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Unusually Stable Aqueous Lyotropic Gyroid Phases from Gemini Dicarboxylate Surfactants

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Supporting Information

ABSTRACT: Aqueous lyotropic liquid crystal (LLC) assemblies with bicontinuous cubic morphologies (Q-phases) have shown promise in applications ranging from selective chemical separations to ion transporting media, yet universal design criteria for amphiphiles that adopt these unique structures remain elusive. Recent reports have demonstrated that cationic gemini surfactants exhibit a tendency to form bicontinuous cubic LLCs as compared to single-tail amphiphiles; however, the universality of this surfactant design motif in stabilizing Q-phases remains untested. Herein, we report the modular synthesis of a new class of anionic gemini surfactants derived from aliphatic carboxylic acids and demonstrate their unexpectedly strong propensity to form gyroid LLC phases with unprecedented stability between 25 and 100 °C over amphiphile concentration windows up to 20 wt % wide. By systematically varying the alkyl spacer length and surfactant counterions (Na^+, K^+, and $(CH_3)_4N^+$), we identify molecular motifs that favor formation of technologically useful bicontinuous cubic LLC morphologies.

Aqueous lyotropic liquid crystal (LLC) assemblies have recently garnered widespread attention in disparate areas of chemistry,[1] by virtue of their utility in highly selective chemical separations such as water desalination[2] and selective ion-transporting membranes,[3] as templates for mesoporous inorganic materials,[4,5] as media for biophysical studies of transmembrane proteins ("cubic lipidic phases"),[6] and very recently, as therapeutic nucleic acid delivery vehicles.[7] LLCs form by the concentration-dependent supramolecular self-assembly of amphiphilic molecules in water into soft materials having distinct hydrophilic and hydrophobic nanoscale domains (~7−100 Å) with long-range periodic order.[8,9] LLCs typically exhibit ordered phases such as lamellae (L_α), bicontinuous cubic (Q; e.g., gyroid, diamond, and primitive), hexagonally packed cylinders (H), and discontinuous cubic (I; e.g., body-centered cubic) morphologies (Figure 1).[10] High symmetry bicontinuous cubic LLC assemblies, exemplified by the gyroid (G) phase (Figure 1), are particularly desirable for membrane applications by virtue of their interpenetrating aqueous and hydrophobic domains with tunable nanopore diameters (~7−50 Å) and well-defined nanopore functionalities that percolate over macroscopic length scales.[2] Q-phases typically exist only in limited water concentration and temperature phase windows, because their interfaces substantially deviate from a constant mean interfacial curvature.[11,12] While "critical packing parameter" models enable correlations of amphiphile structure with the formation of constant mean curvature L_α, H, and I phases,[13] these models fail to provide reliable and general molecular design criteria for amphiphiles that form nonconstant mean curvature Q-phases.[14] Gin and co-workers recently reported that small molecule quaternary ammonium,[15] phosphonium,[2,16] and imidazolium[17] gemini amphiphiles, derived from dimerizing single-tail surfactants with an alkyl spacer through the ionic headgroup,[18] exhibit a greater tendency to form G-phase LLCs. The notion that gemini architectures universally form bicontinuous cubic LLC morphologies remains an untested amphiphile design principle.

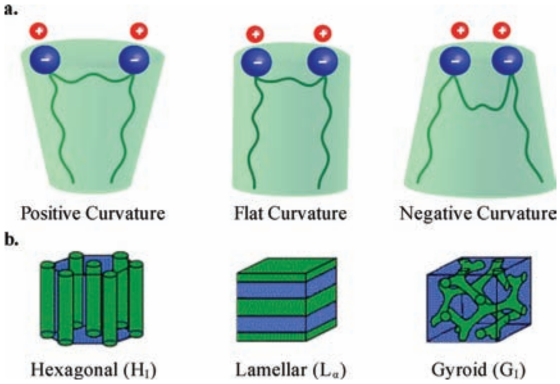

Figure 1. (a) An illustration of the variety of possible curvatures adopted by gemini amphiphiles with flexible hydrophobic alkyl spacers, and (b) observed LLC morphologies formed by gemini surfactants (aqueous domain appear in blue): hexagonal (H_I) with constant positive mean curvature, lamellar (L_α) with flat interfaces, and Gyroid (G_I) that requires substantial positive and negative deviations from constant mean curvature.

Herein, we report the modular synthesis of a new class of anionic gemini surfactants based on aliphatic dicarboxylate salts that form LLC G-phases over unexpectedly large amphiphile concentration ranges (up to 20 wt %) with unprecedented thermal stability in the range 25−100 °C. We also demonstrate that the stability of the G-phase depends sensitively upon the surfactant counterion. By examining the effects of varying both the length of the alkyl spacer between the hydrophilic headgroups and the surfactant counterions (Na^+, K^+, and $(CH_3)_4N^+$), we identify an effective combination of molecular design rules that help to stabilize these technologically useful bicontinuous cubic LLC phases.

Gemini dicarboxylate surfactants derived from decanoic acid with variable hydrophobic alkyl spacers were synthesized according to a modification of the method of Pfeffer et al.[19]

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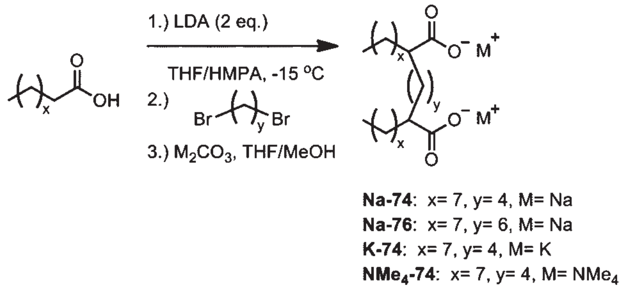
Scheme 1. Syntheses of Gemini Dicarboxylate Surfactants



depicted in Scheme 1. Deprotonation of decanoic acid with lithium diisopropylamide (2 equiv) and subsequent treatment with 1,4-dibromobutane (1 equiv) resulted in the formation of 9,14-dicarboxydocosane as a statistical mixture of diastereomers. Deprotonation of this aliphatic dicarboxylic acid with Na_2CO_3, K_2CO_3, or $(CH_3)_4NOH$ furnished gemini surfactants **Na-74**, **K-74**, and **NMe$_4$-74**, respectively. A surfactant homologue having a six-carbon alkyl spacer between the hydrophilic sodium carboxylate headgroups (**Na-76**) was synthesized analogously (see Supporting Information for synthetic details).

Hydration of these gemini surfactants with varying amounts of water yields well-ordered LLC assemblies having viscous, gel-like properties over a concentration range of 25−90 wt % amphiphile (see Supporting Information for LLC preparation protocols). The LLC phase behavior of these surfactants was interrogated by variable temperature synchrotron X-ray diffraction (XRD) over a temperature range of 25−100 °C for samples having H_2O contents varying in 5 wt % increments. Initial LLC phase behavior studies revealed that samples composed of 80 wt % **Na-74** and 20 wt % H_2O form an optically birefringent L_α-phase at 25 °C (Figure 2), whereas samples with lower H_2O contents formed mixtures of crystalline gemini surfactant and LLC phases. Samples having 60−70 wt % **Na-74** exhibit distinctive XRD patterns with prominent scattering maxima at $q^*\sqrt{6}$, $q^*\sqrt{8}$ with a characteristic ~10:1 intensity ratio, and weaker peaks at $q^*\sqrt{14}$, $q^*\sqrt{16}$, $q^*\sqrt{20}$, $q^*\sqrt{22}$ corresponding to the (211), (220), (321), (400), (420), and (332) reflections of a G-phase LLC with a cubic unit cell dimension of ~70 Å (Figure 2). The lack of observed birefringence upon examining this sample between crossed polarizers at 22 °C is consistent with the cubic symmetry of this LLC phase. Since this G-phase window is situated at higher hydration levels than the L_α phase, we assign it as a Type I ("normal") G_I-phase having interfacial curvature toward the hydrophobic domains.[20] Examination of samples having 40−50 wt % **Na-74** indicates the formation of a "normal" hexagonal (H_I) phase with a modest degree of long-range order, evidenced by XRD peaks that index as $q^*\sqrt{1}$, $q^*\sqrt{3}$, and $q^*\sqrt{7}$ with a ~34 Å intercylinder spacing (Figure 2). From the complete temperature-dependent aqueous lyotropic phase diagram for **Na-74** shown in Figure 3a, one sees that these ordered LLC phases persist up to 100 °C. In contrast to the narrow composition and temperature phase windows in which G-phases are typically observed for monoacylglycerols,[12,21] and ammonium,[15,22] phosphonium,[16] and imidazolium[17] gemini surfactants, the G_I-phase window for **Na-74** is one of the largest reported to date.

Upon increasing the length of the alkyl spacer between the carboxylate headgroups in the decanoic acid-derived gemini surfactant as in **Na-76**, we again observe a large gyroid phase window in the midst of a different sequence of LLC phases upon hydration with >15 wt % H_2O (Figure 3b; see Supporting Information for XRD data). For samples hydrated in the range 75−85 wt % **Na-76**, we observe the formation of stiff, optically nonbirefringent gels characteristic of a Q-phase LLC with order-to-disorder ("clearing") temperatures ~70 °C. Synchrotron XRD patterns exhibit prominent scattering maxima at $q^*\sqrt{2}$, $q^*\sqrt{6}$, $q^*\sqrt{8}$, and $q^*\sqrt{10}$, consistent with either an alternating gyroid structure (Q^{214} space group symmetry) or a primitive (P) structure with a $q^*\sqrt{4}$ extinction, which comprises a network of octahedral connectors (Q^{229}).[4] In accord with convention, we favor the higher symmetry structure and tentatively assign this cubic phase as a P_I-phase. Samples composed of ~70 wt % **Na-76** form stiff yet birefringent gels, which exhibit unusual X-ray scattering patterns that cannot be assigned to any of the classical LLC morphologies; studies are underway to identify the structure of this new LLC. Between ~50 and 65 wt %

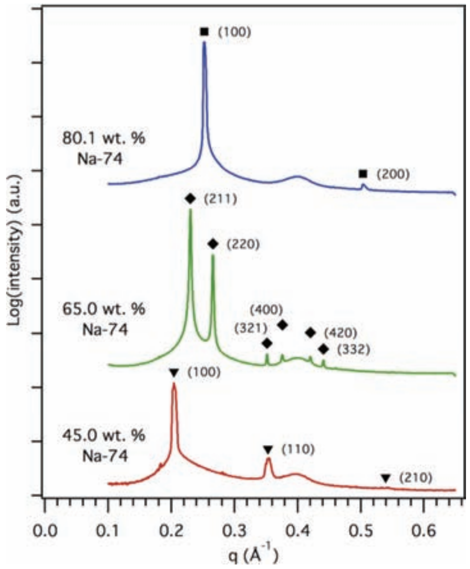


Figure 2. Azimuthally integrated synchrotron XRD patterns of **Na-74** LLCs at various amphiphile weight fractions at 25 °C. Markers on each trace indicate calculated positions for Bragg reflections of the H_I (▼), G_I (◆), and L_α (■) morphologies. The sharp peak ~0.18 Å^{-1} and the broad peak at ~0.4 Å^{-1} are artifacts from the XRD sample holder.

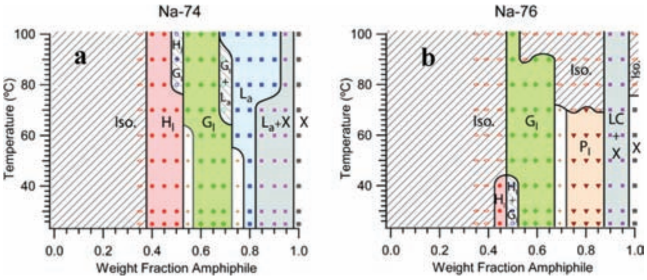


Figure 3. Temperature vs concentration LLC phase diagrams for hydrated sodium carboxylate gemini amphiphiles: (a) **Na-74** and (b) **Na-76**. Iso = fluid isotropic phase, H_I = normal hexagonal, G_I = normal Gyroid, P_I = normal primitive, L_α = Lamellar, X = crystalline surfactant, and + = unknown LLC phase (see Supporting Information for XRD patterns).

amphiphile, **Na-76** unequivocally forms a G_I-phase. Thus, **Na-76** adopts a gyroid morphology with saddle curvature at substantially higher hydration levels than **Na-74**. By comparing XRD data for LLCs composed of hydrated **Na-74** and **Na-76** at comparable water contents that adopt the same morphologies, we find that the unit cell dimensions do not vary significantly in spite of the difference in spacer lengths.

These observations suggest that the combination of gemini architecture and the hydrophilic carboxylate headgroups conspire to stabilize the G-phase more substantially than in the case of previously reported gemini surfactant G-phase LLCs.[15−17,22] In contrast to their single-tail analogues that prefer to form LLCs with constant mean curvature, the flexible, hydrophobic spacer connecting the ionic headgroups in a gemini amphiphile confers a degree of conformational flexibility that enables it to accommodate the substantial deviations from constant mean interfacial curvature required for G-phase stabilization (Figure 1a). Reported calculations demonstrate that the inherent anisotropy of the gemini structure favors the formation of saddle splay and negative curvature interfaces, as compared to their parent single-tail surfactants.[23] In the ammonium, phosphonium, and imidazolium gemini surfactants, the counterion is highly dissociated from the headgroup, causing the flexible spacer to extend fully in order to mitigate Coulombic repulsions between the headgroups. This reduced linker flexibility directs the formation of LLCs with very small deviations in constant mean curvature, while pinning the spacer at the aqueous domain interface and forcing contacts between water and the hydrophobic linker that destabilize the structure.[22] The gemini dicarboxylates behave quite differently, because counterion association with the carboxylate headgroup or protonation of the carboxylates (with attendant formation of HO^- in the aqueous domains) can mitigate Coulombic repulsions between headgroups.[24] Effective charge neutralization through one of these mechanisms allows the alkyl spacer between the carboxylate headgroups to relax, enabling the gemini amphiphile to adopt a wider range of interfacial curvatures over a broader range of headgroup hydration levels to stabilize the nonconstant mean curvature G_I-phase. The flexible spacer likely also pulls away from the aqueous interface to mitigate unfavorable hydrophobic/hydrophilic interactions,[25] inducing alkyl tail chain splay that favors G_I-phase formation (Figure 1).[12] Lengthening the C_4-spacer to a C_6-spacer enhances the conformational flexibility of the surfactant and widens the G_I-phase window (Figure 3), while also inducing a high degree of chain splay (greater hydrophobic volume) that permits the formation of a P_I-phase at low hydration levels (Figure 1). Given that the curvature of a surface displaying densely packed carboxylic acids is known to affect the pK_a of the acid functionality,[26] the possibility for variable protonation states of the gemini carboxylate headgroups may also play an important role in stabilizing the observed G_I-phases.

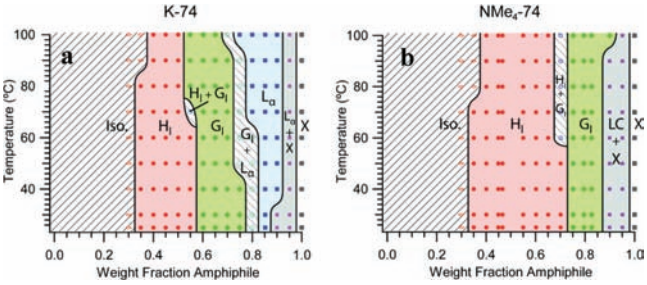


Figure 4. Phase diagrams for (a) **K-74** and (b) **NMe₄-74** gemini amphiphiles in water. Iso = fluid isotropic phase, H_I = normal hexagonal, G_I = normal Gyroid, L_α = Lamellar, X = crystalline surfactant.

Table 1. Counterion Dependence of LLC Unit Cell Dimensions at Similar Hydration Levels (λ) and Morphologies

sample	phase	wt.%	λ[a]	d (nm)[b]
Na-74	H_I	50.1	24.5	3.38
	G_I	69.3	10.9	6.58
K-74	H_I	54.9	21.6	3.37
	G_I	69.9	11.3	6.58
NMe₄-74	H_I	55.0	24.7	3.44
	G_I	75.2	9.98	6.55

[a] λ = mol H_2O/mol amphiphile. [b] Unit cell dimensions (d) were calculated from the position of the principle scattering maxima in azimuthally integrated XRD patterns; calculated values are estimates within ±0.15 nm.

Very few studies of gemini surfactant LLCs have examined their counterion-dependent phase behavior.[27] Variable temperature XRD studies of the phase behavior of **K-74** indicate that the H_I phase window widens substantially and that the G_I window widens and shifts to lower H_2O contents as compared to sodium analogue **Na-74**. The LLC phase diagram for **NMe₄-74** shows an even more pronounced widening of the H_I phase composition window and a large shift in the G_I phase toward lower hydration levels, such that the L_α phase completely vanishes (Figure 4). Comparisons of the principal domain spacings for both the G_I and H_I-phases at comparable hydration levels (λ = (mol H_2O)/(mol gemini)) indicate that the LLC unit cell dimensions are relatively constant at ~34 Å for H_I phases and ~66 Å for G_I phases with different counterions (Table 1). These findings demonstrate that increased counterion dissociation favors the formation of LLCs with high curvature interfaces at constant water content, although the counterion size does not substantially alter the unit cell dimensions of the LLC at similar λ-values. Therefore, changing the surfactant counterion provides a simple means of manipulating LLC phase stability in these gemini surfactant liquid crystals.

The counterion-dependent self-assembly of anionic gemini dicarboxylate surfactants may be rationalized by considering the level of cation dissociation from the anionic carboxylate headgroups. Brun et al. have shown that the association of cations with single tail alkyl carboxylates in dilute solutions increases in the order $(CH_3)_4N^+ < K^+ < Na^+$.[28] In the case of the counterions that strongly associate with the carboxylate headgroups, cation condensation at the interface reduces the repulsive Coulombic interactions between the headgroups to stabilize the G_I-phase over a large concentration window. Since the $(CH_3)_4N^+$ cation is highly dissociated, the lack of headgroup charge screening causes the alkyl spacer to extend fully (*vide supra*) so that it accommodates only very small deviations from constant mean curvature. Therefore, the G_I-phase window shrinks in size at the expense of the more stable H_I-phase. The phase behavior of **NMe₄-74** closely mirrors that of the dissociated gemini phosphonium bromide surfactants previously reported by Gin and coworkers, which favor formation of H_I-phases with only narrow G_I-phases.[16]

We have synthesized a new class of gemini surfactants based on aliphatic carboxylic acid salts and demonstrated their strong propensity to form unusually stable Type I aqueous lyotropic gyroid phases. The stability of these nonconstant mean curvature lyotropic G_I-phases over unexpectedly large concentration (up to 20 wt % wide) and temperature windows (25−100 °C) is ascribed to the conformational flexibility of the aliphatic linker between the two surfactant headgroups, coupled with screening of Coulombic repulsions between the hydrophilic headgroups by counterion association or carboxylate headgroup protonation. Counterion-dependent lyotropic phase behavior studies of these gemini dicarboxylates demonstrate that the counterion plays a pivotal role in stabilizing or destabilizing various phases, whereby highly dissociated counterions drive formation of high constant mean curvature morphologies. By virtue of these data, we are currently investigating the effects of linker flexibility, extent of counterion dissociation, and pH on gemini surfactant LLC self-assembly into both known and new LLC morphologies.

■ ASSOCIATED CONTENT

S Supporting Information. Detailed synthetic procedures and representative 2-D X-ray diffraction patterns. This material is available free of charge via the Internet at http://pubs.acs.org.

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