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Crops: A Green Approach toward Self-Assembled Soft Materials

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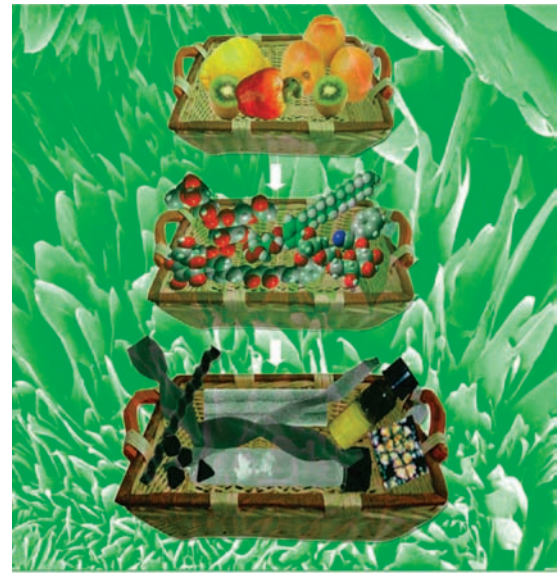
CONSPECTUS



To date, a wide range of industrial materials such as solvents, fuels, synthetic fibers, and chemical products are being manufactured from petroleum resources. However, rapid depletion of fossil and petroleum resources is encouraging current and future chemists to orient their research toward designing safer chemicals, products, and processes from renewable feedstock with an increased awareness of environmental and industrial impact. Advances in genetics, biotechnology, process chemistry, and engineering are leading to a new manufacturing concept for converting renewable biomass to valuable fuels and products, generally known as the biorefinery concept. The swift integration of crop-based materials synthesis and biorefinery manufacturing technologies offers the potential for new advances in sustainable energy alternatives and biomaterials that will lead to a new manufacturing paradigm. This Account presents a novel and emerging concept of generating various forms of soft materials from crops (an alternate feedstock). In future research, developing biobased soft materials will be a fascinating yet demanding practice, which will have direct impact on industrial applications as an economically viable alternative. Here we discuss some remarkable examples of glycolipids generated from industrial byproducts such as cashew nut shell liquid, which upon self-assembly produced soft nanoarchitectures including lipid nanotubes, twisted/helical nanofibers, low-molecular-weight gels, and liquid crystals. Synthetic methods applied to a "chiral pool" of carbohydrates using the selectivity of enzyme catalysis yield amphiphilic products derived from biobased feedstock including amygdalin, trehalose, and vitamin C. This has been achieved with a lipase-mediated regioselective synthetic procedure to obtain such amphiphiles in quantitative yields. Amygdalin amphiphiles showed unique gelation behavior in a broad range of solvents such as nonpolar hexanes to polar aqueous solutions. Importantly, an enzyme triggered drug-delivery model for hydrophobic drugs was demonstrated by using these supramolecularly assembled hydrogels. Following a similar biocatalytic approach, vitamin C amphiphiles were synthesized with different hydrocarbon chain lengths, and their ability to self-assemble into molecular gels and liquid crystals has been studied in detail. Such biobased soft materials were successfully used to develop novel organic–inorganic hybrid materials by in situ synthesis of metal nanoparticles. The self-assembled soft materials were characterized by several spectroscopic techniques, UV–visible, infrared, and fluorescence spectrophotometers, as well as microscopic methods including polarized optical, confocal, scanning, and transmission electron microscopes, and thermal analysis. The molecular packing of the hierarchically assembled bilayer membranes was fully elucidated by X-ray analysis. We envision that the results summarized in this Account will encourage interdisciplinary collaboration between scientists in the fields of organic synthesis, soft materials research, and green chemistry to develop functional materials from underutilized crop-based renewable feedstock, with innovation driven both by material needs and environmentally benign design principles.

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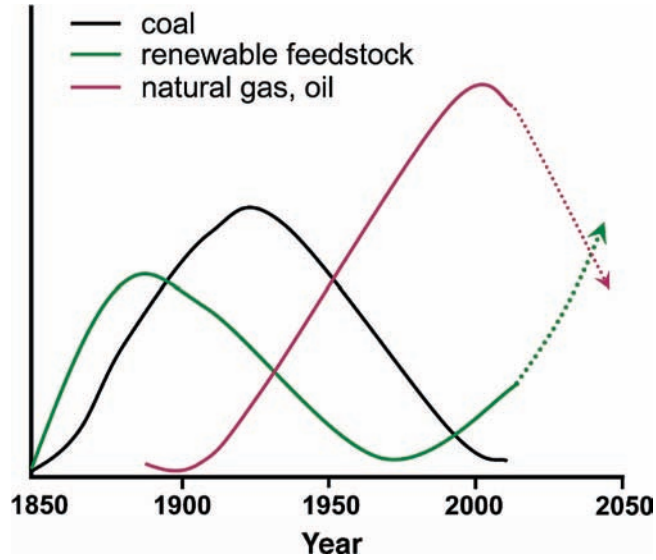
Introduction

In the early part of the 20th century, many industrial materials such as solvents, fuels, synthetic fibers, and chemical products were made from plant/crop-based resources.[1] After the 1950s, most of the biomass-based materials had been replaced by petroleum-derived products. However, the major oil crisis of the 1970s alerted the scientific community to begin to search for efficient processes to use biomass for developing industrial products and materials.[1,2] This scenario is graphically presented in Scheme 1 (adapted from ref 3). The choice of raw materials is now of great significance for both economic reasons and environmental concerns. This challenge then falls on chemists, chemical engineers, and biotechnologists to design suitable methodologies and processes for the effective production of fuels, chemicals, and pharmaceuticals in a biorefinery.

These efforts have produced a new generation of monomers and chemicals for the synthesis of plastics and other products.[2−6] The Technical Advisory Committee (US) has established a national vision for bioenergy and biobased products. The Committee forecasts an optimistic and challenging goal; that biomass will supply five percent of the nation's power, 20% of its transportation fuels, and 25% of its chemicals by 2020. The goal is to replace 30% of current petroleum consumption and will require more than one billion tons of dry biomass annually. With such a dramatic increase in activity from biomass comes a responsibility to increase the capacity and sophistication of waste management systems. Early efforts focused on fermentation byproducts; later researchers' attention turned to developing processes for converting inherently low-value raw materials into chemically sophisticated products. The research took advantage of the selectivity and reactivity of enzymes for unique transformations in a biorefinery concept.

Nature offers an abundance of opportunities for shaping structural and functional materials in its wide variety of raw materials including carbohydrates, nucleotides, and proteins. Recently, Koopman et al. addressed four main themes emphasizing the importance of developing new starting materials from biomass.[7] Much of the work focuses on two areas: green chemistry and industrial/white biotechnology. One aspect of green chemistry refers to the use of biomass to provide alternative starting materials for the production of chemicals, vitamins, pharmaceuticals, colorants, polymers, and surfactants. This use of biomass for chemical syntheses was traditional until its replacement by petrochemicals in the 1950s. Industrial/white biotechnology highlights the use of micro-organisms to provide the chemicals. It also includes the use of enzyme catalysis to yield pure products and consume less energy. Recent literature shows a growing interest in this approach.[8−11]

SCHEME 1. Graphical Presentation of Utility of Various Resources for Generating Value-Added Products, Chemicals, and Fuels, a Historical Perspective[a]



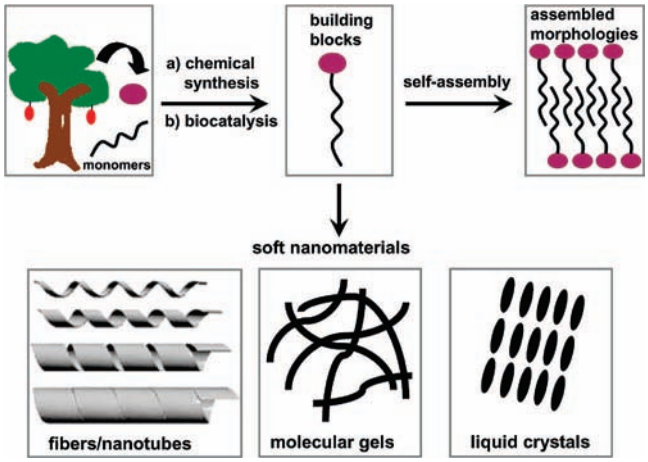
[a] Adapted from ref 3.

Examples using these techniques include composite material such as polymeric foam and biodegradable elastomers generated from soybean oil and keratin fibers.[12] Plastics such as polylactic acid have been developed using this approach, which illustrates biocompatibility due to its trivial hydrolytic degradation.[13] Some examples display a combination of hydrogen bonding and hydrophobic and specific aromatic $\pi-\pi$ interactions in semisynthetic amphiphiles, which generate exotic molecular architectures that facilitate the self-assembly. In this Account, we summarize experimental efforts to develop diverse synthetic intermediates from biomass resources using either chemical processes or biocatalysis. The emphasis is on the use of renewable raw materials (e.g., crops) as a feedstock for new building blocks in supramolecular chemistry and their assembled soft materials. Our current research is focused on generating a wide range of self-assembled soft materials utilizing an array of different crops as feedstock (Scheme 2).

Select Examples of Utilizing Renewable Raw Materials for Value-Added Products

The paradigm shift from petroleum hydrocarbons to biobased feedstocks provides remarkable opportunities for the chemical processing industry. Comprehensive reviews in the literature address the diversity and wealth of renewable monomers

SCHEME 2. Schematic Illustration of Our Research Interest in Developing Soft Materials from Plant- or Crop-Based Resources



and raw materials.[2,3,14–19] Recently, a process for the production of liquid alkanes by aqueous phase processing of carbohydrates was demonstrated.[8,20] A specific reaction pathway for the conversion of biomass-derived glucose into liquid alkanes is shown in Scheme 3. Here, acid-catalyzed dehydration of sugar is followed by aldol condensation of solid base catalysts to produce furans. Subsequent dehydration/hydrogenation over bifunctional catalyst produces liquid alkanes with the number of carbon atoms ranging from C_7 to C_{15}. These liquid alkanes are of the appropriate molecular weight to be tested as transportation fuel components.

Efforts to generate disaccharide intermediates have shown enormous industrial potential. Isomaltulose is amenable to further functional transformations, its industrial production is of great interest.[21,22] Its hydrogenated product, isomalt (Scheme 4), in a 1:1 mixture with the terminally α-glucosylated glucitol and mannitol, which is on the market as a low-calorie sweetner.[23] Amphiphilic derivatives of isomaltulose exhibit liquid-crystalline properties.[24] Families of natural surface active agents (amphiphiles containing either a natural polar headgroup or natural hydrophobic tail), such as, alkylglucosides, alkylglucamides, and sugar esters, have been produced by yeast or bacteria.[19,25–27] Other surfactants have been prepared from carbohydrates and vegetable oils. Their interfacial properties, ecological evaluation, toxicology, and dermatological properties have been investigated.[18] Frost et al. have demonstrated the efficient production of catechol[28] and phenol[29] from D-glucose using genetically engineered *Escherichia coli* (Scheme 5).

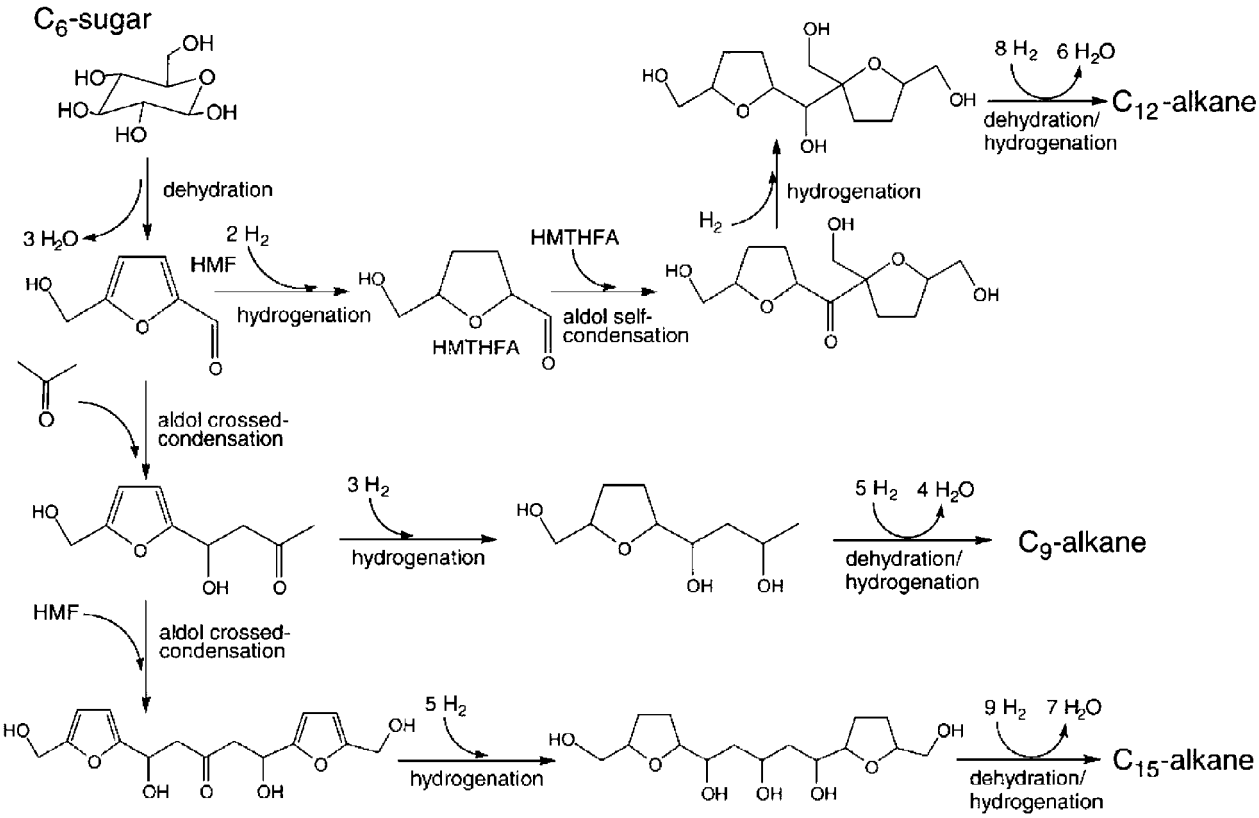
The following section describes the design and synthesis of a wide range of novel amphiphiles from various renewable resources using either chemical synthesis or enzyme-mediated biocatalytic pathways. After selection of a suitable "monomer" (starting material) from renewable resources, appropriate functional groups that can promote intermolecular interactions were systematically introduced by careful design and derivatization. Such amphiphiles were "decorated" with diverse functional groups and were then used to generate an array of self-assembled soft materials such as molecular gels, liquid crystals, fibers, helices, and organic nanotubes. These soft materials were used to develop films, sensors, drug-delivery vehicles, and liquid crystals and also to synthesize and align various metal nanoparticles. This systematic process begins with one of two categories of modifications that are possible with renewable resource-based amphiphiles: either hydrophobic part of the amphiphile can be obtained from biomass and synthetically attached to the polar headgroup, or the polar hydrophilic headgroups can be acquired from renewable feedstock and converted into surfactants by connecting an appropriate hydrophobic group by use of chemical/enzyme-mediated reactions. As an example of the former category, we used cardanol (from cashew nut shell liquid) as the hydrophobic part to which hydrophilic groups were attached. In the latter category, we obtained amygdalin, trehalose, and ascorbic acid as polar headgroups (from crops) and attached a series of hydrophobic tail units to make them amphiphiles to provide self-assembling properties.

Design and Development of New Amphiphiles from Crops

Cashew Nut Shell Liquid (CNSL) Based Products and Intermediates. The biomonomer cardanol, a major constituent of CNSL, is an industrial byproduct from *Anacardium occidentale* L.[30–32] Cardanol (Scheme 6), a distilled product of CNSL, consists of four *meta*-alkyl phenols with alkyl chains differing in their degree of unsaturation. Cardanol possesses interesting functional structural features that allow chemical modification to generate a range of amphiphiles and useful monomer products. A variety of functional groups can be attached to the reactive free hydroxyl group of cardanol for derivatization. For example, cardanyl acrylate (Scheme 6) was synthesized by the reaction of cardanol with acryloyl chloride,[33] which produced a linear polymer upon solution polymerization in toluene using 0.8% azobisisobutyronitrile (AIBN) as radical initiator. Upon removal of solvent and exposure to either air or UV light, the polymer underwent cross-linking to produce an insoluble transparent film.[33] We can attribute the cross-linking to hydroperoxide-mediated autoxidation.[33]

Cardanol-Based Glycolipids. Synthesis of biobased molecular building blocks of aryl glycolipids, GlyLip1 and GlyLip2 (Scheme 7), was achieved by attaching glucopyra-

SCHEME 3. Reaction Pathways for the Conversion of Biomass-Derived Glucose into Liquid Alkanes[a]



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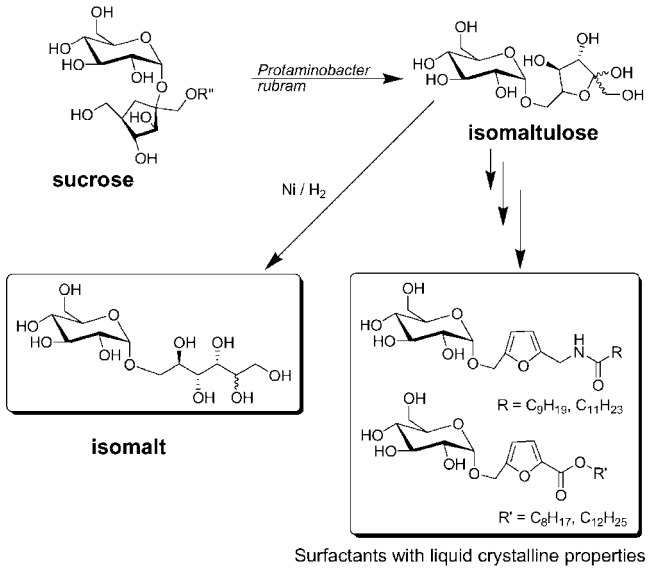
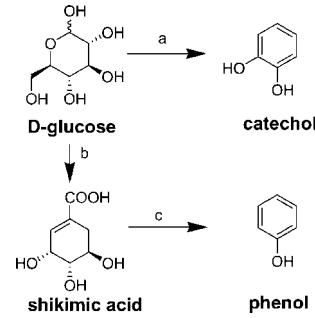
SCHEME 4. Preparation of Isomaltulose from Sucrose and Ensuing Products of Industrial Potential



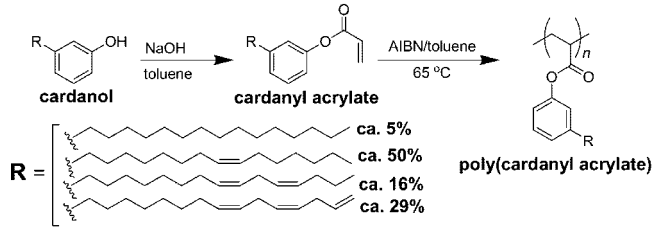
SCHEME 5. Synthesis of Catechol and Phenol from Genetically Modified *E. coli*[a]



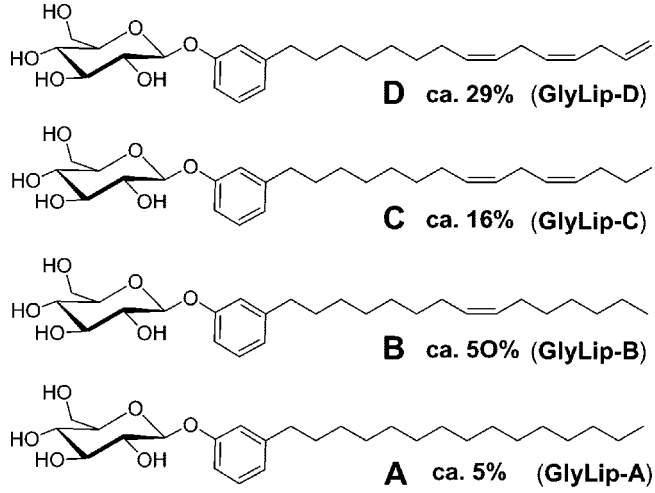
[a] Conditions: (a) *E. coli* AB2834/pKD136/pKD9.069A, 37 °C; (b) *E. coli* SP1.1PTS/Psc6.090B; (c) (1) H_2O, 350 °C, (2) Cu^0, H_2O, 350 °C.

nose to cardanol (for detailed synthesis see ref 34). Self-assembly properties of GlyLip1 and GlyLip2 have been extensively investigated in aqueous solution to generate nanostructures, such as helical and twisted fibers and nanotubes (interestingly, these assemblies exhibited high axial ratios).[34,35] Typically, low concentrations of glycolipids were dispersed in boiling water, and slow cooling of the hot solution and equilibration at room temperature resulted in variety of coiled ribbons and fine fibrous structures within 12−24 h. The fibrous structures were investigated using polarized and phase-contrast light microscopy (POM) and transmission (TEM) and scanning (SEM) electron microscopy. TEM and SEM images showed the presence of ribbons with uniform widths. The lengths of the nanofibers were a few micrometers, and the widths were a few tenths of a nanometer. For saturated GlyLip2, all individual fibers showed twisted morphology, in

SCHEME 6. Synthesis of Cardanol-Based Polymer



SCHEME 7. Chemical Structures of Cardanol-Based Glycolipids with Different Degrees of Unsaturation



GlyLip1 = A + B + C + D
GlyLip2 = A (100%)

contrast to the helical pattern of the fiber from GlyLip1 (Figure 1). The self-assembled nanofibers from GlyLip1 progressively generated tubular structures; TEM images showed that nanotubes were open-ended with uniform shape and uniform internal diameter (Figure 2). The external diameter of nanotubes was between 40 and 60 nm with lengths between 10 and 100 μm and thickness of 8−15 nm. Inspection of noncovalent assembly of nanotubes reveals that they can provide nanostructures with almost the same dimensions as multilayer carbon nanotubes. A schematic illustration of the nanotube wall structure is shown in Figure 3.[35]

To understand the role of the unsaturated hydrophobic tails (mono-, di-, and trienes) in nanotube formation, the individual components were isolated from the cardanyl glucoside mixture. Binary self-assembly of the saturated and monoene derivatives provided a rationale for the control of self-assembled helical structures (Figure 4).[36] In a typical self-assembly, 90:10 (saturated/monoene) mixtures generated twisted ribbons in water. This might have been expected for the 10% doping of the monoene component. The 80:20 compositions also exhibited twisted-ribbon morphology on FE-SEM analysis (Figure 4). No significant effect on the twisted morphology was observed by doping of the monoene component to 30−40%. On the other hand, an equimolar (50:50) composition gave loosely coiled-ribbon morphology between the twisted and tight helical coil. While increasing the monoene content in these experiments, the helical pitch decreased to give tubular morphologies with helical markings.

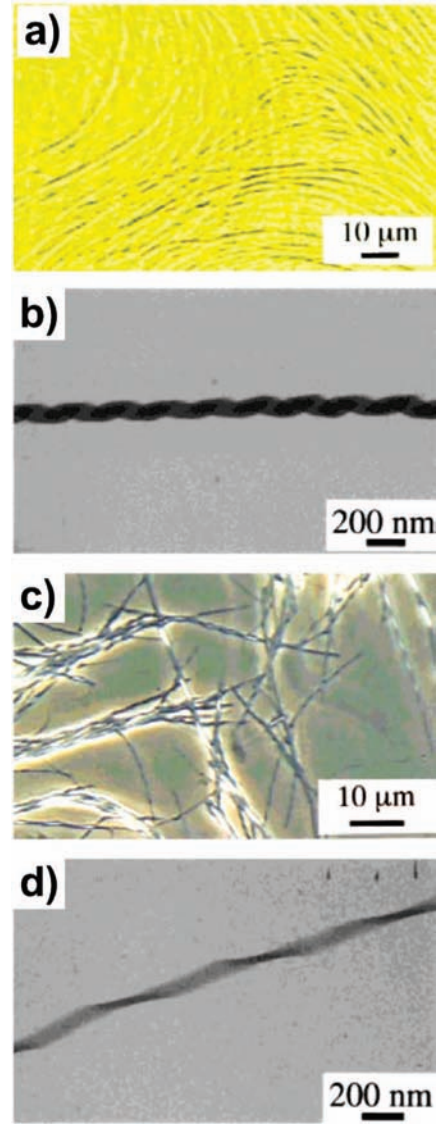


FIGURE 1. A POM image (a) of self-assembled fibers from GlyLip1, an EF-TEM image (b) of an individual coiled nanofiber of GlyLip1, a phase-contrast light microscopy image (c) of self-assembled fibers of GlyLip2, and an EF-TEM image (d) of an individual coiled twisted nanofiber of GlyLip2. Reprinted with permission from ref 34. Copyright 2001 Wiley-VCH.

Novel Synthetic Amphiphiles. The above work encouraged us to design new amphiphiles from common laboratory reagents. Understanding the principles of self-assembly using biobased amphiphiles suggested to us to design new specific synthetic materials. A series of long-chain phenyl glucosides

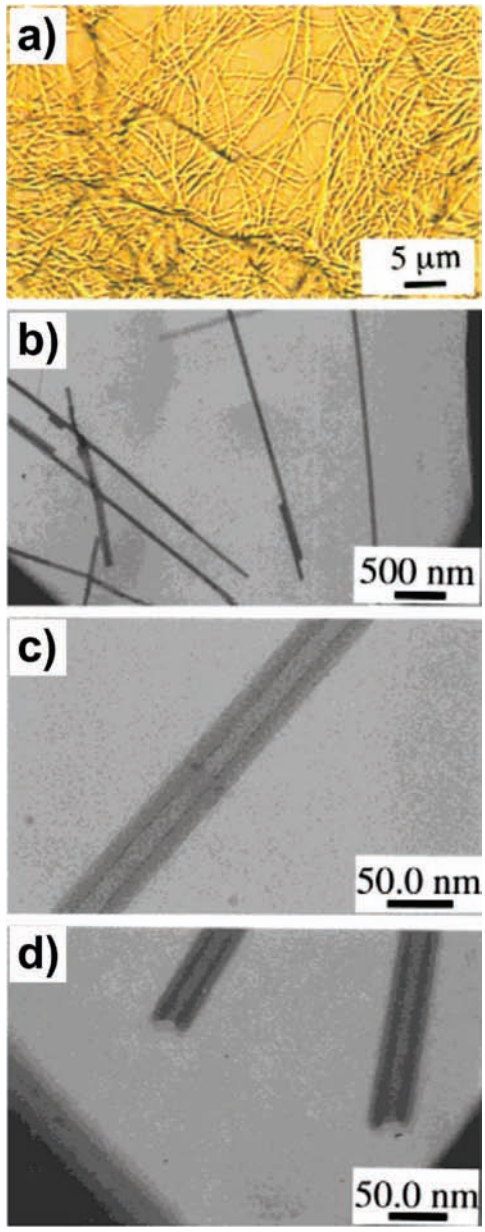


FIGURE 2. A polarized light microscopy image (a) of nanotubes of GlyLip1 and EF-TEM images (b−d) of nanotubes. Reprinted with permission from ref 34. Copyright 2001 Wiley-VCH.

(PheGlu1−5, Scheme 8) were synthesized, and their self-assembling properties were thoroughly examined.[37] In these glycolipids, hydrophobic tails were attached to the phenyl group through an amide bond to increase the possibility of hydrogen bonding. The number of cis double bonds varied (0−3) in the lipophilic component (Scheme 8). Their influence on the formation of nanostructures has been examined by various techniques such as TEM, SEM, CD, FT-IR, and XRD. The glycolipid PheGlu2 showed the twisted fiber structure with 50−200 nm width and several micrometers length, whereas PheGlu3 formed a left-handed coiled tube with 150−200 nm inner diameter and ca. 20 nm wall thickness. In contrast, the

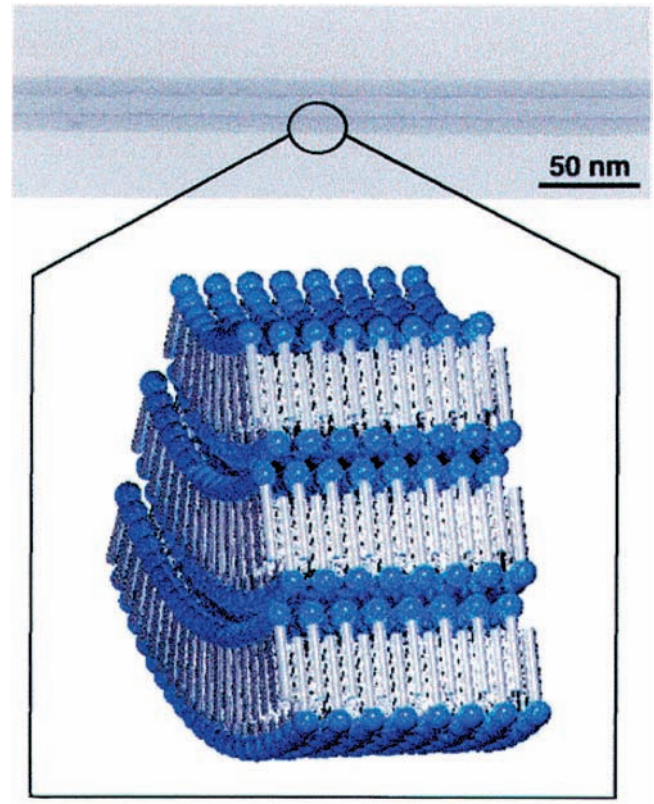


FIGURE 3. TEM image of a lipid nanotube formed from cardanyl glucosides and schematic illustration of the wall structure. Reprinted with permission from ref 35. Copyright 2005 American Chemical Society.

glycolipid with three cis double bonds in the hydrocarbon chain (PheGlu4) displayed a typical nanotubular structure consisting of a 70 nm inner diameter and 80−100 nm outer diameter (Figure 5). The glycolipids containing an amide group as linker exhibited higher gel-to-liquid crystalline phase transition temperatures compared with glycolipids with an *O*-glycosidic linkage.[37]

We then designed analogous synthetic amphiphiles in which molecular recognition units were incorporated using reagents equipped with complementary groups for functional soft materials (Scheme 9). Specifically, by combining simple monosaccharides, saturated or unsaturated fatty acids, and diamino-aromatic linkers, we generated a library of products ranging from fibers that lacked structural regularity to highly uniform nanotubes.[38] Self-assembly of GlyDAP1 (Scheme 9) in water produced helical ribbon morphologies, as expected. Upon aging for an additional 12 h, these helical morphologies converted to lipid nanotubes with an outer diameter of 60−80 nm and an inner diameter of ca. 20 nm.

A hypothetical model for self-assembly of these amphiphiles has been proposed based on the hydrogen bonding, $\pi-\pi$ stacking and interdigitated hydrophobic tails (Figure 6).

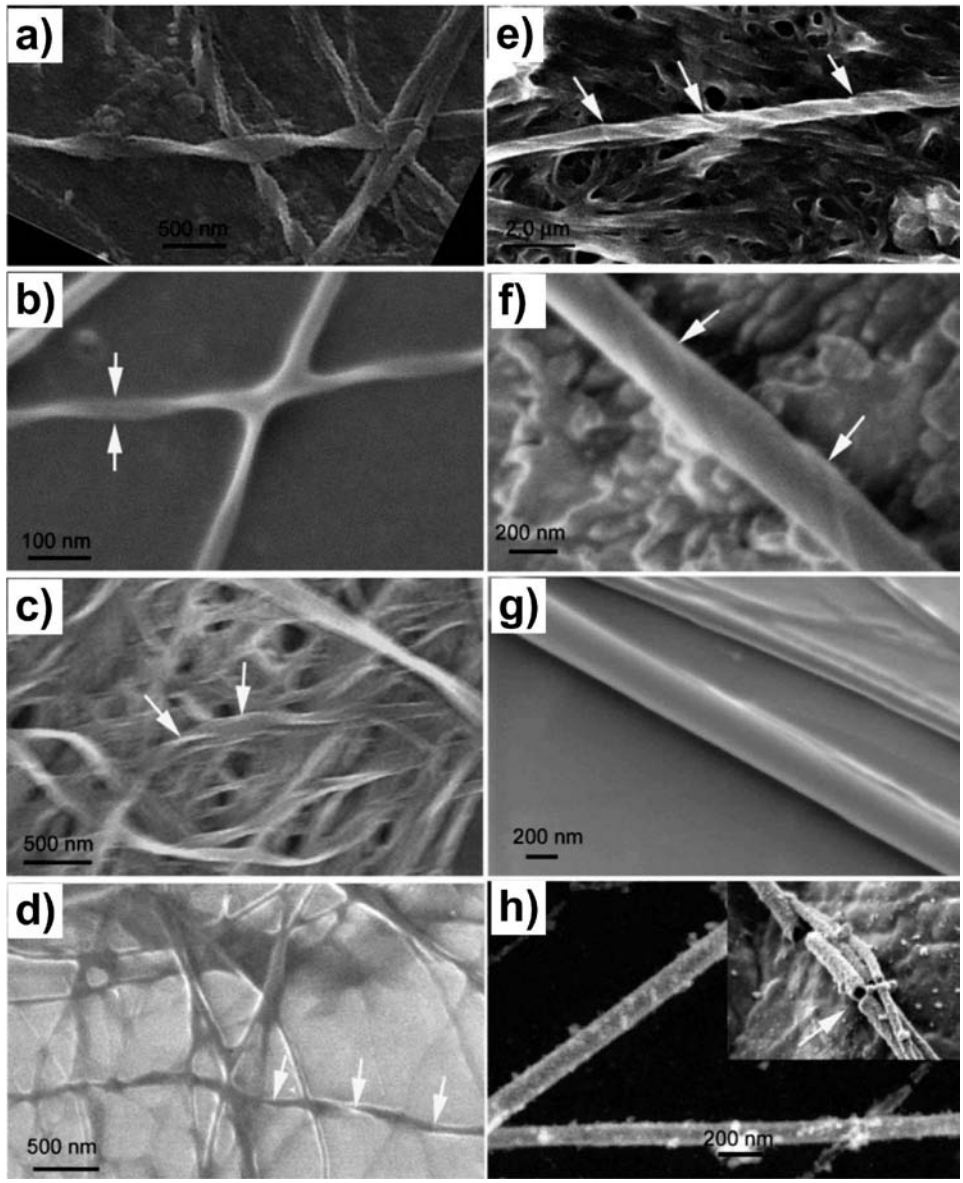
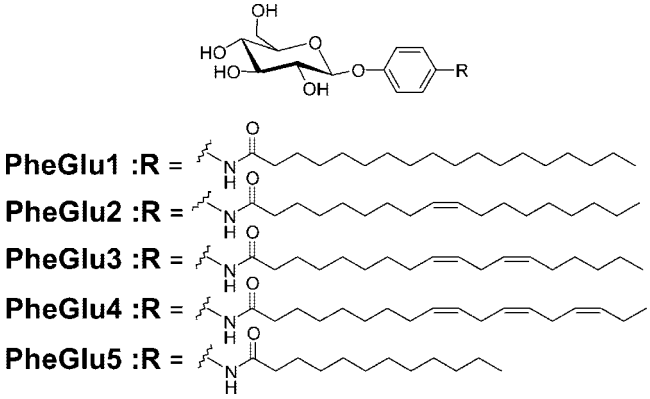


FIGURE 4. FE-SEM Images of Self-Assembled High Axial Ratio Nanostructures after 2 Days Incubation (Saturated/Monoene): (a) 100:0, (b) 90:10,[a] (c) 80:20,[a] (d) 50:50,[a] (e) 20:80,[b] (f) 10:90,[c] (g) 0:100, and (h) cardanyl glucosides mixtures, as a reference. In panels b, c, and d, the white arrows indicate twisted helical morphology. In panel e, the white arrows show the tightly coiled helical ribbons. In panel f, the white arrows show helical markings on the nanotubes. Reprinted with permission from ref 36. Copyright 2002 Wiley-VCH.

Diaminopyridine (DAP) forms three-point hydrogen bonds, which makes this functional group versatile in preparing artificial receptors. Nanotubes made of GlyDAP1 were fluorescent; hence including the DAP group with complementary hydrogen-bonding capability permits the incorporation of fluorescence properties into nanotubes. Indeed, addition of up to 10 mM thymidine caused the quenching of fluorescence presumably due to the formation of multiple hydrogen bonds.[38] Fluorescence quenching was selective for nucleosides over urea and β-D-glucose, which can also form extensive hydrogen bonds. With this design, it was possible to develop novel soft nanomaterials for molecular recognition and other functional applications.

DAP derivatives are also known to serve as ligands for complexing with specific metal ions such as Cu(II), Zn(II), and Co(II).[39,40] The glycolipid GlyDAP1 possesses a metal ion-binding unit in the form of a 2,6-disubstituted DAP moiety. Functional amphiphiles constructed with metal-complexing templates offer additional advantages because they self-assemble in aqueous media to form various nanostructures that apparently can act as templates for patterning the inorganic materials in a desired fashion. In one experiment, novel metal-

SCHEME 8. Series of Synthetic Amphiphilic Glycosides with Different Number of Double Bonds



chelating glycolipid nanotubes were utilized, and Cu nanoparticles were successfully assembled by removing the nanotube templates through an annealing process under argon atmosphere.[41] High-resolution SEM images revealed the dense arrangement of fine Cu nanoparticles on almost the entire surface of the templates, which have directed the nucleation and controlled the assembly of the nanoparticles (Figure 7).[41]

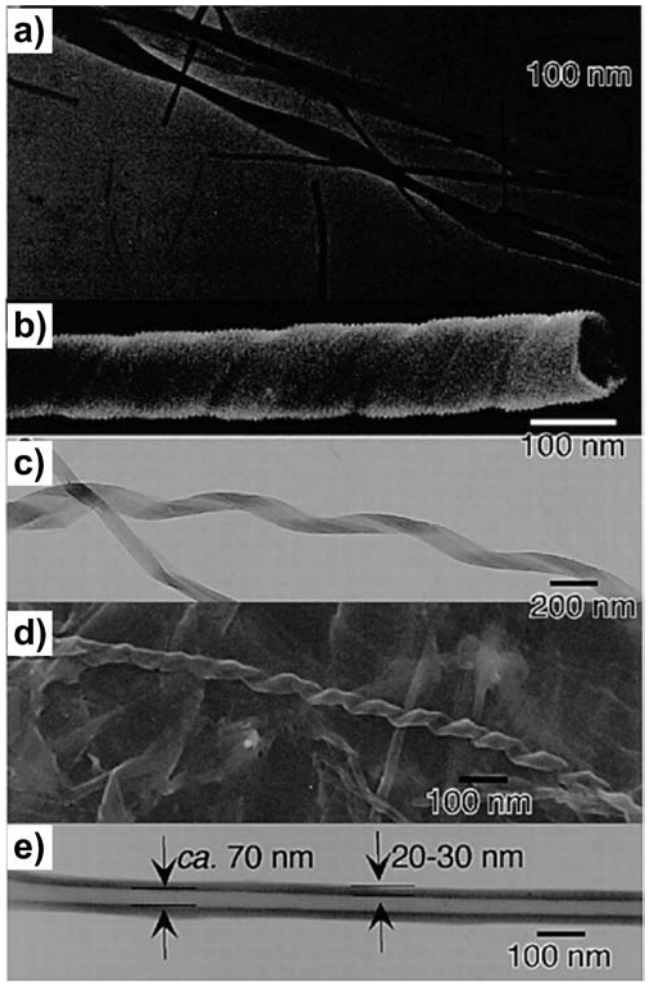
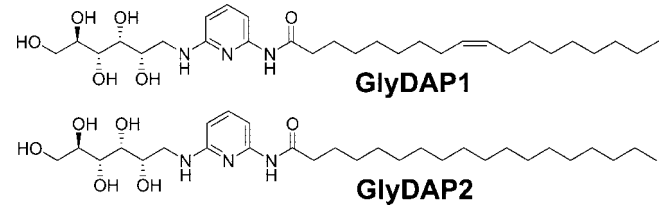


FIGURE 5. EF-TEM and SEM pictures of the self-assembled (a) PheGlu2, (b, c) PheGlu3, and (d, e) PheGlu4. Reprinted with permission from ref 37. Copyright 2002 American Chemical Society.

SCHEME 9. Diaminopyridine-Based Amphiphiles with Open-Chain Sugar Headgroups



A simple conjugated sugar, PheGlu5 (Scheme 8), showed excellent gelation behavior in organic liquids and aqueous solution.[42] Examining the gel microstructure with various spectroscopic techniques revealed that the chiral aggregates consist of predominantly twisted helical ribbons whose helicity was exclusively right-handed with approximately 85 nm width and 315 nm pitch and up to several micrometers length. The XRD, ^{1}H NMR, and FT-IR results suggested that the aqueous gel is stabilized by a combination of hydrogen bonding, $\pi-\pi$ interactions, and hydrophobic forces. We also studied the self-assembling properties of renewable resources-based cardanyl glucosides, GlyLip1 and GlyLip2 (Scheme 7), for generating gels in various solvents. Individual glycolipids GlyLipA−D and mixtures of them (GlyLip1) formed thermally reversible transparent gels in a water/alcohol mixture and a number of organic solvents, which were strongly influenced by the degree of unsaturation in the aliphatic alkyl chain.[43] The amphiphilic nature and self-assembling properties of biomass-based glycolipids GlyLip1 and GlyLip2 prompted us to investigate the possibility of liquid crystal formation.[44] The liquid crystalline properties of GlyLip1 and GlyLip2 were also studied by optical polarizing microscopy, differential scanning calorimetry, and X-ray diffraction. All the phases were identified as lamellar in structure. Introduction of double bonds in the liphophilic portion of the molecule significantly decreased the phase transition temperatures, although these glycolipids all exhibited a common pattern in their phase transitions.

Novel amphiphilic glycolipids were synthesized from cardanol, an industrial byproduct (biomass). The self-association properties of these glycolipids have been investigated extensively. Formation of polymer films, fibers, helices, nanotubules, molecular gels, and liquid crystals from self-assembly of plant- or crop-based glycolipids has elegantly been demonstrated for soft materials development.

Molecular Gels from Amygdalin Amphiphiles. Earlier we obtained the hydrophobic domains of amphiphiles from crops; here we sought polar headgroups from plant- or crop-based resources to synthesize the amphiphiles. While this work shows

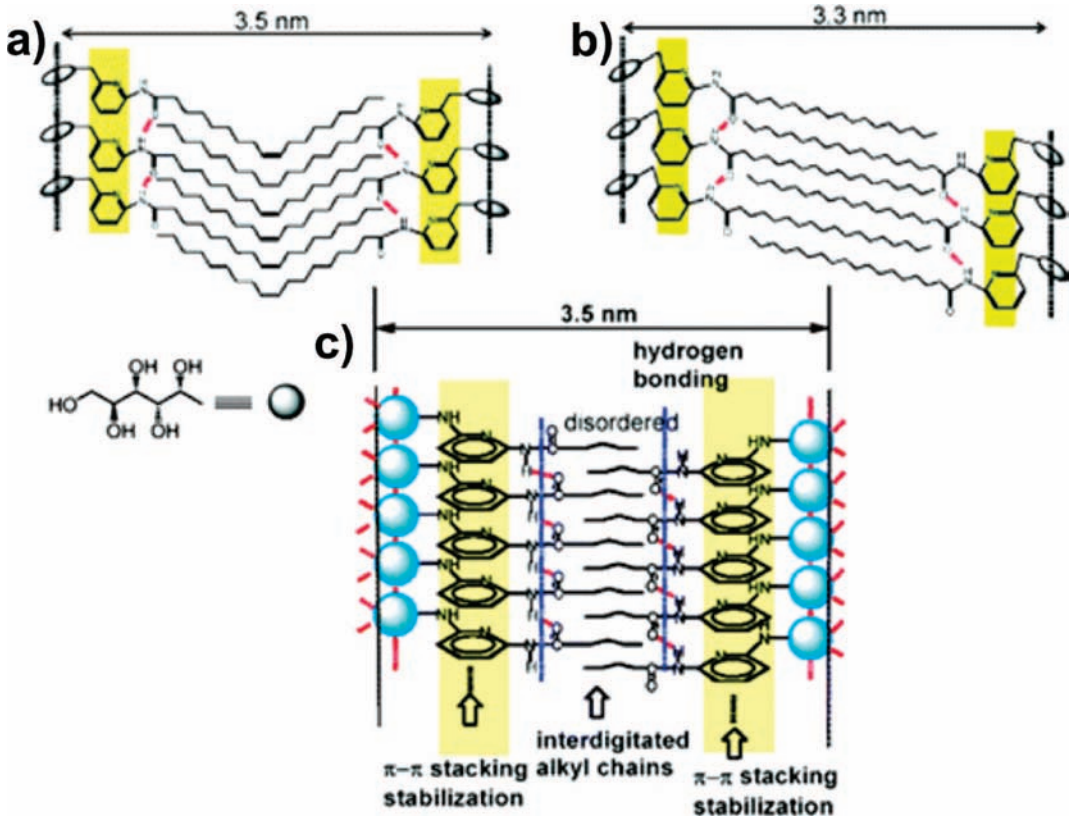


FIGURE 6. Proposed self-assembled nanostructures from GlyDAP1 and GlyDAP2. The unsaturation in GlyDAP1 results in a kink and a slightly less layered interdigitation. Reprinted with permission from ref 38. Copyright 2004 American Chemical Society.

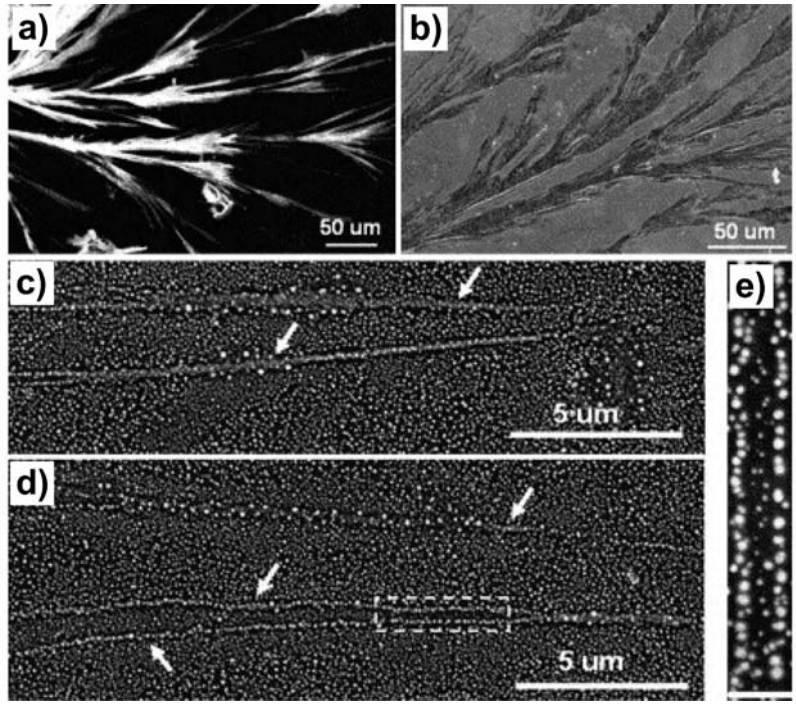
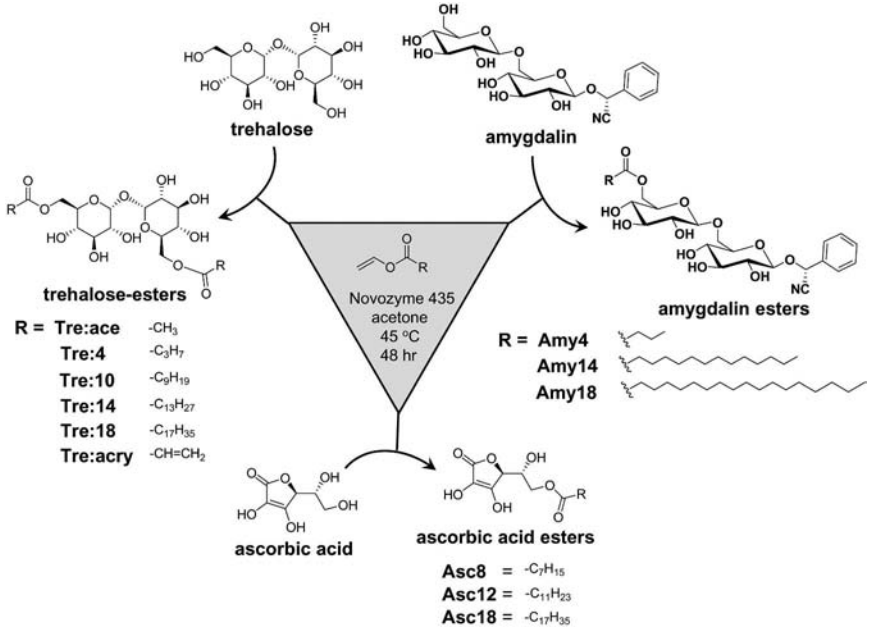


FIGURE 7. SEM images of (a) as produced copper-complexed organic nanotubes, (b) nanoparticles after annealing in argon atmosphere, (c, d) Cu nanoparticles formed on nanotube templates, and (e) an enlarged view of the square area marked in panel d. Scale bar is 500 nm. Reprinted with permission from ref 41. Copyright 2005 Elsevier.

promise in developing unique supramolecular products, at present, multistep syntheses of molecular gels is an encumbrance to commercial operations. Challenges still exist to develop environmentally benign and sustainable production processes. Iden-

SCHEME 10. Enzyme-Catalyzed Regioselective Synthesis of Sugar Amphiphiles from Amygdalin, Trehalose, and Ascorbic Acid



tifying cheap starting materials as well as a sleek synthetic route allow improved commercial development of these products. Synthetic processes that use microbes and enzymes (biocatalysis[45,46]) have greater promise for the expansion of bio-based industries. Unlike thermal and chemical processes, bioprocesses occur under mild reaction conditions, usually result in stereospecific conversions, and produce low or relatively few byproducts. This method can also be used to generate soft materials from biomass at a relatively lower cost and therefore, has economic benefits as well. One drawback is that enzyme-cata-

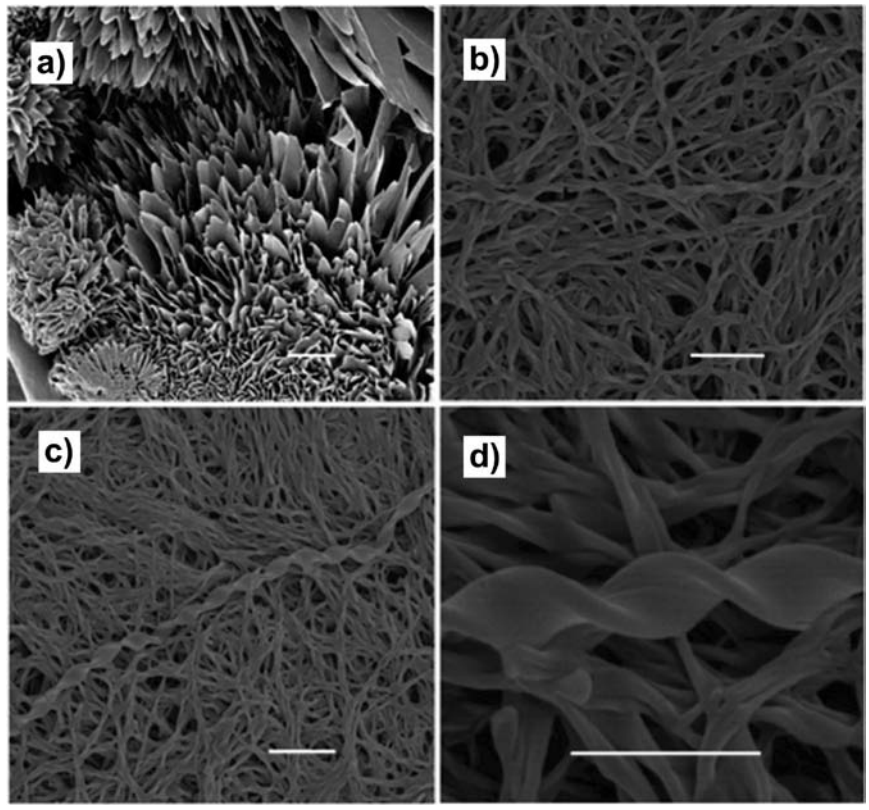


FIGURE 8. SEM micrographs of (a) organogel of Amy4 and aqueous gels of (b) Amy14 and (c) Amy18 and (d) a higher magnification image of the gel in panel b. Scale bar is equivalent to 1 μm. Reprinted with permission from ref 49. Copyright 2006 American Chemical Society.

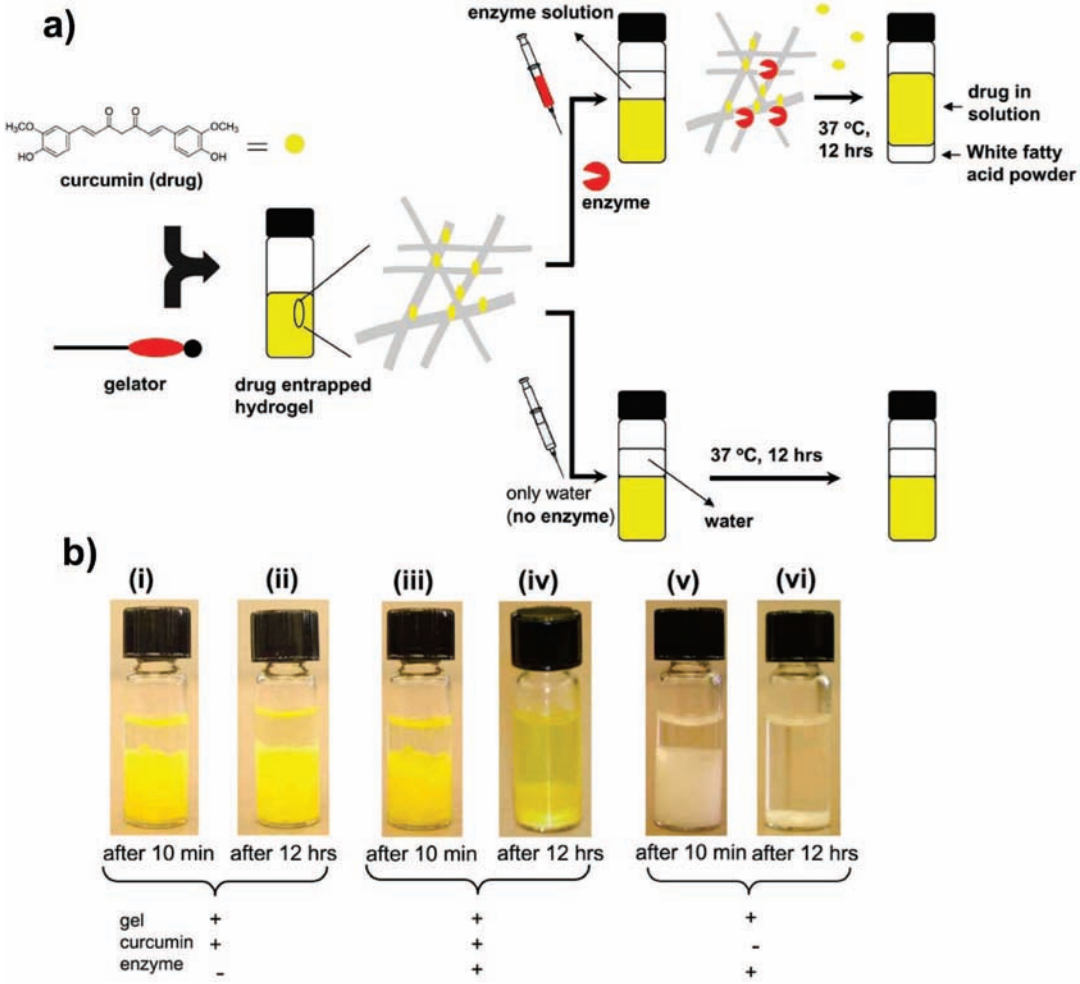


FIGURE 9. (a) Schematic representation of drug encapsulation in hydrogel and subsequent release of drug by enzyme-mediated gel degradation and (b) photos of hydrogels of Amy18 with (i−iv) and without (v, vi) curcumin. Reprinted with permission from ref 49. Copyright 2006 American Chemical Society.

lyzed reactions traditionally lead to low-yield products. Hence, optimization of enzyme-catalyzed reactions with high yields is needed for development of large volumes of materials. Nevertheless, by overcoming these drawbacks, enzyme-mediated feedstock conversion is a suitable solution for bulk production of materials.

We sought new natural starting monomers containing structural features that allow intermolecular associations such as sugar hydrogen bonding and aromatic $\pi-\pi$ stacking. The starting materials also needed to be susceptible to enzyme catalysis. Amygdalin has been used as a main constituent in commercial preparations of laetrile, a purported therapeutic agent.[47] Amygdalin is also a byproduct of the fruit industry. It is a naturally occurring glycoside found in many food plants, such as the kernels of apricots, apples, and almonds.[48] Amygdalin has a phenyl ring and multiple hydroxyl groups, which enhance the aromatic $\pi-\pi$ stacking and the hydrogen bonding, respectively. It also has a primary hydroxyl to which a fatty acid chain can be connected by enzymatic transesterification. Hence, amygdaline-based amphiphiles Amy4, Amy14, and Amy18 (Scheme 10) were designed and synthesized.[49] We demonstrated the utility of enzyme catalysis as a tool to generate amphiphiles from biomass. Biocatalysis offers, in this case, control where the acyl moiety was introduced selectively on the primary hydroxyl group of the sugar in excellent yields (>90%). Generally, multistep synthesis is laborious and often has lower yields, which results in high production costs.[50] This is why low-molecular-weight gelators are not finding niche applications in commercial use.

The amphiphiles Amy4−Amy18 exhibited gelation properties in a broad range of solvents, such as polar solvents, water, and nonpolar cyclohexane, at extremely low concentrations (minimum gelation concentrations are between 0.05−0.2 wt %). They also generate various nanostructures such as grass-like morphologies and helical ribbons in acetonotrile and water gels, respectively (Figure 8).[49] Surpris-

ingly, unpurified crude products showed unprecedented gelation, similar to the purified products, suggesting the utility of this process for industrial-scale applications. The self-assembly of these amphiphiles was characterized with the help of an array of techniques including single-crystal analysis and X-ray diffraction data.

Enzyme-Catalyzed Drug Delivery. Using amygdalin hydrogelators, we have developed a novel approach for encapsulating a hydrophobic drug molecule in a hydrogel. Subsequently, the drug can be released by breaking the gel using a hydrolase (Lipolase 100L, type EX).[49] Encapsulation of the chemotherapeutic hydrophobic drug curcumin[51] in the hydrogel allows subsequent enzyme-triggered drug delivery, as shown in Figure 9. Due to its hydrophobic nature, curcumin is likely to be located at hydrophobic pockets of the gel. The hydrolase enzyme lipolase was added to the preformed gel and kept at 37 °C, lower than the gel melting temperature. After a few hours, the gel was completely degraded and the encapsulated curcumin released into the solution. Drug release was monitored by absorbance studies, and the gel degradation products were characterized. It was shown that during gel degradation, the ester bond formed though biocatalysis was cleaved. The rate of drug release was controlled by manipulating the enzyme concentration, temperature, or both.[49]

Trehalose-Based Organogelators. Trehalose, α-D-glucopyranosyl-(1→1)-β-D-glucopyranoside is an alpha-linked disaccharide. It is synthesized by fungi, plants, and invertebrate animals. Trehalose has been extensively used in the food, pharmaceutical, and cosmetic industries.[52,53] John et al. used a biocatalytic strategy to synthesize a series of highly symmetrical diesters (Scheme 10) that self-assemble in a range of organic solvents to form gels at very low concentrations (0.04% w/v).[54] The gel fibers obtained from short acyl chains were self-assembled and stabilized, most likely through extensive H-bonding networks. In the case of long acyl chains, hydrophobic interactions also play a major role in self-assembly of these gelators. Trehalose−acrylate (Tre:acry) conjugate gave us the opportunity for polymerization of gels. Organogels of Tre:acry (Scheme 10) were polymerized in the presence of the photoinitiator (2,2-dimethoxy-2-phenylacetophenone, 5 mol %) by UV irradiation. Lyophilization of the gel resulted in a highly porous structure. No gel shrinkage occurred during this process. The resulting aerogel remained intact as a self-supporting scaffold. The material behaved as a hydrogel, absorbing 12 times its weight of water to produce a self-supporting transparent material (Figure 10). Such products would be useful in tissue engineering applications.

Vitamin C Based Gels and Liquid Crystals. Our continuing search led us to design amphiphiles from ascorbic acid (vitamin C, of which lime and kiwi fruits are rich sources), which is a powerful antioxidant and is known to inhibit free-radical initiated lipid peroxidation.[55] Ascorbic acid based amphiphiles, Asc8, Asc12, and Asc18 (Scheme 10), were synthesized using *Candida antarctica* Lipase B (CALB) catalyzed transesterfication reactions.[56] The resulting amphiphiles also exhibited gelation behavior in both aqueous solutions and organic solvents. We synthesized gold nanoparticles (GNPs) using these amphiphiles in self-assembled soft materials. Ascorbic acid hydrogels were efficient for in situ synthesis of GNPs, preventing aggregation by capping them yielding GNPs embedded in hydrogels as organic−inorganic hybrid materials.[56]

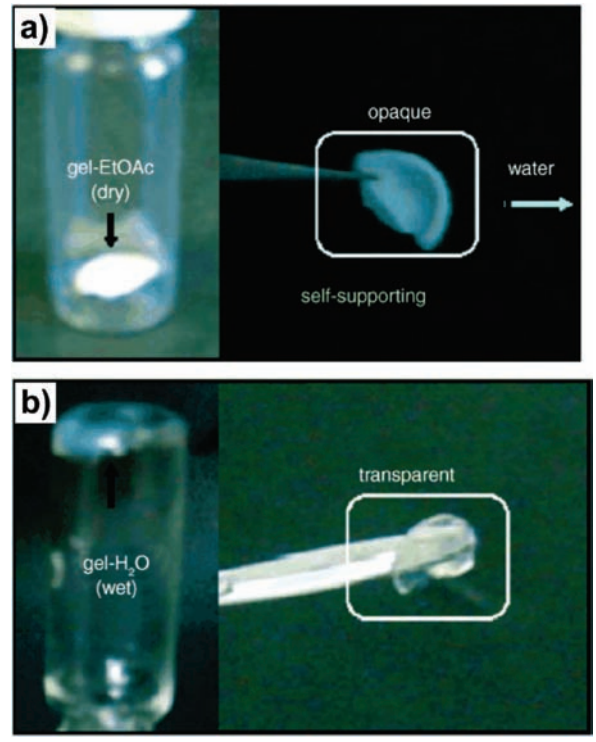


FIGURE 10. Self-supporting (a) organo- and (b) hydrogel from trehalose 6,6′-diacrylate polymerization. Reprinted with permission from ref 54. Copyright 2006 Wiley-VCH.

We examined the ability of ascorbic acid based amphiphiles to generate liquid crystals (LCs), another form of soft materials. Furthermore, LC properties of Asc18 were thoroughly investigated by several techniques. With heating, Asc18 enters an isotropic state; upon cooling, it formed a chiral smectic A (SmA*) phase, which was characterized by polarized optical microscopy (Figure 11).[56] The synthesis of GNPs was carried out in situ. Microscopic examination of the liquid crystal−gold nanoparticle (LC−GNP) hybrids revealed the presence of the GNPs. Under these conditions, the initial SmA* state of the Asc18 amphiphile did not change the inherent phase formation behavior. GNPs were characterized by various techniques such as UV−vis spec-

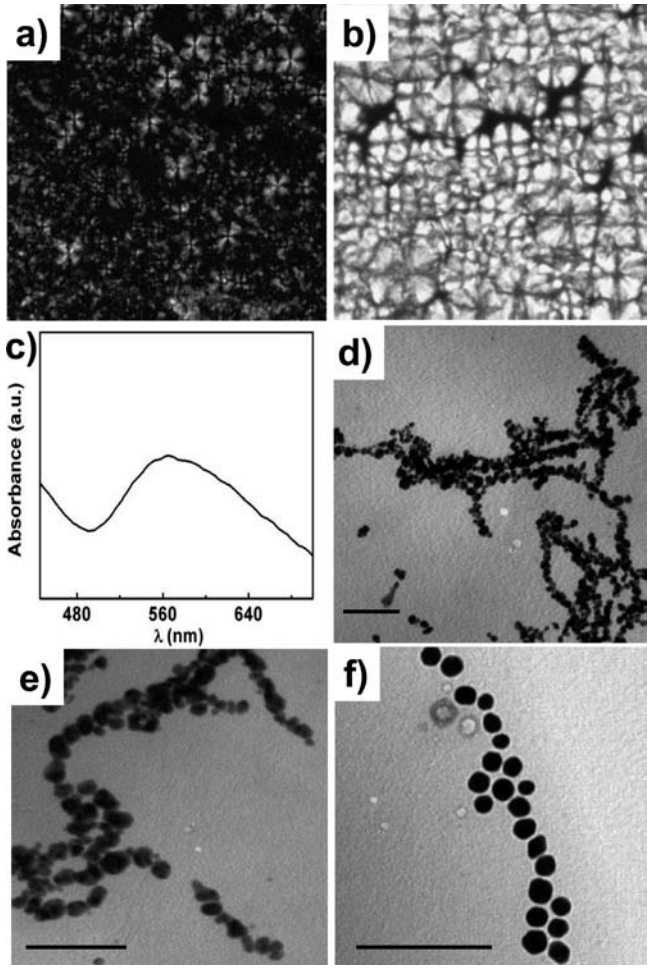


FIGURE 11. POM images of (a) SmA* phase of Asc18 and (b) SmA* phase of Asc18−GNPs, (c) absorption spectra of GNPs embedded in LCs, and (d−f) TEM images of GNPs in LCs at different magnifications. Scale bars represent 100 nm. Reprinted with permission from ref 56. Copyright 2007 American Chemical Society.

troscopy and TEM. GNPs that were embedded in LCs were 16−25 nm thread-like structures showing a characteristic plasmon resonance band (Figure 11).

Conclusions

In conclusion, this Account describes the emerging topic of the production of soft materials designed from crop-based starting materials using green chemistry and self-assembly principles. A series of amphiphilic glycolipids were synthesized from cashew nut shell liquid, a plant- or crop-based raw material. The amphiphiles produced soft nanoarchitectures including lipid nanotubes, twisted or helical nanofibers, low-molecular-weight hydro- or organogels, and liquid crystals. Other sets of amphiphiles have been synthesized from amygdalin, trehalose, and vitamin C. Amygdalin-based amphiphiles showed unique gelation behavior in a wide range of solvents. An enzyme-triggered drug delivery model was demonstrated using these hydrogels for hydrophobic model drugs. Vitamin C based amphiphiles exhibited excellent gelation and liquid crystalline properties. These soft materials were successfully used to develop novel organic−inorganic hybrids by in situ synthesis of metallic nanoparticles. In a nutshell, we find various forms of soft nanomaterials generated from different biomass sources that have applications in a wide range of research fields. These include soft materials, biosensors, liquid crystal displays, medicine, and drug delivery. Overall, this Account demonstrates that utilizing plant- or crop-based resources as starting materials can be "fruitful" in generating useful industrial materials for a sustainable future.

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BIOGRAPHICAL INFORMATION

Dr. Praveen Kumar Vemula is native of Andhra Pradesh, the state of southern India. He received his M.Sc. degree in Organic Chemistry from Osmania University, Hyderabad, and joined in Department of Organic Chemistry at the Indian Institute of Science, Bangalore, India, to pursue research towards his Ph.D. degree under the guidance of Prof. Santanu Bhattacharya. His research was on developing novel catalysts for decontamination reactions in supramolecular aggregates, experimental and computational studies. He received his Ph.D. degree in 2005; currently he is a postdoctoral fellow in Prof. George John's laboratory at the City College of New York. His current research interests include designing and developing novel self-assembled soft materials from renewable resources, molecular gels, liquid crystals, metal nanoparticles, and organic−inorganic hybrid materials.

Prof. George John was born (1962) in Kerala, the southwest coastal state of India. After obtaining his Ph.D. (1993) in Chemistry from Kerala University, India, under the mentorship of Dr. C. K. S. Pillai, Regional Research Laboratory, Trivandrum, he held a postdoctoral position (1994) at the University of Twente, The Netherlands. Subsequently, he was a research scientist at the Agency for Advanced Industrial Science and Technology (AIST), in Japan. In the fall of 2002 he joined the Rensselaer Nanotechnology Center on the research faculty and pursued his research interests in the area of soft materials. Currently, he is an Associate Professor of Chemistry, the City College of the City University of New York. His research interests are in the broad area of organic and macromolecular materials chemistry and specifically include biobased organic synthesis, self-assembled soft materials for functional applications, antimicrobial coatings, green chemistry, understanding growth mechanisms of nanostructures, and designing new structures and multifunctional nanocomposites.

FOOTNOTES

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REFERENCES

1 van Wyk, J. P. H. Biotechnology and the Utilization of Biowaste as a Resource for Bioproduct Development. *Trends Biotechnol.* **2001**, *19*, 172–177.

2 Ragauskas, A. J.; Wiliams, C. K.; Davison, B. H.; Britovsek, G.; Cairney, J.; Eckert, C. A.; Frederick, W. J.; Hallett, J. P.; Leak, D. J.; Liotta, C. L.; Mielenz, L. R.; Murphy, R.; Templer, R.; Tschaplinski, T. The Path Forward for Biofuels and Biomaterials. *Science* **2006**, *311*, 484–489.

3 Lichtenthaler, F. W.; Peters, S. Carbohydrates as Green Raw Materials for the Chemical Industry. *C. R. Chem.* **2004**, *7*, 65–90.

4 Kamm, B.; Kamm, M. Principles of Biorefineries. *Appl. Microbiol. Biotechnol.* **2004**, *64*, 137–145.

5 Herrera, S. Industrial Biotechnology - a Chance at Redemption. *Nat. Biotechnol.* **2004**, *22*, 671–675.

6 Lorenz, P.; Zinke, H. White Biotechnology: Differences in US and EU Approaches. *Trends Biotechnol.* **2005**, *23*, 570–574.

7 Koopmans, R. J. R&D Challenges for the 21st Century. *Soft Matter* **2006**, *2*, 537–543.

8 Corma, A.; Iborra, S.; Velty, A. Chemical Routes for the Transformation of Biomass into Chemicals. *Chem. Rev.* **2007**, *107*, 2411–2502.

9 Rostrup-Nielsen, J. Making Fuels from Biomass. *Science* **2005**, *308*, 1421–1422.

10 Kamm, B. Production of Platform Chemicals and Synthesis Gas from Biomass. *Angew. Chem., Int. Ed.* **2007**, *46*, 5056–5058.

11 Huber, G. W.; Corma, A. Synergies between Bio- and Oil Refineries for the Production of Fuels from Biomass. *Angew. Chem., Int. Ed.* **2007**, *46*, 7184–7201.

12 Hong, C. K.; Richard, P. Development of a Bio-based Material from Soybean Oil and Keratin Fibers. *J. Appl. Polym. Sci.* **2005**, *95*, 1524–1538.

13 Auras, R.; Harte, B.; Selke, S. An Overview of Polylactides as Packaging Materials. *Macromol. Biosci.* **2004**, *4*, 835–864.

14 Mecking, S. Nature or Petrochemistry? Biologically Degradable Materials. *Angew. Chem., Int. Ed.* **2004**, *43*, 1078–1085.

15 Anastas, P. T.; Kirchhoff, M. M. Origins, Current Status, and Future Challenges of Green Chemistry. *Acc. Chem. Res.* **2002**, *35*, 686–694.

16 Lichtenthaler, F. W. Unsaturated O- and N-Heterocycles from Carbohydrate Feedstocks. *Acc. Chem. Res.* **2002**, *35*, 728–737.

17 Biermann, U.; Friedt, W.; Lang, S.; Luhs, W.; Machmuller, G.; Metzger, J. O.; Klass, M. R.; Schafer, H. J.; Schneider, M. P. New Syntheses with Oils and Fats as Renewable Raw Materials for the Chemical Industry. *Angew. Chem., Int. Ed.* **2000**, *39*, 2206–2224.

18 von Rybinski, W.; Hill, K. Alkyl Polyglycosides-Properties and Applications of a New Class of Surfactants. *Angew. Chem., Int. Ed.* **1998**, *37*, 1328–1345.

19 Holmberg, K. Natural Surfactants. *Curr. Opin. Colloid Interface Sci.* **2001**, *6*, 148–158.

20 Huber, G. W.; Chheda, J. N.; Barrett, C. J.; Dumesic, J. A. Production of Liquid Alkanes by Aqueous-Phase Processing of Biomass-Derived Carbohydrates. *Science* **2005**, *308*, 1446–1450.

21 Lichtenthaler, F. W., Ed. *Carbohydrates as Organic Raw Materials*; VCH Publ.: Weinheim/New York, 1991; p 57.

22 Lichtenthaler, F. W.; Klimesch, R.; Muller, V.; Kunz, M. Disaccharide-Building Blocks from Isomaltulose: Glucosyl-α(1→5)-D-arabinoic Acid and Ensuing Products. *Liebigs Ann.* **1993**, 975–980.

23 http://www.isomalt.de/; http://www.isomaltidex.com/html.

24 Hanemann, T.; Haase, W.; Lichtenthaler, F. W. Disaccharide-Derived Liquid Crystals. *Liq. Cryst.* **1997**, *22*, 47–50.

25 Haferburg, D.; Hommel, R.; Claus, R.; Kleber, H.-P. Extracellular Microbial Lipids as Biosurfactants. *Adv. Biochem. Eng. Biotechnol.* **1986**, *33*, 53–93.

26 Guerra-Santos, L. H.; Kappeli, O.; Fiechter, A. Dependence of *Pseudomonas aeruginosa* Continuous Culture Biosurfactant Production on Nutritional and Environmental Factors. *Appl. Microbiol. Biotechnol.* **1986**, *24*, 443–448.

27 Shinoda, K.; Carlsson, A.; Lindman, B. On the Importance of Hydroxyl Groups in the Polar Headgroup of Nonionic Surfactants and Membrane Lipids. *Adv. Colloid Interface Sci.* **1996**, *64*, 253–271.

28 Draths, K. M.; Frost, J. W. Improving the Environment through Process Changes and Product Substitutions In *Green Chemistry: Frontiers in Benign Chemical Syntheses and Processes*; Anastas, P. T., Williamson, T. C., Eds.; Oxford University Press: New York, 1998;Chapter 9.

29 Gibson, J. M.; Thomas, P. S.; Thomas, J. D.; Barker, J. L.; Chandran, S. S.; Harrup, M. K.; Draths, K. M.; Frost, J. W. Benzene-free Synthesis of Phenol. *Angew. Chem., Int. Ed.* **2001**, *40*, 1945–1948.

30 Tyman, J. H. P. Non-isoprenoid Long Chain Phenols. *Chem. Soc. Rev.* **1979**, *8*, 499–537.

31 Antony, R.; Pillai, C. K. S.; Scariah, K. J. GPC Studies on the Cationic Polymerization of Cardanol Initiated by Borontrifluoridediethyletherate. *J. Appl. Polym. Sci.* **1990**, *41*, 1765–1775.

32 John, G.; Pillai, C. K. S. Grafting of Bio-monomers. *Polym. Bull.* **1989**, *22*, 89–94.

33 John, G.; Pillai, C. K. S. Synthesis and Characterization of a Self-crosslinkable Polymer from Cardanol: Autooxidation of Poly(cardanyl acrylate) to Crosslinked Film. *J. Polym. Sci., Part A: Polym. Chem.* **1993**, *31*, 1069–1073.

34 John, G.; Masuda, M.; Okada, Y.; Yase, K.; Shimizu, T. Nanotube Formation from Renewable Resources via Coiled Nanofibers. *Adv. Mater.* **2001**, *13*, 715–718.

35 Yui, H.; Guo, Y.; Koyama, K.; Sawada, T.; John, G.; Yang, B.; Masuda, M.; Shimizu, T. Local Environment and Property of Water Inside of the Hollow Cylinder of a Lipid Nanotube. *Langmuir* **2005**, *21*, 721–727.

36 John, G.; Jung, J.-H.; Minamikawa, H.; Yoshida, K.; Shimizu, T. Morphological Control of Helical Solid Bilayers in High-Axial-Ratio Nanostructures through Binary Self-Assembly. *Chem.—Eur. J.* **2002**, *8*, 5494–5500.

37 Jung, J. H.; John, G.; Yoshida, K.; Shimizu, T. Self-Assembling Structures of Long-Chain Phenyl Glucoside Influenced by the Introduction of Double Bonds. *J. Am. Chem. Soc.* **2002**, *124*, 10674–10675.

38 John, G.; Mason, M.; Ajayan, P. M.; Dordick, J. S. Lipid-Based Nanotubes as Functional Architectures with Embedded Fluorescence and Recognition Capabilities. *J. Am. Chem. Soc.* **2004**, *126*, 15012–15013.

39 Bhattacharya, S.; Snehalatha, K.; George, S. K. Synthesis of Some Copper(II)-Chelating (Dialkylamino)pyridine Amphiphiles and Evaluation of Their Esterolytic Capacities in Cationic Micellar Media. *J. Org. Chem.* **1998**, *63*, 27–35.

40 Bhattacharya, S.; Snehalatha, K.; Kumar, V. P. Synthesis of Copper(II)-Chelating Ligand Amphiphiles and Their Esterolytic Properties in Cationic Micelles. *J. Org. Chem.* **2003**, *68*, 2741–2747.

41 Zhu, H.; John, G.; Wei, B. Synthesis of Assembled Copper Nanoparticles from Copper-chelating Glycolipid Nanotubes. *Chem. Phys. Lett.* **2005**, *405*, 49–52.

42 Jung, J. H.; John, G.; Masuda, M.; Yoshida, K.; Shinkai, S.; Shimizu, T. Self-Assembly of a Sugar-Based Gelator in Water: Its Remarkable Diversity in Gelation Ability and Aggregate Structure. *Langmuir* **2001**, *17*, 7229–7232.

43 John, G.; Jung, J. H.; Masuda, M.; Shimizu, T. Unsaturation Effect on Gelation Behavior of Aryl Glycolipids. *Langmuir* **2004**, *20*, 2060–2065.

44 John, G.; Minamikawa, H.; Masuda, M.; Shimizu, T. Liquid Crystalline Cardanyl β-D-Glucopyranosides. *Liq. Cryst.* **2003**, *30*, 747–749.

45 Koller, K. M.; Wong, C.-H. Enzymes for Chemical Synthesis. *Nature* **2001**, *409*, 232–240.

46 Yan, Y.; Bornschener, U. T.; Schmid, R. D. Lipase-Catalyzed Synthesis of Vitamin C Fatty Acid Esters. *Biotechnol. Lett.* **1999**, *21*, 1051–1054.

47 Syrigos, K. N.; Rowlinson-Busza, G.; Epenetos, A. A. In Vitro Cytotoxicity Following Specific Activation of Amygdalin by β-Glucosidase Conjugated to a Bladder Cancer-Associated Monoclonal Antibody. *Int. J. Cancer* **1998**, *78*, 712–719.

48 Jones, D. A. Why Are so Many Food Plants Cyanogenic. *Phytochemistry* **1998**, *47*, 155–162.

49 Vemula, P. K.; Li, J.; John, G. Enzyme Catalysis: Tool To Make and Break Amygdalin Hydrogelators from Renewable Resources: A Delivery Model for Hydrophobic Drugs. *J. Am. Chem. Soc.* **2006**, *128*, 8932–8938.

50 Zhang, S. Hydrogels: Wet or Let Die. *Nat. Mater.* **2004**, *3*, 7–8.

51 Duvoix, A.; Romain, B.; Sylvie, D.; Michael, S.; Franck, M.; Estelle, H.; Mario, D.; Marc, D. Chemopreventive and Therapeutic Effects of Curcumin. *Cancer Lett.* **2005**, *223*, 181–190.

52 Higashiyama, T. Novel Functions and Applications of Trehalose. *Pure Appl. Chem.* **2002**, *74*, 1263–1269.

53 Elbein, A. D.; Pan, Y. T.; Pastuszak, I.; Carroll, D. New Insights on Trehalose: A Multifunctional Molecule. *Glycobiology* **2003**, *13*, 17R–27R.

54 John, G.; Zhu, G.; Li, J.; Dordick, J. S. Enzymatically Derived Sugar-Containing Self-Assembled Organogels with Nanostructured Morphologies. *Angew. Chem., Int. Ed.* **2006**, *45*, 4772–4776.

55 Nihro, Y.; Miyataka, H.; Sudo, T.; Matsumoto, H.; Satoh, T. 3-O-Alkylascorbic Acids as Free-Radical Quenchers: Synthesis and Inhibitory Effect on Lipid Peroxidation. *J. Med. Chem.* **1991**, *34*, 2152–2157.

56 Vemula, P. K.; Aslam, U.; Mallia, V. A.; John, G. In Situ Synthesis of Gold Nanoparticles Using Molecular Gels and Liquid Crystals from Vitamin-C Amphiphiles. *Chem. Mater.* **2007**, *19*, 138–140.