

Synthesis and Characterization of Maltose-Based Amphiphiles as Supramolecular Hydrogelators

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Supporting Information

ABSTRACT: Low molecular mass amphiphilic glycolipids have been prepared by linking a maltose polar head and a hydrophobic linear chain either by amidation or copper(I)-catalyzed azide—alkyne [3 + 2] cycloaddition. The liquid crystalline properties of these amphiphilic materials have been characterized. The influence of the chemical structure of these glycolipids on the gelation properties in water has also been studied. Glycolipids obtained by the click coupling of the two components give rise to stable hydrogels at room temperature. The fibrillar structure of supramolecular hydrogels obtained by the self-assembly of these gelators have been characterized by electron microscopy. Fibers showed some torsion, which could be related with a chiral



supramolecular arrangement of amphiphiles, as confirmed by circular dichroism (CD). The sol-gel transition temperature was also determined by differential scanning calorimetry (DSC) and NMR.

INTRODUCTION

A gel can be considered as a viscoelastic solidlike material composed of an elastic cross-linked network and a solvent, which is the major component. Macromolecular gels based on polymeric compounds have been widely studied but interest in supramolecular gels has increased in recent years. These types of gels are formed by the self-aggregation of low molecular weight gelator molecules, a process that gives rise to a supramolecular structure that can trap organic or aqueous solvent.¹ Self-assembly occurs through a combination of noncovalent interactions like H-bonding, π - π stacking, donor-acceptor interactions, solvophobic forces, and van der Waals interactions. This self-assembly allows these kinds of material to be considered as supramolecular polymers.² Taking into account the reversibility of these interactions, supramolecular gels can be cycled between free-flowing liquids and nonflowing materials. Furthermore, this reversible behavior can be triggered by external stimuli such as temperature, pH, or irradiation.³ Depending on the medium in which the material can gelate, they have been classified as hydrogels if the solvent is water⁴ or organogels in other cases.⁵ The interest in these soft materials has also increased in recent years due to their possible technological applications, mainly as smart materials or biomaterials, and they have been explored, for instance, as platforms to mediate the growth of tissues and as drug delivery systems.^o

Carbohydrates provide a rich library of water-soluble, hydrophilic building blocks, and these can be used in the preparation of hydrogelators based on the H-bonding of hydroxyl groups. Examples of glyco-amphiphiles, conventional single-head amphiphiles,⁷ and bolaamphiphiles⁸ have been described, with interest focused on the assembled supramolecular structures and their ability to gel in a mixture of water and alcohol or, in some cases, in water alone. In the case of conventional single-headed amphiphiles, mono-⁹ and disaccharides¹⁰ have been used as hydrophilic polar heads. The cyclic forms of carbohydrates have multiple and directional hydroxyl groups that provide a strong cooperative hydrogen bonding network to support the self-assembled fibrous structure of the gels. The presence of amide groups as linking units with the hydrophobic tail or the incorporation of aromatic rings also contributes to the cooperative interactions of glycoamphiphiles and consequently to gelation.¹¹ The gelation process is a consequence of a network resulting from the interpenetration of nanofibers, which are formed by the bottom-up assembly of glyco-amphiphiles.¹² Amphihilic hydrogels based on carbohydrates have been reported, for instance, as drug releasers or sensors¹³ and as a means for cell encapsulation.¹⁴

Apart from their ability to self-assemble in solvents, glycolipids (glyco-amphiphiles) may exhibit liquid crystal (LC) phases due to the polar asymmetry of these compounds. The head groups

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are capable of H-bonding while the alkyl chains self-aggregate into microsegregated regions. Thermotropic LC phases were first observed in alkyl glucopyranosides and these compounds are known to form smectic phases, similar to the lamellar phase formed in aqueous media, but the number of mesogenic glycolipids having di- or polysaccharide head groups remains relatively small.¹⁵

We report here the synthesis and characterization of new amphiphilic glycolipids bearing a disaccharide polar head (see Figure 1) and the study of their liquid crystalline and gel-forming properties. In a previous study by Fitremann et al., it was demonstrated that a mixture of isomers of N-palmitoylphenylalanine sucroesters, obtained by direct esterification of sucrose, can form an "egg-white"-like gel.¹⁶ Here, we describe the synthesis and properties of similar systems composed of a combination of maltose as a hydrophilic head and a palmitic fatty chain as a hydrophobic tail. The polar maltose head and the hydrophobic chain were connected by amidation or, alternatively, by a copper-(I)-catalyzed azide-alkyne [3 + 2] cycloaddition.¹⁷ Furthermore, phenylalanine was incorporated as an alternative in order to favor the gelification by $\pi - \pi$ stacking. The compound Malt-NH-C16 was described previously18 and this material was synthesized as a reference in order to assess the influence of the phenylalanine building block or the triazole ring on the selfassembly properties. The thermotropic properties of these kinds of amphiphiles were also studied. The gelation properties either in water or in mixtures of alcohol and water were also studied. The supramolecular gel structure was characterized by DSC, NMR, SEM, TEM, and CD.

RESULTS AND DISCUSSION

Synthesis of Materials. In a first attempt, the synthesis of glyco-amphiphiles with an amide bond as the connecting group

between the hydrophilic and the hydrophobic part was approached using maltose as the starting material. The aim of this approach was to obtain the product in a reduced number of steps in a similar way to the previously described sucrose derivatives.¹⁶ The synthesis of maltosylamine was carried out using ammonium carbonate as an ammonium donor¹⁹ or, alternatively, by the Liskhosherstov method²⁰ using ammonium carbamate instead of carbonate. In both methods an unstable fluffy product was obtained and the subsequent amide formation was performed directly without further purification. Unfortunately, the final pure compound was obtained in very low yield (5%) by this method (see Supporting Information S1 for experimental details).

In an attempt to increase the yield and facilitate the purification of the intermediates, the synthesis of the glycolipids was accomplished using peracetylated maltose as the starting material, which was amine-functionalized as shown in Scheme 1 by previous preparation of glycosyl azides. Maltosylazide 1 was synthesized in a stereoselective manner by treating maltose octa-acetate with trimethylsilyl azide and tin tetrachloride, as a Lewis acid catalyst, employing the general procedure described by Paulsen et al.²¹ The azide group was reduced to the amine by hydrogenation using a palladium catalyst to yield the acetylated maltosylamine 2 in good yield. This compound can be used in the synthesis of the target amide derivatives. Alternatively, compound 1 can react through a 1,3-dipolar cycloaddition, which opens up new possibilities for the design and preparation of amphiphilic glycolipids.

Amine derivative 2 can react with palmitic acid or *N*-palmitoylphenylalanine derivatives to give the peracetylated precursors of Malt-NH-C₁₆ and Malt-NH-Phe-C₁₆, as shown in Scheme 2. In the case of Malt-NH-C₁₆, palmitoyl chloride was used for the condensation, as described previously,¹⁸ and in the



Scheme 2. Synthesis of Malt-NH-C₁₆ and Malt-NH-Phe-C₁₆

case of Malt-NH-Phe- C_{16} dicyclohexylcarbodiimide and hydroxybenzotriazole were used for the condensation. Yields in both cases were around 45%.

In an alternative approach, the linking of hydrophobic chains derived from palmitic acid can be carried out by a copper(I)catalyzed azide—alkyne [3 + 2] cycloaddition using compound 1 and propargyl derivatives of palmitic acid. For this purpose, the propargylamide of palmitic acid (6) and *N*-palmitoylphenylalanine (7) were synthesized. Click reaction²² was carried out in DMF using CuBr and PMDETA to give the desired product in around 90% yield (Scheme 3). All of the protected derivatives were deacetylated at room temperature according to Zempleńs conditions (MeONa and Amberlyst IR120 in anhydrous MeOH) to give the final product in almost quantitative yield.

All compounds were characterized by ¹H, ¹³C NMR, IR and mass spectrometry. Bidimensional NMR experiments (COSY, TOCSY, NOESY, HSQC, and HMBC) were performed in order to corroborate the chemical structure of the glycolipids. Elemental analysis was performed on peracetylated derivatives **OAc-Malt-NH-C**₁₆, **OAc-Malt-NH-Phe-C**₁₆, **OAc-Malt-Tz-C**₁₆, and **OAc-Malt-Tz-Phe-C**₁₆. In the case of unprotected derivatives (Malt-NH-C₁₆, Malt-NH-Phe-C₁₆, Malt-Tz-C₁₆, and Malt-Tz-**Phe-C**₁₆) elemental analysis was also performed but the water content led to discrepancies between the results and the calculated values. The exact masses were determined by mass spectrometry, in addition to the other spectroscopic studies, and the results confirmed the proposed structures of these materials (see Supporting Information S2 and S3).

Liquid Crystal Properties. The liquid crystal (LC) properties of carbohydrate amphiphiles have been studied mainly because this type of compound has similarities with other carbohydrate related biological systems.^{15d} These compounds have the ability to self-assemble and undergo microphase segregation due to hydrophobic interactions of aliphatic chains and the extensive hydrogen bonded network formed by the polar carbohydrate heads. The LC behavior of these compounds and phase transition temperatures are dependent on the nature of the carbohydrate moiety, the length of the hydrophobic alkyl chain and the type of linker between the two parts (e.g., ether, ester or amide bonds). Most of the glyco-amphiphiles reported to date as liquid crystals are based on a monosaccharide as the polar head. Different maltose derivatives linked by an ether bond to different alkyl chains have been found to exhibit a bilayer smectic A phase.²³ Maltose derivatives linked by an amide bond to aliphatic chains have also been studied. In particular, Malt-NH-C₁₆ was previously reported but the mesophase was not clearly assigned.¹⁸

The thermal properties of the synthesized amphiphilic glycolipids and the peracetylated precursors were studied by thermogravimetric analysis (TGA), polarized light microscopy, and differential scanning calorimetry (DSC).

The thermogravimetric analysis results are gathered in the Supporting Information (S4). In peracetylated precursors, weight loss was observed at temperatures close to 300 °C. However, thermogravimetric curves for glycolipids display weight losses at temperatures around 150-200 °C (in samples previously dried and immediately analyzed).





NaOMe, amberlyst IR-120 MeOH anh.

Malt-Tz-C₁₆

Figure 2. Microphotograph of **Malt-Tz-C**₁₆ taken at 130 °C.

The peracetylated precursors were studied by polarized optical microscopy as a function of temperature and mesomorphic behavior was not observed, with all compounds melting directly from a crystalline state to an isotropic liquid (see Supporting Information S5). However, the final glycolipids exhibited birefringent textures associated with thermotropic liquid crystalline behavior. The poorly defined birefringent texture of the viscous mesophase (see Figure 2) cannot be unambiguously assigned, but it can be postulated that the mesophase is lamellar based on previous results on thermotropic glycolipids with a similar structure. Decomposition of glycolipids was observed by optical microscopy at temperatures around 170 °C and the sample became brown around this point, most probably due to decomposition of the sugar unit.

A DSC study of the glycolipids was performed by heating the compounds to 150 $^{\circ}$ C (maximum) in order to minimize the thermal decomposition of the samples. Under these conditions

Table 1.	DSC Thermal	Cycles in	a Nitrogen	Atmosphere
(10 °C • 1	\min^{-1})		C	-

NaOMe, amberlyst IR-120 MeOH anh.

Malt-Tz-Phe-C16

compound	thermal transition (°C) $[\Delta H]$ (kJ/mol) ^a
Malt-NH-C ₁₆	Cr 49 [6.2] Cr' 67 [5.0] (cold crystallization 75) Cr'' 144 [2.3] $S_A{}^b$
	S _A 62 [3.3] K' 39 [6.9] Cr
Malt-NH-Phe-C ₁₆	Cr 24 [3.7] (cold crystallization 80) Cr'
	127 [7.7] $S_A^{\ b}$
	S _A 11 [2.2] Cr
Malt-Tz-C ₁₆	Cr 31 [2.0] Cr' 49 [6.2] S _A ^b
	S _A 25 [9.18] Cr
Malt-Tz-Phe-C16	Cr 45 [3.0] Cr' 142 [4.0] S _A ^b
	S _A 120 [12.5] Cr' 25 [1.6] Cr
-	

^{*a*} Data corresponding to the second heating and cooling scan. Cr = crystal, I = isotropic phase, S_A = smectic A phase (according to X-ray data). ^{*b*} The heating cycle was only carried out up to 150 °C to avoid decomposition, which occurs before isotropization.

the second and successive scans were reproducible and the transition data (both in heating and cooling scans) are gathered in Table 1. In all cases, broad transition peaks were observed and traces of water were detected, even after drying under vacuum.

Malt-NH-C₁₆ was previously characterized as a glassy material with a transition from a glass to a mesophase (the nature of the mesophase was not described) at around 141 °C.¹⁸ On heating, however, this compound exhibits (once it has been cooled from 150 °C) two endothermic peaks (probably due to crystalline polymorphism) followed by an exothermic transition that can be assigned to a cold crystallization. Finally, the compound melts at around 145 °C into a highly viscous mesophase. On cooling, this compound crystallizes at around 60 °C.

Table 2. Solubility and Gelation Properties of Synthesized Glycolipids in Different Solvents at 1 wt %, after Heating and Cooling Down to RT^a

	Malt-	Malt-NH-	Malt-	Malt-Tz-
solvent	NH-C ₁₆	Phe-C ₁₆	Tz-C ₁₆	Phe-C ₁₆
hexane	Ι	Ι	Ι	Ι
ethyl acetate	Ι	Ι	Ι	Ι
tetrahydrofuran	Р	Ι	S	Ι
dichloromethane	Ι	Ι	Ι	Ι
acetone	Ι	Ι	Ι	Ι
methanol	Р	$P(G^b)$	S	$P(G^b)$
water	Ι	Ι	G	G^{c}
water/methanol	Р	G $(3:2)^d$	not tested	$G(3:1)^{e}$
dimethyl sulfoxide	S	S	S	S

^{*a*} I = insoluble, P = precipitate, S = solution, G = gel. ^{*b*} Gels are formed at higher concentrations (2.5-5% wt) and upon cooling in a fridge. ^{*c*} See text. ^{*d*} 5 mg in 0.3 mL of water and 0.2 mL of methanol. ^{*e*} 3 mg on 0.3 mL of water and 0.1 mL of methanol.

compound is crystalline up to ca. 145 °C and it finally melts to give a mesomorphic liquid. The analogue Mal-NH-Phe-C₁₆ shows similar thermal behavior, but in this case the melting point of the crystalline solid formed by cold crystallization is around 130 °C. The thermal behavior of Malt-Tz-Phe-C₁₆ is similar except that cold crystallization is not observed for this compound and the melting transition occurs at around 140 °C. However, in the case of Malt-Tz-C₁₆, the peak corresponding to the melting transition is depressed and was observed at around 50 °C. Above this temperature the sample is highly viscous and difficult to characterize by optical microscopy. Nevertheless, at temperatures above approximately 90 °C the sample becomes more fluid and can be clearly characterized as liquid crystalline according to the optical observations. In all cases, decomposition was observed in the mesomorphic state at temperatures above approximately 170 °C either by optical microscopy or DSC (deviation of baseline).

In an effort to identify the mesomorphic phase, XRD studies were carried out on the glyco-amphiphile **Malt-Tz-C₁₆** as a representative example. X-ray patterns were recorded at 65 °C for 4.5 h on samples previously heated to 150 °C in order to develop the mesophase. Bragg reflexions in the low-angle region were found that were related to second, third and fifth order. The lamellar spacing was measured close to 51 Å, which indicates an interdigitated bilayer Smectic A phase (see Supporting Information S6). In the high angle region a diffuse, broad maximum was found along with several slightly sharper peaks. These peaks were observed more clearly when the experiment was performed at 150 °C. This fact leads us to suggest that some degradation occurred during the experiment.

Gel Properties. The solubility and gelation ability of the amphiphilic glycolipids were examined in different solvents by dissolving 5 mg of compound in about 0.1-1 mL of the solvent (i.e., 0.5-5 wt %). Glycoamphiphiles are not soluble at room temperature (RT) in the selected solvents, except DMSO. However, in some of the selected solvents, the glycolipids eventually dissolved on heating. The solution was then cooled down to RT, and either a solution, a precipitate, or a gel was observed depending on the solvent. The results are summarized in Table 2 for mixtures with 1 wt % of the sample.

It can be seen that only the compounds that contain a triazole ring give rise to gels in aqueous solution. Malt-Tz- C_{16} can gelate





Figure 3. Hydrogel of Malt-Tz-C₁₆ (1 wt %).

in water to form a homogeneous gel, as can be observed in Figure 3, at a minimum concentration of 1 wt % and in the absence of other organic solvents. Malt-Tz-Phe-C16 also formed a stable gel in water at 1% but it was found to be inhomogeneous as some precipitate was observed within the gel structure once it had cooled. The addition of methanol as an organic solvent led to the formation of a homogeneous and stable gel (in a mixture of water/methanol 3:1). Malt-NH-Phe-C₁₆ can also gelate in a mixture of water/methanol (3:2) but in this case a larger amount of methanol was required to achieve complete solubilization upon heating. In all cases gels are thermoreversible, having a gel-sol transition at around 60-80 °C, and they are stable at RT (for additional gel photos see Supporting Information, S7). Malt-NH-C₁₆ did not form gels even with a 1:1 proportion of water and methanol. The ability of Malt-Tz-C₁₆ to gel in pure water instead of alcoholic mixtures led us to focus our attention on this compound.

Thermal transitions of gels of Malt-Tz-C₁₆ were studied by DSC (under a nitrogen atmosphere, 10 °C min⁻¹). In the first experiment, 5 wt % of solid Malt-Tz-C₁₆ was dispersed in water. In this case, an endotherm was detected at 66 °C. A thermal peak was not observed in the cooling scan. On the second heating, a broad peak was observed at around 65 °C and this could be due to the gel-sol transition. In order to confirm that this peak corresponds to the sol-gel transition, a preformed hydrogel of **Malt-Tz-C₁₆** (1 wt %) was directly studied by DSC (5 $^{\circ}$ C min⁻¹, Figure 4a). An endothermic peak was detected at around 65 °C but a peak was not observed on cooling. However, in the second heating scan the peak corresponding to the gel-sol transition was again observed, which confirms the reversibility of this transition. NMR experiments also provide information about gel-sol transitions. On heating progressively a gel sample of Malt-Tz-C₁₆ at 1 wt % in D₂O the spectrum was fully resolved above 70 °C, the temperature at which a clear solution is obtained (see Supporting Information S8).

The hydrogel derived from **Malt-Tz-Phe-C**₁₆ at 1 wt % was also studied by DSC (5 °C min⁻¹) and two peaks were detected on heating (Figure 4b, top). This observation could be due to the presence of a partial precipitate. The first peak could correspond to a solubilization transition similar to those observed for surfactants that display a Krafft temperature.²⁴ A second endotherm is measured at higher temperature and this corresponds to the gel—sol transition of the gel. DSC measurements (5 °C/min) on the gel formed in a water/methanol/water (3:1) mixture (Figure 4b, bottom) show a peak at around 75 °C corresponding to the gel—sol transition (a small transition can be detected at



Figure 4. Second DSC thermal cycle in a nitrogen atmosphere ($5 \degree C \min^{-1}$): (a) **Malt-Tz-C**₁₆ at 1 wt % water, heating scan (top) and cooling scan (bottom), (b) **Malt-Tz-Phe-C**₁₆ at 1 wt % in water, heating scan (top) and at 1 wt % in a mixture of water/methanol 3:1, heating scan (bottom).



Figure 5. Lyotropic phase observed by optical microscopy on a sample of Malt-Tz- C_{16} in water prepared by the contact method: (a) with polarizers, (b) without polarizers. The concentration increases from left to right; the solid glycolipid sample is shown on the right side.

around 65 °C, probably due to slight insolubility). DSC measurements (10 °C min⁻¹) on a gel of Malt-NH-Phe-C₁₆ obtained in a mixture of water/methanol (3:2) also show a single peak at around 80 °C and this corresponds to the sol–gel transition. In all cases, subsequent heating scans confirmed the reversibility of these transitions.

Compounds with phenylalanine (Malt-NH-Phe-C₁₆ and Malt-Tz-Phe-C₁₆) can gelate in methanol, albeit at a higher concentration (2.5-5%), and on cooling the solution in a freezer. Under other experimental conditions, a swollen transparent precipitate is obtained that is not sufficient to entrap all the solvent.

It has been reported that two of the driving forces that can favor gel formation are H-bonding and $\pi - \pi$ stacking of aromatic rings.⁴ The different behavior of Malt-Tz-C₁₆ and Malt-NH-C₁₆ highlights the effect of the triazole ring. This group can provide $\pi - \pi$ stacking interactions. Hence, an upfield shift in the NMR signal of the H of the triazole ring is detected by adding water to a DMSO solution, which indicates the contribution of $\pi - \pi$ stacking to the aggregation of the amphiphiles as it has been previously reported²⁵ (see ¹H NMR experiments in Supporting Information S9). Moreover, a simultaneous downfield shift of the NH signal in ¹H NMR spectra is also detected, which can be assigned to self-assembly through hydrogen bonding.^{25b} Furthermore, the triazole ring is a rigid fragment of the amphiphile structure and can promote the formation of 1D or 2D aggregates (fibrils and tapes). The dipole moment exhibited by the 1,2,3triazole ring increases the hydrophilicity²⁶ and facilitates the preparation of hydrogels. In the case of Malt-NH-Phe-C₁₆ and Malt-Tz-Phe-C₁₆, the presence of phenyl groups, located in a remote position from the axis of the molecule, also can favor

 $\pi-\pi$ interactions. However, these molecules are more hydrophobic and the presence of an organic cosolvent is required for complete solubilization and subsequent gel formation on cooling. Therefore, in the design of these gelators the presence of the triazole as a linking unit between the hydrophobic and hydrophilic parts seems to play an important role both for the formation of the supramolecular network and also for ensuring an appropriate solubility in water.

Malt-Tz-C₁₆ self-assembled in water to give homogeneous gels at concentrations above 1 wt % and a study of the lyotropic properties of this material was therefore carried out by the contact method.^{15d,27} The sample was heated to 120 °C (mesophase) and then cooled to RT. A small amount of water was then placed on the slide at the edge of the cover glass and this completely surrounded the sample. The slide was placed again for a few seconds on the hot stage at 80 °C and the phase behavior was immediately investigated by polarizing optical microscopy. A concentration effect was observed, as can be seen in Figure 5. A birefringent texture appeared on a gradient of water from pure liquid to solid glass state and this is due to a lyotropic phase with a lamellar organization. However, a precipitate finally appeared over time.

Electron Microscopy. The self-assembled structure of the gels derived from Malt-Tz-C₁₆, Malt-Tz-Phe-C₁₆, and Malt-NH-Phe-C₁₆ were studied by electron microscopy (SEM and TEM), which revealed the typical fibrillar network that characterizes the supramolecular gels (see Figure 6).

SEM measurements on the xerogel obtained from Malt-Tz-C₁₆ (gel in water) show a fibrillar structure with a diameter of around 80 nm and a length of several micrometers (Figure 6a). Gels derived from compounds with phenylalanine, that is, Mal-Tz-Phe-C₁₆ (water or water/methanol) and Malt-NH-Phe-C₁₆ (water/ methanol), also display fibrillar structures by SEM, with estimated diameters of around 80-200 nm (see Suporting Information S9). These fibers can also be measured by TEM (see Experimental Section), but in this case, a dilute solution of the gel must be used. In Malt-NH-Phe-C₁₆, the same diameter was found as in SEM images, that is, around 150 nm (Figure 6f), but in the cases of Malt-Tz-Phe-C₁₆ and Malt-Tz-C₁₆ the estimated diameters were smaller: around 15 nm for Mal-Tz-Phe-C₁₆ in water (Figure 6d) and 40-80 nm for Mal-Tz-Phe-C16 in water/methanol (Figure 6e) and 40 nm for Malt-Tz- C_{16} (Figure 6b). This finding is consistent with the presence of bundles of fibers of tens of nanometers that are further interpenetrated to form the physical network and make the immobilization of the solvent possible.



Figure 6. (a) SEM image of **Malt-Tz-C**₁₆ (1% wt water) xerogel, (b) TEM image of **Malt-Tz-C**₁₆ (0.1% wt water), (c) TEM image of a single fiber of **Malt-Tz-C**₁₆ (0.1% wt water), (d) TEM image of **Malt-Tz-Phe-C**₁₆ (0.1% wt water), (e) TEM image of **Malt-Tz-Phe-C**₁₆ (3 mg in 0.3 mL of water and 0.1 mL of methanol gel, diluted 10 times), and (f) TEM image of **Malt-NH-Phe-C**₁₆ (5 mg in 0.3 mL of water and 0.2 mL of methanol gel, diluted 10 times). TEM images were dried and negatively stained with uranyl acetate (1 wt % water).



Figure 7. CD spectra of aqueous gel: (a) dashed line, acetonitrile solution (0.7% wt) and (b) solid line, aqueous gel 1 wt % of Malt-Tz- C_{16} .

Furthermore, torsion can be detected in the fibrillar structure studied by TEM. For instance, in **Malt-Tz-C**₁₆ (Figure 6c) a twisted helical ribbon was observed in a dried sample of a 0.1% solution of the material in water, with negative staining by uranyl acetate.

Circular Dichroism Measurements. The twisted fibrillar structure observed by TEM may indicate a chiral supramolecular organization in the aqueous gel of **Malt-Tz-C**₁₆. In order to confirm this possibility, circular dichroism (CD) measurements were carried out on both solution and gels and the results are collected in Figure 7.

The λ_{max} value for a **Malt-Tz-C**₁₆ aqueous gel at 1 wt % in the UV absorption spectrum appears at around 232 nm, and this absorption can be assigned to the triazole group. A Cotton effect was not observed in the CD spectrum of a solution of the compound in acetonitrile. However, the hydrogel of this compound (1 wt %), when placed between two quartz discs, exhibited a negative Cotton effect where the θ_{\min} value appeared to be very slightly displaced from the λ_{\max} in the UV spectrum (236 nm). We confirmed that the contribution of the linear



Figure 8. CD (top) and UV–vis (bottom) spectra of a solution of Malt-Tz-C₁₆ (0.01 wt % in water) taken at different times once the solution has been previously heated to 80 °C and left to cool to RT.

dichroism (LD) to the true CD spectrum is negligible by comparing several CD spectra recorded at different angles around the incident light beam. The Cotton effect for the gel sample supports the hypothesis that an ordered chiral structure is formed by selfassembly and gelification in aqueous solution.

In order to gain an insight into the supramolecular aggregates formed in water, a dilute solution was studied by this technique (Figure 8). A solution containing 0.01 wt % of Mal-T- C_{16} was first heated to 80 °C and then cooled down to room temperature. A cloudy solution was obtained due to aggregation. The evolution of the UV-vis and CD spectra was registered at different times. A displacement in the $\lambda_{\rm max}$ from 220 to 235 nm in the UV spectrum was observed. It can also be observed that there is an evolution of the CD signal corresponding to the aggregates formed in solution (it should be remarked that in this concentration, gel formation does not take place). Despite the different experimental conditions, the final CD spectrum of aggregates exhibits as main band a negative Cotton effect at a similar wavelength than the observed in the gel state. This band appears in the region corresponding to the absorption of the triazole ring. This result may indicate a similar supramolecular arrangement of amphiphiles in a chiral fibrillar structure.

CONCLUSIONS

A series of maltose-based amphiphiles have been synthesized and their liquid crystalline and gel-forming properties have been determined. The synthetic approach is based on the use of peracetylated maltose as the starting material. The acetyl group on the anomeric carbon is replaced by an azide group and this can finally be reduced to an amino group. Glycolipids were prepared by amidation of the maltosylamine with palmitic acid derivatives or by a copper(I)-catalyzed azide—alkyne [3 + 2] cycloaddition of the maltosylazide with a palmitoyl derivative bearing an alkyne group.

All of the synthesized compounds exhibit a mesomorphic fluid state and three of the four compounds synthesized form gels in pure water or a mixture of water and alcohol. All compounds are stable at room temperature. Copper(I)-catalyzed azide alkyne [3 + 2] cycloaddition seems to have a beneficial effect in the design and preparation of gelators as a linking strategy for the hydrophilic maltose head and the hydrophobic tail derived from palmitic acid.

The study of the resulting self-assembled fibrillar network was carried out on the maltose/palmitic acid-based molecule with a linking triazole group. This material was chosen because it forms a homogeneous hydrogel at a minimum concentration of 1% wt. The gel was characterized by electron microscopy and fibers of around 40 nm were observed. Furthermore, the formation of twisted fibers was supported by the observation of a CD signal. The sol—gel transition temperature was determined by DSC and NMR studies.

The systems described in this paper are attractive candidates to function as a matrix in tissue engineering or in controlled drug release. The importance of these materials is based on their potential biocompatibility and degradability.

EXPERIMENTAL SECTION

Characterization data (elemental analysis, ¹H and ¹³C NMR, FTIR, and MS) for the intermediate compounds 1-7 are collected in the Supporting Information. Only data corresponding to the peracetylated and final amphiphilic glycolipids are included in this section.

Synthesis of Hepta-O-acetyl- β -maltosyl Azide (1). Trimethylsilyl azide (543 μ L, 4.13 mmol) and tin tetrachloride (173 μ L, 1.48 mmol) were added, at room temperature and under argon, to a solution of β -D-maltose octaacetate (2.00 g, 2.95 mmol) in dry CH₂Cl₂ (6 mL, 0.5 M). The reaction mixture was stirred at room temperature and the reaction was monitored by TLC (6:4 hexane/ethyl acetate). After 24 h, CH_2Cl_2 was added and the solution was washed with saturated Na_2CO_3 and twice with water. The organic layer was dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The product was purified by flash chromatography using hexane/ethyl acetate 6:4. A white solid was obtained (1.59 g, 80%). For characterization data, see the Supporting Information.

Synthesis of Hepta-O-acetyl- β -maltosyl Amide (2). Azidedisaccharide-heptaacetate 1 (1.00 g, 1.51 mmol) was dissolved in 10 mL of anhydrous THF under an argon atmosphere. Palladium hydroxide (20 wt % Pd on carbon wet, 104 mg, 10 wt %) was added and the reaction mixture was stirred for 2 days at room temperature under an atmosphere of hydrogen. The catalyst was removed by filtration and the solvent was removed under reduced pressure. The disappearance of azide was monitored by the IR signal at 2122 cm⁻¹. The product was used without further purification. For characterization data, see the Supporting Information.

Synthesis of Palmitoyl Chloride (3). Palmitic acid (295 mg, 1.15 mmol) was dissolved in 25 mL of anhydrous dichloromethane. Oxalyl chloride (0.30 mL, 2.81 mmol) and *N*,*N*-dimethylformamide (0.3 mL) were added. The reaction mixture was stirred overnight. The solvent was removed under reduced pressure. The acyl chloride formation was monitored by appearance of an IR signal at around 1800 cm⁻¹. The product was used without further purification.

Synthesis of Acetylated Maltose Conjugate OAc-Malt-NH-C₁₆. Amino-disaccharide-heptaacetate 2 was dissolved in 10 mL of anhydrous *N*,*N*-dimethylformamide. Pyridine (130 μ L, 1.61 mmol) was added and the solution was cooled to 0 °C. A solution of palmitoyl chloride (3) in 5 mL of anhydrous *N*,*N*-dimethylformamide was added. The reaction mixture was stirred for 48 h at room temperature and poured into 150 mL of water. The aqueous phase was extracted with 3 × 150 mL of dichloromethane. The combined organic phases were washed once with 150 mL of saturated sodium bicarbonate solution and 2 × 150 mL of water. The organic phase was dried with anhydrous MgSO₄. The solution was filtered and the solvent was removed under reduced pressure. The resulting syrup was purified by flash chromatography with dichloromethane/ethyl acetate 4:6 as eluent. A white solid was obtained (0.369 mg, 45%).

¹H NMR (400 MHz CDCl₃): 0.87 (t, 3H, J = 6.7 Hz) $-(CH_2)_{12} - CH_3$, 1.1–1.38 (m, 24H) $CH_2 - (CH_2)_{12} - CH_3$, 1.52–1.62 (m, 2H) $-CH_2 - CH_2 - (CH_2)_{12}$, 1.99 (s, 3H), 2.00 (s, 3H), 2.02 (s, 3H), 2.06 (s, 3H), 2.09 (s, 3H), 2.12 (s, 3H), 2.16 (s, 3H) $CH_3 - CO - O$, 2.10–2.20 (m, 2H) $CO - CH_2 - CH_2 -$, 3.72 (ddd, 1H, $J_{4'-5'} = 9.0$ Hz, $J_{5'-6'a} = 4.3$ Hz, $J_{5'-6'b} = 2.3$ Hz) H5', 3.85 (ddd, 1H, $J_{4'-5'} = 9.0$ Hz, $J_{5-6a} = 3.8$ Hz, $J_{5-6b} = 2.2$ Hz) H5, 3.89 (dd, 1H, $J_{3'-4'} = 9.5$ Hz, $J_{4'-5'} = 9.0$ Hz) H4', 3.97 (dd, 1H, $J_{5-6b} = 2.2$ Hz, $J_{6b-6a} = 12.4$ Hz) H6b, 4.15 (dd, 1H, $J_{5-6a} = 3.8$ Hz, $J_{6a-6b} = 12.4$ Hz) H6a, 4.17 (dd, 1H, $J_{5'-6'a} = 4.3$ Hz, $J_{6'a-6'b} = 12.3$ Hz) H5' - 3.5 (dd, 1H, $J_{5'-6'a} = 4.3$ Hz, $J_{6'a-6'b} = 12.3$ Hz) $H6'_{2}$, 4.38 (dd, 1H, $J_{5'-6'a} = 4.3$ Hz, $J_{6'a-6'b} = 12.3$ Hz) H2' - 3.5 (dd, 1H, $J_{5'-6'a} = 9.8$ Hz, $J_{4-5} = 9.9$ Hz) H4', 5.21 (dd, 1H, $J_{1'-2'} = 9.4$ Hz, $J_{1'-NH} = 9.4$ Hz) H1' - 5.26 - 5.33 (m, 3H) H1, H3' - H3', 5.97 (d, 1H, $J_{1'-NH} = 9.4$ Hz) mal-NH-CO.

¹³C NMR (100 MHz, CDCl₃): 14.1 $-(CH_2)_{12}-\underline{CH}_3$, 20.6, 20.6, 20.7, 20.8 (<u>CH₃-CO-O)₇</u>, 22.7, 25.2, 29.0, 29.3, 29.3, 29.4, 29.6, 31.9, 36.7 $-CO-\underline{CH}_2-(\underline{CH}_2)_{13}-\underline{CH}_3$, 61.4 <u>C6</u>, 62.8 <u>C6'</u>, 67.9 <u>C4</u>, 68.5 <u>C5</u>, 69.3 <u>C3</u>, 70.0 <u>C2</u>, 71.4 <u>C2'</u>, 72.7 <u>C4'</u>, 73.9 <u>C5'</u>, 75.0 <u>C3'</u>, 77.7 <u>C1'</u>, 95.6 <u>C1</u>, 169.5 CH₃-<u>CO-O-C4</u>, 169.6, 169.8, 170.4 CH₃-<u>CO-O-C2/C6/</u> C6', 170.5, 170.7 CH₃-<u>CO</u>-O-C3/C3', 171.1 CH₃-<u>CO</u>-O-C2', 173.2 NH-CO-CH₂.

MALDI-TOF MS (DCTB+NaTFA): 896.4 $[M + Na]^+$.

Anal. Calcd for C₄₂H₆₇NO₁₈: C, 57.72; H, 7.73; N, 1.60. Found: C, 57.30; H, 7.57; N, 1.60.

IR (KBr, cm⁻¹): 3322 (broad), 2925, 2853, 1747, 1672, 1538, 1371, 1236, 1039, 900, 603.

Synthesis of N-Palmitoyl Succinimide (4). Palmitic acid (5.13 g, 20 mmol) was dissolved in 30 mL of THF, N-hydroxysuccinimide

(3.24 g, 28 mmol) was dissolved in 45 mL of THF, and dicyclohexylcarbodiimide (DCC) (6.60 g, 32 mmol) was dissolved in 35 mL of THF. These solutions were mixed and stirred for 96 h at room temperature. The reaction was monitored by ¹H NMR. The reaction mixture was filtered and the solvent was distilled off. The product was recrystallized from iPrOH to give a white powder (5.55 g, 78%). For characterization data, see the Supporting Information.

Synthesis of *N***-Palmitoylphenylalanine (5).** L-Phenylalanine (1.26 g, 7.63 mmol) and diisopropylethylamine (2.50 mL, 15.26 mmol) were dissolved in 100 mL of water and 50 mL of THF. A solution of *N*-palmitoylsuccinimide (2.70 g, 7.63 mmol) in 115 mL of THF was added. The mixture was stirred at room temperature for 6 h. The reaction was monitored by ¹H NMR. A solution of HCl (37%) was added to give pH = 4. The solvent was partially removed, and the resulting aqueous phase was extracted with dichloromethane (3×100 mL). The organic layer was dried with anhydrous Na₂SO₄ and finally the solvent was evaporated. A white solid was obtained and recrystallized from petroleum ether/dichloromethane (95/5) (2.27 g, 78%). For characterization data, see the Supporting Information.

Synthesis of Acetylated Maltose Conjugate OAc-Malt-NH-Phe-C₁₆. Amino-disaccharide-heptaacetate 2 (700 mg, 1.10 mmol) was dissolved in 10 mL of anhydrous THF, N-palmitoylphenylalanine 5 (680 mg, 1.68 mmol) and hydroxybenzotriazole (255 mg, 1.89 mmol) were added, and the solution was cooled to 0 °C. A solution of dicyclohexylcarbodiimide (330 mg, 1.60 mmol) in 10 mL of anhydrous THF was added. The reaction mixture was stirred for 2 days at room temperature. The reaction was monitored by TLC using a mixture of hexane/ethyl acetate 1:1 as eluent. The mixture was filtered, and the solvent was removed under reduced pressure. Then 150 mL of ethyl acetate was added and the organic phase was washed three times with 1 M KHSO₄ solution and three times with 1 M NaHCO3 solution. The organic layer was dried over anhydrous MgSO4. The solution was filtered, and the solvent was removed under reduced pressure. The resulting white solid was purified by flash chromatography with a mixture of hexane/ethyl acetate 1:1 and recrystallized from ethanol. A white solid was obtained (720 mg, 50%).

¹H NMR (500 MHz, CDCl₃): 0.87 (t, 3H, J = 7.0 Hz) $-(CH_2)_{12} CH_3$, 1.25–1.40 (m, 24H) $-CH_2-(CH_2)_{12}-CH_3$, 1.46–1.60 (m, 2H) $-CH_2-(CH_2)_{12}-CH_3$, 1.93 (s, 3H), 1.99 (s, 6H), 2.02 (s, 3H), 2.05 (s, 3H), 2.10 (s, 3H), 2.15 (s, 3H), CH₃-CO-O-, 2.10-2.20 (m, 2H) CO-CH₂-CH₂, 2.97-3.15 (m, 2H) CH-CH₂-ar, 3.75-3.85 $(m, 1H) H5', 3.91-3.96 (m, 2H) H4', H5, 4.03 (dd, 1H, J_{5-6b} = 2.0 Hz,$ J_{6a-6b} = 12.4 Hz) H6b, 4.20–4.26 (m, 2H) H6a, H6'a, 4.47 (dd, 1H, $J_{5-6'b} = 2.2$ Hz, $J_{6'a-6'b} = 12.3$ Hz) H6'b, 4.57 (m, 1H) NH-CH-CH₂-, 4.67 (dd, 1H, $J_{1'-2'}$ = 9.5 Hz, $J_{2'-3'}$ = 9.5 Hz) <u>H2'</u>, 4.84 (dd, 1H, J_{1-2} = 4.0 Hz, J_{2-3} = 10.5 Hz) H2, 5.06 (dd, 1H, J_{3-4} = 10.0 Hz, J_{4-5} = 10.0 Hz) H4, 5.20 (dd, 1H, $J_{1'-2'} = 9.5$ Hz, $J_{1'-NH} = 9.1$ Hz) H1', 5.33 (dd, 1H, $J_{2'-3'} = 9.5$ Hz, $J_{3'-4'} = 9.2$ Hz, $J_{3'}$, 5.35 (dd, 1H, $J_{3-4} = 10.0$ Hz, $J_{2-3} = 10.5 \text{ Hz}$ H3, 5.37 (d, 1H, $J_{1-2} = 4.0 \text{ Hz}$ H1, 5.77 (d, 1H, $J_{\text{NH-CH}} =$ 7.6 Hz) CH-NH-CO, 6.64 (dd, 1H, J H_{1'-NH} = 9.1 Hz) malt-NH-CO, 7.16-7.11 (m, 2H) ar-CH-C-NH, 7.29-7.21 (m, 3H) ar-CH=CH-CH=ar.

¹³C NMR (125 MHz, CDCl₃): 14.1 (CH₂)₁₃–<u>CH₃</u>, 20.5, 20.6, 20.7, 20.9, (<u>CH₃</u>–CO–O)₇, 22.7, 24.9, 25.4, 25.6, 29.1, 29.3, 29.3, 29.4, 29.6, 29.7, 31.9, 33.9 – <u>CH₂</u>–(<u>CH₂</u>)₁₂–CH₃, 36.4 CO–<u>CH₂</u>–CH₂–, 37.1 CH–<u>CH₂</u>–arom, 53.9 CO–<u>CH</u>–CH₂, 61.4 <u>C6</u>, 62.7 <u>C6'</u>, 67.9 <u>C4</u>, 68.6 <u>C5</u>, 69.3 <u>C3</u>, 70.0 <u>C2</u>, 71.2 <u>C2'</u>, 72.6 <u>C4'</u>, 73.9 <u>C5'</u>, 74.8 <u>C3'</u>, 77.8 <u>C1'</u>, 95.6 <u>C1</u>, 127.1, 128.7, 128.8, 129.1, 129.4 <u>CHarom</u>, 135.9 <u>Carom</u>, 169.5 CH₃–<u>CO</u>–O–C4, 169.7, 169.8 CH₃–<u>CO</u>–O–C3/CH₃– <u>CO</u>–O–C3', 170.4, 170.5, 170.6 CH₃–<u>CO</u>–O–C2/CH₃–<u>CO</u>–O–C2/CH₃–<u>CO</u>–O–C6/CH₃–<u>CO</u>–O–C6', 170.9 CH₃–<u>CO</u>–O–C2', 171.7 mal-NH–CO–CH, 173.3 NH-CO-CH₂–.

MALDI-TOF MS (DCTB+NaTFA): 1043.6 [M + Na]⁺.

Anal. Calcd for C₅₁H₇₆N₂O₁₉: C, 59.99; H, 7.50; N, 2.74. Found: C, 59.60, H, 7.51, N, 2.99.

IR (KBr, cm⁻¹): 3332, 2918, 2849, 1745, 1689, 1649, 1533, 1371, 1226, 1040, 938, 611.

Synthesis of Maltose Conjugates Malt-NH-C₁₆ and Malt-NH-Phe-C₁₆. The protected peracetylated glycolipids OAc-Malt-NH-C₁₆ and OAc-Malt-NH-Phe-C₁₆ (149.7 mg, 0.146 mmol) were dissolved in 7.5 mL of anhydrous methanol and sodium methoxide (55.3 mg, 1.023 mmol) was added. The solution was stirred at room temperature until the reaction was complete (TLC, hexane/ethyl acetate 1:1). Amberlyst IR 120 (H⁺ form) was added to exchange sodium ions. The resin was filtered off and the solvent was evaporated in vacuo to give a white solid (70–85%).

 $\begin{array}{l} \textit{Malt-NH-C}_{16}^{} \overset{1}{} \text{H NMR} \ (400 \ \text{MHz}, \ \text{MeOD}, \ 55 \ ^\circ\text{C}): \ 0.90 \ (t, \ 3H, \ J=\\ 6.7 \ \text{Hz}) \ -(\text{CH}_2)_{12} - \underbrace{\text{CH}_3}_{2}, \ 1.20 - 1.41 \ (m, \ 24H) \ \text{CH}_2 - (\underbrace{\text{CH}_2}_{12})_{12} - \operatorname{CH}_3,\\ 1.56 - 1.67 \ (m, \ 2H) \ \text{CH}_2 - \underbrace{\text{CH}_2}_{2} - (\text{CH}_2)_{12} -, \ 2.23 \ (m, \ 2H) \ -\text{CO} - \underbrace{\text{CH}_2}_{2} - (\text{CH}_2)_{12} -, \ 2.23 \ (m, \ 2H) \ -\text{CO} - \underbrace{\text{CH}_2}_{2} - (\text{CH}_2)_{12} -, \ 2.23 \ (m, \ 2H) \ -\text{CO} - \underbrace{\text{CH}_2}_{2} - (\text{CH}_2)_{12} -, \ 2.23 \ (m, \ 2H) \ -\text{CO} - \underbrace{\text{CH}_2}_{2} -, \ 3.20 - 3.88 \ (m, \ 12H) \ \underline{\text{H2}}, \ \underline{\text{H3}}, \ \underline{\text{H4}}, \ \underline{\text{H5}}, \ \underline{\text{H6a}}, \ \underline{\text{H6b}}, \ \underline{\text{H2}}', \ \underline{\text{H3}}', \ \underline{\text{H4}}', \\ \underline{\text{H5}}', \ \underline{\text{H6}}'a, \ \underline{\text{H6}}'b, \ 4.89 \ (d, \ 1H, \ J_{1'-2'} = 9.2 \ \text{Hz}) \ \underline{\text{H1}}', \ 5.16 \ (d, \ 1H, \ J_{1-2} = 3.7 \ \text{Hz}) \ \underline{\text{H1}}. \end{array}$

¹³C NMR (100 MHz, DMSO):14.5 $-(CH_2)_{12}-CH_3$, 25.4 $-CH_2-CH_2-(CH_2)_{12}-$, 22.5, 29.1 29.2, 29.3, 29.4, 29.5, 29.5, 31.7, $CH_2-(CH_2)_{12}-CH_3$, 35.9 $-CO-CH_2-CH_2-$, 60.9, 61.2, 70.4, 72.4, 73.0, 73.7, 73.9, 77.2, 77.7, 79.6, C2, C3, C4, C5, C6, C2', C3', C4',C5', C6', 80.1 <u>C1'</u>, 101.4 <u>C1</u>, 173.1 NH-CO-CH₂.

Micro-TOF MS: 580.3698 [M + H]⁺ calcd 580.3691; 602.3521[M + Na]⁺ calcd 602.3511.

IR (KBr, cm⁻¹): 3312 (broad), 2914, 2850, 1670, 1548, 1472, 1151, 1083, 1033, 715.

 $\begin{array}{l} \textit{Malt-NH-Phe-C}_{16} \ ^{1}\text{H NMR} \ (400 \ \text{MHz}, \ \text{MeOD}, 55 \ ^{\circ}\text{C}): 0.89 \ (t, 3H, \\ \textit{J} = 6.5 \ \text{Hz}) - (\text{CH}_2)_{12} - \underline{\text{CH}}_3, 1.20 - 1.29 \ (m, 24 \ \text{H}) - \text{CH}_2 - (\underline{\text{CH}}_2)_{12} - \\ \text{CH}_3, 1.42 - 1.49 \ (m, 2H) - \text{CH}_2 - \underline{\text{CH}}_2 - (\text{CH}_2)_{12} -, 2.14 \ (t, 2H, \textit{J} = \\ 7.3 \ \text{Hz}) - \text{CO} - \underline{\text{CH}}_2 - \text{CH}_2 -, 2.89 \ (\text{dd}, 1H, \textit{J}_{\text{CH}-\text{CH}2a} = 9.4 \ \text{Hz}, \\ \textit{J}_{\text{CH2a-CH2b}} = 14.0 \ \text{Hz}) - \text{CH} - (\underline{\text{CH}}_2)_{b} \text{-arom}, 3.18 \ (\text{dd}, 1H, \textit{J}_{\text{CH}-\text{CH}2b} = \\ \textit{4.9 Hz}, \textit{J}_{\text{CH2a-CH2b}} = 14.0 \ \text{Hz}) - \overline{\text{CH}} - (\underline{\text{CH}}_2)_{a} \text{-arom}, 3.27 - 3.88 \ (m, 11H) \\ \underline{\text{H3}}', \ \underline{\text{H4}}', \ \underline{\text{H5}}', \underline{\text{H6}}'_{a}, \ \underline{\text{H6}}'_{b}, \ \underline{\text{H2}}, \ \underline{\text{H3}}, \ \underline{\text{H4}}, \ \underline{\text{H5}}, \ \underline{\text{H6}}_{a}, \ \underline{\text{M6}}_{b}, \ 3.37 \ (\text{dd}, 1H, \\ \vec{J}_{\text{H1'-H2'}} = 9.1 \ \overline{\text{Hz}}, \ \vec{J}_{\text{H2'-H3'}} = 9.2 \ \overline{\text{Hz}}) \ \underline{\text{H2}}', \ 4.67 \ (\overline{\text{dd}}, 1H, \textit{J}_{\text{CH}-\text{CH}2b} = \\ \textit{4.9 Hz} \textit{J}_{\text{CH}-\text{CH}2a} = 9.4 \ \overline{\text{Hz}}) - \underline{\text{CH}} - \overline{\text{CH}}_2 \text{-arom}, \ 4.92 \ (d, 1H, \textit{J}_{\text{H1'-H2'}} = \\ 9.1 \ \overline{\text{Hz}}) \ \underline{\text{H1}}', \ 5.18 \ (d, 1H, \textit{J}_{\text{H1}-\text{H2}} = 3.5 \ \overline{\text{Hz}}) \ \underline{\text{H1}}, \ 7.17 - 7.26 \ (m, \ 5H) \\ \text{CH arom}. \end{aligned}$

¹³C NMR (100 MHz, MeOD, 55 °C): 14.3 $-(CH_2)_{12}-CH_3$, 26.7 $-CH_2-CH_2-(CH_2)_{12}-$, 23.6, 30.3, 30.4, 30.6, 32.9 $-CH_2-(CH_2)_{12}-$ CH₃, 36.9 $-CO-CH_2-CH_2-$, 38.8 $-CH-CH_2$ -arom, 55.7 -CH-CH₂-arom, 62.2, 62.8, 71.7, 74.2, 74.8, 75.2, 78.45, 78.7, 80.9 C2, C3, C4, C5, C6, C3', C4', C5', C6', 73.7 C2', 81.3 C1', 102.8 C1, 127.7, 129.3, 130.4 CH arom, 138.3 Carom, 174.63 malt-NH-CO-CH, 176.1 CH-NH-CO-CH₂.

Micro-TOF MS: 727.4400 [M + H]⁺ calcd 727.4375; 749.4234 [M + Na]⁺, calcd 749.4194.

IR(KBr, cm⁻¹): 3323 (broad), 2919, 2850, 1645, 1540, 1147, 1081, 1034, 698.

Synthesis of N-Propargyl Palmitoylamide (6) and N-Propargyl (N'-palmitoylphenylalanine) Amide (7). Palmitic acid or N-Palmitoyl phenylalanine (5) (1.0 g, 2.48 mmol) and hydroxybenzotriazole were dissolved in 20 mL of anhydrous tetrahydrofuran. Propargylamine (0.16 mL, 2.50 mmol) was added. The solution was cooled to 0 °C. A solution of dicyclohexylcarbodiimide (511 mg mg, 2.48 mmol) in 15 mL of anhydrous THF was added. The reaction mixture was stirred for 2 days at room temperature. The reaction was monitored by TLC with hexane/ ethyl acetate 7:3 as eluent. The mixture was filtered and the solvent was removed under reduced pressure. 250 mL of dichoromethane were added and the organic phase was washed three times with 1 M KHSO₄ solution, and three times with 1 M NaHCO3 solution. The organic layer was dried over anhydrous MgSO₄. The solution was filtered and the solvent was removed under reduced pressure. The resulting white solid was purified by recrystallization from ethanol. A white solid was obtained (yield around 75%). For characterization data see Supporting Information.

Synthesis of Acetylated Maltose Conjugates OAc-Malt-Tz-C₁₆ and OAc-Malt-Tz-Phe-C₁₆. Propargyl derivatives 6 or 7 (266 mg, 0.91 mmol), azide 1 (602 mg, 0.91 mmol), copper(I) bromide (27.7 mg, 0.19 mol) and N-pentamethyldiethylenetriamine (PMDETA) (38 μ L, 0.18 mmol) were dissolved in anhydrous dimethylformamide (6 mL) under an argon atmosphere. The mixture was stirred at room temperature for 2 days. The reaction was monitored by TLC with hexane/ethyl acetate 1:1 as eluent. The catalyst was removed by filtration and the solvent was removed under reduced pressure. The reaction was poured into 150 mL of water. The aqueous phase was extracted three times, each with 150 mL of dichloromethane/ethyl acetate 1:1. The organic phase was dried with anhydrous MgSO₄. The solution was filtered and the solvent was removed under reduced pressure. The resulting white solid was purified by flash chromatography using initially dichloromethane/ethyl acetate 1:1 and then increasing the polarity. A white solid was obtained (756 mg, 87%).

 $\begin{array}{l} OAc-Malt-Tz-C_{16} \ ^{1}\text{H} \ \text{NMR} \ (400 \ \text{MHz}, \text{CDCl}_3): 0.87 \ (\text{t}, 3\text{H}, J = 6.2 \\ \text{Hz} \) -(\text{CH}_2)_{12}-\underline{\text{CH}}_3, \ 1.16-1.35 \ (\text{m}, 24\text{H}) \ -(\underline{\text{CH}}_2)_{12}-, \ 1.55-1.66 \\ (\text{m}, 2\text{H}) \ -\underline{\text{CH}}_2-(\overline{\text{CH}}_2)_{12}, \ 1.84 \ (\text{s}, 3\text{H}) \ \underline{\text{CH}}_3-\overline{\text{CO}}-\overline{\text{O}}-\mathbf{C2'}, \ 2.00 \ (\text{s}, 3\text{H}), \ 2.02 \ (\text{s}, 6\text{H}), \ 2.06 \ (\text{s}, 3\text{H}), \ 2.10 \ (\text{s}, 3\text{H}), \ 2.13 \ (\text{s}, 3\text{H}), \\ \underline{\text{CH}}_3-\overline{\text{CO}}-\overline{\text{O}}, \ 2.17 \ (\text{t}, 2\text{H}, J = 7.7 \ \text{Hz}) \ \text{CO}-\underline{\text{CH}}_2-\overline{\text{CH}}_2, \ 3.96-3.98 \\ (\text{m}, 2\text{H}) \ \underline{\text{H5/H5'}}, \ 4.05 \ (\text{dd}, 1\text{H}, J_{6b-5} = 1.5 \ \text{Hz}, J_{6a-6b} = 1.6 \ \text{Hz}) \ \underline{\text{H6b}}, \ 4.13 \\ (\text{dd}, 1\text{H}, J_{3'-4'} = 9.3 \ \text{Hz}, J_{4'-5'} = 9.3 \ \text{Hz}) \ \underline{\text{H4'}}, \ 4.23-4.27 \ (\text{m}, 2\text{H}) \ \underline{\text{H6a}}/ \\ \underline{\text{H6'}}_{3}, \ 4.44-4.54 \ (\text{m}, 3\text{H}) \ \text{C} = \underline{\text{C}}-\underline{\text{CH}}_2-\overline{\text{NH}}, \ \underline{\text{H6'}}_{5}, \ 4.87 \ (\text{dd}, 1\text{H}, J_{1-2} = 3.9 \ \text{Hz}) \\ \underline{\text{H4'}}, \ 5.31 \ (\text{dd}, 1\text{H}, J_{1'-2'} = 9.1 \ \text{Hz}, J_{2'-3'} = 8.8 \ \text{Hz}) \ \underline{\text{H2'}}, \ 5.37 \ (\text{dd}, 1\text{H}, J_{2-3} = 10.7 \ \text{Hz}, J_{3-4} = 10.0 \ \text{Hz}, J_{3-4} = 9.3 \ \text{Hz}) \\ \underline{\text{H3'}}, \ 5.44 \ (\text{d}, 1\text{H}, J_{1-2} = 3.9 \ \text{Hz}) \ \underline{\text{H1}}, \ 5.84 \ (\text{d}, 1\text{H}, J_{1'-2'} = 9.1 \ \text{Hz}) \ \underline{\text{H1}}', \\ 6.06 \ (\text{t}, 1\text{H}, J = 4.7 \ \text{Hz}) \ -\text{CH}_2-\overline{\text{NH}} - \text{CO}, \ 7.69 \ (\text{s}, 1\text{H}) \ \text{N} - \underline{\text{CH}} = \ \mathbb{C} - \text{CH}_2 \ \text{triazole}. \end{array}$

¹³C NMR (100 MHz, CDCl₃): 14.1 $-(CH_2)_{12}-\underline{CH}_3$, 20.2, 20.6, 20.7, 20.8, 20.8 (\underline{CH}_3-CO-O)₇, 25.6 $CH_2-\underline{CH}_2-(CH_2)_{12}-$, 22.7, 29.3, 29.4, 29.4, 29.5, 29.6, 29.7, 29.7, 31.9, 35.6, $-(\underline{CH}_2)_{12}-$, CO- \underline{CH}_2-CH_2 , 34.8 C- \underline{CH}_2-NH , 61.5 C6, 62.5 C6', 67.9 C4, 68.8 C5, 69.2 C3, 70.0 C2', 70.9 C2, 72.4 C4', 75.1 C3', 75.4 C5', 85.3 C1', 95.9 C1, 120.8 N-CH=C-N triazole, 145.3 CH = C-N triazole, 169.1, 169.4, 169.9 CH₃- $\underline{CO}-O-C2/C6/C6'$, 169.9, 170.3 CH₃- $\underline{CO}-O-C3/3'$, 170.5 CH₃- $\underline{CO}-O-C4$, 170.6 CH₃- $\underline{CO}-O-C2'$, 173.2 NH-CO-CH₂.

MALDI-TOF MS (DCTB+NaTFA): 977.5 [M + Na]⁺.

Anal. Calcd for $\rm C_{45}H_{70}N_4O_{18}:$ C, 56.59; H, 7.39; N, 5.87. Found: C, 56.25; H, 7.28; N, 5.80.

IR (KBr, cm⁻¹): 3303, 2925, 2854, 1754, 1645, 1552, 1369, 1233, 1036.

OAc-Malt-Tz-Phe-C₁₆. ¹H NMR (400 MHz, CDCl₃): 0.87 (t, 3H, J = $(6.8 \text{ Hz}) - (\text{CH}_2)_{12} - \text{CH}_3, 1.14 - 1.40 \text{ (m, 24H)} - (\text{CH}_2)_{12} - 1.47 - 1.58 \text{ Hz}$ 3H), 2.03 (s, 6H), 2.07 (s, 3H), 2.10 (s, 3H), 2.12 (s, 3H), CH₃-CO-O, 2.10-2.17 (m, 2H) CO-CH₂-CH₂, 2.98-3.10 (m, 2H) -CH-CH₂-Phe, 3.94-4.01 (m, 2H) H5/H5', 4.07 (dd, 1H, $J_{5-6b} = 1.8 \text{ Hz}, J_{6a-6b} = 12.4 \text{ Hz}) \text{ H6b}, 4.16 \text{ (dd, 1H, } J_{3'-4'} = 9.4 \text{ Hz}, J_{4'-5'} = 9.4 \text{ Hz}$ 9.4 Hz) <u>H4'</u>, 4.23–4.28 (m, 2H) <u>H6a/H6'</u> a, 4.42 (d, 2H, J = 5.8 Hz) $C-\underline{CH_2}$ -NH, 4.51 (dd, 1H, $J_{5'-6'b}$ = 2.2 Hz, $J_{6'a-6'b}$ = 12.4 Hz) <u>H6'b</u>, 4.60-4.66 (m, 1H) - CO-CH-NH-, $4.88 \text{ (dd, 1H, } J_{1-2} = 3.9 \text{ Hz},$ $J_{2-3} = 10.5$ Hz) H2, 5.07 (dd, 1H, $J_{3-4} = 9.7$ Hz, $J_{4-5} = 10.0$ Hz) H4, 5.32 (dd, 1H, $J_{1'-2'}$ = 9.4 Hz, $J_{2'-3'}$ = 9.2 Hz) H2', 5.38 (dd, 1H, J_{2-3} = 10.5 Hz, $J_{3-4} = 9.7$ Hz) H3, 5.45 (dd, 1H, $J_{2'-3'} = 9.2$ Hz, $J_{3'-4'} = 9.4$ Hz) H3', 5.46 (d, 1H, J_{1-2} = 3.9 Hz) H1, 5.83 (d, 1H, $J_{1'-2'}$ = 9.4 Hz) H1', 6.04 (d, 1H, J = 7.6 Hz) CH-NH-CO, 6.36 (t, 1H, J = 5.7 Hz) CH₂-NH-CO, 7.12-7.13 (m, 2H) Harom, 7.27-7.22 (m, 3H) Harom, 7.54 (s, 1H) N-CH=C.

¹³C NMR (100 MHz, CDCl₃): 14.1 $-(CH_2)_{12}-\underline{CH}_3$, 20.5, 20.6, 20.7, 20.8, $(\underline{CH}_3-CO-O)_7$, 22.7 $-(\underline{CH}_2)_{12}-$, 25.5 $-\underline{CH}_2-(CH_2)_{12}$, 29.2, 29.3, 29.3, 29.4, 29.6, 29.7, 32.0 $-(CH_2)_{12}-$, 34.9 C $-CH_2-NH$,

36.5 $CO-CH_2-CH_2$, 38.2 $CH-CH_2-Phe$, 54.3 $-CO-CH-CH_2$, 61.5 <u>C6</u>, 62.5 <u>C6'</u>, 68.0 <u>C4</u>, 68.8 <u>C5</u>, 69.3 <u>C3</u>, 70.0 <u>C2</u>, 70.9 <u>C2'</u>, 72.5 <u>C4'</u>, 75.2 <u>C3'</u>, 75.5 <u>C5'</u>, 85.0 <u>C1'</u>, 96.0 <u>C1</u>, 120.8 N-<u>CH</u>=C-N triazole, 127.0, 128.9, 129.2 <u>CHarom</u>, 136.5 <u>Carom</u>, 144.9 <u>CH</u>=C-N triazole, 169.1 CH₃-<u>CO</u>-O-C2', 169.3 CH₃-<u>CO</u>-O-C4, 169.8 CH₃-<u>CO</u>-O-C3, 169.9 CH₃-<u>CO</u>-O-C3', 170.4 CH₃-<u>CO</u>-O-C2, 170.5, 170.3 CH₃-<u>CO</u>-O-C6/C6', 171.0 NH-<u>CO</u>-CH-, 173.2 NH-CO-CH₂-.

MALDI-TOF MS (DCTB): 1124.4 [M + Na]⁺.

Anal. Calcd for C₅₄H₇₉N₅O₁₉: C, 58.84; H, 7.22; N, 6.35. Found: C, 58.24; H, 7.12; N, 6.28.

IR (KBr, cm⁻¹): 3306, 2923, 2852, 1753, 1640, 1546, 1370, 1234, 1037.

Synthesis of Maltose Conjugates Malt-Tz- C_{16} and Malt-Tz-Phe- C_{16} . The protected triazole-disaccharide-octaateate derivatives (OAc-Malt-Tz- C_{16} and OAc-Malt-Tz-Phe- C_{16}) (149.7 mg, 0.146 mmol) were dissolved in 7.5 mL of anhydrous methanol. Sodium methoxide (55.3 mg, 1.023 mmol) was added. The solution was stirred at room temperature until the reaction was complete (TLC, hexane/ ethyl acetate 1:1). Amberlyst IR 120 (H⁺ form) was added to exchange sodium ions, the resin was filtered off, and the solvent was evaporated in vacuo. A white solid was obtained (85–90%).

 $\begin{array}{l} \textit{Malt-Tz-C}_{16}. \ ^{1}\text{H NMR} (400 \text{ MHz, MeOD, 55 °C}): 0.90 (t, 3H, J = 6.9 \text{ Hz}) - (CH_2)_{12}-\underline{CH}_{3i} 1.20-1.36 (m, 24H), -(\underline{CH}_2)_{12}-CH_3, 1.56-1.60 (m, 2H) \underline{CH}_2-CH_2-(CH_2)_{12}, 2.21 (t, 2H, J = 7.4 \text{ Hz}) \\ \textit{CO-}\underline{CH}_2-CH_2, 3.28 (dd, 1H, J_{3-4} = 9.6 \text{ Hz}, J_{4-5} = 9.5 \text{ Hz}) \underline{H4}, 3.47 \\ (dd, 1H, J_{1-2} = 3.8 \text{ Hz}, J_{2-3} = 9.7 \text{ Hz}) \underline{H2}, 3.64 (dd, 1H, J_{2-3} = 9.7 \text{ Hz}, J_{3-4} = 9.6 \text{ Hz}) \underline{H3}, 3.65-3.90 (m, 8H) \underline{H5}, H6a, H6b, H3', H4', H5', \underline{H6'a, H6'b}, 3.93 (dd, 1H, J_{1'2'} = 9.1 \text{ Hz}, J_{2'3'} = 9.0 \text{ Hz}) \underline{H2'}, 4.34 (s, 2H) C-\underline{CH}_2-NH, 5.13 (d, 1H, J_{1-2} = 3.8 \text{ Hz}) \underline{H1}, 5.50 (d, 1H, J_{1'2'} = 9.1 \text{ Hz}) \underline{H1'}, 7.95 (s, 1H) N-\underline{CH}-C-\text{triazole}. \end{array}$

¹³C NMR (100 MHz, MeOD, 55 °C):13.0 $-(CH_2)_{12}-\underline{CH}_3$, 22.3, 25.4, 28.9, 29.2, 31.6 $-\underline{CH}_2-(\underline{CH}_2)_{12}-$, 34.1 $C-\underline{CH}_2-NH-$, 35.5 $CO-\underline{CH}_2-CH_2$, 60.4, 61.3, 73.7, 76.8, 78.2, <u>C6</u>, C3', <u>C4'</u>, <u>C5'</u>, <u>C6'</u>, 70.1 <u>C4</u>, 72.2 <u>C2'</u>, 72.8 <u>C2</u>, 73.5 <u>C3</u>, 78.9 <u>C5</u>, 88.0 <u>C1'</u>, 101.5 <u>C1</u>, 120.0 $N-\underline{CH}=C$ triazole, 145.0 $CH=\underline{C}-CH_2$ triazole, 174.9 $NH-\underline{CO}-CH_2$. MicroTOF MS: 683.383 [M+ Na]⁺, calcd: 683.384.

IR (KBr, cm⁻¹): 3313 (broad), 2917, 2849, 1643, 1543, 1464, 1429, 1241, 1050, 719.

 $\begin{array}{l} \mbox{Malt-Tz-Phe-C}_{16} \ ^{1}\mbox{H} \ {\rm NMR} \ (400 \ {\rm MHz}, \ {\rm MeOD}, \ 55 \ ^{\circ}\ C): \ 0.86 \ (t, \ 3H, \\ J = 6.8 \ {\rm Hz}) \ -({\rm CH}_2)_{12} \ - \underline{\rm CH}_3, \ 1.10 \ - 1.32 \ (m, \ 24H), \ {\rm CH}_2 \ - {\rm CH}_2 \ - \ (\underline{\rm CH}_2)_{12}, \ 1.38 \ - 1.48 \ (m, \ 2H) \ \underline{\rm CH}_2 \ - {\rm CH}_2 \ - \ ({\rm CH}_2)_{12}, \ 2.15 \ (t, \ 2H, \\ J = 7.5 \ {\rm Hz}) \ {\rm CO} \ - \underline{\rm CH}_2 \ - {\rm CH}_2, \ 2.89 \ (dd, \ 1H, \ J_{\rm CH-CH2a} = 8.9 \ {\rm Hz}, \\ J_{\rm CH2a-CH2b} = 13.9 \ {\rm Hz}) \ {\rm CH} \ - \ (\underline{\rm CH}_2)_{2} \ {\rm a} \ - {\rm Phe}, \ 3.11 \ (dd, \ 1H, \ J_{\rm CH-CH2b} = 8.9 \ {\rm Hz}, \\ J_{\rm CH2a-CH2b} = 13.9 \ {\rm Hz}) \ {\rm CH} \ - \ (\underline{\rm CH}_2)_{2} \ {\rm b} \ - {\rm Phe}, \ 3.34 \ (dd, \ 1H, \ J_{3-4} = 8.8 \ {\rm Hz}, \ J_{2-3} = 9.6 \ {\rm Hz}) \ {\rm H2}, \ 3.67 \ (dd, \ 1H, \ J_{2-3} = 9.6 \ {\rm Hz}, \ J_{3-4} = 8.8 \ {\rm Hz}) \ {\rm H3}, \ 3.70 \ - 3.93 \ (m, \ 9H) \ {\rm H5}, \ {\rm H6a}, \ {\rm H6b}, \ {\rm H2}', \ {\rm H3}', \ {\rm H4}', \ {\rm H5}', \ {\rm H6}'a, \ {\rm H6}'b, \ 4.42 \ (s, \ 2H) \ {\rm C} \ - \ {\rm CH}_2 \ - {\rm NH}, \ 4.61 \ (dd, \ 1H, \ J_{2-3} = 8.8 \ {\rm Hz}) \ {\rm Hz}, \ J_{\rm CH-CH2b} = 6.4 \ {\rm Hz}) \ {\rm CO} \ - \ {\rm CH}_2 \ - {\rm NH}, \ 4.61 \ (dd, \ 1H, \ J_{2-1} = 3.8 \ {\rm Hz}) \ {\rm H1}, \ 5.59 \ (d, \ 1H, \ J_{1^{-2}} = 3.8 \ {\rm Hz}) \ {\rm H1}, \ 5.59 \ (d, \ 1H, \ J_{1^{-2}}' = 8.8 \ {\rm Hz}) \ {\rm H1}, \ 5.59 \ (d, \ 1H, \ J_{1^{-2}}' = 8.8 \ {\rm Hz}) \ {\rm H1}, \ 5.59 \ (d, \ 1H, \ J_{1^{-2}}' = 8.8 \ {\rm Hz}) \ {\rm H1}, \ 5.59 \ (d, \ 1H, \ J_{1^{-2}}' = 8.8 \ {\rm Hz}) \ {\rm H1}, \ 5.59 \ (d, \ 1H, \ J_{1^{-2}}' = 8.8 \ {\rm Hz}) \ {\rm H1}, \ 5.59 \ (d, \ 1H, \ J_{1^{-2}}' = 8.8 \ {\rm Hz}) \ {\rm H1}, \ 5.59 \ {\rm (d, \ 1H}, \ 5.59$

¹³C NMR (100 MHz, MeOD, 55 °C): 13.0 $-(CH_2)_{12}-CH_3$, 25.3 $CH_2-CH_2-(CH_2)_{12}-$, 22.1, 28.5 28.7, 28.8, 28.9, 31.4 $-(CH_2)_{12}-$, 34.4 $C-CH_2-NH-$, 35.6 $CO-CH_2-CH_2$, 37.5 $CH-CH_2$ -arom, 54.7 CO-CH-NH-, 60.6, 61.3, 73.3, 76.8, 78.2, 78.3 <u>C5</u>, C6, C3', <u>C4'</u>, C5', C6', 70.2 <u>C4</u>, 72.3 <u>C2'</u>, 72.6 <u>C2</u>, 73.7 <u>C3</u>, 87.9 <u>C1'</u>, 101.1 <u>C1</u>, 122.4 N-CH=C triazole, 126.5 <u>Carom</u>, 128.2, 128.9, 136.9 <u>CHarom</u>, 144.8 CH = <u>C</u>-CH₂ triazole, 175.6 NH-<u>CO</u>-CH, 175.2 NH-CO-CH₂-.

Micro-TOF MS: 808.4666 [M + H]⁺ calcd: 808.4702; 830.4495 [M + Na]⁺, calcd: 830.4521.

IR (KBr, cm⁻¹): 3297 (broad), 2919, 2850, 1638, 1543, 1456, 1377, 1036, 699.

Characterization Techniques. ¹H and ¹³C NMR spectra were recorded on a BRUKER AV-400 spectrometer. IR spectra were measured on Thermo NICOLET Avatar 360 FT-IR spectrophotometer using KBr pellets. Mass analysis was performed using a MALDI+/TOF Brüker Microflex system with a different matrix depending on the compound (DCTB or DHB) and MicroTOF Brüker equipment for exact mass measurements. Elemental analysis was performed using a Perkin-Elmer CHN2400 microanalyzer.

The mesogenic behavior was studied by optical microscopy with an Olympus BH-2 polarizing microscope equipped with a Linkam THMS hot-stage central processor and a CS196 cooling system. Differential scanning calorimetry (DSC) was performed using a DSC Q2000 from TA Instruments with samples sealed in aluminum pans and a scanning rate of 10 or 5 $^{\circ}$ C/min under a nitrogen atmosphere. Temperatures were read at the maximum of the transition peaks. Thermogravimetric analysis (TGA) was performed using a TGA Q5000IR instrument from TA Instruments at a rate of 10 $^{\circ}$ C/min under a nitrogen atmosphere. Circular dichroism was measured using Jasco J-180 equipment. The CD spectra of the samples were registered by rotating the sandwich every 60 $^{\circ}$ around the light beam axis.

SEM measurements were performed using a JEOL JSM 6400 at the laboratory of "Servicio de Microscopia de la Universidad de Zaragoza". The sample was fixed onto glass and coated with gold.

TEM measurements were performed using a TECNAI G^2 20 (FEI COMPANY) at the laboratory of Advanced Microscopy of the "Instituto de Nanociencia de Aragon". For TEM sample preparation, a drop of the solution (0.1 wt % gel diluted) was placed on a copper grid and left to dry for 15 min. The copper grid was then placed again over a drop of 1% uranyl acetate solution as a negative stain for 30 s and was then left to dry.

Gelation Test. The gelator and the solvent were placed in a septumcapped test tube. The resulting mixture was heated until a clear solution was obtained. The solution was cooled to room temperature, and if the tube was turned upside down and the solution did not flow, the formation of a gel was registered.

ASSOCIATED CONTENT

Supporting Information. Synthesis of Malt-NH-Phe-C₁₆ using maltose as starting material; characterization data of compounds 1–7; NMR spectra, EM, and FTIR of OAc-Malt-Tz-C₁₆ and Malt-Tz-C₁₆; thermogravimetric analysis; DSC thermal cycles of peracetylated compounds; models of the Malt-Tz-C₁₆ molecules on the lamellar phase; Malt-Tz-Phe-C₁₆ and Malt-NH-Phe-C₁₆ gel photos; NMR studies of the gel—sol transition of the Malt-Tz-C₁₆ gel; ¹H NMR spectra of Malt-Tz-C₁₆ in DMSO-d₆ with increasing H₂O content; SEM images of Malt-Tz-Phe-C₁₆ and Malt-NH-Phe-C₁₆. This material is available free of charge via the Internet at http://pubs.acs.org

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REFERENCES

(a) Terech, P.; Weiss, R. G. Chem. Rev. 1997, 97, 3133–3159. (b)
 Ajayaghosh, A.; Praveen, V. K.; Vijayakumar, C. Chem. Soc. Rev. 2008, 37, 109–122. (c) Smith, D. K. Chem. Soc. Rev. 2009, 38, 684–694. (d)
 Banerjee, S.; Das, R. K.; Maitra, U. J. Mater. Chem. 2009, 19, 6649–6687.

(2) (a) Brunsveld, L.; Folmer, B. J. B.; Meijer, E. W.; Sijbesma, R. P. *Chem. Rev.* 2001, *101*, 4071–4097. (b) De Greef, T. F. A.; Smulders, M. M. J.; Wolffs, M.; Schenning, A. P. H. J.; Sijbesma, R. P.; Meijer, E. W. *Chem. Rev.* 2009, *109*, 5687–5754.

(3) Sangeetha, N. M.; Maitra, U. Chem. Soc. Rev. 2005, 34, 821-836.

(4) Estroff, L. A.; Hamilton, A. D. Chem. Rev. 2004, 104, 1201–1217.

(5) Abdallah, D. J.; Weiss, R. G. Adv. Mater. 2000, 12, 1237–1247.

(6) Hirst, A. R.; Escuder, B.; Miravet, J. F.; Smith, D. K. Angew. Chem., Int. Ed. 2008, 47, 8002–8018.

(7) (a) Yoza, K.; Ono, Y.; Yoshihara, K.; Akao, T.; Shinmori, H.; Takeuchi, M.; Shinkai, S.; Reinhoudt, D. N. *Chem. Commun.* 1998, 8, 907–908. (b) Yoza, K.; Amanokura, N.; Ono, Y.; Akao, T.; Shinmori, H.; Takeuchi, M.; Shinkai, S.; Reinhoudt, D. N. *Chem.—Eur. J.* 1999, 5, 2722–2729. (c) Gronwald, O.; Shinkai, S. *J. Chem. Soc., Perkin Trans.* 2 2001, 10, 1933–1937.

(8) (a) Shimizu, T.; Masuda, M. J. Am. Chem. Soc. 1997, 119, 2812–2818. (b) Nakazawa, I.; Masuda, M.; Okada, Y.; Hanada, T.; Yase, K.; Asai, M.; Shimizu, T. Langmuir 1999, 15, 4757–4764. (c) Masuda, M.; Hanada, T.; Okada, Y.; Yase, K.; Shimizu, T. Macromolecules 2000, 33, 9233–9238. (d) Bhattacharya, S.; Acharya, S. N. G. Langmuir 2000, 16, 87–97.

(9) (a) John, G.; Masuda, M.; Okada, Y.; Yase, K.; Shimizu, T. Adv.
 Mater. 2001, 13, 715–718. (b) Kiyonaka, S.; Sugiyasu, K.; Shinkai, S.;
 Hamachi, I. J. Am. Chem. Soc. 2002, 124, 10954–10955.

(10) Bhattacharya, S.; Acharya, S. N. G. *Chem. Mater.* **1999**, *11*, 3504–3511.

(11) (a) Jung, J. H.; John, G.; Masuda, M.; Yoshida, K.; Shinkai, S.;
 Shimizu, T. *Langmuir* 2001, *17*, 7229–7232. (b) Jung, J. H.; Shinkai, S.;
 Shimizu, T. *Chem.—Eur. J.* 2002, *8*, 2684–2690.

(12) (a) Fuhrhop, J. H.; Schnieder, P.; Boekema, E.; Helfrich, W.
J. Am. Chem. Soc. 1988, 110, 2861–2867. (b) Shimizu, T.; Masuda, M.;
Minamikawa, H. Chem. Rev. 2005, 105, 1401–1443. (c) Kamiya, S.;
Minamikawa, H.; Jung, J. H.; Yang, B.; Masuda, M.; Shimizu, T.
Langmuir 2005, 21, 743–750. (d) Lee, C. C.; Grenier, C.; Meijer,
E. W.; Schenning, A. Chem. Soc. Rev. 2009, 38, 671–683.

(13) (a) Kiyonaka, S.; Sada, K.; Yoshimura, I.; Shinkai, S.; Kato, N.; Hamachi, I. Nat. Mater. 2004, 3, 58–64. (b) Yoshimura, I.; Miyahara, Y.; Kasagi, N.; Yamane, H.; Ojida, A.; Hamachi, I. J. Am. Chem. Soc. 2004, 126, 12204–12205. (c) Yang, Z. M.; Xu, K. M.; Wang, L.; Gu, H. W.; Wei, H.; Zhang, M. J.; Xu, B. Chem. Commun. 2005, 35, 4414–4416. (d) Tamaru, S.; Kiyonaka, S.; Hamachi, I. Chem.—Eur. J. 2005, 11, 7294–7304. (e) Mohan, S. R. K.; Hamachi, I. Curr. Org. Chem. 2005, 9, 491–502. (f) Bhuniya, S.; Kim, B. H. Chem. Commun. 2006, 1842–1844. (g) Park, J.; Rader, L. H.; Thomas, G. B.; Danoff, E. J.; English, D. S.; DeShong, P. Soft Matter 2008, 4, 1916–1921. (h) Matsumoto, S.; Yamaguchi, S.; Ueno, S.; Komatsu, H.; Ikeda, M.; Ishizuka, K.; Iko, Y.; Tabata, K. V.; Aoki, H.; Ito, S.; Noji, H.; Hamachi, I. Chem.—Eur. J. 2008, 14, 3977–3986.

(14) (a) Ikeda, M.; Ueno, S.; Matsumoto, S.; Shimizu, Y.; Komatsu, H.; Kusumoto, K. I.; Hamachi, I. *Chem.—Eur. J.* 2008, *14*, 10808–10815.
(b) Song, F.; Zhang, L. M.; Shi, J. F.; Li, N. N. *Colloids Surf., B.* 2010, *81*, 486–491.

(15) (a) Smits, E.; Engberts, J.; Kellogg, R. M.; VanDoren, H. A. *Liq. Cryst.* **1997**, *23*, 481–488. (b) Hato, M.; Minamikawa, H.; Tamada, K.; Baba, T.; Tanabe, Y. *Adv. Colloid Interface Sci.* **1999**, *80*, 233–270. (c) Hato, M. *Curr. Opin. Colloid Interface Sci.* **2001**, *6*, 268–276. (d) Goodby, J. W.; Gortz, V.; Cowling, S. J.; Mackenzie, G.; Martin, P.; Plusquellec, D.; Benvegnu, T.; Boullanger, P.; Lafont, D.; Queneau, Y.; Chambert, S.; Fitremann, J. *Chem. Soc. Rev.* **2007**, *36*, 1971–2032. (e) Ho, M. S.; Hsu, C. S. *Liq. Cryst.* **2010**, *37*, 293–301.

(16) Fitremann, J.; Bouchu, A.; Queneau, Y. Langmuir 2003, 19, 9981–9983.

(17) (a) Fazio, F.; Bryan, M. C.; Blixt, O.; Paulson, J. C.; Wong, C. H. J. Am. Chem. Soc. **2002**, 124, 14397–14402. (b) Marmuse, L.; Nepogodiev, S. A.; Field, R. A. Org. Biomol. Chem. 2005, 3, 2225–2227. (c) Wilkinson, B. L.; Bornaghi, L. F.; Houston, T. A.; Innocenti, A.; Supuran, C. T.; Poulsen, S. A. J. Med. Chem. 2006, 49, 6539–6548. (d) Paul, K. J. V.; Loganathan, D. Tetrahedron Lett. 2008, 49, 6356–6359. (e) Neto, V.; Granet, R.; Krausz, P. Tetrahedron 2010, 66, 4633–4646. (f) Song, S. X.; Zhang, H. L.; Kim, C. G.; Sheng, L.; He, X. P.; Long, Y. T.; Li, J.; Chen, G. R. Tetrahedron 2010, 66, 9974–9980.

(18) Gerber, S.; Wulf, M.; Milkereit, G.; Vill, V.; Howe, J.; Roessle, M.; Garidel, P.; Gutsmann, T.; Brandenburg, K. *Chem. Phys. Lipids* **2009**, *158*, 118–130.

(19) (a) Meinjohanns, E.; Meldal, M.; Paulsen, H.; Dwek, R. A.; Bock, K. *J. Chem. Soc., Perkin Trans.* 1 **1998**, *3*, 549–560.(b) Vetter D. Methods for the solid phase synthesis of glycoconjugates. Patent number WO 95/18971.

(20) (a) Likhosherstov, L. M.; Novikova, O. S.; Shibaev, V. N. *Dokl. Chem.* **2002**, 383, 89–92. (b) Hackenberger, C. P. R; O'Reilly, M. K.; Imperiali, B. *J. Org. Chem.* **2005**, 70, 3574–3578. (c) Somsak, L.; Felfoldi, N.; Konya, B.; Huse, C.; Telepo, K.; Bokor, E.; Czifrak, K. *Carbohydr. Res.* **2008**, 343, 2083–2093.

(21) (a) Gyorgydeak, Z.; Szilagyi, L.; Paulsen, H. J. Carbohydr. Chem. 1993, 12, 139–163. (b) Bianchi, A.; Bernardi, A. J. Org. Chem. 2006, 71, 4565–4577.

(22) (a) Kolb, H. C.; Fin, M. G.; Sharpless, K. B. Angew. Chem., Int. Ed. 2001, 40, 2004–2021. (b) Tornøe, C. W.; Christensen, C.; Meldal, M. J. Org. Chem. 2002, 67, 3057. (c) Wu, P.; Feldman, A. K.; Nugent, A. K.; Hawker, C. J.; Scheel, A.; Voit, B.; Pyun, J.; Fréchet, J. M. J.; Sharpless, K. B. Angew. Chem., Int. Ed. 2004, 43, 3928–3932. (d) Dedola, S.; Nepogodoviev, A. S.; Field, R. A. Org. Biomol. Chem. 2007, S, 1006–1017.

(23) (a) Vill, V.; Bocker, T.; Thiem, J.; Fischer, F. *Liq. Cryst.* **1989**, 6, 349–356. (b) von Minden, H. M.; Brandenburg, K.; Seydel, U.; Koch, M. H. J.; Garamus, V.; Willumeit, R.; Vill, V. *Chem. Phys. Lipids* **2000**, *106*, 157–179. (c) Vill, V.; von Minden, H. M.; Koch, M. H. J.; Seydel, U.; Brandenburg, K. *Chem. Phys. Lipids* **2000**, *104*, 75–91.

(24) Shinoda, K.; Yamaguchi, N.; Carlsson, A. J. Phys. Chem. 1989, 93, 7216–7218.

(25) (a) Suzuki, M.; Yumoto, M.; Kimura, M.; Shirai, H.; Hanabusa, K. *Chem.—Eur. J.* **2003**, *9*, 348–354. (b) Ikeda, M.; Nobori, T.; Schmutz, M.; Lehn, J. M. *Chem.—Eur. J.* **2005**, *11*, 662–668.

(26) Juwarker, H.; Lenhardt, J. M.; Castillo, J. C.; Zhao, E.; Krishnamurthy, S.; Jamiolkowski, R.; Kim, K. H.; Craig, S. L. J. Org. Chem. 2009, 74, 8924–8934.

(27) Van Doren, H. A.; Wingert, L. M. Recl. Trav. Chim. Pays-Bas 1994, 113, 260–265.