 90 °C. After evaporation the solvents, water and DCM were added to the residue, and the mixture was acidified with dilute

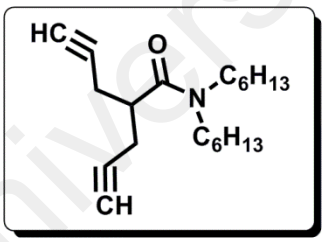
hydrochloric acid to pH 1. The organic phase was washed with brine water and dried over $MgSO_4$, The crude was purified by flash chromatography followed by subsequent crystallization to give 1.7 g from the corresponding carboxylic acid (60 % yield). ^{1}H NMR ($CDCl_3$) δ =10.29 (bs, 1H, OH); 2.86- 2.79 (m, 1H, $CH(CH_2)_2$), $J_{1,2;\ 1,3}$ = 6.21, 12.76; 2,68 (bs, 4H, 2x CH_2); 2.05 (t, 2H, 2x CH-propargyl). ^{13}C NMR ($CDCl_3$) δ = 178.48 (COOH); 80.15 (2x C =CH); 70.84 (2x C= CH); 42.89 (CH); 19.60 (2x CH_2).



Chemical Formula: C_8H_7ClO
Molecular Weight: 154.5936

5.2.2.4 2-Bis (propynyl) acetic chloride (6)

To a stirred solution of 2-bis (propynyl) acetic acid (2 g, 14.80 mmole) in $CHCl_3$ 100 mL, oxalyl chloride (3.75 g, 29.60 mmol) was added slowly. The reaction mixture was reflux at 50 °C for overnight, then concentrated in a rotary evaporator and used directly for the next reaction. The residue was yellowish 2.2 g (98 % yield).

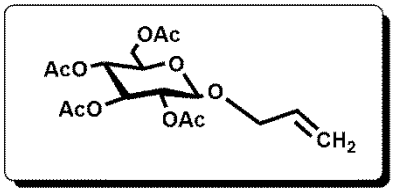


Chemical Formula: $C_{20}H_{33}NO$
Molecular Weight: 303.4821

5.2.2.5 *N,N*-dihexyl-2-bis (propynyl) acetanamide (7)

2-bis(propynyl) acetic chloride (2 g, 12.93 mmole), dihexylamine (3.6 g, 19.4 mmole) and triethylamine (5.41 mL, 38.54 mmole) were mixed in acetoneitrile, then the mixture was refluxed for overnight. The solvent was evaporatord and the residue purified by flash chromatography column using 20 % ethyl acetate in hexane as the eluent to give 2.6 g of a pale yellow oil (66 % yield). ^{1}H NMR ($CDCl_3$) δ =3.34 (t, 4H,

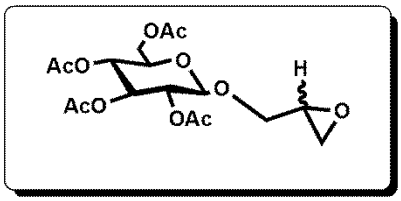
$N(CH_2)_2$; 3.06 (p, 1H, CH); 2.50- 2.48 (m, 4H, 2x CH_2-propargyl); 2.00- 1.98 (m, 2H, 2x CH propargyl); 1.65- 1.58, 1.55- 1.49 (2x m, 2x 2H, 2x B-CH_2); 1.30 (bd, 12H, bulk-CH_2); 0.92- 0.86 (m, 6H, 2x CH_3). ^{13}C NMR ($CDCl_3$) δ =172.15 (CO); 81.46 (2x C≡CH); 70.00 (2x C≡ CH); 48.26, 46.66 (2x $N(CH_2)_2$); 39.81 (CH); 31.59, 31.51 (2x ∞-2); 29.69, 27.49 (2x ∞-1); 26.63, 26.53 (bulk-CH_2); 22.57, 22.55 (2x B-CH_2); 21.85 (2x CH_2-propargyl); 13.99, 13.93(2x CH_3).



Chemical Formula: $C_{17}H_{24}O_{10}$
Molecular Weight: 388.3665

5.2.2.6 Allyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (1)

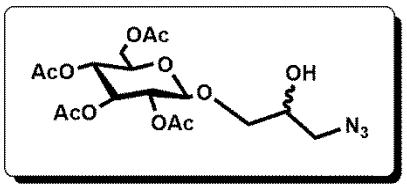
(10 g, 25.6 mmol) glucose pentaacetate and 1.9 mL (27.8 mmol, 1.1 eq.) allyl alcohol were dissolved in 120 mL dichloromethane and treated with 4.8 mL (38.2 mmol, 1.5 eq.) BF_3xEt_2O. The reaction was stirred at room temperature for 3h and then washed with an aqueous solution of $NaHCO_3$ and dried over $MgSO_4$. The solvent was concentrate and crystalized by ethanol to get (6.4 g) white crystal and the residue was purified by column chromatography using hexane: ethyl acetate (3:1) as eluent to obtain (2.3 g), total yield was 87 %. ^{1}H NMR ($CDCl_3$) δ = 5.80-5.65 (m, 1H, allylic CH=); 5.20-5.10 (m, 2H, allylic CH_2=); 5.08 (dd~t, 1H, H-3); J=9.50 Hz; 4.95 (dd~t, 1H, H-4); J=10.00 Hz; 4.87 (dd~t, 1H, H-2); J=9.50 Hz; 4.47 (d, 1H, H-1); J=8.07 Hz; 4.25-4.09 (m, 2H, H-6); 4.06-3.91 (2m, 4H, H-6, OCH_2); 3.64 (ddd, 1H, H-5); J=4.5, 2.5 Hz; 1.97, 1.93, 1.91, 1.89 (4x s,3H, 4x Ac); ^{13}C NMR ($CDCl_3$) δ = 170.51, 170.11, 169.31,169.20 (4x COCH_3); 133.26 (C$H=CH_2$); 117.46 (CH=CH_2); 99.43 (B C1); 72.72 (C4); 71.62 (C2); 71.16 (OCH2); 69.88 (C6); 68.31 (C3); 61.82 (C5); 20.60, 20.53, 20.47 (4x OCH_3).



Chemical Formula: $C_{17}H_{24}O_{11}$
Molecular Weight: 404.3659

5.2.2.7 2,3-Epoxypropyl 2,3,4,6-Penta-*O*-acetyl-*β*-D-glucopyranoside (3a + 3b)

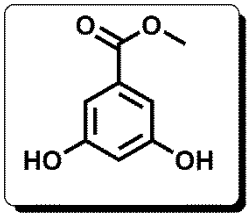
Compound **1** (2 g, 5.15 mmol) was dissolved in 100 mL dichloromethane, MCPBA (2.2g, 12.8mmol, 2.5eq.) was added to the solution and the mixture left stirred overnight at room temperature. The reaction mixture washed with an aqueous solution of $NaHCO_3$ twice. The organic layer was dried over $MgSO_4$ and evaporatord in vacuo to concentrate. 20 mL of ethyl acetate was added to the mixture to crystalize to give pure compound **2** (1 g) white crystal and the residue was purified by flash chromatography over silica gel (3:1 hexane: ethyl acetate) to give (0.6 g) pure, total yield was 77 %. ^{1}H NMR ($CDCl_3$) δ = 5.12/5.05 (2 dd~t, 1H, H-3); J=9.50 Hz; 5.00/4.95 (2 dd~t, 1H, H-4); J=10.0, 4.91/4.89 (2 dd, 1H, H-2); J=9.50 Hz; 4.57/4.48 (2 d, 1H, H-1); J=8.00 Hz; 4.19/4.16 (dd, 1H, H-6a); J=12.00 Hz; 4.04 (dd~bd, 1H, H-6b); 3.91, 3.79 (2 dd, 1H, OC$\underline{H}_2$ I); J=3.00 Hz; 3.74, 3.64 (2 dd, 1H, OCH_2 II); J=6.50 Hz; 3.64 (m, 1H, H-5); 3.05 (m, 1H, $CH_2C\underline{H}OCH_2$); J=2.50 Hz; 2.69 (m, 1H, $CH_2CHOC\underline{H}_2$ I); 2.56/2.46 (m, 1H, CH2CHOC$\underline{H}_2$ II); 2.08, 2.07, 2.04, 2.01 (4x s, 3H, 4x $COCH_3$); ^{13}C NMR ($CDCl_3$) δ =170.96, 170.46, 170.05, 169.31 (4x $\underline{C}OCH_3$); 100.90, 100.39 (2 x C1); 72.69, 72.65 (2x C3); 71.79 (C5); 71.02 (C2); 70.43, 68.99 (OCH_2); 68.20, 68.19 (C4); 61.62 (C6); 50.41, 50.15 ($CH_2C\underline{H}OCH_2$); 43.97, 43.92 ($CH_2CHOC\underline{H}_2$); 20.57, 20.52, 20.45 (4x $CO\underline{C}H_3$).



Chemical Formula: $C_{17}H_{25}N_3O_{11}$
Molecular Weight: 447.3939

5.2.2.8 (2′-hydroxy-3′-azidopropyl)-2,3,4,6-Penta-*O*-acetyl-*β*-D-glucopyranoside (4a + 4b)

Anhydrous NaN_3 (0.8 g, 12.3 mmol, 2.5 eq.) was added to a DMF solution of compound **2** (2 g, 4.9mmol, 1eq.) and the solution was stirred at 80 °C for overnight. Removed the solvent by evaporation in vacuo, washed the residue with water and DCM, separated the organic layer and dried over $MgSO_4$ and then concentrated to give compound **3** as a syrup (2 g, yield 90 %). ^{1}H NMR ($CDCl_3$) δ = 5.22 (dd~t, 1H, H-3); J= 9.44; 5.10-5.03 (2 dd~t, 1H, H-4); J=10.0; 4.97 (2 dd, 1H, H-2); J=9.50; 4.55 (2 d, 1H, H-1); J=8.00; 4.25-4.15 (m, 2H, H-4, H-6); 3.99-3.69 (m, 4H, H-5, O$\underline{C}H_2$CHOH, $OCH_2\underline{C}HOH$); 3.40-3.27 (m, 2H, CHOH$\underline{C}H_2N_3$); 2.10, 2.06, 2.04, 2.01 (4x s, 3H, 4x Ac); ^{13}C NMR ($CDCl_3$) δ = 170.61, 170.14, 169.42, 169.38 (4x $\underline{C}OCH_3$); 101.40, 101.28 (C1); 72.72,72.57 (C3); 72.16 ($OCH_2\underline{C}HOH$); 71.95 (O$\underline{C}H_2$); 71.24, 71.22 (C2); 69.66, 69.53 (C5); 68.41, 68.35 (C4); 61.97, 61.95 (C6); 53.00, 52.98 (CHOH$\underline{C}H_2N_3$); 20.58, 20.29 (CO$\underline{C}H_3$).

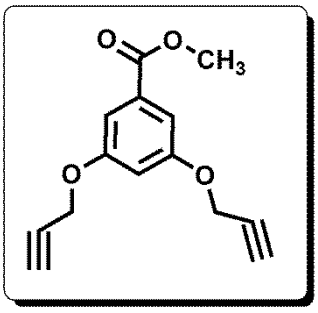


Chemical Formula: $C_8H_8O_4$
Molecular Weight: 168.1467

5.2.2.9 Methyl 3,5-dihydroxybenzoate

2 mL of concentrate H_2SO_4 was added to a stirred solution of 3,5-dihydroxybenzoic acid (4.0 g, 25.95 mmole) in methanol. The reaction mixture was then refluxed for 2h at 100 °C. The solvent was evaporatord and the residue was taken

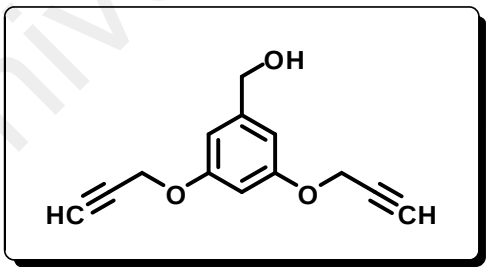
up in water and extracted with ethyl acetate three times. The combined organic phases were washed with brine water and dried over $MgSO_4$, then concentrate in a rotary evaporator to give 4.2 g from the corresponding carboxylic acid (98 % yield).



Chemical Formula: $C_{14}H_{12}O_4$
Molecular Weight: 244.2427

5.2.2.10 Methyl 3,5-dipropynylbenzoate

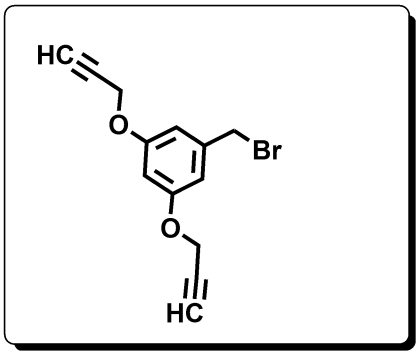
To a stirred solution of methyl 3,5-dihydroxybenzoate (4.0 g, 23.78 mmole) and K_2CO_3 (9.84 g, 71.36 mmole) in acetonitrile, propargyl bromide (7.85 mL, 89.20 mmole) was added. The reaction mixture was refluxed at 80 °C for overnight. The mixture was filtered, then the solvent was evaporatord and the residue extracted three times with DCM and water. The combined organic phases were washed with brine water and dried over $MgSO_4$, then concentrated in a rotary evaporator to give 5.0 g yellowish solid (86 % yield).



Chemical Formula: $C_{13}H_{12}O_3$
Molecular Weight: 216.2326

5.2.2.11 3,5-Dipropynylbenzayl alcohol

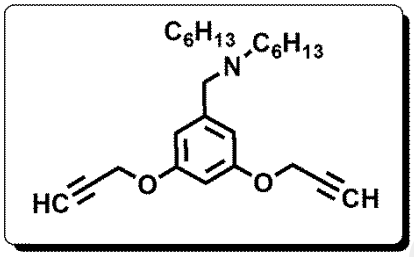
A similar procedure to that reported in literature (Cai, Jiang, Shen, & Fan, 2012a) was employed.



Chemical Formula: $C_{13}H_{11}BrO_2$
Molecular Weight: 279.1292

5.2.2.12 3,5-Dipropynylbenzayl bromide

The synthesis procedure was carried out according to the method reported in the literature (Cai, Jiang, Shen, & Fan, 2012b).

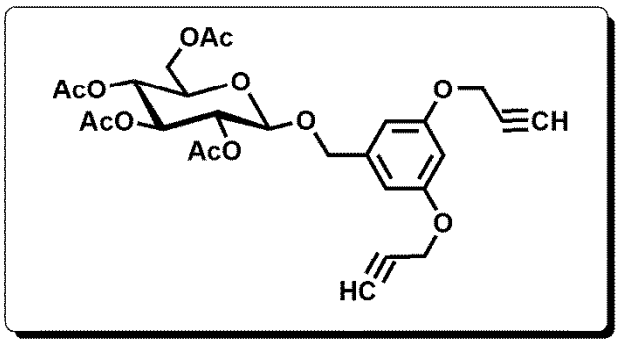


Chemical Formula: $C_{25}H_{37}NO_2$
Molecular Weight: 383.5668

5.2.2.13 *N*-(3,5-dipropynylbenzayl)-*N*,*N*-dihexylamine (8)

Tetrabutylammonium bromide (0.5 g, 1.55 mmole) was added to a solution of 3,5-dipropynylbenzayl bromide (1.7 g, 6.1 mmole) and dihexylamine (2 mL, 8.6 mmole) in DCM (40 mL) and 2N of sodium hydroxide solution. The reaction mixture was stirred for overnight at room temperature, then poured into distilled water and extracted with DCM three times. The combined organic phases were washed with brine water and dried over $MgSO_4$, and concentrate in a rotary evaporator to give yellow oil. The crude oil was purified by flash chromatography column using 20% ethyl acetate in hexane as the eluent to give 2.0 g of a colorless oil (87 % yield). ^{1}H NMR ($CDCl_3$) δ =6.58 (s, 2H, 2x CH-benzene); 6.43 (s, 2H, CH-benzene); 4.60, 4.59 (2x s, 4H, 2x OCH_2); 3.46 (s, 2H, CH_2N); 2.44 (t, 2H, 2x CH propargyl); 2.37- 2.34 (m, 4H, $N(CH_2)_2$); 1.43- 1.36 (m, 4H, 2x B-CH_2); 1.25- 1.15 (m, 12H, bulk-CH_2); 0.80 (t, 6H,

2x CH_3). ^{13}C NMR ($CDCl_3$) δ =158.56 (2x C-benzene); 137.00 (C-benzene); 108.24 (2x CH-benzene); 100.91 (CH-benzene); 78.54 (2x C =CH); 75.42 (2x C= CH); 58.57 ($CH_{2benzyl}N$); 55.90 (2x CH_2-propargyl); 53.76 ($N(CH_2)_2$); 31.78 (2x ∞-2); 27.11 (2x ∞ -1); 22.66 (2x B-CH_2); 14.05 (2x CH_3).



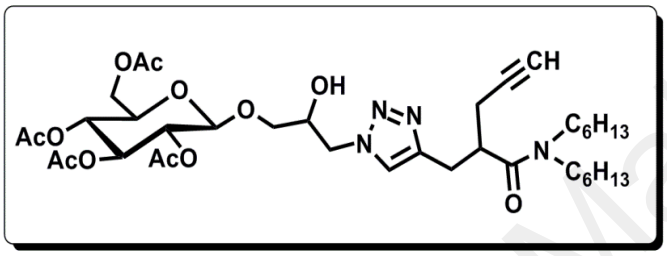
Chemical Formula: $C_{27}H_{30}O_{12}$
Molecular Weight: 546.5199

5.2.2.14 3,5-Di-propynyl banzayl-2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranoside (2)

(10g, 25.6mmol) glucose pentaacetate and 6.0 g (28.17 mmol, 1.2 eq.) 3,5-dipropynylbenzayl alcohol were dissolved in 120 mL dichloromethane and treated with 9.6 mL (76.4 mmol, 1.5 eq.) BF_3xEt_2O. The reaction was stirred at room temperature for 3h and then washed with an aqueous solution of $NaHCO_3$ and dried over $MgSO_4$. The solvent was concentrate and purified by column chromatography using hexane: ethyl acetate (3:2) as eluent to obtain (9.5 g), yield was 67 %. ^1H NMR ($CDCl_3$) δ = 6.55 (bs, 3H, CH-benzene); 5.20-5.04(m, 2H, H-3, H-4); 4.83 (d, 1H, H-1), J= 12.74; 4.67 (d, 4H, $(OCH_2)_2$), J=2.36; 4.59- 4.55 (m, 2H, CH_2-benzyl); 4.28, 4.25 (dd, 1H, H-2), J=4.68; 4.18- 4.09 (m, 2H, H-6); 3.70- 3.66 (ddd, 1H, H-5), J=7.00, 4.60; 2.55 (t, 2H, $(C\equiv H)_2$), J=2.34; 2.10, 2.03, 2.02, 2.00 (4x s, 12H, OCH_3). ^{13}C NMR ($CDCl_3$) δ = 170.67, 170.24, 169.39, 169.36 (4x CO); 158.75 (2x C benzene); 139.21 (C benzene); 107.23 (2x CH benzene); 101.57 (CH benzene); 99.25 (C-1); 78.29 (C-propargyl); 75.80 (CH-propargyl); 72.80 (C-4); 71.85 (C-2); 71.28 (C-5); 70.30 (CH_2-benzyl); 68.36 (C-3); 61.90 (C-6); 55.89 (2x OCH_2); 20.73, 20.67, 20.58, 20.56 (4x $COCH_3$).

5.2.3 General Procedure for Click-Chemistry

A solution of the azide compound and the dendrimer propargyl building blocks compound in methanol (5mL) was treated with copper chloride or copper iodide. The mixture was stirred at room temperature for overnight. The reaction mixture was filtered through ciliate and concentrated under reduced pressure, the residue was purified through silica gel with 9:1 chloroform: methanol as eluent to result the corresponding mono-click propargyl compounds.

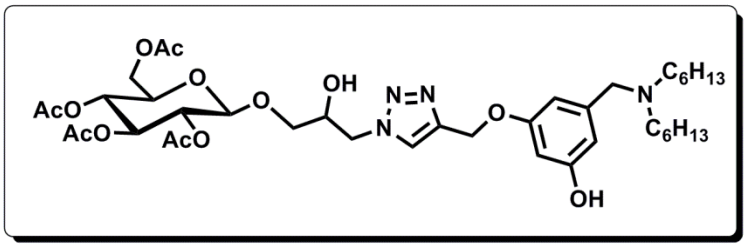


Chemical Formula: $C_{37}H_{58}N_4O_{12}$
Molecular Weight: 750.8760

5.2.3.1 2-((2′-hydroxypropyl-2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranosyloxy)methyl -1,2,3-mono-triazole)-*N*,*N*-dihexylpent-4-yn amide (10)

3.2 g (7.15 mmole) of sugar azide **4** and 1.0 g (3.35 mmole) of di-propargyl compound **7** were subjected to click chemistry reaction, according to general procedure **5.2.3** to give 2.0 g product (yield 79 %). ^{1}H NMR ($CDCl_3$) δ =7.50- 7.46 (m, 1H, CH-triazole); 5.24- 5.20 (m, 1H, H-3); 5.08- 5.04 (m, 1H, CHOH); 5.03- 4.98 (m, 1H, H-1); 4.60- 4.56 (m, 1H, H-2); 4.48- 4.13 (m, 4H, OCH_2, H-4, H-5); 3.90- 3.59 (m, 4H, H-6, CH_2-triazole); 3.50- 3.10 (m, 4H, $N(CH_2)_2$, triazole-CH_2); 3.01- 2.78 (m, 4H, COCH, $CHCH_2$, CH-propargyl); 2.08, 2.07, 2.06, 2.05, 2.02, 2.00 (s, 12H, CH_3CO); 1.37-1.13 (m, 16H, bulk-CH_2); 0.88- 0.86 (m, 6H, CH_3). ^{13}C NMR ($CDCl_3$) δ =173.74 (CON); 171.34, 170.63, 170.15, 169.55, 169.41 (4x $COCH_3$); 144.66 (m, C-triazole); 123.77 (m, CH-triazole); 101.30, 101.14 (C-1); 77.23 (C-propargyl); 73.99 (CH-propargyl); 72.57 (C-4); 72.02, 71.93 (CHOH); 71.66, 71.60 (OCH_2); 71.24 (C-2); 69.12, 69.08 (C-5); 68.34 (C-3); 61.83 (C-6); 52.67, 52.51, 52.41 (m, CH_2-triazole); 48.12, 48.01, 46.38,

47.73 ($N(CH_2)_2$); 45.73 (CH_2-triazole); 41.60 (COCH); 31.55, 31.44 (∞-2); 29.68, 29.34, 29.30, 28.29 (bulk-CH_2); 27.55 (CH2-propargyl); 26.61, 26.42 (B-CH_2); 22.57, 22.53 (∞-1); 20.68, 20.55 (CH_3CO); 14.02, 13.99 (CH_3). HRMS (MALDI) mono-coupling calcd. for $C_{37}H_{58}N_4O_{12}$ [M+Na]: 773.39; found: 774.64; di-coupling calcd. for $C_{54}H_{83}N_7O_{23}$ [M+Na]: 1220.54; found: 1220.64.

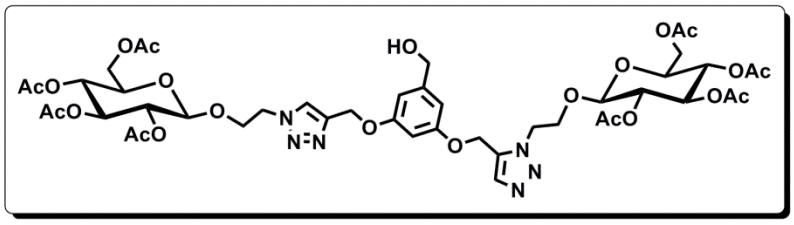


Chemical Formula: $C_{39}H_{60}N_4O_{13}$
Molecular Weight: 792.9127

5.2.3.2 3-((2′-hydroxypropyl-2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranosyloxy) methyl -1,2,3-mono-triazole)-5- propynyl benzyl-*N*,*N*-dihexyl amine (11)

3.2 g (7.15mmole) of sugar azide **4** and 1.28 g (3.35 mmole) of di-propargyl compound **9** were subjectedto click chemistry reaction according to general produre **5.2.3** to give 2.1 g product (yield 77 %). ^{1}H NMR ($CDCl_3$) δ =8.15- 8.09 (m, 1H, CH-benzene); 6.61-6.31 (m, 3H, (CH-benzene)$_2$, CH-triazole); 5.38 (d, 1H, H-1); 5.28 (t, 1H, H-3), J=9.2; 5.08 (d, 2H, OCH_2-triazole), J=4.3; 5.02- 4.74 (m, 3H, CHOH, OCH_2); 4.46- 4.41 (m, 1H, H-2); 4.30- 4.16 (m, 3H, H-4, H-6); 4.05- 3.99 (m, 3H, H-5, CH_2-benzyl); 3.74- 3.66 (m, 2H, triazole-CH_2); 2.40- 2.30 (m, 4H, $N(CH_2)_2$); 2.03, 2.01, 1.98, 1.94 (s, 12H, CH_3CO); 1.41- 122 (m, 16H, bulk-CH_2); 0.82 (t, 6H, CH_3). ^{13}C NMR ($CDCl_3$) δ =170.68, 170.11, 169.66, 169.44 (4x $COCH_3$); 159.34 (Cbenzene); 158.46 (C-benzene); 146.98 (C-triazole); 142.71 (Cbenzene-benzyl); 124.90 (b, CH-triazole); 108.53 ($(CH)_2$ benzene); 101.26 (m, C-1, CH benzene); 74.41 (CH-propargyl); 72.56 (C-4); 72.01, 71.91 (C-2); 71.60, 71.56 (OCH_2, OCH_2triazole); 71.23 (C-3); 71.04 (CH_2-benzyl); 68.90 (CHOH); 68.32 (C-5); 61.80 (C-6); 58.44 (OCH_2-propargyl); 56.32 ($N(CH_2)_2$); 53.50 (b, CH_2-triazole); 31.65, 31.38 (∞-2); 27.01, 26.68 (B-CH_2);

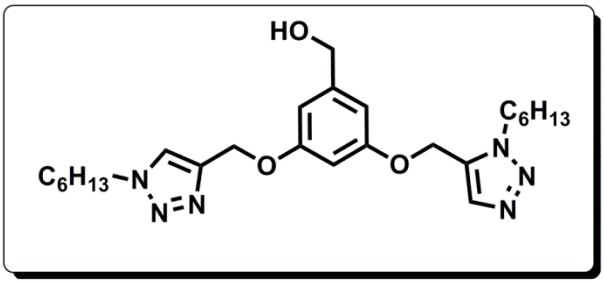
22.59, 22.48 (∞-1); 20.66, 20.54 (CH_3CO); 14.01, 13.94 (CH_3). HRMS (MALDI) calcd. for $C_{39}H_{60}N_4O_{13}$ [M+Na]: 793.43; found: 793.42.



Chemical Formula: $C_{45}H_{58}N_6O_{23}$
Molecular Weight: 1050.9684

5.2.3.3 3,5-Bis(ethayl-2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranosyloxy-1H-1,2,3-triazol-1-yl-4,4'-methoxyl) benzyl alcohol (12)

1.3 g (3.11 mmole) of sugar azide **9** with 0.33 g (1.55 mmole) of 3,5-Dipropynylbenzayl alcohol were subjectedto click chemistry reaction according to general produre **5.2.3**, to gave 1.2 g product (yield was 75 %). ^{1}H NMR (400 MHz, $CDCl_3$) 7.63 (s, triazole), 6.57 (d, 2H, $CH_{\text{-benzene}}$), $^3J_{CH}$ = 2.0, 6.47 (bt, $CH_{\text{-benzene}}$), 5.12-5.08 (m, 6H, H-3, OCH_2), 4.98 (t, H-2), $^3J_{2,3}$ = 9.5, 4.91 (dd, H-4), $^3J_{4,5}$ = 9.5, 4.56 (s, $CH_{2\text{-Benzyl}}$), 4.54 (t, $CH_{2a}N$), 4.46 (dd, H-6a), ^2J = 3.4, 4.41 (d, H-1), $^3J_{1,2}$ = 7.9, 4.19-4.14 (m, OCH_2), 4.05 (dd, H-6b), ^2J= 2.2, 3.89-3.84 (m, $CH_{2b}N$), 3.63 (ddd, H-5), $^3J_{5,6}$ = 9.9, 7.52, 2.00, 1.94,1.92, 1.87 (4s, 3x4 H, Ac). ^{13}C NMR (100MHz, $CDCl_3$) 170.61, 170.13, 169.44, 169.42 (4x $COCH_3$), 159.50 (2x C_{benzene}), 144.13, 144.10 ($C_{\text{-triazole}}$), 143.74 (C_{benzene}), 124.26, 123.96 ($CH_{\text{-triazole}}$), 105.88, 105,82 (2x CH_{benzene}), 100.02, 100.93 (CH_{benzene}), 100.45 (C-1), 72.45 (C-3), 71.93 (C-4), 70.93 (C-2), 68.22 (C-5), 67.68 (2x OCH_2), 64.82 ($CH_{2\text{-benzyl}}$), 61.80 (OCH_2), 61.74 (C-6), 50.08, 49.74 (CH_2N), 20.70, 20.55 (Ac). HRMS (MALDI) calcd. for $C_{45}H_{58}N_6O_{23}$ [M+Na]: 1073.34, [M+K]: 1089.31; found: 1073.84, 1089.81.



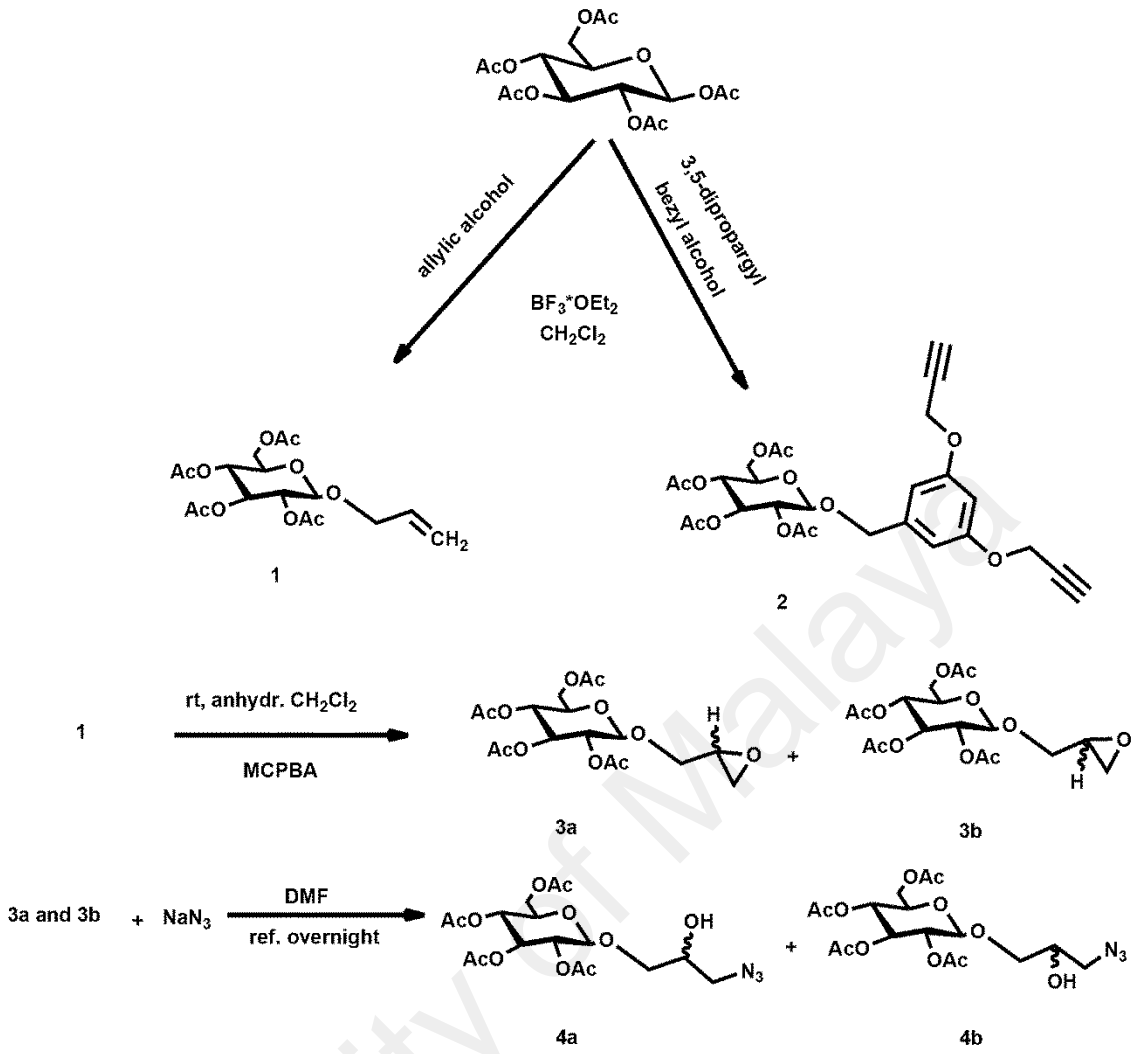
Chemical Formula: $C_{25}H_{38}N_6O_3$
Molecular Weight: 470.6076

5.2.3.4 3,5-Bis(1H-1,2,3-triazol-1-yl-4,4'-methoxyl)benzyl alcohol (13)

0.7 g (5.55 mmole) of hexylazide with 0.5 g (2.31 mmole) of 3,5-Dipropynylbenzayl alcohol di-propargyl were subjectedto click chemistry reaction according to general produre **5.2.3** to gave 0.7 g product (yield was 66 %). ^{1}H NMR (400 MHz, $CDCl_3$) 7.63 (s, triazole), 6.57 (bd, 2H, $CH_{\text{-benzene}}$), 6.48 (bt, $CH_{\text{-benzene}}$), 5.11 (s, 2x2 H, OCH_2) 4.60 (s, $CH_{2\text{-Benzyl}}$), 4.32 (t, 2x2 H, NCH_2), 1.88 (p, 2x2 H, B-CH_2), 1.29 (bs, 12 H, bulk-CH_2), 086 (t, 3x2 H, CH_3). ^{13}C NMR (100MHz, $CDCl_3$) 159.43 (2x C_{benzene}), 144.10 ($C_{\text{-triazole}}$), 144.19 (C_{benzene}), 122.78 ($CH_{\text{-triazole}}$), 105.79 (2x CH_{benzene}), 100.97 (CH_{benzene}), 64.62 (CH_2-benzyl), 61.93 (2x OCH_2), 50.49 (2x $CH_{2\text{-triazole}}$), 31.10 (ω-2), 30.17 (bulk-CH_2), 26.12 (B-CH_2), 22.37 (ω-1); 13.921 (2x CH_3).

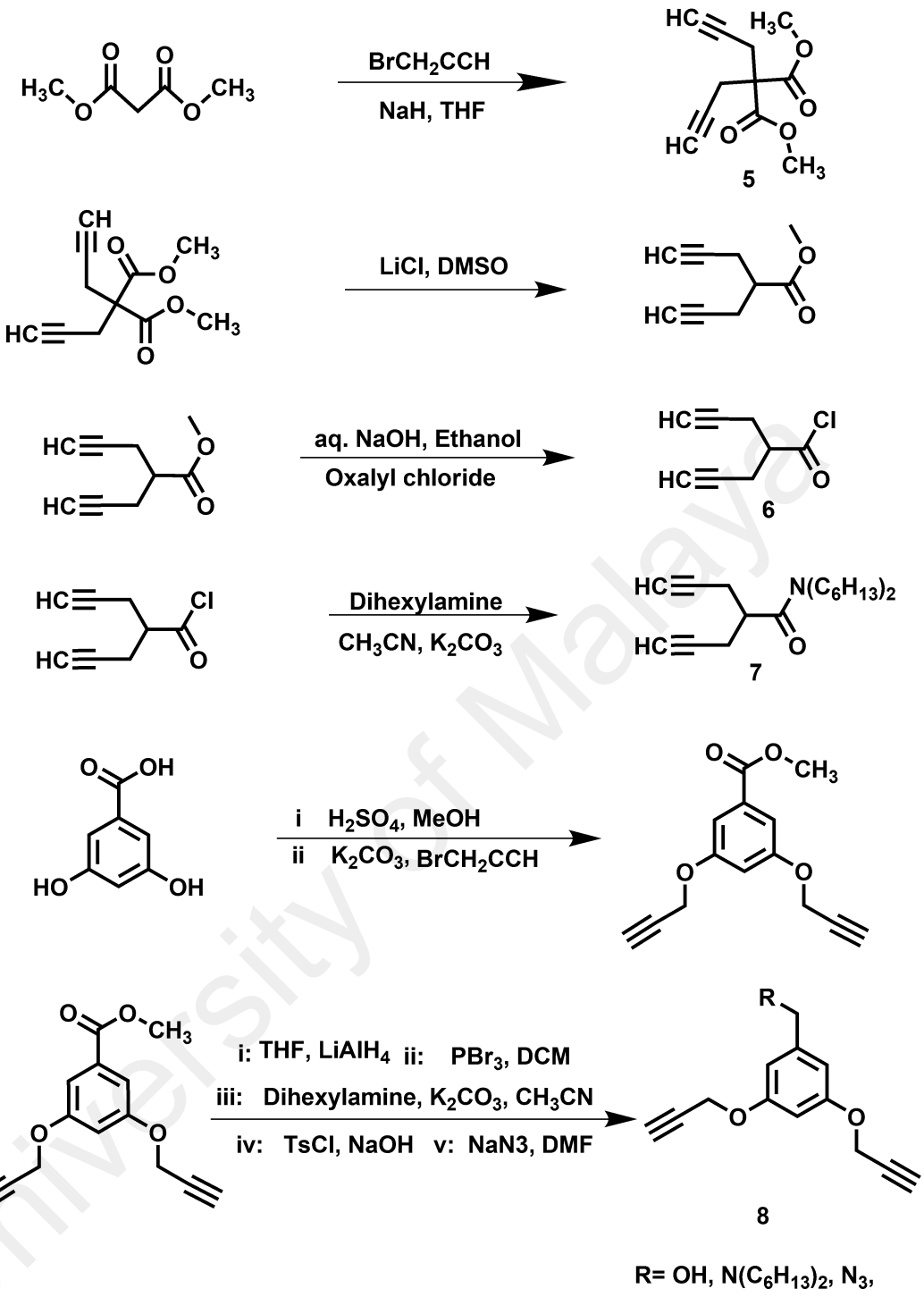
5.3 Results and Discussion

The general strategy used for the synthesis of the target carbohydrate-triazole derivatives is based on the regioselective CuAAC of organic azides with terminal alkynes. The synthesis starts with the preparation of 2′-hydroxy-3′-azidopropyl 2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranoside (**4a + 4b**) (Scheme 5-1), which was synthesized by epoxidation and subsequent ring-openning azidation of allyl 2,3,4,6-tetra-O-acetyl-B-D-glucopyranoside (**1**). mCPBA was applied to prepare the epoxide (**3**) (Barnett & Ralph, 1971; Legler & Bause, 1973), which furnished azide (**4**) in 90 % yield. The alternatively used azide building block (**9**) was prepared according to a literature procedure (Mattarella & Siegel, 2012). For the preparation of the dipropargylated building block (**2**) β-glucose pentaacetate was reacted with 3,5-dipropnyloxy benzyl alcohol (Cai *et al*., 2012a) under BF_3-catalysis (Barnett & Ralph, 1971), affording **2** in 67 % (Scheme 5-1).



Scheme 5-1: Synthesis of glucose pyranoside precursor compounds.

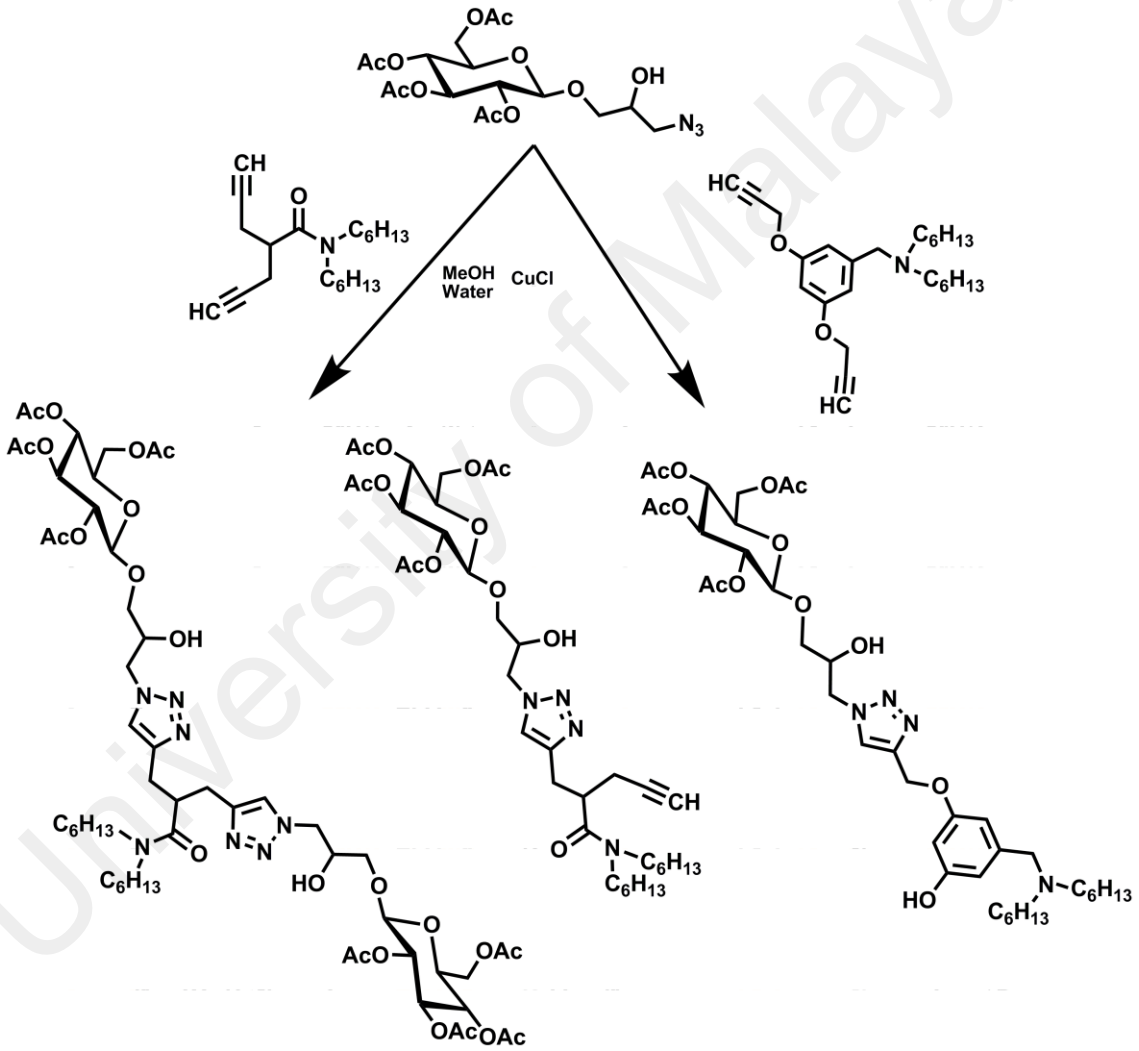
The synthesis of methyl-2-(2-propnyl)-4-pentynoate was carried out according to the literature (Carney *et al.*, 2008). The hydrolysis of methyl-2-(2-propnyl)-4-pentynoate was achieved by treatment with strong base in aqueous alcohol at elevated temperature (reflux) to give the products in conversion yield 60%. Although the 2-bis(propnyl) acetic acid **6** was refluxed with oxallylic chloride in $CHCl_3$ and the product conduct to next reaction with dihexyl amine in present of K_2CO_3 to affording the corresponding compound **7** (Scheme 5-2) (66%).



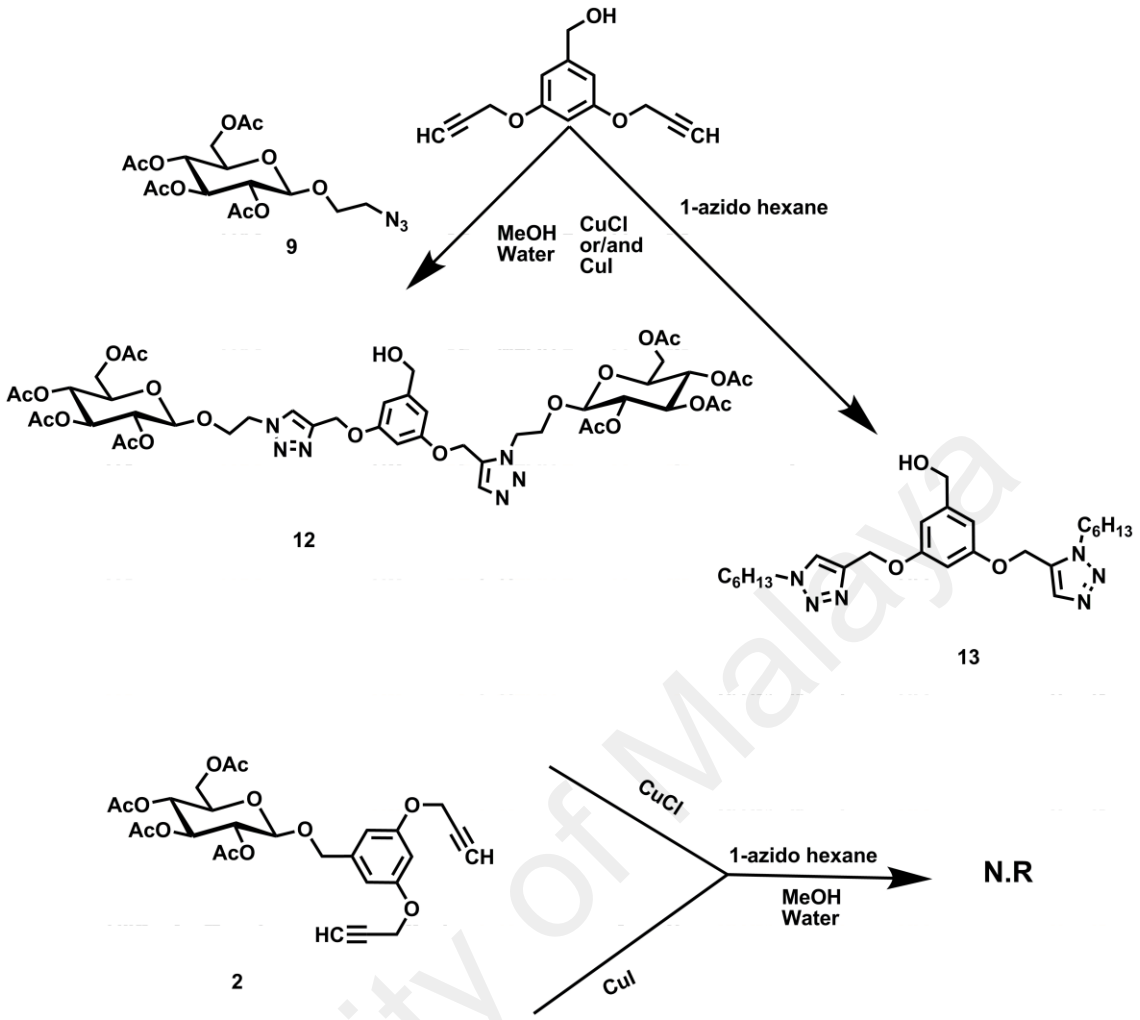
Scheme 5-2: Synthesis of di-propargyl compounds.

The click reaction was studies using differing molar ratios of azido glucosides and bis-propargyls of 2:1 and 3:1. However, the variation did not alter the reaction output at all; only mono-triazole products were obtained. The reaction was performed in methanol as the solvent leading to isolated product yields for the mono-triazole as high as 70-80 %. In contrast, the reaction of sugar di-propargyl compound (**2**) with hexyl

azide did not furnish any click product. This could be due to steric hindrance or/and some kind of coordination obstacle blocking the active side of the click chemistry reaction. The reaction was investigated for altogether three different copper catalysts, *i.e*. CuCl, CuI and $CuSO_4$/Na-ascorbate, but reproducibly furnished no triazole. This result is surprising, since in general no significant differences in the reactivity were observed for propargyls connected with an aromatic and aliphatic group.



A) Mono coupling of dipropargylic system.



B) Di-coupling of of dipropargylic system.

Scheme 5-3: Synthesis of unexpected "click" chemistry compounds.

The mono-coupling was confirmed by a detailed spectroscopic analysis of the reaction products using FT-IR, ^{1}H NMR and ^{13}C NMR. Spectra for the mono-click products **10** and **11** are displayed in Figures 5-1 to 5-3. The FT-IR spectra in Figure 5-1 showed OH-stretching vibrations at 3358, 3351 and 3350 cm^{-1} and correlated bending vibrations at 1221, 1218 and 1224 cm^{-1}, reflecting the presence of the carbohydrate azide. The peaks at 2117 and 2119 cm^{-1}, on the other hand, confirmed the presence of the terminal triple bond. Triazole related C-N stretching vibrations were found at 1369, 1159 and 1035 cm^{-1}. More pronounced than in the IR was the triazole presence in the NMR spectra, shown in Figures 5-2 and 5-3. The triazole CH appeared in the ^{1}H NMR

spectra as singlet peaks between 7 and 7.5 ppm, while the corresponding ^{13}C NMR signals were found between 141 and 145 ppm for the triazole-C and at 122-125 ppm for the aromatic CH. The presence of diastereomers, owing to the racemic stereo-centre (CHOH) at the linker between the sugar and the triazole complicates a detailed NMR analysis.

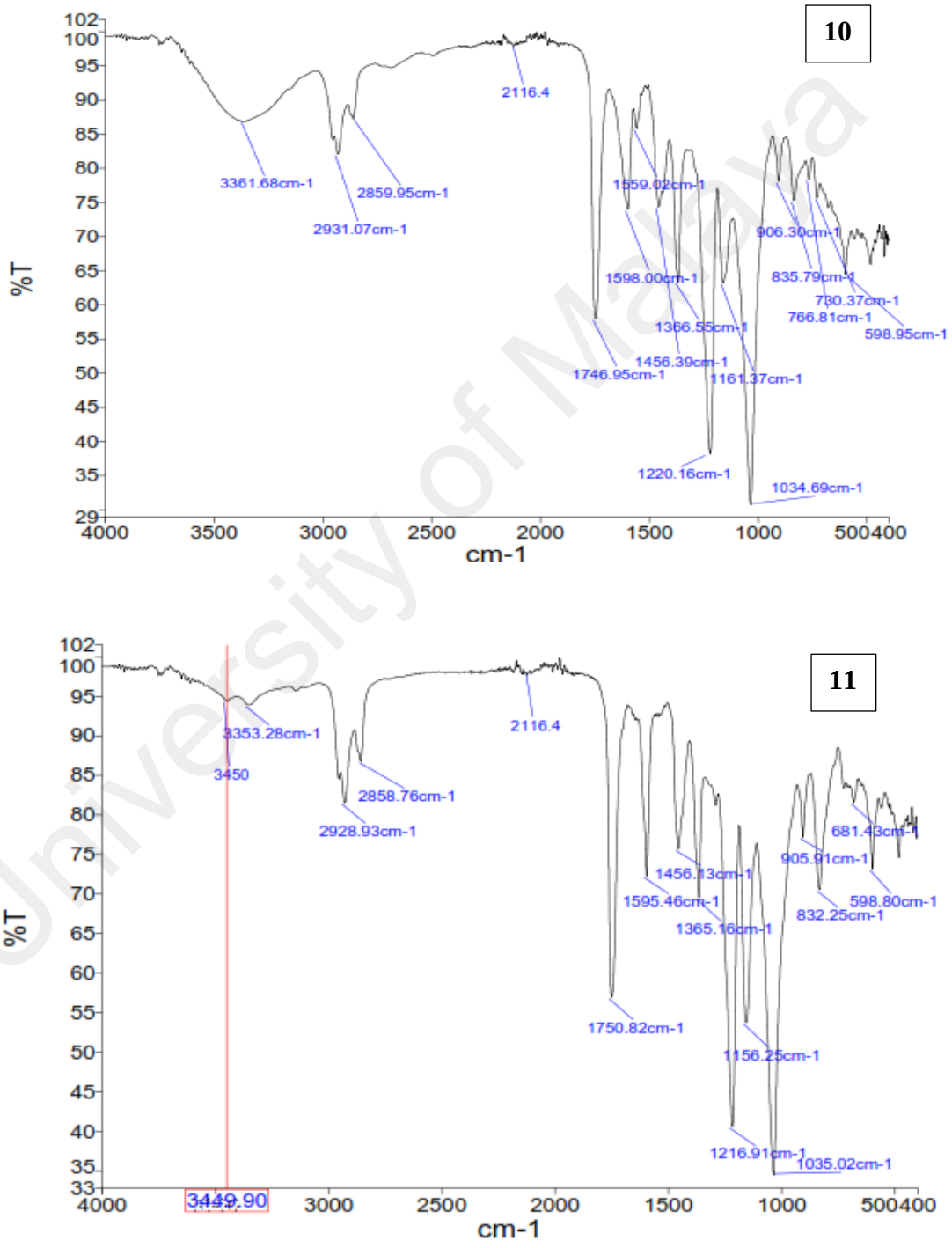


Figure 5-1: FT-IR spectrum for mono-coupling compounds 10 and 11.

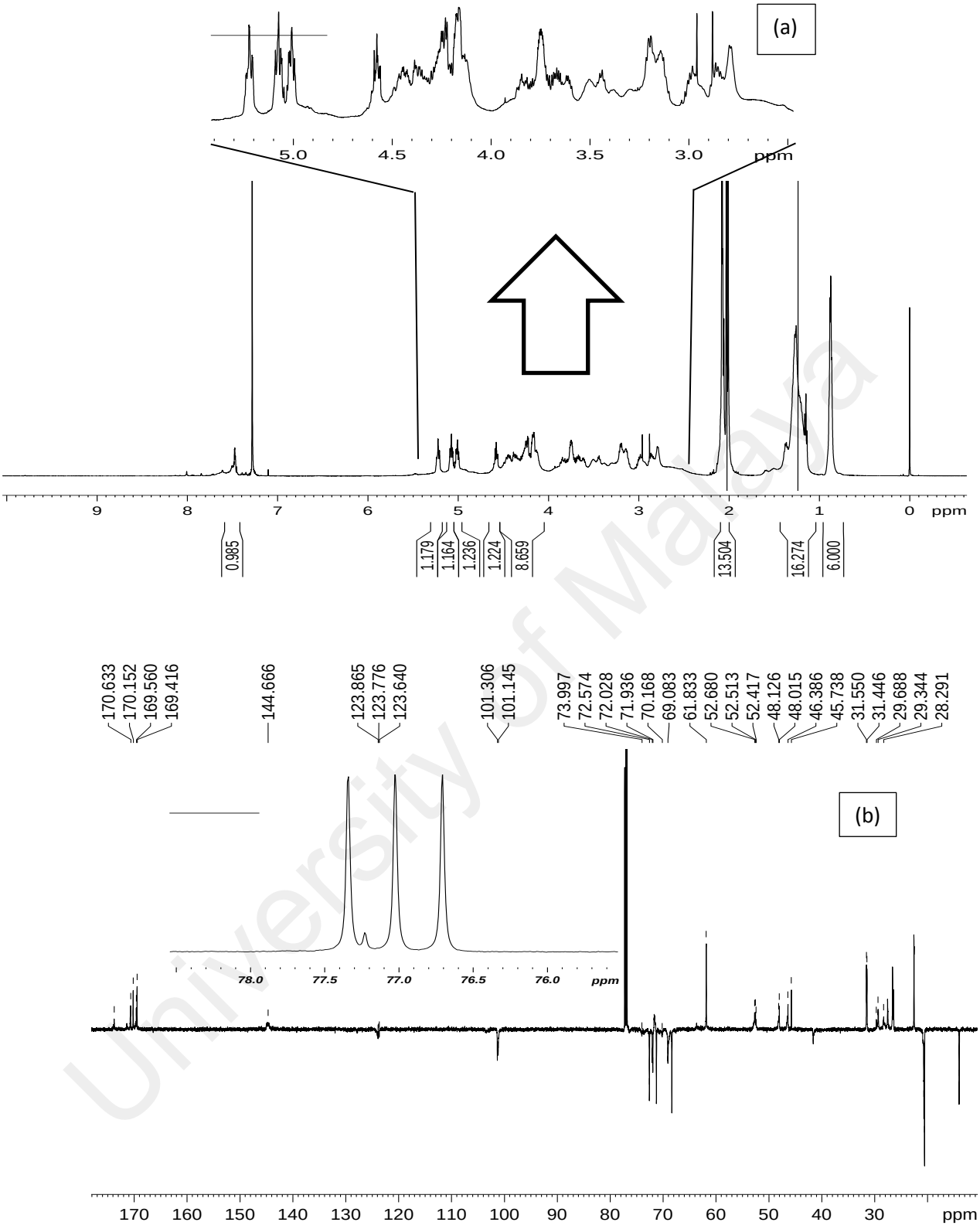


Figure 5-2: The evolution of a) ^{1}H NMR b) ^{13}C NMR spectra (600 MHz, $CDCl_3$, 298 K) for mono-coupling compound 10.

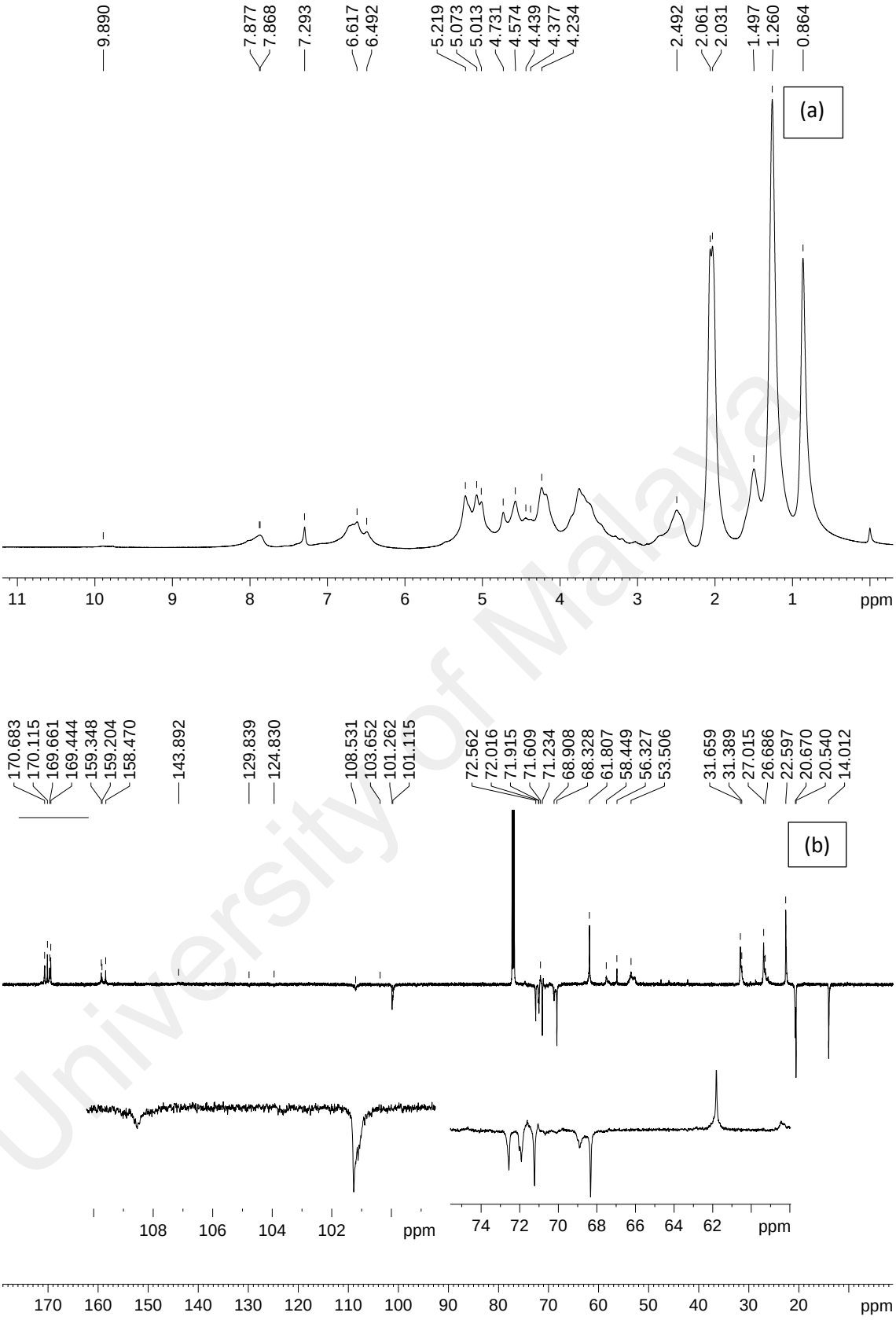


Figure 5-3: The evolution of a) ^{1}H NMR b) ^{13}C NMR spectra (600 MHz, $CDCl_3$, 298 K) for mono-coupling compound 11.

5.4 Conclusion

A number of mono-triazoles with remaining terminal alkyne function have been prepared by coupling of dialkynes with azidoalkyl glucosides in CuAAC "click chemistry" fashion. The spectroscopic characterization of the products, which were obtained in high reaction yields, confirmed both the single coupling and the remaining alkyne function.

Chapter 6 : The effect of aromatic groups on the behaviour of reverse Y-shaped sugar-based surfactants

6.1 Introduction

Synthesis of surfactants has dramatically increased in recent years, reflecting the wide range of applications, these compounds are used for in daily life. Particular interesting surfactants are non-ionic, as their application potential is least restricted by salinity and pH variations. Among the non-ionic surfactants sugar-derived compounds experience highest interest, due to biocompatibility concerns and omnipresent renewable resources. Many studies have been aiming on industrial processes for these compounds as well as on their formulation, trying to optimize the economy of sugar-based surfactants (Fukada, 2000; Lim *et al*., 2000; Penfold & Thomas, 2010; Rybinski & Hill, 1998). Glycolipids, as they are also termed, are associated with environmental independent performance, biological degradability as well as inexpensive and abundant resources. Moreover, their multi-hydroxy head-group ensures good water interaction despite missing ionic charges. This combination makes them highly interesting surfactants (Auvray, Petipas, & Anthore, 1995; Hoffmann & Platz, 2001; Imura *et al*., 2007; Kocherbitov & Soderman, 2003; Ogawa & Osanai, 2012; Soderberg, Drummond, Furlong, Godkin, & Matthews, 1995). The structural diversity of sugar-based surfactants exceeds other surfactant classes by far, owing to the large number of stereo-centres, which adds onto the regio-diversity. This variety potentially provide opportunities to fine-tune both biological and physical properties of sugar-based surfactants, in particular the assembly behaviour, thus giving rise to a vast number of applications in various fields, Features of particular interest involve i) the creation of bio-related ordered systems, *i.e*. vesicles, ii) a chiral environment, iii) potential

biological activity and iv) the ability to form ordered macroscopic assemblies, or liquid crystalline phases.

Besides regio- and stereochemical effects of carbohydrate configurations, the linkage between the sugar head group and the hydrophobic chain affects the surfactant behaviour. This refers not only to the functional group that mediates the connection, but in particular to small molecular spacers and linkers that may be introduced between the two surfactant-antipodes, *i.e*. head group and tail. The current work focuses on the chemical synthesis and phase behaviour study of new reverse Y-shaped surfactants. This term refers to bi-antennary sugar-based surfactants exhibiting two hydrocarbon chains for the hydrophobic, and a single sugar for the hydrophilic domain. In between these two antipodes a variety of different linkers of both aliphatic and aromatic nature have been introduced in order to investigate the effect of the nature of this linker on the surfactant properties.

6.2 Materials and methods

6.2.1 Material

All Chemicals were purchased from various commercial sources and used without further purification. The purification of all products applied column chromatography using the flash technique on silica gel 35-60 mesh (Merck). TLC was performed on precoated plates of silica gel 60 (GF254 by Merck). Visualization was achieved by treatment with 15 % ethanolic sulfuric acid and subsequent heating.

6.2.2 Characterization

Structural identities are based on NMR spectra (^{1}H and ^{13}C, recorded on a Bruker AVN-400 MHz spectrometer). Matrix-assisted laser desorption ionization (MALDI) time of flight (TOF) mass spectra were recorded at the Mass Spectral Service Centre of the National University of Singapore on a Shimadzu/Kratos (Columbia, MD) AXIMA CFR mass spectrometer in reflectron mode. The samples were co-precipitated with 2,5-dihydroxy-benzoic acid (DHB, 5 mg/100 µl in MeOH/H_2O 1:1) and were irradiated by a N_2-laser at λ =335 nm.

6.2.3 Determination of phase behaviour and interfacial properties

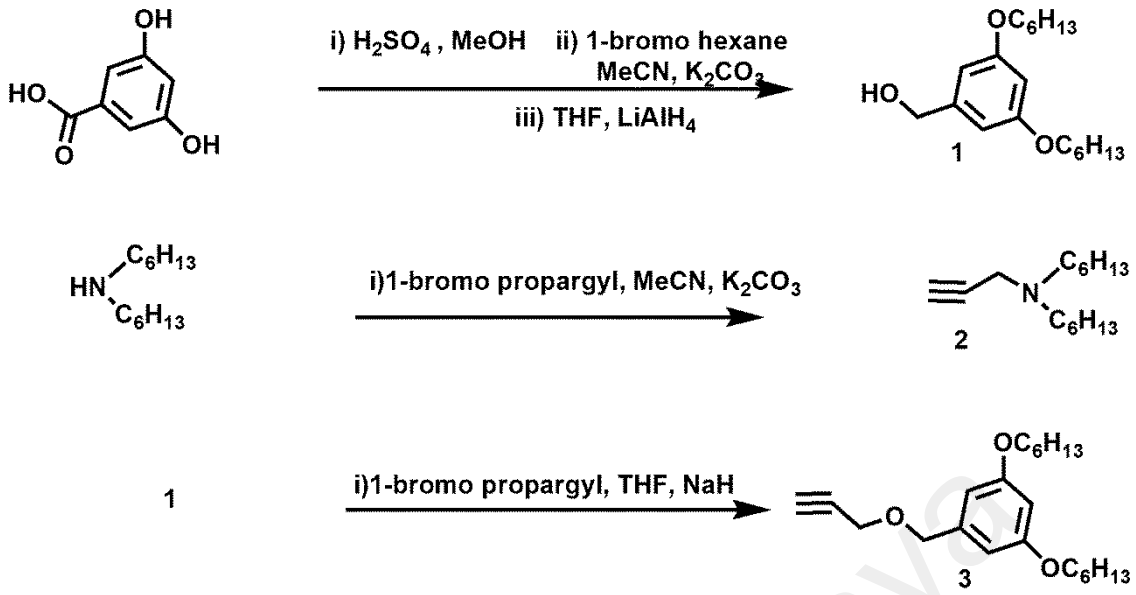
Surface tension measurements were performed at 25 °C under atmospheric pressure using a KSV Sigma 702 tensiometer. This instrument applies the DuNouy ring method. The critical micelle concentration (CMC) was assessed as the intersection of the linear regressions of the surface tension against the logarithmic surfactant concentration for the concentration depending region and the concentration independent region at high surfactant concentration. The surface tension at this intersection point is called the surface tension at the CMC.

The lyotropic phase behaviour of the glycolipids was investigated on an optical polarizing microscope (OPM) (Olympus BH-2 OPM equipped with Mettler FF82 hot

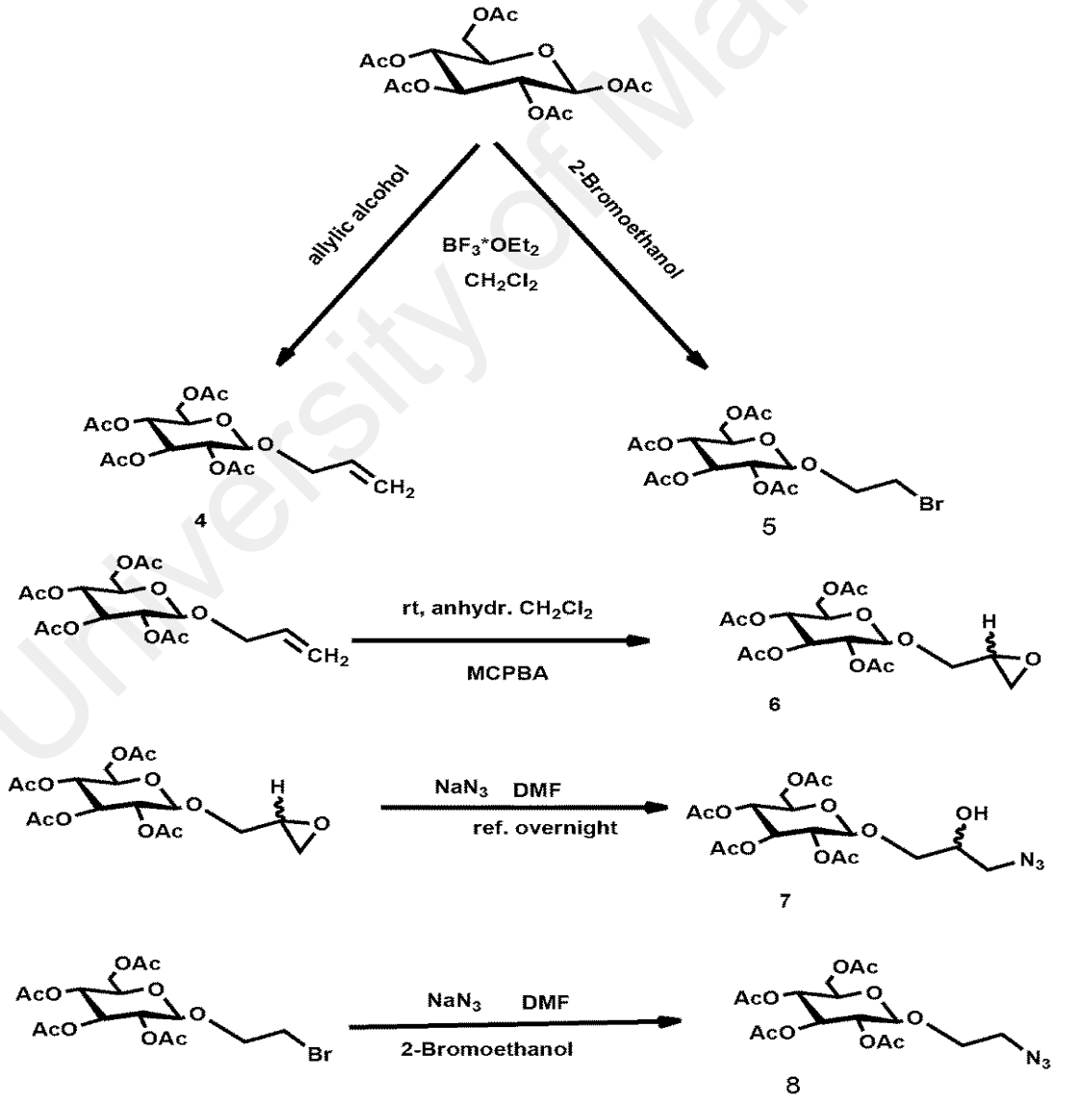
stage and Mettler FP80 Central Processor). The investigation was carried out at room temperature (around 27 ºC) applying two different solvents, one of which is polar (water) and the other one non-polar (1-undecanol). The stability investigation of emulsions applied a composition of 19 volumetric (4.75 mL) parts water and 1 part oil (methyl laurate) with a surfactant content of 0.5 %. The formulation was mixed with a homogenizer (T10 basic, IKA) for approximately 2 minutes at room temperature at a speed of 14,450 rpm. The emulsion samples were stored at room temperature and monitored on phase separation over a period of a few weeks.

6.2.4 Experimental

Non-ionic surfactants with reversed Y-shape (compounds **9**, **11**, **13** and **15**) have been synthesized involving various spacers as shown in Scheme 6.1. In brief, 3,5-dihydroxybenzoic acid was converted to its methyl ester, and subsequently bis-alkylated with hexyl bromide in the presence of potassium carbonate. Reduction of the ester with $LiAlH_4$ furnished 3,5-bis(hexyloxy)benzyl alcohol **1**, which was glycosylated with B-D-Glucose pentaacetate in the presence of $BF_3 \times OEt_2$. Alternatively applied azidoalkyl glycosides for a 'click-chemistry'-based synthesis of reverse Y-shaped surfactants were already described in chapter 3. N-(2-propynyl)-dihexyl amine **2** was prepared by refluxing dihexyl amine with excess of propargyl bromide in the presence of potassium carbonate. Compounds **2** and **7** were coupled in CuAAC click chemistry-fashion to afford the surfactant precursor **13** in good yields, see Scheme 6-3.

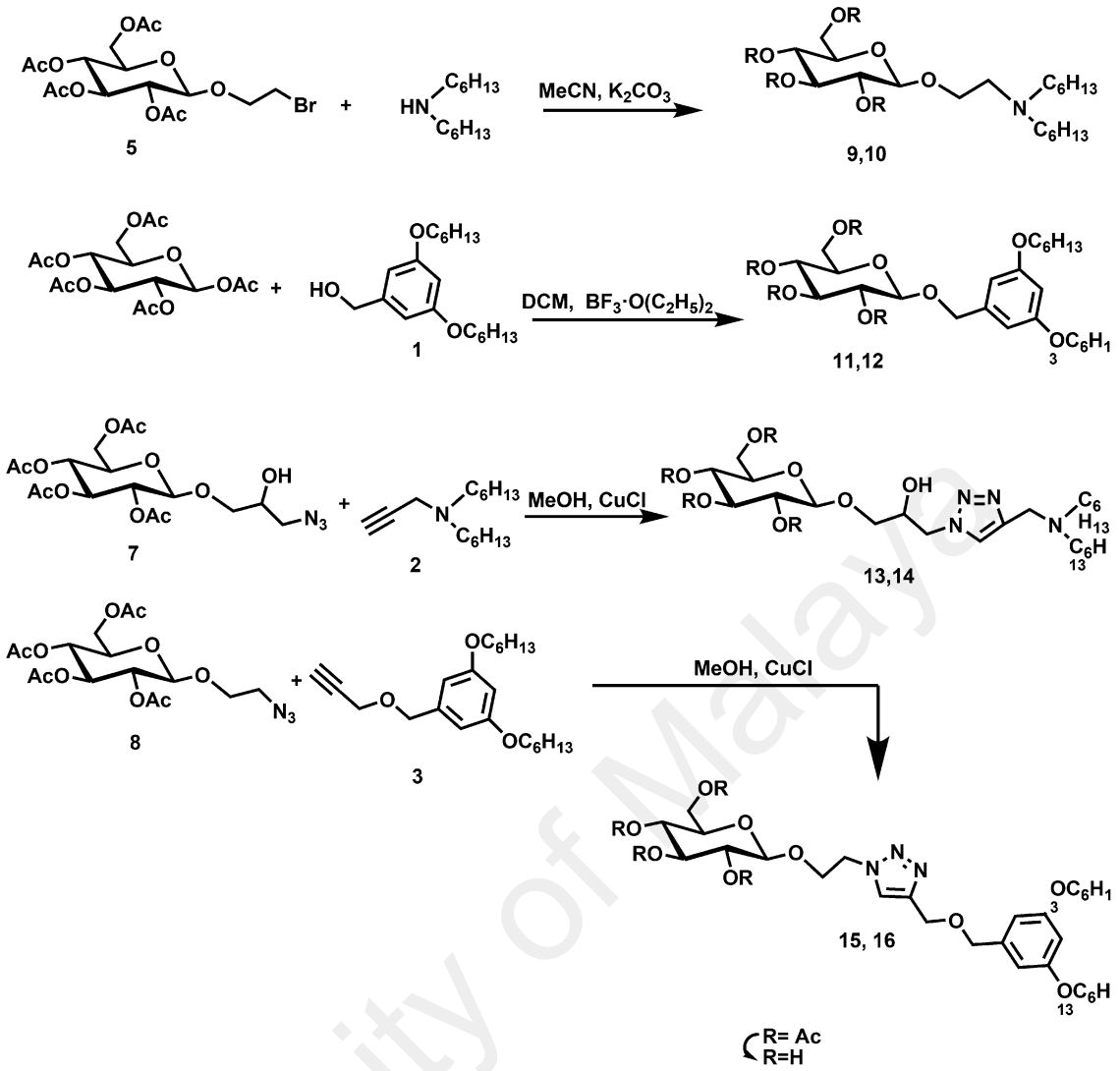


Scheme 6-1: Synthesis Scheme for the hydrophobic parts.

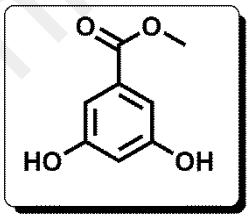


Scheme 6-2: Synthesis of hydrophilic part.

Surfactant precursor **9** was prepared by reacting 2-bromoethyl-2,3,4,6-tetra-O-acetyl-beta-D-glucopyranoside **5** (C. Li & Wong, 2003) with dihexyl amine in a nucleophilic replacement reaction, whereas surfactant **15** applied a click coupling of azidoalkyl glucoside **8** (Mattarella & Siegel, 2012) with alkyne compound **3**. The structures of all synthesized compounds were confirmed by NMR spectroscopy and mass spectrometry. The most important ^{1}H NMR peaks for surfactants **11** and **12** are the signals of the p-substituted benzene ring, found at δ = 6.41 and 6.38 ppm. The signals for the secondary sugar hydrogen-atoms at acetylated oxygen (H-2 to H-4) appear between δ 5.20 and 5.04 ppm, while the anomeric proton (H-1) is found around 4.80 ppm. The benzyl-protons were observed at 4.54 ppm. Upon deacetylation the sugar signals shift towards high field, while the signal reflecting the acetates at around 2.00 ppm disappears. The ^{1}H NMR for **9** shows hydrogens at the acetylate sugar carbons (H-2 to H-4 and H-6) between 5.19 to 3.91 ppm. The protons of the linker were found at 3.75 ppm for OCH_2, at 2.76 ppm for CH_2N and at 2.5 ppm for $N(CH_2)_2$. The corresponding ^{13}C NMR indicates the nitrogen linked methylene groups at 54.77 and 53.33 ppm. The deacetylation is reflected in the loss of signals for the acetates and an up-field shift for corresponding sugar proton in the ^{1}H NMR. The triazole-hydrogen for the acetylated surfactant precursor **13** was found at 7.43 ppm. The sugar acetylate proton peaks appear in multiple broad system due to the high possibility of hydrogen bond, The corresponding ^{13}C NMR indicates triazole-hydrogen shown at 130.02, 130.04 while the signal of the C-1 shows two peaks at 101.14 and 100.85 due to the anomeric system. Upon deprotection acetate-related peaks disappear both in the ^{1}H as well as in the ^{13}C NMR spectrum, thus confirming the success of the reaction. Unlike the NMR-spectra for compounds **13** and **14**, which suffer from the presence of a diastereomeric product mixture, surfactant precursor **15** and its deacetylated analogue **16** exhibited very clear spectra for a distinct, single isomer.



Scheme 6-3: Synthesis of reverse Y-shape sugar-based surfactants.

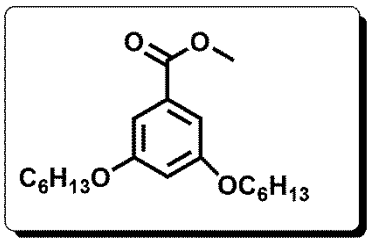


Chemical Formula: $C_8H_8O_4$
Molecular Weight: 168.1467

6.2.4.1 Methyl-3,5-dihydroxybenzoate

2 mL of concentrated H_2SO_4 was added to a stirred solution of 3,5-dihydroxybenzoic acid (4.0 g, 25.95 mmole) in methanol. The reaction mixture was then refluxed for 2h at 100 °C. The solvent was evaporatord and the residue was taken

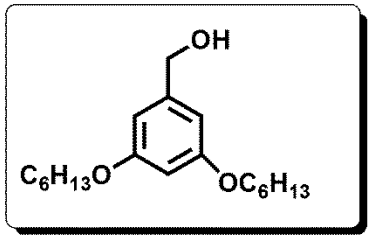
up in water and ethyl acetate for three times. The combined organic phases were washed with brine water and dried over $MgSO_4$, then concentrate in a rotary evaporator to give 4.2 g from the corresponding ester (98 % yield).



Chemical Formula: $C_{20}H_{32}O_4$
Molecular Weight: 336.4657

6.2.4.2 Methyl-3,5-bis(hexyloxy)benzoate

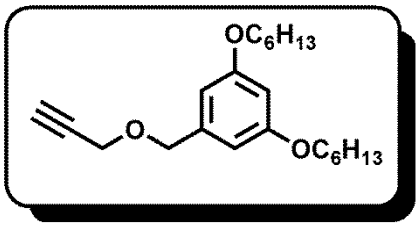
1-bromohexane (7 mL, 49.86 mmole) was added to a stirred solution of methyl-3,5-dihydroxybenzoate (4.0 g, 23.78 mmole) and K_2CO_3 (9.84 g, 71.36 mmole) in DMF,. The reaction mixture was refluxed at 80 °C for overnight. The mixture was filtered, and then the solvent was evaporatord. The residue was extracted with DCM and water for three times. The combined organic phases was washed with brine water and dried over $MgSO_4$, then concentrated in a rotary evaporator to gave 7.2 g green dark oil (90 % yield). ^{1}H NMR ($CDCl_3$) δ = 7.61 (s, 2x CH-benzene); 6.63 (s, CH-benzene); 3.96 (t, 4H, $(OCH_2)_2$); 1.77 (p, 4H, B-CH_2); 1.45 (p, 4H, ∞-CH_2); 1.33 (bs, 8H, bulk-CH_2); 0.90 (t, 6H, 2x CH_3). ^{13}C NMR ($CDCl_3$) δ = 166.99 (CO); 160.16 (2x $C_{benzene}$); 131.82 ($C_{benzene}$); 107.63 (2x $CH_{benzene}$); 106.59 ($CH_{benzene}$); 68.32 (2x OCH_2); 31.54 (ω-2); 29.14 (bulk-CH_2); 25.67 (B-CH_2); 22.58 (ω-1); 14.00 (2x CH_3).



Chemical Formula: $C_{19}H_{32}O_3$
Molecular Weight: 308.4556

6.2.4.3 3,5-Bis(hexyloxy)benzyl alcohol (1)

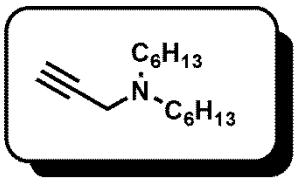
Lithium aluminium hydride (0.5 g, 13.51 mmol) was added to a stirred solution of methyl-3,5-bis(hexyloxy)benzoate (3.0 g, 8.91 mmol) in (100 mL) anhydrous THF at 10 ° C. The reaction mixture was allowed to warm to room temperature and stirred for overnight. 0.5 mL of water was added slowly to stop the reaction, an aq. 10 % NaOH solution (1 mL), and then additional water (2 mL). Then the reaction mixture was left to stir for around 30 min. until the suspended solids become white. The reaction mixture was filtered and the solid rinsed with CH_2Cl_2, the filtrate dried over $MgSO_4$ and concentrated in rotary evaporator to produce 2.2 g green dark oil (80 % yield). ^{1}H NMR ($CDCl_3$) δ = 6.48 (d, 2x CH-benzene), J= 2.48; 6.36 (t, CH-benzene), J= 2.28; 4.59 (s, CH_2-benzyl); 3.92 (t, 4H, $(OCH_2)_2$); 1.75 (p, 4H, B-CH_2); 1.44 (p, 4H, ∞-CH_2); 1.34 - 1.30 (m, 8H, bulk-CH_2); 0.90 (t, 6H, 2x CH_3). ^{13}C NMR ($CDCl_3$) δ = 160.51 (2x $C_{benzene}$); 143.28 ($C_{benzene}$); 105.06 (2x $CH_{benzene}$); 100.56 ($CH_{benzene}$); 68.07 ($(OCH_2)_2$); 65.34 (CH_2-benzyl); 31.57 (ω -2); 29.22 (bulk-CH_2); 25.71 (B-CH_2); 22.59 (ω -1); 14.01 (2x CH_3).



Chemical Formula: $C_{22}H_{34}O_3$
Molecular Weight: 346.5036

6.2.4.4 3,5-Bis(hexyloxy)-1-(propargyl methyl) benzene (3)

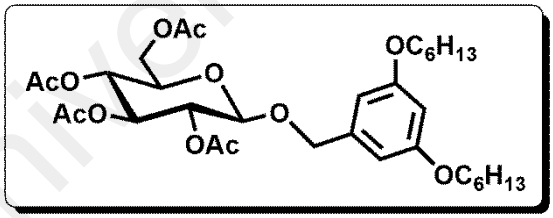
3,5-bis(hexyloxy)benzyl alcohol (5 g, 16.21 mmole) was added slowly to a suspension of NaH (0.85 g, 21.25 mmole) in THF at 10 °C and leaved stirrer for 15min. Propargyl bromide (80% w/w in toluene, 3.5 mL 32.42 mmole) was added dropwise to the reaction mixture which was stirring at 10 °C. Then the reaction mixture was kept stirring for 10 min., and then allowed to warm to room temperature and stirred for overnight. The reaction mixture was extracted three times with water and CH_2Cl_2. The combine organic phases was washed with brine water, dried over $MgSO_4$, filtered and concentrated on a rotary evaporator leaving 5.2 g dark brown oil (93 % yield). ^{1}H NMR ($CDCl_3$) δ = 6.51 (d, 2H, 2x CH-benzene), J= 2.40; 6.41 (t, CH-benzene), J= 2.24; 4.56 (s, CH_2-benzyl); 4.18 (d, CH_2-propargyl), J=2.4; 3.92 (t, 4H, $(OCH_2)_2$); 2.48 (t, CH-propargyl), J=2.36; 1.78 (p, 4H, B-CH_2); 1.50-1.43 (m, 4H, ∞-CH_2); 1.37- 1.28 (m, 8H, bulk-CH_2); 0.93 (t, 6H, 2x CH_3). ^{13}C NMR ($CDCl_3$) δ = 160.43 (2x $C_{benzene}$); 139.41 ($C_{benzene}$); 106.23 (2x $CH_{benzene}$); 100.88 ($CH_{benzene}$); 79.67 (C-propargyl); 74.57 (CH-propargyl); 71.53 ($(OCH_2)_2$); 68.04 (CH_2-benzyl); 59.70 (OCH_2-propargyl); 31.58 (ω-2); 29.36 (bulk-CH_2); 25.73 (B-CH_2); 22.60 (ω-1); 14.03 (2x CH_3).



Chemical Formula: $C_{15}H_{29}N$
Molecular Weight: 223.3975

6.2.4.5 2-*N*-propynyl-*N*,*N*-dihexyl amine (2)

To a stirred solution of dihexyl amine (3 mL, 12.89mmole) and K_2CO_3 (1.8 g, 13.17 mmole) in acetonitrile, propargyl bromide (80 % w/w in toluene, 2.9 mL, 25.78 mmole) was added. The reaction mixture was refluxed at 70°C for overnight. The mixture was filtered, then the solvent was evaporatord and the residue was extracted with DCM and water three times. The combined organic phase was washed with brine water and dried over $MgSO_4$, then concentrated in a rotary evaporator to obtain (2.7 g) as brown syrup, (yield 94 %).^{1}H NMR ($CDCl_3$) δ = 4.68 (d, CH_2N), J=2.47; 3.66- 3.51 (m, 4H, $N(CH_2)_2$); 2.99 (t, CH-propargyl); 1.82 (p, 4H, 2x B-CH_2); 1.32- 1.23 (m, 12H, bulk-CH_2); 0.82 (t, 6H, CH_3). ^{13}C NMR ($CDCl_3$) δ = 79.80 (C-propargyl); 75.62 (CH-propargyl); 59.98 (CH_2N); 58.52 ($N(CH_2)_2$); 28.97 (B-CH_2); 24.00 (ω*-1); 20.36 (ω-1); 11.86 (CH_3).

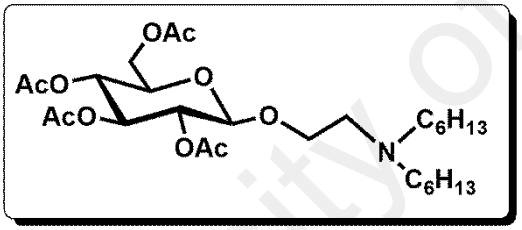


Chemical Formula: $C_{33}H_{50}O_{12}$
Molecular Weight: 638.7429

6.2.4.6 1-Ethoxyl-(3,5-bis(hexyloxy)benzyloxy)-2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (11)

Glucose pentaacetate (3 g, 7.78 mmol, 1.2eq.) and 2.00 g (6.48 mmol) 3,5-bis(hexyloxy)benzyl alcohol were dissolved in 60 mL dichloromethane and treated with 3 mL (24.30 mmol, 3 eq.) BF_3xEt_2O. The reaction was stirred at room temperature for 3 hours and then washed with an aqueous solution of $NaHCO_3$ and dried over $MgSO_4$.

The solvent was concentrated and purified by column chromatography using hexane: ethyl acetate (3:1) as eluent to obtain (4 g) white solid. (Yield 81 %). ^{1}H NMR ($CDCl_3$) δ = 6.41 (s, 2H, 2x CH-benzene); 6.38 (s, CH-benzene); 5.20- 5.04 (m, 3H, H-3, H-4, H-2); 4.80 (d, H-1); 4.54 (d, CH_2-benzyl); 4.29, 4.26 (dd, H-6a); 4.18-4.09 (m, H-5); 3.92 (t, 4H, 2x OCH_2); 3.67 (d, H-6b); 2.10, 2.02, 2.01, 1.98 (ms, 12H, CH_3CO); 1.79-1.72 (p, 4H,2x B-CH_2); 1.48- 1.23 (m, 12H, bulk-CH_2); 0.92-0.86 (m, 6H, 2x CH_3). ^{13}C NMR ($CDCl_3$) δ = 170.61, 170.19, 169.35, 169.27 (4x $COCH_3$); 160.43 (2x $C_{benzene}$); 138.74 ($C_{benzene}$); 106.09 (2x $CH_{benzene}$); 100.45 ($CH_{benzene}$); 99.08 (C-1); 72.87 (C-4); 71.80 (C-2); 71.32 (C-3); 70.49 (CH_2benzyl); 68.42 (C-5); 67.99 (2x CH_2O); 61.92 (C-6); 31.54 (ω-2); 29.20 (bulk-CH_2); 25.70 (B-CH_2); 22.60, 22.55 (ω-1); 20.66, 20.57, 20.53, 20.51 (4x CH_3CO); 14.05, 13.96 (2x CH_3).



Chemical Formula: $C_{28}H_{49}NO_{10}$
Molecular Weight: 559.6894

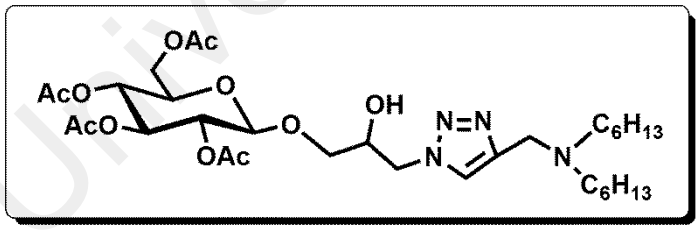
6.2.4.7 1-Ethoxyl-(dihexylamino)-2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (9)

To a mixture solution of 2-bromoethyl 2,3,4,6-tetra-O-acetyl-beta-D-glucopyranoside (4.0 g, 8.78 mmole) and K_2CO_3 (1.8 g, 13.17 mmole) in acetonitrile, dihexyl amine (1.9 mL, 8.16 mmole) was added. The reaction mixture was refluxed at 80°C for overnight. The mixture was filtered, then the solvent was evaporatord and the residue extracted with DCM and water for three times. The combined organic phases were washed with brine water and dried over MgSO4, then concentrated in a rotary evaporator and purified by column chromatography using hexane: ethyl acetate (3:1) as eluent to obtain (3 g) as brown syrup, (yield 61 %). ^{1}H NMR ($CDCl_3$) δ = 5.19 (t, H-3), $^{3}J_{3,4}$ = 9.40; 5.07 (t, H-4), $^{3}J_{4,5}$ = 9.26; 4.96 (t, H-2), $^{3}J_{2,3}$ = 8.54; 4.57 (d, H-1), $^{3}J_{1,2}$ =

7.84; 4.26 (d, H-6a); 4.14 (d, H-6b); 3.97-3.91 (m, H-5); 3.75- 3.68 (m, OCH_2); 2.76 (d, CH_2N); 2.53 (t, 4H, $N(CH_2)_2$); 2.08, 2.04, 2.02, 2.00 (4x s, 12H, 4x CH_3CO); 1.46 (bs, 4H, 2x B-CH_2); 1.28 (bs, 12H, bulk-CH_2); 0.89 (t, 6H, 2x CH_3). ^{13}C NMR ($CDCl_3$) δ = 170.65, 170.28, 169.39, 169.24 (4x $COCH_3$); 100.81 (C-1); 72.91 (C-4); 71.75 (C-2); 71.31 (C-3); 68.45 (C-5); 68.34 (OCH_2); 61.99 (C-6); 54.77 ($N(CH_2)_2$); 53.33 (CH_2N); 31.80 (ω -2); 27.16, 27.10 (B-CH_2); 22.64 (ω -1); 20.70, 20.66, 20.58, 20.57 (4x CH_3CO); 14.04 (2x CH_3).

6.2.4.8 General method for click chemistry

A solution of the sugar azide **5** and/or **6** (2 g, 4.47 mmole and/or 2 g, 4.79 mmole) with terminal alkyne compound **2** and/or **3** (1.1 g, 4.92 mmole and/or 1.7 g, 4.90 mmole) in 40 mL methanol was treated with copper chloride. The solution was stirred at room temperature for overnight. The reaction mixture was filtered through ciliate and concentrated under reduced pressure, the residue was purified by filtrating through 5 cm silica gel with 2:1 ethyl acetate: hexane as eluent to remove the unreactant from sugar and alkyl chain, finally the product was filling down by 4:1 methanol: $CHCl_3$ to result the corresponding product.

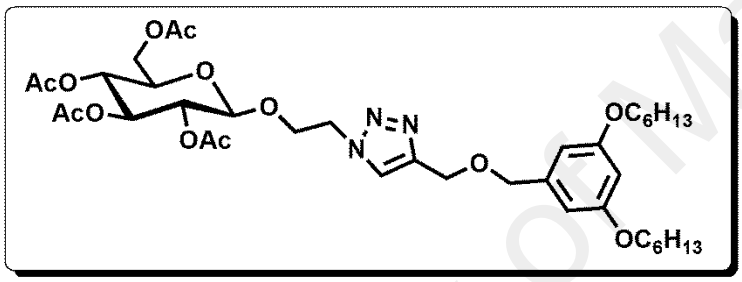


Chemical Formula: $C_{32}H_{54}N_4O_{11}$
Molecular Weight: 670.7914

6.2.4.8.1 3-((2′-hydroxypropyl-2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranosyloxy) methyl-1,2,3-mono-triazole)-*N*,*N*-dihexyl amine (13)

Sugar azide **7** (2.0 g, 4.5 mmol) and propargyl **2** (1.1 g, 4.9 mmol) were coupled with CuCl (40 mg, 0.2 mmol) in MeOH according to the general procedure for click chemistry to provide **13** (2.1 g, 70 %) as a brown syrup. ^{1}H NMR ($CDCl_3$) δ = 8.20-

7.43 (m, triazole), 5.24/ 5.20 (2dd~2t, H-3), 5.08 (dd~t, H-4), 5.00 (dd~bt, H-2), 4.63 (d, H-1), 4.50- 2.96 (14H, OCH_2, H-$6_{a,b}$, H-5 CHOH, CH_2-triazole, $N(CH_2)_2$, CH_2N), 2.17, 2.09, 2.03, 2.01 (4s, 12H, Ac), 1.88- 1.65 (m, 4H, 2x β-CH_2), 1.38- 1.25 (m, 12H, bulk-CH_2), 0.93- 0.86 (m, 6H, CH_3). $^3J_{1,2}$ = 8.0, $^3J_{3,4}$ = 9.2, $^3J_{4,5}$ = 9.5 Hz. ^{13}C NMR ($CDCl_3$) δ =170.84, 170.23, 169.82, 169.52 (CO), 134.26 (C-triazole), 130.02/130.04 (CH-triazole), 101.14/100.85 (C-1), 72.75 (C-4), 71.86/71.99 (C-2), 71.27/71.21 (C-3), 71.11 (OCH_2), 68.35 (CHOH, C-5), 61.85 (C-6), 58.84 (NCH), 53.50 (CH_2-triazole), 53.25($N(CH_2)_2$), 31.18 (ω-2), 29.69 (bulk-CH_2), 25.93 (β-CH_2), 22.42 (ω-1), 20.85, 20.79, 20.61 (Ac), 13.93, 13.89 (CH_3).



Chemical Formula: $C_{38}H_{57}N_3O_{13}$
Molecular Weight: 763.8715

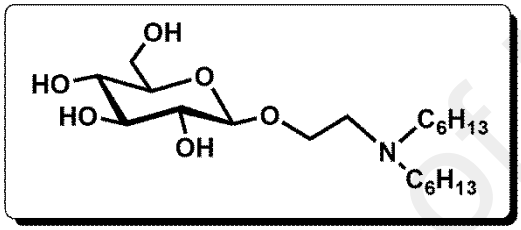
6.2.4.8.2 1-[4-(1-ethoxyl-2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranosyloxy)methyl-1,2,3-mono-triazole)]-3,5-bis(hexyloxy)benzyloxy (15)

Sugar azide **8** (2.0 g, 4.4 mmol) and propargyl **3** (1.7 g, 4.9 mmol) were coupled with CuCl (40 mg, 0.2 mmol) in MeOH according to the general procedure for click chemistry to provide **15** (2.6 g, 71 %) as a brown syrup. ^1H NMR ($CDCl_3$) 7.63 (s, CH-triazole), 6.46 (bs, 2H, CH-benzene), 6.38 (bs, CH-benzene), 5.18 (dd~t, H-3), 5.07 (dd~t, H-4), 5.00 (dd, H-2), 4.64- 4.47 (m, 7H, OCH_2, CH_2N, $CH_{2\text{-benzyl}}$, H-1), 4.24 (d, H-6a), 4.20 (d, H-6b), 4.12/ 4.09 (2 s, 2H CH_2O), 3.93 (t, 4H, OCH_2), 3.70 (ddd, H-5), 2.08, 2.02, 1.99, 1.96, (4 s, 4x3H, Ac), 1.76 (p, 4H, β-CH_2), 1.45 (p, 4H, γ-CH_2), 1.35- 1.33 (m, 8H, bulk-CH_2), 0.90 (t, 6H, CH_3); $^3J_{1,2}$ = 8.0, $^3J_{2,3}$ = 9.5, $^3J_{3,4}$ = 9.0, $^3J_{5,\,6a}$ = 4.5, $^3J_{5,\,6B}$ = 7.5, $^2J_6$ = 12.0 Hz. ^{13}C NMR ($CDCl_3$) 170.57, 170.08, 169.39, 169.36 (O), 160.40 (2x $C_{benzene}$), 139.92 ($C_{benzene}$), 139.63 (C-triazole), 126 (CH-

triazole), 106.12 (2x $CH_{benzene}$), 100.68 ($CH_{benzene}$), 100.51 (C-1), 72.66 (CH_2-benzyl), 72.48 (C-3), 71.98 (C-4), 70.89 (C-2), 68.21 (C-5), 68.03 (OCH_2), 67.73 (OCH_2-triazole), 63.48 (OCH_2Ph), 61.70 (C-6), 50.0 (CH_2N), 31.56 (ω-2), 29.22 (bulk-CH_2), 25.71 (β-CH_2), 22.58 (ω-1), 20.70, 20.55, 20.48 (Ac), 14.02 (CH_3).

6.2.4.9 General procedure for de-acetylation

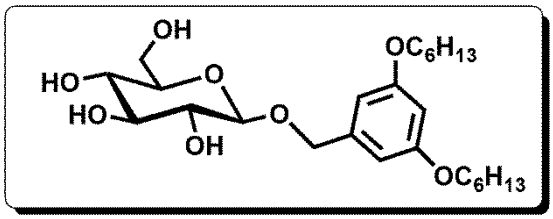
The deprotection was carried out by using methanol as a solvent and a catalytic amount of NaOMe. The mixture was stirred for 4h at room temperature. The catalyst was removed by neutralization with Amberlite IR120 (H^+) and then the solvent was evaporatord to give the final pure compound.



Chemical Formula: $C_{20}H_{41}NO_6$
Molecular Weight: 391.5426

6.2.4.9.1 (*N,N*-Dihexyl-2-aminoethyl)*β*-D-glucopyranoside (10)

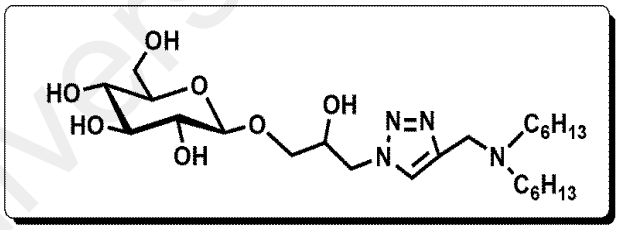
9 (2.9 g, 5.3 mmol) was reacted according to general procedure for de-acetylation to produce **10** (1.9 g, 91 %). as brown syrup. ^{1}H NMR (DMSO-d_6) δ = 4.18 (d, H-1, $^3J_{1,2}$ = 7.5 Hz) 3.94 (dd~bt, H-3); 3.80- 3.60 (m, 2H, OCH_2); 3.22- 2.95 (m, 7H, H-4, H-2, H-5, H-6, CH_2N); 2.81 (bt, 4H, $N(CH_2)_2$); 1.51 (m, 4H, 2x β-CH_2); 1.25 (m_c, 12H, bulk-CH_2); 0.85 (t, 6H, CH_3). ^{13}C NMR (DMSO-d_6) δ = 103.33 (C-1); 77.33 (C-4); 76.92 (C-2); 73.82 (C-3); 70.51 (C-5); 64.85 (OCH_2); 61.56 (C-6); 53.26 ($N(CH_2)_2$); 52.37 (CH_2N); 31.34 (ω-2); 26.49, 26.45 (β-CH_2); 22.42 (ω-1); 14.21 (CH_3).



Chemical Formula: $C_{25}H_{42}O_8$
Molecular Weight: 470.5962

6.2.4.9.2 (2-[3,5-Bis-(hexyloxy)-benzoxy]ethyl)β-D-glucopyranoside (12)

31 (4.0 g, 6.2 mmol) was reacted according to general procedure for de-acetylation to produce **12** (2.8 g, 95 %) as white solid. ^{1}H NMR (DMSO-d_6) δ = 6.54 (s, 2x CH-benzene); 6.33 (s, CH-benzene); 4.73 (d, Bn-A); 4.53 (d, Bn-B); 4.20 (d, H-1); 3.91 (t, 4H, 2x OCH_2); 3.70 (dd~bd, H-6_a); 3.46 (dd, H-6_b); 3.18- 3.06 (m, 3H, H-3, H-4, H-5), 3.04 (dd, H-2); 1.67 (p, 4H, 2x β-CH_2); 1.41-1.29 (m, 12H, bulk-CH_2); 0.87 (m_c, 6H, CH_3). $^3J_{1,2}$ = 8.0, $^3J_{2,3}$ = 9.5, $^3J_{5,6a}$ < 1.0, $^3J_{5,6B}$ = 5.0, $^2J_6$ = 12.0, $^2J_{Bn}$ = 13.0 Hz. ^{13}C NMR (DMSO-d_6) δ = 160.20 (2x $C_{benzene}$); 140.89 ($C_{benzene}$); 106.02 (2x $CH_{benzene}$); 102.39 (C-1); 100.39 ($CH_{benzene}$); 77.38 (C-4); 77.15 (C-2); 73.98 (C-3); 70.60 (C-5); 69.63 (Bn); 67.86 (CH_2O); 61.61 (C-6); 31.45 (ω-2); 29.12 (γ-CH_2); 25.66 (β-CH_2); 22.53 (ω-1); 14.35 (CH_3).

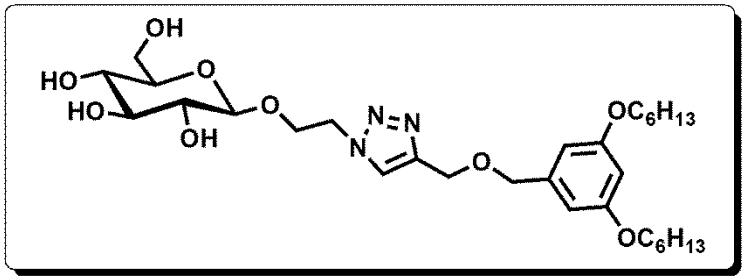


Chemical Formula: $C_{24}H_{46}N_4O_7$
Molecular Weight: 502.6446

6.2.4.9.3 *N,N*-Dihexyl-[4-aminomethyl-1-(2-hydroxy-3-β-D-glucopyranosyloxy-propyl)-1,2,3-triazole(14)

13 (2.0 g, 3.1 mmol) was reacted according to general procedure for de-acetylation to produce **14** (1.5 g, 96 %.) as brown syrup. ^{1}H NMR (CD_3OD) δ = 8.52-7.43 (m, triazole), 4.62 (bs, H-1), 4.35 (dd~t, H-3), 4.24 (m_c, CHOH), 3.98-3.17 (15H, H-2, H-4, OCH_2, H-6_a, H-6_b, CH_2, $N(CH_2)_2$, CH_2N, H-5) with solvent peak, 1.88 (m_c, 4H, β-CH_2), 1.43-1.30 (m, 12H, bulk-CH_2), 0.97- 0.86 (m, 6H, CH_3). ^{13}C NMR

(CD_3OD) δ = 134.89 (C-triazole), 132.50 (CH-triazole), 103.30/103.19 (C-1), 76.68 (C-4), 76.55/76.50 (C-2), 73.73/73.65 (C-3), 70.62/70.51 (OCH_2), 68.80/68.72 (CHOH, C-5), 61.30 (C-6), 57.97 (NCH), 52.99 (CH_2-triazole), 52.10 ($N(CH_2)_2$), 30.94 (ω-2), 29.69 (γ-CH_2), 25.87, 25.57 (β-CH_2), 22.14, 21.64 (ω-1), 12.89 (CH_3).



Chemical Formula: $C_{30}H_{49}N_3O_9$
Molecular Weight: 595.7248

6.2.4.9.4 1-[4-(1-ethoxyl-2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranosyloxy) methyl-1,2,3-mono-triazole)]-3,5-bis(hexyloxy)benzyloxy(16)

15 (2.6 g, 3.4 mmol) was reacted according to general procedure for de-acetylation to produce **16** (1.9 g, 95 %.) as brown syrup. ^{1}H NMR (CD_3OD) 8.29 (bs, CH-triazole), 6.52 (bd, 2H, CH-benzene), 6.39 (bt, CH-benzene), 4.72 (t, 2 H, CH_2N), 4.67 & 4.55 (2 s, 2×2 H, CH_2OAr), 4.34 (d, H-1), 4.28 (ddd~dt,CH_2O-A), 4.07 (ddd~dt, CH_2O-B), 3.95 (t, 4H, α-CH_2), 3.89 (dd, H-6a), 3.66 (dd, H-6b), 3.37- 3.24 (m, 3H, H-3, H-4, H-5), 3.18 (dd, H-2), 1.76 (p, 4H, β-CH_2), 1.52- 1.45 (p, 4H, γ-CH_2), 1.39-1.30 (m, 8H, bulk-CH_2), 0.94 (t, 6H, CH_3); $^3J_{1,2}$ = 8.0, $^3J_{2,3}$ = 9.0, $^3J_{5,6a}$ = 2.0, $^2J_{6a,b}$ = 5.0, $^2J_6$ = 12.0, $^2J_{A,B}$ = 12.0 Hz. ^{13}C NMR (CD_3OD) 160.45 (2x $C_{benzene}$), 139.76 ($C_{benzene}$), 139.63 (C-triazole), 126 (CH- triazole), 105.87 (2x $CH_{benzene}$), 103.14 ($CH_{benzene}$), 100.34 (C-1), 76.70 (C-3), 76.56 (C-4), 73.49 (C-2), 72.27 (CH_2-benzyl), 70.11 (C-5), 67.66 (2x OCH_2), 67.35 (OCH_2-triazole), 61.89 (OCH_2), 61.27 (C-6), 51.10 (CH_2N), 31.38 (ω-2), 28.98 (bulk-CH_2), 25.74 (β-CH_2), 22.27 (ω-1), 12.97 (2x CH_3).

6.3 Results and Discussion

The synthesis of the surfactants followed the sequential approach, in which the surfactant alkyl chains were first attached to a linker, which was subsequently coupled to the carbohydrate by glycosylation, alkylation of an amine or click-chemistry. All surfactants were obtained in overall yields ranging from 29 to 56 % based on glucose pentaacetate. Chromatographic purification was required due to remaining starting material and side products. The ^{1}H NMR spectra of the surfactants indicated high purity for all products and confirmed the complete removal of protecting groups in the final surfactants. Examples are shown in Figure 6-1. High-resolution mass spectra, recorded by MALDI-TOF mode, as displayed in Figure 6-2, were in line with the structure proposals. Click-chemistry-based surfactant **14** and its precursor **13** exhibited complex NMR spectra with doubled peaks for most signals, owing to the presence of two diastereomers originating from missing stereo-selectivity for the preparation of epoxide intermediate **6**. The close structural similarity of surfactant precursors **13** and **15** is reflected in their ^{13}C NMR spectra, confirming a diastereomeric relationship between two products in **13**. A closer look on chemical shift differences of diastereo-related peaks reveal more significant effects in the close environment of 'racemic' stereo-centre. So is the chemical shift difference for C-1 substantially larger than for any other carbon inside the glucose.

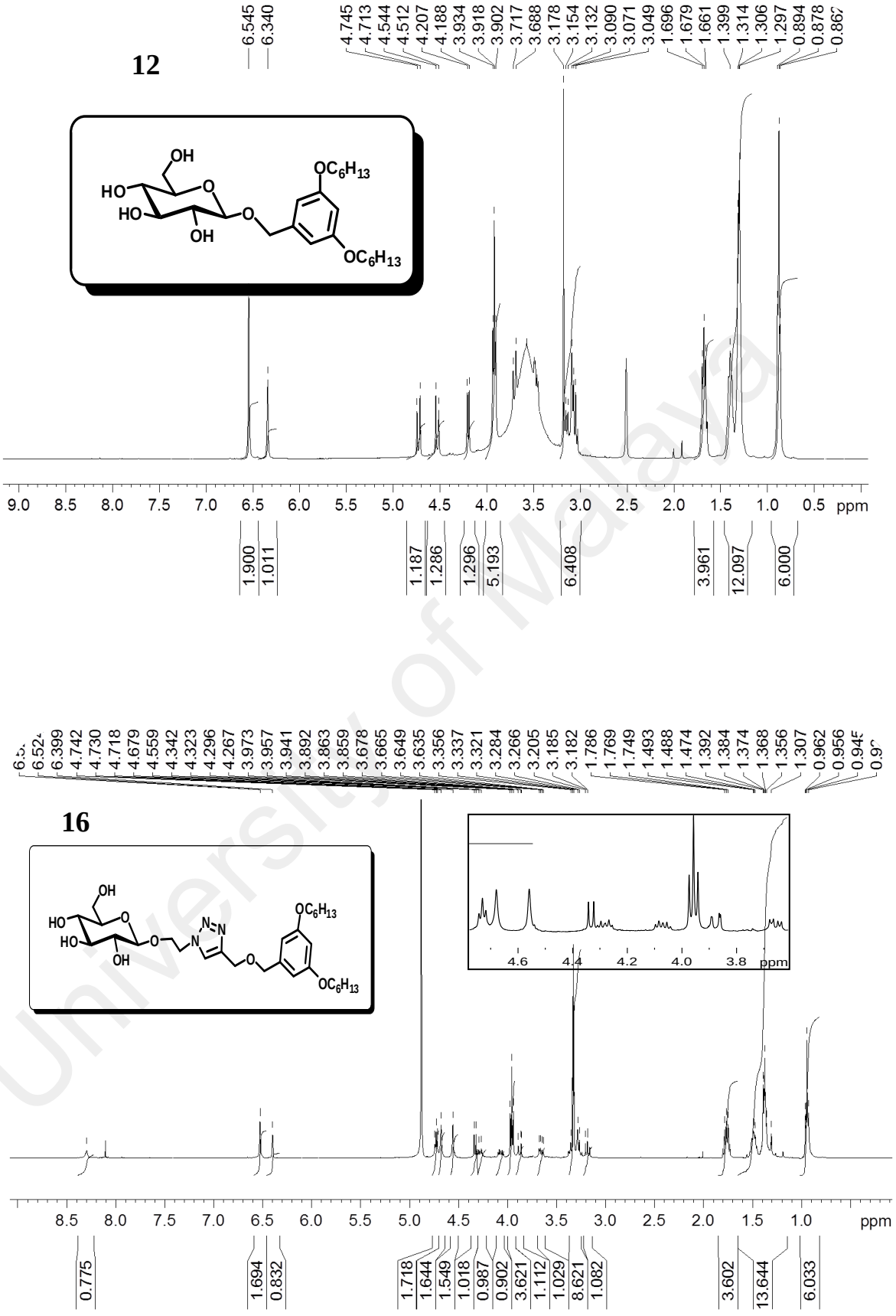


Figure 6-1: The evolution of ^{1}H NMR spectra (400 MHz, $CDCl_3$, 298 K) for compound 12 and 16.

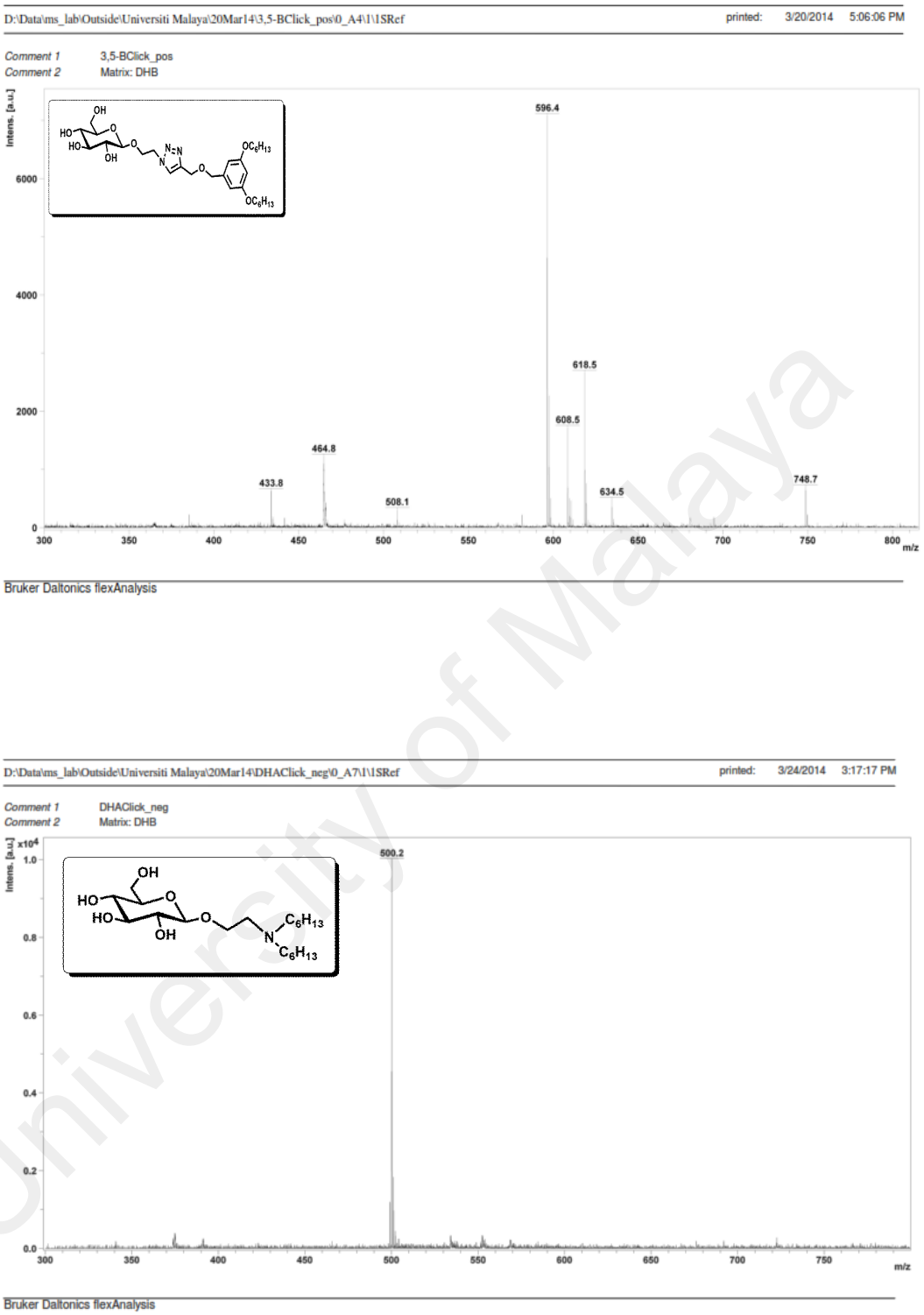


Figure 6-2: MALDI TOF mass spectrum for surfactant 10 and 16.

6.3.2 Liquid crystalline behaviour

The lyotropic liquid crystal phases were investigated by optical polarizing microscopy (OPM) at room temperature using the contact penetration technique (Milkereit *et al*., 2005; von Minden *et al*., 2000). In contact with water no liquid crystal phase was observed for surfactants **10**, **14** and **16**. The compounds on their own appeared as viscous fluids (syrup) at room temperature. While no texture was observed for compound **10**, probably reflecting an isotropic liquid based on rather low viscosity and that could be due to the short tail volume, For compound **14** also no textures could be observed, owing to the dark colouring of the material. Therefore the missing observation of a texture does not exclude liquid crystalline phases. Compound **12** again exhibited low water solubility. However, at the contact zone with water a phase showing birefringence emerged, which likely reflects a hexagonal phase as depicted in the Figure 6-3b. The compound itself also exhibited birefringence, but in contrast to the water penetrated assembly the fan shape texture is more in line with a smectic A phase (lamellar). The observation of La phases suggests that the present of aromatic ring with duple short alkyl tail groups in the surfactants has made the width of the hydrophilic and hydrophobic portions more comparable, promoting the formation of the lamellar phase. The textures are shown in Figure 6-3b.

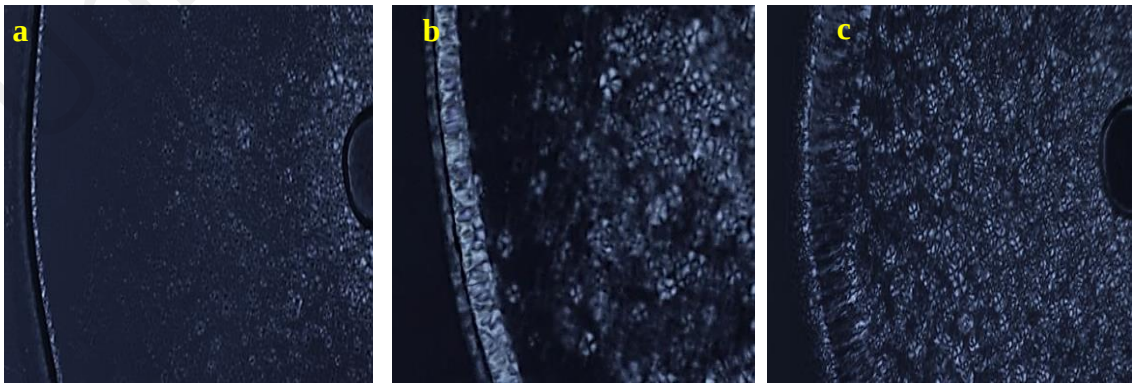


Figure 6-3: OPM texture for compound **12** (a) texture of the pure sample (b) Water penetration scans shows hexagonal H_1 and lamellar phases L_α at room temperature (c) in contact with 1-undecanol penetrate.

Upon contact with the non-polar solvent (1-undecanol), surfactants **14** and **16** did not show visible solubilisation, but lead to a swelling of the surfactant. No liquid crystalline phase, however, was observed. Compound **10**, on the other hand, exhibited a significant solubility in 1-undecanol. Like in the cases reported before, no liquid crystalline phase was observed. Finally, surfactant **12** also indicated solubility in undecanol. Besides, the penetration scan revealed the formation of a new phase with exhibiting birefringence. The texture of this new phase appears to be closely related to those observed for the pure surfactant, see Figure 6-3c.

In terms of molecular assembly, a change of the assembly behaviour upon altering the water concentration is expected. Figure 6-4 illustrates this expectation. For the molecular shape a parallel alignment of the alkyl chains are assumed, as shown in Figure 6-4(a). For the pure compound and in presence of low water concentration the molecules preferably to arrange in a lamellar phase as depicted in Figure 6-4(b). Upon increasing water content, however, the interaction of the surfactant head with water increases, resulting in a welling of that domain that causes the aggregate to rearrange into a curved hexagonal assembly, as shown in Figure 6-4(c). The expected behaviour, however, only reflects the observations for compound **12**.

The presence of aromatic groups, reflecting both benzene and triazole, reduced the water-solubility of the surfactants. This is supposed to be expected, owing to a substantially increased hydrophobicity of the aglycon comprising not only the alkyl chains, but the linking unit as well. Surprisingly the addition of aromatic rings did not substantially enhance the interactions with an oil phase. This may be due to the section of the latter, which did not contain aromatic components. The observed low interaction of surfactants involving triazole linkages and oil might discourage the application of click coupling for the preparation of sugar-based surfactants. However, a more

extensive study involving different types of oil as well as a wider range of surfactants is required to investigate the effect.

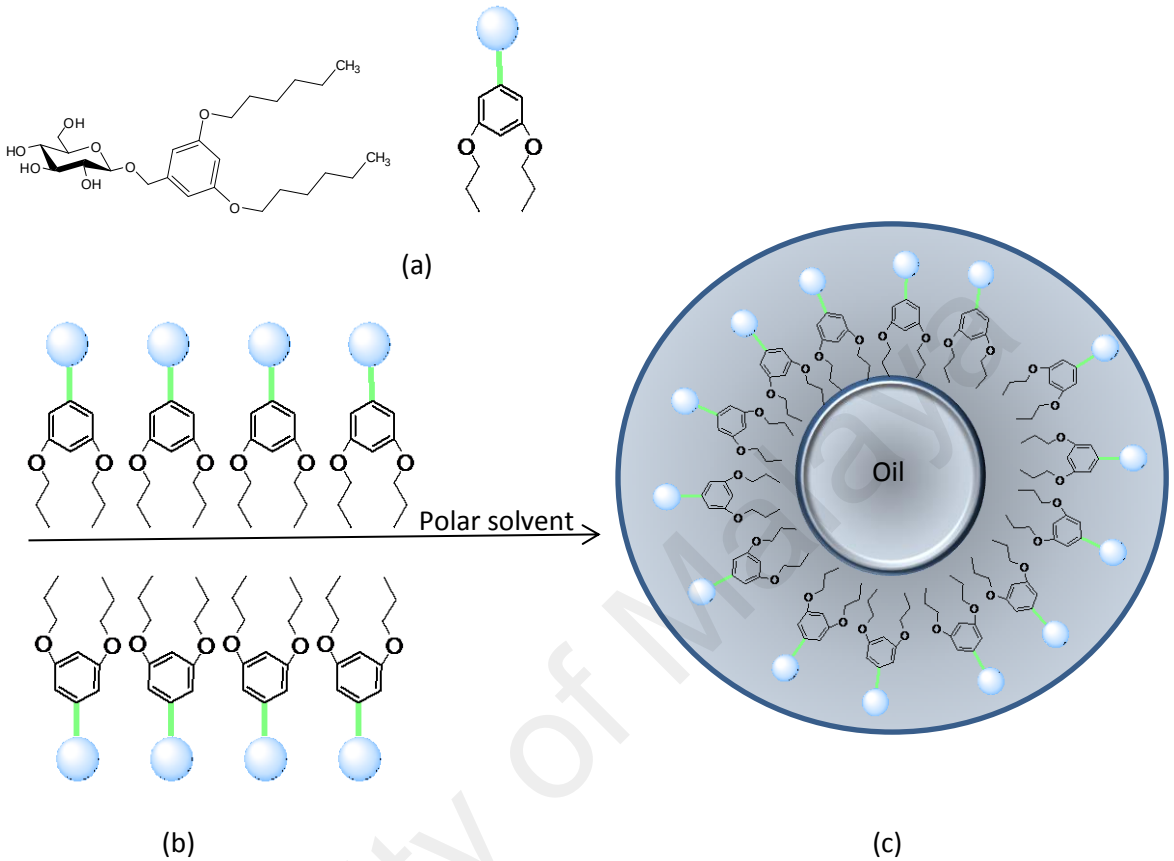


Figure 6-4 : Structure diagram of surfactant assembly for compound 2 shows (a) single surfactant molecules, (b) the surfactant molecules at low water concentration assemble in a lamellar phase, (c) at higher water concentration the surfactant molecules arrange in a hexagonal H_1 phase.

6.3.3 Air-water interface behaviour and emulsion stability

The behaviour of the surfactants at the air-water interphase was investigated by systematic surface tension measurements over a wide range of concentrations. With exception of compound 10, for which no CMC could be determined even at high concentration, data regarding the micellar assembly for the surfactants are tabulated in Table 6-1.

Table 6-1: CMC, surface tension at CMC, minimum area per surfactant molecule and standard free energy of micellization.

Compound	cmc (mM)	γ_{cmc} (mN/m)	A_{min} (Å^2)	ΔG_{mic} (KJ.mole^{-1})
12	**0.7**	**34**	**48**	**10.9**
14	**3.7**	**37**	**29**	**6.7**
16	**0.4**	**27.9**	**40**	**12.5**

The CMC decreases by one decade upon introduction of a benzene ring, as seen in the lower values for compounds **12** and **16**. The drastic reduction of the CMC is expected, since the benzene ring increases the hydrophobicity of the aglycon, *i.e*. the non-sugar component of the surfactant, significantly. On the other hand, the triazole affected the CMC significantly less. This observation is in line with previous observations for ATGs (Sani *et al*., 2012). A comparison of compounds **12** and **16** indicates a significant reduction of the minimum surface tension (γ_{min}) upon introduction of the triazole linkage, whereas the CMC itself is not much affected. This surface tension affect might originate out of a conformational more flexible linkage between the sugar core and the hydrophobic domain, represented by the bis-alkoxylated benzene. A higher molecular surface area for compound **12** is in line with this hypothesis. The lower surface tension of surfactant **16** with respect to **14**, on the other hand, can be attributed to the benzene ring, which increases the efficiency of the otherwise rather small hydrophobic domain. Surfactant **12** exhibited an unusual decrease of the surface tension above the CMC. Such behaviour has been previously associated with presence of poly-disperse micelles or the formation of a gel-monolayer at air-water interface (Swanson-vethamuthu, Feitosa, & Brown, 1998). A mathematical analysis of the slope of the surface tension at the concentration dependent region near the CMC enables the determination of the molecular surface area A_{min} and the

micellization energy (ΔG_{misc}). The calculation based on the Gibbs isotherm adsorption equation, displayed in equation 6.1, which enables the determination of the amount of surfactant molecules adsorbed per unit area at the air-water interface. This value can be related with A_{min} according to equation 6.2 (Soderberg *et al*., 1995). A_{min} increased upon presence of the benzene ring. The decrease of the surface area upon introduction of the triazole linker has been already stated above. The standard free energy of micellization was determined by using equation 6.3 (Soderberg *et al*., 1995). The value increases with the introduction of aromatic rings, both for the benzene and the triazole.

$$\Gamma_{max} = -\frac{1}{2.303nRT}\left(\frac{\partial\gamma}{\partial \log C}\right)_{maxT} \qquad \text{eq. 6.1}$$

$$A_{min} = \frac{10^{20}}{N_A \Gamma_{max}} \qquad \text{eq. 6.2}$$

$$\Delta G_{mic} = RTLn(cmc/55.5) \qquad \text{eq.6.3}$$

With exception of surfactant **10**, all surfactants exhibited reasonable good oil-in-water emulsion stabilities, requiring five days for the separation of a homogenized formulation in absence of polymeric stabilizers. Pictures of the emulsions before and after separation are shown in Figure 6-5. A reason for poor emulsion stabilization of compound **10** could be repulsive ionic interactions originating from a partial protonation of the amine in combination with relatively week hydrophobic effects for the relatively short alkyl chains. Surfactant **12** exhibited a remarkably good water-in-oil emulsion stabilitization, resulting in a separation time as long as two-month. Pictures are shown in Figure 6-6.

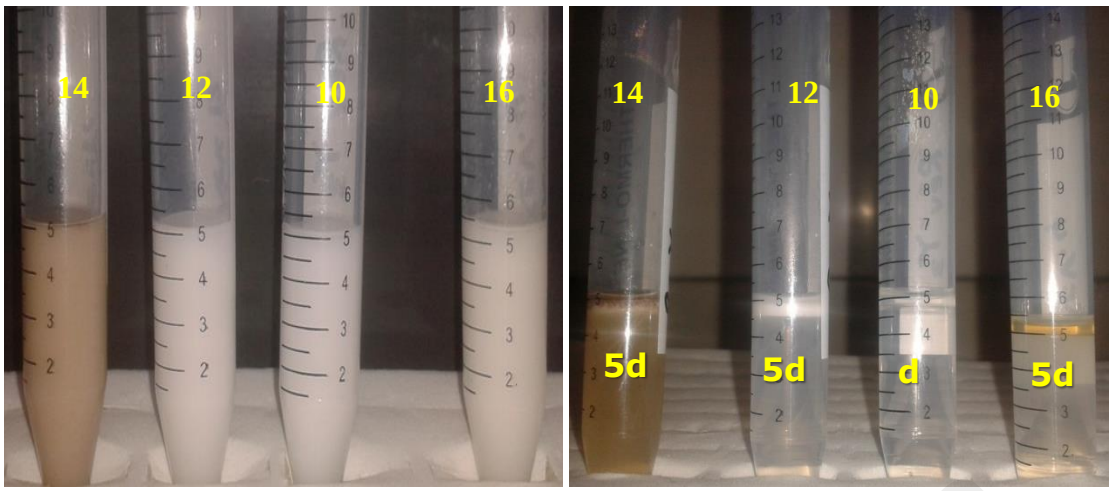


Figure 6-5: Emulsion stability (O/W).

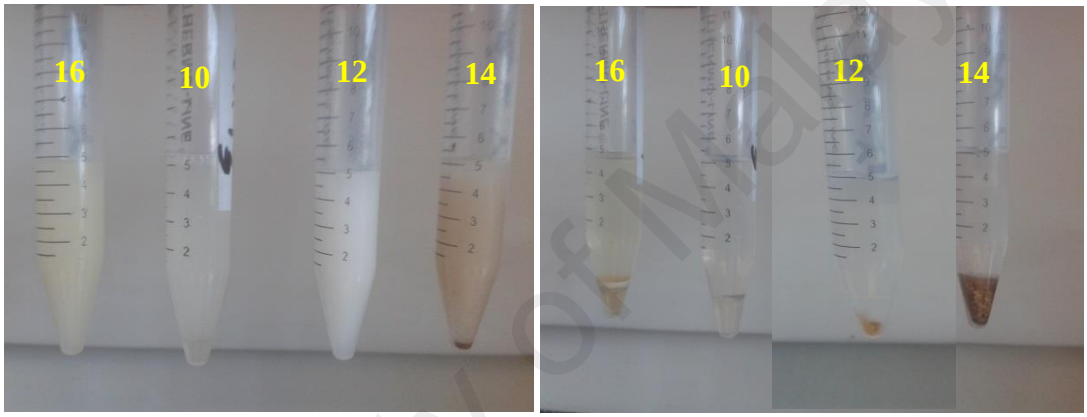


Figure 6-6: Emulsion stability (W/O).

6.4 Conclusion

A series of Y-shaped sugar-based surfactants involving aromatic and aliphatic linkers has been designed and synthesized. The incorporation of a benzene ring increases the molecular surface area, resulting in less curvature of the assembly towards the hydrophilic side, thereby enhancing the surfactants emulsifier potential for water-in-oil formulations.

Chapter 7 : A new class design of X-shape sugar-based surfactants by "click" chemistry and studies their self-assembling

7.1 Introduction

At the end of last century, carbohydrate derived surfactants have attracted increasing attention in both scientific and technical fields (Baba *et al*., 1999; Balzer, 1993; M Hato, Minamikawa, Tamada, Baba, & Tanabe, 1999; Korchowiec *et al*., 2001). The reasons cover both biological and industrial (performance) aspects, in particular for applications related to cosmetics, pharmaceuticals, food and detergents (Kitamoto *et al*., 2002; Sharma & Rakshit, 2004). Their increasing utilization for various applications is driven by environmental awareness and emphasis on a sustainable resources (Holmberg, 2001; Kitamoto *et al*., 2002). Sugar-based surfactants are considered biodegradable and reasonably non-toxic (Bazito & El Seoud, 2001; Nilsson *et al*., 1998). Since the development of surfactants from on natural products including sugar (Aveyard *et al*., 1998; Boyd, Drummond, Krodkiewska, & Grieser, 2000; Garofalakis, Murray, & Sarney, 2000; Kjellin, Claesson, & Vulfson, 2001; Retailleau, Laplace, Fensterbank, & Larpent, 1998; Rico-Lattes & Lattes, 1997; Soderberg *et al*., 1995; Zhang & Marchant, 1996) various products have been synthesized and investigated. However, the compound design is commonly based on synthetic convenience rather than on structure-property based application optimization. Only few investigations aiming for application-designed surfactants have been reported. For example, Stein and Gellman (Stein & Gellman, 1992) have been prepared a family of amphiphiles, derived from a rigid dicarboxylic acid head group unit of unusual topology. Cheng *et al.* (Cheng, Ho, Gottlieb, Kahne, & Bruck, 1992) deal in the design and study of facial amphiphiles. These are material comprised of glycosylate bile acids, have hydrophobic and hydrophilic faces as opposed to a linear hydrophobic tail attached to a hydrophilic head

group. Nusselder and Engberts (Nusselder & Engberts, 1989) examined and focus on the relationship between the molecular architecture of the surfactant and aggregate morphology in 1,4-dialkylpyrimidinium salts. Menger *et al.* have reported unnatural amphiphilies, in which the hydrophobic moiety was a polynuclear aromatic ring system (Menger & Whitesell, 1987) or a hyperextended linear chain (Menger & Yamasaki, 1993). The ratio of surface areas for the hydrophilic and hydrophobic antipodes affects the shape of a micellar assembly (Fisher, 2000) and hence the application potential of a surfactant. While typical surfactant designs enable a rather easy prediction of the shape of micelles, the assembly of more complex structures is difficult. However, in view of potential applications, a systematic study of the relationship of chemical structure and assembly geometry is needed. This leads to the need of new surfactants with unusual shape (Menger & Littau, 1993; Nusselder & Engberts, 1989; Stein & Geiiman, 2003). Conventional sugar-based surfactants contain one head group and one or two alkyl chains. The structure types are termed as a and b in Figure 7-1. Their assembly leads to a random distribution of hydrophilic groups at interphases, including the surface of micelles (Engberts & Kevelam, 1996). Bola-shaped and so-called Gemini-surfactants, on the other hand, consist of two head groups, referring to types c to f in Figure 7-1. The idea underlying the use of two head groups is to enhance the molecular solubility in water and oil by decreasing the aggregation number, hence it increases the critical aggregation concentration (Castro, Cirelli, & Kovensky, 2006; Pestman, 1998). Based on this concept, new surfactants with X-shape design, reflecting type f in Figure 7-1, varying in the structure of the central connector of the hydrophilic and hydrophobic antipodes, were prepared and their interfacial behaviours were investigated. Both aliphatic and aromatic core were applied to cover a wide structural diversity.

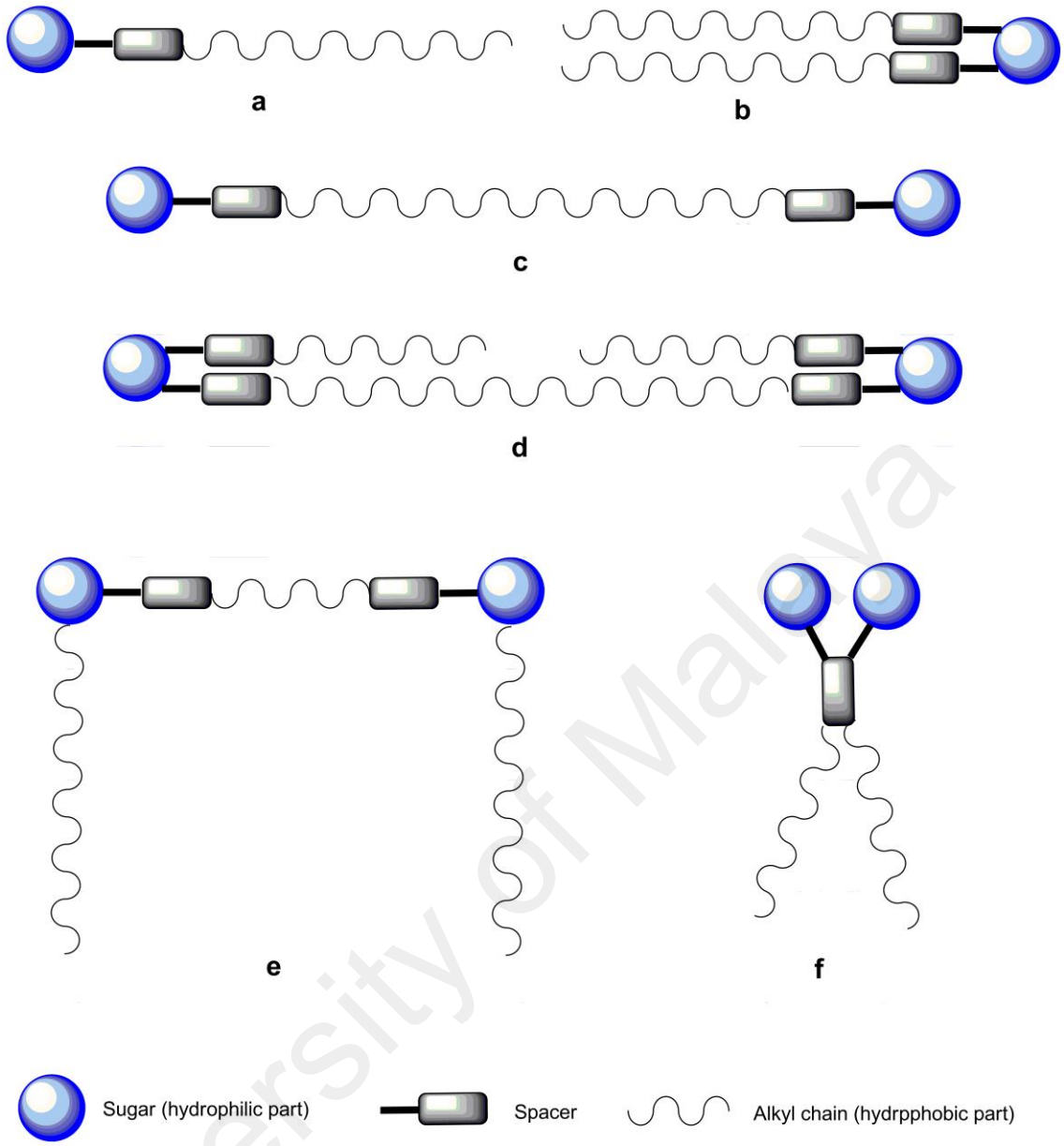


Figure 7-1: Showing surfactant design shape where (a) single-chained surfactant, (b) double-chained surfactant, (c and d) bolaform surfactant and (e and f) gemini surfactants.

7.2 Materials and methods

7.2.1 Material

All Chemicals were purchased from various commercial sources and were used without further purification. Purification of all products applied column chromatography on silica gel 35-60 mesh (Merck) using the flash technique. TLC was performed on pre-coated plates of silica gel 60 (GF254 by Merck). Visualization of carbohydrate compounds applied treatment with 15 % ethanolic sulfuric acid and subsequent heating.

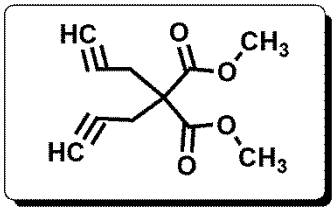
7.2.2 Characterization and determination of interfacial properties

Structural identities are based on NMR spectra (^{1}H and ^{13}C, recorded on a Bruker AVN-400 MHz spectrometer). Matrix-assisted laser desorption/ionization (MALDI) time of flight (TOF) mass spectra were recorded at the Mass Spectrometric Service Centre of the National University of Singapore on a Shimadzu/Kratos (Columbia, MD) AXIMA CFR mass spectrometer in reflexion mode. The samples were co-precipitated with 2,5-dihydroxy-benzoic acid (DHB, 5 mg/100 µl in MeOH/H_2O 1:1) and irradiated by a N_2-laser at λ =335 nm. Physicochemical property investigation applied distilled water. The surface tension was measured on a KSV Sigma 702 tensiometer applying the DuNouy ring method. Surface tension measurements of aqueous solutions of the surfactants were recorded at 298 K under atmospheric pressure. The critical micelle concentration (CMC) value was assessed as the intersection of the linear regressions of the surface tension against the logarithmic surfactant concentration. The surface tension at this intersection point is called the surface tension at CMC. The experiments were repeated twice, leading to coinciding curves.

The phase behaviour of the glycolipids was investigated lyotropically under an optical polarizing microscope (OPM) (Olympus BH-2 equipped with Mettler heating stage FF82 and central processor FP80). Two different solvents, one of which is polar

(water) while the other one non-polar (1-undecanol), were applied at 27 °C. Emulsion were prepared based on ratio of 19 parts water containing 0.5% surfactant to 1 part of oil. Samples were homogenized at room temperature for approximately 2 minutes using an IKA T10 basic at a speed of 14,450 rpm. The emulsion samples were stored at room temperature and monitored on phase separation over a period of a few weeks.

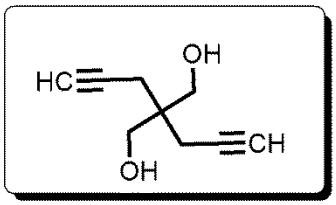
7.2.3 Experimental



Chemical Formula: $C_{11}H_{12}O_4$
Molecular Weight: 208.2106

7.2.3.1 Dimethyl 2,2-bis-(2-propynyl)-malonate

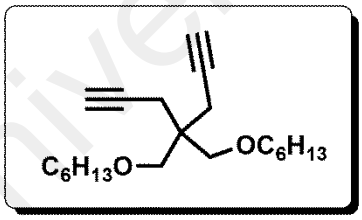
A procedure similar to that reported in literature (Carney *et al*., 2008) was employed. Dimethyl malonate (6.0 mL, 52 mmole) was added dropwise to a suspension of sodium hydride (60 % wt in mineral oil, 4.22 g, 105.5 mmol) in dry THF (100 mL) which was stirring at 10°C. Then the reaction mixture was left stirring for 10min., and then propargyl bromide (80 % wt. in toluene, 12.0 mL, 107.7 mmol) was added dropwise. The reaction mixture was warmed to room temperature and stirred for overnight. The reaction mixture was extracted three times with water and Et_2O. The combined organic phases were washed with brine water, dried over $MgSO_4$, filtered and concentrated on a rotary evaporator leaving white solid. The solid was crystallized from ethyl acetate to give 9.4 g of a crystalline white solid (84 % yield).



Chemical Formula: $C_9H_{12}O_2$
Molecular Weight: 152.1904

7.2.3.2 4,4-Bis-(hydroxymethyl)-1,6-heptadiyne (1)

Lithium aluminium hydride (1.2 g, 32.43 mmol) was added to a stirred solution of the Dimethyl 2,2-di(propynyl)malonate (3.0 g, 14.42 mmol) in anhydrous THF at 10 ° C. The reaction mixture was allowed to warm to room temperature and stirred for overnight. 1.2 mL of water was added slowly to stop the reaction, an aq. 10 % NaOH solution (1.2 mL), and then additional water (3.6 mL). Then the reaction mixture was left to stir for around 30 min. until the suspended solids become white. The reaction mixture was filtered and the solid rinsed with CH_2Cl_2, the filtrate dried over $MgSO_4$ and concentrate in rotary evaporator to resulting 2.0 g colorless crystal (91 % yield). ^{1}H NMR ($CDCl_3$) δ = 3.71 (s, 2x2 H, O$\underline{CH_2}$); 2.35 (d, 2x2 H, CH_2 propargyl); 2.05 (t, 2x1 H, CH propargyl). ^{13}C NMR ($CDCl_3$) δ =80.34 (2x $\underline{C}$ =CH); 71.22 (2x C= $\underline{C}$H); 66.26 (2x $\underline{C}H_2OH$); 42.08 (C quaternary); 21.65 (CH_2 propargyl).

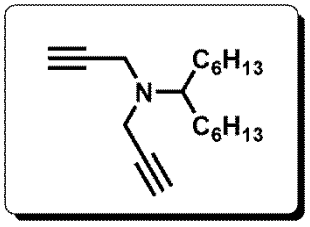


Chemical Formula: $C_{21}H_{36}O_2$
Molecular Weight: 320.5093

7.2.3.3 4,4-Bis-(hexyloxymethyl)-1,6-heptadiyne (2)

Compound **1** (2.4 g, 15.78 mmol), 1-bromododecane (8.34 mL, 34.73 mmole) and KOH (2 g, 35.71 mmole) were dissolved in DMSO and stirred for overnight at room temperature. The reaction mixture was extracted with water and CH_2Cl_2, the organic phases were washed with brine water and dried over $MgSO_4$. Then the mixture was concentrated in rotary evaporator and the residue was purified by column

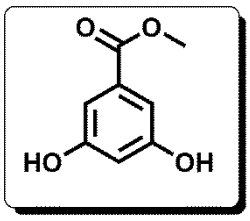
chromatography with 10 % ethyl acetate in hexane as eluent to resulting 3.0 g (60 %yield). ^{1}H NMR ($CDCl_3$) δ =3.42 (s, 2x2 H, CCH_2O); 3.37 (t, 2x2 H, OCH_2); 2.73 (t, 2x1 H, CH propargyl); 1.95 (t, 2x2 H, CH_2 propargyl), J=2.7; 1.52- 1.45 (m, 2x2 H, B-CH_2); 1.29- 1.17 (m, 12H, CH_2-bulk); 0.82 (t, 3x2 H, CH_3). ^{13}C NMR ($CDCl_3$) δ = 80.35 (2x C $\equiv$CH); 74.47 (2x CCH_2); 71.91 (2x C$\equiv$ CH); 70.84 (2x OCH_2); 31.55 (C quaternary); 29.41 (α-2); 25.70 (α-1); 22.53 (B-CH_2); 21.88 (CH_2-propargyl) 13.80 (CH_3).



Chemical Formula: $C_{19}H_{33}N$
Molecular Weight: 275.4720

7.2.3.4 *N,N*-Di-(2-propynyl)-7-trideyl-amine (3)

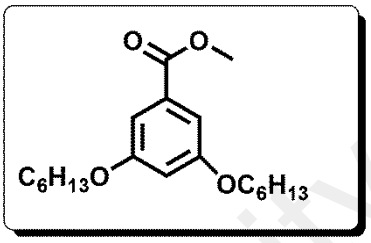
The synthesis of tridecan-7-amine was carried out according to the method reported in the literature (Che, Datar, Balakrishnan, & Zang, 2007; Manning, Bogen, & Kelly, 2011; Myahkostupov, Prusakova, Oblinsky, Scholes, & Castellano, 2013). To a solution of tridecan-7-amine (2.0 g, 10.03 mmole) and K_2CO_3 (4.5 g, 32.60 mmole) was added propargyl bromide (3 mL, 34.06 mmole) in DMF. The reaction mixture was reflux at 80°C for overnight. The reaction mixture filtered and the solvent was evaporatord, and then the residue purified by flash chromatography column using 10 % ethyl acetate in hexane as the eluent to give 1.65g as a di-substitute and 0.5 g as mono-substitute of a yellow oil (78 % yield). ^{1}H NMR ($CDCl_3$) δ = 3.40 (d, 2x2 H, CH_2-propargyl), J=2.3; 2.63 (p, CHN); 2.11 (t, 2x1 H, CH-propargyl); 1.46- 1.20 (m, 20H, bulk-CH_2); 0.81 (t, 3x2 H, CH_3). ^{13}C NMR ($CDCl_3$) δ = 81.00 (2x C $\equiv$CH); 71.98 (2x C$\equiv$ CH); 60.79 (CHN); 38.77 (2x CH_2- propargyl); 31.83 (∞-2); 30.57 (∞° -2); 29.51 (bulk-CH_2); 26.66 (B-CH_2); 22.66 (∞-1); 14.08 (CH_3).



Chemical Formula: $C_8H_8O_4$
Molecular Weight: 168.1467

7.2.3.5 Methyl 3,5-dihydroxybenzoate

2 mL of concentrate H_2SO_4 was added to a stirred solution of 3,5-dihydroxybenzoic acid (4.0 g, 25.95 mmole) in methanol. The reaction mixture was then refluxed for 2h at 100 °C. The solvent was evaporated and the residue was taken up in water and extracted with ethyl acetate three times. The combined organic phases were washed with brine water and dried over $MgSO_4$, then concentrated in a rotary evaporator to produce 4.2 g from the corresponding ester (98 % yield).

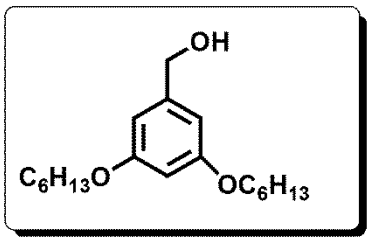


Chemical Formula: $C_{20}H_{32}O_4$
Molecular Weight: 336.4657

7.2.3.6 Methyl 3,5-bis-(hexyloxy)-benzoate

To a stirred solution of Methyl 3,5-dihydroxybenzoate (4.0 g, 23.78 mmole) and K_2CO_3 (9.84 g, 71.36 mmole) in DMF, 1-bromohexane (7 mL, 49.86 mmole) was added. The reaction mixture was refluxed at 80°C for overnight. The mixture was filtrate, then the solvent was evaporatord and the residue extracted with DCM and water three times. The combined organic phases were washed with brine water and dried over MgSO4, then concentrated in a rotary evaporator to produce 7.2 g green dark oil (90 % yield). ^{1}H NMR ($CDCl_3$) δ = 7.61 (s, 2x1 H, CH-benzene); 6.63 (s, CH-benzene); 3.96 (t, 2x2 H, OCH_2); 1.77 (p, 2x2 H, B-CH_2); 1.45 (p, 2x2 H, ∞-CH_2); 1.33 (bs, 8H, bulk-CH_2); 0.90 (t, 3x2 H, CH_3). ^{13}C NMR ($CDCl_3$) δ = 166.99 (CO); 160.16 (2x $C_{benzene}$);

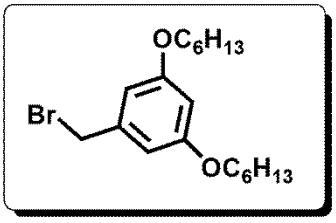
131.82 ($C_{benzene}$); 107.63 (2x $CH_{benzene}$); 106.59 ($CH_{benzene}$); 68.32 ($(OCH_2)_2$); 31.54 (ω -2); 29.14 (bulk-CH_2); 25.67 (B-CH_2); 22.58 (ω -1); 14.00 (2x CH_3).



Chemical Formula: $C_{19}H_{32}O_3$
Molecular Weight: 308.4556

7.2.3.7 3,5-Bis(hexyloxy)-benzyl alcohol (4)

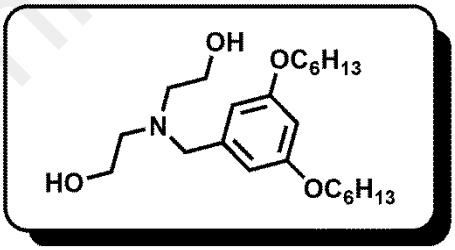
Lithium aluminium hydride (0.5 g, 13.51 mmol) was added to stirred solution of Methyl 3,5-bis(hexyloxy)benzoate (3.0 g, 8.91 mmol) in anhydrous THF at 10 ° C. The reaction mixture was allowed to warm to room temperature and stirred for overnight. 0.5 mL of water was added slowly to stop the reaction, an aq. 10 % NaOH solution (1 mL), and then additional water (2 mL). Then the reaction mixture was left to stir for around 30 min. until the suspended solids become white. The reaction mixture was filtered and the solid rinsed with CH_2Cl_2, the filtrate dried over $MgSO_4$ and concentrated in rotary evaporator to give 2.2 g green dark oil (80 % yield). ^{1}H NMR ($CDCl_3$) δ = 6.48 (d, 2x1 H, CH-benzene), J= 2.5; 6.36 (t, CH-benzene), J= 2.3; 4.59 (s, CH_2-benzyl); 3.92 (t, 2x2 H, OCH_2); 1.75 (p, 2x2 H, B-CH_2); 1.44 (p, 2x2 H, ∞-CH_2); 1.34- 1.30 (m, 8H, bulk-CH_2); 0.90 (t, 3x2 H, 2x CH_3). ^{13}C NMR ($CDCl_3$) δ = 160.51 (2x $C_{benzene}$); 143.28 ($C_{benzene}$); 105.06 (2x $CH_{benzene}$); 100.56 ($CH_{benzene}$); 68.07 ($(OCH_2)_2$); 65.34 (CH_2-benzyl); 31.57 (ω -2); 29.22 (bulk-CH_2); 25.71 (B-CH_2); 22.59 (ω -1); 14.01 (2x CH_3).



Chemical Formula: $C_{19}H_{31}BrO_2$
Molecular Weight: 371.3522

7.2.3.8 3,5-Bis(hexyloxy)-benzyl bromide

5 g, 16.21 mmole of 3,5-bis(hexyloxy)benzyl alcohol in anhydrous CH_2Cl_2 (100 mL) at 0 °C was phosphorus tribromide (3 mL, 32.42 mmole) added dropwise to a solution. The stirred solution was continued at 0 °C for 30 min. and then at ambient temperature for 2h. The reaction mixture was poured into ice/water and extracted three times with CH_2Cl_2. The combine organic phases were washed with brine water, dried over $MgSO_4$, filtered and concentrated on a rotary evaporator leaving 5.6 g yellow oil (93 % yield). ^{1}H NMR ($CDCl_3$) δ = 6.54 (d, 2H, $(CH)_2$-benzene), J= 2.2; 6.41 (t, 1H, CH-benzene), J= 2.0; 4.48 (s, 2x1 H, CH_2-benzyl); 3.95 (t, 2x2 H, OCH_2); 1.79 (p, 2x2 H, B-CH_2); 1.51- 1.44 (m, 2x2 H, ∞-CH_2); 1.38- 1.34 (m, 8H, bulk-CH_2); 0.94 (t, 3x2 H, CH_3). ^{13}C NMR ($CDCl_3$) δ = 160.43 (2x $C_{benzene}$); 139.54 ($C_{benzene}$); 107.40 (2x $CH_{benzene}$); 101.44 ($CH_{benzene}$); 68.12 ($(OCH_2)_2$); 33.79 (CH_2-benzyl); 31.59 (ω-2); 29.25 (bulk-CH_2); 25.73 (B-CH_2); 22.62 (ω-1); 14.05 (2x CH_3).

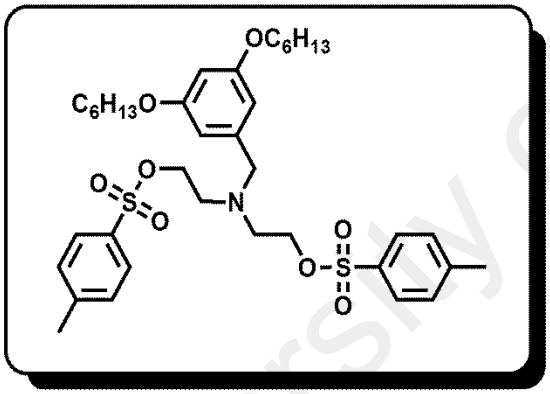


Chemical Formula: $C_{23}H_{41}NO_4$
Molecular Weight: 395.5759

7.2.3.9 *N*-(3,5-dihexyloxy-benzyl)-diethanolamine

Diethanol amine (1.7 g, 16.17 mmole) was added to a mixture of 3,5-bis(hexyloxy)benzyl bromide (3.0 g, 8.07 mmol) with K_2CO_3 (2.2 g, 15.94 mmole) in ethanol (100 mL) which was stirring at 75 °C for overnight. The reaction mixture was

filtrate and the ethanol was evaporatord. The reaction mixture was extracted three times with water and Et_2O. The combine organic phases were washed with brine water, dried over $MgSO_4$, filtered and concentrated on a rotary evaporator leaving 3.0 g (94% yield) brown whish oil. ^{1}H NMR ($CDCl_3$ 400MHz) 6.46 (d, 2x1 H, CH-benzene), J= 2.2, 6.36 (t, CH-benzene), J= 2.0, 3.92 (t, 2x2 H, OCH_2), 3.63 (bt, 3x2 H, CH_2-benzyl, CH_2OH), 2.70 (t, 2x2 H, CH_2N), 1.76 (p, 2x2H, B-CH_2), 1.49- 1.42 (m, 2x2 H, ∞-CH_2), 1.36-1.32 (m, 8H, bulk-CH_2), 0.92 (t, 3x2 H, CH_3). ^{13}C NMR ($CDCl_3$ 100MHz) 160.43 (2x $C_{benzene}$), 140.70 ($C_{benzene}$), 107.87 (2x $CH_{benzene}$), 99.89 ($CH_{benzene}$), 67.99 (2x OCH_2), 59.46 (2x CH_2OH), 59.18 (CH_2-benzyl), 55.77 (2x CH_2N), 31.61 (ω-2), 29.28 (bulk-CH_2), 25.75 (B-CH_2), 22.60 (ω-1), 14.03 (CH_3).

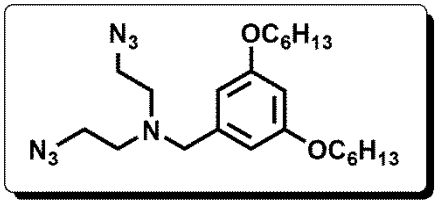


Chemical Formula: $C_{37}H_{53}NO_8S_2$
Molecular Weight: 703.9486

7.2.3.10 *N,N*-Bis-[2-(4-methylphenylsulfonyloxy)ethyl]-(3,5-dihexyloxy-benzyl amine

To a solution of 3,5-bis(hexyloxy)benzyl alcohol (4.0 g, 12.96 mmol) in 50 mL DCM was added 10 mL of 40 % NaOH followed by 4-toluenesulfonyl chloride (5.0 g, 26.22 mmol, 2 eq) then the reaction mixture were stirred for overnight. The reaction mixture was poured into an aqueous solution of $NaHCO_3$ and extracted three times with DCM. The combine organic phase was dried over $MgSO_4$ and concentrated in rotary evaporator to providea colorless oil 5.4g (97 % yield). ^{1}H NMR (400 MHz, $CDCl_3$) 7.94 (d, 2x1H, $CH_{\text{-tosyl}}$), 7.43 (d, 2x1H, $CH_{\text{-tosyl}}$), 6.53 (d, 2x1 H, $CH_{\text{-benzene}}$), J = 2.0, 6.38 (t,

$CH_{\text{-benzene}}$), J = 2.1, 3.95 (t, 2x2 H, OCH_2), 3.68 (s, $CH_{2\text{-Benzyl}}$), 3.53 (t, 2x2 H, CH_2O-tosyl), 2.94 (t, 2x2 H, CH_2N), 2.50 (s, $CH_{3\text{-tosyl}}$), 1.78 (p, 2x2 H, B-CH_2), 1.51-1.44 (p, 2x2 H, ∞-CH_2), 1.37-1.32 (m, 8H, bulk-CH_2), 0.92 (t, 2x3 H, CH_3). ^{13}C NMR (100MHz, $CDCl_3$) 160.38 (2x C_{benzene}), 146.90 ($\underline{C}SO_3$ tosyl), 141.66 ($\underline{C}CH_3$ tosyl), 141.31 (C_{benzene}), 130.28, 127.02 (4x CH-tosyl), 106.72 (2x CH_{benzene}), 100.22 (CH_{benzene}), 68.01 (2x OCH_2), 59.32 (CH_2-benzyl), 56.39 (2x CH_2O-tosyl), 42.04 (2x CH_2N), 31.61 (ω-2), 29.27 (bulk-CH_2), 25.76 (B-CH_2), 22.62 (ω-1), 21.80 ($CH_{3\text{-tosyl}}$), 14.06 (CH_3).



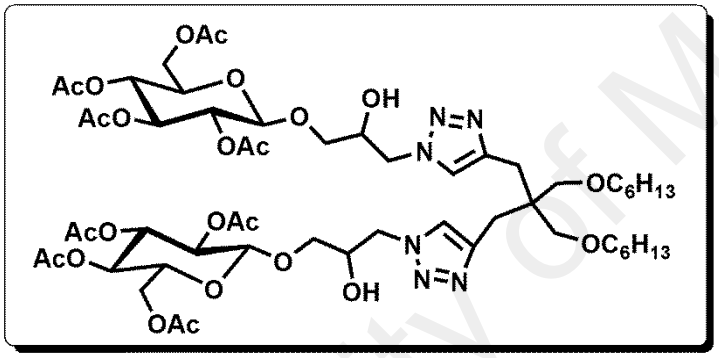
Chemical Formula: $C_{23}H_{39}N_7O_2$
Molecular Weight: 445.6015

7.2.3.11 *N*,*N*-Bis-(2-azidoethyl)-3,5-dihexyloxy-benzylamine

3,5-bis(hexyloxy)benzyl-4- methylbenzenesulfonate (4 g, 8.64 mmol) and anhydrous NaN_3 (1.2 g, 18.4 6mmol, 2 eq.) were added to DMF and the mixture was stirred at 80 °C for 2days. The solvent was removed by evaporation in vacuum, and the residue was extracted with water against DCM. The organic layer was dried over $MgSO_4$ and then concentrated to give a yellowish oil 2.7 g (94 % yield). ^{1}H NMR (400 MHz, $CDCl_3$) 6.52 (d, 2x1 H, $CH_{\text{-benzene}}$), J = 2.2, 6.37 (t, $CH_{\text{-benzene}}$), J = 2.2, 3.94 (t, 2x2 H, OCH_2), 3.64 (s, $CH_{2\text{-benzyl}}$), 3.33 (t, 2x2 H, CH_2N_3), 2.78 (t, 2x2 H, CH_2N), 1.78 (p, 2x2 H, B-CH_2), 1.46 (p, 2x2 H, ∞-CH_2), 1.36- 1.31 (m, 8H, bulk-CH_2), 0.92 (t, 2x3 H, CH_3). ^{13}C NMR (100MHz, $CDCl_3$) 160.41 (2x C_{benzene}), 140.86 (C_{benzene}), 106.75 (2x CH_{benzene}), 100.40 (CH_{benzene}), 68.04 (2x OCH_2), 59.59 ($CH_{2\text{-benzyl}}$), 53.86 (2x CH_2N_3), 49.47 (2x CH_2N), 31.58 (ω-2), 29.25 (bulk-CH_2), 25.72 (B-CH_2), 22.60 (ω-1), 14.03 (CH_3).

7.2.3.12 General Procedure for Click-Chemistry

A solution of the sugar azide (4 mmole, 2.1 eq.) and the divalent hydrocarbon precursor (2 mmol, 1 eq.) in methanol (50 mL) was treated with copper (II) salt ($Cu(OAc)_2$ or $CuSO_4$ 0.4 mmol, 15 % eq.) and sodium ascorbate (0.4 g, 2.0 mmol, 45 % eq.). The solution was stirred at room temperature overnight, then filtered and concentrated under reduced pressure. The residue was purified by filtration through a 5 cm layer of silica gel with 1:1 ethyl acetate: hexane as eluent to remove remaining starting materials (sugar and alkyl chain), followed by chloroform: methanol 4:1 to collect the surfactant precursors.

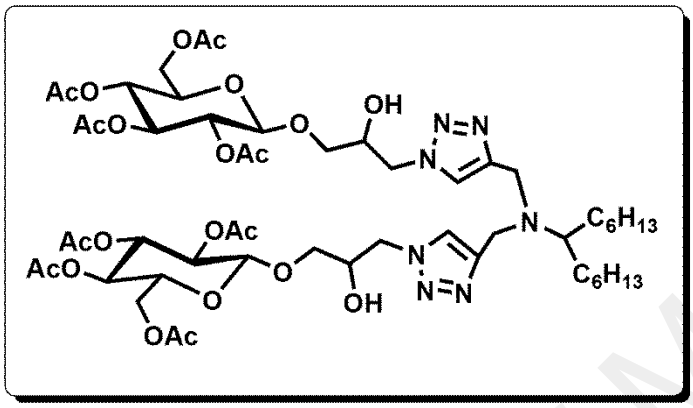


Chemical Formula: $C_{55}H_{86}N_6O_{24}$
Molecular Weight: 1215.2971

7.2.3.12.1 4,4'-Bis(2′-hydroxypropyl-2,3,4,6-Penta-*O*-acetyl-*β*-D-glucopyranosyl oxy)-2,2-bis(hexyloxymethyl)propane-1,3-diyl)bis(1H-1,2,3-triazole)(8)

Sugar azide **6** (2.0 g, 4.4 mmol) and dipropargyl **2** (0.68 g, 2.1 mmol) were coupled with Cu(OAc) (80 mg, 0.4 mmol) and Na-ascorbate (0.4 g,2 mmol) in MeOH according to the general procedure **I** to provide **8** (2.1 g yield 82 %) as a brown syrup. ^{1}H NMR (DMSO D6) δ =7.81 (bs, 2H, CH-triazole); 5.36 (bd, 2H, 2x H-1); 5.27 (t, 2H, 2x H-3), J=8.53; 4.19 (t, 2H, 2x H-4), J=9.7; 4.85-4.77 (m, 4H, 2x OCH_2); 4.44-4.33 (m, 2H, 2x H-5); 4.29-4.13 (m, 6H, 2x (H-6, H-2)); 4.04-3.89 (m, 8H, 2x(CCH_2O, CH_2-triazole)); 3.71-3.50 (m, 6H, 2x(CHOH, OCH_2-chain)); 2.00, 1.98, 1.94 (s, 24H, 8x CH_3CO); 1.56-1.46 (m, 4H, 2x B-CH_2); 1.37- 1.19 (m, 12H, bulk-CH_2); 0.87 (t,6H, 2x CH_3). ^{13}C NMR ($CDCl_3$) δ =169.99, 169.62, 169.51, 169.24, 169.14, 169.10 (8x

$COCH_3$); 144.66 (C-triazole); 124.66 (CH-triazole); 99.83, 99.61 (2x C-1); 73.20 (2x C-4); 71.97, 71.90 (2x C-2); 70.68 (2x C-3); 70.72 (2x (CH_2O, OCH_2)); 70.56 (2x CHOH); 70.49 (2x OCH_2-chain); 68.10, 67.81 (2x C-5); 61.65 (2x C-6); 52.37 (2x CH_2-triazole); 42.63 (C- quaternary); 31.12 (∞-2); 29.18 (2x C$\underline{C}H_2$); 25.37 (B-CH_2); 22.04 (∞-1); 20.42, 20.32, 20.23 (8x CH_3CO); 13.88 (2x CH_3).

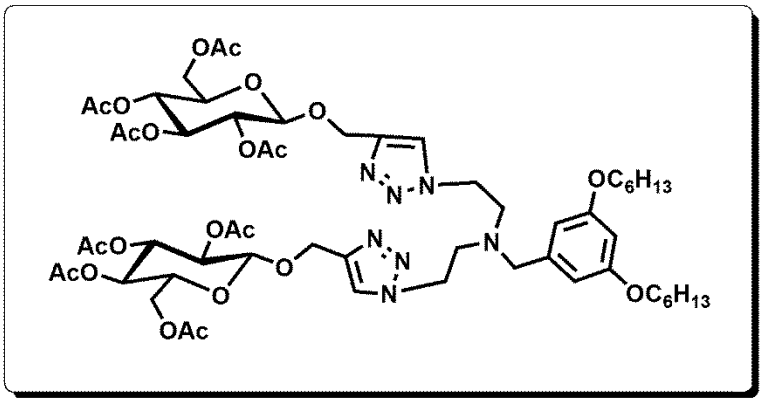


Chemical Formula: $C_{53}H_{83}N_7O_{22}$
Molecular Weight: 1170.2598

7.2.3.12.2 *N,N*-Bis((4,4'-bis(2′-hydroxypropyl-2,3,4,6-Penta-*O*-acetyl-*β*-D-glucopyranosyloxy) -1H-1,2,3-triazol)methyl)tridecan-7-amine (10)

Sugar azide **6** (2.0 g, 4.4 mmol) and dipropargyl **3** (0.58 g, 2.1 mmol) were coupled with Cu(OAc) (80 mg, 0.4 mmol) and Na-ascorbate (0.4 g,2 mmol) in MeOH according to the general procedure **I** to provide **10** (2.0 g yield 77 %) as a brown syrup. ^{1}H NMR (CD_3OD) δ = 7.58 (bs, 2H, 2x CH-triazole); 5.25 (t, 2H, 2x H-3), J=9.3; 5.09 (t, 2H, 2x H-4), J=9.5; 5.04 (ddd, 2H, 2x H-2), J=2.9; 4.62 (d, 2H, 2x H-1), J=7.92; 4.56-4.40 (m, 4H, 2x OCH_2); 4.28 (d, 2H, 2x H-6a), J=5.0; 4.25 (d, 2H, 2x H-6b), J=4.3; 4.22-4.12 (m, 4H, 2x CH_2-triazole); 3.91-3.65 (m, 8H, 2x(H-5, CHOH, CH_2N)); 2.62-2.53 (m, 1H, NCH); 2.18, 2.09, 2.04, 2.02 (s, 24H, 8x CH_3CO); 1.62-1.14 (m, 20H, bulk-CH_2); 0.90 (s, 6H, 2x CH_3). ^{13}C NMR (CD_3OD) δ =170.69, 170.18, 169.72, 169.45 (8x $COCH_3$); 147.30 (C-triazole); 124.58 (CH-triazole); 101.25, 101.22, 101.07 (2x C-1); 72.58 (2x C-4); 71.97, 71.89 (2x C-2); 71.52, 71.24 (2x OCH_2); 71.30, 71.24 (2x C-3); 69.08 (2x CHOH); 68.96 (NCH); 68.33 (2x C-5); 61.82 (2x C-6); 53.00 (2x

CH_2-triazole); 45.46 (2x triazole-CH_2); 31.84 (∞-2); 30.74, 30.56, 30.49, 29.51 (bulk-CH_2); 27.28 (B-CH_2); 22.69 (∞-1); 20.78, 20.71, 20.58 (8x CH_3CO); 14.11 (2x CH_3).



Chemical Formula: $C_{57}H_{83}N_7O_{22}$
Molecular Weight: 1218.3026

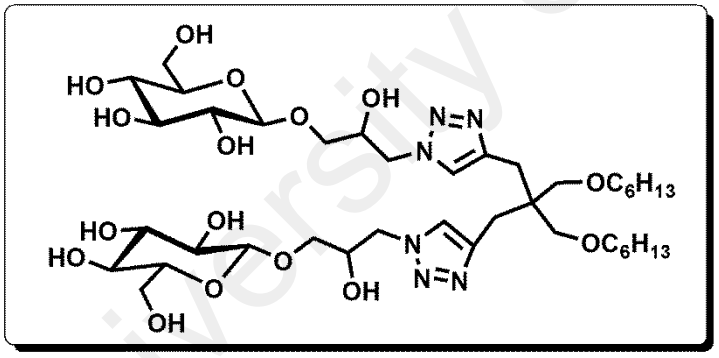
7.2.3.12.3 *N,N*-(3,5-bis(hexyloxy)benzyl)-2-(4,4'-bis(2,3,4,6-Penta-*O*-acetyl-*β*-D-glucopyranosyl-oxymethyl)-1H-1,2,3-triazol-1-yl)diethyl amine (12)

(1.1g, 2.46mmol, 1eq.) azido compound **4** with propargyl sugar **7** (2.0 g, 5.17 mmol, 2.1 eq.) in methanol were treated with $CuSO_4.5H_2O$ (0.1 g, 0.33 mmole, 15% eq.) and sodium ascorbate (0.4 g, 2.0 mmole, 45 % eq.). The solution was stirred at room temperature for overnight. The reaction mixture was filtered through celite and concentrated under reduced pressure. The residue was purified by filtrating through 5 cm silica gel with 1:1 ethyl acetate: hexane as eluent to remove remaining reactants. The product was eluted with chloroform: methanol 4:1 to provide **12** (2.4g yield 80%). ^{1}H NMR (400 MHz, $CDCl_3$) 7.42 (s, 2x1 H, $CH_{\text{-triazole}}$), 6.37 (t, $CH_{\text{-benzene}}$), J = 2.18, 6.27 (d, 2x1 H, $CH_{\text{-benzene}}$), J = 2.0, 5.21 (t, 2x1 H, H-3), $^3J_{3,4}$ = 9.4, 5.11 (t, 2x1 H, H-2), $^3J_{2,3}$ = 9.7, 5.01 (dd~t, 2x1 H, H-4), $^3J_{4,5}$ = 8.0, 4.94 (d, 2x1 H, H-6a), $^2J_6$ = 12.58, 4.83 (d, 2x1 H, H-6b), $^2J_6$ = 12.6, 4.71 (d, 2x1 H, H-1), $^3J_{1,2}$ = 7.9, 4.36-4.29 (m, 2x2 H, $CH_{2\text{-triazole}}$), 4.27 (d, 1x1 H, OCHa$_{\text{-triazole}}$), J = 4.5, 4.20 (d, OCHb$_{\text{-triazole}}$), J = 2.2, 4.20 (d, OCHb`$_{\text{-triazole}}$), J = 2.2, 3.90 (t, 2x2 H, OCH_2), 3.78 (ddd, 2x1 H, H-5), $^3J_{5,6a}$ = 2.0, $^3J_{5,6b}$ = 9.90, 3.60 (s, $CH_{2\text{-benzyl}}$), 3.05 (t, 2x2 H, CH_2N), 2.10, 2.04, 2.01, 1.98 (4x s, 8x3 H, Ac), 1.78 (p, 2x2 H, B-CH_2), 1.47 (p, 2x2 H, ∞-CH_2), 1.38-1.34 (m, 8H, bulk-CH_2),

0.93 (t, 2x3 H, CH_3). ^{13}C NMR (100MHz, $CDCl_3$) 170.67, 170.18, 169.34, 169.39 (8x COO), 160.45 (2x $C_{\text{-benzene}}$), 144.05 ($C_{\text{-triazole}}$), 139.95 ($C_{\text{-benzene}}$), 123.58 ($CH_{\text{-triazole}}$), 107.19 (2x $CH_{\text{-benzene}}$), 100.05 ($CH_{\text{-benzene}}$), 99.98 (2x C-1), 72.78 (2x C-3), 71.89 (2x C-5), 71.20 (2x C-4), 68.30 (2x C-2), 68.09 (2x OCH_2), 62.90 (2x C-6), 61.75 (2x OCH_2-triazole), 59.24 ($CH_{2\text{-benzyl}}$), 54.17 (2x CH_2N), 48.69 (2x $CH_{2\text{-triazole}}$), 31.60 (ω-2), 29.25 (bulk-CH_2), 25.752 (B-CH_2), 22.60 (ω-1), 20.77, 20.65, 20.59 (8x CH_3CO), 14.04 (CH_3).

7.2.3.14 General procedure for de-acetylation

The acetylated surfactant was carried out using methanol as solvent and treated with a catalytic amount of NaOMe. TLC revealed complete conversion after 4 hours stirring at room temperature. The catalyst was neutralization by Amberlite IR120 (H^+) and then the solvent was evaporatord to give the final surfactant

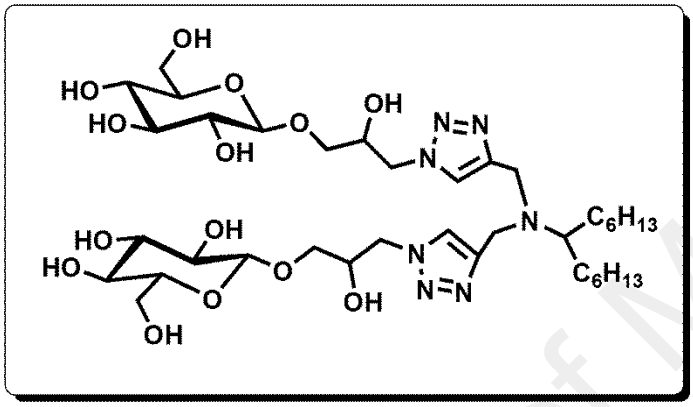


Chemical Formula: $C_{39}H_{70}N_6O_{16}$
Molecular Weight: 879.0037

7.2.3.14.1 4,4'-Bis(2′-hydroxypropyl-β-D-glucopyranosyloxy)-2,2-bis(hexyloxy methyl)propane-1,3-diyl)bis(1H-1,2,3-triazole) (9)

8 (2 g, 1.6 mmol) was reacted according to general procedure **II** to produce **9** (1.4 g, 96 %) as brown syrup. ^1H NMR (600 MHz, Pyridine 5d) 8.21 (s, 2x1 H, CH-triazole), 4.91- 4.88 (bm, 4x1 H, H-1, $CHa_{\text{-triazole}}$), 4.61- 4.44 (bm, 6x1 H, $CHb_{\text{-triazole}}$, H-5, H-6a), 4.28 – 4.15 (m, 6x1 H, H-6b, H-3, CHOH), 3.98 – 3.77 (m, 4x1 H; 2x2 H, H-4, H-2; OCH_2), 3.43 – 3.32 (bd, 4x2 H, CCH_2O, $OCH_{2\text{-chain}}$), 2.97 (bs, 2x2 H, CH_2C)

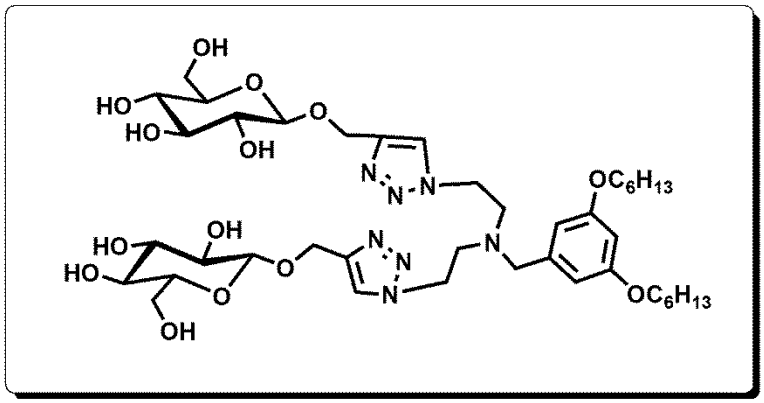
1.46 (bs, 2x2 H, CH_2), 1.21 (bd, 6x2 H, bulk-CH_2), 0.71 (bs, 2x3 H, CH_3). ^{13}C NMR (100MHz, Pyridine 5d) 143.86 (C-triazole), 125.42 (CH-triazole), 105.08, 104.81 (C-1), 78.32 (C-4), 78.20 (C-3), 74.92, 74.83 (C-2), 72.71 (C$\underline{C}$H$_2$O), 72.12 (OCH$_{2\text{-chain}}$), 71.27 (OCH$_2$), 71.27 (CHOH), 69.55, 69.50 (C-5), 64.22, 62.37 (C-6), 53.69, 53.42 (CH_2-triaole), 43.69 (C-quaternary), 31.60 (ω-2), 29.78 (bulk-CH_2), 27.75, 27.71 ($\underline{C}$H$_2$C), 25.89 (B-CH_2), 22.54 (ω-1), 13.91 (CH_3).



Chemical Formula: $C_{37}H_{67}N_7O_{14}$
Molecular Weight: 833.9664

7.2.3.14.2 *N,N*-Bis((4,4'-bis(2′-hydroxypropyl-*β*-D-glucopyranosyloxy)-1H-1,2,3-triazol)methyl) tridecan-7-amine (11)

10 (2 g, 1.7 mmol) was reacted according to general procedure **II** to produce **11 (**1.4 g, 98 %) as brown syrup. ^{1}H NMR (CD_3OD) δ = 7.98/7.58 (d~bs, 2H, 2x CH-triazole); 4.68-4.17 (m, 20H, 2x H-3, 2x H-4, 2x H-2, 2x H-1, 2x OCH$_2$, 2x H-6a, 2x H-6b, 2x CH_2-triazole); 3.94-3.25 (m, 9H, 2xH-5, CHOH, CH_2N, NCH); 1.75 (m$_c$, 20H, bulk-CH_2); 0.94 (s, 6H, 2x CH_3). ^{13}C NMR (CD_3OD) δ = 155.70 (C-triazole); 131.89 (CH-triazole); 103.31, 103.22 (2x C-1); 76.64, 76.50 (2x C-4), (2x C-3); 73.72, 73.64 (2x C-2), (2x OCH$_2$); 72.62 (2x CHOH); 70.43 (NCH); 70.16 (2x C-5); 61.28 (2x C-6); 52.20 (2x CH_2-triazole); 46.44 (2x triazole-CH_2); 31.66, 31.30 (∞-2); 28.81, 28.78 (bulk-CH_2); 24.38 (B-CH_2); 22.37, 22.20 (∞-1); 13.10, 12.98 (2x CH_3).



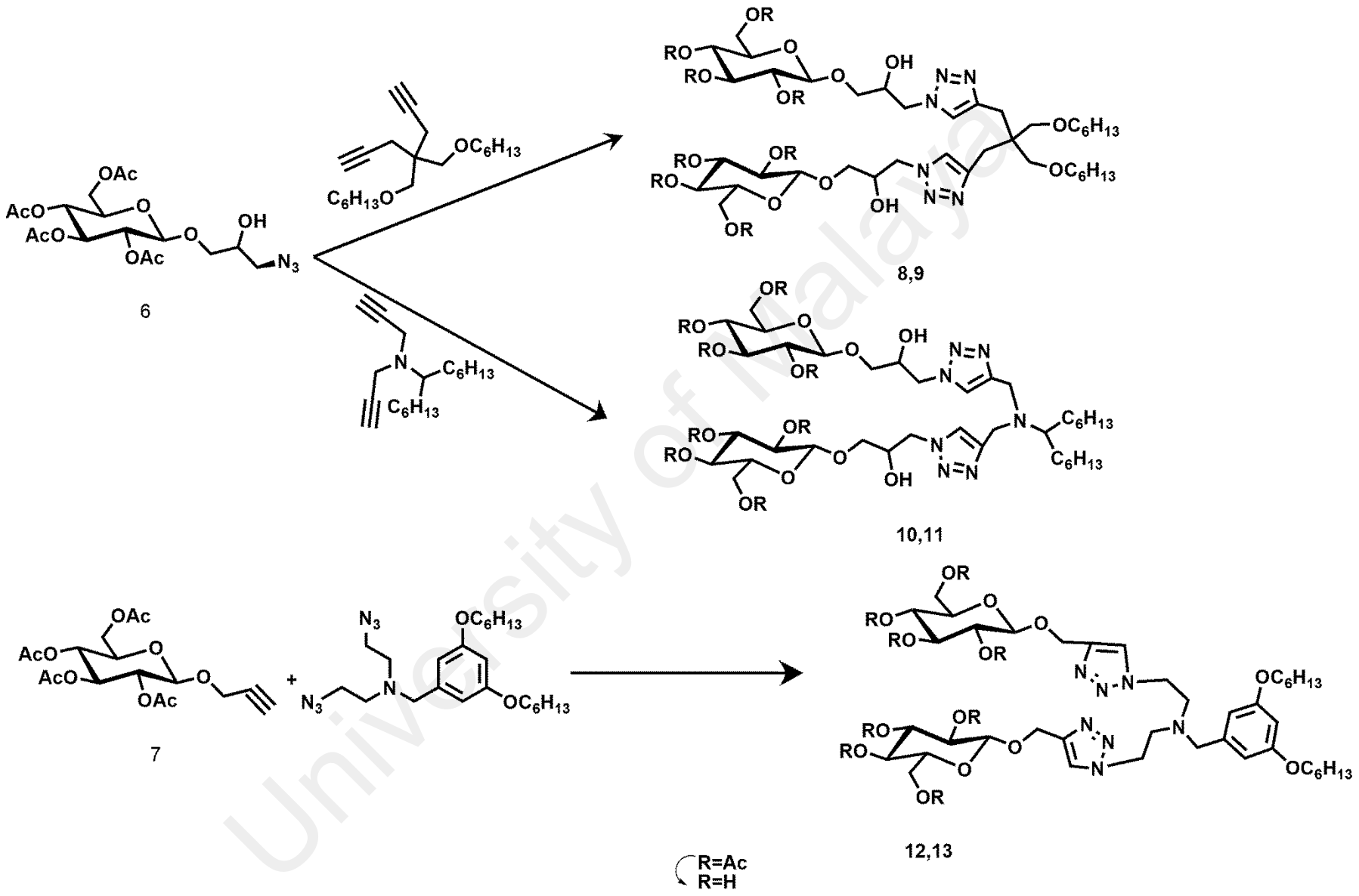
Chemical Formula: $C_{41}H_{67}N_7O_{14}$
Molecular Weight: 882.0092

7.2.3.14.3 *N,N*-(3,5-bis(hexyloxy)benzyl)-2-(4,4'-bis(*β*-D-glucopyranosyl-oxymethyl)-1H-1,2,3-triazol-1-yl)diethyl amine (13)

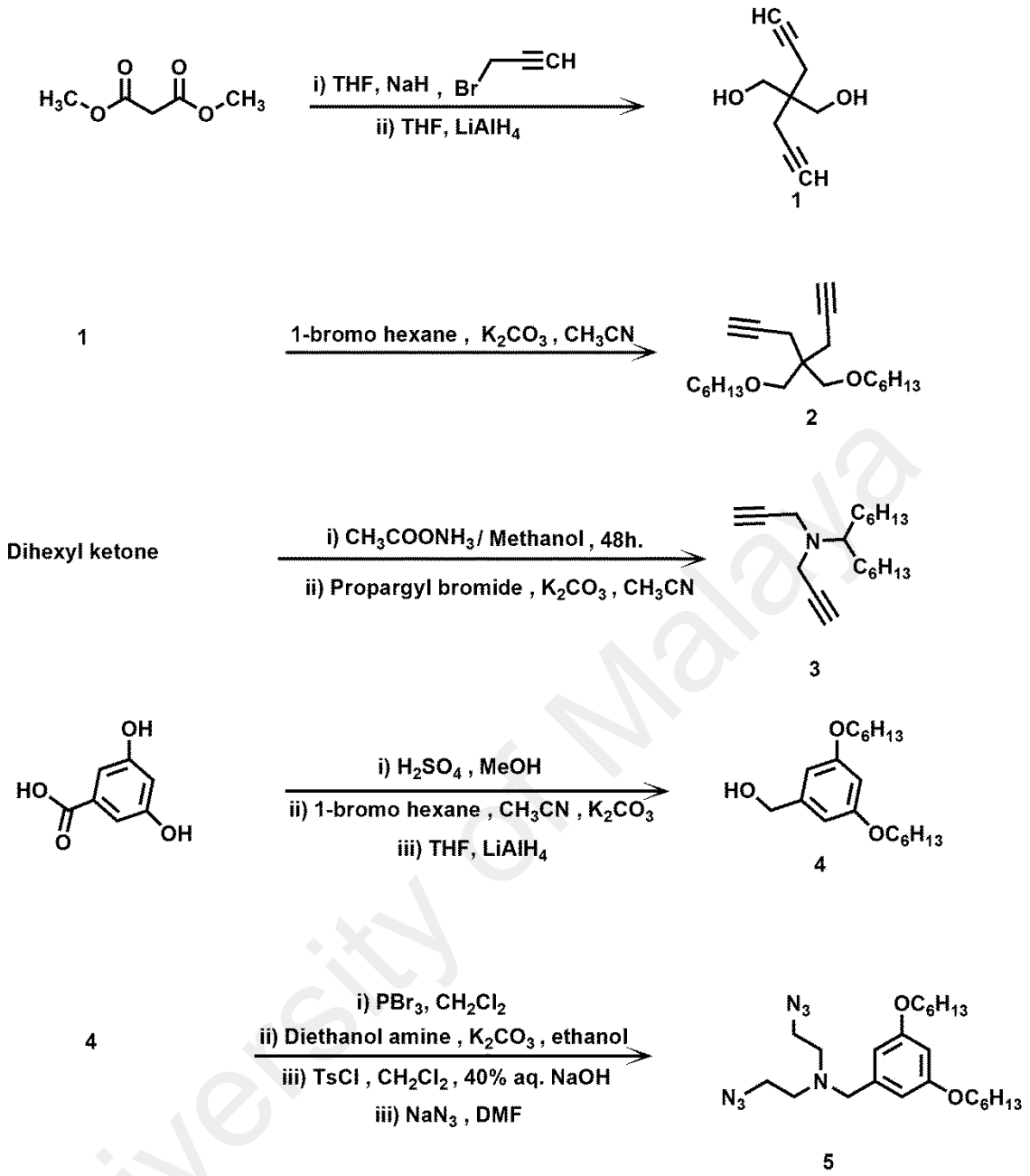
12 (2 g,1.64 mmol) was reacted according to general procedure **II** to produce **13** (1.4g, 97 %) as brown syrup. ^{1}H NMR (400 MHz, Pyridine 5d) 8.04 (s, 2x1H, $CH_{\text{-triazole}}$), 6.72 (bs, $CH_{\text{-benzene}}$), 6.65 (bs, 2x1 H, $CH_{\text{-benzene}}$), 5.40, 5.20 (2x d, $OCH_{2\text{-triazole}}$), J = 12.2, 5.08 (d, 2x1 H, H-1), $^{3}J_{1,2}$ = 7.56, 4.58 (d, 2x1 H, H-6a), $^{2}J_{6}$ = 11.7, 4.44 (bt, 2x2 H, $CH_{2\text{-triazole}}$), 4.40 (d, 1H, H-6b), $^{2}J_{6}$ = 4.8, 4.37 (d, 1H, H-6b`), $^{2}J_{6}$ = 4.88, 4.26 (d, 4x1 H, H-3; H-5), $^{3}J_{3,4;\ 5,6a}$ = 6.6, 4.09 (bt, 2x1 H, H-2), 4.03- 3.98 (m, 2x1; 2x2 H, OCH_2; H-4), 3.70 (s, $CH_{2\text{-benzyl}}$), 3.03 (bt, 2x2 H, CH_2N), 1.78 (bp, 2x2 H, B-CH_2), 1.44 (bp, 2x2 H, ∞-CH_2), 1.24 (bs, 8H, bulk-CH_2), 0.82 (bt, 2x3 H, CH_3). ^{13}C NMR (100MHz, Pyridine 5d) 160.74 (2x $C_{\text{-benzene}}$), 145.03 ($C_{\text{-triazole}}$), 141.10 ($C_{\text{-benzene}}$), 124.30 ($CH_{\text{-triazole}}$), 107.28 (2x $CH_{\text{-benzene}}$), 103.87 (2x C-1), 100.72 ($CH_{\text{-benzene}}$), 78.31 (2x C-4), 78.26 (2x C-3), 74.88 (2x C-2), 71.36 (2x C-5), 67.98 (2x OCH_2), 62.89 (2x OCH_2-triazole), 62.47 (2x C-6), 58.39 ($CH_{2\text{-benzyl}}$), 53.73 (2x CH_2N), 48.08 (2x $CH_{2\text{-triazole}}$), 31.53 (ω-2), 29.37 (bulk-CH_2), 25.81 (B-CH_2), 22.58 (ω-1), 13.91 (CH_3).

7.3 Results and Discussion

Three X-shape sugar-based surfactants (**9**, **11** and **13**) were designed. Their synthetic pathway is shown in Scheme 7-1. The main challenge for X-shaped surfactants involving carbohydrates as hydrophilic domains is the combination of the carbohydrates with the double alkyl chain. Click chemistry (Baier *et al*., 2012; Xu *et al*., 2009) provided a powerful synthetic tool in a modular synthesis by efficiently and reliably joining the two surfactant antipodes. The designed surfactants were targeted for the stabilization of particularly oil-in-water emulsions, emphasizing a similar geometry than Y-shape surfactants but with increased coverage of interphases by the hydrophobic domain. The synthesis of sugar azide precursors followed the approach towards Y-shaped surfactants, reported in chapter 3. The alkyne functionalized hydrophobic domain, on the other hand, based on core structures involving malonic acid, ammonia and a symmetrical functionalized benzene derivative. In the first approach dimethyl malonate was alkylated with propargyl bromide, followed by reduction of the two carbonyl groups with $LiAlH_4$ to produce linker **1**, which provided the hydrophobic domain precursor **2** upon alkylation with the surfactant hydrocarbon chains. More straightforward was the synthesis of the second hydrophobic building block. It was synthesized in two-step reaction, starting with a reductive amination of dihexyl-ketone with sodium cyanoborohydride (Manning *et al*., 2011) in quantitative yield, followed by subsequent alkylation with propargyl bromide to produce the mono and bis-alkyne in yields of 17% and 61%, respectively. The last building block originated from 3,5-dihydroxy-benzoid acid. 3,5-Bis-(hexyloxy)-benzyl alcohol was prepared and converting the corresponding bromide by treatment with PBr_3 following an analogue literature procedure (Cai *et al*., 2012b). The bromide was replaced by substitution with diethanol amine to provide the core of the hydrophobic domain.



Scheme 7-1: Synthesis of X-shape sugar-based surfactants.



Scheme 7-2: Synthesis of di-terminal alkyne and azide compounds as a hydrophobic part.

The crude compound was tosylated to finally introduce azides at the position of the former hydroxyl groups, see Scheme 7-2. Unlike for the previous two building blocks, click coupling of this compound required an alkyne terminated sugar building block, which is easily found in propargyl glucoside (Du, Linhardt, & Vlahov, 1998).

The coupling of the surfactant antipodes proceeded by click chemistry in high yields. All surfactants, as well as their various respective precursors, were fully

characterized by NMR spectroscopy. The disappearance of resonance signals for the triplet between δ = 2.8 and 1.8 ppm, reflecting the terminal alkyne, was accompanied by a new peak around δ = 8.0 – 7.2 ppm, which indicates the triazole ring, as shown in Figures 7-2 and 7-3.

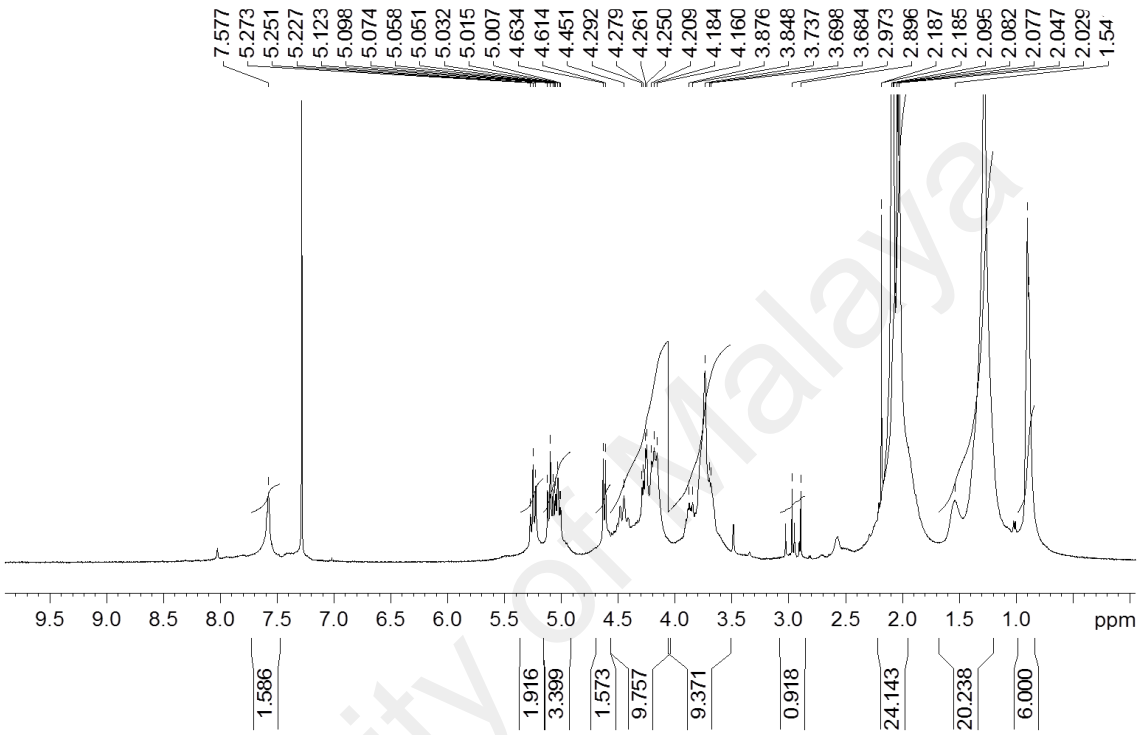


Figure 7-2: The evolution of ^{1}H NMR spectra (400 MHz, $CDCl_3$, 298 K) for acetylated surfactant precursor 10.

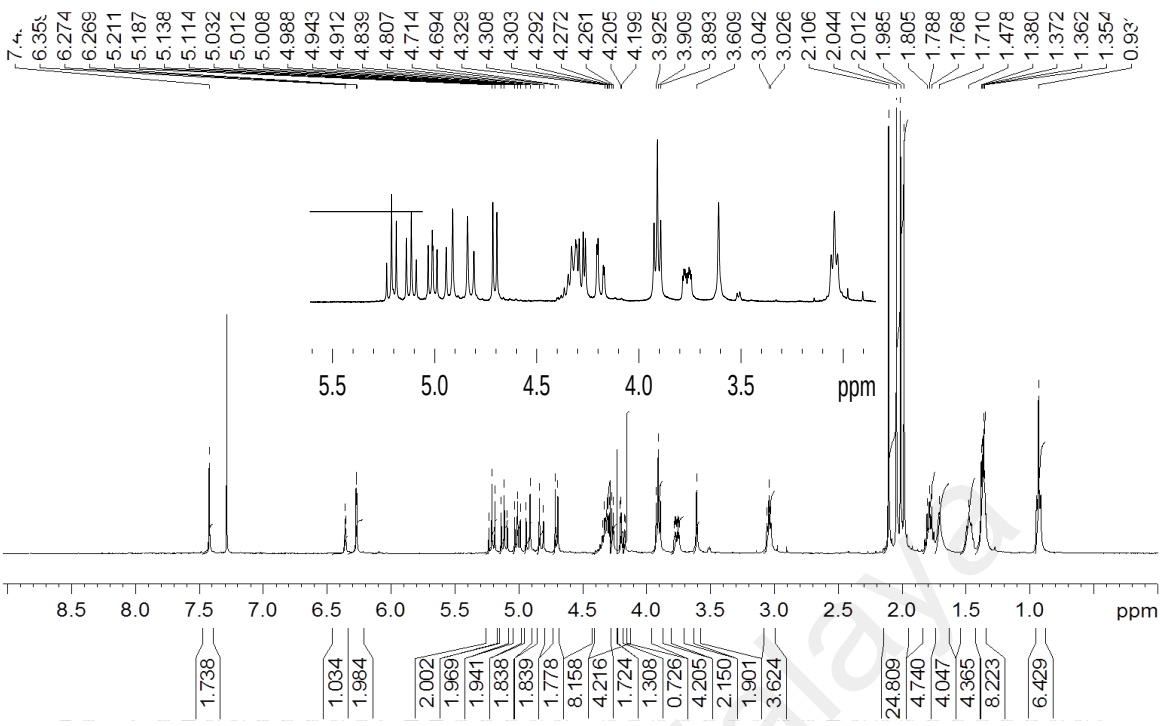


Figure 7-3: The evolution of ^{1}H NMR spectra (400 MHz, $CDCl_3$, 298 K) for acetylated surfactant precursor 12.

The identification of the structure elements for the final X-shaped surfactants was complicated due to striking ambiguities observed in both ^{1}H and ^{13}C NMR spectra, such as extensive regional spectral broadening, leading to insufficient resolution for the identification of the carbohydrate in the ^{1}H NMR, seen Figure 7-4, as well as the vast number of ^{13}C NMR signals in Figure 7-5. These features reflect a set on diastereomers, due to the presence of two 'racemic' centres in the surfactant product, originating from missing stereoselectivity for the epoxidation of allyl glucoside, which was already highlighted for Y-shaped surfactants in chapter 3. In order to enable assignments and distinguish the peaks, a heteronuclear (^{1}H, ^{13}C) multidimensional correlation NMR technique was applied, shown in Figures 7-6 – 7-9.

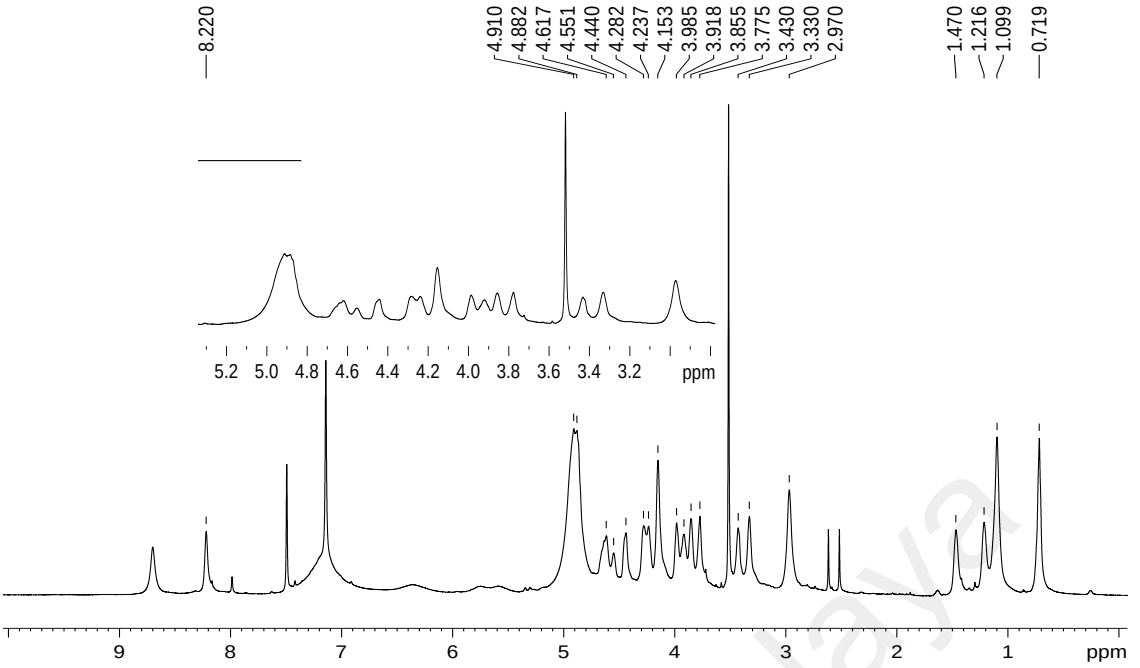


Figure 7-4: The evolution of ^{1}H NMR spectra (600 MHz, $CDCl_3$, 298 K) for de-acetylated surfactant 9.

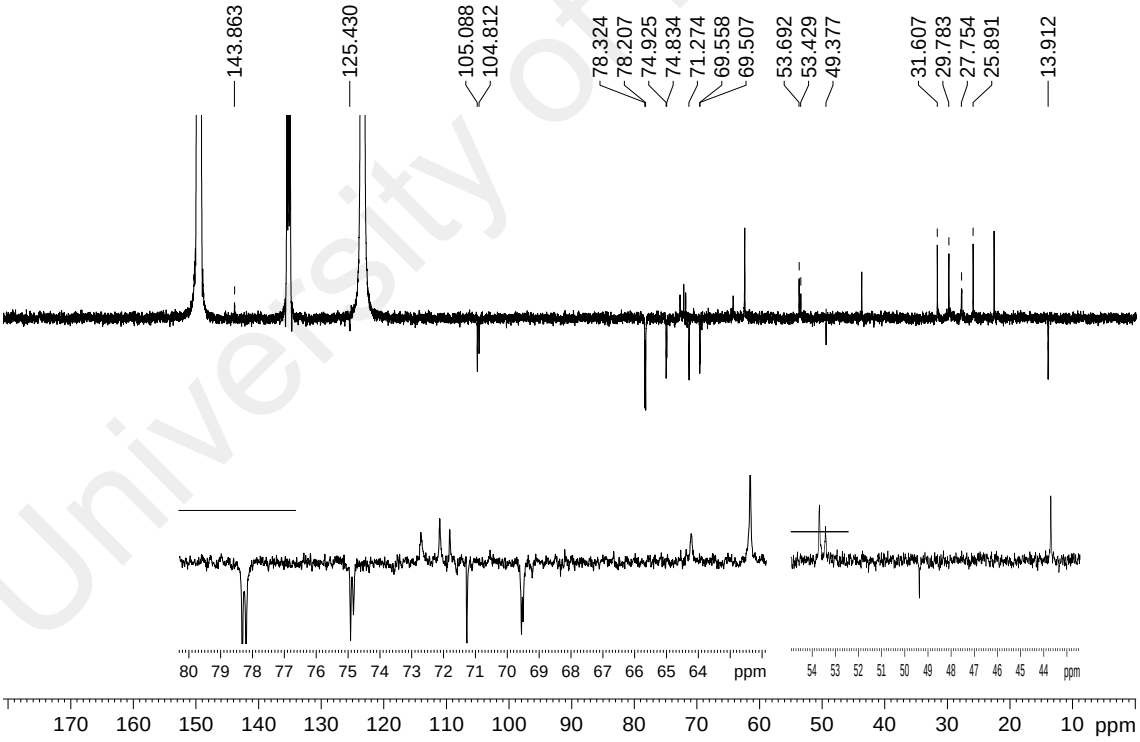


Figure 7-5: The evolution of ^{13}C NMR spectra (400 MHz, pyridine d5, 298 K) for de-acetylated surfactant 9.

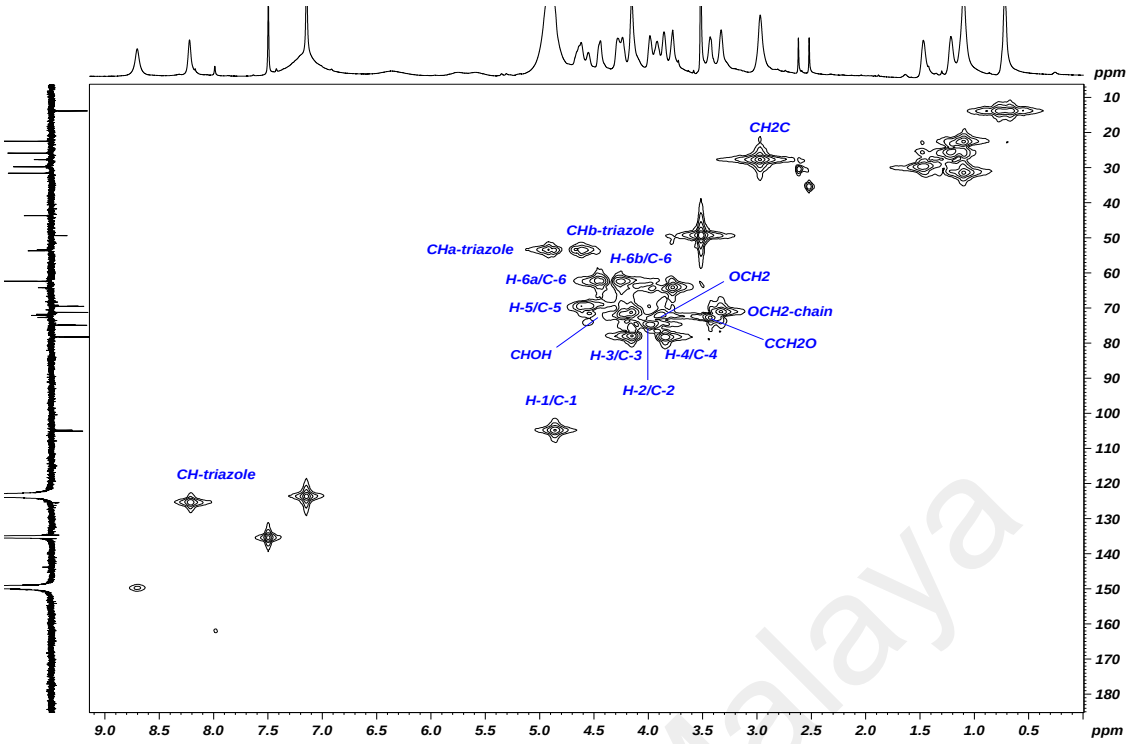


Figure 7-6: The 2-D NMR correlation spectra (^{1}H-^{13}C-HSQC, 400 MHz, pyridine d5, 300 K) are displayed for de-acetylated surfactant **9** with complete peak assignments.

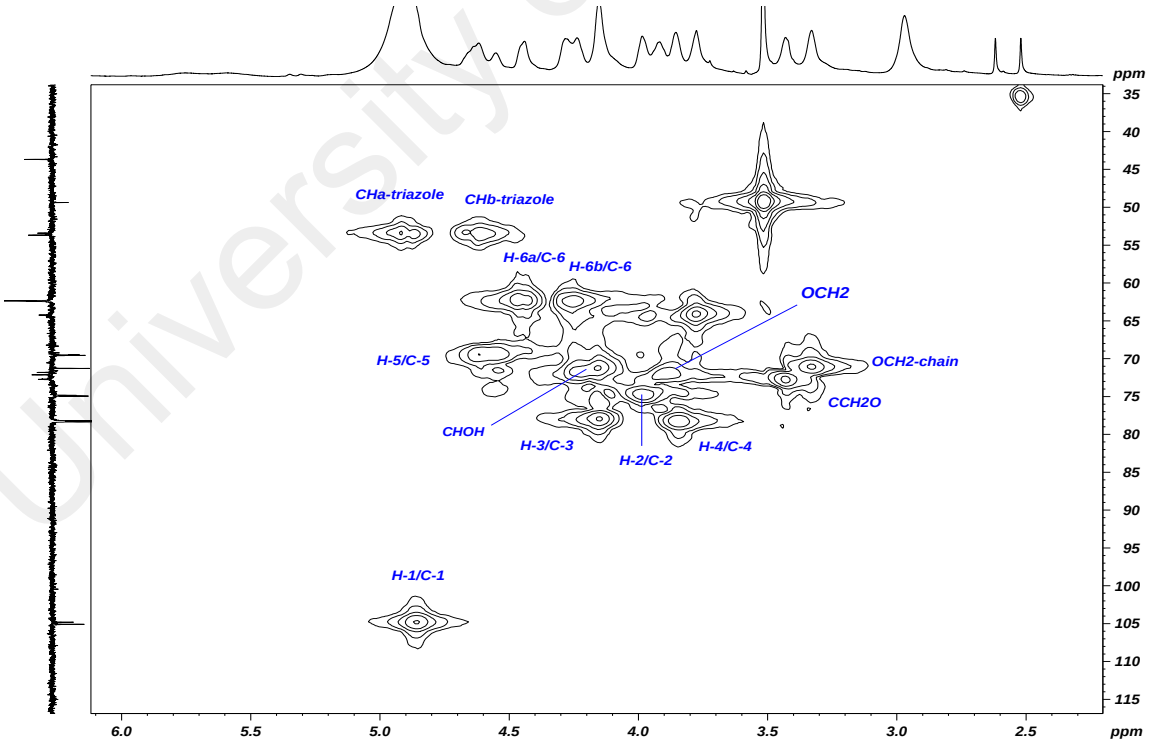


Figure 7-7: Selected regions of interest 2-D NMR correlation spectra (^{1}H-^{13}C-HSQC, 400 MHz, pyridine d5, 300 K) are displayed for de-acetylated surfactant **9** with complete peak assignments.

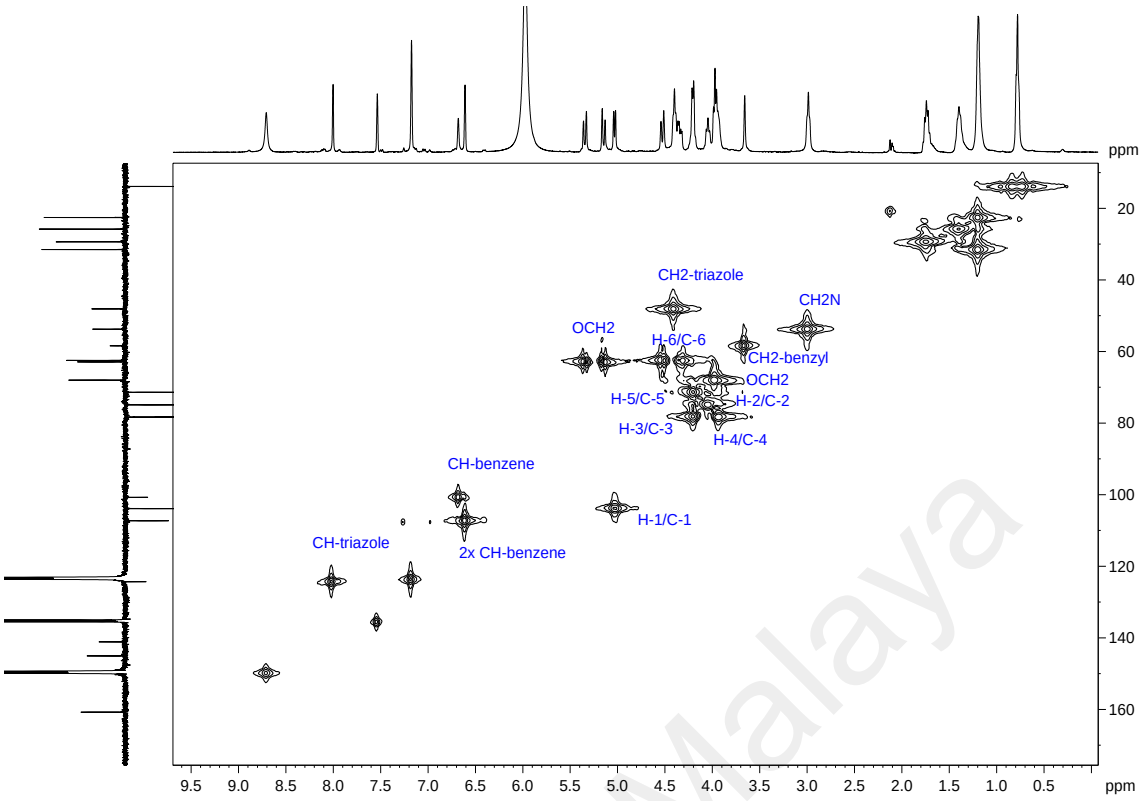


Figure 7-8: The 2-D NMR correlation spectra (^{1}H-^{13}C-HSQC, 400 MHz, pyridine d5, 298 K) are displayed for de-acetylated surfactant **13** with complete peak assignments.

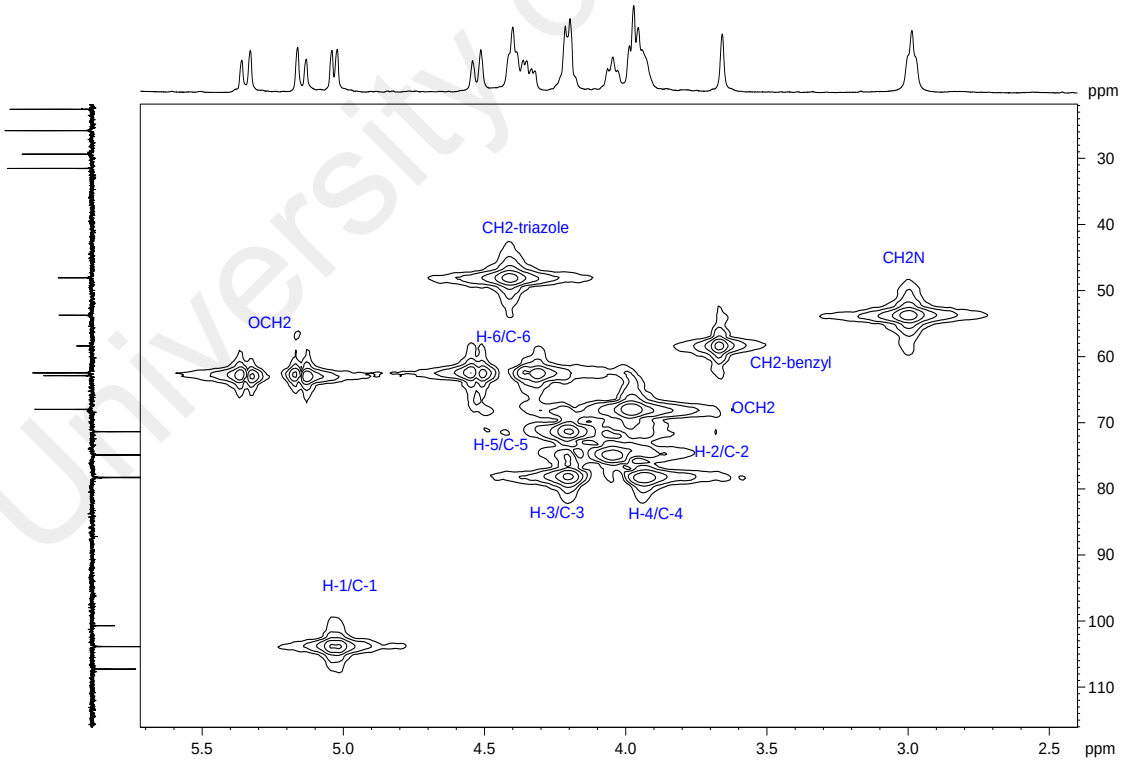


Figure 7-9: Selected regions of interest 2-D NMR correlation spectra (^{1}H-^{13}C-HSQC, 400 MHz, pyridine d5, 298 K) are displayed for de-acetylated surfactant **13** with complete peak assignments.

7.4 Phase behaviour

7.4.1 Liquid crystalline behaviour

Water penetration scans under an optical polarizing microscope (Milkereit *et al*., 2005; von Minden *et al*., 2000) were performed to provide information about the phase behaviour. All compounds were very viscous syrups, which did not exhibit birefringence, thus suggesting an isotropic phase for the pure surfactants. Upon contact with water, on the other hand, fine needles emerged, as shown in Figure 7-10. The observation of the formation of the same needle-type texture upon longer exposure to a humid environment illustrates a significant hygroscopic behaviour for the anhydrous surfactants. When sample **9** was contacted with 1-undecanol overnight, a texture emerged that most likely reflects an inverted hexagonal phase, see Figure 7-10 A (c). The penetration profile of **11** at 25 °C was showing in Figure 7-10 B. As water penetrated, the sample does not show any solubility in water and immediately the big sizes of needle crystal started to form (Figure 7-10 B (a, b)). Typically, only inverted micellar solution was observed in 1-undecanol penetrated system (Figure 7-10 B(c)) and this reflects the dominant tail volume of the hydrophobic domain, which leads to a curving of surfactant assemblies towards the hydrophilic domain. When dried, the surfactant **13** could show lamellar phase, in weak observation of the birefringent region and there was no evidence of observation any other phase (Figure 7-10 C (a)). During the contact with water, the sample was forming L1-normal micelle solution as showing in Figure 7-10 C (b), whereas reversing hexagonal phase was observed after prolonged time of penetration with 1-undecanol ((Figure 7-10 C (c)).

7.4.2 Air-water interface behaviour and emulsion stability

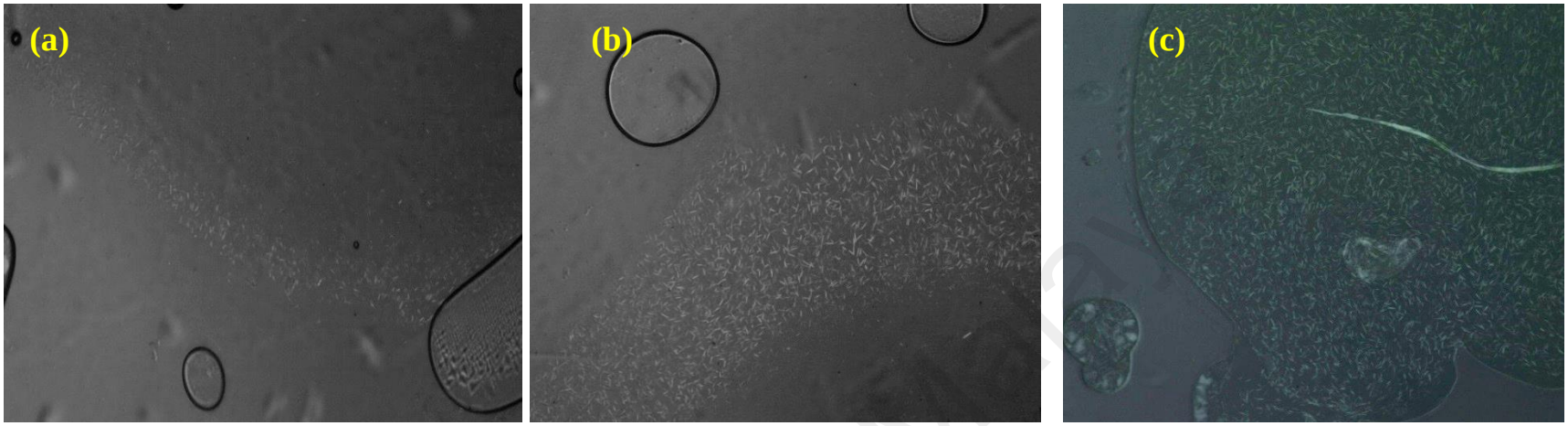
Since the critical micelle concentration (CMC) is considered a key feature for a surfactant, the surface tension for aqueous solutions of all three surfactants was

investigated systematically over a wide range of concentration. The determined values of the CMC at 25 °C are presented in table 7-1. The surface tension above the CMC was found to be in the range of 32–36 mNm^{-1}. This is considerably lower than the corresponding values for Y-shaped surfactants, see chapter 3, and can be explained with an increased coverage of the air-water interphase by the hydrophobic domain, which is split into two chains. The presence of a benzene ring decreases the CMC by about a decade. This trend is in line with analogue observations for Y-shape surfactants, and originates out of the hydrophobic effect of the aromatic linker.

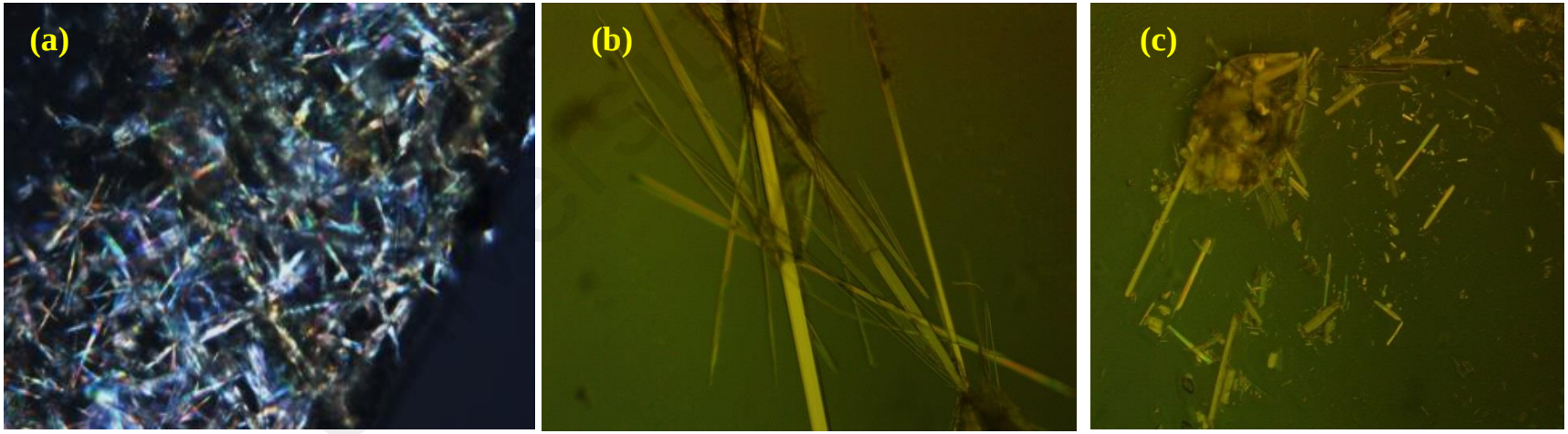
With exception of surfactant **11,** all the surfactants exhibited good oil-in-water emulsion stabilities, requiring five days for separation of an emulsion in the absence of a polymeric stabilizer, as showing in Figure 7-11. The poor performance of surfactant **11** as emulsifier can be related to the amine core of the hydrophobic domain, which already affected the emulsion stabilities for Y-shaped surfactants, see chapter 3.

Table 7-1: CMC and surface tension at CMC.

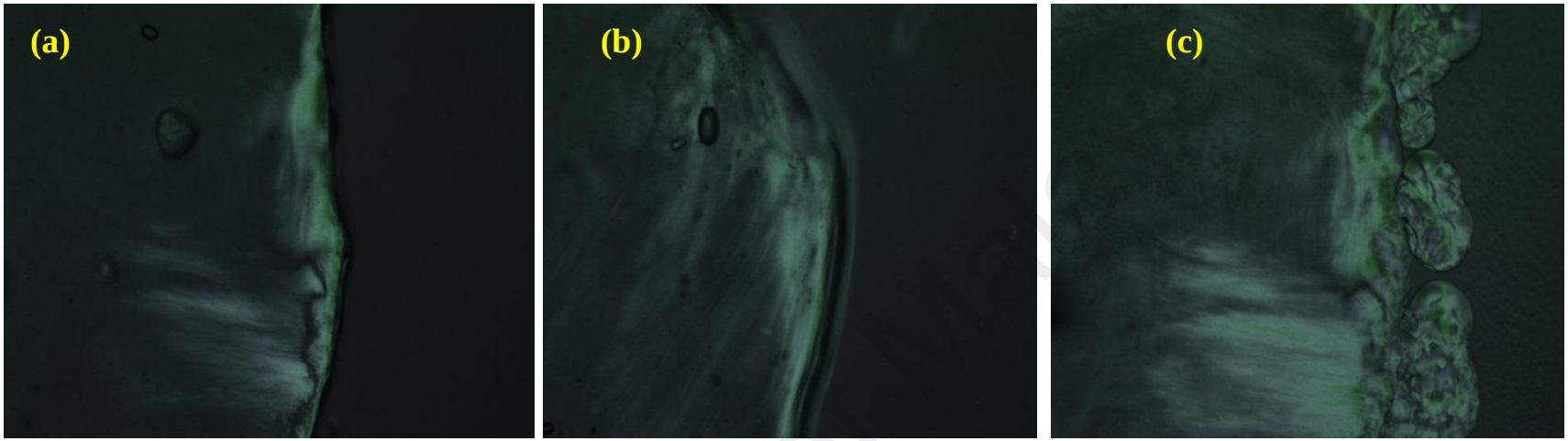
Compound	cmc (mM)	γ_{cmc} (mN/m)
9	**4.6**	**36.4**
11	**4.3**	**31.7**
13	**0.12**	**31.6**



A: OPM texture for surfactant **9** (a) texture of the pure sample (b) Water penetration scans (c) 1-undecanol penetrate at room temperature.



B: OPM texture for surfactant **11**, (a) texture of the pure sample (b) Water penetration scans (c) 1-undecanol penetrate at room temperature.



C: OPM texture for surfactant **13**, (a) texture of the pure sample (b) Water penetration scans (c) 1-undecanol penetrate at room temperature.

Figure 7-10: Microscopy images of lyotropic liquid crystalline phases viewed through crossed polarizers for X-shape sugar-based surfactant.

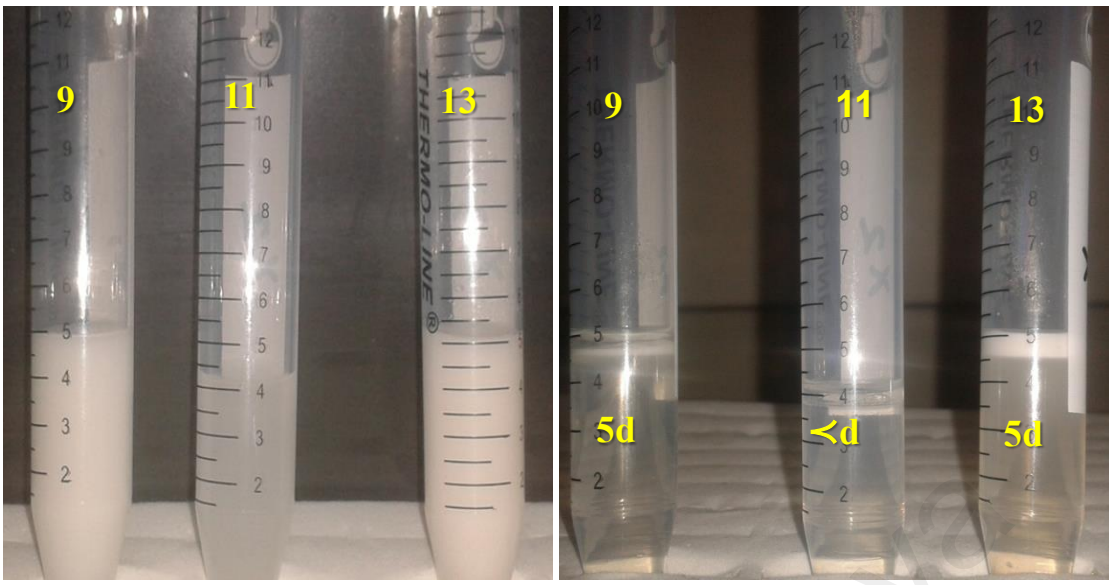


Figure 7-11: Emulsion stability (O/W).

7.5 Conclusion

A series of X-shaped surfactants with carbohydrate hydrophilic doamins have been prepared by applying "click" coupling of functionalized precursors, leading to high reaction yields. Two of the compounds exhibited crystallization in needle shape upon water contact, including environmental humidity, while another appeared to form a micellar solution instead. The structural design of the surfactants led to an increase of the packing parameter, compared to the previously discussed Y-shape surfactants (chapter 3), thus stabilizing a lamellar phase for compounds involving an aromatic linker. The minimum surface tension of surfactant solutions decreases with respect to Y-shape analogues, reflecting a more efficient surface coverage of the hydrophobic domain. The previously reported CMC lowering effect of a benzene ring for Y-shaped surfactants was confirmed for X-shaped analogues.

Chapter 8 : Conclusion and recommendation for future work

8.1 Conclusions

Click chemistry-based coupling enables an easy access to synthetic glycolipids. Variation of linkers in combination with either one or two linking triazoles enables a variety of different surfactant shapes, referring to molecular design based on the arrangement of hydrophilic and hydrophobic domains. The surfactants belong to the previously defined class of alkyl triazole glycosides (ATGs) (Sani *et al*., 2012), which in general exhibit similar surfactant behaviour to APGs (Nilsson *et al*., 1998), but provide a potential more economic approach due to reduced reaction temperature requirements and improved surfactant purity (Baier *et al*., 2012; Xu *et al*., 2009).

The primary focus of this research was the development of new sugar-based surfactants that retain the favourable attributes found in APGs, while varying their physical properties, e.g. enhancing their water solubility, and attempting to improve the synthetic access in terms of economic viability. In the attempt of the latter, the previously reported coupling strategy for ATGs (Sani *et al*., 2012) was reverted, to utilize a lipid based alkyne and an azide-containing glycoside. The latter is easily accessible based on the epoxidation of allyl glucoside followed by a ring-opening azidation. The major advantage of this approach is a potentially more direct access to the functionalized lipid component of the surfactant.

Three distinctly different surfactant classes, *i.e*. Y-, reverse Y-, and X-shape surfactants, each of them comprising of a series of structurally different compounds, were synthesized and characterized. This enabled the investigation of the effect of the generic shape of a surfactant on its surface and emulsion properties. The presence of the additional hydroxyl groups in the spacer between the sugar ring and triazole linkage enhances the water solubility of surfactants, thus affecting the phase behaviour.

Glucose based ATGs of both Y- and X-shape exhibit good interaction with water but do not interact effectively with lipid-based oil, like methyl laurate. Most Y-shape surfactants exhibited exclusively micellar solutions (L_1-phase) but no liquid crystal phases. This reflects the good water solubility based on high curvature of the surfactant. X-shape surfactants, on the other hand, formed needle shaped crystals in contact with water. Although the X-shape surfactant also formed the micellar L_1 phase, the phase behaviour in contact with water showed more diversity than the Y-shape analogues, involving lamellar phases. In contact with oil the reverse hexagonal H_2 phase was observed. Low Krafft points, indicate both X- and Y-shape surfactants as potentially good emulsifiers Indeed, most of the investigated surfactants, including the reverse Y-shaped compounds exhibited good emulsion stabilities for an oil-in-water system. Exceptions, however, were compounds containing amine linkages.

8.2 Recommendation

The present work leads to the following suggestions for future work:-

1-Study the effect of salinity on the micro emulsion system. This study may be expanded to compare the effects of different salts, such as NaCl, LiCl, NH_4Cl, KI, $CaCl_2$, $MgCl_2$ and $ALCl_3$, and varying ionic strength.

2- Compare the emulsion behaviour of the surfactants for different types of oil, like vegetable and petrochemical oil with and without aromatic components.

3- Vary the carbohydrate source and study the effect on the emulsion and surface behaviour of the surfactant.

4- The current investigation indicates high solubility and low Krafft points for Y-and X-shaped sugar-based surfactants. Since the investigation is limited to C_{12} hydrophobic

chains, it will be interesting to confirm this phenomenon for surfactants with different chain lengths.

References

Abrams, S. R., & Shaw, A. C. (1987). On the Mechanism of 1,3-Prototropic Shifts in Acetylene-Allene Isomerizations. *Journal of Organic Chemistry*, *52*(7), 1835–1839.

Aizpurua, J. M., Azcune, I., Fratila, R. M., Balentova, E., Sagartzazu-Aizpurua, M., & Miranda, J. I. (2010). "Click" Synthesis Of Nonsymmetrical Bis(1,2,3-Triazoles). *Organic Letters*, *12*(7), 1584–7.

Akeroyd, N., & Klumperman, B. (2011). The Combination Of Living Radical Polymerization And Click Chemistry For The Synthesis Of Advanced Macromolecular Architectures. *European Polymer Journal*, *47*(6), 1207–1231.

Alargova, R. G., Vakarelsky, I. Y., Paunov, V. N., Stoyanov, S. D., Kralchevsky, P. A., Mehreteab, A., & Broze, G. (2003). Properties of Amphoteric Surfactants Studied by -Potential Measurements with Latex Particles. *Langmuir*, *7463*(15), 1996–2003.

Albrecht, M. (2008). C4-Bound Imidazolylidenes: From Curiosities To High-Impact Carbene Ligands. *Chemical Communications (Cambridge, England)*, *31*, 3601–10.

Alkhatib, M. H. (2006). *PH-Degradable 1, 3-Dioxolane Surfactants: Synthesis And Application In Mixed Surfactant Systems*. University of Alabama.

Allen, D. K., & Tao, B. Y. (1999). Carbohydrate-Alkyl Ester Derivatives as Biosurfactants. *Journal of Surfactants and Detergents*, *2*(3), 383–390.

Aniansson, E. A. G., & Wali, S. N. (1974). On the Kinetics of Step-Wise Micelle Association. *The Journal of Physical Chemistry. B*, *78*(10), 1024–1030.

Appukkuttan, P., Dehaen, W., Fokin, V. V, & Eycken, E. Van Der. (2004). A Microwave-Assisted Click Chemistry Synthesis of 1 , 4-Disubstituted Three-Component Reaction. *Organic Letters*, *6*(23), 4223–4225.

Auvray, X., Petipas, C., & Anthore, R. (1995). X-ray Diffraction Study of the Ordered Lyotropic Phases Formed by Sugar-Based Surfactants. *Langmuir*, *11*, 433–439.

Aveyard, R., Binks, B. P., Chen, J., Esquena, J., Fletcher, P. D. I., Buscall, R., & Davies, S. (1998). Surface and Colloid Chemistry of Systems Containing Pure Sugar Surfactant. *Langmuir*, *7463*(9), 4699–4709.

Avti, P. K., Maysinger, D., & Kakkar, A. (2013). Alkyne-Azide "Click" Chemistry In Designing Nanocarriers For Applications In Biology. *Molecules (Basel, Switzerland)*, *18*(8), 9531–49.

Baba, T., Minamikawa, H., Hato, M., Motoki, a, Hirano, M., Zhou, D., & Kawasaki, K. (1999). Synthetic Phytanyl-Chained Glycolipid Vesicle Membrane As A Novel Matrix For Functional Reconstitution Of Cyanobacterial Photosystem II Complex. *Biochemical and Biophysical Research Communications*, *265*(3), 734–8.

Baier, G., Siebert, J. M., Landfester, K., & Musyanovych, A. (2012). Surface Click Reactions on Polymeric Nanocapsules for Versatile Functionalization. *Macromolecules*, *45*(8), 3419–3427.

Bajpai, D., & Tyagi, V. K. (2006). Fatty Imidazolines : Chemistry , Synthesis , Properties and Their Industrial Applications. *Journal of Oleo Science*, *55*(7), 319–329.

Balazs, D. a, & Godbey, W. (2011). Liposomes For Use In Gene Delivery. *Journal of Drug Delivery*, *2011*, 326497.

Balzer, D. (1993). Cloud Point Phenomena In The Phase Behavior Of Alkyl Polyglucosides In Water. *Langmuir*, *9*(11), 3375–3384.

Banerjee, S. (2012). ON MICELLES, VESICLES AND ARTIFICIAL CELLS-The Magic Of Directed Self Assembly (Can physics be the secret to artificial life) | Physics de Pristine. Retrieved February 19, 2015, from http://physics-depristine.blogspot.com/2012/01/on-micelles-vesicles-and-artificial.html

Barnett, J. E. G., & Ralph, A. (1971). The Preparation Of 2,3-Epoxypropyl B-D-Glucopyranoside. *Carbohydrate Research*, *17*(1), 231–233.

Bazito, R. C., & El Seoud, O. a. (2001). Sugar-Based Anionic Surfactants: Synthesis And Micelle Formation Of Sodium Methyl 2-Acylamido-2-Deoxy-6-O-Sulfo-D-Glucopyranosides. *Carbohydrate Research*, *332*(1), 95–102.

Beach, E., & Wendy, H. (2011). Novel, Sugar-Based Surfactants More Stable And Sustainable. Environmental Health News. Retrieved April 21, 2014 from http://www.environmentalhealthnews.org/ehs/newscience/surfactants-from-sugars

Boyd, B. J., Drummond, C. J., Krodkiewska, I., & Grieser, F. (2000). How Chain Length , Headgroup Polymerization , and Anomeric Configuration Govern the Thermotropic and Lyotropic Liquid Crystalline Phase Behavior and the Air - Water Interfacial Adsorption of Glucose-Based Surfactants. *Langmuir*, (27), 7359–7367.

Bräse, S., Gil, C., Knepper, K., & Zimmermann, V. (2005). Organic Azides: An Exploding Diversity Of A Unique Class Of Compounds. *Angewandte Chemie (International Ed. in English)*, *44*(33), 5188–240.

Brummond, K. M., Davis, M. M., & Huang, C. (2009). Rh(I)-Catalyzed Cyclocarbonylation Of Allenol Esters To Prepare Acetoxy 4-Alkylidenecyclopent-3-En-2-Ones. *Journal of Organic Chemistry*, *74*(21), 8314–20.

Brummond, K. M., Lu, J., & Virginia, W. (1999). A Short Synthesis of the Potent Antitumor Agent-Hydroxymethylacylfulvene Using an Allenic Pauson-Khand Type Cycloaddition. *Journal of the American Chemical Society*, *121*(12), 5087–5088.

Cai, H., Jiang, G., Shen, Z., & Fan, X. (2012a). E ff ects of Dendron Generation and Salt Concentration on Phase Structures of Dendritic − Linear Block Copolymers with a Semirigid Dendron Containing PEG Tails. *Macromolecules*, *45*, 6176–6184.

Cai, H., Jiang, G., Shen, Z., & Fan, X. (2012b). Effects of Dendron Generation and Salt Concentration on Phase Structures of Dendritic−Linear Block Copolymers with a Semirigid Dendron Containing PEG Tails. *Macromolecules*, *45*, 6176–6184.

Carney, J. M., Donoghue, P. J., Wuest, W. M., Wiest, O., & Helquist, P. (2008). Intramolecular Hydroamination Of Aminoalkynes With Silver-Phenanthroline Catalysts. *Organic Letters*, *10*(17), 3903–6. Carpenter, C. a., Kenar, J. a., & Price, N. P. J. (2010). Preparation of saturated and unsaturated fatty acid hydrazides and long chain C-glycoside ketohydrazones. *Green Chemistry*, *12*(11), 2012.

Castro, M. J. L., Cirelli, A. F., & Kovensky, J. (2006). Synthesis And Interfacial Properties Of Sugar-Based Surfactants Composed Of Homo-And Heterodimers. *Journal of Surfactants and Detergents*, *9*(3), 279–286.

Cenini, S., Gallo, E., Caselli, A., Ragaini, F., Fantauzzi, S., & Piangiolino, C. (2006). Coordination Chemistry Of Organic Azides And Amination Reactions Catalyzed By Transition Metal Complexes. *Coordination Chemistry Reviews*, *250*(11-12), 1234–1253.

Che, Y., Datar, A., Balakrishnan, K., & Zang, L. (2007). Ultralong Nanobelts Self-Assembled From An Asymmetric Perylene Tetracarboxylic Diimide. *Journal of the American Chemical Society*, *129*(23), 7234–5.

Cheng, Y., Ho, D. M., Gottlieb, C. R., Kahne, D., & Bruck, M. A. (1992). Facial Amphiphiles. *Journal of the American Chemical Society*, *114*(18), 7319–7320.

Columbia, B. (1999). *Canadian Water Quality Guidelines for the Protection of Aquatic Life* (pp. 1–4).

Dalgleish, D. G. (2006). Food Emulsions—Their Structures And Structure-Forming Properties. *Food Hydrocolloids*, *20*(4), 415–422. Dedola, S., Nepogodiev, S. a, &

Field, R. a. (2007a). Recent Applications Of The Cu(I)-Catalysed Huisgen Azide-Alkyne 1,3-Dipolar Cycloaddition Reaction In Carbohydrate Chemistry. *Organic & Biomolecular Chemistry*, *5*(7), 1006–17.

Dedola, S., Nepogodiev, S. a, & Field, R. a. (2007b). Recent Applications Of The Cu(I)-Catalysed Huisgen Azide-Alkyne 1,3-Dipolar Cycloaddition Reaction In Carbohydrate Chemistry. *Organic & Biomolecular Chemistry*, *5*(7), 1006–17.

Desai, J. D., & Banat, I. M. (1997). Microbial Production Of Surfactants And Their Commercial Potential . Microbial Production Of Surfactants And Their Commercial Potential. *Microbiology Molecular Biology Reviews*, *61*(1), 47–64.

Doak, B. C., Scanlon, M. J., & Simpson, J. S. (2011). Synthesis of Unsymmetrical Using Monosilylbutadiynes. *Organic Letters*, *13*(3), 537–539.

Du, Y., Linhardt, R. J., & Vlahov, I. R. (1998). Recent Advances In Stereoselective C-Glycoside Synthesis. *Tetrahedron*, *54*(462), 9913–9959.

Emmanuel, E., Hanna, K., Bazin, C., Keck, G., Clement, B., & Perrodin, Y. (2005). Fate Of Glutaraldehyde In Hospital Wastewater And Combined Effects Of Glutaraldehyde And Surfactants On Aquatic Organisms. *Environment International*, *31*, 399–406.

Engberts, J. B., & Kevelam, J. (1996). Formation And Stability Of Micelles And Vesicles. *Current Opinion in Colloid & Interface Science*, *1*(6), 779–789.

Eremin Vadim V. (2009). phase behaveor amphiphilic. Retrieved April 21, 2014 from http://eng.thesaurus.rusnano.com/wiki/article513

FernLey, G. W. (1978). Zwitterionic Surfactants: Structure And Performance. *Journal of the American Oil Chemists' Society*, *55*(1), 98–103.

Fiandanese, V., Bottalico, D., Marchese, G., Punzi, A., & Capuzzolo, F. (2009). An Easy Access To Unsymmetrically Substituted 4,4′-bi-1,2,3-triazoles. *Tetrahedron*, *65*(51), 10573–10580.

Fisher, K. (2000). *Formation of Self-Assembling Structures : Micelles , Bilayers , and Vesicles*. Retrieved April 21, 2014 from http://willson.cm.utexas.edu/Research/Sub_Files/Surface_Phenomena/Spring%202000/Self_Assembling_Structures.pdf

Foley, P. M., Phimphachanh, A., Beach, E. S., Zimmerman, J. B., & Anastas, P. T. (2011). Linear And Cyclic C-Glycosides As Surfactants. *Green Chemistry*, *13*(2), 321.

Foley, P. M. (2012). *Derivation And Synthesis Of Renewable Surfactants : Past , Present , And Into The Future*. Yale University.

Fukada, K. (2000). *Sugar-based Surfactants*. (C. C. Ruiz, Ed.) (143rd ed., Vol. 49, pp. 1035–1040,1293). Boca Raton, London, New York: Taylor & Francis Group.

Garofalakis, G., Murray, B., & Sarney, D. (2000). Surface Activity and Critical Aggregation Concentration of Pure Sugar Esters with Different Sugar Headgroups. *Journal of Colloid and Interface Science*, *229*(2), 391–398.

Gawish, S. M., Hazzaa, A. A. B., Zourab, S., & El-Din Gebril, B. (1981). Synthesis And Properties Of Amphoteric Surfactants. *Journal of the American Oil Chemists' Society*, *58*(6), 757–760.

Gilmore, K., & Alabugin, I. V. (2011). Cyclizations Of Alkynes: Revisiting Baldwin's Rules For Ring Closure. *Chemical Reviews*, *111*(11), 6513–56.

Goldsmith, W. T., McKinney, W., Jackson, M., Law, B., Bledsoe, T., Siegel, P., … Frazer, D. (2011). A Computer-Controlled Whole-Body Inhalation Exposure System For The Oil Dispersant COREXIT EC9500A. *Journal of Toxicology and Environmental Health. Part A*, *74*(21), 1368–80.

Gonzalez, D. P. O. (2009). *Effect of Surfactants on Asphaltene Interfacial Films and Stability of Water-in-Oil Emulsions*. University of Calgart.

Goodby, J. W., Görtz, V., Cowling, S. J., Mackenzie, G., Martin, P., Plusquellec, D., … Fitremann, J. (2007). Thermotropic Liquid Crystalline Glycolipids. *Chemical Society Reviews*, *36*(12), 1971–2032.

Goyal, P. S., & Aswal, V. K. (2001). Micellar Structure And Inter-Micelle Interactions In Micellar Solutions : Results Of Small Angle Neutron Scattering Studies. *Current Science*, *80*(8), 972–979.

Greener Industry. Retrieved February 19, 2015, from http://greener-industry.org.uk /pages/protecting/protecting_3_pop_up.htm

Hamme, J. D. Van, Singh, A., & Ward, O. P. (2003). Recent Advances in Petroleum Microbiology. *Microbiology Molecular Biology Reviewe*, *67*(4), 503–549.

Hato, M., Minamikawa, H., Tamada, K., Baba, T., & Tanabe, Y. (1999). Self-Assembly Of Synthetic Glycolipid/Water Systems. *Advances in Colloid and Interface Science*, *80*(3), 233–70.

Hato, M., Minamikawa, H., Tamada, K., Baba, T., & Tanabe, Y. (1999). Self-Assembly Of Synthetic Glycolipid/Water Systems. *Advances in Colloid and Interface Science*, *80*(3), 233–70.

Hayashi, S., & Ikeda, S. (1980). Micelle Size and Shape of Sodium Dodecyl Sulfate in Concentrated NaCl Solutions. *Journal of the American Chemical Society*, *84*(7), 744–751.

Heckenroth, M., Kluser, E., Neels, A., & Albrecht, M. (2008). Palladation Of Diimidazolium Salts At The C4 Position: Access To Remarkably Electron-Rich Palladium(II) Centers. *Journal of the American Chemical Society*, *130*(41), 13534–13535.

Hein, J. E., & Fokin, V. V. (2010a). Copper-Catalyzed Azide-Alkyne Cycloaddition (Cuaac) And Beyond: New Reactivity Of Copper(I) Acetylides. *Chemical Society Reviews*, *39*(4), 1302–15.

Hersant, Y., Abou-Jneid, R., Canac, Y., Lubineau, A., Philippe, M., Semeria, D., Scherrmann, M.-C. (2004). One-Step Synthesis Of Beta-C-Glycolipid Derivatives From Unprotected Sugars. *Carbohydrate Research*, *339*(3), 741–5.

Himo, F., Lovell, T., Hilgraf, R., Rostovtsev, V. V, Noodleman, L., Sharpless, K. B., & Fokin, V. V. (2005). Copper(I)-Catalyzed Synthesis Of Azoles. DFT Study Predicts Unprecedented Reactivity And Intermediates. *Journal of the American Chemical Society*, *127*(1), 210–6.

Hoffmann, B., & Platz, G. (2001). Phase And Aggregation Behaviour Of Alkylglycosides. *Current Opinion in Colloid & Interface Science*, *6*(2), 171–177.

Holmberg, K. (2001). Natural Surfactants. *Current Opinion in Colloid & Interface Science*, *6*(2), 148–159.

Holmberg, K., Jonsson, B., Kronberg, B., & Lindman, B. (2002). *Surfactants and polymers in aqueous solution* (pp. 0–471). England: John Wiley & Sons, Ltd.

Huisgen, R., Knorr, R., Möbius, L., & Szeimies, G. (1965). 1.3-Dipolare Cycloadditionen, XXIII. Einige Beobachtungen zur Addition organischer Azide an CC-Dreifachbindungen. *Chemische Berichte*, *98*(12), 4014–4021.

How to disperse and stabilize pigments. Retrieved February 19, 2015, from http://www.inkline.gr/inkjet/newtech/tech/dispersion/

Imura, T., Hikosaka, Y., Worakitkanchanakul, W., Sakai, H., Abe, M., Konishi, M., … Kitamoto, D. (2007). Aqueous-Phase Behavior Of Natural Glycolipid Biosurfactant Mannosylerythritol Lipid A: Sponge, Cubic, And Lamellar Phases. *Langmuir : The ACS Journal of Surfaces and Colloids*, *23*(4), 1659–63.

Janshekar, H., Inoguchi, Elvira O. Camara Greiner, Y., & Ma, X. (2013). Surfactants IHS Chemical. Retrieved April 21, 2014 from http://www.ihs.com/products/chemical/ planning/scup/surfactants.aspx

Jensen, G. V., Lund, R., Gummel, J., Monkenbusch, M., Narayanan, T., & Pedersen, J. S. (2013). Direct Observation Of The Formation Of Surfactant Micelles Under Nonisothermal Conditions By Synchrotron SAXS. *Journal of the American Chemical Society*, *135*(19), 7214–22.

Jiao, J. (2002). *Physical Stabilty Of Water-In-Oil-In-Water Multiple Emulsions*. University o f Connecticut.

Judith Taylor. (2010). Market Intelligence: Surfactants Employed To Break Up BP Oil Spill In US Gulf. Retrieved April 21, 2014 from http://www.icis.com/Articles/2010/05/31/9363397/market-intelligence-surfactants-employed-to-break-up-bp-oil-spill-in-us.html

Kaasgaard, T., & Drummond, C. J. (2006). Ordered 2-D And 3-D Nanostructured Amphiphile Self-Assembly Materials Stable In Excess Solvent. *Physical Chemistry Chemical Physics : PCCP*, *8*(43), 4957–75.

Kang, E., Lee, B. M., Hwang, H. A., & Lim, J. C. (2011). A Novel Cationic Surfactant Having Two Quaternary Ammonium Ions. *Journal of Industrial and Engineering Chemistry*, *17*(5-6), 845–852.

Karthikeyan, T., & Sankararaman, S. (2009). Palladium Complexes With Abnormal N-Heterocyclic Carbene Ligands Derived From 1,2,3-Triazolium Ions And Their Application In Suzuki Coupling. *Tetrahedron Letters*, *50*(42), 5834–5837.

Kitagaki, S., Teramoto, S., & Mukai, C. (2007). Ring-Closing Reaction Of Allenic/Propargylic Anions Generated By Base Treatment Of Sulfonylallenes. *Organic Letters*, *9*(13), 2549–52.

Kitamoto, D., Isoda, H., & Nakahara, T. (2002). Functions And Potential Applications Of Glycolipid Biosurfactants--From Energy-Saving Materials To Gene Delivery Carriers. *Journal of Bioscience and Bioengineering*, *94*(3), 187–201.

Kjellin, U. R. M., Claesson, P. M., & Vulfson, E. N. (2001). Studies Of N -Dodecyllactobionamide , Maltose 6- O -Dodecanoate , And Octyl-B-Glucoside With Surface Tension , Surface Force , And Wetting Techniques. *Langmuir*, *17*(5), 1941–1949.

Kocherbitov, V., & Soderman, O. (2003). Phase Diagram And Physicochemical Properties Of The N-Octyl A-D-Glucoside/Water System. *Physical Chemistry Chemical Physics: PCCP*, *5*(23), 5262.

Kolb, H. C., Finn, M. G., & Sharpless, K. B. (2001). Click Chemistry: Diverse Chemical Function from a Few Good Reactions. *Angewandte Chemie (International Ed. in English)*, *40*(11), 2004–2021.

Kolb, H. C., & Sharpless, K. B. (2003). The Growing Impact Of Click Chemistry On Drug Discovery. *Drug Discovery Today*, *8*(24), 1128–37.

Kopeliovich, D. D. (2013). Surfactants. Retrieved July 20, 2014, from http://www.substech.com/dokuwiki/doku.php?id=surfactants

Korchowiec, B. M., Baba, T., Minamikawa, H., & Hato, M. (2001). Forces that Control pH-Dependent Aggregation of Nonionic Glycolipid Vesicles. *Langmuir*, *17*(6), 1853–1859.

Kwak, J. M., Moon, J. S., Choi, J. I., Murugan, R. N., & Park, W. K. (2013). Construction of a Library of Arylpiperazinyl 1,2,3-Triazole Derivatives as Ligands for Dopamine D3 / D4 Receptor. *Bulletin of the Korean Chemical Society*, *34*(11), 7–10.

Laha, S., & Luthy, R. G. (1991). Inhibition Of Phenanthrene Mineralization By Nonionic Surfactants In Soil-Water Systems. *Environmental Science & Technology*, *25*(11), 1920–1930.

Lallana, E., Riguera, R., & Fernandez-Megia, E. (2011). Reliable And Efficient Procedures For The Conjugation Of Biomolecules Through Huisgen Azide-Alkyne Cycloadditions. *Angewandte Chemie (International Ed. in English)*, *50*(38), 8794–804.

Lalrempuia, R., McDaniel, N. D., Müller-Bunz, H., Bernhard, S., & Albrecht, M. (2010). Water Oxidation Catalyzed By Strong Carbene-Type Donor-Ligand Complexes Of Iridium. *Angewandte Chemie (International Ed. in English)*, *49*(50), 9765–8.

Lee, B.-Y., Park, S. R., Jeon, H. B., & Kim, K. S. (2006). A New Solvent System For Efficient Synthesis Of 1,2,3-Triazoles. *Tetrahedron Letters*, *47*(29), 5105–5109.

Legler, G., & Bause, E. (1973). Epoxyalkyl Oligo-(1→4)-B-D-Glucosides As Active-Site-Directed Inhibitors Of Cellulases. *Carbohydrate Research*, *28*(1), 45–52.

Lewis, W. G., Green, L. G., Grynszpan, F., Radić, Z., Carlier, P. R., Taylor, P., … Sharpless, K. B. (2002). Click Chemistry In Situ: Acetylcholinesterase As A Reaction Vessel For The Selective Assembly Of A Femtomolar Inhibitor From An

Array Of Building Blocks. *Angewandte Chemie (International Ed. in English)*, *41*(6), 1053–7.

Li, C., & Wong, W.-T. (2003). A Simple , Regioselective Synthesis Of Tetraazacyclododecane Lanthanide (III) Ions . The Resulting Complexes Show High Thermodynamic And Kinetic Stability In Aqueous Solution And Have Been Widely Used As Magnetic Resonance Pendant Chelating Moieties , e. *Journal of Organic Chemistry*, *68*(19), 2956–2959.

Li, M.-H. (2008). Effects Of Nonionic And Ionic Surfactants On Survival, Oxidative Stress, And Cholinesterase Activity Of Planarian. *Chemosphere*, *70*(10), 1796–803.

Lim, M.-Y., Chou, T.-C., Lin, X.-Z., Chen, C.-Y., Ling, T.-R., & Shiesh, S.-C. (2000). Application Of Nonionic Surfactants Combining Hydrophobic And Hydrophilic Cholelitholytic Solvents On Dissolution Of Gallstones. *Colloids and Surfaces B: Biointerfaces*, *17*(4), 265–274.

Liu, H., & Houghton, M. (2012). Fluorescent Conjecated Polymers With A Bodipy-Based Backbone And Uses Thereof. US 2012/0070382 A1.

Lu, S., Jin, T., Bao, M., & Yamamoto, Y. (2010). Palladium-Catalyzed Three-Component [3+2] Cycloaddition Of Propargyl Trifluoroacetates , Ethylidene Malononitriles , And Allyltributylstannane . *Organic Letters*, *12*(4), 864–866.

Lutz, J.-F., & Zarafshani, Z. (2008). Efficient Construction Of Therapeutics, Bioconjugates, Biomaterials And Bioactive Surfaces Using Azide-Alkyne "Click" Chemistry. *Advanced Drug Delivery Reviews*, *60*(9), 958–70.

Manetsch, R., Krasiński, A., Radić, Z., Raushel, J., Taylor, P., Sharpless, K. B., & Kolb, H. C. (2004). In Situ Click Chemistry: Enzyme Inhibitors Made To Their Own Specifications. *Journal of the American Chemical Society*, *126*(40), 12809–18.

Manning, S. J., Bogen, W., & Kelly, L. a. (2011). Synthesis, Characterization, And Photophysical Study Of Fluorescent N-Substituted Benzo''swallow Tail" Monoimides. *Journal of Organic Chemistry*, *76*(15), 6007–13.

Matoba, M., Kajimoto, T., Nishide, K., & Node, M. (2006). Preparation And Application Of Odorless 1,3-Propanedithiol Reagents. *Chemical & Pharmaceutical Bulletin*, *54*(1), 141–6.

Mattarella, M., & Siegel, J. S. (2012). Sym-(CH_2X)5-Corannulenes: Molecular Pentapods Displaying Functional Group And Bioconjugate Appendages. *Organic & Biomolecular Chemistry*, *10*(30), 5799–802.

Meldal, M., & Tornøe, C. W. (2008). Cu-Catalyzed Azide-Alkyne Cycloaddition. *Chemical Reviews*, *108*(8), 2952–3015.

Menger, F. M., & Littau, C. a. (1993). Gemini surfactants: a new class of self-assembling molecules. *Journal of the American Chemical Society*, *115*(22), 10083–10090.

Menger, F. M., & Whitesell, L. G. (1987). Binding Properties Of 1-Pyrenesulfonic Acid In Water. *Journal of Organic Chemistry*, *52*(17), 3793–3798.

Menger, F. M., & Yamasaki, Y. (1993). Hyperextended Amphiphiles. Bilayer Formation From Single-Tailed Compounds. *Journal of the American Chemical Society*, *115*(9), 3840–3841.

Milkereit, G., Brandenburg, K., Gerber, S., Koch, M. H. J., Morr, M., Andrä, J., Vill, V. (2005). Synthesis And Mesomorphic Properties Of Glycosyl Dialkyl- And Diacyl-Glycerols Bearing Saturated, Unsaturated And Methyl Branched Fatty Acid And Fatty Alcohol Chains. Part II. Mesomorphic Properties. *Chemistry and Physics of Lipids*, *135*(1), 15–26.

Moulik, S. P. (1996). Micelles: Self-Organized Surfactant Assemblies. *Current Science*, *71*(5), 368– 376.

Muthuprasanna, P., Surya, K., Sobhita, P., Satish, I. A., Chandiran, I. S., Arunachalam, G., & Shalini, S. (2009). Basics And Potential Applications Of Surfactants - A Review. *International Journal of PharmTech Research*, *1*(4), 1354–1365.

Myahkostupov, M., Prusakova, V., Oblinsky, D. G., Scholes, G. D., & Castellano, F. N. (2013). Structural Refinement of Ladder-Type Perylenediimide Dimers: A Classical Tale of Conformational Dynamics. *Journal of Organic Chemistry*, *78*, 8634–8644.

Nagarajan, R. (2002). Molecular Packing Parameter and Surfactant Self-Assembly : The Neglected Role of the Surfactant Tail. *Langmuir*, *18*, 31–38.

Nakamura, T., Terashima, T., Ogata, K., & Fukuzawa, S. (2011). Complexes As Efficient Catalysts For Click Reactions Of Azides With Alkynes. *Organic Letters*, *13*(4), 620–623.

National Commission on the BP Deepwater Horizon Oil Spill and Offshore Drilling, Dispersant use during the BP Deepwater Horizon oil spill. (2011). Retrieved February 17, 2015, from http://www.eoearth.org/view/article/160620/

Nguan, H. S., Heidelberg, T., Hashim, R., & Tiddy, G. J. T. (2010). Quantitative Analysis Of The Packing Of Alkyl Glycosides: A Comparison Of Linear And Branched Alkyl Chains. *Liquid Crystals*, *37*(9), 1205–1213.

Nilsson, F., Soderman, O., & Johansson, I. (1998). Four Different C 8 G 1 Alkylglucosides . Anomeric Effects And The Influence Of Straight Vs Branched Hydrocarbon Chains. *Journal of Colloid and Interface Science*, *139*(203), 131–139.

Nusselder, J. J. H., & Engberts, J. B. F. N. (1989). Surfactant Structure And Aggregate Morphology. The Urge For Aggregate Stability. *Journal of the American Chemical Society*, *111*(13), 5000–5002.

Ogawa, S., & Osanai, S. (2012). Glass Transition Behavior of Aqueous Solution of Sugar-Based Surfactants. In P. Wilson (Ed.), (p. 134). Japan: Publisher InTech.

Opawale, F. O. (1997). *The Formulation And Stability Of Water-In-Oil-In-Water Emulsions*. University of Connecticut.

Oskarsson, H., Frankenberg, M., Annerling, A., & Holmberg, K. (2007). Adsorption of Novel Alkylaminoamide Sugar Surfactants at Tailor-made Surfaces. *Journal of Surfactants and Detergents*, *10*(1), 41–52.

Oss, C., & Jan, V. (2008). The Water – Air Interface. In *The Properties of Water and their Role in Colloidal and Biological Systems* (Vol. 16, pp. 149–160). Interface Science and Technology. (book section)

Oyelere, A. K., Chen, P. C., Yao, L. P., & Boguslavsky, N. (2006). Heterogeneous Diazo-Transfer Reaction: A Facile Unmasking Of Azide Groups On Amine-Functionalized Insoluble Supports For Solid-Phase Synthesis. *Journal of Organic Chemistry*, *71*(26), 9791–6.

Penfold, J., & Thomas, R. K. (2010). Mixed Surfactants At The Air–Water Interface. *Annual Reports Section "C" (Physical Chemistry)*, *106*, 14.

Perkin, W. H., & Simonsen, J. L. (1907). The Action Of Tribromopropane On The Sodium Derivative Of Ethyl Malonate. *Journal of the Chemical Society, Transactions*, *91*, 840.

Pestman, J. M. (1998). *Carbohydrate-derived Surfactants Containing an N-acylated Amine Functionality: Fundumental Aspects and Practical Applications*. Rijksuniversiteit Groningen University.

Pianoforte, K. (2012). Surfactants Update - Coatings World. Retrieved April 21, 2014 from http://www.coatingsworld.com/issues/2012-03/view_features/surfactants-update-282696/

Pichot, R. (2010). *Stability and Characterisation of Emulsions in the presence of Colloidal Particles and Surfactants*. University of Birmingham.

Piispanen, P. S. (2002). *Synthesis and Characterization of Surfactants Based on Natural Products*. Kungl Tekniska Högskolan,Stockholm.

Pourceau, G., Meyer, A., Vasseur, J.-J., & Morvan, F. (2008). Combinatorial And Automated Synthesis Of Phosphodiester Galactosyl Cluster On Solid Support By Click Chemistry Assisted By Microwaves. *Journal of Organic Chemistry*, *73*(15), 6014–7.

Ranoux, A., Lemiègre, L., Benoit, M., Guégan, J.-P., & Benvegnu, T. (2010). Horner-Wadsworth-Emmons Reaction Of Unprotected Sugars In Water Or In The Absence Of Any Solvent: One-Step Access To C-Glycoside Amphiphiles. *European Journal of Organic Chemistry*, *2010*(7), 1314–1323.

Reddya, C. M., Areyb, J. S., Seewalda, J. S., Sylvaa, S. P., Lemkaua, K. L., Nelsona, R. K., Camillic, R. (2011). Composition and fate of gas and oil released to the water column during the Deepwater Horizon oil spill. *Proceedings of the National Academy of Sciences*, *109*(50), 20229–20234.

Retailleau, L., Laplace, A., Fensterbank, H., & Larpent, C. (1998). Synthesis, Structural Analysis, and Properties of N-Alkylglucosyl(meth)acrylamides: New Reactive Sugar Surfactants. *Journal of Organic Chemistry*, *63*(3), 608–617.

Rico-Lattes, I., & Lattes, A. (1997). Synthesis Of New Sugar-Based Surfactants Having Biological Applications: Key Role Of Their Self-Association. *Colloids and Surfaces A: Physicochemical and Engineering Aspects*, *123-124*(5), 37–48.

Rodrigues, F., Canac, Y., & Lubineau, A. (2000). A Convenient, One-Step, Synthesis Of B-C-Glycosidic Ketones In Aqueous Media. *Chemical Communications*, *6*(20), 2049–2050.

Romero, T., Orenes, R. A., Tárraga, A., & Molina, P. (2013). Preparation, Structural Characterization, Electrochemistry, And Sensing Properties Toward Anions And Cations Of Ferrocene-Triazole Derivatives. *Organometalics*, *32*, 5740–5753.

Rosen, M. J. (2004). *Surfactants and interfacial phenomena surfactants and interfacial phenomena* (third, p. 455). University of New York: Wiley- Interscience.

Rosen, M. J., Li, F., Morrall, S. W., & Versteeg, D. J. (2001). The Relationship Between The Interfacial Properties Of Surfactants And Their Toxicity To Aquatic Organisms. *Environmental Science & Technology*, *35*(5), 954–9.

Rostovtsev, V. V, Green, L. G., Fokin, V. V, & Sharpless, K. B. (2002). A Stepwise Huisgen Cycloaddition Process: Copper(I)-Catalyzed Regioselective "Ligation" Of Azides And Terminal Alkynes. *Angewandte Chemie (International Ed. in English)*, *41*(14), 2596–9.

Rybinski, W. Von, & Hill, K. (1998). Alkyl Polyglycosides-Properties And Application Of A New Class Of Surfactants. *Angewandte Chemie (International Ed. in English)*, *37*, 1328–1345.

Salkar, R. a, Minamikawa, H., & Hato, M. (2004). Alkylglucosides With Isoprenoid-Type Hydrophobic Chains-Effects Of Hydrophobic Chain Size On The Aqueous Phase Behavior. *Chemistry and Physics of Lipids*, *127*(1), 65–75.

Sani, F. A., Heidelberg, T., Hashim, R., & Farhanullah. (2012). Alkyl Triazole Glycosides (Atgs)--A New Class Of Bio-Related Surfactants. *Colloids and Surfaces. B: Biointerfaces*, *97*, 196–200.

Schuster, O., Yang, L., Raubenheimer, H. G., & Albrecht, M. (2009). Beyond Conventional N-Heterocyclic Carbenes: Abnormal, Remote, And Other Classes Of NHC Ligands With Reduced Heteroatom Stabilization. *Chemical Reviews*, *109*(8), 3445–78.

Schwuger, M.-J., & Stickdornt, K. (1995). Microemulsions in Technical Processes. *Chemical Reviews*, *95*, 849–864.

Sharma, K. S., & Rakshit, A. K. (2004). Investigation of the Properties of Decaoxyethylene n-Dodecyl Ether , $C_{12}E_{10}$, in the Aqueous Sugar-rich Region. *Journal of Surfactants and Detergents*, *7*(3), 305–316.

Shibata, Y., Noguchi, K., & Tanaka, K. (2010). Cationic Rhodium(I) Complex-Catalyzed Cotrimerization Of Propargyl Esters And Arylacetylenes Leading To Substituted Dihydropentalenes. *Organic Letters*, *12*(23), 5596–9.

Shin, K.-H., Ahn, Y., & Kim, K.-W. (2005). Toxic Effect Of Biosurfactant Addition On The Biodegradation Of Phenanthrene. *Environmental Toxicology and Chemistry / SETAC*, *24*(11), 2768–74.

Shinoda, K., Carlsson, a, & Lindman, B. (1996). On The Importance Of Hydroxyl Groups In The Polar Head-Group Of Nonionic Surfactants And Membrane Lipids. *Advances in Colloid and Interface Science*, *64*, 253–71.

Siwakunakorn, S. (2006). *Formation And Stability Of Oil-In-Water Emulsion Made With B-Casein Hydrophobic Peptides*. University of Guelph.

Soderberg, I., Drummond, C. J., Furlong, D. N., Godkin, S., & Matthews, B. (1995). Non-Ionic Sugar-Based Surfactants: Self Assembly And Air/Water Interfacial Activity. *Colloids and Surfaces A: Physicochemical and Engineering Aspects*, *102*, 91–97.

Spence, J. D., Wyatt, J. K., Bender, D. M., Moss, D. K., & Nantz, M. H. (1996). Stereogenic Propargylic Centers Via Base-Mediated Terminal Allene Isomerization. *Journal of Organic Chemistry*, *61*(12), 4014–4021.

Stefani, H. a., Canduzini, H. a., & Manarin, F. (2011). Modular Synthesis Of Mono, Di, And Tri-1,4-Disubstituted-1,2,3-Triazoles Through Copper-Mediated Alkyne–Azide Cycloaddition. *Tetrahedron Letters*, *52*(46), 6086–6090.

Stein, T. M., & Geiiman, S. H. (2003). Synthesis And Aggregation Properties Of A New Family Of Amphiphiles With An Unusual Headgroup Topology. *Journal of the American Chemical Society*, (2), 3943–3950.

Stein, T. M., & Gellman, S. H. (1992). Synthesis And Aggregation Properties Of A New Family Of Amphiphiles With An Unusual Headgroup Topology. *Journal of the American Chemical Society*, *114*(10), 3943–3950.

Straub, B. F. (2007). μ-Acetylide And μ-Alkenylidene Ligands In "Click" Triazole Syntheses. *Chemical Communications*, (37), 3868.

Such, G. K., Johnston, A. P. R., Liang, K., & Caruso, F. (2012). Synthesis And Functionalization Of Nanoengineered Materials Using Click Chemistry. *Progress in Polymer Science*, *37*(7), 985–1003.

Swanson-vethamuthu, M., Feitosa, E., & Brown, W. (1998). Salt-Induced Sphere-to-Disk Transition of Octadecyltrimethylammonium Bromide Micelles. *Langmuir*, *7463*(10), 1590–1596.

Tadros, T. (2013). *Encyclopedia of Colloid and Interface Science*. (T. Tadros, Ed.). Berlin, Heidelberg: Springer.

Tay, K. S., Rahman, N. A., & Abas, M. R. Bin. (2009). Degradation of DEET by Ozonation In Aqueous Solution. *Chemosphere*, *76*(9), 1296–302.

Tornøe, C. W., Christensen, C., & Meldal, M. (2002). Peptidotriazoles On Solid Phase: [1,2,3]-Triazoles By Regiospecific Copper(I)-Catalyzed 1,3-Dipolar Cycloadditions Of Terminal Alkynes To Azides. *Journal of Organic Chemistry*, *67*(9), 3057–64.

Tran, H.-A., Kitov, P. I., Paszkiewicz, E., Sadowska, J. M., & Bundle, D. R. (2011). Multifunctional Multivalency: A Focused Library Of Polymeric Cholera Toxin Antagonists. *Organic & Biomolecular Chemistry*, *9*(10), 3658–71.

Trost, B. M., & Rudd, M. T. (2002). An Unusual Ruthenium-Catalyzed Cycloisomerization Of Alkynes And Propargyl Alcohols. *Journal of the American Chemical Society*, *124*(16), 4178–9.

Turnbull, K., & Scriven, E. F. V. (1988). Azides: Their Preparation And Synthetic Uses. *Chemical Reviews*, *88*(2).

Vasilevsky, S. F., Baranov, D. S., Mamatyuk, V. I., Gatilov, Y. V, & Alabugin, I. V. (2009). An Unexpected Rearrangement That Disassembles Alkyne Moiety Through Formal Nitrogen Atom Insertion Between Two Acetylenic Carbons And Related Cascade Transformations: New Approach To Sampangine Derivatives And Polycyclic Aromatic Amides. *Journal of Organic Chemistry*, *74*(16), 6143–50.

Volkering, F., Breure, a M., & Rulkens, W. H. (1998). Microbiological Aspects Of Surfactant Use For Biological Soil Remediation. *Biodegradation*, *8*(6), 401–17.

Von Minden, H. M., Brandenburg, K., Seydel, U., Koch, M. H., Garamus, V., Willumeit, R., & Vill, V. (2000). Thermotropic And Lyotropic Properties Of Long Chain Alkyl Glycopyranosides. Part II. Disaccharide Headgroups. *Chemistry and Physics of Lipids*, *106*(2), 157–79.

Von Rybinski, W., & Hill, K. (1998). Alkyl Polyglycosides—Properties And Applications Of A New Class Of Surfactants. *Angewandte Chemie (International Ed. in English)*, *37*(10), 1328–1345.

Weissleder, R., Ross, B. D., Rehemtulla, A., & Gambhir, S. S. (2010). *Molecular Imaging: Principles and Practice* (p. 1357). PMPH-USA. Retrieved April 21, 2014 from http://books.google.com/books?id=Q4USPF4 Lm08C&pgis=1

Winsor, P. A., Thornton, L., & Great, C. (1968). Binary And Multicomponent Solutions Of Amphiphilic Compounds. Solubilization And The Formation, Structure, And Theoretical Significance Of Liquid Crystalline Solutions. *Chemical Reviews*, *68*(1), 1–40.

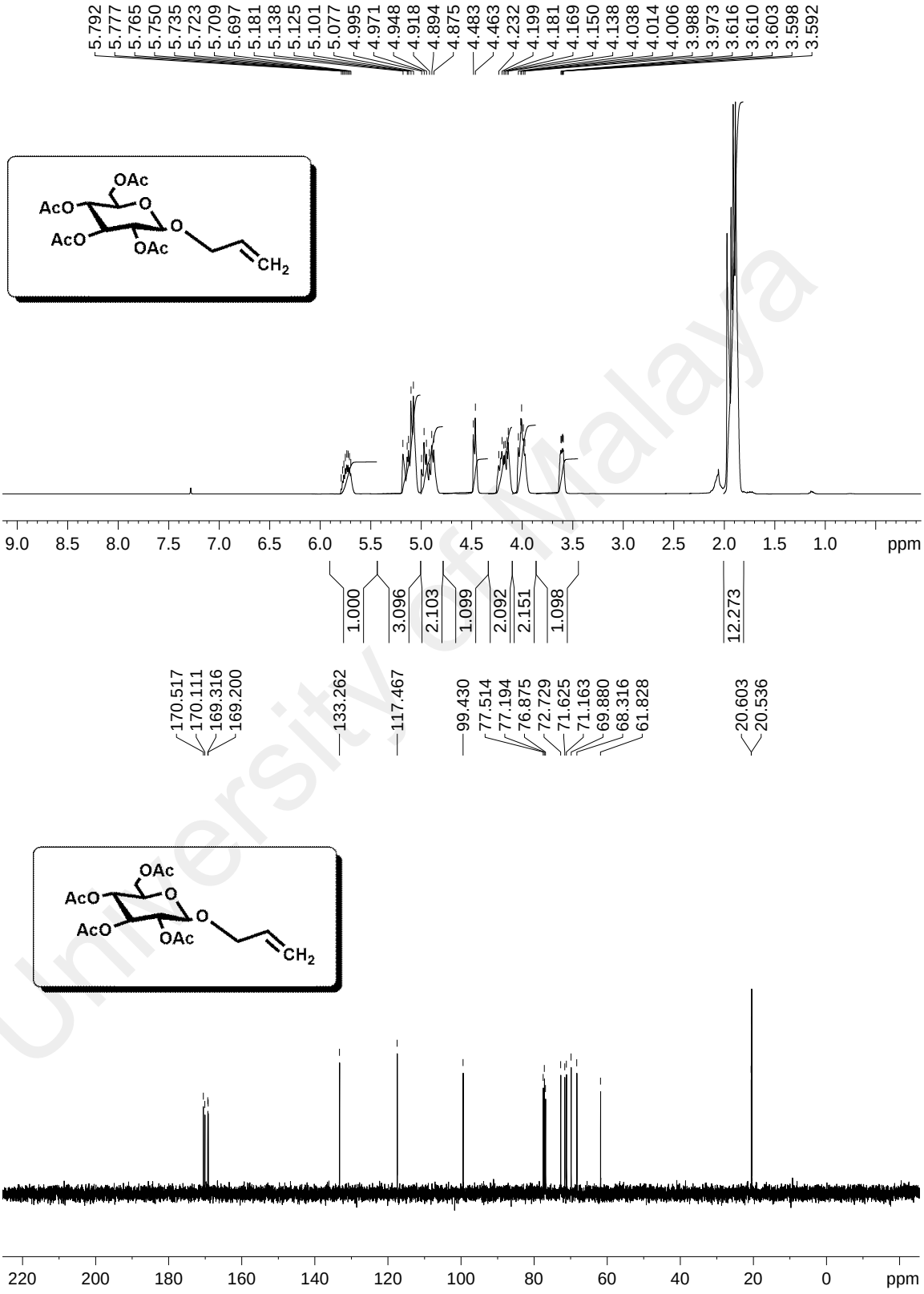
Wotiz, J. H., Barelski, P. M., & Koster, D. F. (1973). The Mechanism Of The Base-Catalyzed Pratotropic Propargylic Rearrangement In Vicinal Diamines. *Journal of Organic Chemistry*, *38*(3), 489–493.

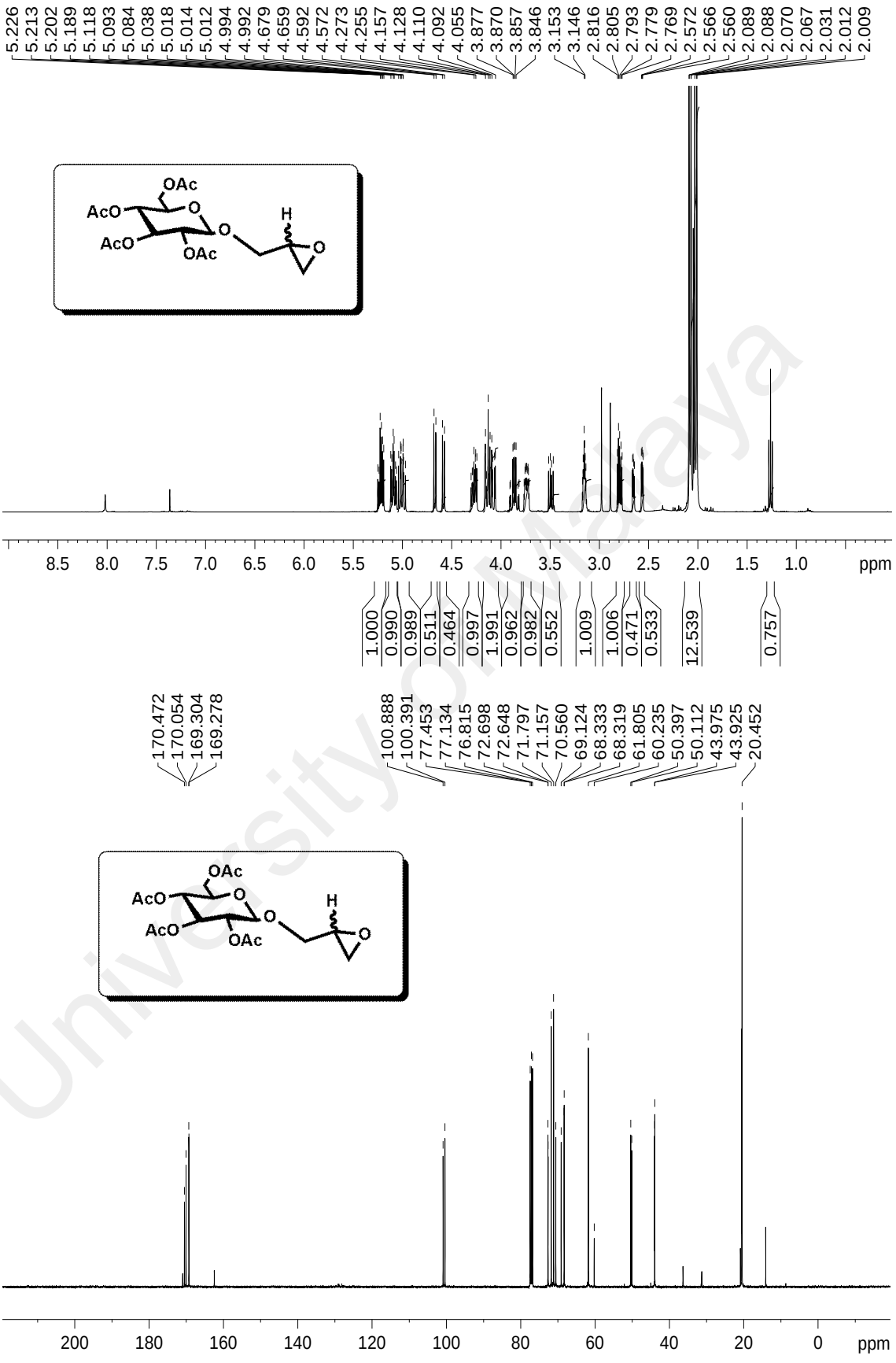
Xu, L. Q., Yao, F., Fu, G.-D., & Shen, L. (2009). Simultaneous "Click Chemistry" and Atom Transfer Radical Emulsion Polymerization and Prepared Well-Defined Cross-Linked Nanoparticles. *Macromolecules*, *42*(17), 6385–6392.

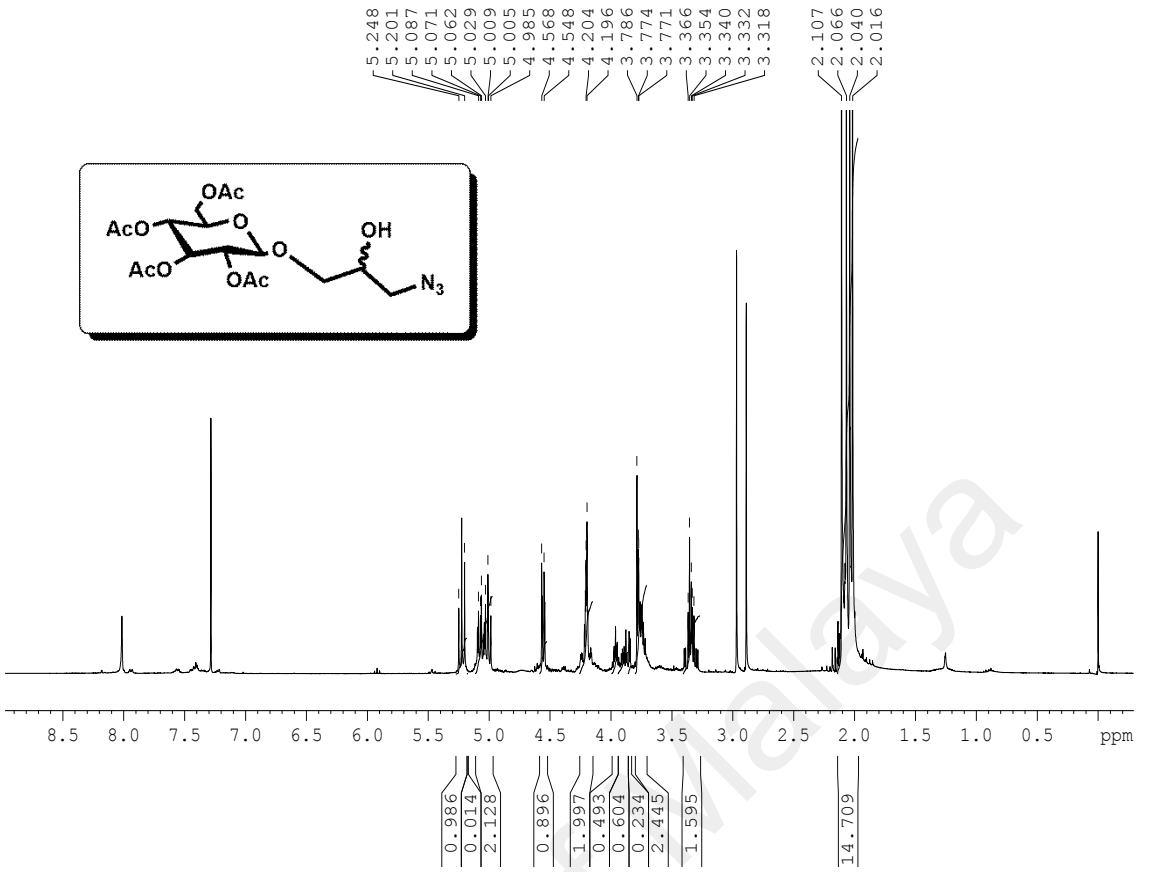
Zhang, T., & Marchant, R. E. (1996). Novel Polysaccharide Surfactants: The Effect Of Hydrophobic And Hydrophilic Chain Length On Surface Active Properties. *Journal of Colloid and Interface Science*, *177*(2), 419–426.

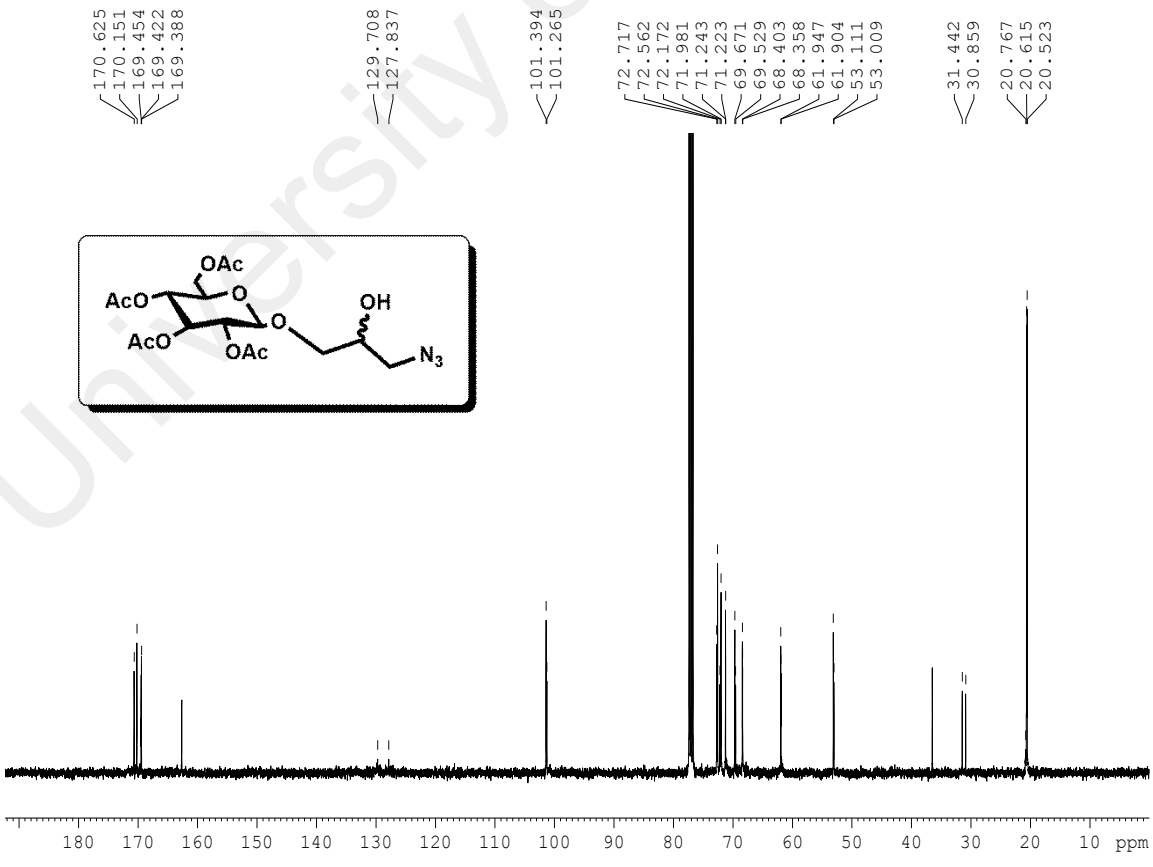
Zhang Xiaoxa. (2010). *Surfactant Enhanced Biodegradation Of Petroleum Hydrocarbons In Oily Sludge*. Xiangtan University.

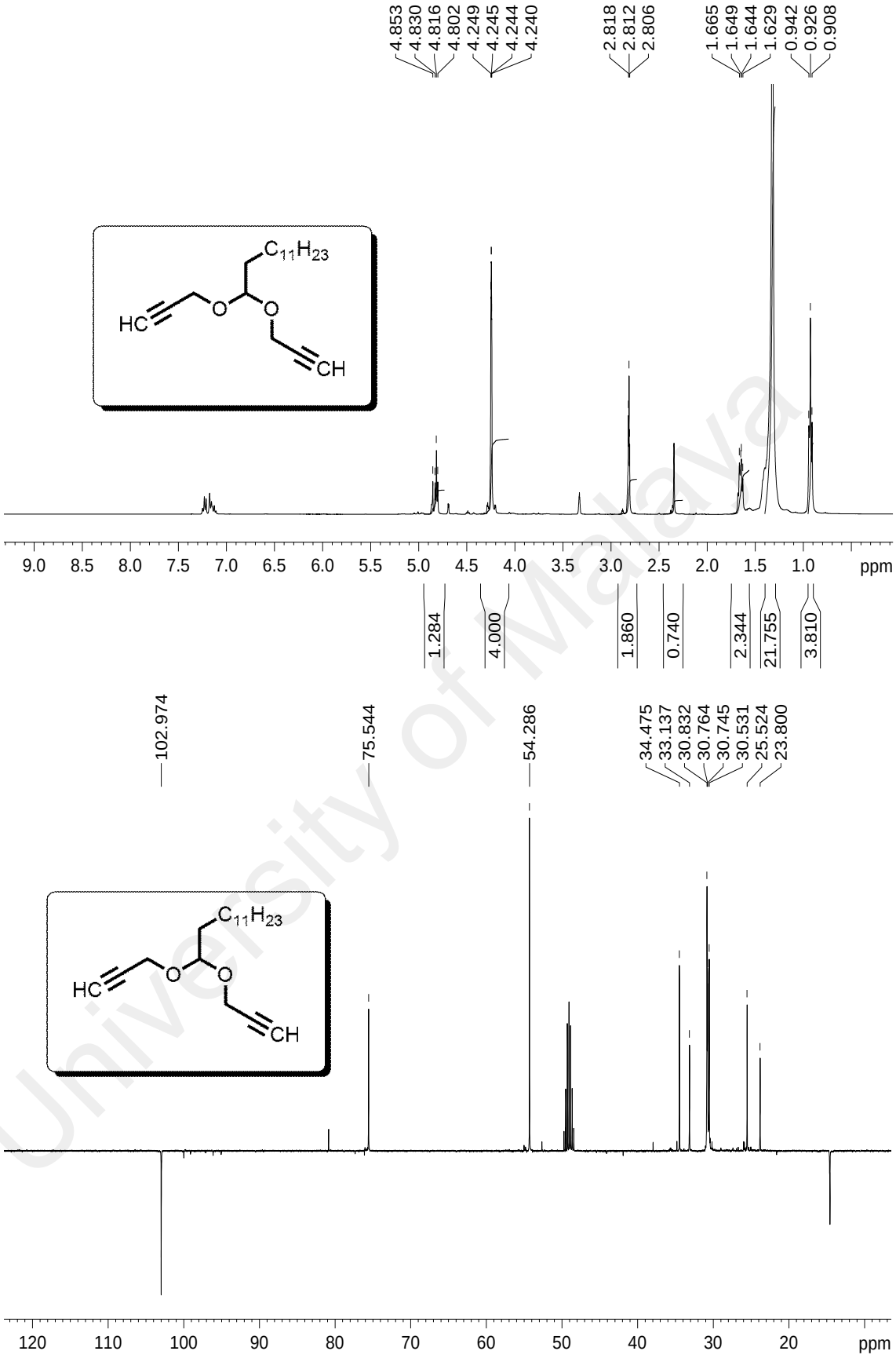
Appendix A: NMR (^{1}H and ^{13}C/Pendant) spectra for new Y-shaped surfactants from renewable resources

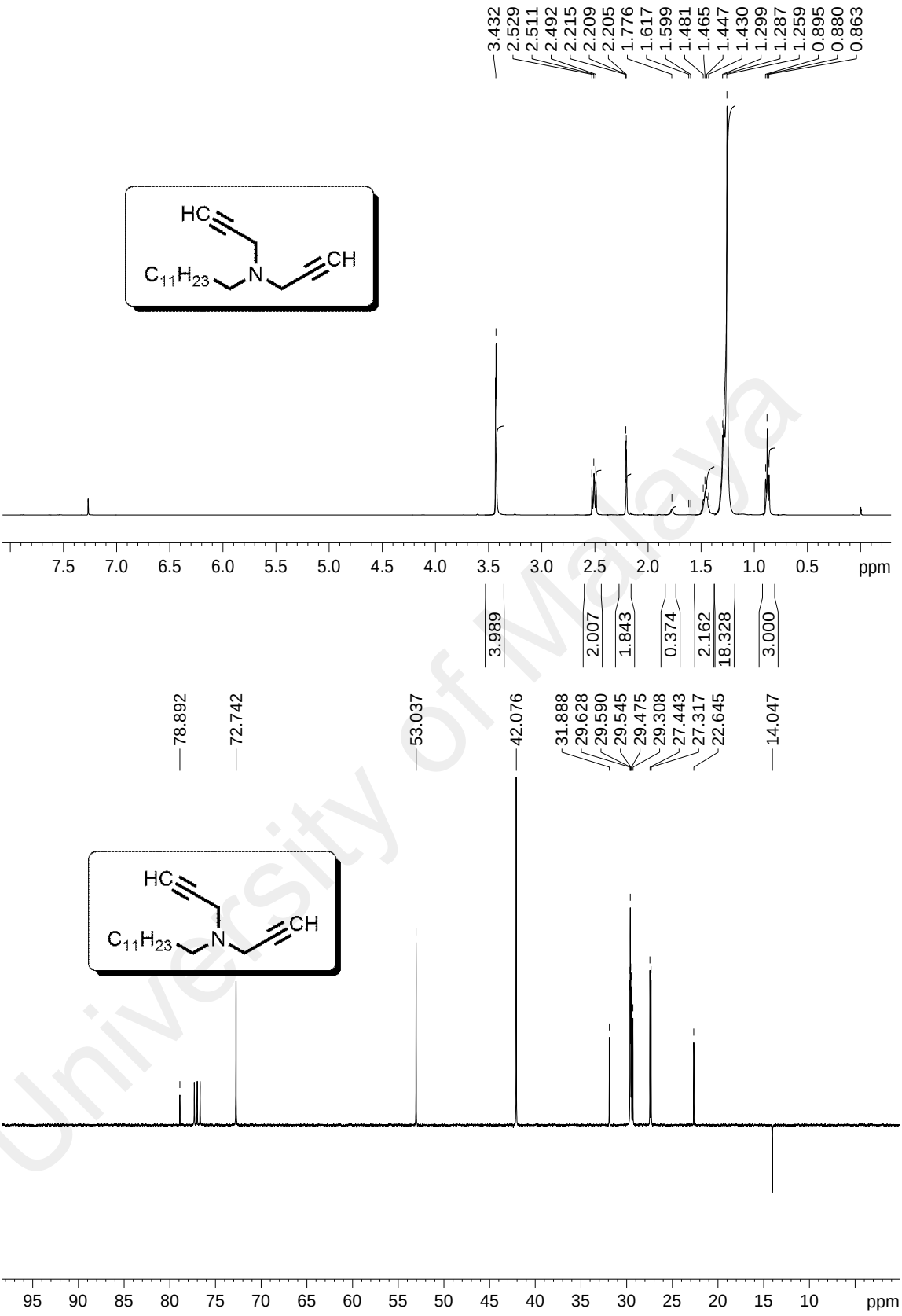


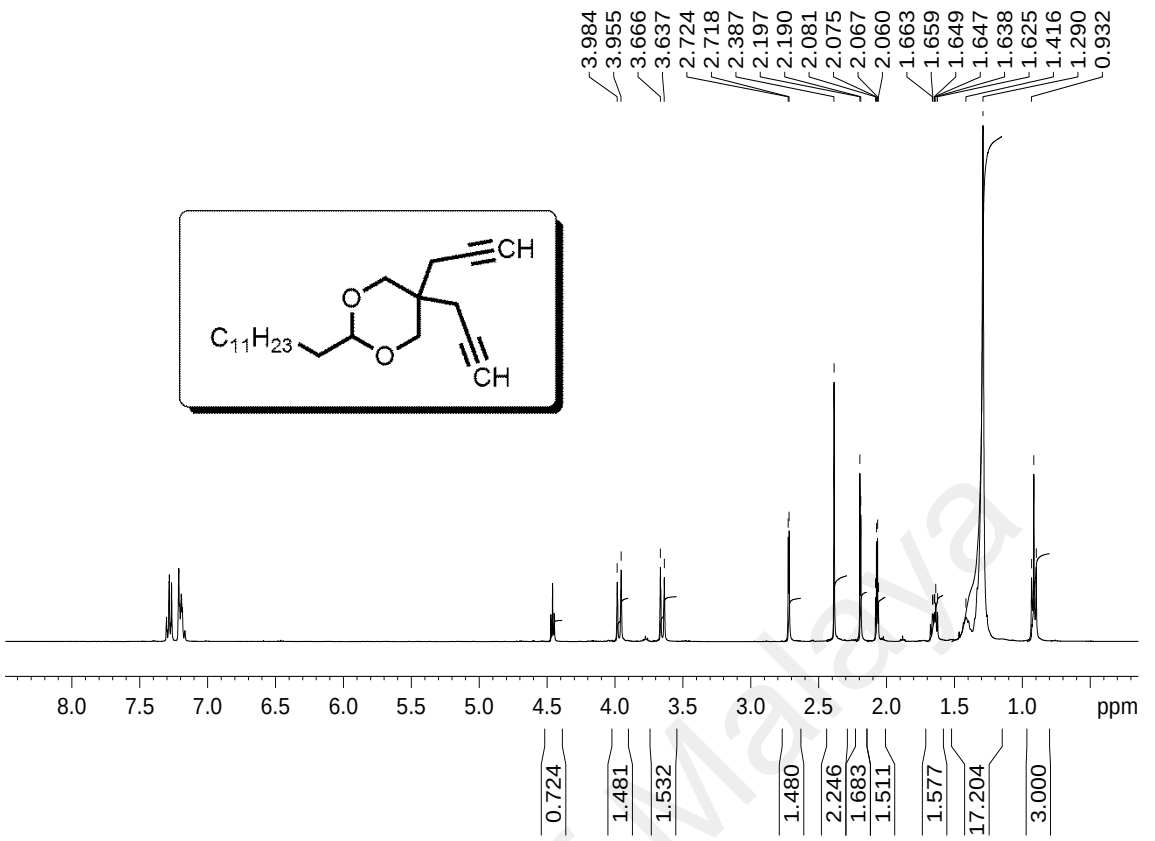


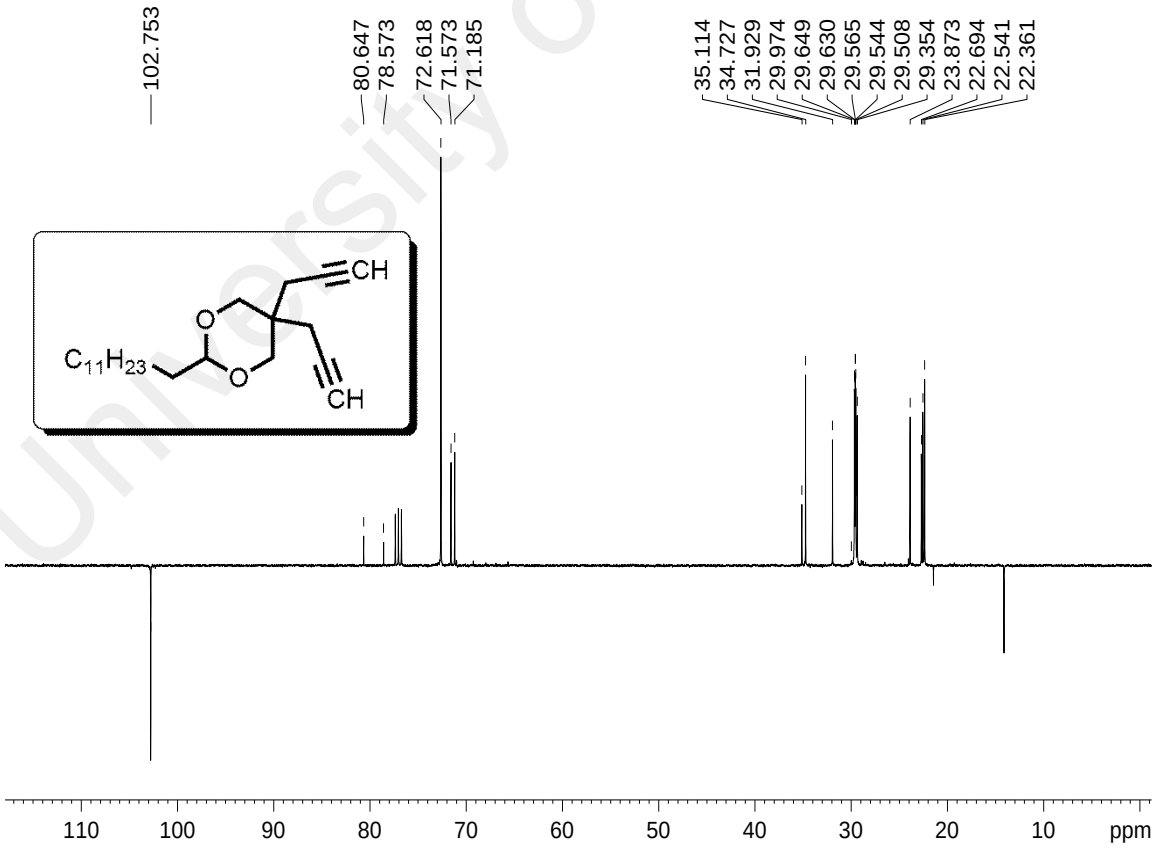


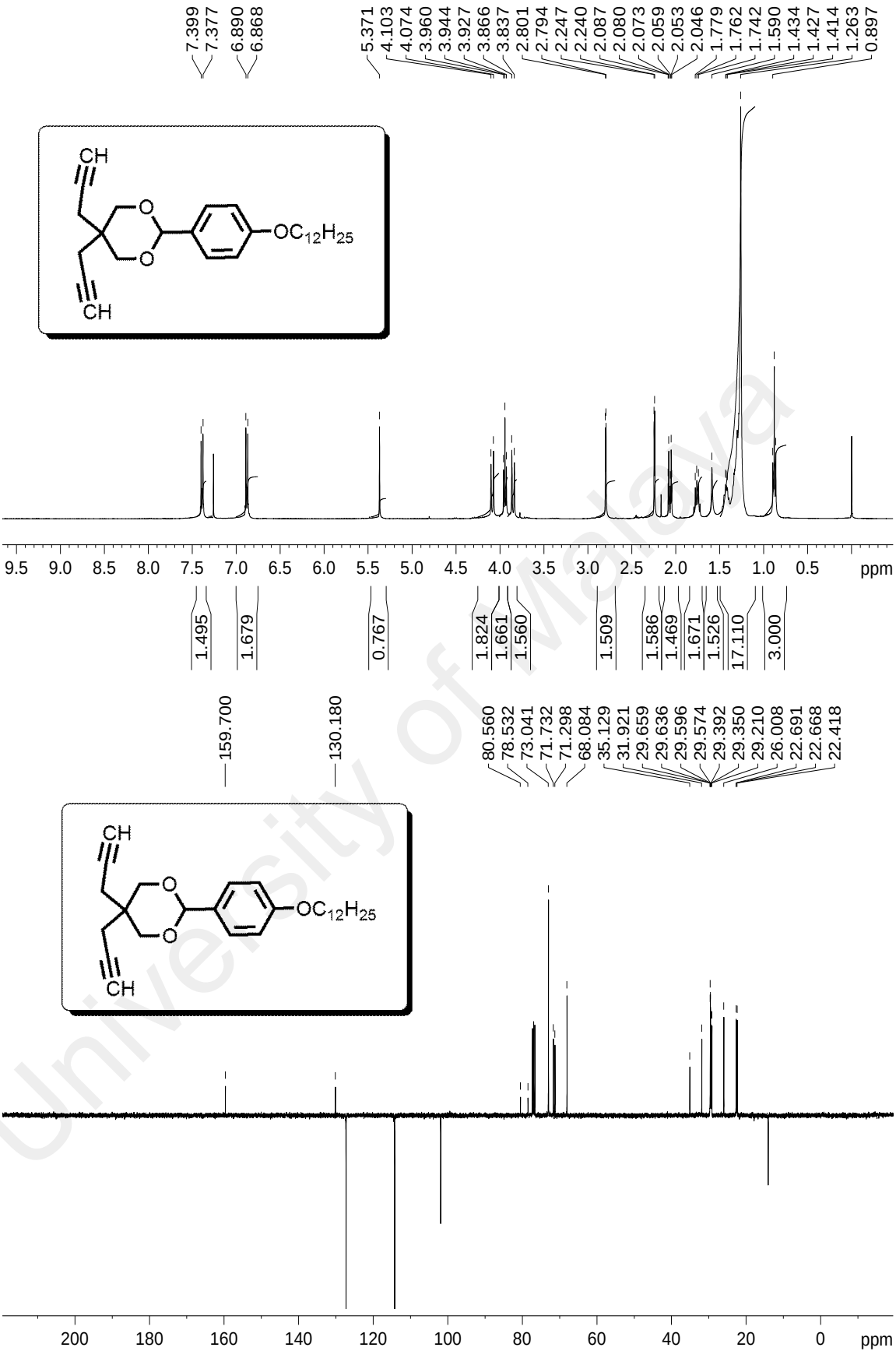


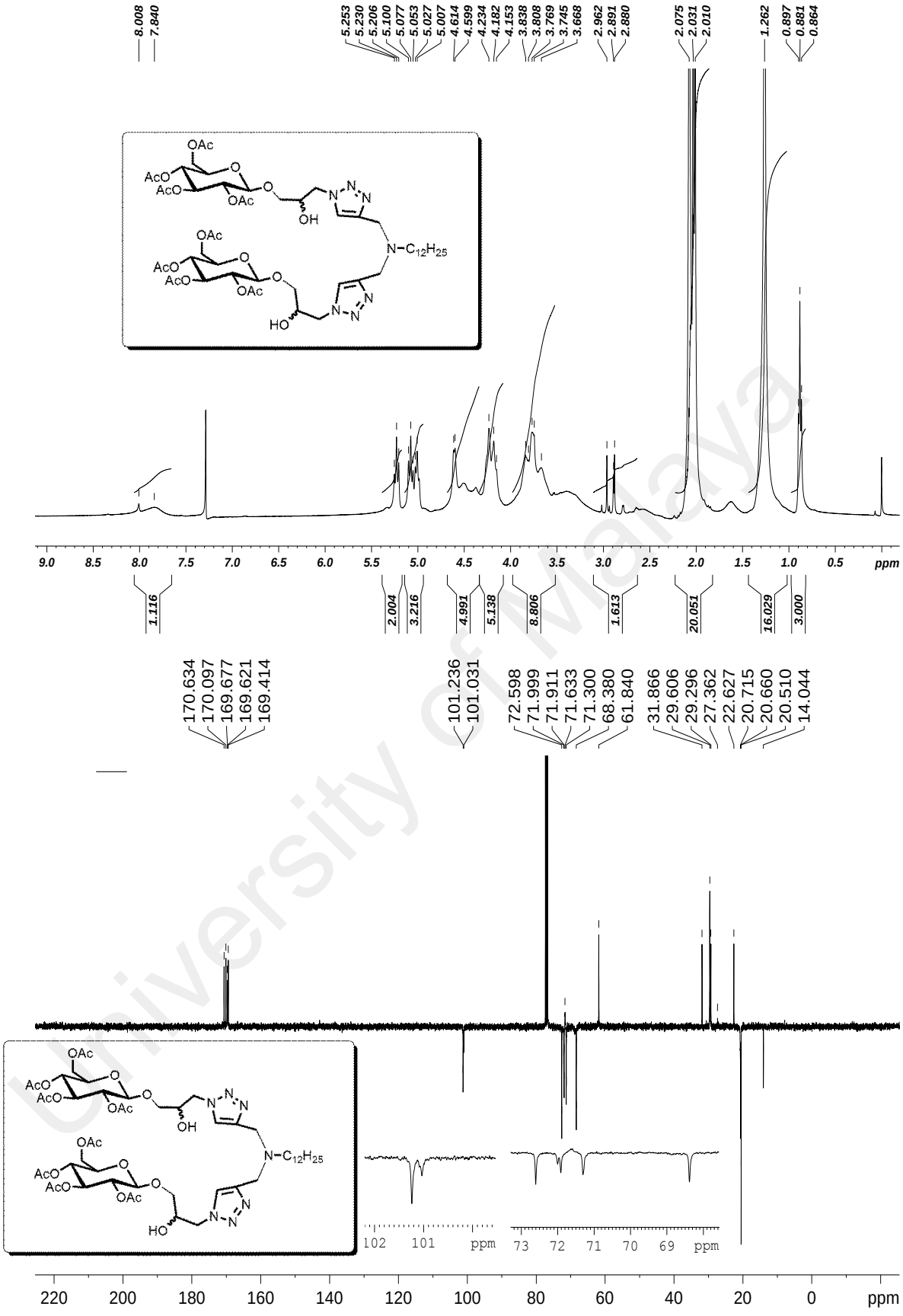


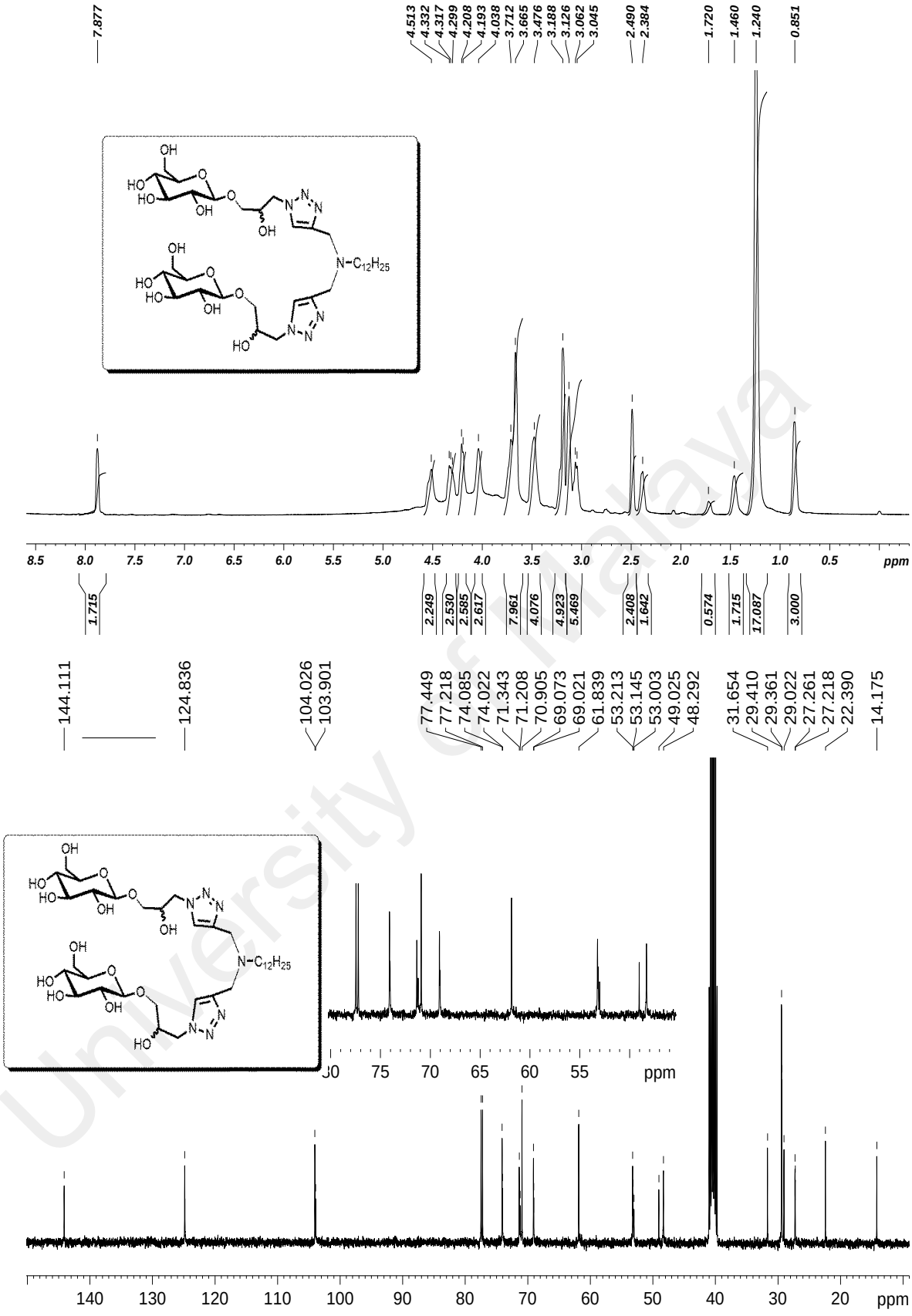


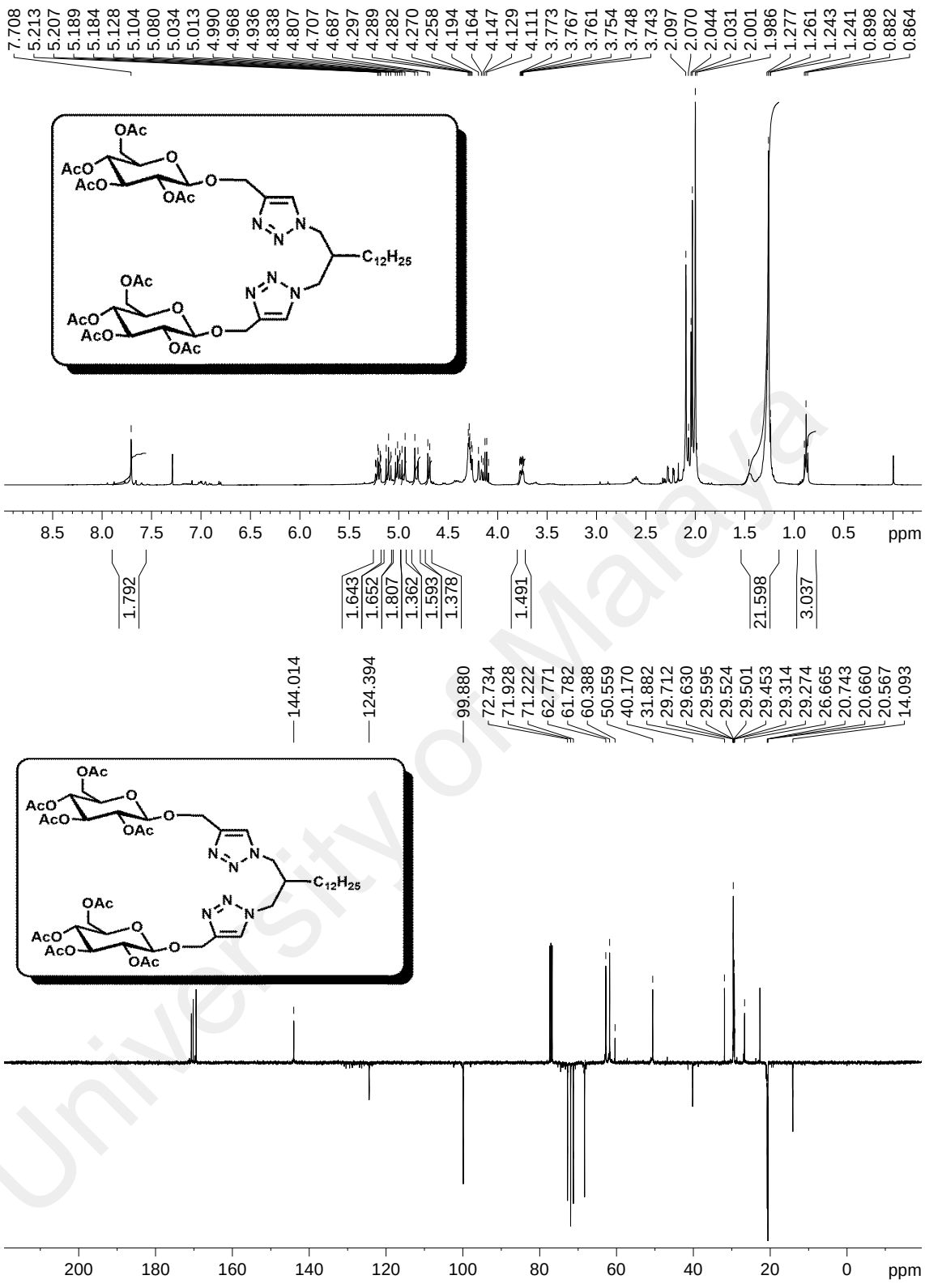


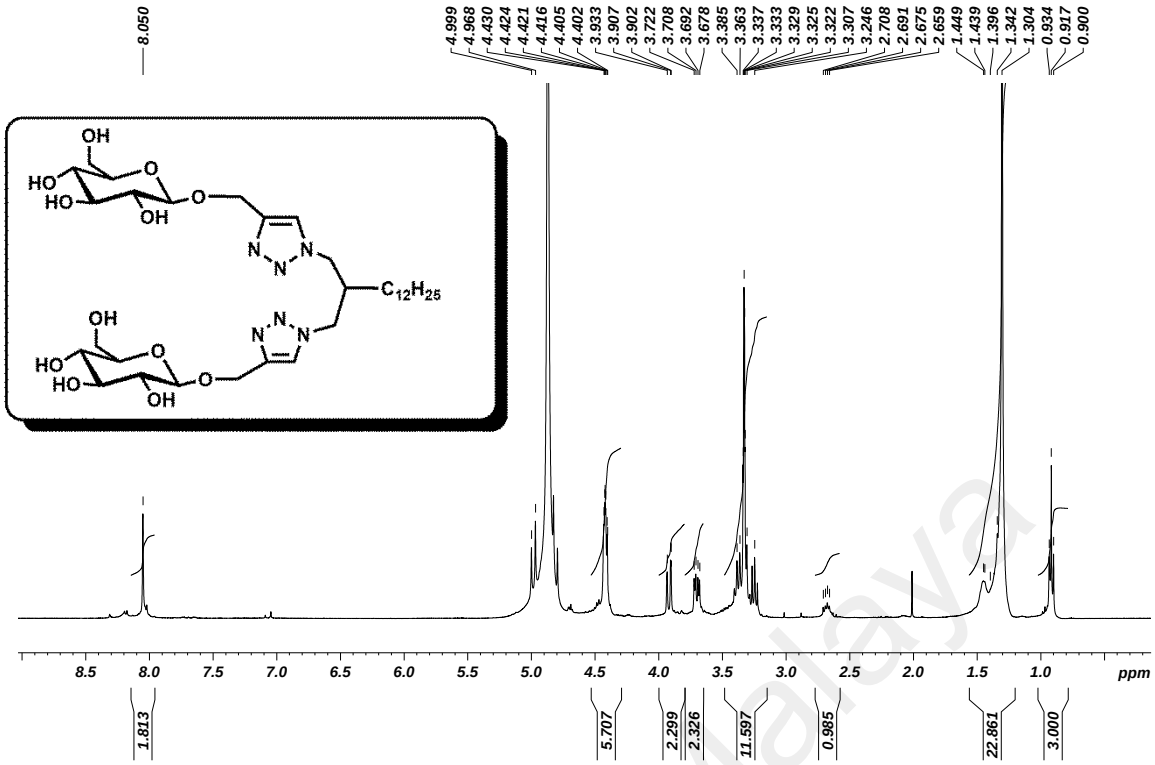


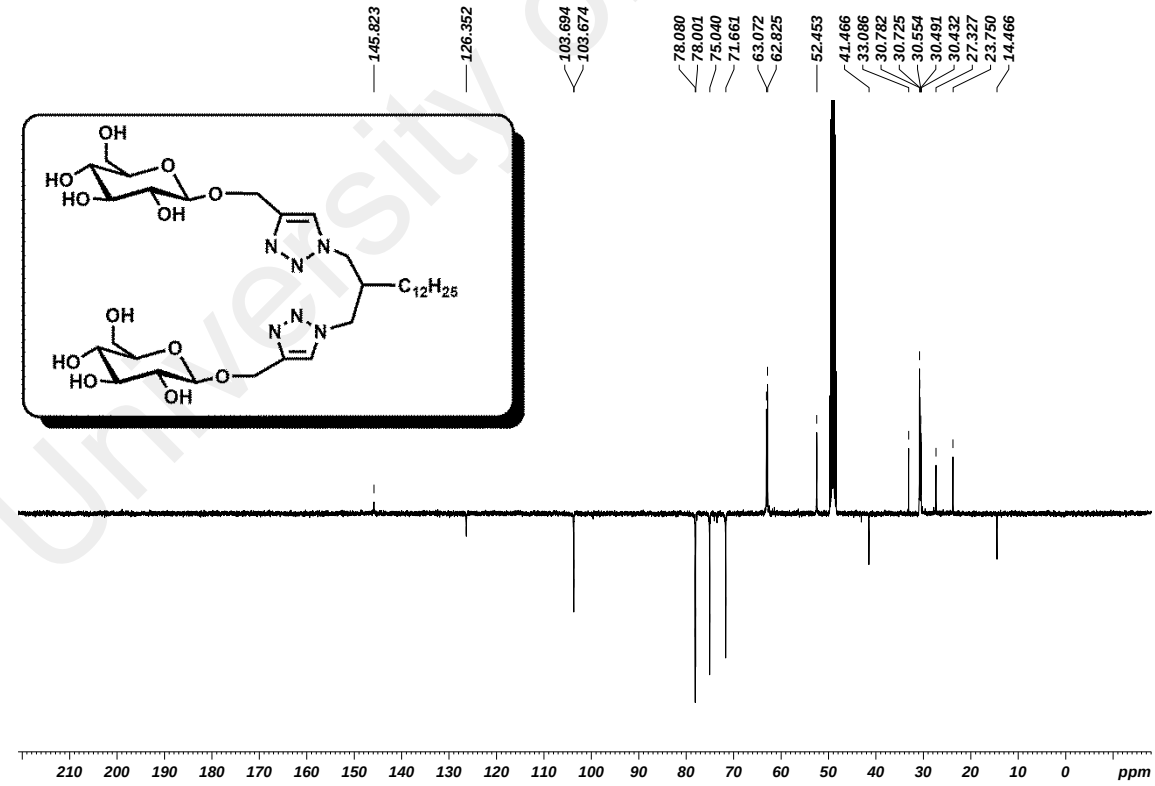


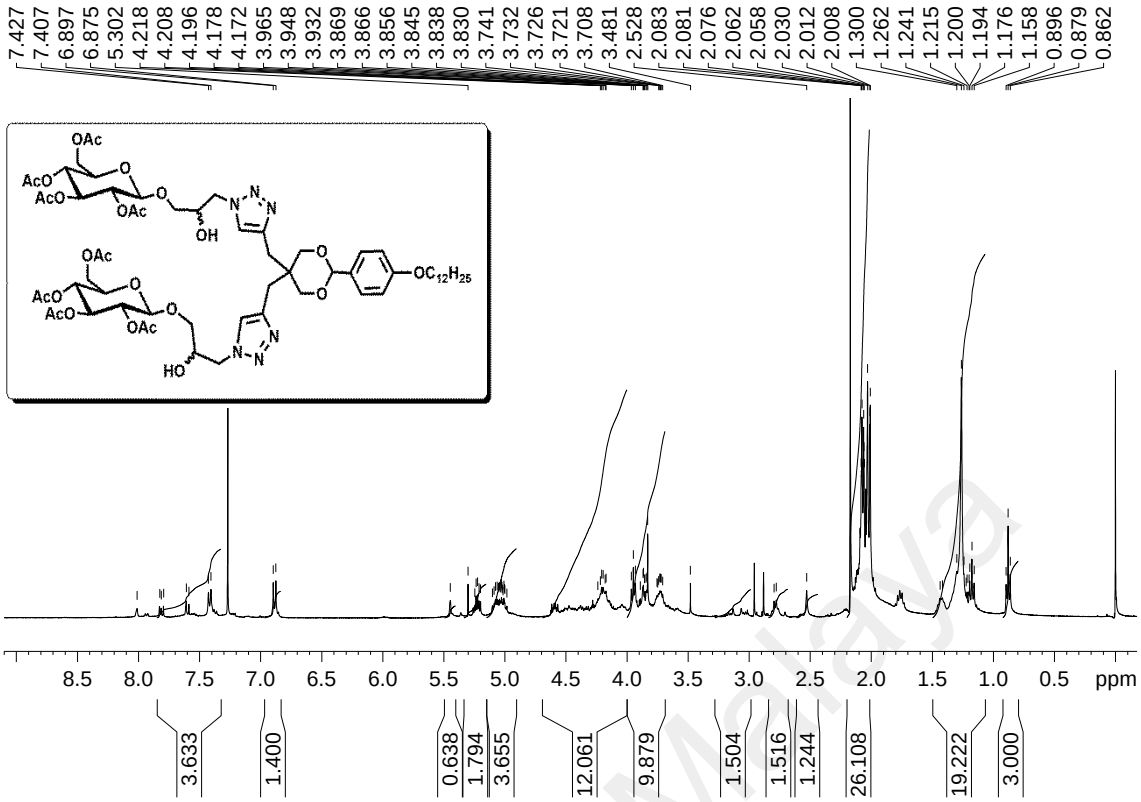


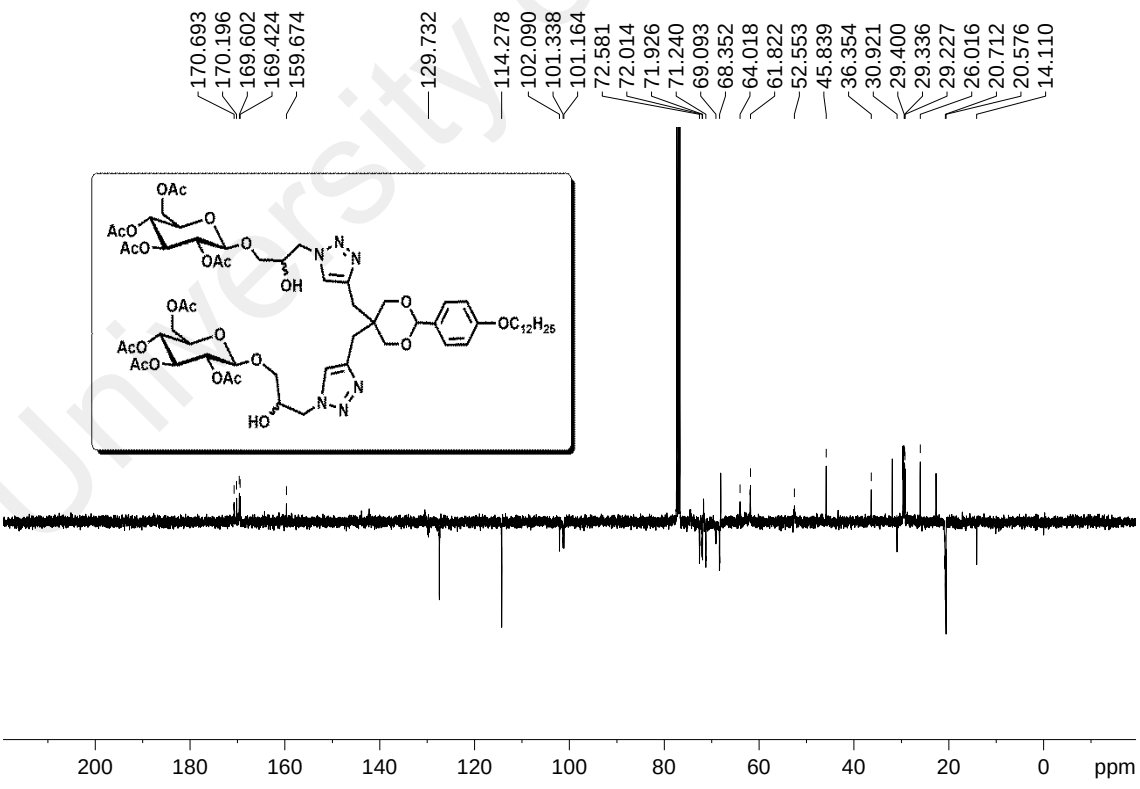


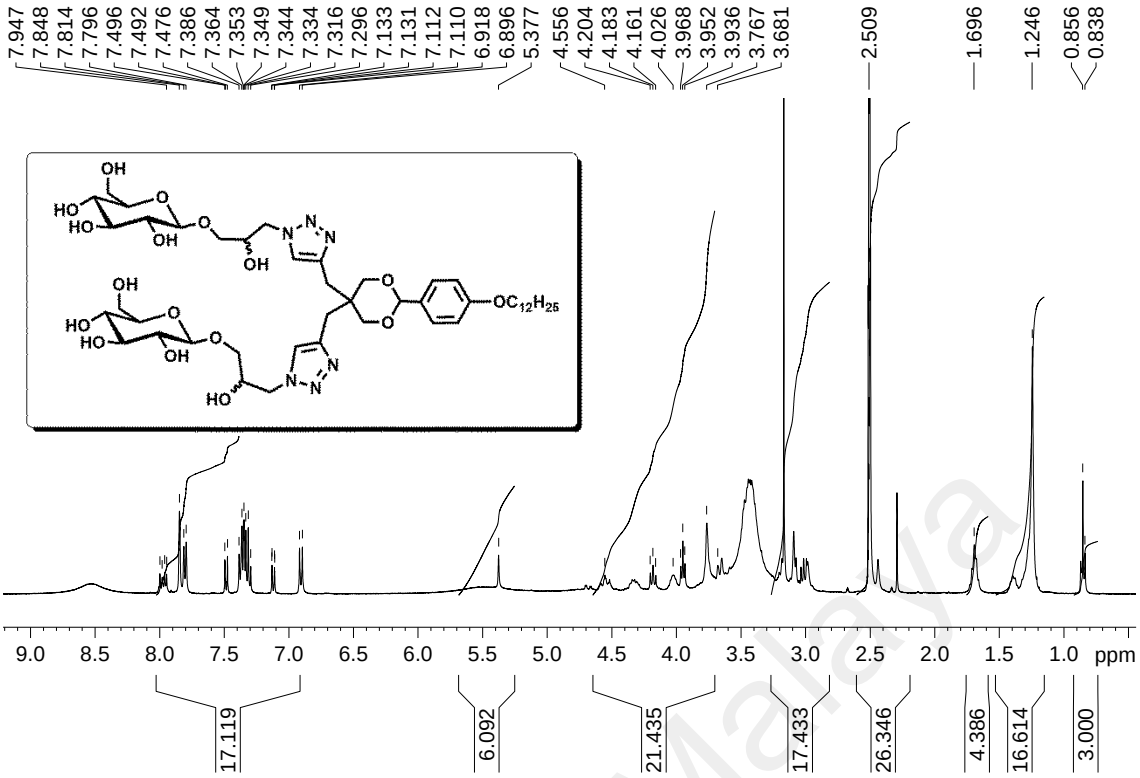


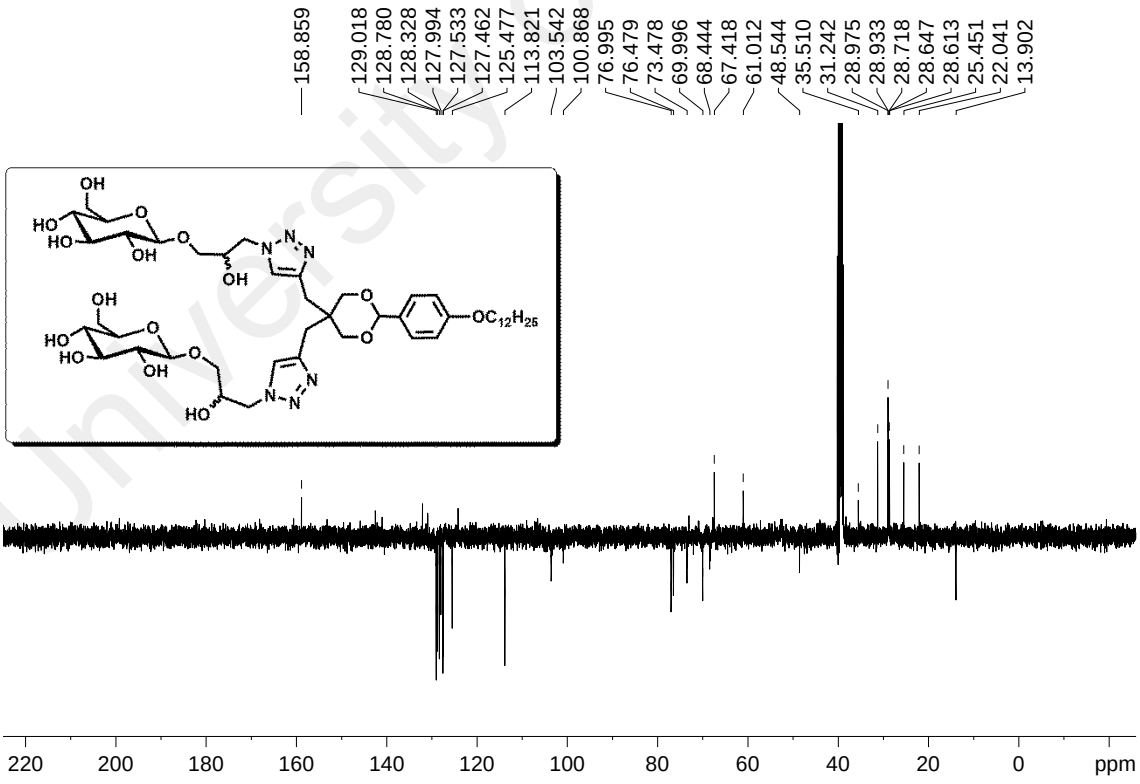


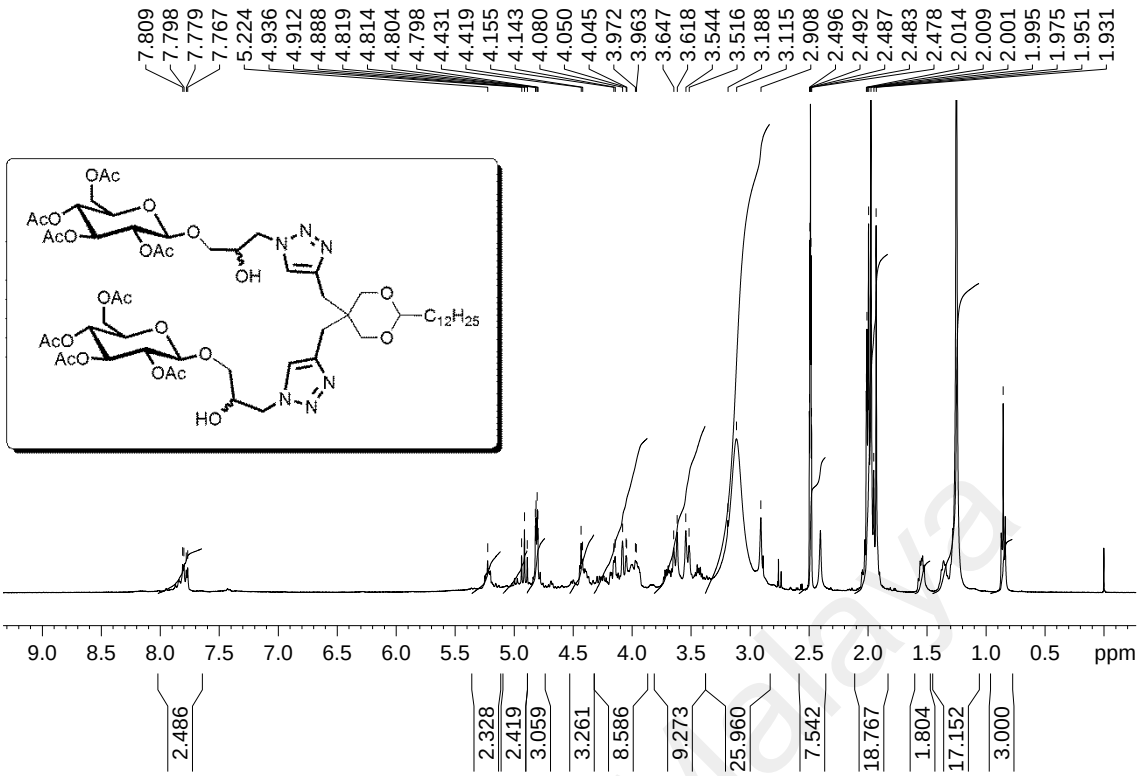


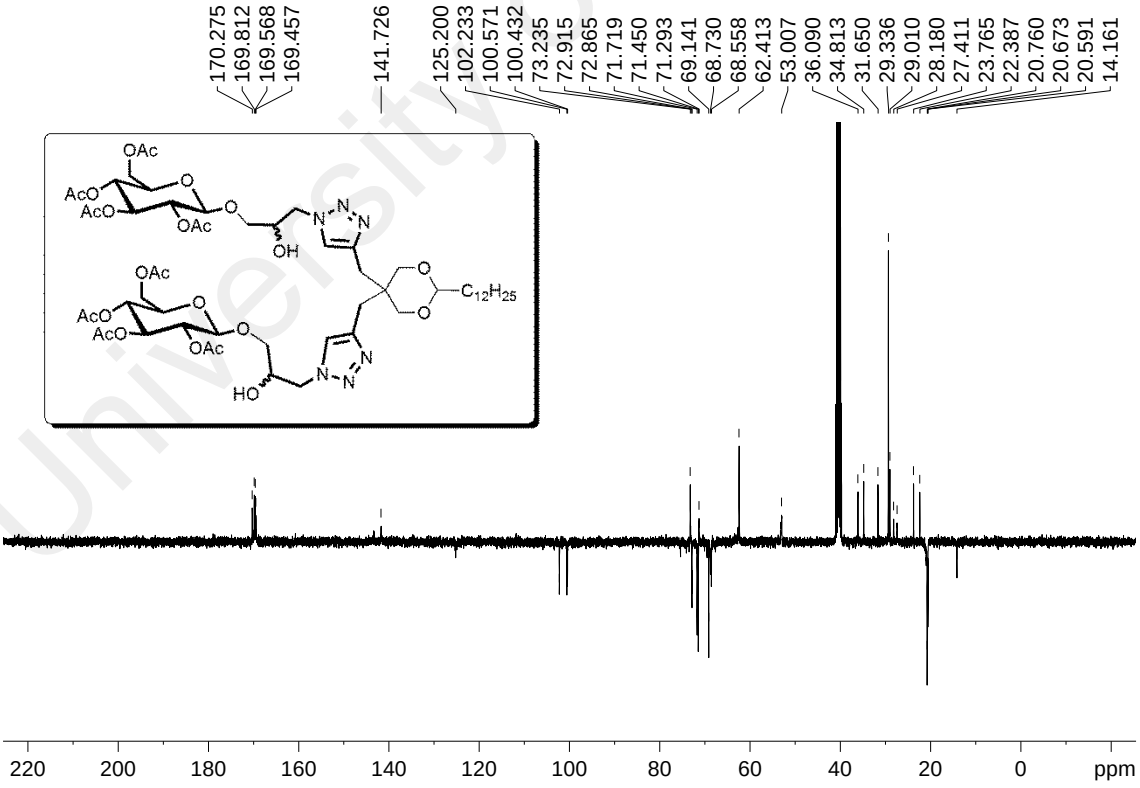


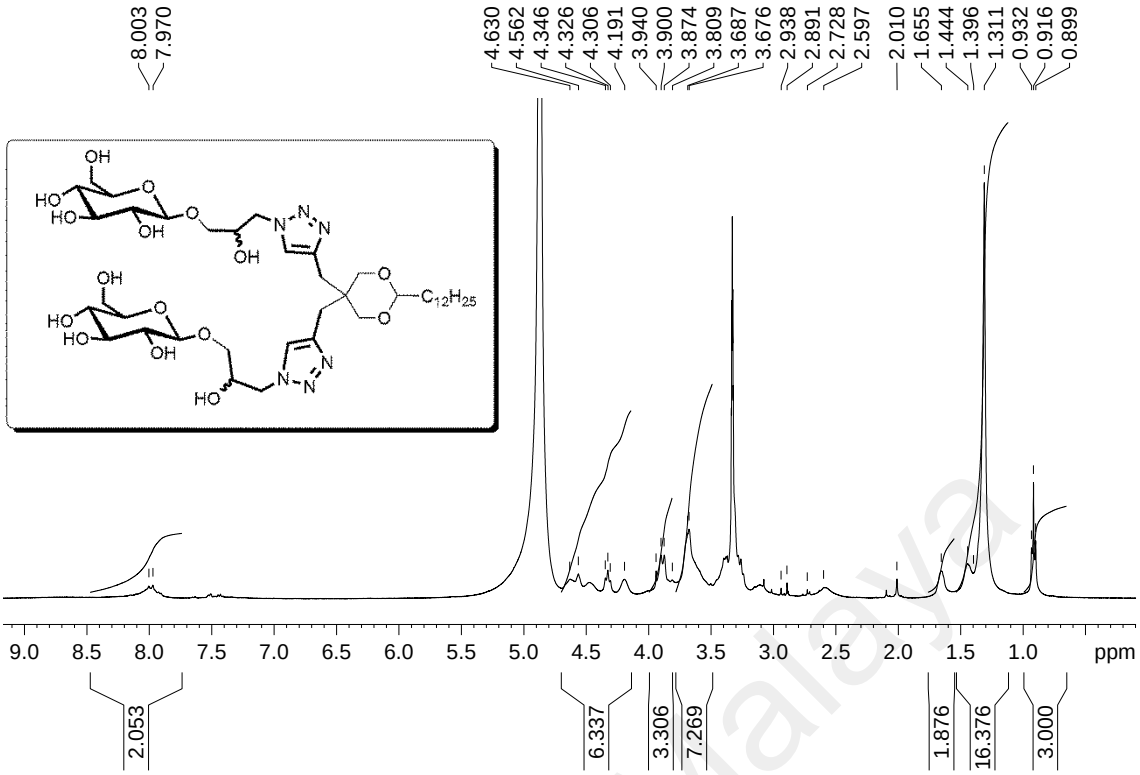


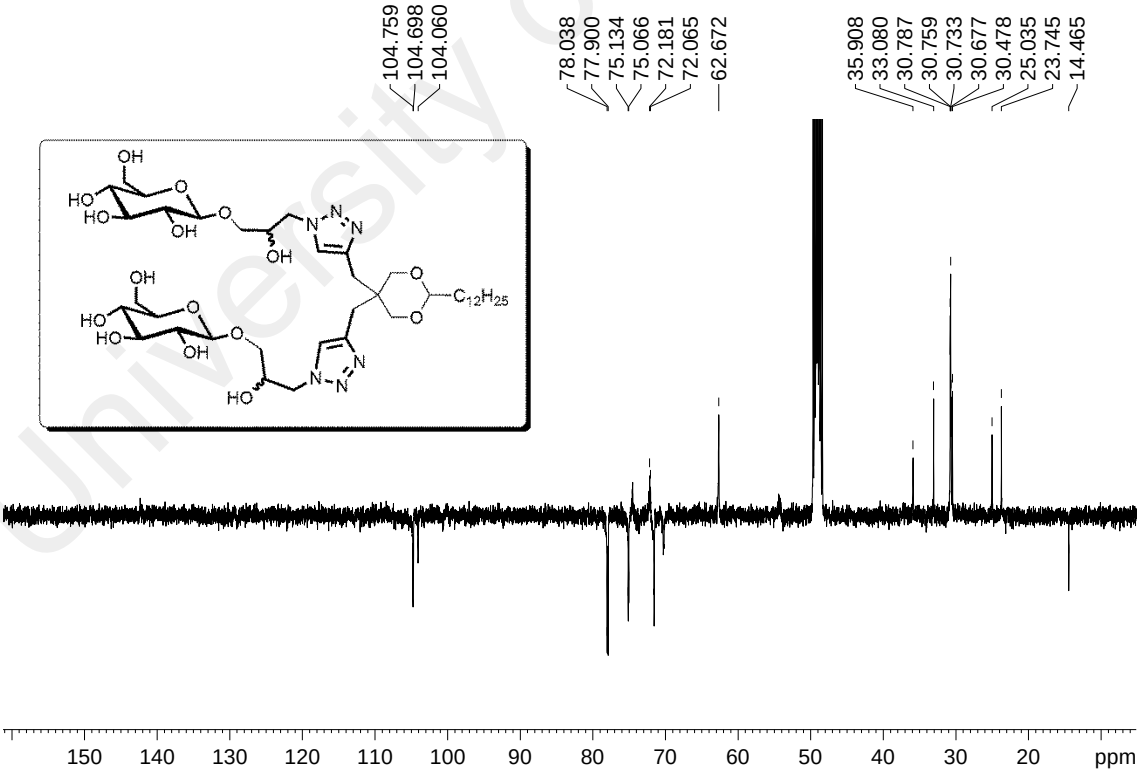


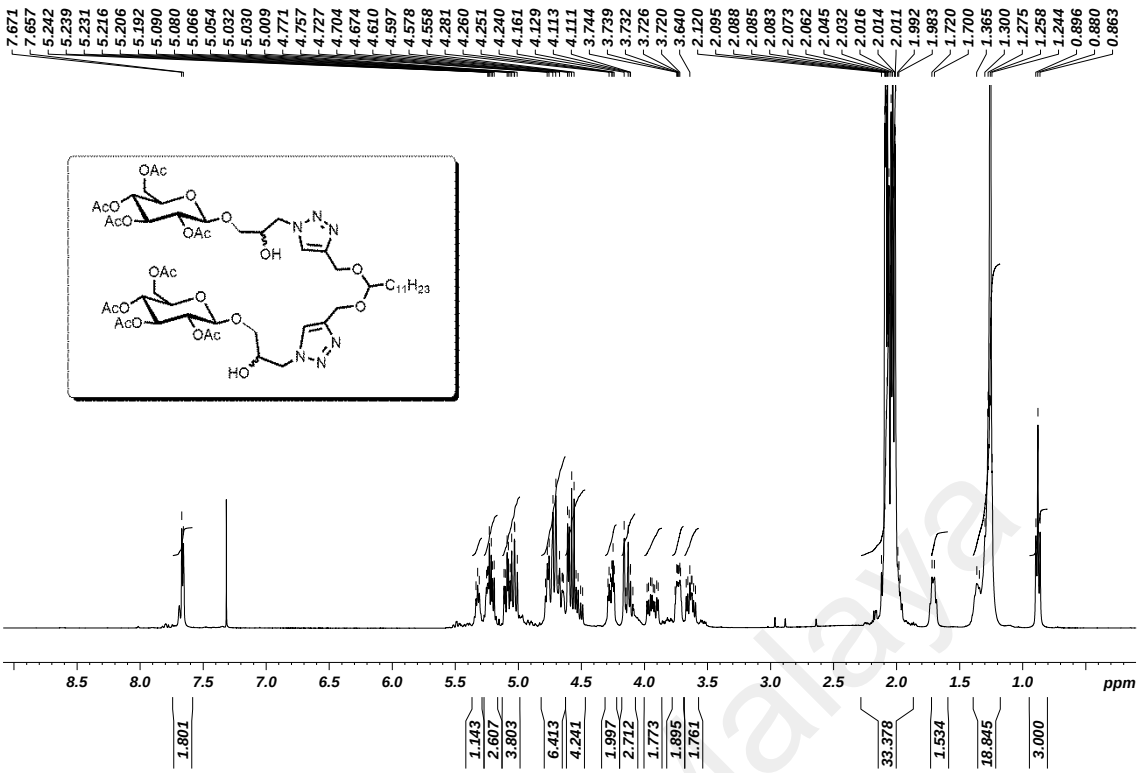


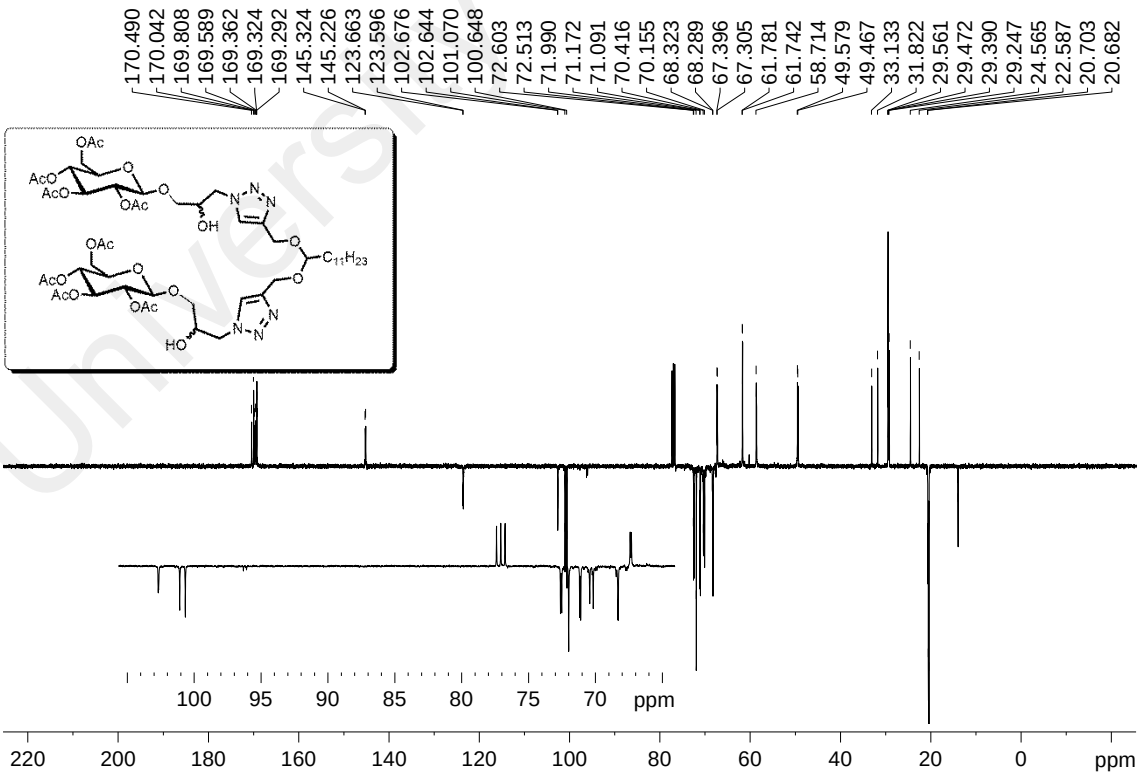


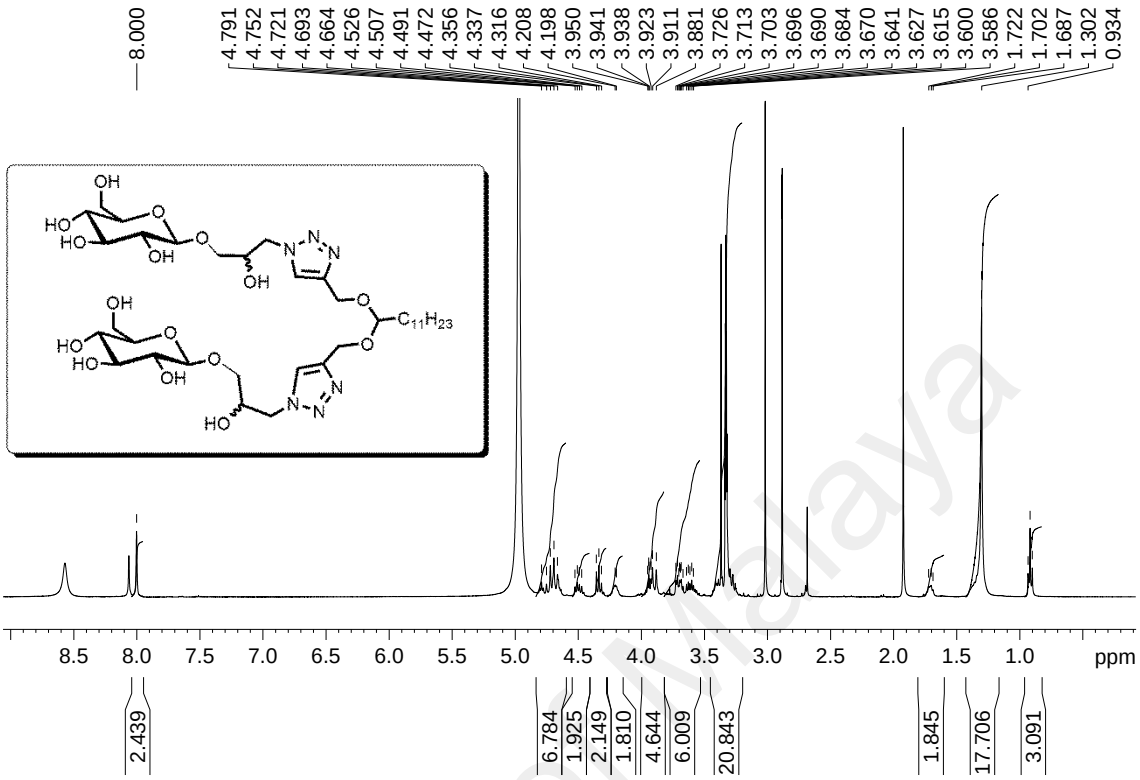


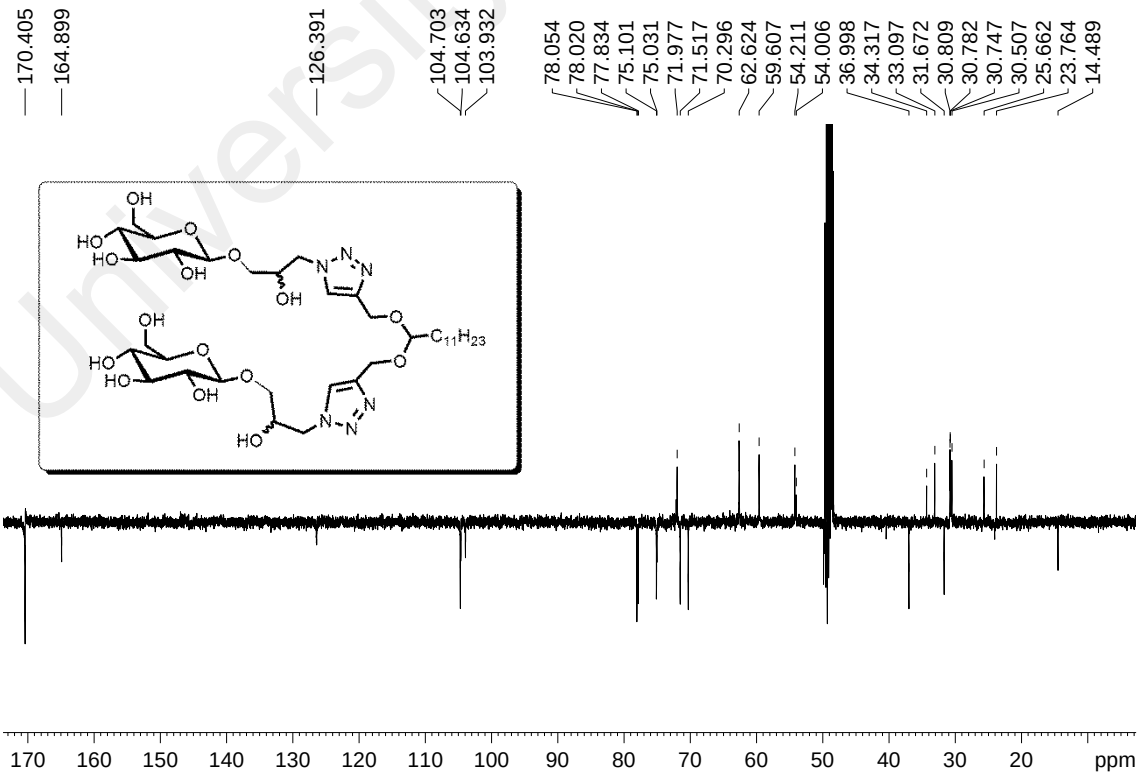




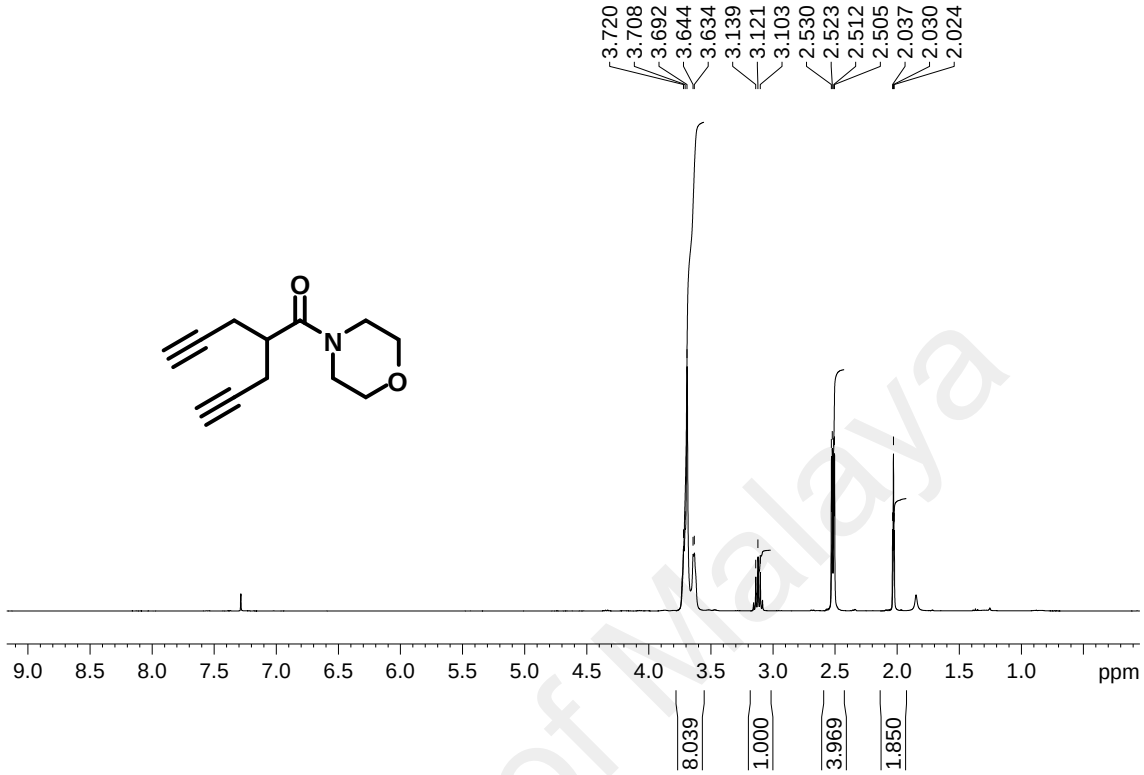


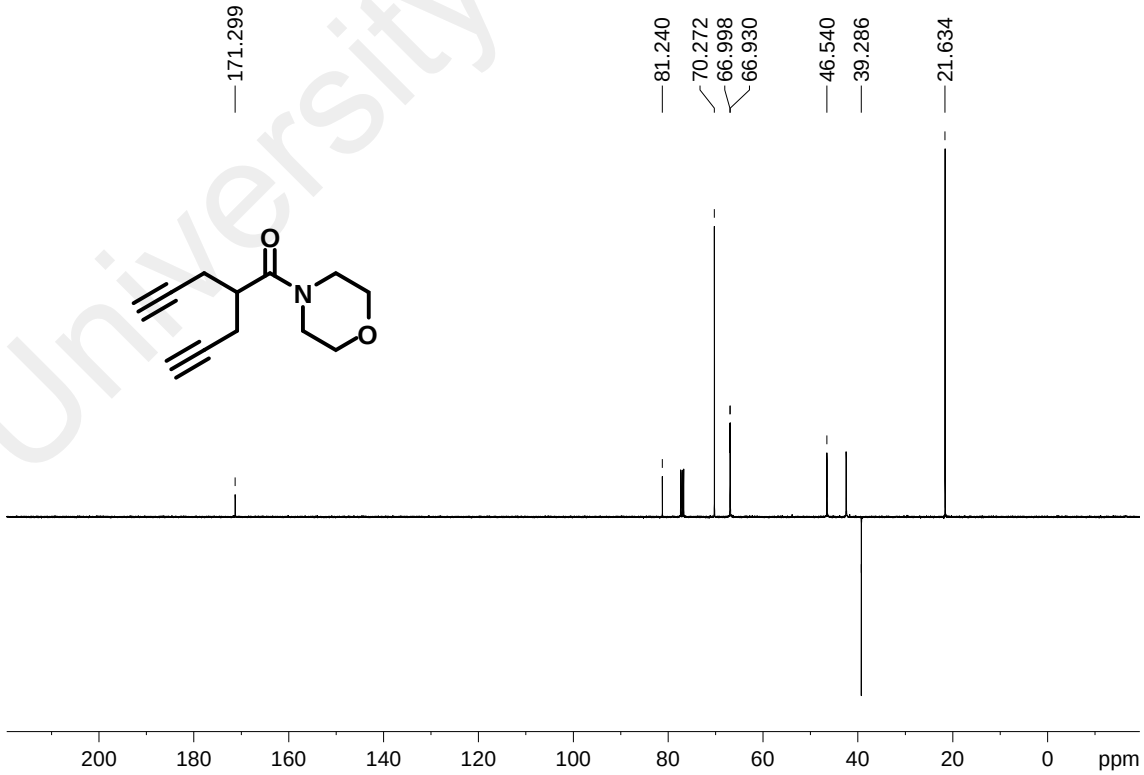


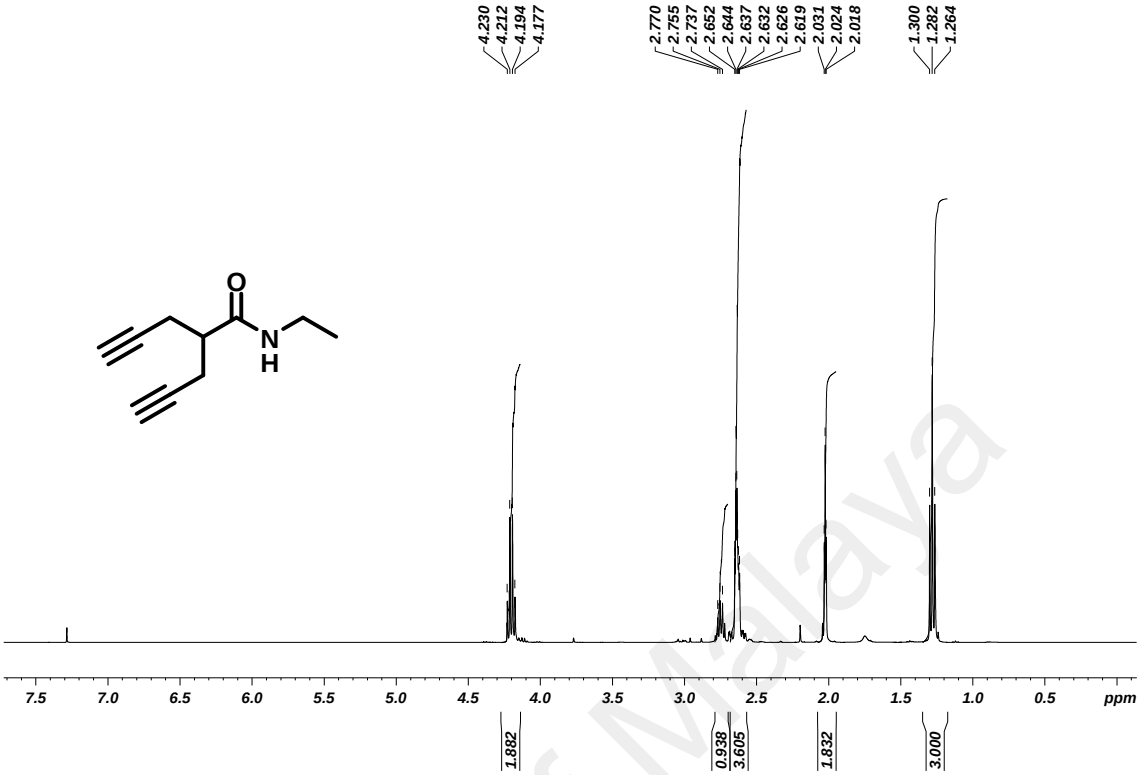


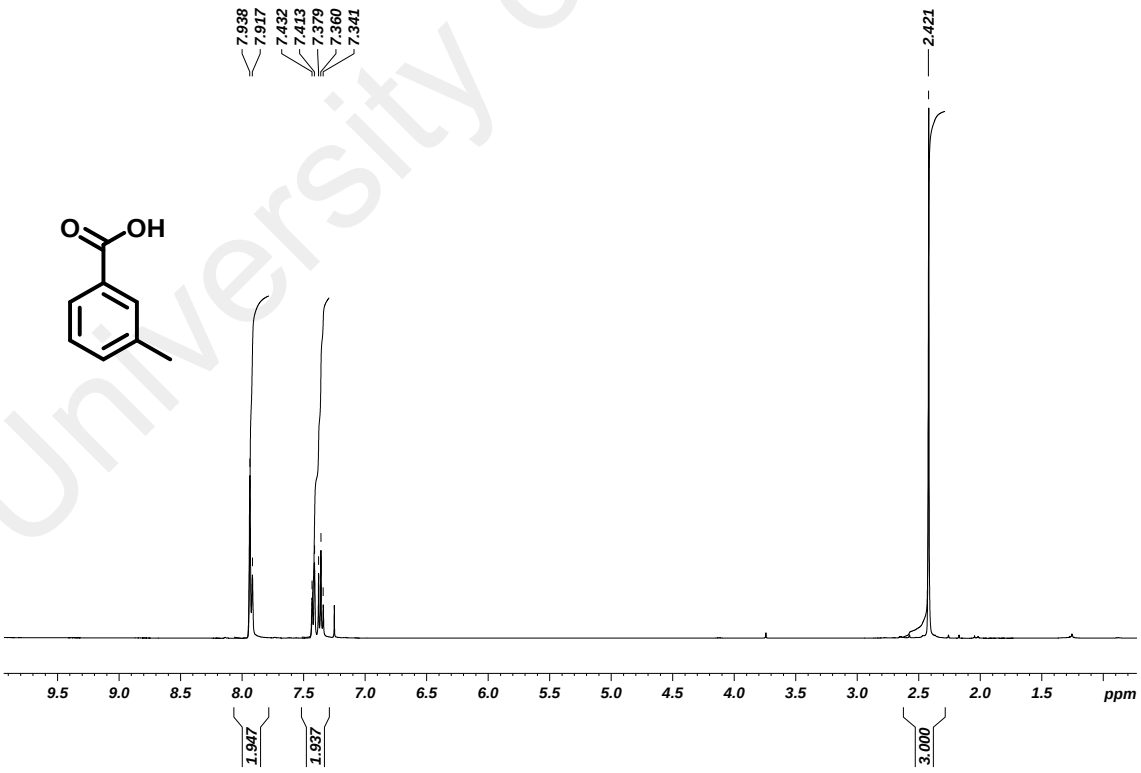


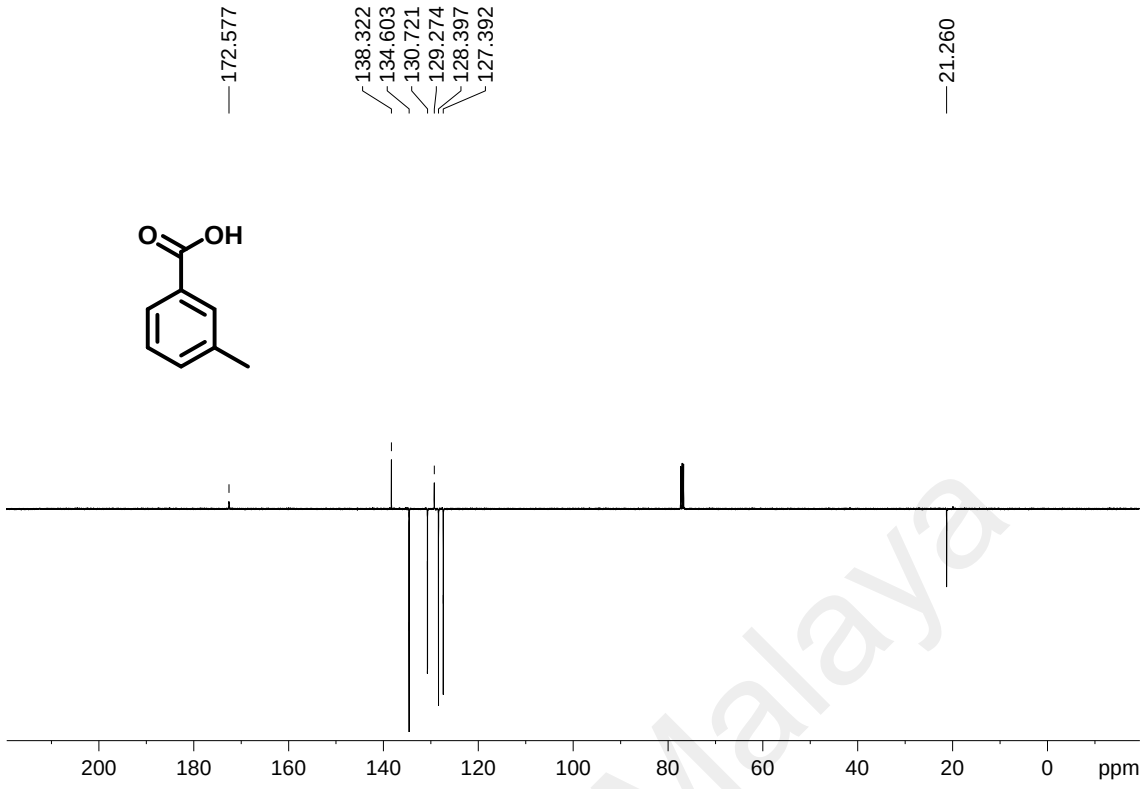
Appendix B: NMR (^{1}H and ^{13}C/Pendant) spectra for unusual base-induced cyclization of dipropargylic systems to m-substituted toluenes

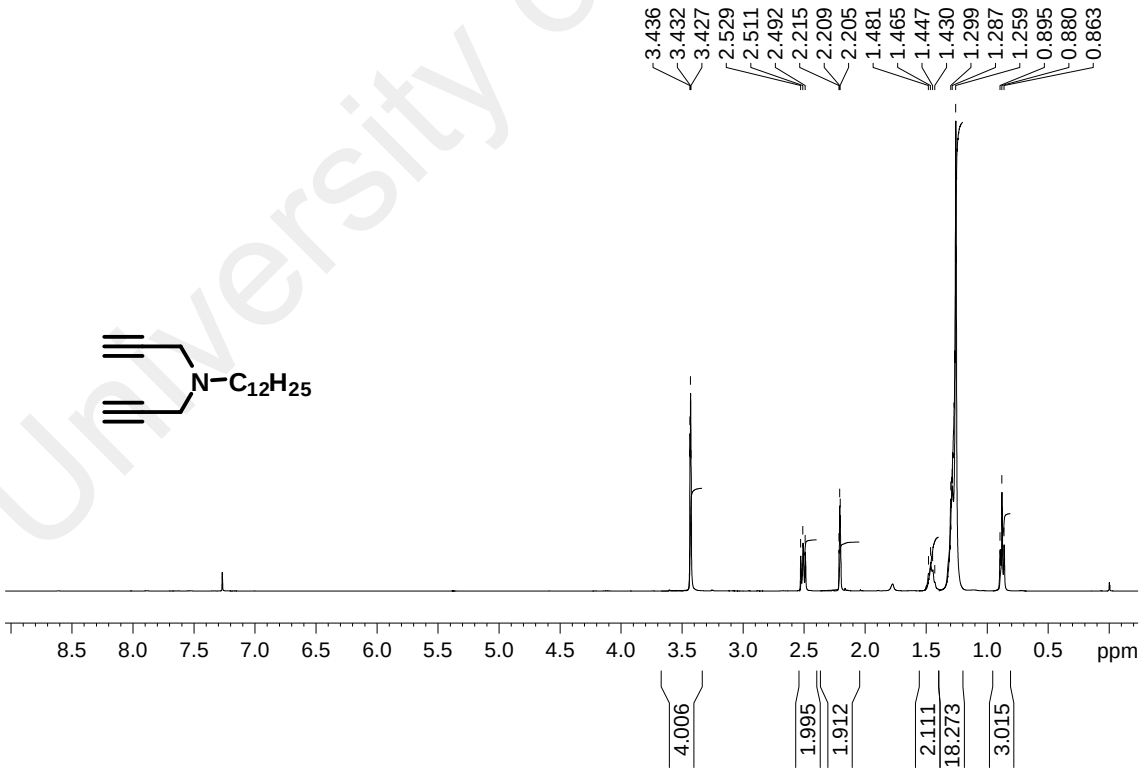


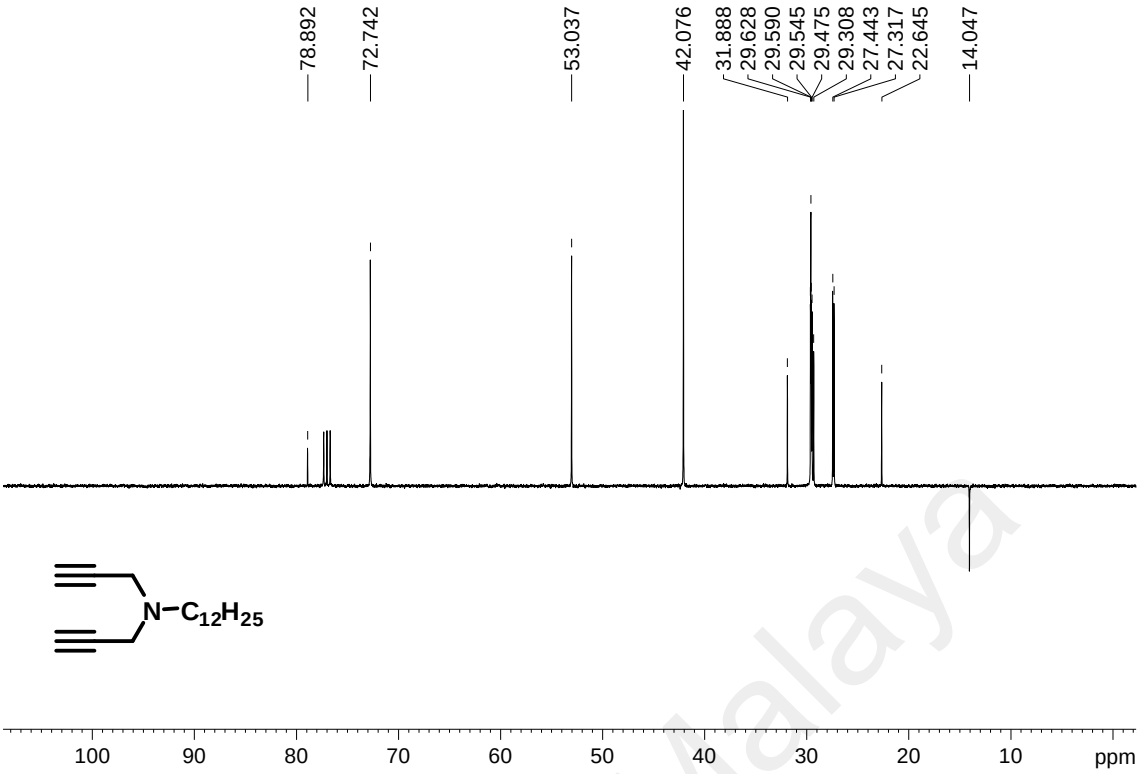




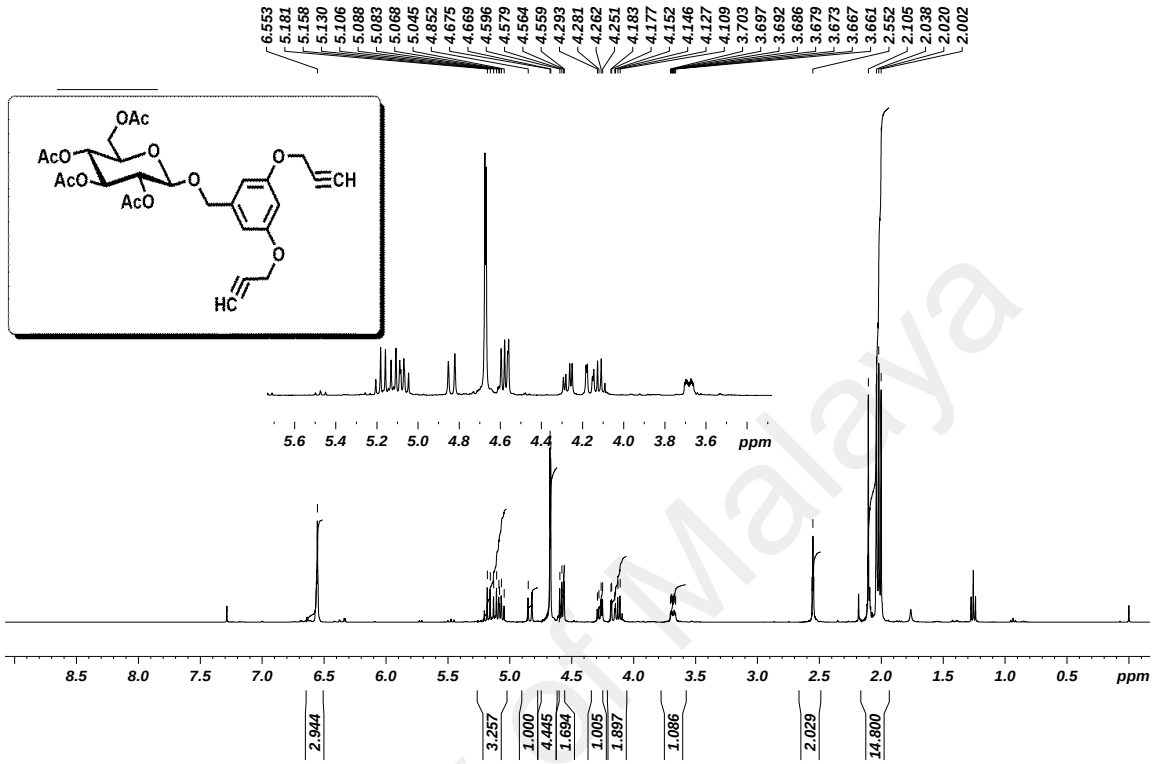


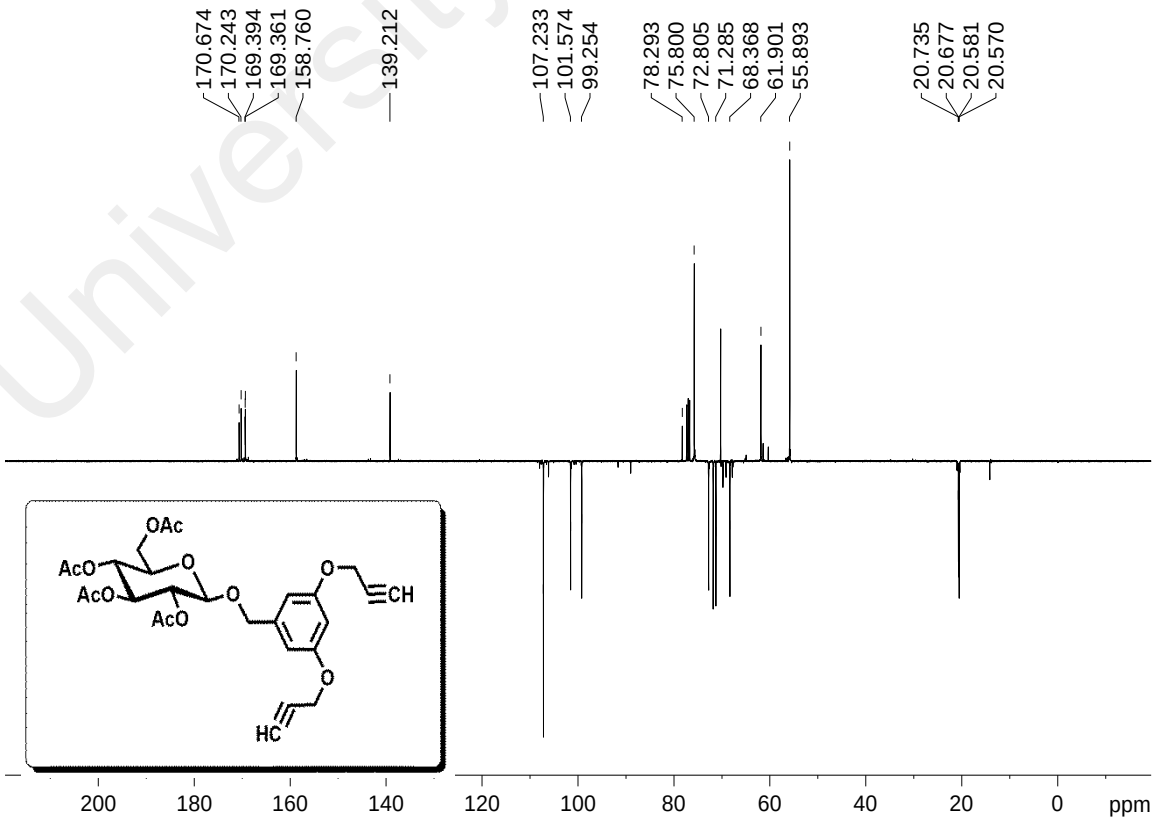


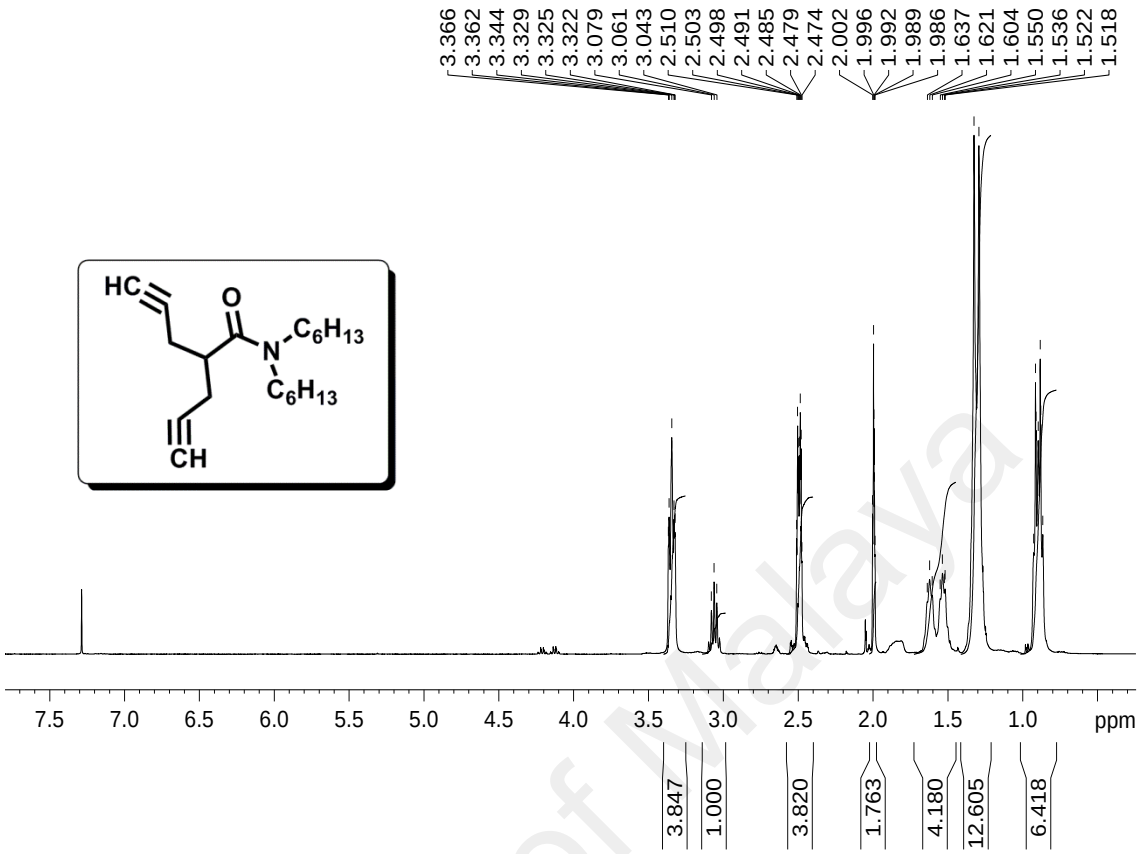


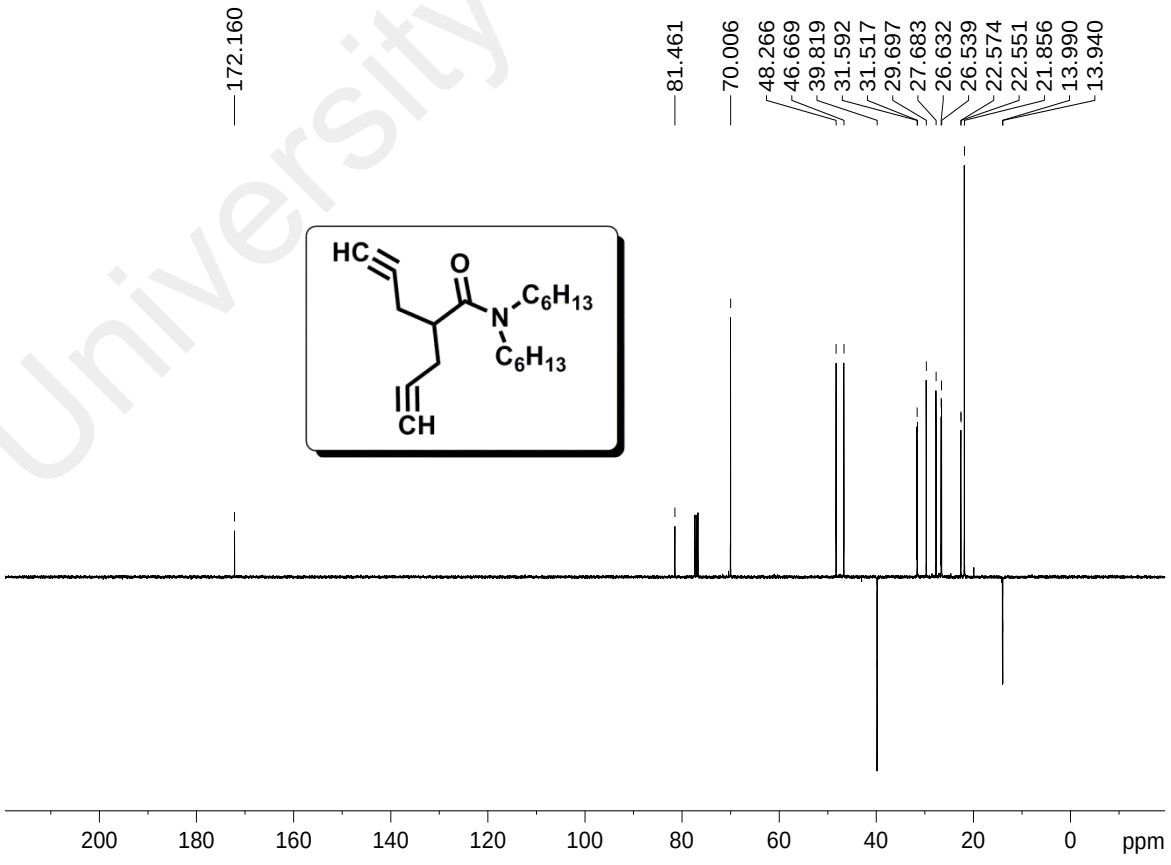


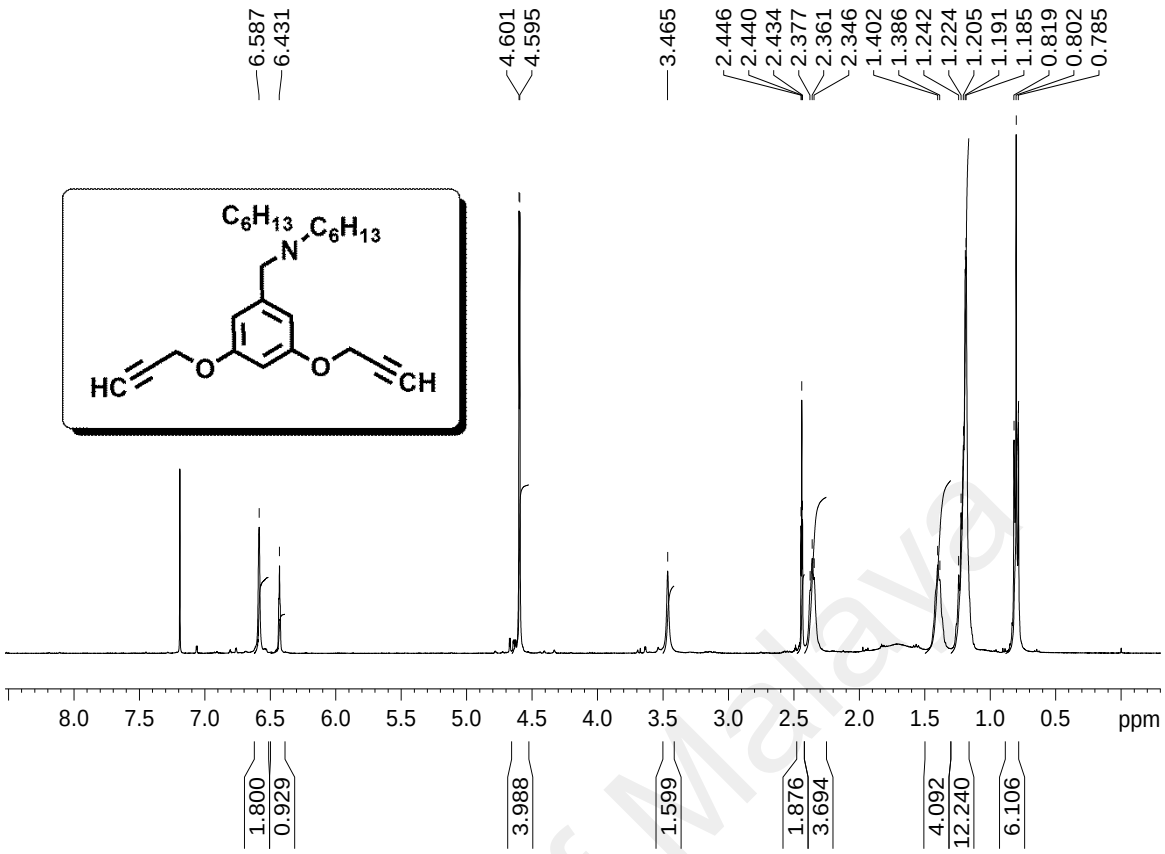
Appendix C: NMR (^{1}H and ^{13}C/Pendant) and maldi tof mass spectra for Unexpected mono-coupling "click chemistry'' of di-terminal alkyne

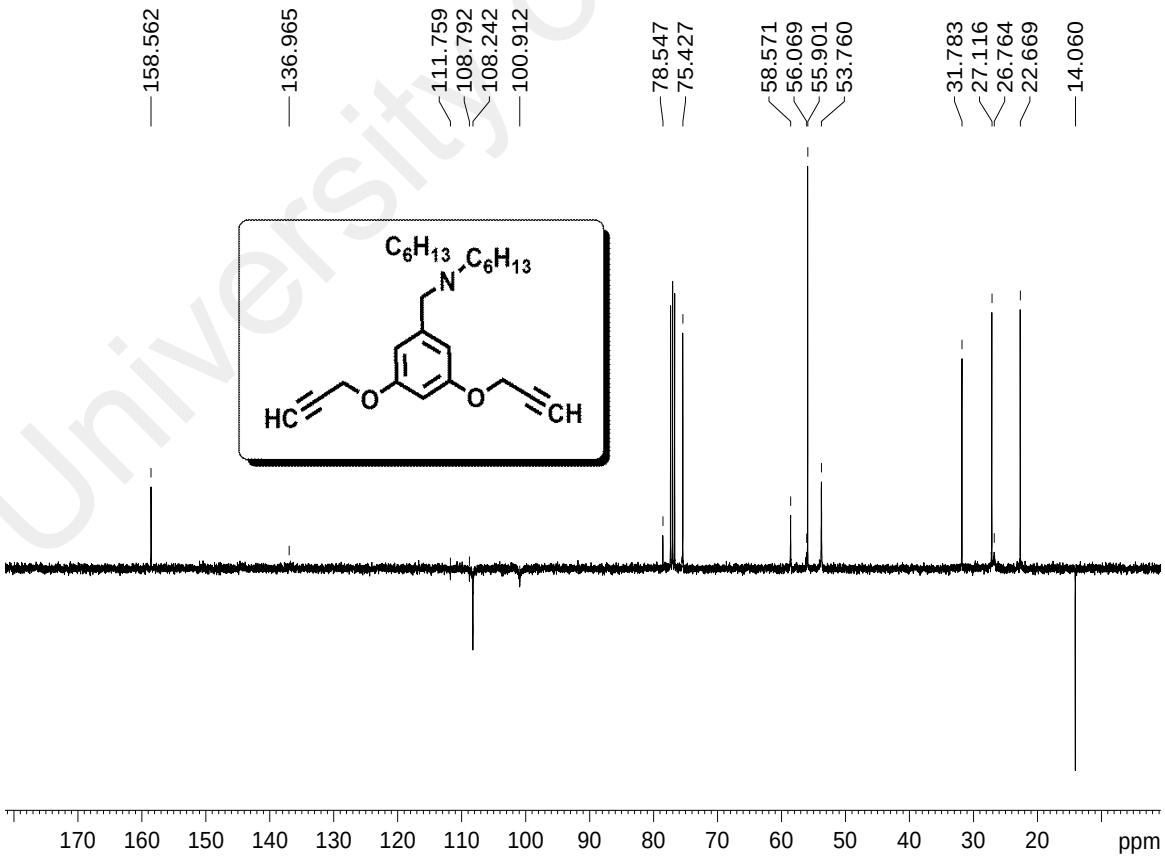


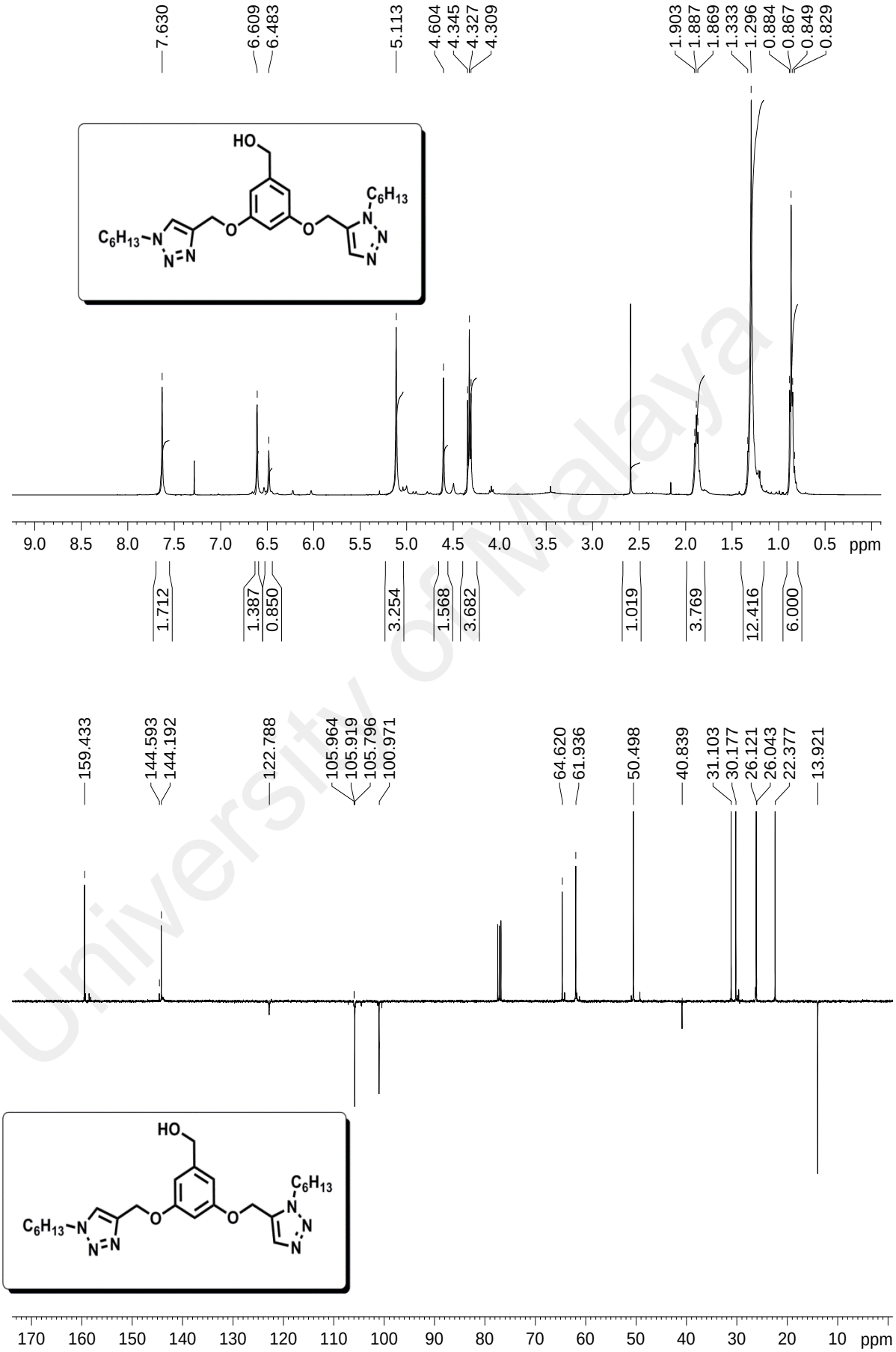


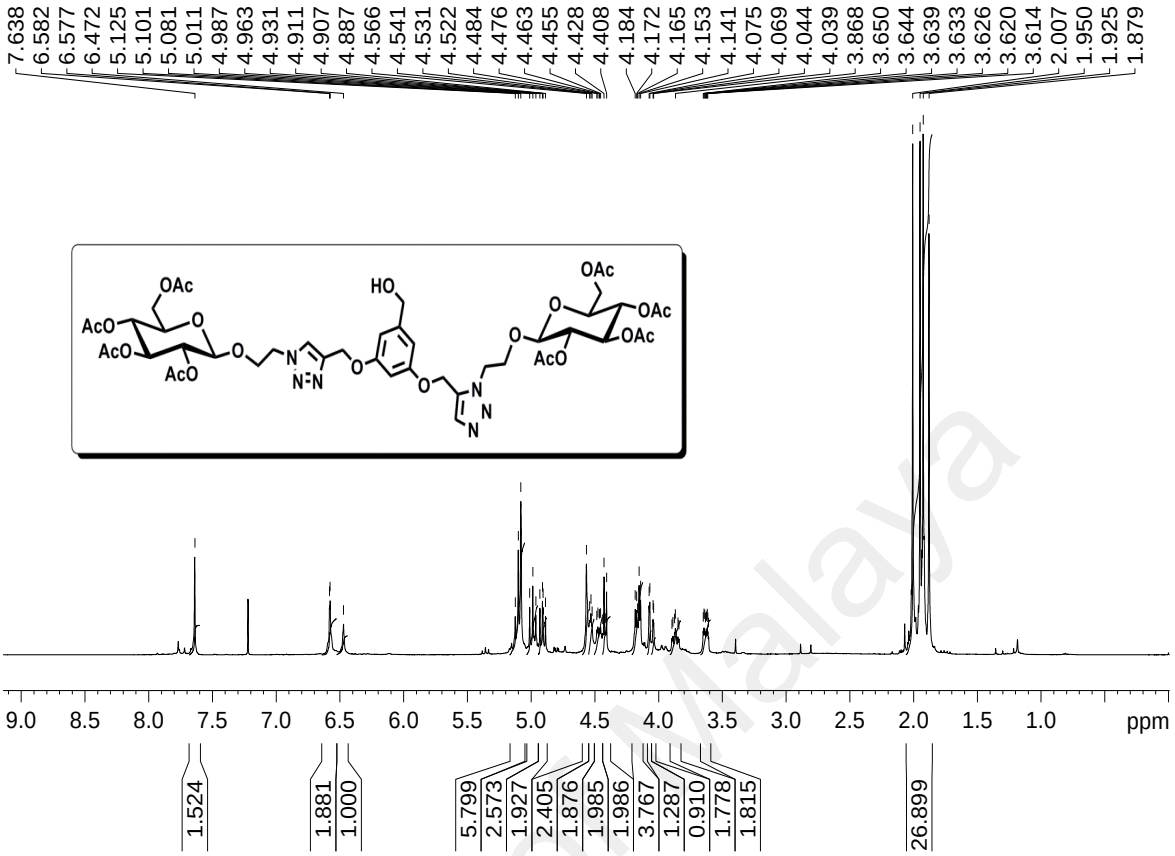


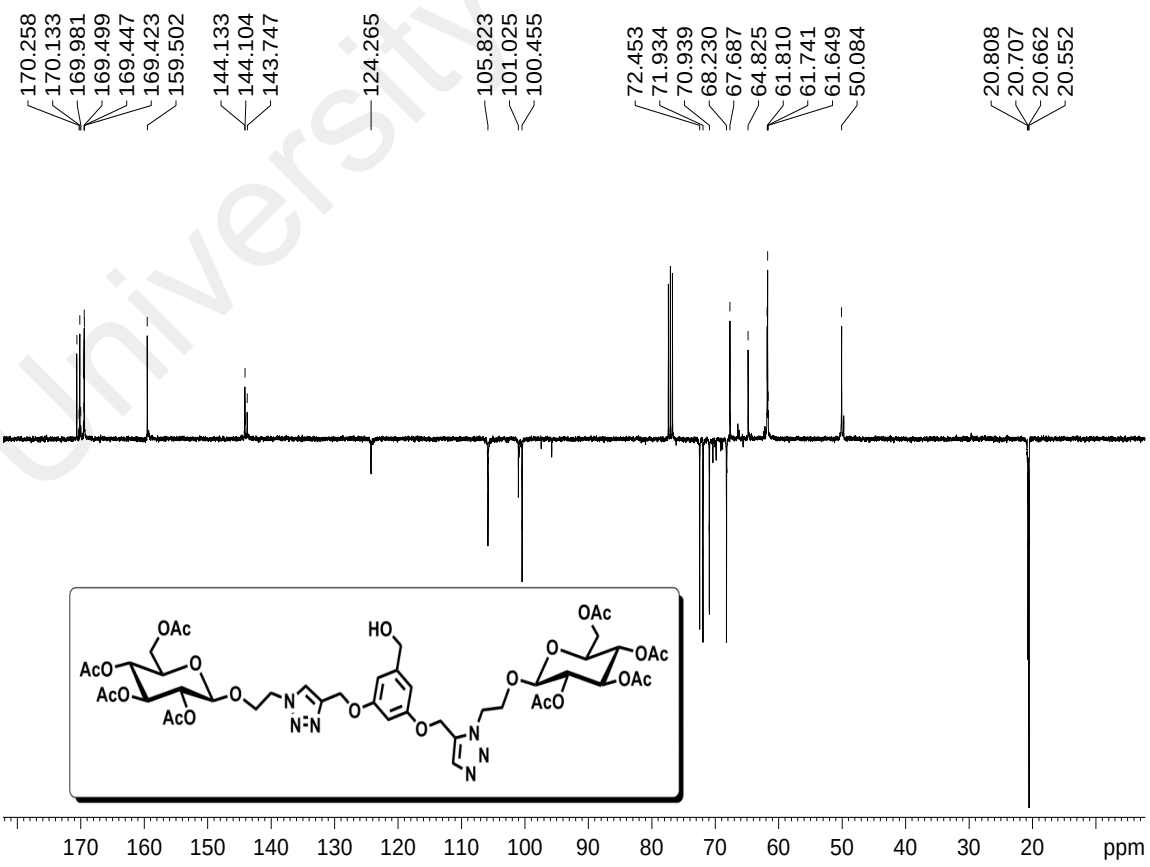


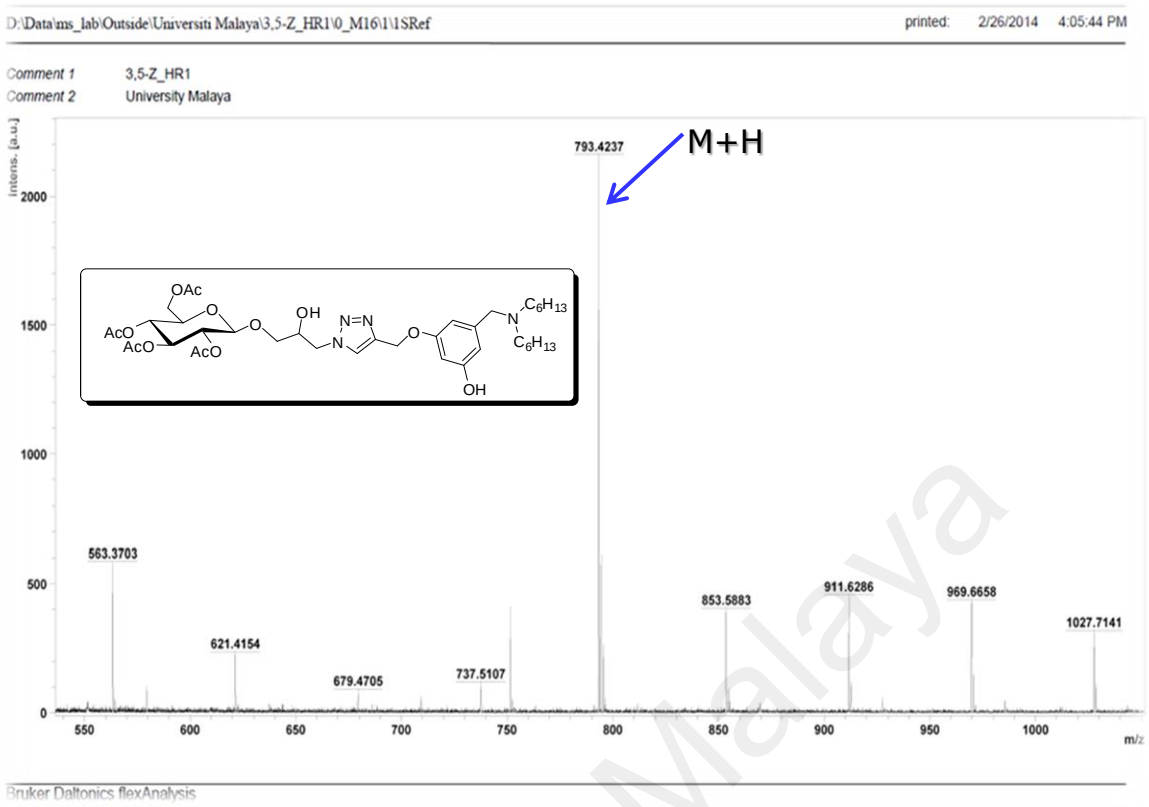


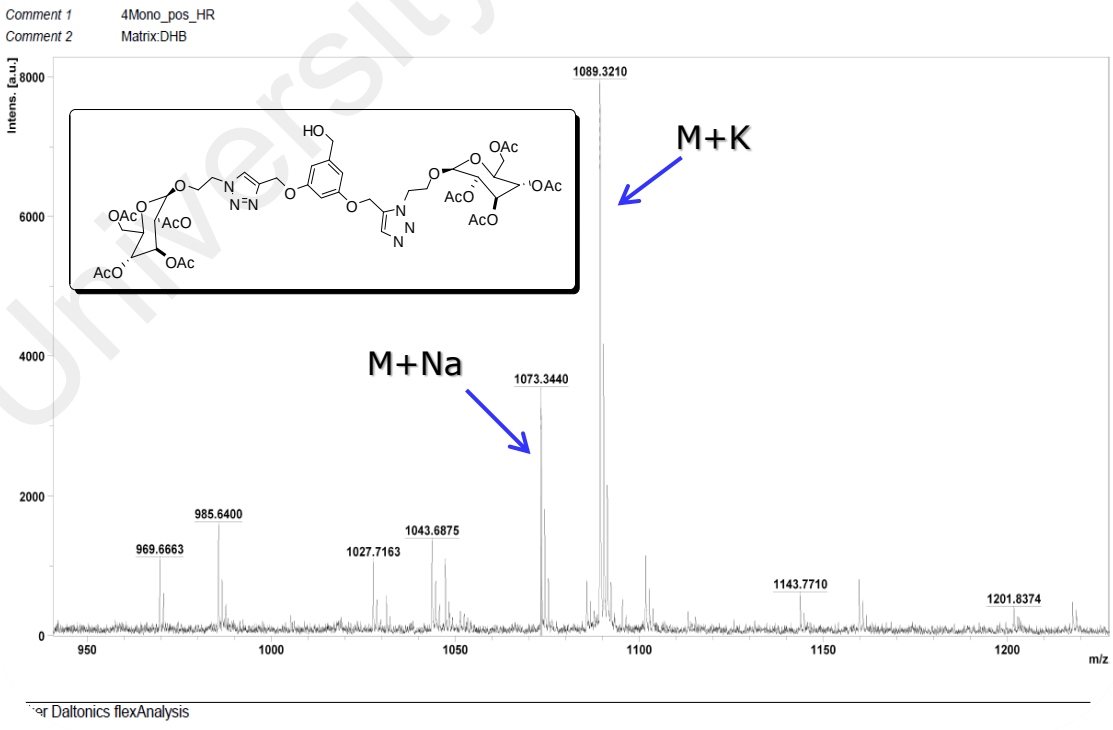






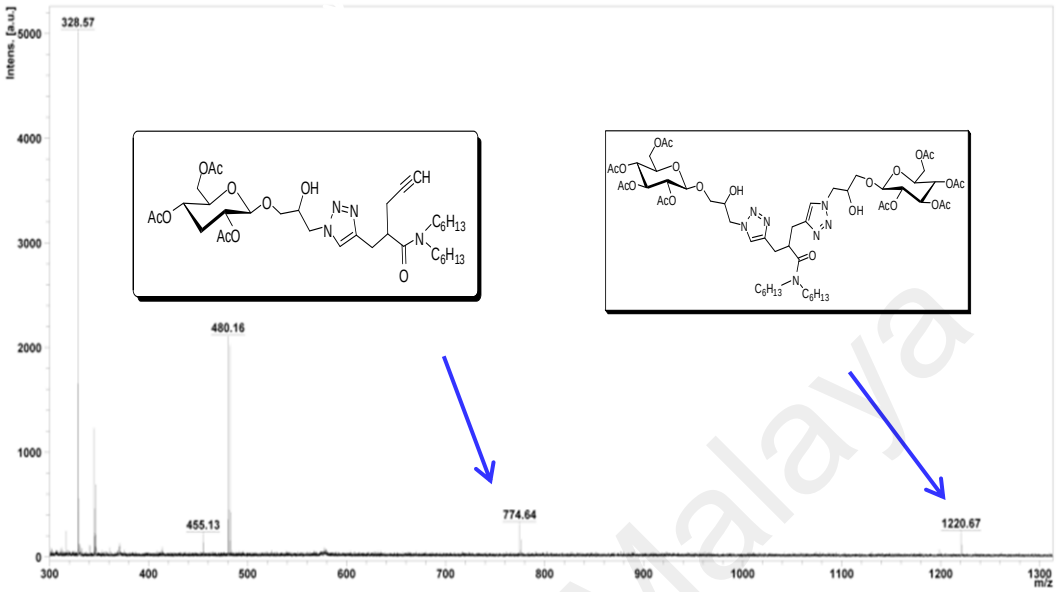






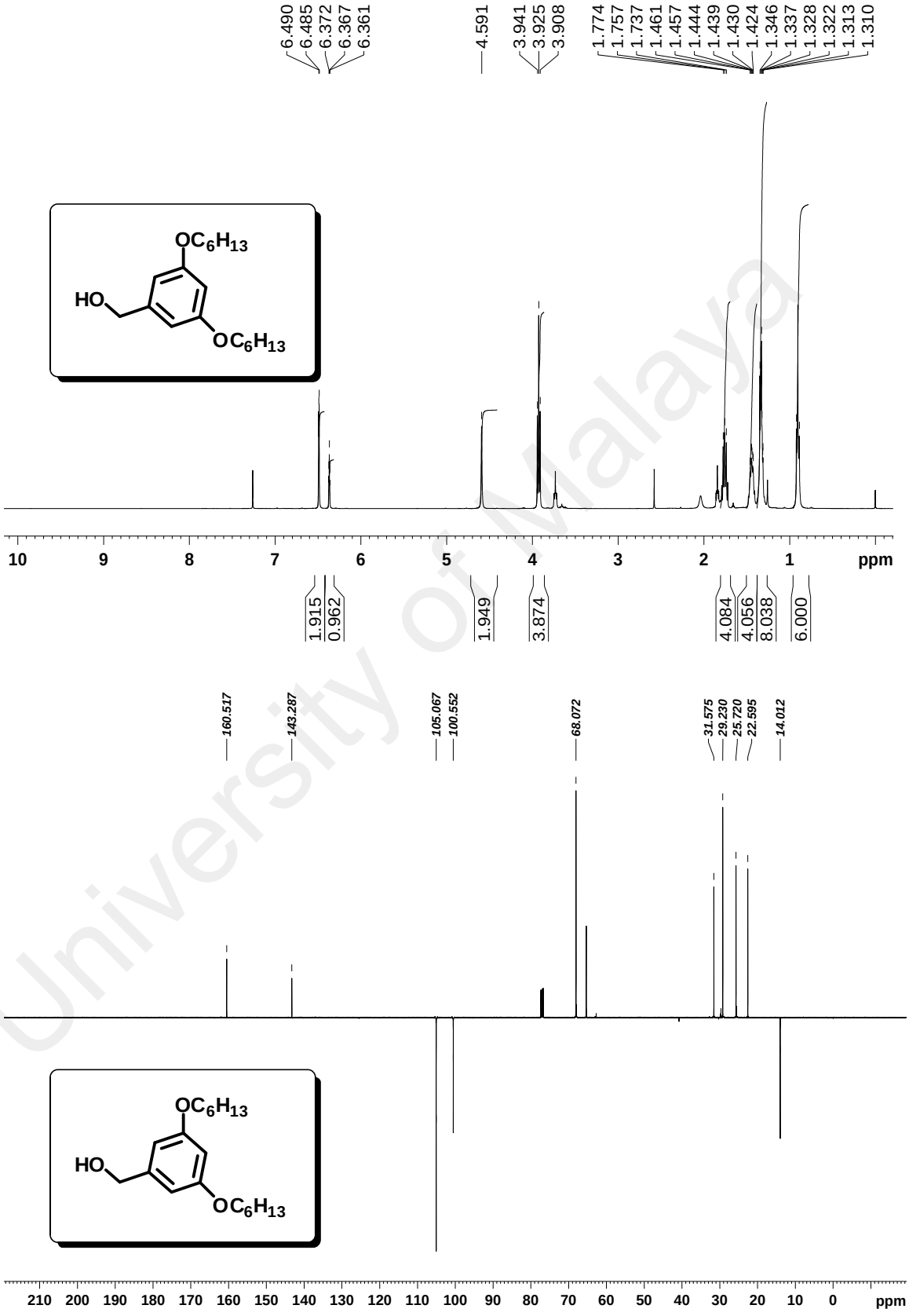
D:\Data\ms_lab\Outside\Universiti Malaya\MZ_pos\0_J3\1\1SRef printed: 1/8/2014 11:47:46 AM

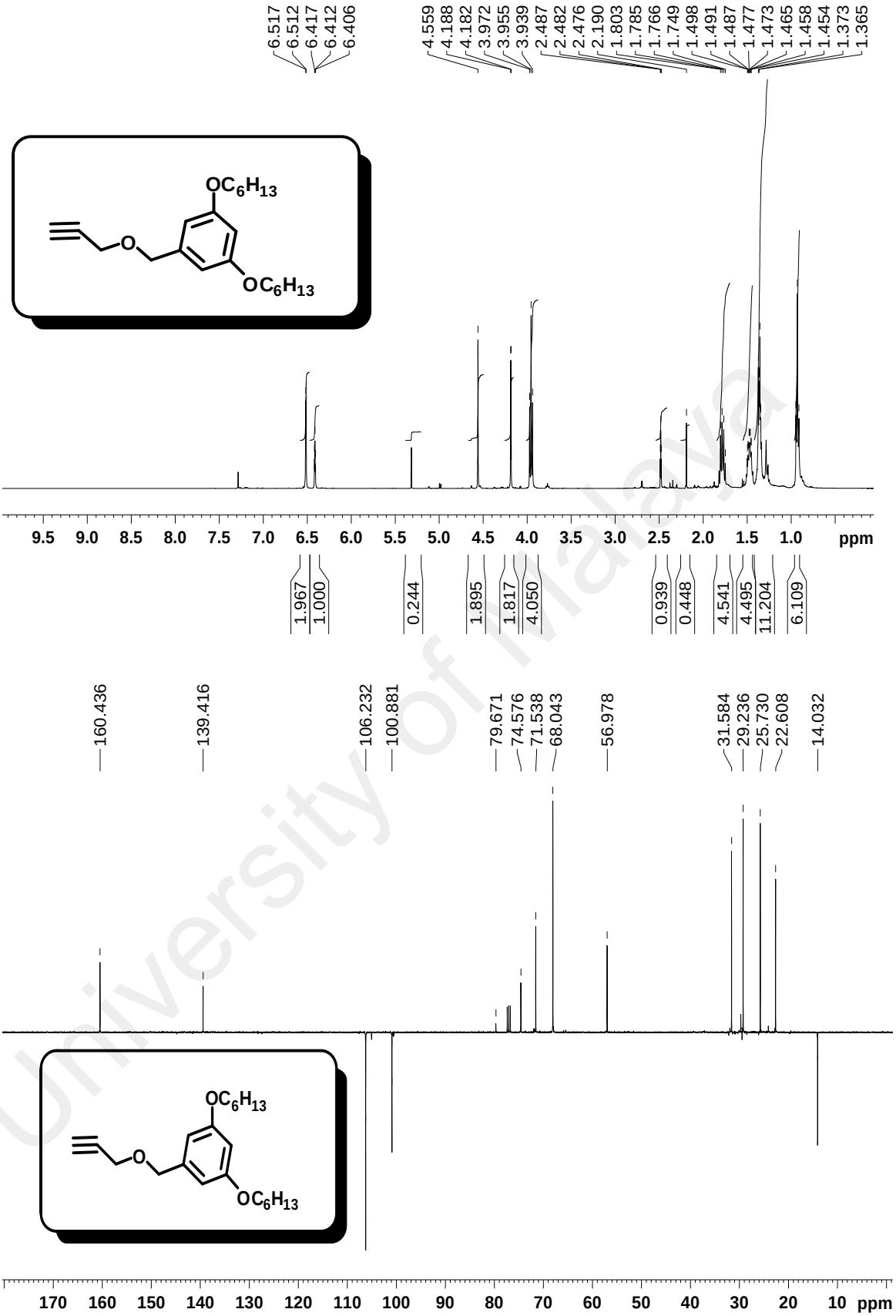
Comment 1 MZ_pos
Comment 2 Matrix:DHB

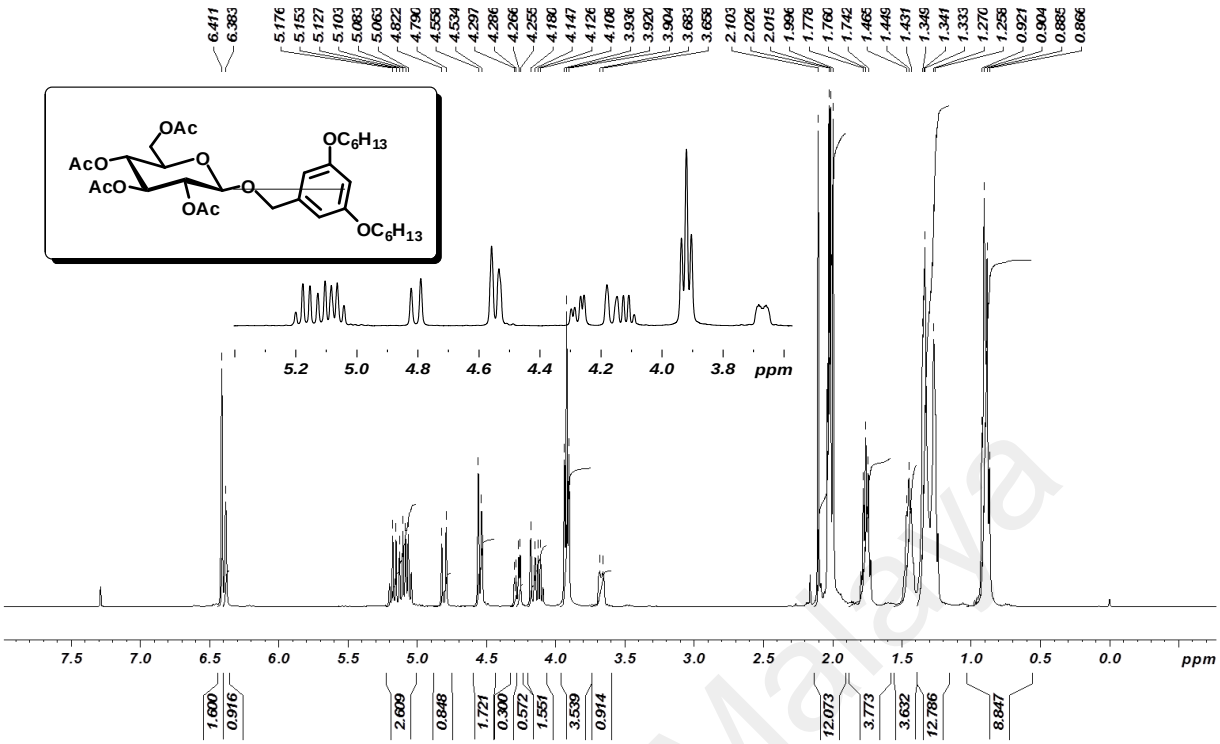


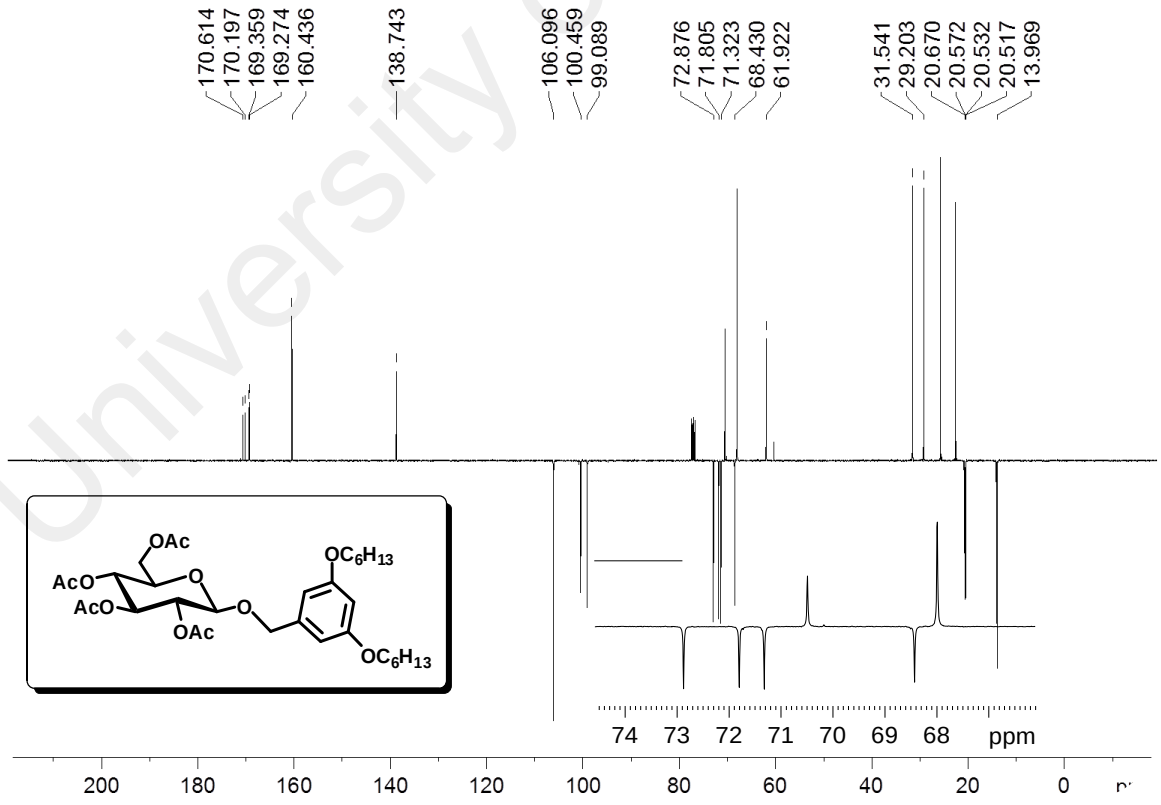
Bruker Daltonics flexAnalysis

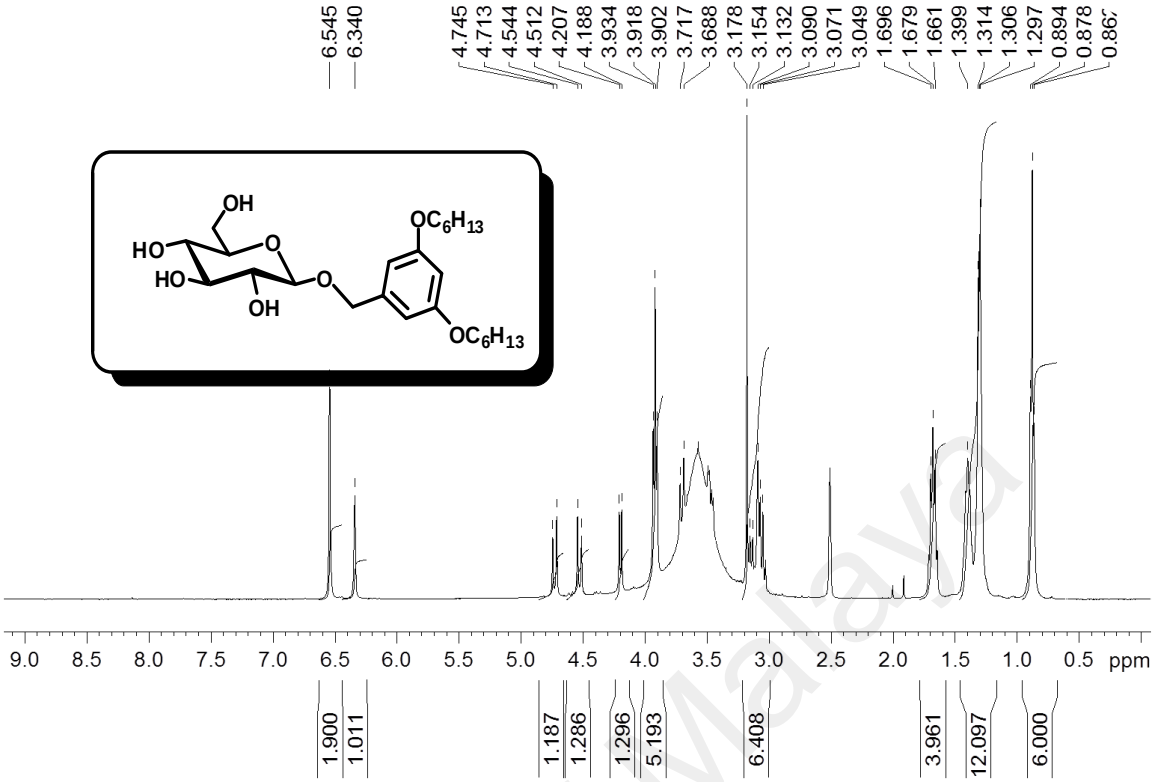
Appendix D: NMR (^{1}H, ^{13}C/Pendant and HMQC) spectra for the effect of aromatic groups on the behaviour of reverse Y-shaped sugar-based surfactants

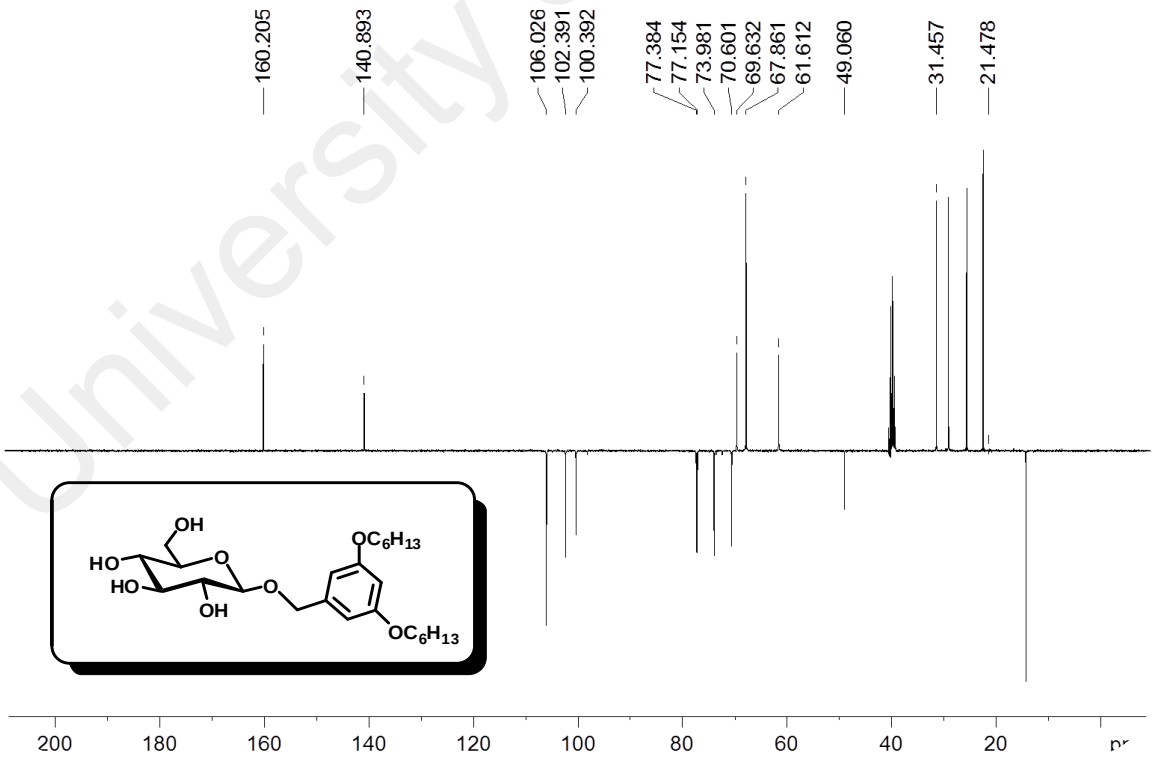


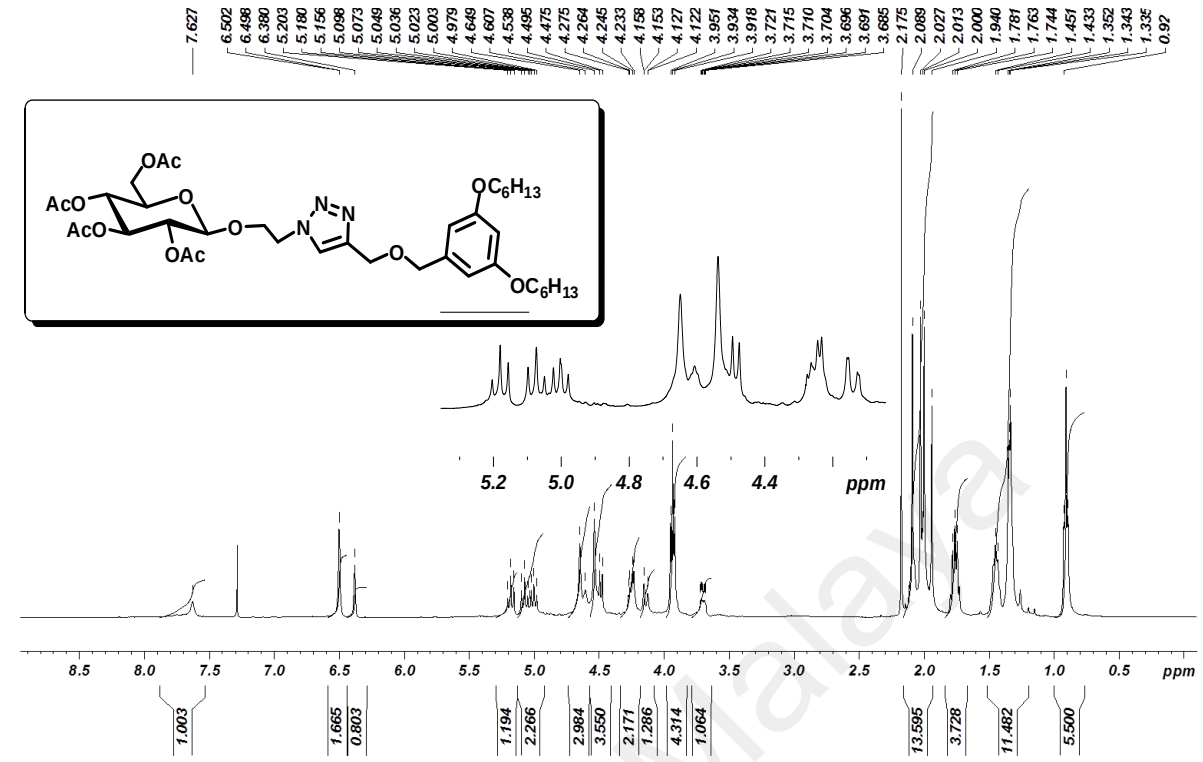


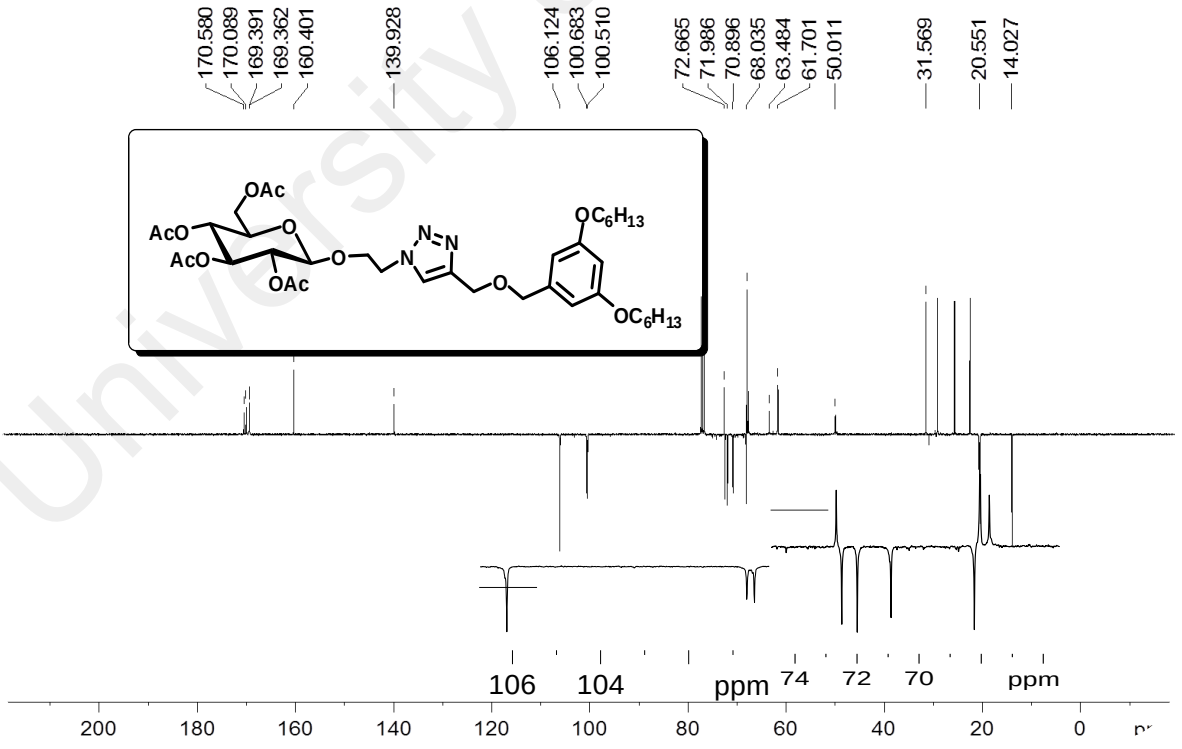


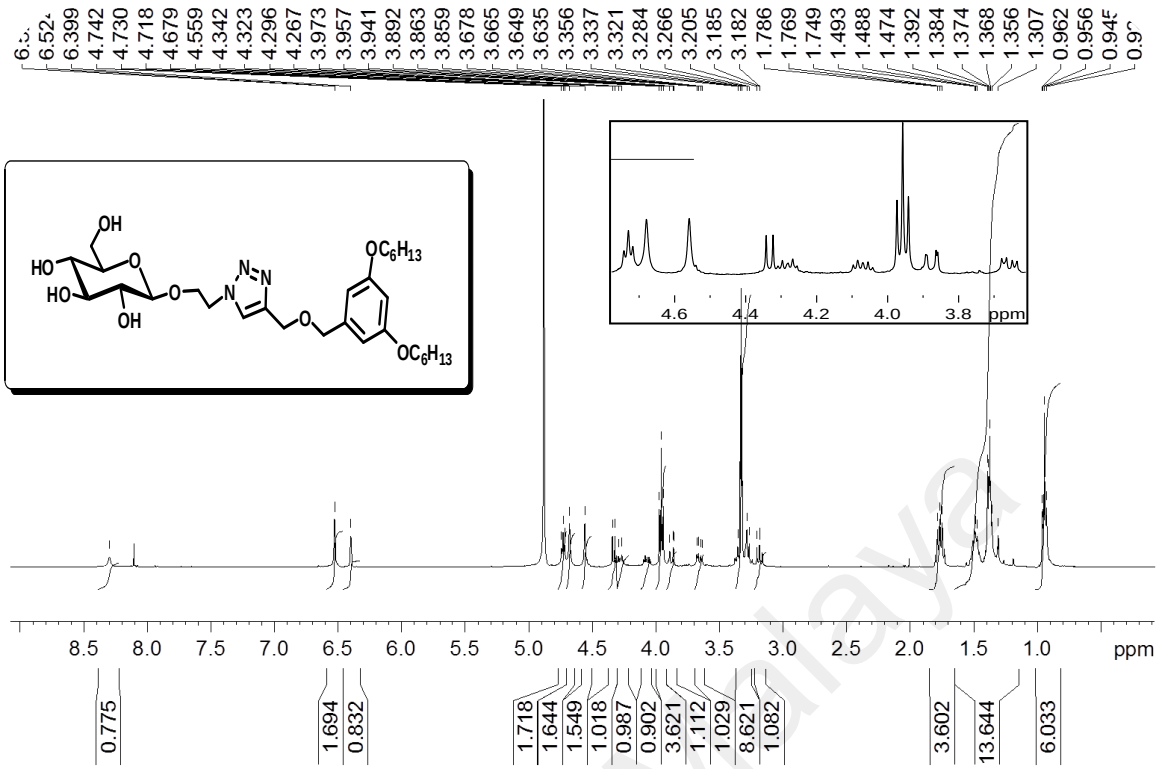


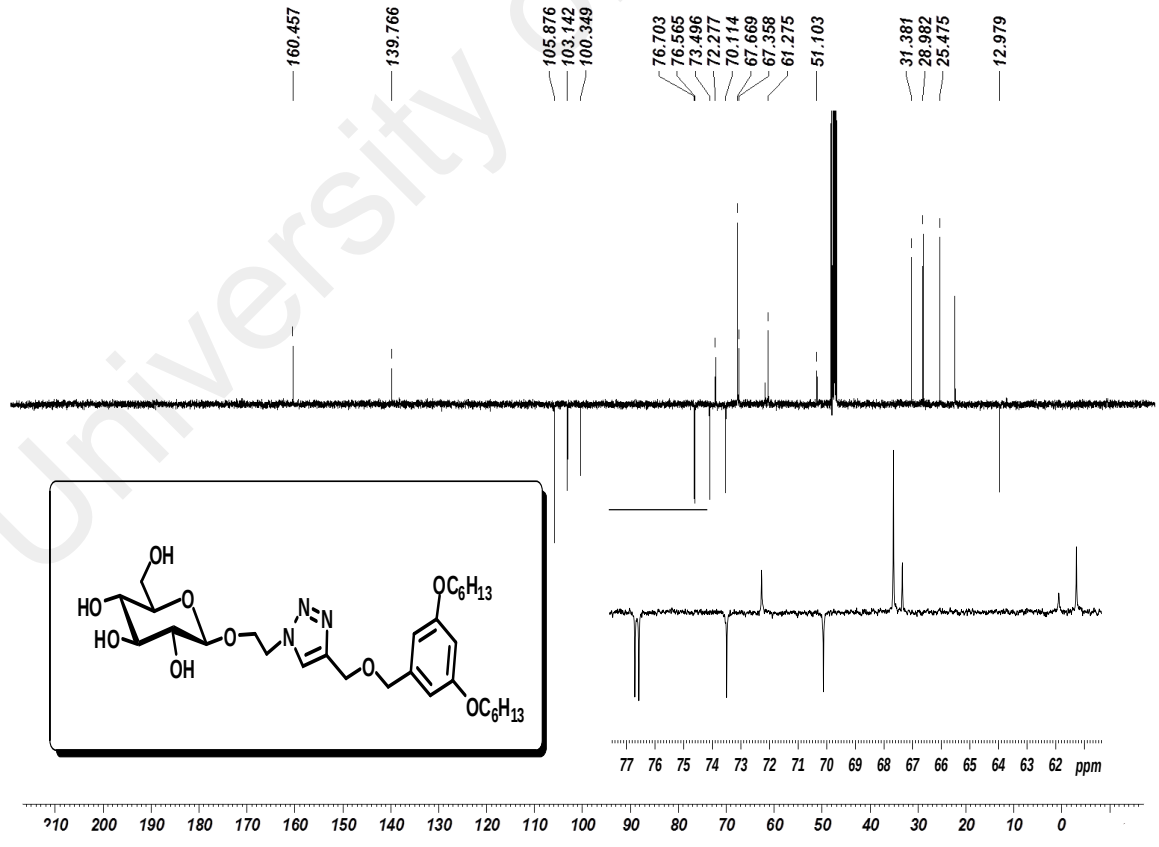


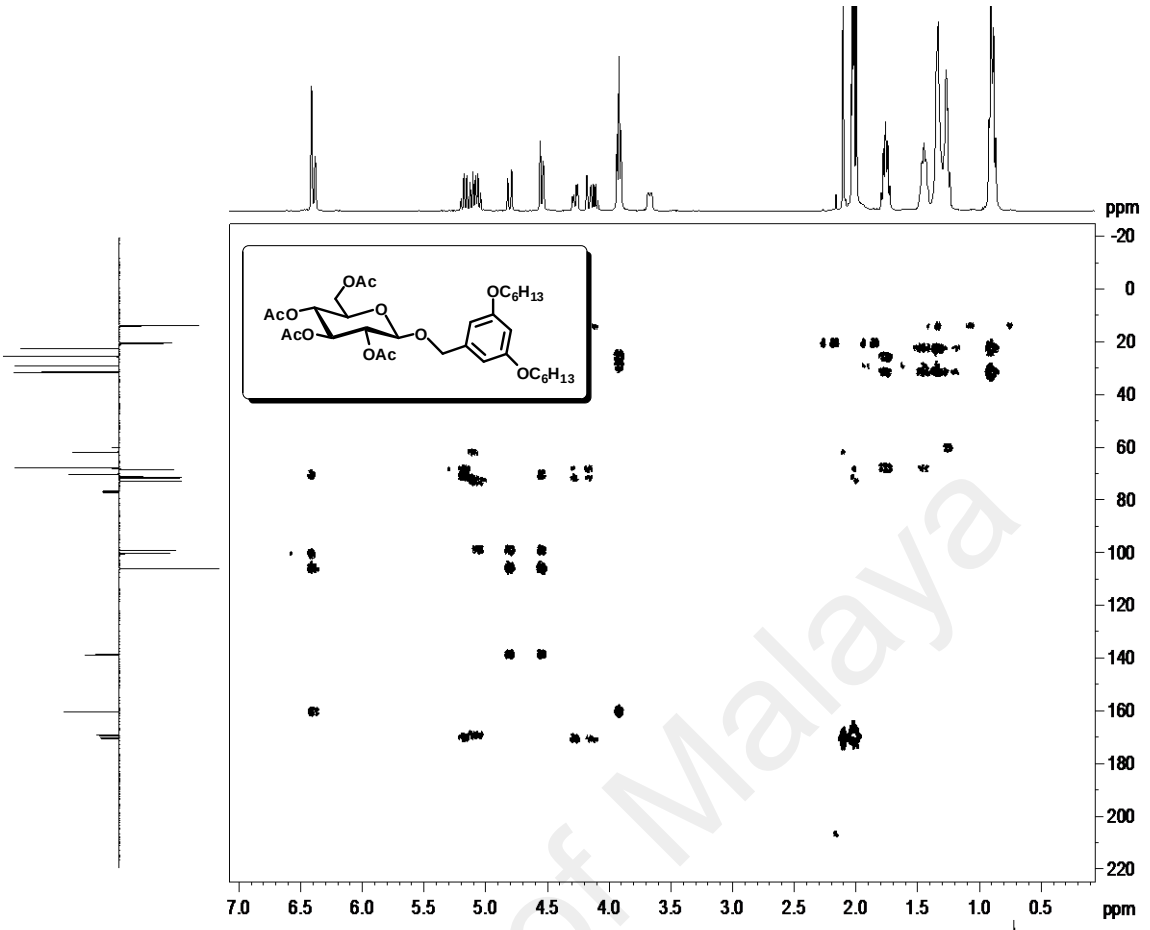


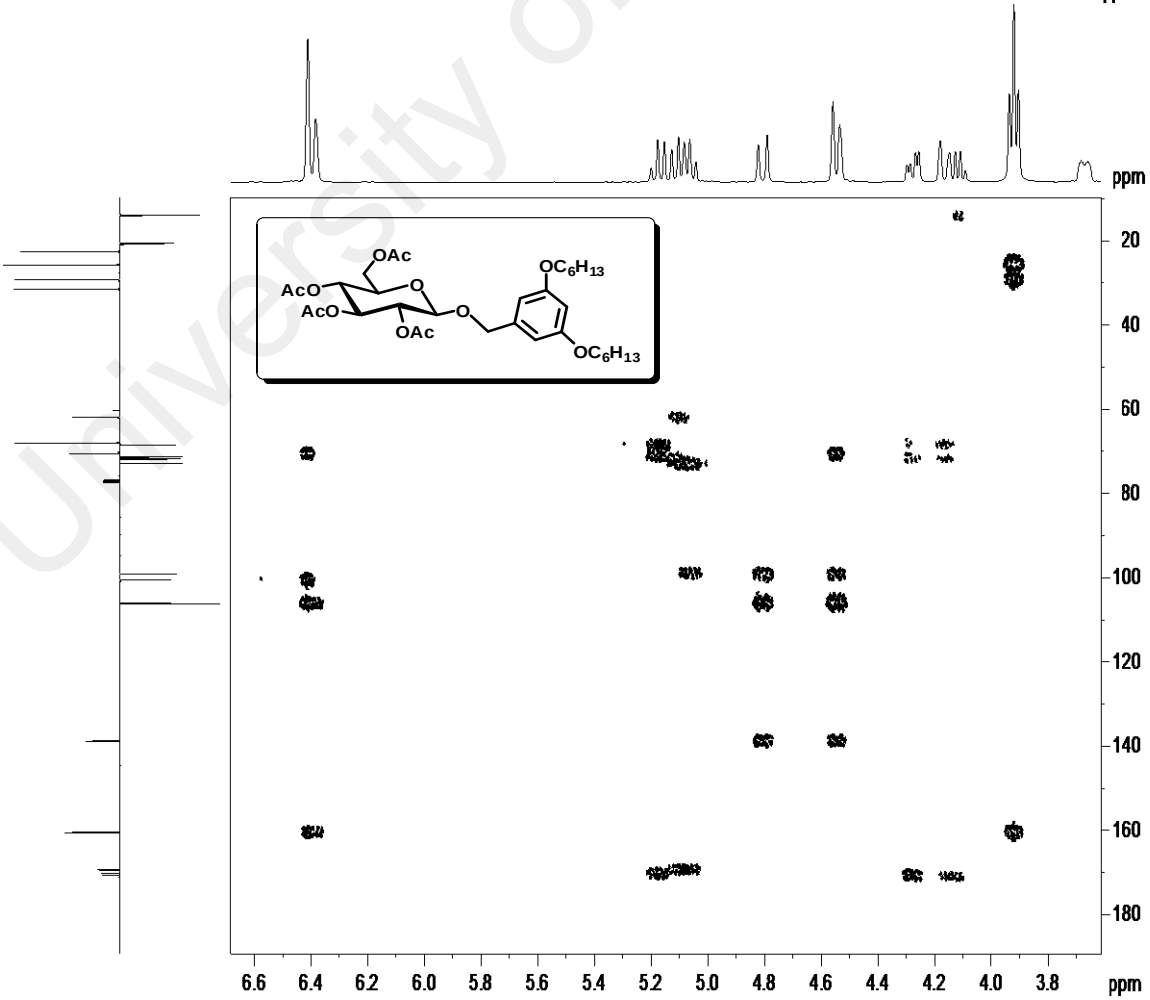


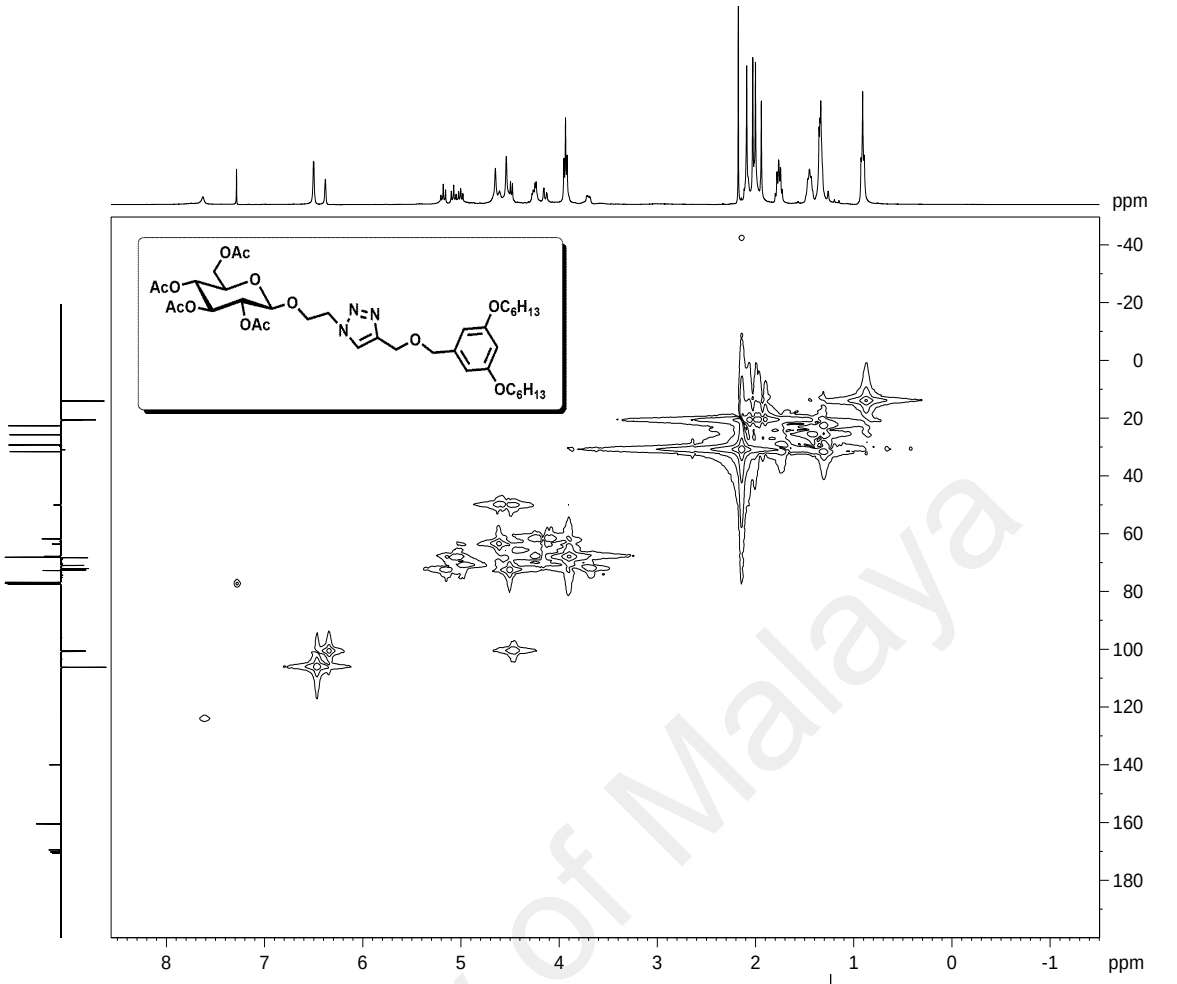


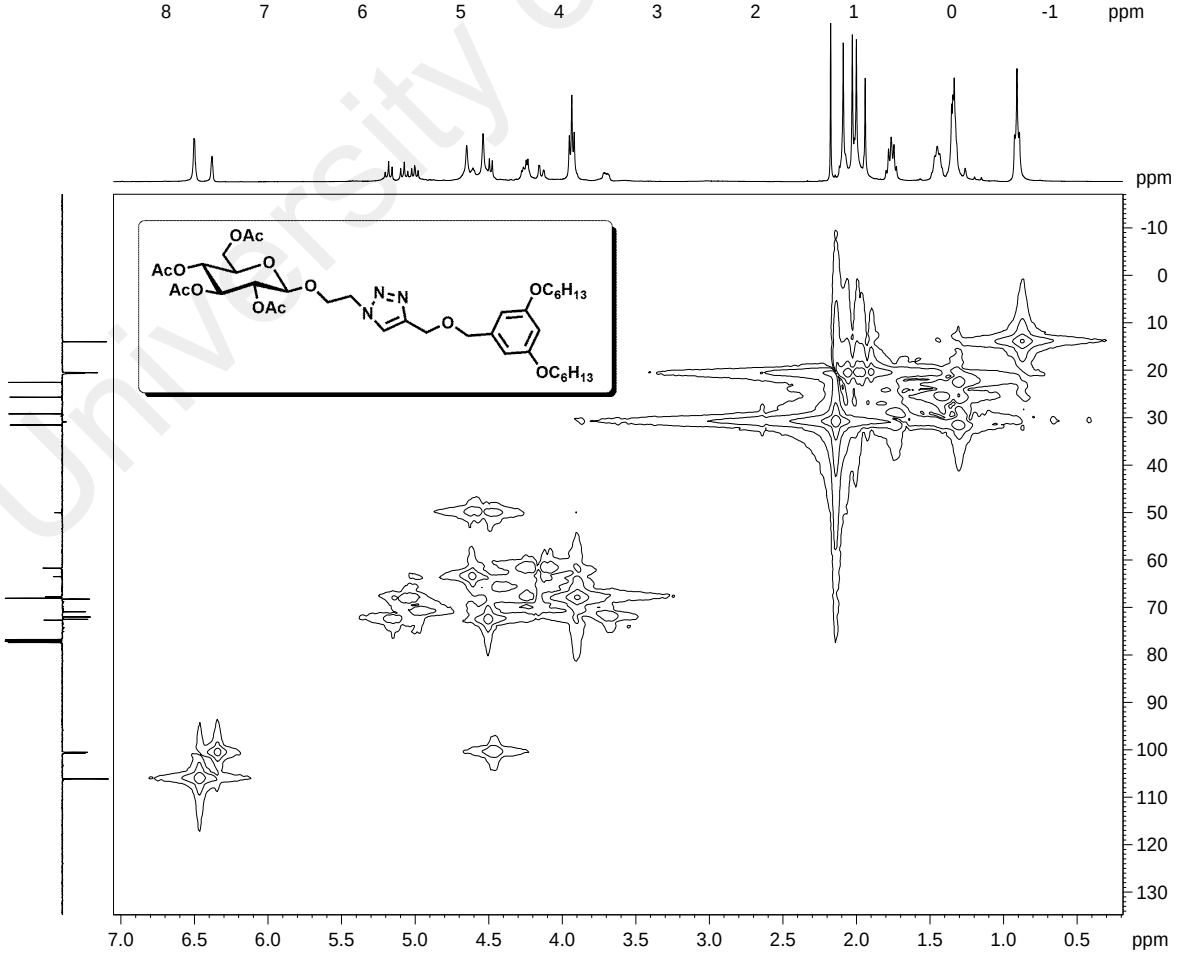












Appendix E: NMR (^{1}H, ^{13}C/Pendant and HMQC) spectra for a new class design of X-shape sugar-based surfactants by "click" chemistry and studies their self-assembling