STUDY OF NON-COVALENT INTERACTIONS IN THE SELF-ASSEMBLY OF CARDANOL AZODYE AMPHIPHILES

A Project Report submitted for the Partial fulfilment of
the requirement for the degree of

MASTER OF SCIENCE IN CHEMISTRY

By

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SEPTEMBER 2022

DEPARTMENT OF CHEMISTRY

PAVANATMA COLLEGE, MURICKASSERY

CERTIFICATE

This is to certify that the project work entitled **“STUDY OF NON-COVALENT INTERACTIONS IN THE SELF-ASSEMBLY OF CARDANOL AZODYE AMPHIPHILES”** is a bonafide report of the work carried out Ms. Arya Murali, at Nirmala College, Muvattupuzha under the supervision of Dr. Jyothish Kuthanapillil, for the partial fulfillment of the degree of Master of Science in Chemistry from Pavanatma College, Murickassery.

Place : Murickassery

Date :

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DECLARATION

I, Arya Murali**,** hereby declare that this project work entitled as **“STUDY OF NON-COVALENT INTERACTIONS IN THE SELF-ASSEMBLY OF CARDANOL AZODYE AMPHIPHILES”**, submitted to Pavanatma College, Murickassery for the partial fulfilment of the requirements for the Master’s Degree in Chemistry, is a record of original work done by me during the study period at the college, under the guidance of Dr. Jyothish Kuthanapillil, Assistant Professor, Department of chemistry, Nirmala college , Muvattupuzha.

Murickassery **Arya Murali**

Date:

ACKNOWLEDGEMENT

With deep regards and profound respect I take this opportunity to express my deep sense of gratitude and indebtedness to my project guide **Dr. Jyothish Kuthanapillil**, Assistant Professor, Department of Chemistry, Nirmala College, Muvattupuzha for giving me an incredible opportunity to carry out my project in a fascinating area of chemistry. The blessing, help and guidance given by him from time to time carried me a long in the journey of life on which I am about to embark.

I also take this opportunity to express a deep sense of gratitude to **Mr. Saji K Jose**, Head of the Department of Chemistry, Pavanatma College, Murickassery for allowing me to be at Nirmala College, Muvattupuzha for my project. Moreover, I am grateful to **Ms. Ardra C Mathew**, Class Tutor for helping to choose the right place.

I owe my sincere thanks to **Ms. Anjali Raju** for her endless support, suggestions, inspiration and patience which helped in guiding me in the right direction.

I would also acknowledge my family, friends and teachers for their complete support and encouragement.

Last but not the least; I express my heartfelt gratitude to the Lord Almighty for strengthening me to work hard and for the endless blessing showered on me throughout my project work.

Arya Murali

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1. INTRODUCTION

To date, a wide range of industrial materials such as solvents, fuels, synthetic fibers and chemical products are being manufactured from petroleum resources. However, questions on environmental safety/ pollution about the use of petroleum resources necessitate the search for alternate resources and have opened a new manufacturing paradigm – one that will spawn "biorefineries" as opposed to oil refineries. The environmental impact of such biorefineries will be low (fewer harsh chemicals, less toxic waste streams), and their energy consumption will also be much lower than conventional chemical plants. Moreover, biobased organic synthesis have distinct advantages for the generation of new building blocks such as, a) they are obtainable from renewable resources, b) they are likely to be biodegradable and non-hazardous to the environment, and c) natural compounds have a wealth of structural diversity that has yet to be explored. These inherent advantages of biobased building blocks and biocatalysis methods have led to a rise in interest in plant/crop based materials and made them at the top in the priority list for future technologies.

In this background, **cardanol**, obtained from Cashew Nut Shell Liquid (CNSL), a side product of the cashew industry, is the active constituent of CNSL, which is cheap, and renewable natural source. Cashew nut shells (CNS), which are agro - wastes from cashew nut processing factories, have proven to be among the most versatile bio-based renewable materials in the search for functional materials and chemicals from renewable resources. Hence, CNSL became one of the few major and economic sources of naturally occurring phenols[1].

CNSL is essentially a mixture of four phenolic compounds namely anacardic acid, cardol, cardanol and 2-methylcardol.The vacuum distillation of cashew nut shell liquid finally affords cardanol. Cardanol is a yellow pale liquid comprising four meta-alkyl phenols differing by the degree of unsaturation of the aliphatic chain: saturated chains (SC) 8.4%, mono olefinic 48.5%, diolefinic 16.8% and triolefinic 29.33% chains[2,3]. Cardanol, a mixture of meta alkylphenols with variable degree of unsaturation attached to the benzene ring, is indeed a mixture of saturated (3-npentadecylphenol), monoolefinic [3-(n-pentadeca-8- enyl)phenol], diolefinic [3-(npentadeca-8,11-dienyl)phenol], and triolefinic [3-(n-pentadeca-8,11,14-trienyl)phenol]; remarkably in the mixture, both E and Z isomers are present, typically major ones are Z components.Cardanol is hydrophobic and remains flexible and liquid at very low temperatures; its freezing point is below −20 °C, it has a density of 0.930 g/mL, and boils at 225 °C under reduced pressure (10 mmHg)[4].

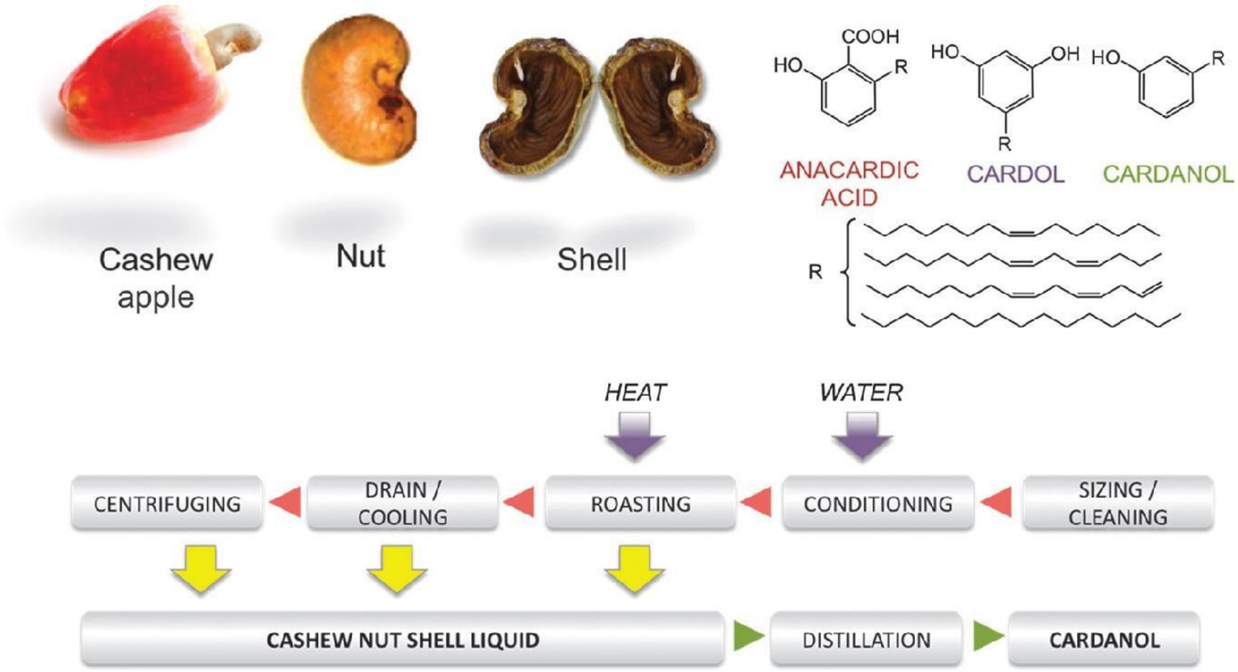

Figure 1.1: The synthesis of cardanol from CNSL

The major structural advantages of cardanol having reactive phenolic group and unsaturated hydrophobic alkyl side chain at the meta-position of phenolic group. Due to this unique nature, cardanol and its derivative could be recognized as amphiphilic building blocks with supramolecular architecture. Cardanol displays several biological activities including antimicrobial, antioxidant and antitumor however strong cytotoxicity of this kind of compound limits its application as lack of biocompatibility. Cardanol contributes to improved flexibility, good drying after baking, high electric insulation properties and thermal stability. These properties make Cardanol an effective substitute for the petroleum-based Phenol.

These mono/ di/ tri unsaturated components possess exciting functional flexibility due to three main structural and chemical features. First is the reactive phenolic –OH group offering synthetic flexibility, and second is the meta alkyl chain with non-isoprenoic cis double bonds attributing amphiphilic and lipidic character. Lastly, the aromatic ring allows for p–p stacking and functionalization. These features make cardanol a tenable precursor for chemical modifications to generate a library of amphiphiles and functional monomers. A variety of functional groups can be attached to the reactive phenoxy group of cardanol for further derivatization. Therefore, cardanol has remained a vital building block for the synthesis of various chemicals that find applications in fine chemicals, as well as in synthesis of functional materials and polymers.

The proposed work involves the rational design and synthesis of new amphiphilic building blocks from renewable resource monomer cardanol and characterization of their selfassembled structures. Of particular interest is the phenomenon of gelation, where the amphiphiles (gelators) assemble initially into fibrils or tubules which then interact to form 3dimensional networks that entrap the liquid.[8,9] In this context, while there is immense structural diversity in low-molecular-weight gelators (LMWGs) that can gel organic liquids, LMWGs that can gel water are few and far between.[8-10] The present work will look into the possibility of new LMWGs from renewable resources and would ideally expand the diversity of LMWGs for water (i.e., of hydrogelators). Moreover, we expect the new LMWGs to be suitable for applications such as the structuring of optically modulated material.

Due to the recent importance of ‘Sustainable Electronics’ - an emerging area of research aimed at identifying compounds of natural origin and establishing economically efficient routes for the production of synthetic materials that have applicability in electronic materials/Devises.[11] Azobenzene systems are inimitable light responsive molecules suitable for the development of optically modulated materials.[12,13]Thus, by having the flexibility of synthesizing a wide range of molecules with small structural changes, one can generate vastly different self-assembled nanomaterials Cardanol. So our aim is to synthesise a photo responsive molecule posess azo group as photo responsive part from cardanol and connect the molecule with glucose to convert in an amphiphile. The amphiphile synthesized envisaged to posess photo responsive soft material propertiese. The synthesized azo dyes will be characterized using techniques such as NMR and LC-MS. Then the self-assembly properties of the synthesized amphiphile will be studied in aqueous as well as organic solvents. The morphology of self-assembled structures will be studied using techniques such as SEM.

2. AIM AND OBJECTIVES

The objective of this proposal is the rational design and synthesis of new amphiphilic molecules from renewable resources and study of the self-assembly of the amphiphiles in different organic solvents.

The three major goals of this study are;

i) **Design and synthesis of amphiphiles from renewable resource monomers such as cardanol and glucose**

The amphiphilic building blocks to be synthesized will have a hydrophilic head group selected from plant-based sugars, and a hydrophobic part (tail) selected from non-polar aliphatic or aromatic moieties of plant origin, using mitsunobu reaction as a tool for the high yield synthesis.

(a) For the head groups of these amphiphiles, glucose is envisioned with an eye on specific structural features such as ability to form strong intermolecular interactions through its multiple hydrogen bonds, chiral properties and easy functionalization. The sugars will be regioselectively converted to an amphiphile after coupling to the hydrophobic component.

(b) For the hydrophobic part, natural monomers such as Cardanol (obtained by the fractional distillation of cashew nut shell liquid) will be used. It is aimed to make phenyl azo cardanol first by using simple diazotization reactions, then it will be coupled with cardanol using novel mitsunobu reaction. The reactions will be monitored using thin layer chromatography and the desired compound will be separated using column chromatography. The amphiphile synthesized will be characterized by using techniques such as ^{1}H NMR, ^{13}C NMR and mass spectroscopy.

ii) **Study of cis-trans isomerization of azodyes**

We will study the light induced cis –trans isomerization of the azodyes in organic solvents. The azo-dye solution will be irradiated with a suitable light source and cis-transe isomerization will be monitored using UV-Visible spectroscopy.

iii) <u>**Study of the self-assembly of azo dyes in different organic solvents**</u>

Self-assembly of the above amphiphiles in organic solvents will be investigated using SEM and spectroscopic techniques. The goal will be to understand how molecular structure and interactions dictate the nature and properties of the corresponding assemblies.

3. REVIEW OF LITERATURE

a) Cardanol; A versatile monomer as a soft material precursor

Categorically in the strictest sense soft materials are selfassembled nano- or mesostructures obtained from small molecules, but occasionally include polymer–based materials as well. Self-assembly is one of the few practical strategies for making such assembled nanostructures and has emerged as an essential tool in the field of nanotechnology. Nature offers myriad of opportunities to generate functional materials from its multifarious raw materials including small molecules, carbohydrates, lipids and nucleotides, to highlight a few. The production of chemicals and/or materials from biomass is emerging as a reliable approach for the furtherance of a balanced environment and economic system. Devising processes which convert bio- or industrial waste into value-added chemicals and hitherto functional materials have been proven to be an alternate platform to build the concept of biorefinery. Several successful efforts are now known to convert raw materials into molecular precursors and applied end-materials.

Supramolecular gels are prepared by bringing a solution of the precursor, also known as gelator, to an elevated temperature, and subsequently allowing it to cool down to room temperature. During that process, the gelator forms reversible physical cross-links in organic solvents through non-covalent interactions, resulting in a consistent network of self-assembled molecules. The solvent used varies depending on the desired application and properties of the gel, but usually consists of an organic liquid. In supramolecular gels, the gelators are referred to as low molecular weight gelators (LMWGs) because of their relatively small molar masses, which favor the non-covalent interactions necessary for the gel formation[11].

Cardanol, a byproduct from cashew nut processing, is an excellent candidate as a starting material for making supramolecular gels. The chemical structure of cardanol, containing the phenol unit and the long aliphatic chain, which can have different degrees of unsaturation varying from 0 to 3, provide opportunities for self- assembly and therefore use as an LMWG[11]. Additionally, cardanol also contains an aromatic ring that promotes pi-pi interactions.

LMWGs can be used individually or in combination with other species in order to obtain specific properties. Cardanol-based LMWGs can have a variety of intermolecular forces that contribute to the formation of supramolecular gels. For example Cardanol modified with diaminopyridine (DAP) has three types of intermolecular forces: hydrogen bonding, pi–pi stacking, and van der Waals interactions. The DAP head group forms three hydrogen bonds, the aromatic rings interact with each other via pi–pi stacking, and the hydrophobic tails have van der Waals interactions[14]. Interestingly, unsaturation in the hydrophobic tails influences the shapes of nanostructures formed by self-assembly. A variety of hydrophilic head groups can be used to modify cardanol for the formation of supramolecular gels.

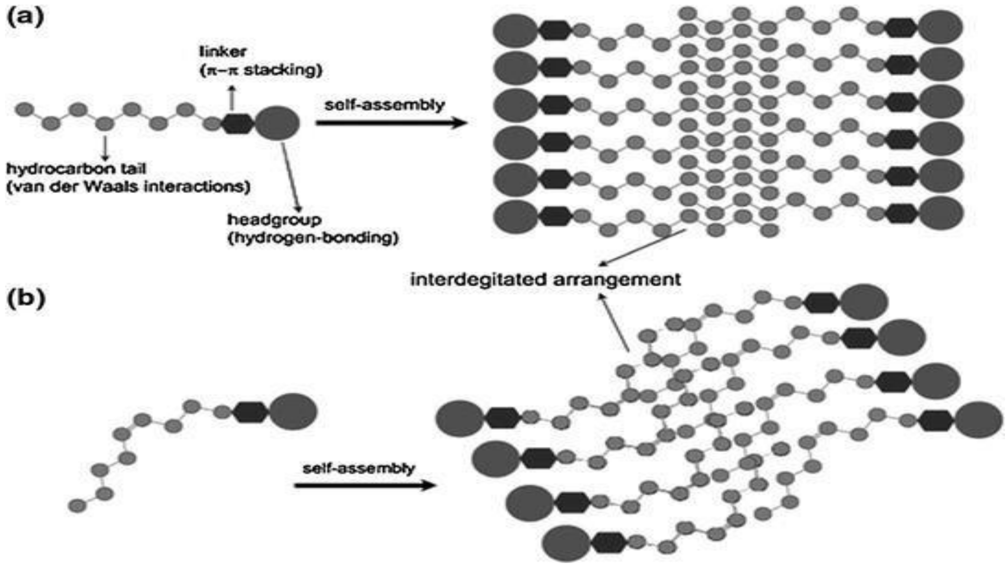

Figure 3.1: Schematic representation of the self-assembly of cardanol–diaminopyridine based amphiphiles with (a) saturated and (b) unsaturated alkyl chains (the alkyl chains do not represent the exact number of carbons, and it is only representative).

Cardanol possesses this functional flexibility allowing for simple chemical modification for the synthesis of structurally diverse amphiphilic molecules, that self-assemble to generate distinctive softmaterials. Besides creating functional soft-materials, the development of cardanol-based amphiphiles also provides an opportunity to study the influence of hydrophobic groups on the self-assembly of amphiphiles.[13] Glycolipids, were synthesized by attaching glucopyranose to cardanol . The sugar moiety acts as a nonionic polar head group and bestows chirality to the molecule. Soft materials, such as twisted fibers, helical coils and high axial ratio nanotubes, were formed through the selfassembly of amphiphilic glycolipid.[14]

Cardanol liquid crystals Much like gels exhibit properties of both solids and liquids; liquid crystals straddle the line separating solid and liquids as they flow like a liquid, yet they possesses either positional and/ or orientational order like solid crystals. They exhibit interesting properties in response to changes in heat (thermotropic) or with respect to concentration (lyotropic). The cardanol derived glycolipid and was found to be both thermotropic and lyotropic liquid crystalline materials .The presence of alkyl side chain unsaturations and the effect of hydration played a pivotal role on the phase behavior of the cardanol-based glycolipids.[15]

Cardanol possesses a similar structure to linear alkyl benzenes (LABs), which are the most commonly used as industrial and household surfactants. . Fittingly, chemically unmodified cardanol does have inherent surfactant-like properties due to its slightly polar phenolic ring and longhydrophobic hydrocarbon chain. An extracted pure form of cardanol was able to stabilize the phospholipid liposomes akin to cholesterol, a well-known liposome/membrane/lamellar stabilizer.[16] Similarly, cardanol-based quaternary ammonium surfactants could catalyze the transformation of benzyl alcohol into corresponding aldehydes in an efficient manner. Interestingly, cardanol-based phase transfer catalysts consistently outperformed the commercially available phase transfer catalyst Aliquats to produce high yields.[13] Since cardanol contains phenols with a varying degree of cis-double bond unsaturations, one can envision an amphiphile which exhibits a stimuli-responsive behavior, that could be utilized to reconfigure them into functional architectures. Judicious conjugation of hydrophilic taurine (a vital amino sulfonic acid) and hydrophobic cardanol generated an amphiphile, N-cardanyl tauramide . An amide linker was used to facilitate hydrogen-bonded association. At room temperature, a 5 mM aqueous solution of NCT formed micellar aggregates .Upon heating the micellar solution’s thermal fluctuations were developed in the alkyl chains, increasing the mobility of alkyl chains. This phenomenon facilitated favorable conformations for micellular transformation into bilayers, and during re-assembly the shorter kinked and longer extended alkyl chains interlocked in a bilayer arrangement and eventually underwent curvature forming individual vesicular structures.[17]

Azobenzene is a photoswitchablechemical compound composed of two phenyl rings linked by a N=Ndouble bond. It is the simplest example of an aryl azo compound. The term 'azobenzene' or simply 'azo' is often used to refer to a wide class of similar compounds. These azo compounds are considered as derivatives of diazene (diimide),and are sometimes referred to as 'diazenes[18]'. The diazenes absorb light strongly and are common dyes.trans-Azobenzene is planar. The N-N distance is 1.189 Å. cis-Azobenzene is nonplanar with a C-N=N-C dihedral angle of 173.5°. The N-N distance is 1.251 Å. The isomerization process involves a decrease in the distance between the two carbon atoms in position 4 of the aromatic rings of azobenzene, from 9.0 Å in the trans form to 5.5 Å in the cis form. The trans-azobenzene is almost flat and has no dipole moment, whereas the cis isomer presents an angular geometry and a dipole moment of 3.0 D. One of the rings rotates to avoid steric repulsions due to facing of one of the π clouds of one aromatic ring to the other . The arrangement of the aromatic rings is also reflected in the proton nuclear magnetic resonance spectrum (^{1}H NMR). The signals of the cis isomer appear at higher field than the signals corresponding to the trans isomer, due to the anisotropic effect of the π cloud of the aromatic ring.

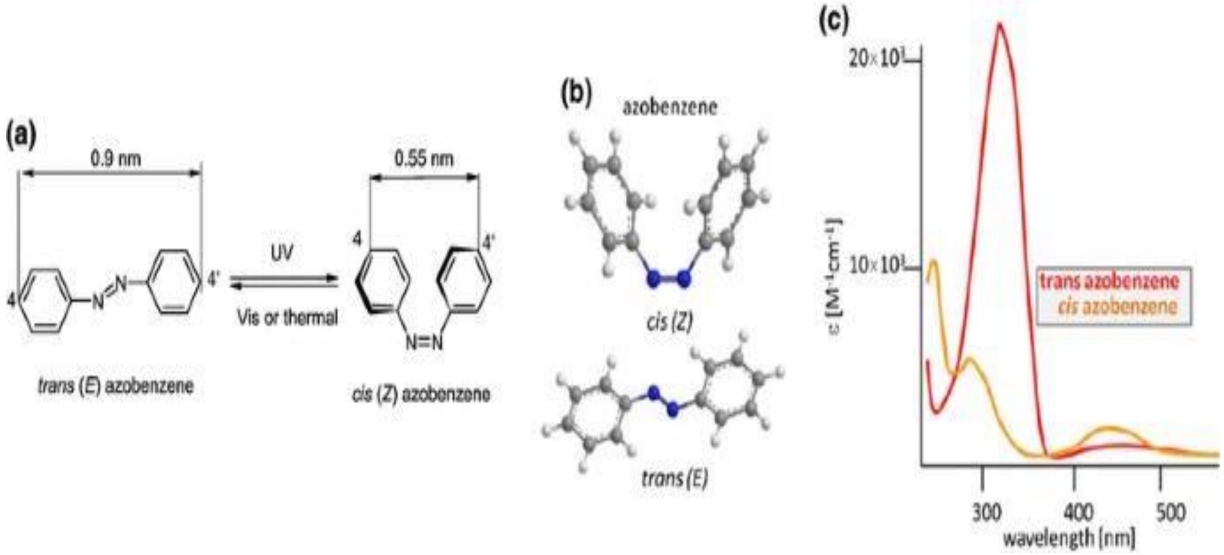

Figure 3.2: The cis trans isomers of azobenzene and their UV-Visible spectrum

Azo or azobenzene is commonly used to refer to a wide class of molecules containing core azobenzene structures and various functional groups extending from the phenyl rings. These azobenzene-based compounds are also called diazenes and are used as dyes in various industries. Photoisomerization is the most interesting property of azobenzene and azobenzene-based compounds. The cis and trans isomers of the compounds can be switched reversibly with each other by the application of light of a particular wavelength. UV light of > 400 nm wavelength can be used to switch the cis form to the trans form and, by using UV light between 300–400 nm wavelength, we can switch back to the cis form. This photochemical property of these compounds is the reason for their photoresponsive behavior and this makes them suitable for use in various applications, such as in the development of various sensors[19].

The development of soft nanomaterials by the controlled self-assembly of molecules derived from renewable sources has become a major area of interest for scientists across the World. Recent trends in scientific research show an increasing interest in studying nanostructures fabricated from. This is on account of their ability for specific molecular recognition, simple chemical and biological modification and easy availability for bottom- up fabrication. Plant/crop based feed stocks are already used extensively in the preparation of various materials such as plastics, solvents, lubricants etc. Among the various bioresources, cardanol has been considered the most exciting molecule based on its functional flexibility due to three main structural and chemical features: (i) the presence of reactive phenolic –OH group offering synthetic flexibility, (ii) the presence of meta alkyl chain with non-isoprenoic cis double bonds that lead to amphiphilic and lipidic character and (iii) the existence of the aromatic ring which allows for π–π stacking and functionalization. These features make cardanol an acceptable precursor for chemical modifications to generate a library of amphiphiles and functional monomers used in the production of soft materials.There exists a plethora of reports based on cardanol centered polymers and polymeric materials in scientific literature and they continue to enjoy their status as a major focus of research.

The self-assembly of cardanol and its derivatives into diverse nanostructures have been intensely studied by various research groups. However, studies on the self-assembly of cardanol based molecules are limited to extended architectures, fibers and gels. Controlling their selfassembly is important for the development of novel soft materials from bioresources (Cardanol). Self- assembly can be controlled by various stimuli such as pH, temperature, molecular design and light. Among these, light happens to be a powerful tool to manipulate the properties of molecules and materials. For example, light induced changes of azobenzene derived photochromic molecules have been exploited to control properties of molecular, macromolecular and supramolecular architectures. Among various photochromic molecules, azobenzene is of immense scientific relevance due to its reversible E-Z photoisomerization that proceeds with large dipole moment and volume change leading to significant modulation of the macroscopic properties. Like the self-assembly of Cardanol based photoswitchable molecule in non-polar solvents such as cyclohexane can be taken as an example.To conclude, the light triggered growth of nanospheres through the self-assembly of an azobenzene derivative into microspheres. The trans-cis photoisomerization and the associated surface dipole moment increase are responsible for the association of the nanospheres into microspheres. There arepotential possibilities of using the versatile azobenzene chromophore[20].

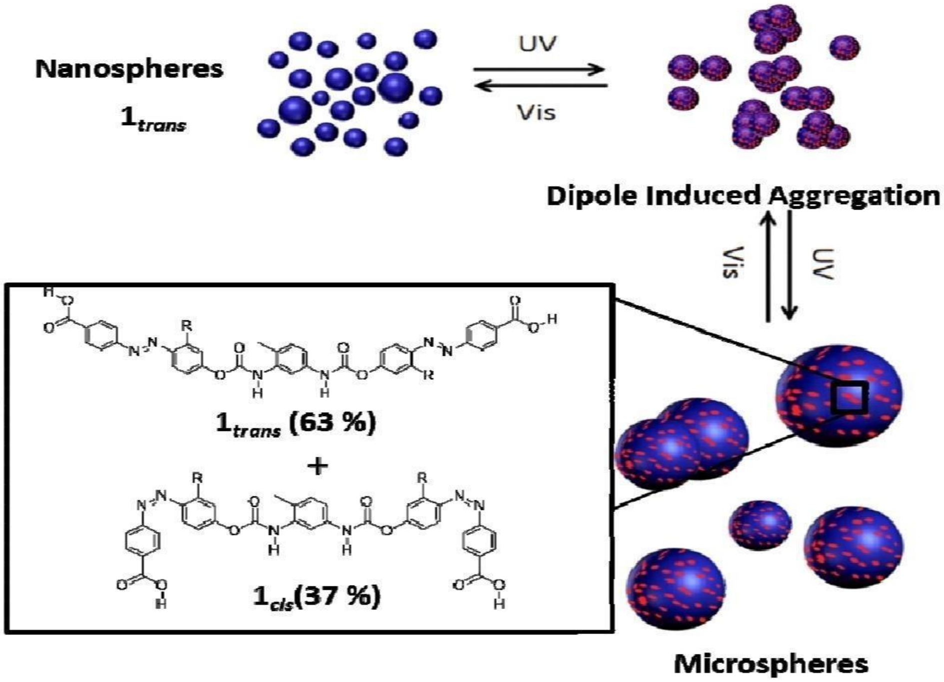

Figure 3.3: Light Induced Size variation at Nanoscale-Schematic representation of transformation of nanospheres to microspheres.

The Mitsunobu reaction is the dehydrative coupling of a primary or secondary alcohol (occasionally, tertiary alcohols have been used) to a pronucleophile (NuH), which is mediated by the reaction between a dialkyl azodicarboxylate and a trialkyl- or triarylphosphine. When chiral, secondary alcohols are employed, complete inversion of stereochemistry is observed in all but a

few cases. The Mitsunobu reaction occurs under mild, essentially neutral conditions, and typically at 0 °C to room temperature. Standard solvents for the reaction include THF, diethyl ether, dichloromethane and toluene, although sometimes more polar solvents including ethyl acetate, acetonitrile and DMF have been used. In "conventional" Mitsunobu chemistry, there is a wide range of pronucleophiles that can participate in the reaction. Suitable pronucleophiles include (thio)carboxylic acids, (thio)phenols, imides and sulfonamides, permitting the formation of C-O, C-S and C-N bonds (and C-C bonds as will be seen shortly). It is generally agreed that the pKa of the pronucleophile must be around 12 or below for a successful reaction with the typical Mitsunobu reagents diethyl azodicarboxylate (DEAD; R3 = Et) or diisopropyl azodicarboxylate (DIAD; R3 = iPr) and triphenylphosphine (PPh3). This "pKa rule" stems from the mechanism of the reaction wherein the betaine that results from the reaction between DEAD and PPh3 has a pKa of about 12 and removes the acidic proton from the pronucleophile, otherwise alkylation of DEAD will occur, which is a known side reaction of the
Mitsunobureaction[21].

The reaction generally represented as:

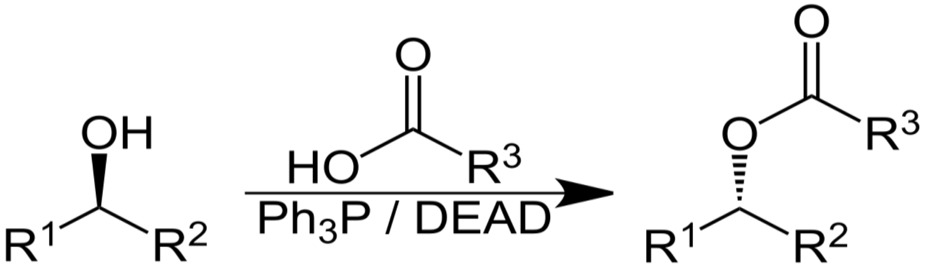

Figure 3.4: The standard Mitsunbou reaction

The standard Mitsunobu reaction involves coupling of an alcohol and a nucleophile in a dehydrative SN_2 process activated by a reactive combination of a triaryl- or trialkylphosphine as reducing agent and a dialkyl azodicarboxylate as oxidant. In a redox process, the phosphine species is oxidized to the respective phosphine oxide and the azo reagent is reduced to the corresponding 1,2-hydrazinodicarboxylate[22].

The reaction proceeds under mild, neutral conditions that are compatible with a wide range of functional groups. In the case where a stereogenic center is involved, the reaction takes place with stereochemical inversion. The reaction partners are mostly primary or secondary alcohols, while the nucleophilic species needs to be acidic with a $pKa < 11$. Otherwise the azo reagent would compete with the acidic nucleophile and participate in the substitution reaction.

Various compounds comply with that condition: carboxylic acids, phenols, hydrazoic acid, some other NH acids, and thiols.The standard azo reagents used are diethyl- (DEAD) or diisopropyl(DIAD) azodicarboxylate. However, alternative reagents such as azodi-carboxamides or stabilized phosphoranes were also developed to allow reaction with nucleophiles of weaker acidity. The typical phosphine reagents are triphenyl-(Ph_3P) or tributyl- phosphine ($n\text{-}Bu_3P$). In recent years, advances have been made using solid supported reagents, thus facilitating work-up conditions. The polarity of the commonly aprotic solvents used in the Mitsunobu reaction, including toluene, tetrahydrofuran or dimethylformamide, has been shown to be effective in terms of efficiency and stereoselectivity[22] .

Since its infancy, the Mitsunobu reaction has found applications in carbohydrate chemistry, as its broad scope and mild conditions are ideal for the formation of conjugates with sensitive natural products. Standard applications of Mitsunobu reaction in glycochemistry have mostly dealt with the functionalization of the primary hydroxy group of sugars and, to a lesser extend, with modifications of the secondary alcohol array in carbohydrate rings, for example for halogenation. However, the Mitsunobu reaction can also be profitably utilized for the anomeric modification of carbohydrates.

Perhaps the single, most important feature of the Mitsunobu reaction is that secondary alcohols undergo clean inversion of their stereo genic centres.1-5 Thus, hydrolysis of the ester that is yielded from the dehydrative coupling of a carboxylic acid and a secondary alcohol will furnish the inverted alcohol generally in high enantiomeric purity. In addition to carboxylic acids, other oxygen nucleophiles that have become popular coupling partners in the Mitsunobu reaction include phenols and also alcohols themselves in intramolecular reactions.

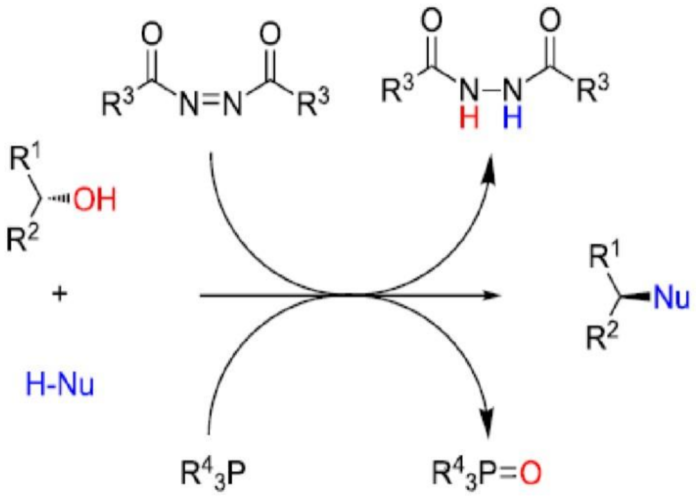

Figure 3.5: The Mitsunobu reaction is essentially a nucleophilic substitution of alcohols occurring with inversion of configuration at the alcohol stereocenter. The auxiliary reagents are involved in a redox process.

To rationalize the outcome of the Mitsunobu reaction with reducing sugars, special mechanistic considerations have to be taken into account. On the one hand, the equilibrium between the azodicarboxylate, the phosphine, and the acidic component,Nu-OH, is important.

Mutarotation of the sugar hemiacetal results in an equilibrium of both, α- and β-anomers. However, full anomerization is often not observed as the rate and the extent of mutarotation depends on various parameters such as anchimeric effects of neighboring groups and the reaction conditions[15].

Hence it has been frequently observed in Mitsunobu reactions with carbohydrate hemiacetals, that sugar anomerization is either absent or slower than the formation of the *O*glycosyloxyphosphonium salt, which can play the intermediate during the reaction.

Another possible explanation for limited anomerization lies in the different stability of anomeric glycosyloxyphosphonium salts, where one anomer can be sterically favored over the other, thereby pushing the equilibrium to a product with the respective anomeric configuration.

Regardless of the rate of mutarotation, the Mitsunobu reaction can proceed through a mechanistic pathway A or B as depicted below. Especially when the sugar alcohol is not sterically hindered, phosphorus transfer occurs to yield a phosphine-activated anomeric alcohol (a glycosyloxyphosphonium ion, pathway A). This in turn can be attacked by the deprotonated nucleophile resulting in an anomerically modified carbohydrate with inversion of configuration at the anomeric center, according to a SN^2 mechanism. Pathway A can also proceed through a SN_1 mechanism when the intermediate glycosyloxyphosphonium ion is less stable. Then, it can decompose into the corresponding anomeric oxocarbenium ion and phosphine oxide. The oxocarbenium ion would then react with the NuO−anion in a SN^1 mechanism. While this would lead to racemization under normal circumstances, in most carbohydrates, participation effects of neighboring groups in the vicinity (typically at the 2-position of the sugar ring) affect the reaction outcome, favoring nucleophile attack from a preferred face of the sugar ring[24].

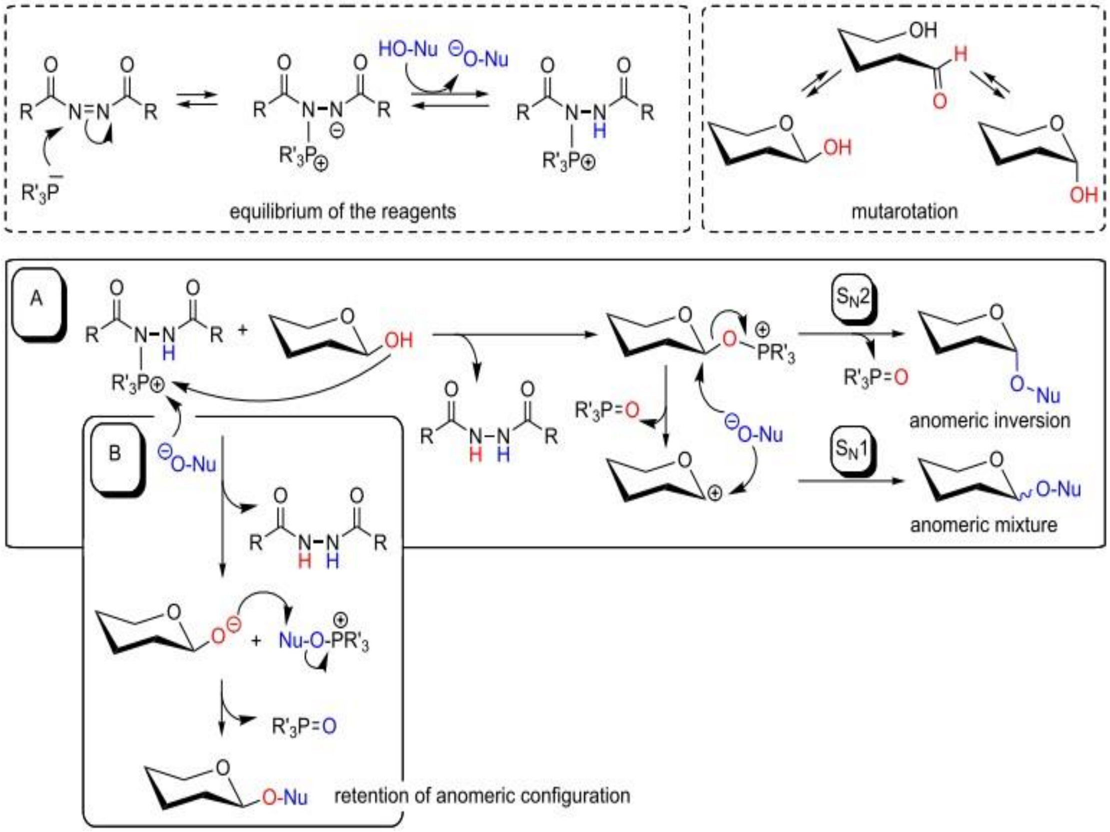

Figure 3.6: Mechanistic considerations on the Mitsunobu reaction with carbohydrate hemiacetals (depicted in simplified form). Two equilibria are rele-vant for this reaction (top dashed boxes), (i) the formation of the “Mitsunobu reagent” from the employed azodicarboxylate, phosphine and the acidic nucleophile, and (ii) the mutarotation equilibrium of the reducing sugar in solution. These can give rise to at least two different reaction pathways, A and B, as explained in the main text. Depending on various parameters, the anomerically modified sugar, a glycoside or an anomeric ester, respec-tively, is obtained with full inversion of anomeric configuration or as anomeric mixture (A), or with retention of the anomeric configuration via O-alkyl-ation (B). For clarity both reaction pathways are exemplified with only one sugar anomer.

4. MATERIALS AND METHODS

All starting materials were obtained from commercial suppliers and used as received, except otherwise mentioned. Double distilled cardanol was supplied by Golden Cashew Pvt Ltd and was purified by column chromatography before use. 3-Pentadecyl phenol was purchased from TCI America. Glucose, maltose and triphenylphosphine were purchased from Nice chemicals, India. Aniline, 4-Nitroaniline, 2-methoxy aniline and Diisopropyl azodicarboxylate were purchased from Spectrochem, India. Column chromatography was carried out using silica gel (100-200 mesh). ^{1}H NMR (400 MHz) spectra were recorded on a Bruker-400 MHz NMR spectrometer instrument.

Proton chemical shifts are reported in parts per million downfield from tetramethyl silane (TMS). Mass spectra were recorded on a Schimadzu 8045 LC/MS spectrometer instrument. SEM images were obtained using a Jeol-JSM-6490-LA scanning electron microscope (SEM) with an accelerating voltage of 15 KV and a FE-SEM Gemini 300 Carlzeiss instrument. Samples were prepared by spinning the samples on glass slices and coating with Au. The electronic absorption spectra were recorded on a Shimadzu UV-3101 scanning spectrophotometer. All the solvents used were purified by distillation before use. The progress of the reaction was monitored by looking at the TLC of the reaction mixture at various time intervals.

4.1 Preparation of diazonium chloride solution of amine :

The aromatic amine about 1g was dissolved in a mixture of concentrated hydrochloric acid about 3 ml and distilled water about 15 ml. About 0.9g of sodium nitrite is dissolved in distilled water about 3 ml and this solution was added dropwise to the acidic solution of amine over a period of 10 min at 0°C and then the mixture was stirred at 0°C for 50 min in a magnetic stirrer.

4.1.1 Synthesis of the cardanol azo dyes[25] (I)

The pre-cooled solution of cardanol about 3.21g in ethanol (15 ml) was added dropwise to the previously prepared solution of diazonium salt in presence of KOH at 0°C. The reaction mixture was stirred at 0°C for 40 min by which time the product was precipitated. The water insoluble layer was extracted with diethyl ether; the organic layer was washed repeatedly for 2-3 times with 50 ml distilled water and solvent was removed under reduced pressure. The resulting oily viscous dyes (**a/b**) were dried at 50°C for 2 hours.

The reaction was monitored using thin layer chromatography and the desired compound was separated using the column chromatography using 10% Ethyl acetate/ Hexane. These qualitative tests were performed only after the complete removal of the solvent.

i) 4-(Phenylazo)cardanol:

Yellowish-brown viscous liquid; Yield 62%. ^{1}H NMR (400 MHz, DMSO d6) δppm: 9.1 (s), 7.77 (d, J = 7.6 Hz, 2H), 7.52 (d, J = 7.6 Hz, 2H), 7.45 (t, J = 7.2 Hz, 2H), 6.98 (br s, 1H), 6.74 (dd, J = 2.0 Hz, 1H), 5.80 (m), 5.30 (m), 5.20 (m), 3.02 (t, J = 7.6 Hz), 2.90 (m), 2.76 (t, J = 7.2 Hz), 2.0 (m), 1.60 (t), 1.20 (m), 0.80 (m).IR: 3346, 3008, 2923, 2852, 1600, 1483, 1468, 1455, 1365, and 1225cm^{-1}; LC-MS; m/z = 407.

ii) 4-(2-methoxyphenylazo)cardanol:

Dark red viscous liquid; Yield 60%. ^{1}H NMR(400 MHz, DMSO d6), δppm: 9.1 (s), 7.77 (d, J = 8.8 Hz, 2H), 7.53 (d, J = 8.8 Hz, 1H), 6.71 (d, 2H), 6.66 (br d, J = 6.4 Hz, 1H), 5.80 (m), 5.31 (m), 4.92 (m), 3.76 (s, 3H), 3.25 (t), 2.90 (m), 2.68 (t, J = 5.6 Hz), 1.91 (m), 1.62 (m), 1.35 (m), 0.80 (m); IR: 3400, 3010, 3090, 2923, 2842, 1640, 1484, 1463, 1398, 1366, 1247, and 1181cm^{-1}; LC-MS; m/z = 437.6.

4.1.2 Synthesis of acetic anhydride

20 g of powered sodium acetate is taken in 500 ml 2-necked RB flask. One neck is tightly fitted with stopper. Then flask is dipped in ice and 13 ml of acetyl chloride added drop wise by means of syringe. The reaction mixture is continuously shaken with magnetic stirrer.After completion of reaction the flask is removed from ice bath and shaken well. Then it is allowed to

stand for a while at room temperature. After one hour, the whole mixture is distilled and distillate is collected in 250 ml RB flask.

4.1.3 Synthesis of D-Glucopyranose, 1,2,3,4,6- pentacetate[26]

To a solution of D-Glucose (1g, 0.0055 mmol) in acetic anhydride (5ml) was added sodium acetate (0.45g, 0.0055 mol) and is heated at reflux for 4 Hrs. After cooling to room temperature the solution is poured into ice water and stirred for 2 hrs. The solid was collected by filtration, dried and recrystallized from water to obtain peracetylated glucose as colourless crystals. White solid (53%,mp 131-132^0 C), ^{1}H NMR (400MHz, $CDCl_3$)δ: 5.72 (1H, d, J=8.4), 5.26 (1H, t, J=9.2), 5.14 (2H, m), 4.29 (1H, m), 4.12(1H, m), 3.84(1H, m), 2.10 (15H, m), LC-MS m/z = 390.

4.1.4 Synthesis of D-Glucopyranose, 2,3,4,6-tetraacetate[27](II)

General procedure: Zinc acetate (0.056g, 0.256mmol) was added to a solution of peracetylated glucose (1g, 2.56mmol) in 25 mL of methanol and the mixture was stirred for 3 hrs at 50-55^{0}C. The solvent was then evaporated from the mixture under reduced pressure, and the crude product was purified by column chromatography upon silica gel (100-200 mesh) using hexane and EtOAc (3: 1). Compounds gave acceptable ^{1}H NMR spectra that matched the data reported in the literature. Colorless syrup (60%), ^{1}H NMR (400 MHz, $CDCl_3$) ^{1}HNMR.: 6 2.02-2.09 (3 s, 12 H, 4 AC), 3.74.3 (m, 3H, H-5,6,6'), and 4.7-5.6 (m, 5H, H-1,2,3,4, and OH).^{13}C NMR (400 MHz, $CDCl_3$) δ: 170.9, 170.8, 170.19, 170.18, 170.16, 169.7, 169.5, 95.5, 90.1, 73.1, 72.1, 72.0, 71.0, 69.8, 68.4, 68.3, 67.1, 61.90, 61.88, 20.72, 20.69, 20.67, 20.60, 20.57, 20.56.

4.1.5 Synthesis of Phenylazocardanol glucosides

General procedure: The carbohydrate starting material (0.01mol), phenyl azocardanol (0.012mol) and triphenylphosphine (0.013 mol) were dissolved in 40 ml dry Toluene/2:1 Toluene - dichloromethane mixture (for the synthesis of maltose azocardanol derivatives). The solution was cooled to 0 ^{0}C , and a solution of Diisopropyl azodicarboxylate (DIAD, 0.012 mol) in dry Toluene (5.00 mL) was added drop wise over 30 min. The reaction mixture was stirred at room temperature until the TLC showed no further consumption of the carbohydrate starting material. The solvent was evaporated in vacuum, and the crude mixture was subjected to deprotection without further purification. To the crude product, 30% of triethylamine (13ml) was added followed by 75 ml of methanol, and stirred at room temperature for 24 hrs. The reaction mixture was then washed with 10% sodium bicarbonate solution and purified by column chromatography using chloroform and hexane (1:9). The chromatography afforded the azodyes as coloured solids.

i) 1-O-(4-phenylazo(cardanyl))glucopyranoside (**1a):**

Orange red solid; yield 75%,mp 173 ^{0}C. ^{1}H NMR (DMSO-d6), δ ppm: 7.84 (2H, d, J = 7.6),7.65 (1H,d, J = 8.8), 7.58 (2H, t, 7.2), 7.57 (2H, t, 6.8), 7.06 (1H, s), 6.98 (1H, d, J =9.4), 5.39 (1H, d, J =4.8), 5.33 (3H, m), 5.14 (1H, d, J = 4.4), 5.077 (1H, d, J = 5.2), 5.00 (1H, d, J = 7.2), 4.98, 4.59 (1H, t, J = 5.6), 3.71 (1H, d, J = 5.2), 3.49 (1H, m), 3.402 (1H, m), 3.30 (2H, m), 3.22 (1H, m), 3.09 (2H, t, J =7.2), 2.74 (2H, m), 1.936 (4H, m), 1.62(2H,m), 1.26 (16H, m), 0.82 (3H, t, J =7.2).

[1]C NMR (100 MHz, DMSO-d6), δ ppm: 160.43, 152.87, 145.36, 144.92, 137.14, 131.19, 130.14, 130.19, 129.90, 129.84, 128.40, 128.18, 127.89, 126.95, 122.76, 117.63,116.85, 115.30, 114.98, 100.32, 77.60, 77.10, 73.68, 73.10, 61.07, 32.16, 32.02, 31.75, 31.56, 31.44, 31.06, 29.52, 29.45, 29.15, 29.06, 29.03, 29.00, 23.95, 23.71, 27.03, 25.99, 25.66, 25.59, 22.67,14.38**,**14.04**.** LC-MS**;** m/z = 569.

ii) 1-O-(4-2-methoxyphenylazo(cardanyl))glucopyranoside (**1b):**

Orange yellow stiky solid ;Yield 67% mp 127 ^{0} C.^{1}H NMR (400MHz, DMSOd6), δ ppm: 7.56 (1H, d, J = 8), 7.48 (2H, m), 7.25 (1H, d, J = 8),7.03 (2H, m), 7.013(1H, d, J

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[1] C NMR (100 MHz, DMSO-d6), δ ppm: 160.11, 156.97, 145.54, 144.92, 142.31, 137.15, 132.62,130.40, 130.18, 130.06, 129.91, 129.38, 128.91, 128.18, 127.89, 126.96,

=7.6), 6.97 (1H, J = 9), 5.38 (1H,d, J = 5.2), 5.34 (3H, m), 5.14 (1H, d, J = 4.4), 5.07 (1H, d, J = 5.2), 4.99 (1H, J = 7.2), 4.995, 4.59 (1H, t, J = 5.6), 3.954 (3H, s), 3.71 (1H, m), 3.495 (1H, m), 3.39 (1H, m), 3.32 (2H, m), 3.22 (1H, m), 3.076 (2H, t, J = 7.6), 2.66 (2H, m),1.94 (3H, m), 1.617 (2H, m), 1.28 (15H, m), 0.83(2H, t, J = 7).

120.96, 117.54, 116.66, 115.30, 114.96, 113.92, 100.36, 77.61, 77.13, 73.68, 61.08, 56.47, 31.97, 31.76, 31.57, 31.45, 31.08, 29.53, 29.47, 29.16,28.97,28.71, 27.04, 25.67, 22.68,14.38, 14.04. LC-MS; m/z = 601.

4.2 Cis-trans isomerization.

Light induced cis- trans isomerization of azodyes were observed using UV-Visible spectroscopy. Azodye in toluene was irradiated with 350nm uv light and absorption spectra were recorded at regular time intervals (each 5 minutes).

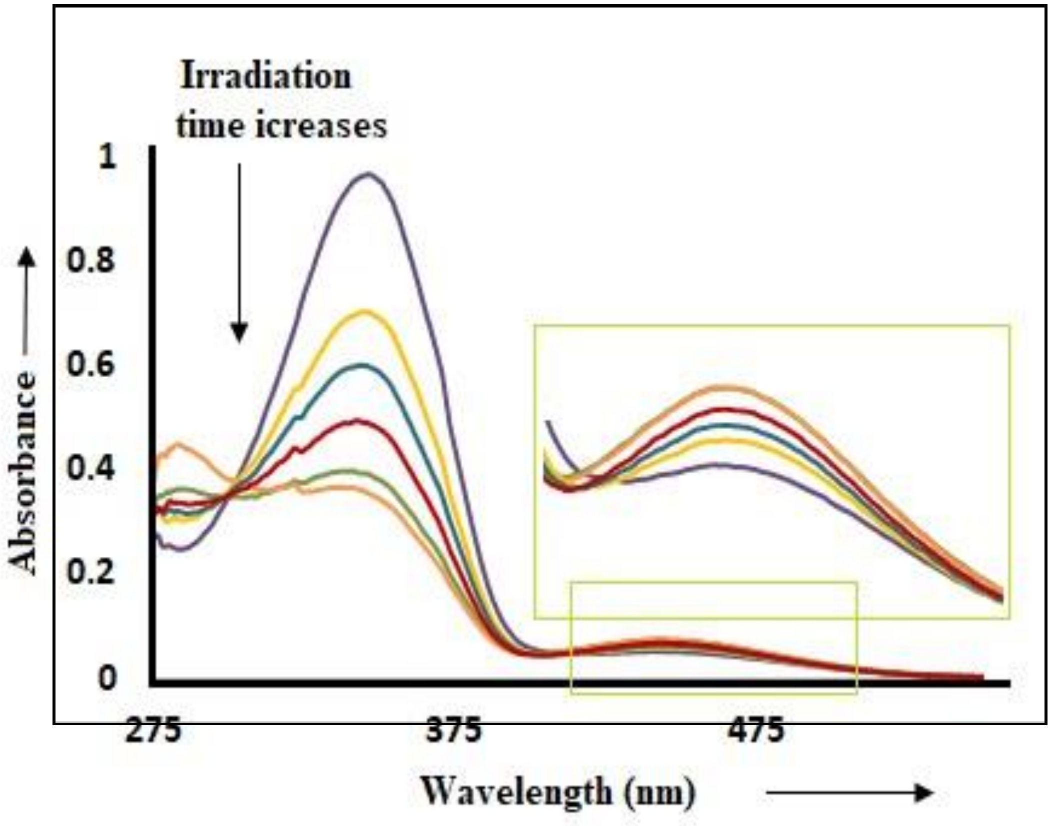

Figure 4.1: Absorption spectra showing cis trans isomerization of **1a** in toluene (0.05molL^{-1}).

4.3 Study of self-assembly of the azo dyes in different solvents

UV-Visible spectrum of azodye were recorded in different compositions of Toluene: hexane.The spectrum were recorded suddenly after hot dissolving (0.85molL^{-1}) in different compositions of Toluene and hexane mixture. The spectrum shows decrease in absorbance with increase in composition of the non-solvent (hexane), which could be due to the formation of aggregates.

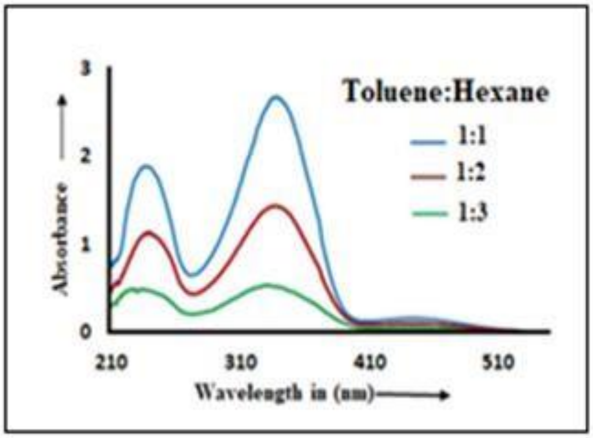

Figure 4.2: Absorption spectrum of **1a** different compositions of toluene and hexane.

4.4 Preparation and characterization of viscous phase:

1. 1-3 wt% of **1a** in toluene was found to form wet string at 35 ^{0}C, this solution was then diluted with toluene, drop casted on a glass plate and analysed using FE-SEM.

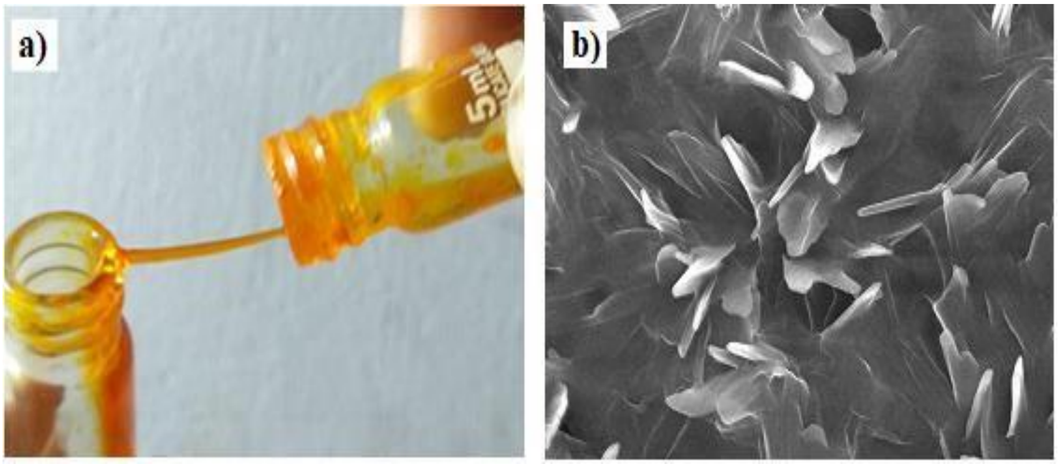

Figure 4.3: (a) Photograph of wet string formed by the azodye**1a** in toluene (1.5wt %)

(b) FE-SEM images of the wet string drop casted on an aluminium foil.

4.4.1 Characterization of gel phase formed by Azocardanol glucosides 1a and 1b

The gelation experiments were carried out with various solvents using a test tube inversion method. The gelators and the solvents were put in a glass vial and heated (> 65 ºC) until the solid was dissolved. Then the sample vial was cooled to 25 ºC (prepared sample).It was then left for few minutes to obtain the gel at the ambient conditions. Qualitatively, gelation was considered successful if no sample flow was observed upon inverting the container at room temperature.

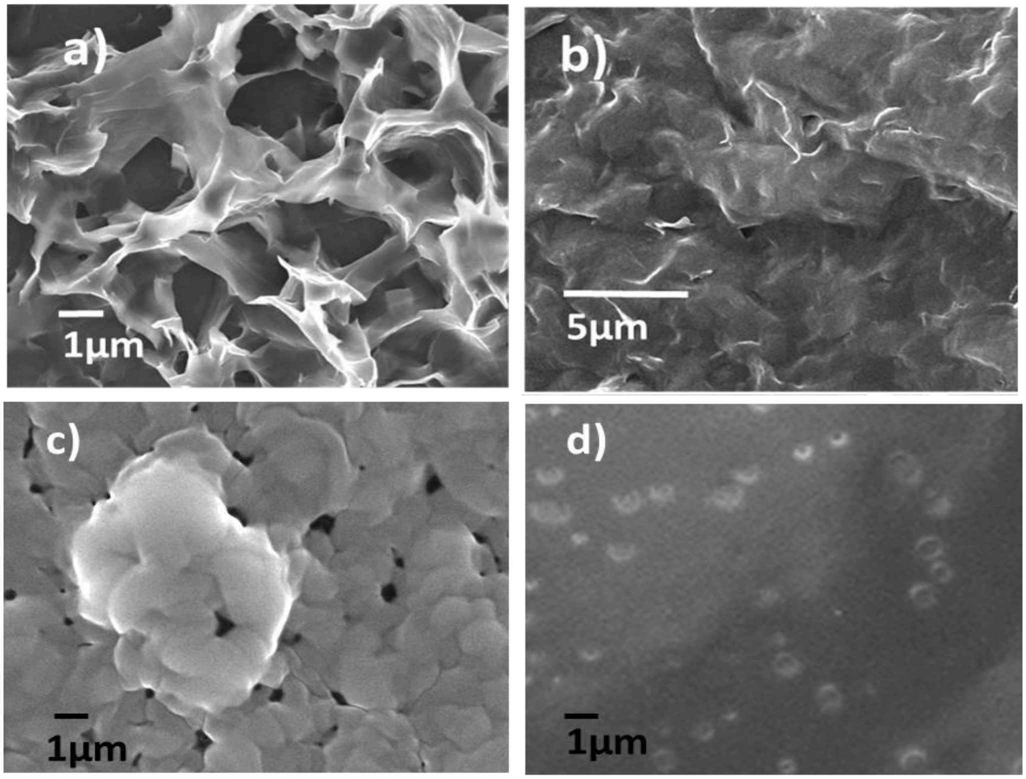

Figure 4.5: SEM images of azodye**1a** in a) acetonitrile, b) toluene and **1b** in c) toluene d) toluene hexane

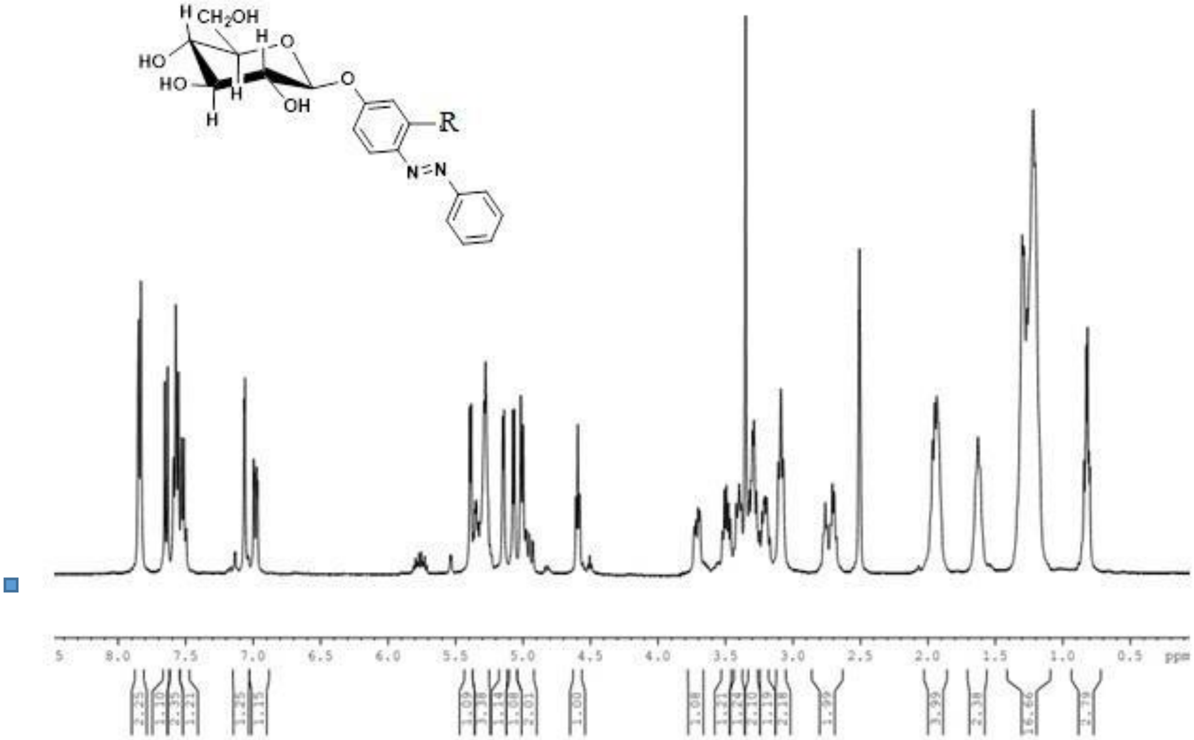

Figure 4.6: ^{1}H NMR spectrum of phenyl azocardanol glucoside **1a** in DMSO.

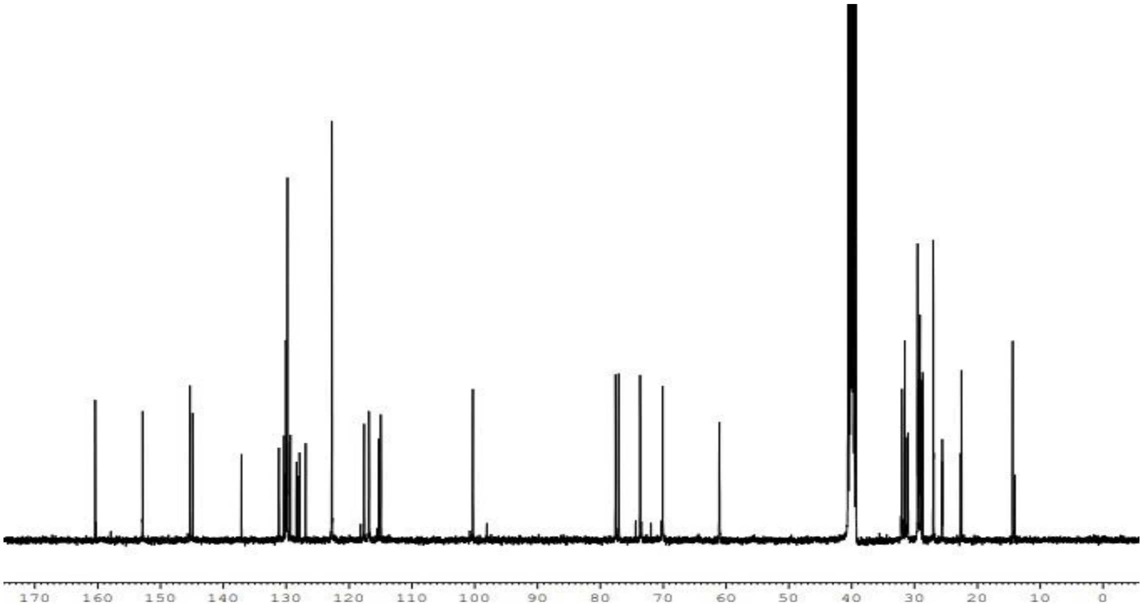

Figure 4.7: ^{13}C NMR spectrum of phenyl azocardanol glucoside **1a** in DMSO.

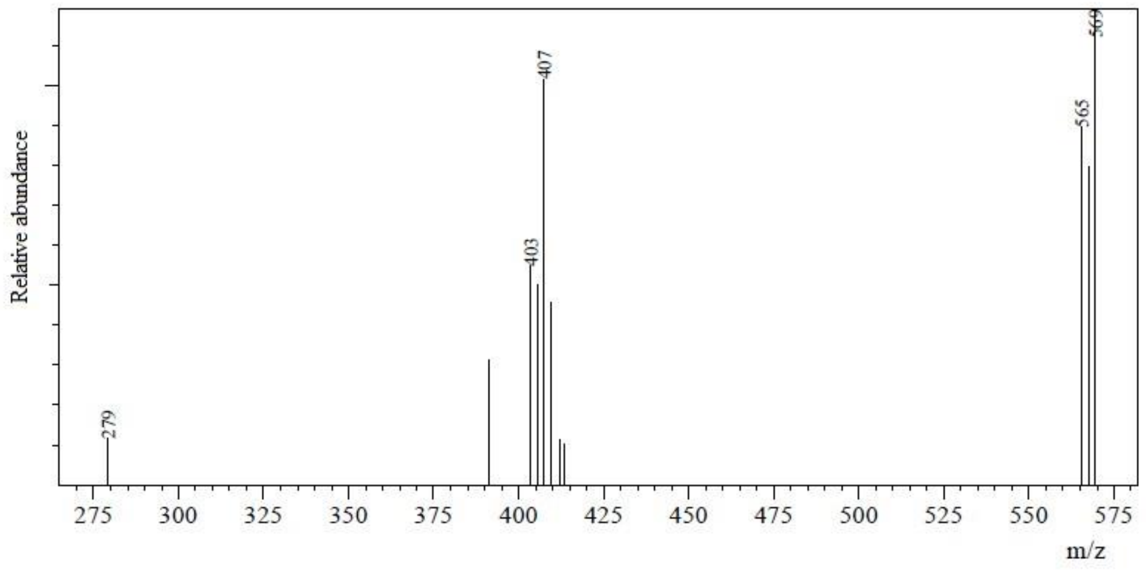

Figure 4.8: LC-MS Spectrum of phenyl azocardanol glucoside **1a** in Acetonitrile.

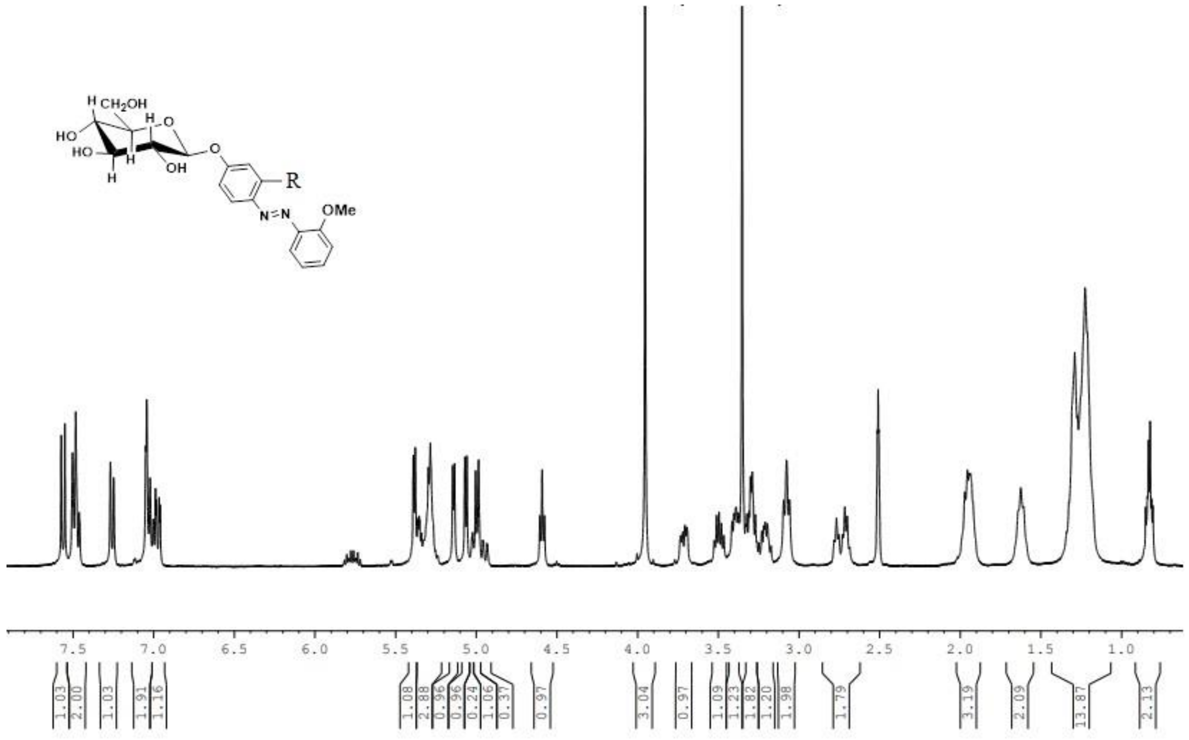

Figure 4.9: ^{1}H NMR spectrum of phenyl azocardanol glucoside **1b** in DMSO.

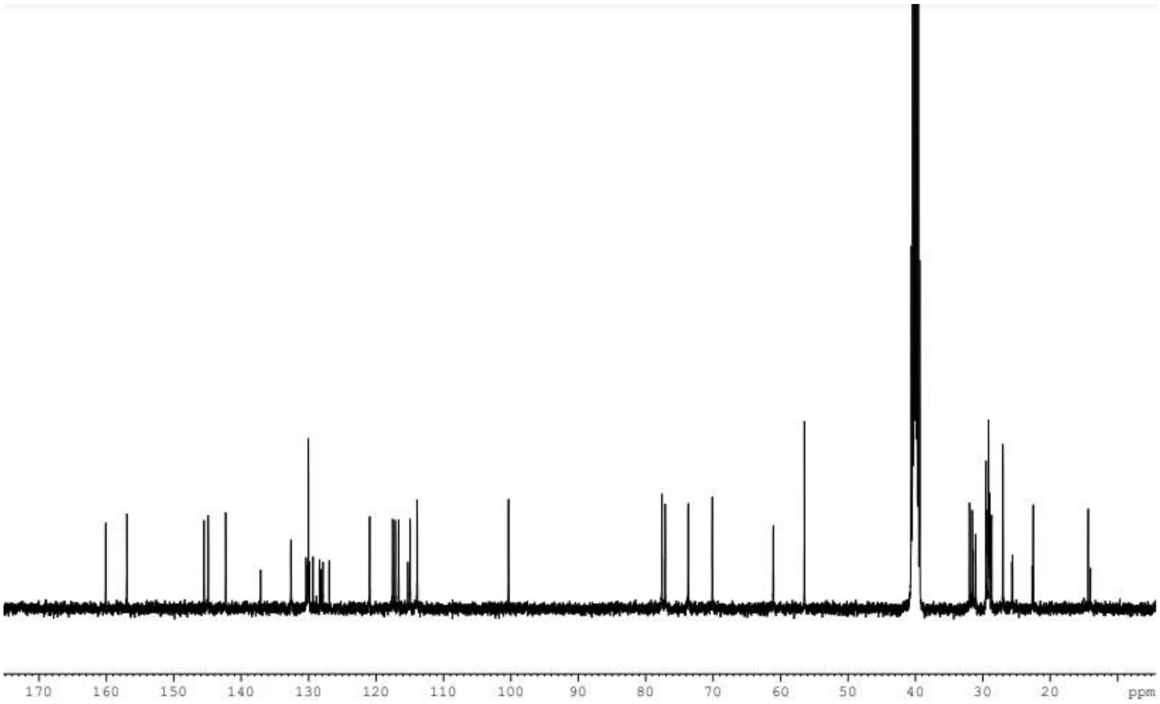

Figure 4.10: ^{13}C NMR spectrum of phenyl azocardanol glucoside **1b** in DMSO.

5. CONCLUSION

This study was aimed at Azocardanol Amphilies; their design, synthesis and selfassembly properties. And the outcomes from this study can be described as the following:

1) Design and synthesis of amphiphiles from cardanol were achieved in good yields using novel mitsunobu reaction. The azodyes were characterised by using the techniques such as NMR and LC-MS.

2) The light induced cis –trans isomerization of the azodyes in organic solvents were studied. The azo-dye solution was irradiated with a suitable light source and cis-trans isomerization was monitored using UV-Visible spectroscopy.

3) Self-assembly of the above amphiphiles in organic solvents was investigated using SEM and spectroscopic techniques. The azo dyes form a gel phase and a viscous phase depending upon the concentration and composition of solvents. Through which we understood how molecular structure and interactions dictate the nature and properties of the corresponding assemblies.

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