

Article

Synthesis and Mesomorphic Properties of Geometric and Conformation-Modulated Amphiphilic β -Cyclodextrin Liquid Crystals

Austin Che ¹, Homayoun Ghaseminezhad ², Carson O. Zellmann-Parrotta ² , Jessica Duong ¹, Vance E. Williams ^{2,*}  and Chang-Chun Ling ^{1,*}

¹ Department of Chemistry, University of Calgary, 2500 University Drive NW, Calgary, AB T2N 1N4, Canada; austin.che@ucalgary.ca (A.C.)

² Department of Chemistry, Simon Fraser University, Burnaby, BC V5A 1S6, Canada; homayoun_ghaseminezhad@sfu.ca (H.G.)

* Correspondence: vancew@sfu.ca (V.E.W.); ccling@ucalgary.ca (C.-C.L.); Fax: +1-604-291-3765 (V.E.W.); +1-403-289-9488 (C.-C.L.)

Abstract: This study explores the liquid crystalline properties of novel amphiphilic β -cyclodextrin derivatives functionalized with seven oligoethylene glycol chains at the primary face, terminated with either an O-methyl or an O-cyanoethyl group, and fourteen hydrophobic aliphatic chains (elaidic or oleic acids) at the secondary face. These derivatives were designed to study the impact of chain conformation and terminal group polarity on their mesomorphic behavior. Thermal, microscopic, and X-ray diffraction studies revealed that the elaidic derivatives form columnar hexagonal mesophases, with the O-cyanoethyl derivative undergoing a slow, temperature-dependent transition to a bicontinuous cubic phase. The oleic derivatives, although less stable, also exhibit columnar hexagonal phases, but clear differences were observed in the clearing temperatures between these two groups of molecules, and they are also different from analogous derivatives containing no alkene functionalities. This work provides direct insights into the structure–mesomorphic property relationships of amphiphilic cyclodextrins in terms of the geometry and conformation flexibility of the hydrophobic regions, as well as the functional group attached to the end of the polar region.

Keywords: amphiphilic cyclodextrin; liquid crystals; hexagonal columnar mesophase; cis/trans-alkenes



Citation: Che, A.; Ghaseminezhad, H.; Zellmann-Parrotta, C.O.; Duong, J.; Williams, V.E.; Ling, C.-C. Synthesis and Mesomorphic Properties of Geometric and Conformation-Modulated Amphiphilic β -Cyclodextrin Liquid Crystals. *Molecules* **2024**, *29*, 5633. <https://doi.org/10.3390/molecules29235633>

Academic Editors: Georgia N. Valsami, Natassa Pippa and Paraskevi Papakyriakopoulou

Received: 22 October 2024
Revised: 15 November 2024
Accepted: 23 November 2024
Published: 28 November 2024



Copyright: © 2024 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

1. Introduction

Cyclodextrins (CDs) are well recognized for their truncated cone-shaped hydrophobic cavities, which are sandwiched between two hydrophilic surfaces [1]. Remarkably, the narrower end of the hydrophilic surfaces of a CD (primary face) is formed with the more reactive primary hydroxyl groups of constituent D-glucopyranosyl building blocks, while the opposite end (wider, secondary face) is formed with the less reactive secondary hydroxyl groups (OH-2s and OH-3s) of the same building blocks. The regioselective modification of primary hydroxyl groups permits the introduction of different functional groups to opposite faces of the cavity in a programmable manner [2–6]; this structural feature differentiates CDs from most other macrocyclic hosts, making them unique and versatile scaffolds. A regioselective per-substitution either of the primary hydroxyl groups or of the secondary hydroxyl groups with the same functionalities would serve to pre-organize the functionalities, facilitating the creation of ordered materials. To take advantage of this, amphiphilic CD derivatives [7–20] have been developed as a class of very useful materials for drug delivery because of their ability to self-assemble in solutions into micelles, liposomes, and vesicles.

In the solid state, amphiphilic CDs have been found to self-assemble into thermotropic liquid crystals (LCs) [21–25]. The first class of LCs based on amphiphilic CDs, reported

in 1993 by Ling et al. [23], featured the covalent introduction of seven aliphatic chains to the primary face of β -CD via thioester linkages, forming a family of per-6-thioalkyl-substituted β -CDs bearing 14 secondary hydroxyl groups, and these amphiphilic CD materials, especially those bearing C18 and C16 alkyl lengths, showed a strong ability to self-assemble into smectic LCs above $\sim 215^\circ\text{C}$, but had very high clearing temperatures ($>295^\circ\text{C}$ with decomposition). To elucidate the roles played by the hydrogen bond strength, a structure–LC property relationship study was subsequently carried out [26] by keeping the C18-thioalkyl substitution at the primary face, while substituting part or all of the secondary hydroxyl position alkyl groups of different sizes; they were all found to either completely lose their ability to self-assemble or to retain partially their ability to form LCs [26]. By shifting away from relying on inter/intramolecular H-bonding as the strong intermolecular forces to promote LC mesophases, during the last few years, we have started to pre-organize oligoethylene glycols (OEG) onto β -CD scaffolds using the well-known copper (I)-catalyzed Huisgen [2+3] dipolar cycloaddition reaction (“click” chemistry) [27,28], either linking them to the primary O-6 positions while leaving the other face per-functionalized with C18-aliphatic [29,30], or vice versa [31]. This has resulted in several families of amphiphilic CDs capable of forming LCs. It is worth noting that the mesophases formed by these materials greatly depend on the substitution patterns. For example, by placing seven C18-aliphatic chains at the primary face and fourteen OEG groups at the secondary face, we obtained amphiphilic CD derivatives capable of forming smectic mesophases, which showed enhanced fluidity and thermostability [31]. On the other hand, reversing the faces on which the polar OEG groups and apolar C18-aliphatic chains are attached dramatically changes the formed mesophases from smectic A (SmA) to columnar liquid crystals (Col_h) [29,30]. Further chemical modifications have been carried out on the ends of OEG groups (such as compounds 1 and 2, Figure 1) and the introduced chemical functionalities further influence the properties of the mesophases. These novel OEG-based materials have found different applications, such as proton or lithium conduction [30,32,33].

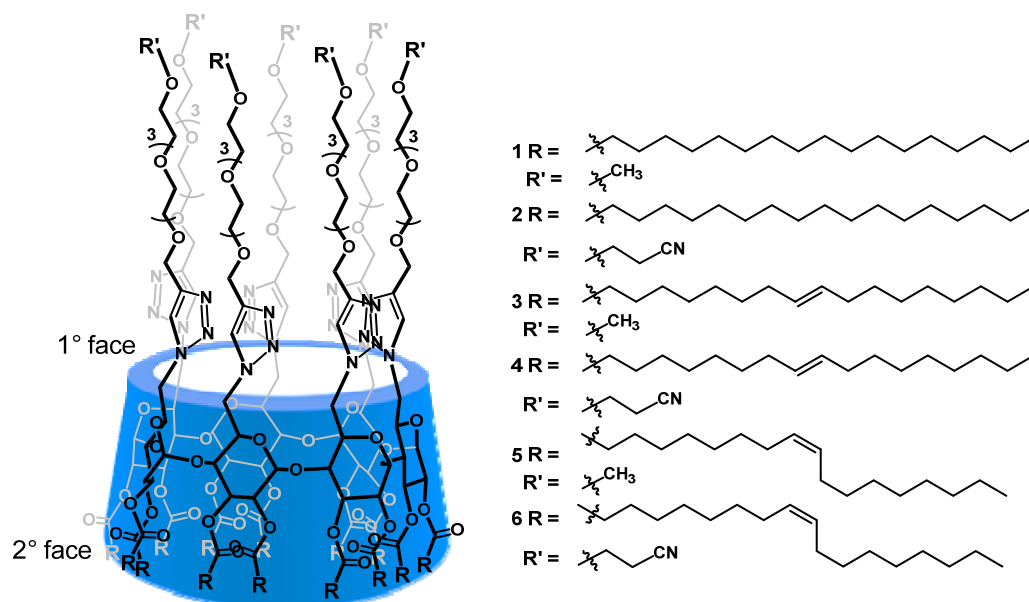


Figure 1. Structures of the target amphiphilic β -CD derivatives (3–6) bearing elaidic or oleic functionalities, with either a terminal methyl or a 2-cyanoethyl group on the tetraethylene glycol chain, in comparison with previously reported saturated analogs (1–2) [30].

To further understand the structure–property relationship of amphiphilic CDs, in this study, we present the synthesis of a novel series of amphiphilic β -CDs that incorporate seven tetraethylene glycol groups at the primary face that are terminated with either a methyl or a 2-cyanoethyl group, and fourteen hydrophobic aliphatic chains em-

bedded with a *trans*- or *cis*-alkene functionality (compounds 3/4, elaidic acid and 5/6, oleic acid, Figure 1). Compared to compounds containing only saturated aliphatic chains (compounds 1/2, stearic acid, Figure 1), it is expected that the geometry and conformation flexibility of the unsaturated chains will be altered, which would further influence the packing/preorganization of these groups on a CD-scaffold, ultimately affecting the mesomorphic properties of the materials. Research reports showed that the incorporations of unsaturated *cis*-C₁₈-aliphatic chains can influence the self-assembly behavior of glycosurfactants [34] and other LC materials [35–37]; additionally, it was reported that the incorporation of these functionalities could affect the drug loading in certain lipid nanoparticles [38].

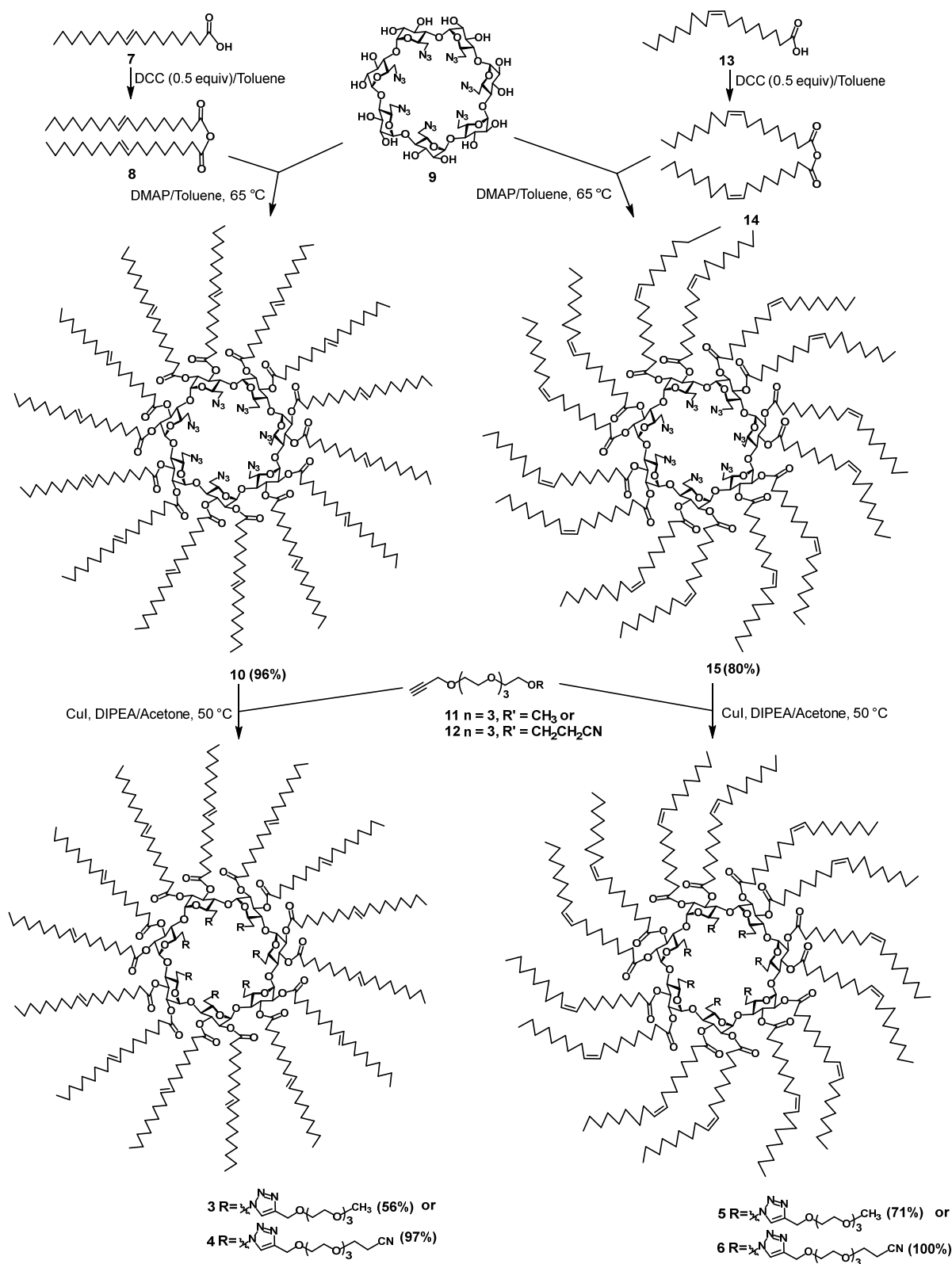
2. Results and Discussion

2.1. Chemical Synthesis and Characterization

The desired polyester targets 3/4 (per-2,3-*O*-elaidic esters) and 5/6 (per-2,3-*O*-oleyl esters) were synthesized according to Scheme 1. To introduce fourteen elaidate residues to the secondary face of per-6-azido- β -CD (9), the commercial elaidic acid (7) was activated to the corresponding anhydride (8) by a treatment with *N,N'*-dicyclohexylcarbodiimide as the dehydrating reagent in toluene at 65 °C. The crude anhydride (8, 2.0 equivalents per OH) was not purified, but combined with per-6-azido- β -CD (8) in the same solvent at 65 °C, using 4-*N,N*-dimethylpyridine as a base [39]. After 16 h, the resulting compound (10) was isolated with excellent yield (96%). The per-esterification of compound 10 was confirmed by ¹H NMR (Figure S1), which showed a doublet at 5.08 ppm (*J* = 3.8 Hz) and two sets of doublets of doublets at 5.32 ppm (*J* = 9.4, 9.4 Hz) and 4.80 ppm (*J* = 10.1, 3.7 Hz), corresponding to the three types of protons, H-1s, H-3s, and H-2s, of the seven glucopyranosyl units of β -CD. Both signals that correspond to the seven H-2s and seven H-3s respectively, appear at a rather deshielded region, confirming the direct attachment of electron-withdrawing elaidate ester groups. A multiplet peak was observed at 5.45–5.37 ppm, corresponding to the unsaturated *trans*-double bond of the elaidic ester chains. The fact that only one set of signal was observed for each type of protons is consistent with the presence of axial symmetry, confirming the per-*O*-esterifications at all O-2 and O-3 positions of the β -CD. Interestingly, in the C-13 NMR spectra (Figure S2), four peaks of alkenic carbons were observed, corresponding to the two types of double bonds embedded in elaidate groups that are attached to the O-2 and O-3 positions of the glucopyranosyl units.

The verification of complete per-2,3-*O*-esterifications in compound 10 was further conducted using mass spectroscopy. Unfortunately, high-resolution mass spectrometry using electrospray ionization (positive, ESI HRMS) failed to give us the peaks corresponding to the adducts of molecular ions, likely due to the high molecular weight and lack of adequate polar functionalities; however, low-resolution MALDI-TOF (positive) showed a peak at *m/z* 5031.3 (100%), which correlated closely with the anticipated sodium adduct of the expected structural formula C₂₉₄H₅₁₁N₂₁O₄₂Na (M + Na)⁺, which has a calculated *m/z* value of 5034.8 (100%), based on simulated isotope distributions of the expected compound 10.

To obtain the targeted per-2,3-*O*-elaidate-modified compounds 3/4, the mono-*O*-propargylated tetraethylene glycol derivatives 11 and 12 were synthesized as previously reported [30]. Each of these derivatives was then covalently linked to compound 10 via a copper (I)-catalyzed Huisgen [2+3] dipolar cycloaddition [27] in the presence of *N,N*-diisopropylethylamine (DIPEA) in acetone. The reaction was heated at 55 °C for approximately 96 h, and the desired amphiphilic β -CD derivatives (3–4) were successfully isolated. The copper catalyst was removed through multiple extractions with a 5% EDTA solution in water, followed by repeated precipitation–centrifugation in a mixture of dichloromethane and methanol. The final products were obtained in 56% and 97% yields. Structural characterizations of the final targets 3 and 4 were carried out using NMR experiments. As an example, Figure 2 shows the 1D ¹H and 2D ¹H-¹³C GHSQC correlation spectra of compound 3.



Scheme 1. Synthetic scheme for β -CD targets 3–6 with 14 elaidate or 14 oleate ester groups on the secondary face and seven tetraethylene glycol chains, terminated with either a methyl or 2-cyanoethyl group, on the primary face.

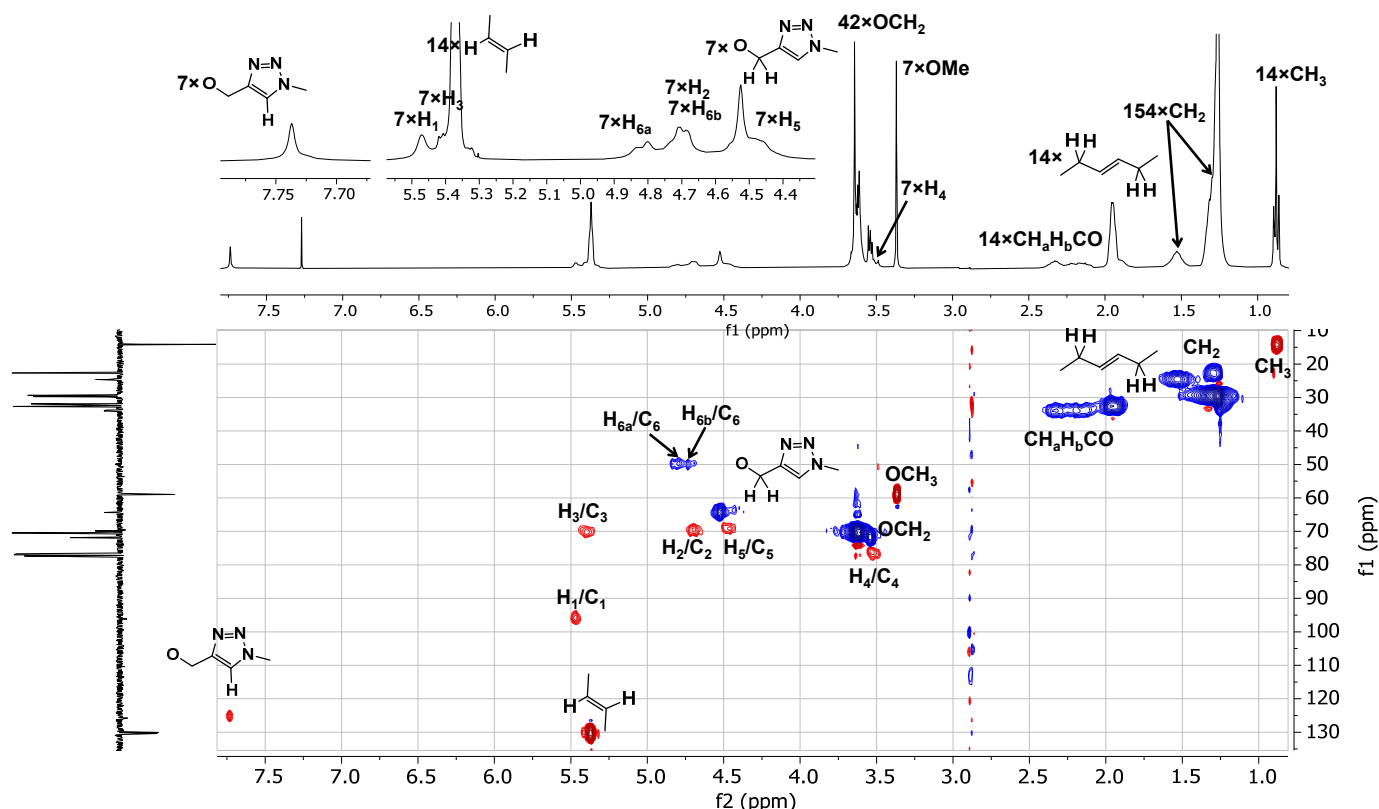


Figure 2. ^1H NMR Spectrum (top) and ^1H - ^{13}C HSQC spectrum (bottom) of compound 3.

As can be seen, the per-substitutions in compound 3 were supported by the presence of axial symmetry, as only one set of signals was observed for each type of proton in both ^1H and ^{13}C spectra. In the 1D ^1H (Figure S5) and 2D ^1H - ^1H GCOSY (Figure S7) spectra, the signals of the H-6a and H-6b protons of the glucopyranose units are observed at a highly deshielded region (~ 4.8 and ~ 4.7 ppm, respectively); this confirms the success of the [2+3] dipolar cycloaddition, as all the C-6s of the glucopyranose units are now directly attached to the newly formed aromatic 1,2,3-triazole rings, making them experience a deshielding effect due to the aromatic π -electrons. Similarly, the H-5 protons also experience some deshielding effect, as they are found to resonate at ~ 4.5 ppm. Most of the proton signals in the ^1H -NMR spectra of compounds 3–4 exhibit broadness (Figures S5 and S9), attributed to the limitation of molecular rotation imposed by the substantial size of these molecules. Finally, the structures of compounds 3–4 were confirmed by high-resolution mass spectrometry (HRMS). For example, for compound 3, HRMS (positive electrospray ionization, positive) showed a triple-charged peak at 2244.9593, which correlated well with the expected $\text{C}_{378}\text{H}_{665}\text{N}_{21}\text{O}_{77} (\text{M} + 3\text{H})^{3+}$ molecular formula, which has a calculated m/z of 2244.9662 ($\text{M} + 3\text{H})^{3+}$. For compound 4, the observed peak at m/z 2335.9890 also correlated well with the expected molecular formula $\text{C}_{392}\text{H}_{672}\text{N}_{28}\text{O}_{77} (\text{M} + 3\text{H})^{3+}$, which has a calculated m/z at 2335.9916.

With the success of both elaidate-substituted targets 3 and 4, we next continued our synthesis of the two oleate-substituted targets 5 and 6. As shown in Scheme 1, the desired oleic anhydride 14 was first prepared from the commercially available oleic acid (13), as above. The crude anhydride (2.0 equiv. per OH) was then directly used to carry out polyesterification of all O-2 and O-3 positions of per-6-azido- β -CD (9) using the same conditions to afford the key intermediate 15, which was isolated in pure form (80% yield). The structure of compound 15 was characterized similarly, using NMR spectroscopy (See Figures S13–S16) and low-resolution MALDI-TOF mass spectrometry, which showed the anticipated sodium adduct peak at m/z 5029.6 (100%), corresponding closely to the expected

structure of compound **15**, which has the molecular formula $C_{294}H_{511}N_{21}O_{42}Na$ ($M + Na$)⁺, with a calculated m/z of 5034.8 (100%).

With the key compound **15** in hand, we subjected it to reactions with the two mono-O-propargylated tetraethylene glycol derivatives **11** and **12**, using the copper (I)-catalyzed Huisgen [2+3] dipolar cycloaddition in a similar manner as above. After 96 h, the targeted amphiphilic β -CD derivatives (**5–6**) were successfully formed and isolated in 71% and almost quantitative yields, respectively. Structural characterizations of the final targets **5** and **6** were also carried out using NMR experiments (see experiments, Figures S17–S24) and HRMS. Notably, the alkene protons on the *cis*-double bonds were observed at the 5.20–5.41 ppm regions (Figures S17 and S21) and HRMS (positive electrospray ionization, positive) also confirmed the structural identification of both amphiphilic targets: with compound **5** having a peak observed at m/z 2244.9490 (calculated m/z for $C_{378}H_{665}N_{21}O_{77}$ ($M + 3H$)³⁺ ion: 2244.9662) and compound **6** having a peak observed at m/z 2335.9915 (calculated m/z for $C_{392}H_{672}N_{28}O_{77}$ ($M + 3H$)³⁺ ion: 2335.9782).

2.2. Mesomorphic Properties

The DSC thermogram of compound **3** (Figure 3a) displayed two endothermic transitions upon heating: a broad peak at ~ 4 °C and a second, lower-intensity peak at 88.3 °C. Integrations of the two peaks revealed a large enthalpic change (81.3 kJ/mol) for the lower transition and a much smaller enthalpic change (2.7 kJ/mol) for the higher transition (Table 1). Polarized optical microscopy (POM) revealed that the latter transition corresponded to the change from a birefringent liquid crystal phase to an isotropic liquid. POM images of the liquid crystal phase of compound **3** during the cooling cycle exhibited fan-shaped domains, characteristic of a columnar hexagonal (Col_h) phase (Figures 4a and S29). This phase assignment was confirmed by variable temperature X-ray diffraction (vt-XRD), which showed four distinct peaks in the low-angle region that indexed to the (100), (110), (200), and (210) reflections of a Col_h liquid crystal (Figure 5 and Table 2). Due to instrumental limitations, we were unable to investigate the lower-temperature phase, denoted as X (Table 1), by vt-XRD or POM.

Table 1. Phase behavior of compounds **3–6**. Unless otherwise noted, transition temperatures and enthalpies (in parentheses) were determined by DSC on the first heating run at a scan rate of 10 °C/min.

Compound	Phase Transitions	
3	Heating	X ~ 4 °C (81.3 kJ/mol) Col_h 88.3 °C (2.7 kJ/mol) Iso
	Cooling	Iso 82.1 °C (6.6 kJ/mol) Col_h -21.3 °C (86.8 kJ/mol) X
4	Heating	X -0.2 °C (79.7 kJ/mol) Cub_{bi} ~ 70 °C ^a Col_h 161.4 °C (2.6 kJ/mol) Iso
	Cooling	Iso 154.0 °C (4.8 kJ/mol) Col_h -19.7 °C (68.7 kJ/mol) X
5	Heating	Col_h 51 °C ^a Iso
	Cooling	Iso 44 °C ^a Col_h
6	Heating	Col_h 150 °C ^a Iso
	Cooling	Iso 147 °C ^a Col_h

^a Determined by POM. **Col_h**: hexagonal columnar mesophase; **Cub_{bi}**: bicontinuous cubic mesophase; **X**: an unknown phase; **Iso**: isotropic phase.

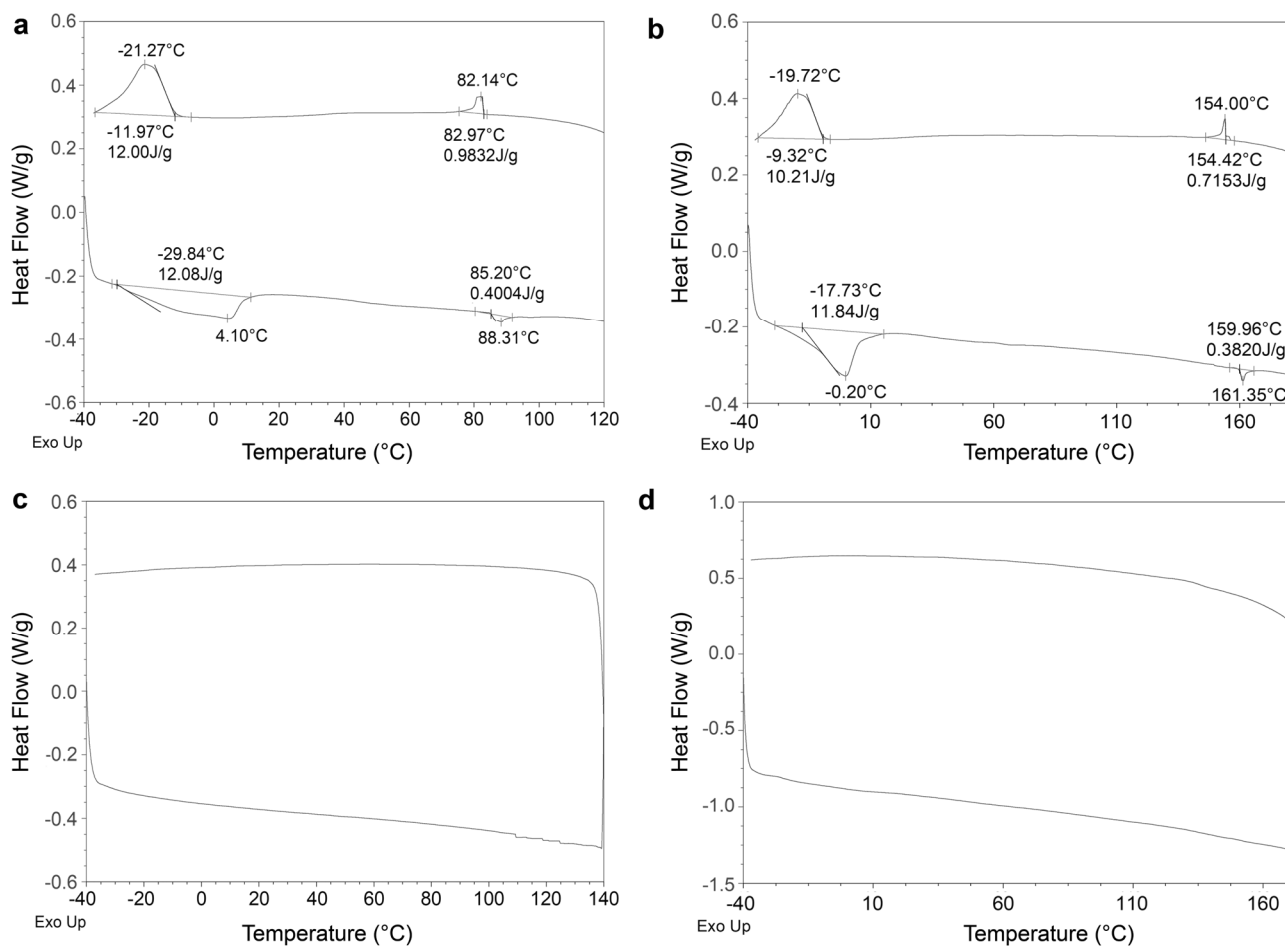


Figure 3. DSC thermograms of (a) 3, (b) 4, (c) 5, and (d) 6.

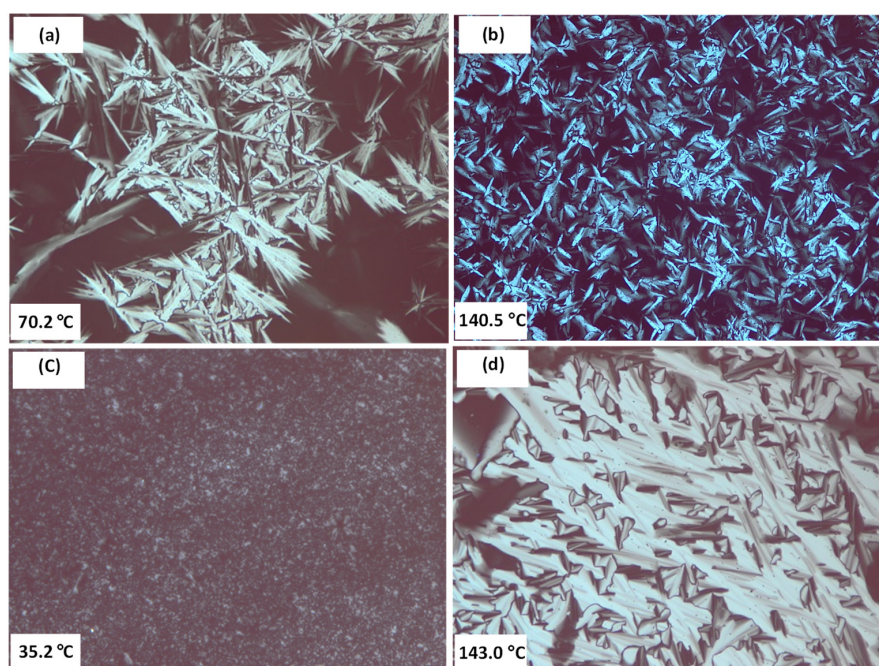


Figure 4. Polarized micrographs showing the cooling cycles of (a) compound 3 at 70.2 °C, (b) compound 4 at 140.5 °C, (c) compound 5 at 35.2 °C, and (d) compound 6 at 143.0 °C, with all compounds in the Col_h phase.

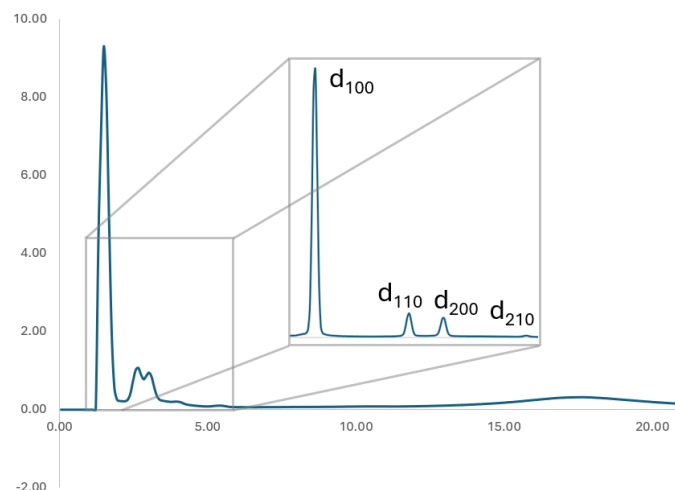


Figure 5. XRD of compound **3** at room temperature.

Table 2. Summary of X-ray diffraction data for compounds **3**, **4**, **5**, and **6**, showing d-spacing values, Miller indices, and the identified phases at various temperatures. The table includes lattice constants for each compound phase where applicable.

	T (°C)	d-Spacing (Å)	Miller Index (hkl)	Phase (Lattice Constants)
3	70	49.57	(100)	Col _h (a = 57.2 Å)
		28.55	(110)	
		24.64	(200)	
		18.61	(210)	
		5.1	alkyl halo	
4	140	52.5	(100)	Col _h (a = 60.6 Å)
		30.2	(110)	
		26.3	(200)	
		5.1	alkyl halo	
	RT	57.7	(211)	Cub _{bi} (Ia3d) (a = 141 Å)
		50.4	(220)	
		37.7	(321)	
		35.2	(400)	
		33.3	Col _h	
		31.5	(420)	
		30.2	(332)	
		27.7	(510)	
		5.0	alkyl halo	
5	RT	47.7	(100)	Col _h (a = 55.1 Å)
		27.1	(110)	
		5.0	alkyl halo	
6	140	52.8	(100)	Col _h (a = 61.0 Å)
		30.2	(110)	
		26.3	(200)	
		4.9	alkyl halo	

Note: alkyl halo determined from WAXS; all other peaks from MAXS.

Compound **4** exhibits more complex phase behavior. Upon heating, compound **4** exhibits two transitions in the DSC (Figure 3b), at -0.2 °C (79.7 kJ/mol) and 161.4 °C (2.6 kJ/mol); the latter transition was identified as the clearing temperature to the isotropic phase, which was confirmed by POM and XRD experiments. Upon cooling from the isotropic phase, the POM images show fluid fan-shaped textures typical of a columnar hexagonal (Col_h) phase (Figures 4b and S29). The X-ray diffractogram of this liquid crystal shows three low-angle peaks, indexed to the (100), (110), and (200) Miller planes

of a Col_h structure (Table 2). Both the POM textures and XRD patterns initially remain unchanged upon cooling to room temperature. However, samples left at room temperature for extended periods (days to weeks) gradually developed additional diffraction peaks, which index to a bicontinuous cubic phase (Cub_{bi}, *1a3d* space group) [40–43]. This is likely because the high viscosity of the Col_h phase slows the transition to the Cub_{bi} phase during cooling. As evidence, room-temperature POM images show a progressive decrease in birefringence (Figures 4 and S29), consistent with a slow transformation from the Col_h phase to an optically isotropic and more thermally stable Cub_{bi} phase. Upon reheating, the Cub_{bi} phase remains optically isotropic until ~65 °C, where a sudden increase in birefringence is observed (Figures 4 and S29), and the POM textures gradually increase in brightness upon further heating (Figures 4 and S29), indicating the reformation of the columnar phase, although no corresponding transition was detected by DSC. Finally, compound 4 completely clears into isotropic liquid phase at 160.3 °C (Figures 4 and S29). This phase behavior, including the supercooling of the columnar phase, is reproducible across subsequent heating and cooling cycles. Similarly to compound 3, the transition at −0.2 °C to an unknown phase, which is denoted as X (Table 1), could not be directly examined by POM or XRD due to instrumental limitations.

No phase transitions were observed in the DSC traces for compounds 5 and 6 (Figure 3c,d), which is likely to have been due to the very small enthalpy changes between the relatively disordered Col_h phase and the isotropic liquid. The melting transitions of compounds 5 and 6 could be below the detectable range of our DSC experiments, which is further supported by the absence of crystallization observations. However, the POM studies revealed the characteristic textures of columnar hexagonal (Col_h) phases for both compounds (Figure 4c for compound 5, Figure 4d for compound 6; also see Figure S29), with compound 5 having a clearing transition at 51 °C, and at 150 °C for compound 6.

The XRD pattern for 5 showed two low-angle peaks, indexed to the (100) and (110) reflections of a Col_h phase (Table 2). These peaks were significantly broadened, indicating a relatively disordered sample, which is likely to contribute to the compound's tendency to polymerize. However, it should be noted that no significant polymerization occurred during the POM experiment for compound 5, as the POM experiments can be repeated and the sample remained birefringent and fluid during cooling cycle. The polymerization of compound 5 was confirmed by dissolving a small amount of the nearly insoluble material and analyzing the ¹H NMR spectra. The spectra displayed asymmetrical peaks and a reduction in the integration values of the cis-alkene protons, further supporting polymerization. In contrast, the XRD pattern of compound 6 exhibited three sharp peaks corresponding to the (100), (110), and (200) reflections of a well-ordered Col_h phase (Table 2). Compound 6 was also observed undergoing polymerization, but this occurred over a much longer period (several months). No polymerization was observed during the POM and XRD experiments for compound 6.

The clearing temperatures of each compound are also influenced by the geometry of the alkene functionalities of the aliphatic chains region and the terminal group of the oligoethylene glycol segments. Using the two *O*-methyl-terminated derivatives as an example, the compound containing the trans-alkene functionalities, 3, has a higher clearing temperature (88.3 °C) than its cis-alkene analog 5, which clears at 51 °C, but lower than the 107.7 °C (previously reported for the *O*-methylated analog 1 [30]), which contains only fully saturated octadecanoyl groups. The same trend was observed for the three *O*-2-cyanoethyl-terminated derivatives (4 (trans) clears at 161.4 °C, 6 (cis) clears at 150 °C, and fully saturated compound 2 clears at 167.3 °C [30]). These results indicate that, compared to the amphiphilic CD derivatives containing cis-alkene functionalities, the analogs containing the linear trans-alkene chains have stronger van der Waals forces, because higher orders can be established among the trans-alkene-functionalized aliphatic chains to allow better packing efficiency, whereas higher degrees of disorder take place among the cis-alkene-functionalized analogs due to their bent geometry. On the other hand, the two compounds containing fully saturated *n*-octadecyl chains consistently exhibit the highest

clearing temperatures in each family, suggesting that the higher conformation flexibility of the fully saturated *n*-octadecyl chains permits more efficient packing. Finally, all three amphiphilic CD derivatives containing *O*-2-cyanoethyl-terminated tetraethylene glycol groups exhibit significantly higher clearing temperatures than their *O*-methyl derivatives; this difference is ascribed to the much larger dipole moment of the nitrile groups compared to the methyl groups.

3. Conclusions

In this study, we successfully synthesized a series of novel amphiphilic β -CD derivatives featuring seven *O*-methyl- or *O*-2-cyanoethyl-functionalized tetraethylene glycol groups at the primary face and fourteen elaidic or oleic chains at the secondary face of β -CD. The availability of these series of amphiphilic CD derivatives enabled a first-hand appreciation of their liquid crystalline properties. Our results demonstrate that the phase behavior of these materials is strongly influenced by the geometry of the aliphatic chains and the terminal group of the OEG segments. The elaidic derivatives exhibit stable columnar hexagonal phases, with compound **4** undergoing a transformation to a bicontinuous cubic phase over time, highlighting its unique phase transition dynamics. The oleic derivatives also show columnar mesophases but display lower stability and a tendency to polymerize (especially compound **5**). The presence of nitrile groups significantly increases the clearing temperatures of these materials due to the larger dipole moment. These findings contribute to the broader understanding of the role of chain geometry/conformation flexibility and terminal group polarity in determining the mesomorphic properties of amphiphilic CDs and open new possibilities for their application in advanced materials design.

4. Materials and Methods

4.1. Methods

General methods. All commercial reagents were used as supplied unless otherwise stated. Analytical thin-layer chromatography was performed on Silica Gel 60-F₂₅₄ (Sigma-Aldrich® TLC Plates, Oakville, ON, Canada) with detection by quenching of fluorescence and/or by charring with 5% sulfuric acid in water or with a ceric ammonium molybdate dip. Column chromatography was performed on Silica Gel 60 (Silicycle, Quebec City, QC, Canada). Organic solutions from extractions were concentrated under vacuum with the assistance of a heat bath. The ¹H NMR spectra were recorded at 400 MHz and ¹³C NMR spectra were recorded at 100 MHz on a Bruker spectrometer. Chemical shifts δ_H and δ_C are reported in δ (ppm) and referenced to residual CHCl₃ (δ_H 7.24, δ_C 77.0, CDCl₃). First-order coupling constants were reported in Hz for proton nuclei. The ¹H and ¹³C NMR spectra were assigned with the assistance of DEPTQ, COSY, and HSQC spectra. Low-resolution mass spectra were obtained using mass spectrometry with Autoflex III Smartbeam (Bruker Daltonics Inc., Billerica, MA, USA) matrix-assisted laser desorption/ionization (MALDI-TOF/TOF). High-resolution ESI-QTOF mass spectra were recorded on an Agilent 6520 Accurate Mass Quadrupole Time-of-Flight LC/MS spectrometer.

DSC. Phase transition temperatures and enthalpies were investigated using differential scanning calorimetry (DSC) on a DSC Q200 instrument (TA Instruments, New Castle, DE, USA) equipped with a refrigerated cooling system (TA Instruments, Refrigerated Cooling System 90). Heating and cooling measurements were performed at a rate of 10 °C/min. DSC thermograms of the first heating and cooling cycles for all compounds are shown in the main text, while any subsequent runs are shown in the ESI.

POM. Polarized optical microscopy experiments were carried out using an Olympus BX50 microscope equipped with a Nikon D90 DSLR camera. Sample temperatures were controlled using a Linkam LTS350 heating stage coupled with a TMS94 temperature controller.

XRD. XRD measurements were conducted on a SAXSLAB Ganesha 300XL small-angle X-ray scattering (SAXS) instrument (Cu source, 45 kV, 0.6 mA). All samples were loaded into thin-walled quartz capillary tubes (Charles Supper Company, Westborough, MA, USA)

with an outer diameter of 1.5 mm. All measurements were performed on a Linkam T95-PE heating stage. Each spectrum was collected for 8 min.

4.2. Chemical Synthesis

Compound 10.

Elaidic acid (**7**, 3.02 g, 10.69 mmol) was dissolved in anhydrous toluene (40 mL). DCC (1.10 g, 5.35 mmol) was added to the reaction flask and the reaction was stirred for 4 h under an inert argon atmosphere at 65 °C. The solid precipitate was filtered off and the filtrate containing anhydride **8** was reheated to 65 °C. Compound **9** (0.25 g, 0.19 mmol) and DMAP (1.47 g, 12.02 mmol) were added to the warm solution and the reaction was stirred overnight under an inert argon atmosphere. The reaction flask was concentrated before adding methanol (3.0 mL) to form a precipitate. The solution was centrifuged and the solid was redissolved in DCM (5 mL) and precipitated again with methanol (30 mL). The precipitate was precipitated and centrifuged twice more to afford compound **10** as a solid (0.92 g, 96%). $R_f = 0.58$ (EtOAc:Hexanes, 10:90). $[\alpha]_{25}^D + 54.4$ (c 0.57, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 5.45–5.37 (m, 28H, 28 × C=CH), 5.32 (dd, $J = 9.4, 9.4$ Hz, 7H, 7 × H-3), 5.08 (d, $J = 3.8$ Hz, 7H, 7 × H-1), 4.80 (dd, $J = 10.1, 3.7$ Hz, 7H, 7 × H-2), 4.03 (br ddd, 7H, 7 × H-5), 3.80–3.69 (m, 14H, 7 × H-4, 7 × H-6_a), 3.64 (br dd, 7H, 7 × H-6_b), 2.44–2.11 (m, 28H, 14 × CH₂COO), 2.03–1.93 (m, 56H, 28 × C=CHCH₂), 1.65–1.52 (m, 28H, 14 × CH₂CH₂COO), 1.42–1.22 (m, 280H, 140 × CH₂), 0.90 (t, $J = 7.1$ Hz, 42H, 14 × CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.4, 171.9, 130.48, 130.46, 130.10, 130.07, 96.5, 76.8, 70.9, 70.4, 70.3, 51.7, 34.3, 34.0, 32.8, 32.1, 29.96, 29.94, 29.87, 29.7, 29.60, 29.57, 29.50, 29.44, 29.40, 29.37, 25.0, 24.9, 22.9, 14.3. LRMS (MALDI-TOF, positive) m/z calc'd for C₂₉₄H₅₁₁N₂₁O₄₂Na (M + Na⁺): 5031.8 (15.65%) and 5034.849 (100%); found 5031.3.

Compound 3

Compound **11** [30] (0.14 g, 0.56 mmol), DIPEA (4.9 μ L, 27.95 μ mol), and CuI (5.3 mg, 27.95 μ mol) were added to a solution of compound **10** (0.20 g, 39.93 μ mol) dissolved in acetone (7.0 mL). The reaction was heated to 55 °C and stirred for 4 d. The solution was concentrated and then diluted with dichloromethane (75 mL) and washed with 5% ethylenediamine-*N,N,N',N'*-tetraacetic acid in water (2 × 75 mL). The organic phase was dried with sodium sulfate before being evaporated and then redissolved in DCM (2 mL), before the addition of methanol (30 mL) to form a precipitate, which was centrifuged and decanted. Precipitation and centrifugation were repeated two more times to obtain the target compound **3** as a waxy solid (0.15 g, 56%). $R_f = 0.63$ (CH₃OH:CH₂Cl₂, 10:90). $[\alpha]_{25}^D + 19.2$ (c 0.50, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 7.74 (s, 7H, 7 × 1,2,3-triazole), 5.52–5.27 (m, 42H, 7 × H-1, 7 × H-3, 28 × C=CH), 4.89–4.61 (m, 21H, 7 × H-2, 7 × H-6_a, 7 × H-6_b), 4.58–4.40 (m, 21H, 7 × H-5, 7 × OCH₂-1,2,3-triazole), 3.71–3.43 (m, 119H, 7 × H-4, 56 × OCH₂), 3.37 (s, 21H, 7 × OCH₃), 2.43–2.06 (m, 28H, 14 × CH₂COO), 2.01–1.82 (m, 56H, 28 × C=CHCH₂), 1.63–1.42 (m, 28H, 14 × CH₂CH₂COO), 1.39–1.16 (m, 280H, 140 × CH₂), 0.88 (t, $J = 7.0$ Hz, 42H, 14 × CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.0, 171.7, 130.41, 130.37, 130.08, 130.02, 125.8, 96.2, 71.9, 70.53, 70.48, 70.45, 70.37, 69.8, 69.5, 64.4, 59.0, 34.0, 33.9, 32.71, 32.66, 31.9, 29.8, 29.7, 29.52, 29.46, 29.43, 29.39, 29.33, 29.29, 29.24, 29.22, 24.7, 24.6, 22.7, 14.1. HRMS (ESI-QTOF, positive) m/z calc'd for C₃₇₈H₆₆₅N₂₁O₇₇ (M + 3H⁺): 2244.9662 found 2244.9593.

Compound 4

Compound **12** [30] (0.14 g, 0.56 mmol), DIPEA (4.9 μ L, 27.95 μ mol), and CuI (5.3 mg, 27.95 μ mol) were added to a solution of compound **10** (0.20 g, 39.93 μ mol) dissolved in acetone (6.0 mL). The reaction was heated to 55 °C and stirred for 4 d. The solution was concentrated and then diluted with dichloromethane (40 mL) and washed with 5% ethylenediamine-*N,N,N',N'*-tetraacetic acid in water (2 × 100 mL). The aqueous phase was washed with DCM (25 mL) and separated. The organic extracts were combined and dried with sodium sulfate before being evaporated. The crude product was redissolved in DCM (2 mL) before the addition of methanol (35 mL) to form a precipitate, which was centrifuged and decanted. Precipitation and centrifugation were repeated two more

times to obtain the target compound **4** as a solid (0.27 g, 97%). $R_f = 0.44$ (CH₃OH:CH₂Cl₂, 10:90). $[\alpha]_{25}^D + 22.2$ (c 0.40, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 7.73 (s, 7H, 7 $\times$ 1,2,3-triazole), 5.50–5.26 (m, 42H, 7 $\times$ H-1, 7 $\times$ H-3, 28 $\times$ C=CH), 4.86–4.61 (m, 21H, 7 $\times$ H-2, 7 $\times$ H-6_a, 7 $\times$ H-6_b), 4.56–4.40 (m, 21H, 7 $\times$ H-5, 7 $\times$ OCH₂-1,2,3-triazole), 3.75–3.44 (m, 133H, 7 $\times$ H-4, 63 $\times$ OCH₂), 2.61 (t, $J = 6.3$ Hz, 14H, 7 $\times$ CH₂CN), 2.42–2.01 (m, 28H,), 1.99–1.87 (m, 56H, 28 $\times$ C=CHCH₂), 1.61–1.42 (m, 28H, 14 $\times$ CH₂CH₂COO), 1.37–1.17 (m, 280H, 140 $\times$ CH₂), 0.86 (t, $J = 7.1$ Hz, 42H, 14 $\times$ CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.0, 171.7, 144.6, 130.41, 130.36, 130.06, 130.00, 125.8, 118.0, 96.2, 70.7, 70.6, 70.47, 70.45, 70.35, 65.9, 64.3, 34.0, 33.8, 32.70, 32.68, 32.65, 31.9, 29.8, 29.7, 29.50, 29.45, 29.41, 29.38, 29.32, 29.27, 29.23, 29.21, 24.7, 24.6, 22.7, 18.8, 14.1. HRMS (ESI-QTOF, positive) m/z calc'd for C₃₉₂H₆₇₂N₂₈O₇₇ (M + 3H⁺): 2335.9916; found 2335.9890.

Compound 15

Oleic acid (**13**, 12.08 g, 42.77 mmol) was dissolved in anhydrous toluene (200 mL). DCC (4.41 g, 21.38 mmol) was added to the reaction flask and the reaction was stirred for 3.5 h under an inert argon atmosphere at 65 °C. The solid precipitate was filtered off and the filtrate containing the intermediate anhydride **14** was reheated to 65 °C. Compound **9** (1.0 g, 0.76 mmol) and DMAP (5.22 g, 42.77 mmol) was added to the warm solution and the reaction was stirred for 24 h under an inert argon atmosphere. The reaction flask was concentrated before adding methanol (200 mL) to form a precipitate. The solution was decanted, redissolved in DCM (5 mL) and precipitated again with methanol (100 mL). The precipitate was precipitated and centrifuged twice more to afford compound **15** as a solid (3.06 g, 80%). $R_f = 0.40$ (EtOAc:Hexanes, 10:90). $[\alpha]_{25}^D + 68.4$ (c 0.58, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 5.42–5.26 (m, 35H, 7 $\times$ H-3, 28 $\times$ C=CH), 5.07 (d, $J = 3.8$ Hz, 7H, 7 $\times$ H-1), 4.79 (dd, $J = 10.1, 3.7$ Hz, 7H, 7 $\times$ H-2), 4.00 (br ddd, 7H, 7 $\times$ H-5), 3.79–3.67 (m, 14H, 7 $\times$ H-4, 7 $\times$ H-6_a), 3.63 (br dd, 7H, 7 $\times$ H-6_b), 2.42–2.12 (m, 28H, 14 $\times$ CH₂COO), 2.01 (m, 56H, 28 $\times$ C=CHCH₂), 1.64–1.49 (m, 28H, 14 $\times$ CH₂CH₂COO), 1.40–1.20 (m, 280H, 140 $\times$ CH₂), 0.93–0.83 (t, $J = 7.2$ Hz, 42H, 14 $\times$ CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.1, 171.7, 129.98, 129.95, 129.57, 129.53, 96.3, 76.6, 70.7, 70.3, 70.1, 51.6, 34.1, 33.8, 31.9, 29.87, 29.84, 29.8, 29.6, 29.5, 29.4, 29.34, 29.32, 29.27, 29.2, 27.3, 27.2, 24.8, 24.7, 22.7, 14.1. LRMS (MALDI-TOF, positive) m/z calc'd for C₂₉₄H₅₁₁N₂₁O₄₂Na (M + Na⁺): 5031.8 (15.65%) and 5034.849 (100%); found 5029.6.

Compound 5

Compound **11** (0.14 g, 0.56 mmol), DIPEA (4.9 μ L, 27.95 μ mol), and CuI (5.3 mg, 27.95 μ mol) were added to a solution of compound **15** (0.20 g, 39.93 μ mol) dissolved in acetone (5.0 mL). The reaction was heated to 55 °C and stirred for 4 d. The solution was concentrated and then diluted with ethyl acetate (100 mL) and washed with 5% ethylenediamine-*N,N,N',N'*-tetraacetic acid in water (3 $\times$ 100 mL). The organic phase was dried with sodium sulfate before being evaporated and then redissolved in DCM (2 mL) before the addition of methanol (35 mL) to form a precipitate, which was centrifuged and decanted. Precipitation and centrifugation were repeated two more times to obtain the target compound **5** as a waxy solid (0.19 g, 71%). $R_f = 0.63$ (CH₃OH:CH₂Cl₂, 10:90). $[\alpha]_{25}^D + 17.0$ (c 0.44, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 7.72 (s, 7H, 7 $\times$ 1,2,3-triazole), 5.47 (br d, 7H, 7 $\times$ H-1), 5.41–5.24 (m, 35H, 7 $\times$ H-3, 28 $\times$ C=CH), 4.87–4.62 (m, 21H, 7 $\times$ H-2, 7 $\times$ H-6_a, 7 $\times$ H-6_b), 4.58–4.37 (m, 21H, 7 $\times$ H-5, 7 $\times$ OCH₂-1,2,3-triazole), 3.69–3.46 (m, 119H, 7 $\times$ H-4, 56 $\times$ OCH₂), 3.36 (s, 21H, 7 $\times$ OCH₃), 2.42–2.06 (m, 28H, 14 $\times$ CH₂COO), 1.99 (m, 56H, 28 $\times$ C=CHCH₂), 1.64–1.43 (m, 28H, 14 $\times$ CH₂CH₂COO), 1.38–1.17 (m, 280H, 140 $\times$ CH₂), 0.92–0.81 (t, $J = 7.1$ Hz, 42H, 14 $\times$ CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.0, 171.6, 144.7, 129.93, 129.89, 129.57, 129.51, 125.7, 96.2, 76.7, 71.9, 70.5, 70.48, 70.45, 70.37, 69.8, 64.4, 59.0, 34.0, 33.7, 31.9, 29.9, 29.8, 29.54, 29.52, 29.45, 29.40, 29.33, 29.30, 29.27, 29.2, 27.3, 27.24, 27.21, 24.8, 24.6, 22.7, 14.1. HRMS (ESI-QTOF, positive) m/z calc'd for C₃₇₈H₆₆₅N₂₁O₇₇ (M + 3H⁺): 2244.9662; found 2244.9490.

Compound 6

Compound **12** (0.14 g, 0.56 mmol), DIPEA (4.9 μ L, 27.95 μ mol), and CuI (5.3 mg, 27.95 μ mol) were added to a solution of compound **15** (0.20 g, 39.93 μ mol) dissolved

in acetone (6.0 mL). The reaction was heated to 55 °C and stirred for 4 d. The solution was concentrated and then diluted with dichloromethane (40 mL) and washed with 5% ethylenediamine-*N,N,N',N'*-tetraacetic acid in water (2 × 100 mL). The organic phase was dried with sodium sulfate before being evaporated and then redissolved in DCM (2 mL) before the addition of methanol (35 mL) to form a precipitate, which was centrifuged and decanted. Precipitation and centrifugation were repeated two more times to obtain the target compound **6** as a waxy solid (0.29 g, 100%). $R_f = 0.47$ (CH₃OH:CH₂Cl₂, 10:90). $[\alpha]_{25}^D + 20.1$ (c 0.61, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 7.75 (s, 7H, 7 × 1,2,3-triazole), 5.53–5.20 (m, 42H, 7 × H-1, 7 × H-3, 28 × C=CH), 4.85–4.58 (m, 21H, 7 × H-2, 7 × H-6_a, 7 × H-6_b), 4.57–4.39 (m, 21H, 7 × H-5, 7 × OCH₂-1,2,3-triazole), 3.75–3.45 (m, 133H, 7 × H-4, 63 × OCH₂), 2.60 (t, $J = 6.4$ Hz, 14H, 7 × CH₂CN), 2.39–2.04 (m, 28H, 14 × CH₂COO), 2.05–1.87 (m, 56H, 28 × C=CHCH₂), 1.63–1.40 (m, 28H, 14 × CH₂CH₂COO), 1.37–1.12 (m, 280H, 140 × CH₂), 0.85 (t, $J = 6.7$ Hz, 42H, 14 × CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.0, 171.7, 144.5, 129.94, 129.90, 129.55, 129.48, 125.9, 118.0, 96.2, 76.8, 70.62, 70.55, 70.4, 70.3, 69.8, 69.5, 65.9, 64.3, 50.6, 50.0, 34.0, 33.7, 31.9, 29.87, 29.85, 29.7, 29.53, 29.50, 29.44, 29.39, 29.32, 29.29, 29.2, 27.3, 27.2, 24.8, 24.6, 22.6, 18.8, 14.1. HRMS (ESI-QTOF, positive) m/z calc'd for C₃₉₂H₆₇₂N₂₈O₇₇ (M + 3H⁺): 2335.9916; found 2335.9782.

Supplementary Materials: The following supporting information can be downloaded at: <https://www.mdpi.com/article/10.3390/molecules29235633/s1>. Figure S1: ¹H NMR spectrum of compound **10**; Figure S2: ¹³C NMR spectrum of compound **10**; Figure S3: ¹H-¹H COSY NMR spectrum of **10**; Figure S4: ¹H-¹³C HSQC NMR spectrum of **10**; Figure S5: ¹H NMR spectrum of compound **3**; Figure S6: ¹³C NMR spectrum of compound **3**; Figure S7: ¹H-¹H COSY NMR spectrum of **3**; Figure S8: ¹H-¹³C HSQC NMR spectrum of **3**; Figure S9: ¹H NMR spectrum of compound **4**; Figure S10: ¹³C NMR spectrum of compound **4**; Figure S11: ¹H-¹H COSY NMR spectrum of **4**; Figure S12: ¹H-¹³C HSQC NMR spectrum of **4**; Figure S13: ¹H NMR spectrum of compound **15**; Figure S14: ¹³C NMR spectrum of compound **15**; Figure S15: ¹H-¹H COSY NMR spectrum of **15**; Figure S16: ¹H-¹³C HSQC NMR spectrum of **15**; Figure S17: ¹H NMR spectrum of compound **5**; Figure S18: ¹³C NMR spectrum of compound **5**; Figure S19: ¹H-¹H COSY NMR spectrum of **5**; Figure S20: ¹H-¹³C HSQC NMR spectrum of **5**; Figure S21: ¹H NMR spectrum of compound **6**; Figure S22: ¹³C NMR spectrum of compound **6**; Figure S23: ¹H-¹H COSY NMR spectrum of **6**; Figure S24: ¹H-¹³C HSQC NMR spectrum of **6**; Figure S25: DSC thermogram of **3**; Figure S26: DSC thermogram of **4**; Figure S27: DSC thermogram of **5**; Figure S28: DSC thermogram of **6**; Figure S29: Cross-polarized micrographs of **3** during cooling cycle at 70.2 °C (a) and 35.7 °C (b), **4** during cooling cycle at 140.5 °C (c) and 48.3 °C (d), followed by standing at ambient temperature after several days (e), and reheating cycle to 67.1 °C (f), 150.0 °C (g), and. Finally, 160.3 °C (h), with five during cooling cycle at 35.2 °C (i), and six during cooling cycle at 143.0 °C (j) and 72.7 °C (k); Figure S30: XRD of **3**; Figure S31: XRD of **4**; Figure S32: XRD of **5**; Figure S33: XRD of **6**.

Author Contributions: Chemical synthesis, A.C. and J.D.; POM, A.C.; XRD, H.G.; writing—original draft preparation, A.C., C.-C.L. and V.E.W.; writing—review and editing, A.C., H.G., C.O.Z.-P., J.D., V.E.W. and C.-C.L.; project administration and supervision, C.-C.L. and V.E.W.; fund acquisition, C.-C.L.; conceptualization, C.-C.L. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by the Natural Sciences and Engineering Research Council of Canada (NSERC), grant number RGPIN/04320-2018 (C.-C.L.).

Data Availability Statement: The data are contained within the article.

Acknowledgments: We are grateful to the Department of Chemistry, University of Calgary, for the support for the current work.

Conflicts of Interest: The authors declare no conflicts of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

References

1. Dodziuk, H. (Ed.) *Cyclodextrins and Their Complexes: Chemistry, Analytical Methods, Applications*, 1st ed.; Wiley-VCH: Weinheim, Germany, 2006; ISBN 978-3-527-31280-1.
2. Khan, A.R.; Forgo, P.; Stine, K.J.; D'Souza, V.T. Methods for Selective Modifications of Cyclodextrins. *Chem. Rev.* **1998**, *98*, 1977–1996. [[CrossRef](#)] [[PubMed](#)]
3. Ashton, P.R.; Ellwood, P.; Staton, I.; Stoddart, J.F. Synthesis and Characterization of Per-3,6-Anhydro Cyclodextrins. *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 80–81. [[CrossRef](#)]
4. Fügedi, P. Synthesis of Heptakis(6-*O*-*tert*-Butyldimethylsilyl)Cyclomaltoheptaose and Octakis(6-*O*-*tert*-Butyldimethylsilyl)Cyclomaltooctaose. *Carbohydr. Res.* **1989**, *192*, 366–369. [[CrossRef](#)]
5. Gabelle, A.; Defaye, J. Selective Halogenation at Primary Positions of Cyclomaltooligosaccharides and a Synthesis of Per-3,6-Anhydro Cyclomaltooligosaccharides. *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 78–80. [[CrossRef](#)]
6. Wang, A.; Li, W.; Zhang, P.; Ling, C.-C. Synthesis of a Novel Class of Cyclodextrin-Based Nanotubes. *Org. Lett.* **2011**, *13*, 3572–3575. [[CrossRef](#)]
7. Sallas, F.; Darcy, R. Amphiphilic Cyclodextrins—Advances in Synthesis and Supramolecular Chemistry. *Eur. J. Org. Chem.* **2008**, *2008*, 957–969. [[CrossRef](#)]
8. Rivero-Barbarroja, G.; Benito, J.M.; Ortiz Mellet, C.; García Fernández, J.M. Cyclodextrin-Based Functional Glyconanomaterials. *Nanomaterials* **2020**, *10*, 2517. [[CrossRef](#)]
9. Bilensoy, E.; Hincal, A.A. Recent Advances and Future Directions in Amphiphilic Cyclodextrin Nanoparticles. *Expert Opin. Drug Deliv.* **2009**, *6*, 1161–1173. [[CrossRef](#)]
10. Parrot-Lopez, H.; Ling, C.C.; Zhang, P.; Baszkin, A.; Albrecht, G.; De Rango, C.; Coleman, A.W. Self-Assembling Systems of the Amphiphilic Cationic per-6-Amino- β -Cyclodextrin 2,3-Di-O-Alkyl Ethers. *J. Am. Chem. Soc.* **1992**, *114*, 5479–5480. [[CrossRef](#)]
11. Zhang, P.; Chang-Chun, L.; Coleman, A.W.; Parrot-Lopez, H.; Galons, H. Formation of Amphiphilic Cyclodextrins via Hydrophobic Esterification at the Secondary Hydroxyl Face. *Tetrahedron Lett.* **1991**, *32*, 2769–2770. [[CrossRef](#)]
12. Badi, N.; Jarroux, N.; Guégan, P. Synthesis of Per-2,3-Di-O-Heptyl- β and γ -Cyclodextrins: A New Kind of Amphiphilic Molecules Bearing Hydrophobic Parts. *Tetrahedron Lett.* **2006**, *47*, 8925–8927. [[CrossRef](#)]
13. Díaz-Moscoso, A.; Guilloteau, N.; Bienvenu, C.; Méndez-Ardoy, A.; Blanco, J.L.J.; Benito, J.M.; Le Gourriérec, L.; Di Giorgio, C.; Vierling, P.; Defaye, J.; et al. Mannosyl-Coated Nanocomplexes from Amphiphilic Cyclodextrins and pDNA for Site-Specific Gene Delivery. *Biomaterials* **2011**, *32*, 7263–7273. [[CrossRef](#)] [[PubMed](#)]
14. Wazynska, M.; Temeriusz, A.; Chmurski, K.; Bilewicz, R.; Jurczak, J. Synthesis and Monolayer Behavior of Amphiphilic per(2,3-Di-O-Alkyl)- α - and β -Cyclodextrins and Hexakis(6-Deoxy-6-Thio-2,3-Di-O-Pentyl)- α -Cyclodextrin at an Air–Water Interface. *Tetrahedron Lett.* **2000**, *41*, 9119–9123. [[CrossRef](#)]
15. Roux, M.; Perly, B.; Djedaini-Pilard, F. Self-Assemblies of Amphiphilic Cyclodextrins. *Eur. Biophys. J.* **2007**, *36*, 861–867. [[CrossRef](#)]
16. Falvey, P.; Lim, C.W.; Darcy, R.; Revermann, T.; Karst, U.; Giesbers, M.; Marcelis, A.; Lazar, A.; Coleman, A.W.; Reinhoudt, D.N. Bilayer Vesicles of Amphiphilic Cyclodextrins: Host Membranes That Recognize Guest Molecules. *Chem.-A Eur. J.* **2005**, *11*, 1171–1180. [[CrossRef](#)]
17. Mazzaglia, A.; Forde, D.; Garozzo, D.; Malvagna, P.; Ravoo, B.J.; Darcy, R. Multivalent Binding of Galactosylated Cyclodextrin Vesicles to Lectin. *Org. Biomol. Chem.* **2004**, *2*, 957–960. [[CrossRef](#)]
18. Ravoo, B.J.; Darcy, R. Cyclodextrin Bilayer Vesicles. *Angew. Chem. Int. Ed.* **2000**, *39*, 4324–4326. [[CrossRef](#)]
19. Bienvenu, C.; Martínez, Á.; Blanco, J.L.J.; Giorgio, C.D.; Vierling, P.; Mellet, C.O.; Defaye, J.; Fernández, J.M.G. Polycationic Amphiphilic Cyclodextrins as Gene Vectors: Effect of the Macrocyclic Ring Size on the DNA Complexing and Delivery Properties. *Org. Biomol. Chem.* **2012**, *10*, 5570–5581. [[CrossRef](#)]
20. McMahon, A.; O'Neill, M.J.; Gomez, E.; Donohue, R.; Forde, D.; Darcy, R.; O'Driscoll, C.M. Targeted Gene Delivery to Hepatocytes with Galactosylated Amphiphilic Cyclodextrins. *J. Pharm. Pharmacol.* **2012**, *64*, 1063–1073. [[CrossRef](#)]
21. Champagne, P.-L.; Kumar, R.; Ling, C.-C. Supramolecular Liquid Crystals Based on Cyclodextrins. In *Cyclodextrin Applications in Medicine, Food, Environment and Liquid Crystals*; Fourmentin, S., Crini, G., Lichtfouse, E., Eds.; Springer International Publishing: Cham, Switzerland, 2018; pp. 183–240; ISBN 978-3-319-76162-6.
22. Votava, M.; Ravoo, B.J. Principles and Applications of Cyclodextrin Liquid Crystals. *Chem. Soc. Rev.* **2021**, *50*, 10009–10024. [[CrossRef](#)]
23. Ling, C.-C.; Darcy, R.; Risse, W. Cyclodextrin Liquid Crystals: Synthesis and Self-Organisation of Amphiphilic Thio- β -Cyclodextrins. *J. Chem. Soc. Chem. Commun.* **1993**, 438–440. [[CrossRef](#)]
24. Chen, L.; Hu, T.-H.; Xie, H.-L.; Zhang, H.-L. A Mixed Cyclodextrin-Biphenyl Thermotropic Liquid Crystal: Synthesis, Liquid-Crystalline Properties, and Supramolecular Organization. *J. Polym. Sci. Part A Polym. Chem.* **2010**, *48*, 2838–2845. [[CrossRef](#)]
25. Yang, F.; Zhang, Y.; Guo, H. Novel Supramolecular Liquid Crystals: Cyclodextrin-Triphenylene Column Liquid Crystals Based on Click Chemistry. *New J. Chem.* **2013**, *37*, 2275–2279. [[CrossRef](#)]
26. Ward, S.; Calderon, O.; Zhang, P.; Sobchuk, M.; Keller, S.N.; Williams, V.E.; Ling, C.-C. Investigation into the Role of the Hydrogen Bonding Network in Cyclodextrin-Based Self-Assembling Mesophases. *J. Mater. Chem. C* **2014**, *2*, 4928–4936. [[CrossRef](#)]
27. Kolb, H.C.; Finn, M.G.; Sharpless, K.B. Click Chemistry: Diverse Chemical Function from a Few Good Reactions. *Angew. Chem. Int. Ed.* **2001**, *40*, 2004–2021. [[CrossRef](#)]

28. Geng, Z.; Shin, J.J.; Xi, Y.; Hawker, C.J. Click Chemistry Strategies for the Accelerated Synthesis of Functional Macromolecules. *J. Polym. Sci.* **2021**, *59*, 963–1042. [\[CrossRef\]](#)
29. Champagne, P.-L.; Ester, D.; Zeeman, M.; Zellman, C.; Williams, V.E.; Ling, C.-C. Inverting Substitution Patterns on Amphiphilic Cyclodextrins Induces Unprecedented Formation of Hexagonal Columnar Superstructures. *J. Mater. Chem. C* **2017**, *5*, 9247–9254. [\[CrossRef\]](#)
30. Che, A.; Zellman, C.O.; Sarkar, D.; Trudel-Lachance, S.; Espejo, J.; Michaelis, V.K.; Williams, V.E.; Ling, C.-C. Functional Group Polarity-Modulated Formation of Liquid Crystals of Amphiphilic Cyclodextrins. *J. Mater. Chem. C* **2023**, *11*, 4153–4163. [\[CrossRef\]](#)
31. Champagne, P.-L.; Ester, D.; Ward, S.; Williams, V.E.; Ling, C.-C. A Family of Amphiphilic Cyclodextrin Liquid Crystals Governed by Dipole–Dipole Interactions. *ChemPlusChem* **2017**, *82*, 423–432. [\[CrossRef\]](#)
32. Champagne, P.-L.; Ester, D.; Polan, D.; Williams, V.E.; Thangadurai, V.; Ling, C.-C. Amphiphilic Cyclodextrin-Based Liquid Crystals for Proton Conduction. *J. Am. Chem. Soc.* **2019**, *141*, 9217–9224. [\[CrossRef\]](#)
33. Champagne, P.-L.; Ester, D.; Bhattacharya, A.; Hofstetter, K.; Zellman, C.; Bag, S.; Yu, H.; Trudel, S.; Michaelis, V.K.; Williams, V.E.; et al. Liquid Crystalline Lithium-Ion Electrolytes Derived from Biodegradable Cyclodextrin. *J. Mater. Chem. A* **2019**, *7*, 12201–12213. [\[CrossRef\]](#)
34. Moore, J.E.; McCoy, T.M.; Marlow, J.B.; Pottage, M.J.; Mudie, S.T.; Pearson, G.R.; Wilkinson, B.L.; Tabor, R.F. Rich Liquid Crystal Phase Behavior of Novel Alkyl-Tri(Ethylene Glycol)-Glucoside Carbohydrate Surfactants. *J. Colloid Interface Sci.* **2019**, *540*, 410–419. [\[CrossRef\]](#) [\[PubMed\]](#)
35. Alamro, F.S.; Ahmed, H.A.; Bedowr, N.S.; Naoum, M.M.; Mostafa, A.M.; Al-Kadhi, N.S. New Liquid Crystals Based on Terminal Fatty Chains and Polymorphic Phase Formation from Their Mixtures. *Crystals* **2022**, *12*, 350. [\[CrossRef\]](#)
36. Alnoman, R.; Al-Nazawi, F.K.; Ahmed, H.A.; Hagar, M. Synthesis, Optical, and Geometrical Approaches of New Natural Fatty Acids' Esters/Schiff Base Liquid Crystals. *Molecules* **2019**, *24*, 4293. [\[CrossRef\]](#)
37. Varia, M.C.; Srinivasa, H.T.; Kumar, S. Effects of Chain Branching and Lateral Fluorine Substitution on Mesomorphism of Cholesteryl Benzoates. *Liq. Cryst.* **2014**, *41*, 883–890. [\[CrossRef\]](#)
38. Funakoshi, Y.; Iwao, Y.; Noguchi, S.; Itai, S. Effect of Alkyl Chain Length and Unsaturation of the Phospholipid on the Physico-chemical Properties of Lipid Nanoparticles. *Chem. Pharm. Bull.* **2015**, *63*, 731–736. [\[CrossRef\]](#)
39. Díaz-Moscoso, A.; Vercauteren, D.; Rejman, J.; Benito, J.M.; Mellet, C.O.; De Smedt, S.C.; Fernández, J.M.G. Insights in Cellular Uptake Mechanisms of pDNA–Polycationic Amphiphilic Cyclodextrin Nanoparticles (CDplexes). *J. Control. Release* **2010**, *143*, 318–325. [\[CrossRef\]](#)
40. Cao, Y.; Alaasar, M.; Nallapaneni, A.; Salamończyk, M.; Marinko, P.; Gorecka, E.; Tschierske, C.; Liu, F.; Vaupotič, N.; Zhu, C. Molecular Packing in Double Gyroid Cubic Phases Revealed via Resonant Soft X-Ray Scattering. *Phys. Rev. Lett.* **2020**, *125*, 027801. [\[CrossRef\]](#)
41. Do, T.H.; Kim, H.-J.; Nguyen, M.L.; Cho, B.-K. Bicontinuous Cubic and Hexagonal Columnar Liquid Crystalline Ion-Conductors at Room Temperature in Ion-Doped Dendritic Amphiphiles. *Crystals* **2020**, *10*, 193. [\[CrossRef\]](#)
42. Ichikawa, T.; Kato, T.; Ohno, H. 3D Continuous Water Nanosheet as a Gyroid Minimal Surface Formed by Bicontinuous Cubic Liquid-Crystalline Zwitterions. *J. Am. Chem. Soc.* **2012**, *134*, 11354–11357. [\[CrossRef\]](#)
43. Ichikawa, T.; Yoshio, M.; Hamasaki, A.; Taguchi, S.; Liu, F.; Zeng, X.; Ungar, G.; Ohno, H.; Kato, T. Induction of Thermotropic Bicontinuous Cubic Phases in Liquid-Crystalline Ammonium and Phosphonium Salts. *J. Am. Chem. Soc.* **2012**, *134*, 2634–2643. [\[CrossRef\]](#)

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.