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PAT

Synthesis of polymerizable amphiphiles with critical packing parameters systematically varied†

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In this paper the design and synthesis of a group of polymerizable amphiphiles with different ratios of the number of hydrophilic heads and the number of hydrophobic tails are reported. The head/tail number ratio could be viewed as an approximate equivalent of the critical packing parameter. The synthetic procedure was optimized to be extendable. The design is expected to furnish a robust library of polymerizable amphiphiles for formation and immobilization of surfactant phases.

KEYWORDS: amphiphiles; synthesis; critical packing parameter; systematic variation; phase behavior

INTRODUCTION

An amphiphile is a molecule composed of a hydrophilic part and a hydrophobic part, which are incompatible and tend to separate from each other. The tendency of separation is often promoted by addition of water and sometimes also oil. Under balanced conditions the mixtures form macroscopically homogeneous phases, including isotropic solution phases and liquid crystalline phases. Correlation of the amphiphile structure with its phase behavior could be understood with a simple geometric model,[1] which defines a dimensionless critical packing parameter (CPP) to describe the relative bulkiness of the hydrophobic part and the hydrophilic part in an amphiphile. With the CPP increasing from a small value to a high value the amphiphile changes from hydrophilic to hydrophobic, its preferred phase structure from direct structures via lamellar structure to reverse structures. This model provides a basis for the molecular design of amphiphiles.

To immobilize the microstructure of the phases formed by amphiphiles is a challenge for current material chemists. Techniques of both inorganic polymerization[2] and organic polymerization[3] have been developed. With organic polymerization the molecular design of the polymerizable amphiphiles is critical for the successful immobilization of the vulnerable precursor microstructures. To our knowledge only Gin's group has ever reported molecular design of polymerizable amphiphiles with the molecular shape systematically varied. They synthesized three series of polymerizable amphiphiles: sodium alkyl carboxylates with styryl ether group attached at different positions of the alkyl chain,[4] tapered amphiphiles with three alkyl tails end-capped with two conjugated C=C double bonds[5] and gemini amphiphiles with two polymerizable alkyl tails and two hydrophilic head groups.[6] These amphiphiles were very effective in forming lyotropic liquid crystalline phases and Gin's attempts of immobilizing these phases were also very successful.

Inspired by Gin's work the authors have designed and synthesized a new series of polymerizable amphiphiles with the CPPs systematically varied. The synthetic procedure was optimized to be flexible for CPP variation and extendable. The design is expected to furnish a robust library of polymerizable amphiphiles for formation and immobilization of surfactant phases.

EXPERIMENTAL

Reagents and chemicals

Most commercial chemicals except those referred to later were purchased in A.R. or C.P. grades and used without further treatment. 11-Bromoundecanol was synthesized with the standard procedure.[7] Methyl gallate and methyl 3,4-dihydroxybenzoate were synthesized as in the literature.[8] 2-Bromoethyl acetate was synthesized with the patented procedure.[9] *p*-Toluenesulfonic acid (TsOH) was dehydrated by azeotropic distillation with benzene and dried in vacuo. 4-Dimethylaminopyridinium *p*-toluenesulfonate (DPTS) was prepared as in the literature.[10] 1,3-Dicyclohexylcarbodiimide

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(DCC) was dissolved in petroleum ether (30–60°C), filtered, and evaporated to dryness. 2,6-Di-*tert*-butyl-4-methylphenol (BHT) and nitrobenzene were used as the polymerization inhibitors. *N*,*N*-Dimethyl formamide (DMF) was dried over activated molecular sieves (4 Å) for 2–3 days. Dichloromethane and acetonitrile were refluxed and distilled over CaH_2. Column chromatography (flash) was performed with silica gel H (Qingdao Haiyang Chemicals).

3,4,5-Tris-(11-acryloyloxy-undecyloxy)-benzoic acid (3Acrylate-Ph-COOH)

*3,4,5-Tris-(11-hydroxy-undecyloxy)-benzoic acid methyl ester (**1**)*[8]. Methyl gallate (6.44 g, 34.8 mmol), 11-bromoundecanol (29.0 g, 115 mmol), K_2CO_3 (52 g, 377 mmol), KI (0.42 g) was added to dry DMF (200 ml) and stirred with a powerful stirrer. With dry N_2 bubbled for ~40 min, the mixture was stirred in a bath at 75°C for 24 hr. It was then cooled to room temperature, poured into water and stirred for ~10 min. The solid was filtered, washed by water and dissolved in warm EtOAc (~40°C). The solution was washed with dilute HCl (1 N, 25 ml × 2) and saturated brine (50 ml × 2) and then cooled slowly to below 0°C for recrystallization. The crystals were further recrystallized twice in EtOAc (180 ml + 250 ml). Drying in air overnight gave an off-white fine powder (21.2 g, 87.2%). Thin-layer chromatography (TLC) showed only one point (Petroleum/EtOAc = 2 : 3, $R_f = 0.15$).

*3,4,5-Tris-(11-hydroxy-undecyloxy)-benzoic acid (**2**)*[8]. Compound **1** (21.2 g, 30.5 mmol) and KOH (13.73 g, 245 mmol) were dissolved in a mixture of methanol/water (3 : 1 v/v, 170 ml) and stirred in a bath at 67°C for 24 hr. Then a mixture of concentrated. HCl (36%, 25 ml) and methanol (38 ml) was added to the hot reaction mixture. The mixture was then poured into cold water (1000 ml) and stirred for 10 min. The solid was filtered, dissolved in hot EtOAc (~50°C) and washed with dilute HCl (1 N) and saturated brine. The solution was cooled slowly to 5°C for recrystallization. The collected crystals were again dissolved in warm $CHCl_3$ (38°C) and stirred over $MgSO_4$ in a bath at 38°C for 15 min. The dried solution was filtered quickly and cooled slowly to 5°C. Filtration and drying *in vacuo* gave a white fine powder (20.64 g, 99%). Spectral data agreed with those in the literature.[8]

3Acrylate-Ph-COOH. Compound **2** (4.8 g), TsOH (0.29 g) and BHT (0.29 g) were added to methyl acrylate (97 ml), to which a fast stream of dry N_2 was bubbled for 40 min. The mixture was heated in a bath at 75°C for 18 hr. Then the solution was cooled and evaporated to dryness. Fresh methyl acrylate (20 ml) was added to the residue, which was evaporated to dryness again. The co-evaporation was repeated for another time. To the residue fresh methyl acrylate (97 ml) was added. With N_2 bubbled for 40 min the solution was heated in a bath at 75°C for another 18 hr. Then the solution was cooled, washed with water and saturated brine, and dried over Na_2SO_4. After evaporation of methyl acrylate, the residue was chromatographed on silica gel (150 g) with at first petroleum ether/EtOAc (1260 ml/140 ml) and then petroleum ether/EtOAc (700ml/350ml) as eluents. Evaporation of solvents and drying *in vacuo* gave a white solid powder (4.82 g, 81.5%). ^{1}H-NMR shows the presence of very small amount of methyl ester (<5%). If a smaller loading was used in flash chromatography, all methyl ester could be removed. But small amounts of methyl ester left could be removed in future synthesis. Chemical shifts in ^{1}H-NMR (500 MHz, $CDCl_3$, ppm): 7.32 (s, 2H), 6.40 (d, 3H), 6.12 (q, 3H), 5.81 (q, 3H), 4.15 (t, 6H), 4.02 (t, 6H), 1.82 (m, 4H), 1.74 (m, 2H), 1.66 (m, 6H), 1.49 (m, 6H), 1.30 (m, 36H).

3,4-Bis-(11-acryloyloxy-undecyloxy)-benzoic acid (2Acrylate-Ph-COOH)

3,4-Bis-(11-hydroxy-undecyloxy)-benzoic acid methyl ester. This compound was synthesized using the same procedure as for **1**. But methyl 3,4-dihydroxybenzoate was used instead of methyl gallate. The yield was 95.8%. TLC showed only one point (petroleum/EtOAc = 1 : 1).

3,4-Bis-(11-hydroxy-undecyloxy)-benzoic acid. This compound was synthesized using the same procedure as for **2**. But 3,4-bis-(11-hydroxy-undecyloxy)-benzoic acid methyl ester was used instead of **1**. The yield was 92.8%.

2Acrylate-Ph-COOH. This compound was synthesized using the same procedure as for 3Acrylate-Ph-COOH. But 3,4-bis-(11-hydroxy-undecyloxy)-benzoic acid was used instead of **2**. The yield was 71.8%. Chemical shifts in ^{1}H-NMR (500 MHz, $CDCl_3$, ppm): 7.71 (m, 1H), 7.58 (d, 1H), 6.89 (m, 1H), 6.40 (d, 2H), 6.12 (q, 2H), 5.81 (q, 2H), 4.15 (t, 4H), 4.05 (t, 4H), 1.84 (m, 4H), 1.66 (m, 4H), 1.47 (m, 4H), 1.33 (m, 24H).

4-(11-Acryloyloxy-undecyloxy)-benzoic acid (1Acrylate-Ph-COOH)

4-(11-Hydroxy-undecyloxy)-benzoic acid methyl ester. This compound was synthesized using the same procedure as for **1**. But methyl 4-hydroxybenzoate was used instead of methyl gallate. The yield was 84.0%.

4-(11-Hydroxy-undecyloxy)-benzoic acid. This compound was synthesized using the same procedure as for **2**. But 4-(11-hydroxy-undecyloxy)-benzoic acid methyl ester was used instead of **1**. The yield was 95.3%.

1Acrylate-Ph-COOH. This compound was synthesized using the same procedure as for 3Acrylate-Ph-COOH. But 4-(11-hydroxy-undecyloxy)-benzoic acid was used instead of **2** and only one process of transesterification (18 h × 1) was adopted. The yield was 73.2%. Chemical shifts in ^{1}H-NMR (500 MHz, $CDCl_3$, ppm): 8.05 (d, 2H), 6.93 (d, 2H), 6.40 (d, 1H), 6.12 (q, 1H), 5.81 (q, 1H), 4.15 (t, 2H), 4.02 (t, 2H), 1.81 (m, 2H), 1.66 (m, 2H), 1.45 (m, 2H), 1.33 (m, 12H).

3,4,5-Tris-(2-bromo-ethoxy)-benzoic acid 4-hydroxy-butyl ester (3Br-Ph-OH)

*3,4,5-Tris-(2-acetoxy-ethoxy)-benzoic acid methyl ester (**3**).* Methyl gallate (10 g, 0.0543 mol), K_2CO_3 (75 g, 0.543 mol)

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and KI (0.51 g) were added to dry DMF (300 ml). A fast stream of dry N_2 was bubbled to the violently stirred mixture for 0.5 hr and the mixture was heated in a bath at 75°C. 2-Bromoethyl acetate (20 ml, 0.181 mol) was dropped slowly into the mixture, which was stirred in N_2 atmosphere for 20 hr. Then the reaction mixture was cooled and filtered to remove solids. With a small amount of acetic acid (~8 ml) added it was then evaporated *in vacuo* at 85°C. After most of the DMF was removed, the residue was partitioned in 100 ml water and 80 ml CH_2Cl_2. The organic layer was separated, washed by water and saturated brine and dried over $MgSO_4$. After filtration and evaporation the crude dark brown solid residue was chromatographed on silica gel (200 g) with at first petroleum ether/ethyl acetate (1260 ml/140 ml) and then petroleum ether/ethyl acetate (800 ml/610 ml) as eluents. Evaporation of solvents and drying *in vacuo* gave a white solid powder (17.8 g, 74.2%). TLC showed petroleum/EtOAc = 4 : 3, $R_f = 0.42$. Chemical shifts in ^{1}H-NMR (500 MHz, $CDCl_3$, ppm): 7.31 (s, 2H), 4.45 (t, 4H), 4.38 (t, 2H), 4.26 (m, 6H), 3.90 (s, 3H), 2.10 (s, 6H), 2.06 (s, 3H).

*3,4,5-Tris-(2-hydroxy-ethoxy)-benzoic acid methyl ester (**4**).* Compound **3** (19.6 g) and *p*-toluenesulfonic acid (1.28 g) were dissolved in dry methanol (160 ml). Under the protection of a $CaCl_2$ tube the solution was refluxed for 24 hr. Then it was cooled to room temperature. With stirring and cooling activated alkaline alumina (20 g) was added to adsorb *p*-toluenesulfonic acid. After stirring for a while the alumina was removed by filtration through a combined plug with a layer of fresh alkaline alumina (1.5 cm, top) and a layer of silica gel H (1.5 cm, bottom). The resulted clear light-yellow solution was evaporated to a white solid, which was then taken up by dry chloroform (70 ml) and stirred for 1 hr. Filtration and drying *in vacuo* gave a white fine powder (12.15 g, 86.7%). Chemical shifts in ^{1}H-NMR (500 MHz, $CDCl_3$, ppm) 7.30 (s, 2H), 4.13 (m, 6H), 3.89 (t, 4H), 3.83 (s, 3H), 3.76 (t, 2H).

*3,4,5-Tris-(2-bromo-ethoxy)-benzoic acid methyl ester (**5**).* Compound **4** (12.16 g, 38.4 mmol), Ph_3P (54.40 g, 207 mmol) were added to dry CH_2Cl_2 (380 ml) and stirred in an ice/water bath. CBr_4 (69.00 g, 208 mmol) was added in four portions over 1 hr. Ten minutes after addition of CBr_4 the ice/water bath was removed. After an additional 10 min the solution turned into a thick white slurry, which was stirred at room temperature for a further 3 hr. Then the slurry was filtered to give a light-brown clear solution. With some methanol (3.8 ml, 94 mmol) added the solution was stirred for 3 hr and evaporated at 1 atm until solids appeared. Then dry Et_2O (150 ml) was added slowly with stirring. The resulting suspension was filtered to remove solids and evaporated to dryness. The residue was again dissolved in Et_2O (120 ml) and filtered to remove solids. All the filtered solids were combined, extracted with Et_2O (150 ml) and removed by filtration. Both ethereal filtrates were combined and evaporated to a light-yellow solid, which was taken up in some CH_2Cl_2 (20 ml) and chromatographed on silica gel (360 g) with petroleum ether/EtOAc (3840 ml/960 ml) as eluent. Evaporation and drying *in vacuo* gave a white cotton-like solid (16.16 g, 83.3%). TLC shows petroleum/THF = 1 : 1, $R_f = 0.85$. Chemical shifts in ^{1}H-NMR (500 MHz, $CDCl_3$, ppm): 7.30 (s, 2H), 4.38 (m, 6H), 3.91 (s, 3H), 3.70 (m, 6H).

3Br-Ph-OH. Compound **5** (3.53 g, 6.99 mmol) and Ti(O^iPr)$_4$ (2.06 ml, 6.99 mmol) were added to 1,4-butanediol (60 ml) and stirred in a bath at 80°C for 24 hr. The mixture was then cooled and poured into dilute HCl (0.1 N, 350 ml) with stirring. The precipitated solids was collected by filtration, washed with fresh water and dissolved in Et_2O (30 ml). The solution was washed with dilute HCl (1 N), dilute aqueous $NaHCO_3$ and saturated brine. After drying over Na_2SO_4 and evaporation, the residue solid was chromatographed on silica gel (70 g) with petroleum ether/EtOAc (600 ml/600 ml) as eluent. Evaporation and drying *in vacuo* gave a white powder (2.86 g, 73%). Chemical shifts in ^{1}H-NMR (500 MHz, $CDCl_3$, ppm): 7.30 (s, 2H), 4.37 (m, 8H), 3.70 (m, 8H), 1.87 (m, 2H), 1.71 (m, 2H), 1.34 (m, 1H).

3,4-Bis-(2-bromo-ethoxy)-benzoic acid 4-hydroxy-butyl ester (2Br-Ph-OH)

3,4-Bis-(2-acetoxy-ethoxy)-benzoic acid methyl ester. This compound was synthesized using the same procedure as for **3**. But methyl 3,4-dihydroxybenzoate was used instead of methyl gallate and the product after flash chromatography was further recrystallized in Et_2O. The yield was 78.2%. TLC showed only one point.

3,4-Bis-(2-hydroxy-ethoxy)-benzoic acid methyl ester. This compound was synthesized using the same procedure as for **4**. But 3,4-bis-(2-acetoxy-ethoxy)-benzoic acid methyl ester was used instead of **3**. The product from evaporation of the filtrate was washed with dry Et_2O instead of dry chloroform. The yield was 93.2%.

3,4-Bis-(2-bromo-ethoxy)-benzoic acid methyl ester. This compound was synthesized using the same procedure as for **5**. But 3,4-bis-(2-hydroxy-ethoxy)-benzoic acid methyl ester was used instead of **4**. The eluent used in flash chromatography was petroleum ether/EtOAc (4.2 : 0.8) instead of petroleum ether/EtOAc (4 : 1). The yield was 89.5%.

2Br-Ph-OH. This compound was synthesized using the same procedure as for 3Br-Ph-OH. But 3,4-bis-(2-bromo-ethoxy)-benzoic acid methyl ester was used instead of **5**. The yield was 38.7%. Chemical shifts in ^{1}H-NMR (500 MHz, $CDCl_3$, ppm): 7.70 (m, 1H), 7.61 (s, 1H), 6.93 (d, 1H), 4.39 (t, 4H), 4.34 (t, 2H), 3.70 (m, 6H), 1.87 (m, 2H), 1.72 (m, 2H), 1.38 (m, 1H).

4-(2-Bromo-ethoxy)-benzoic acid 4-hydroxy-butyl ester (1Br-Ph-OH)

4-(2-Acetoxy-ethoxy)-benzoic acid methyl ester. This compound was synthesized using the same procedure as for **3**. But methyl 4-hydroxybenzoate was used instead of methyl gallate and the product after flash chromatography was further recrystallized in Et_2O. The eluent used in flash chromatography was petroleum ether/EtOAc (4.1 : 0.9) instead of two gradient eluents. The yield was 77.7%.

4-(2-Hydroxy-ethoxy)-benzoic acid methyl ester. This compound was synthesized using the same procedure as

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for **4**. But 4-(2-acetoxy-ethoxy)-benzoic acid methyl ester was used instead of **3**. The product from evaporation of the filtrate was directly dried *in vacuo* without being washed with chloroform or Et_2O. The yield was 96.6%.

4-(2-Bromo-ethoxy)-benzoic acid methyl ester. This compound was synthesized using the same procedure as for **5**. But 4-(2-hydroxy-ethoxy)-benzoic acid methyl ester was used instead of **4**. The eluent used in flash chromatography was petroleum ether/EtOAc (4.6 : 0.4) instead of petroleum ether/EtOAc (4 : 1). The yield was 93.6%.

1Br-Ph-OH. This compound was synthesized using the same procedure as for 3Br-Ph-OH. But 4-(2-bromo-ethoxy)-benzoic acid methyl ester was used instead of **5**. The eluent used in flash chromatography was petroleum ether/EtOAc (3 : 2) instead of petroleum ether/EtOAc (1 : 1). It took 2 days of standing in a vacuum desiccator for the product to solidify. The yield was 72.3%. Chemical shifts in ^{1}H-NMR (500 MHz, $CDCl_3$, ppm): 8.00 (d, 2H), 6.93 (d, 2H), 4.34 (m, 4H), 3.73 (t, 2H), 3.66 (t, 2H), 1.87 (m, 2H), 1.72 (m, 2H).

3,4,5-Tris-(2-trimethylammonio-ethoxy)-benzoic acid 4-[3,4,5-tris-(11-acryloyloxy- undecyloxy)-benzoyloxy]-butyl ester tribromide (3Acrylate-Ph-3Ammonium)

3,4,5-Tris-(2-bromo-ethoxy)-benzoic acid 4-[3,4,5-tris-(11-acryloyloxy-undecyloxy)-benzoyloxy]-butyl ester (3Acrylate-Ph-3Br). 3Acrylate-Ph-COOH (0.60 g, 0.71 mmol), 3Br-Ph-OH (0.42 g, 0.75 mmol) and DPTS (45 mg, 0.153 mmol) were dissolved in dry CH_2Cl_2 (6 ml) and stirred in an ice/water bath. DCC (0.22 g, 1.07 mmol) diluted in CH_2Cl_2, was added dropwise. The clear solution turned turbid in 2–3 min and was stirred at 20–30°C for 24 hr. Then the mixture was filtered and the clear filtrate was evaporated to dryness. The residue thick slurry was taken up in petroleum ether/EtOAc (4 ml/1 ml) and filtered to remove solids. The filtrate was evaporated to dryness and was chromatographed on silica gel (20 g) with petroleum ether/EtOAc (254 ml/76 ml) as eluent. Evaporation and drying *in vacuo* gave a wax-like solid (0.75 g, 76%). TLC shows petroleum/EtOAc = 3.5 : 1.5, $R_f = 0.48$. Chemical shifts in ^{1}H-NMR (500 MHz, $CDCl_3$, ppm): 7.28 (s, 2H), 7,23 (s, 2H), 6.39 (d, 3H), 6.12 (q, 3H), 5.80 (d, 3H), 4.39 (m, 10H), 4.15 (t, 6H), 4.00 (t, 6H), 3.68 (m, 6H), 1.93 (t, 4H), 1.80 (m, 4H), 1.73 (m, 2H), 1.66 (m, 6H), 1.46 (m, 6H), 1.38 (m, 36H).

3Acrylate-Ph-3Ammonium. 3Acrylate-Ph-3Br (1.00 g, 0.72 mmol), trimethylamine (33 wt% in alcohol, $d \approx 0.75$) (1.6 ml, 6.7 mmol), BHT (0.04 g), nitrobenzene (0.48 ml) and acetonitrile (22 ml) were charged into a sealed ball ampule and stirred at 50°C for 2 days. After filtration for removal of small amount of solids present, the reaction mixture was cooled at less than 20°C in a refrigerator for 3–4 hr and filtered at about −22°C (CCl_4/N_2(liquid) bath) in dry N_2 atmosphere. The solid was further recrystallized in dry acetonitrile three times (20 ml × 3). Lyophilization of the crystals lead to a white hygroscopic solid (0.66 g, 58.5%). Chemical shifts in ^{1}H-NMR (500 MHz, $CDCl_3$, ppm): 7.29 (d, 2H), 7.20 (d, 2H), 6.39 (d, 3H), 6.12 (q, 3H), 5.80 (d, 3H), 4.61 (m, 6H), 4.46 (t, 4H), 4.37 (t, 4H), 4.23 (t, 2H), 4.14 (t, 6H), 4.00 (t, 6H), 3.60 (s, 27H), 1.93 (m, 4H), 1.80 (m, 4H), 1.73 (m, 2H), 1.66 (m, 6H), 1.47 (m, 6H), 1.38 (m, 36H).

3,4,5-Tris-(2-trimethylammonio-ethoxy)-benzoic acid 4-[3,4-bis-(11-acryloyloxy-undecyloxy)-benzoyloxy]-butyl ester tribromide (2Acrylate-Ph-3Ammonium)

3,4,5-Tris-(2-bromo-ethoxy)-benzoic acid 4-[3,4-bis-(11-acryloyloxy-undecyloxy)- benzoyloxy]-butyl ester (2Acrylate-Ph-3Br). This compound was synthesized using the same procedure as for 3Acrylate-Ph-3Br.

2Acrylate-Ph-3Ammonium. This compound was synthesized using the same procedure as for 3Acrylate-Ph-3Ammonium except that the reaction mixture was filtered and evaporated to dryness before recrystallization. Lyophilization of the crystals lead to a white hygroscopic solid. The combined yield of both esterification and amination was about 61%. Chemical shifts in ^{1}H-NMR (500 MHz, DMSO-d_6, ppm): 7.56 (d, 1H), 7.41 (m, 3H), 7.05 (m, 1H), 6.31 (d, 2H), 6.16 (q, 2H), 5.93 (d, 2H), 4.57 (t, 4H), 4.38 (m, 4H), 4.32 (t, 2H), 4.07 (t, 4H), 4.02 (t, 2H), 3.97 (t, 2H), 3.91 (t, 4H), 3.82 (t, 2H), 3.25 (m, 27H), 1.86 (m, 4H), 1.71 (m, 4H), 1.58 (m, 4H), 1.43 (m, 4H), 1.28 (m, 24H).

3,4,5-Tris-(2-trimethylammonio-ethoxy)-benzoic acid 4-[4-(11-acryloyloxy- undecyloxy)-benzoyloxy]-butyl ester tribromide (1Acrylate-Ph-3Ammonium)

3,4,5-Tris-(2-bromo-ethoxy)-benzoic acid 4-[4-(11-acryloyloxy-undecyloxy)-benzoyloxy]-butyl ester (1Acrylate-Ph-3Br). This compound was synthesized using the same procedure as for 3Acrylate-Ph-3Br.

1Acrylate-Ph-3Ammonium. This compound was synthesized using the same procedure as for 3Acrylate-Ph-3Ammonium except that the reaction mixture was filtered and evaporated to dryness before recrystallization. Lyophilization of the crystals lead to a white hygroscopic solid. The combined yield of both esterification and amination was about 74%. Chemical shifts in ^{1}H-NMR (500 MHz, DMSO-d_6, ppm): 7.89 (d, 2H), 7.42 (s, 2H), 7.04 (d, 2H), 6.31 (d, 1H), 6.17 (q, 1H), 5.93 (d, 1H), 4.58 (t, 4H), 4.39 (t, 4H), 4.32 (t, 2H), 4.09 (t, 2H), 4.04 (t, 2H), 3.93 (t, 4H), 3.84 (t, 2H), 3.27 (m, 27H), 1.87 (m, 4H), 1.72 (m, 2H), 1.59 (m, 2H), 1.40 (m, 2H), 1.29 (m, 12H).

3,4-Bis-(2-trimethylammonio-ethoxy)-benzoic acid 4-[3,4,5-tris-(11-acryloyloxy-undecyloxy)-benzoyloxy]-butyl ester dibromide (3Acrylate-Ph-2Ammonium)

3,4-Bis-(2-bromo-ethoxy)-benzoic acid 4-[3,4,5-tris-(11-acryloyloxy-undecyloxy)-benzoyloxy]-butyl ester (3Acrylate-Ph-2Br). This compound was synthesized using the same procedure as for 3Acrylate-Ph-3Br. The yield was calculated in combination with the next step (amination). Chemical shifts in ^{1}H-NMR (500 MHz, $CDCl_3$, ppm): 7.69 (m, 1H), 7.60 (d, 1H), 7.24 (s, 2H), 6.93 (d, 1H), 6.39 (d, 3H), 6.12 (q, 3H), 5.80 (d, 3H), 4.39 (m, 8H), 4.15 (t, 6H), 4.00 (t, 6H), 3.68 (m, 4H), 1.93 (t, 4H), 1.80 (m, 4H), 1.73 (m, 2H), 1.66 (m, 6H), 1.47 (m, 6H), 1.38 (m, 36H).

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3Acrylate-Ph-2Ammonium. This compound was synthesized using the same procedure as for 3Acrylate-Ph-3Ammonium. Lyophilization of the crystals lead to a white hygroscopic solid. The combined yield of both esterification and amination was about 76%. Chemical shifts in ^{1}H-NMR (500 MHz, $CDCl_3$, ppm): 7.72 (d, 1H), 7.53 (s, 1H), 7.23 (s, 2H), 7.07 (d, 1H), 6.39 (d, 3H), 6.12 (q, 3H), 5.80 (d, 3H), 4.62 (t, 2H), 4.51 (t, 2H), 4.36 (m, 8H), 4.14 (t, 6H), 4.00 (t, 6H), 3.62 (s, 18H), 1.92 (m, 4H), 1.80 (m, 4H), 1.73 (m, 2H), 1.66 (m, 6H), 1.47 (m, 6H), 1.38 (m, 36H).

3,4-Bis-(2-trimethylammonio-ethoxy)-benzoic acid 4-[3,4-bis-(11-acryloyloxy-undecyloxy)-benzoyloxy]-butyl ester dibromide (2Acrylate-Ph-2Ammonium)

3,4-Bis-(2-bromo-ethoxy)-benzoic acid 4-[3,4-bis-(11-acryloyloxy-undecyloxy)-benzoyloxy]-butyl ester (2Acrylate-Ph-2Br). This compound was synthesized using the same procedure as for 3Acrylate-Ph-3Br. The yield was calculated in combination with the next (amination).

2Acrylate-Ph-2Ammonium. This compound was synthesized using the same procedure as for 3Acrylate-Ph-3Ammonium. Lyophilization of the crystals lead to a white hygroscopic solid. The combined yield of both esterification and amination was about 39%. Chemical shifts in ^{1}H-NMR (500 MHz, $CDCl_3$, ppm): 7.68 (d, 1H), 7.61 (d, 1H), 7.51 (s, 2H), 7.07 (d, 1H), 6.86 (d, 1H), 6.39 (d, 2H), 6.12 (q, 2H), 5.80 (d, 2H), 4.61 (t, 2H), 4.52 (t, 2H), 4.32 (m, 8H), 4.14 (t, 4H), 4.02 (t, 4H), 3.58 (s, 18H), 1.89 (m, 4H), 1.82 (m, 4H), 1.66 (m, 4H), 1.45 (m, 4H), 1.33 (m, 24H).

3,4-Bis-(2-trimethylammonio-ethoxy)-benzoic acid 4-[4-(11-acryloyloxy-undecyloxy)-benzoyloxy]-butyl ester dibromide (1Acrylate-Ph-2Ammonium)

3,4-Bis-(2-bromo-ethoxy)-benzoic acid 4-[4-(11-acryloyloxy-undecyloxy)-benzoyloxy]-butyl ester (1Acrylate-Ph-2Br). This compound was synthesized using the same procedure as for 3Acrylate-Ph-3Br. The yield was calculated in combination with the next step (amination).

1Acrylate-Ph-2Ammonium. This compound was synthesized using the same procedure as for 3Acrylate-Ph-3Ammonium. Lyophilization of the crystals lead to a white solid. The combined yield of both esterification and amination was about 82%. Chemical shifts in ^{1}H-NMR (500 MHz, DMSO-d_6, ppm): 7.89 (d, 2H), 7.78 (d, 1H), 7.59 (d, 1H), 7.22 (d, 1H), 7.03 (d, 2H), 6.31 (d, 1H), 6.17 (q, 1H), 5.93 (d, 1H), 4.54 (t, 4H), 4.32 (t, 4H), 4.08 (t, 2H), 4.04 (t, 2H), 3.84 (t, 4H), 3.22 (s, 18H), 1.85 (m, 4H), 1.72 (m, 2H), 1.59 (m, 2H), 1.41 (m, 2H), 1.28 (m, 12H).

4-(2-Trimethylammonio-ethoxy)-benzoic acid 4-[3,4,5-tris-(11-acryloyloxy-undecyloxy)-benzoyloxy]-butyl ester bromide (3Acrylate-Ph-1Ammonium)

4-(2-Bromo-ethoxy)-benzoic acid 4-[3,4,5-tris-(11-acryloyloxy-undecyloxy)-benzoyloxy]-butyl ester (3Acrylate-Ph-1Br). This compound was synthesized using the same procedure as for 3Acrylate-Ph-3Br. The yield was calculated in combination with the next step (amination).

3Acrylate-Ph-1Ammonium. This compound was synthesized using the same procedure as for 3Acrylate-Ph-3Ammonium. Lyophilization of the crystals lead to a white hygroscopic solid. The combined yield of both esterification and amination was about 39%. Chemical shifts in ^{1}H-NMR (500 MHz, $CDCl_3$, ppm): 8.03 (d, 2H), 7.24 (s, 2H), 6.94 (d, 2H), 6.39 (d, 3H), 6.12 (q, 3H), 5.82 (d, 3H), 4.58 (t, 2H), 4.44 (t, 2H), 4.38 (t, 4H), 4.14 (t, 6H), 4.00 (t, 6H), 3.58 (s, 9H), 1.93 (m, 4H), 1.80 (m, 4H), 1.73 (m, 2H), 1.66 (m, 6H), 1.47 (m, 6H), 1.38 (m, 36H).

4-(2-Trimethylammonio-ethoxy)-benzoic acid 4-[3,4-bis-(11-acryloyloxy- undecyloxy)-benzoyloxy]-butyl ester bromide (2Acrylate-Ph-1Ammonium)

4-(2-Bromo-ethoxy)-benzoic acid 4-[3,4-bis-(11-acryloyloxy-undecyloxy)-benzoyloxy]-butyl ester (2Acrylate-Ph-1Br). This compound was synthesized using the same procedure as for 3Acrylate-Ph-3Br. The yield was calculated in combination with the next step (amination).

2Acrylate-Ph-1Ammonium. This compound was synthesized using the same procedure as for 3Acrylate-Ph-3Ammonium. Lyophilization of the crystals lead to a white hygroscopic solid. The combined yield of both esterification and amination was about 33%. Chemical shifts in ^{1}H-NMR (500 MHz, $CDCl_3$, ppm): 8.03 (d, 2H), 7.63 (d, 1H), 7.53 (s, 1H), 6.96 (d, 2H), 6.86 (d, 1H), 6.39 (d, 2H), 6.12 (q, 2H), 5.82 (d, 2H), 4.58 (t, 2H), 4.38 (m, 6H), 4.14 (t, 4H), 4.04 (t, 4H), 3.61 (s, 9H), 1.93 (m, 4H), 1.83 (m, 4H), 1.66 (m, 4H), 1.47 (m, 4H), 1.32 (m, 24H).

4-(2-Trimethylammonio-ethoxy)-benzoic acid 4-[4-(11-acryloyloxy-undecyloxy)-benzoyloxy]-butyl ester bromide (1Acrylate-Ph-1Ammonium)

4-(2-Bromo-ethoxy)-benzoic acid 4-[4-(11-acryloyloxy-undecyloxy)-benzoyloxy]-butyl ester (1Acrylate-Ph-1Br). This compound was synthesized using the same procedure as for 3Acrylate-Ph-3Br. The yield was calculated in combination with the next step (amination).

1Acrylate-Ph-1Ammonium. This compound was synthesized using the same procedure as for 3Acrylate-Ph-3Ammonium. Lyophilization of the crystals lead to a white solid. The combined yield of both esterification and amination was about 72%. Chemical shifts in ^{1}H-NMR (500 MHz, $CDCl_3$, ppm): 8.03 (d, 2H, 7.98 (d, 2H), 6.96 (d, 2H), 6.90 (d, 2H), 6.39 (d, 1H), 6.12 (q, 1H), 5.82 (d, 1H), 4.59 (t, 2H), (t, 2H), 4.38 (m, 6H), 4.15 (t, 2H), 4.00 (t, 2H), 3.59 (s, 9H), 1.93 (m, 4H), 1.79 (m, 2H), 1.66 (m, 2H), 1.45 (m, 2H), 1.32 (m, 12H).

RESULTS AND DISCUSSION

The series of polymerizable amphiphiles with the CPP systematically varied is composed of nine members (Scheme 1) which are assembled from three hydrophobic modules and three hydrophilic modules. They can be arranged in a sequence according to the ratios of the number

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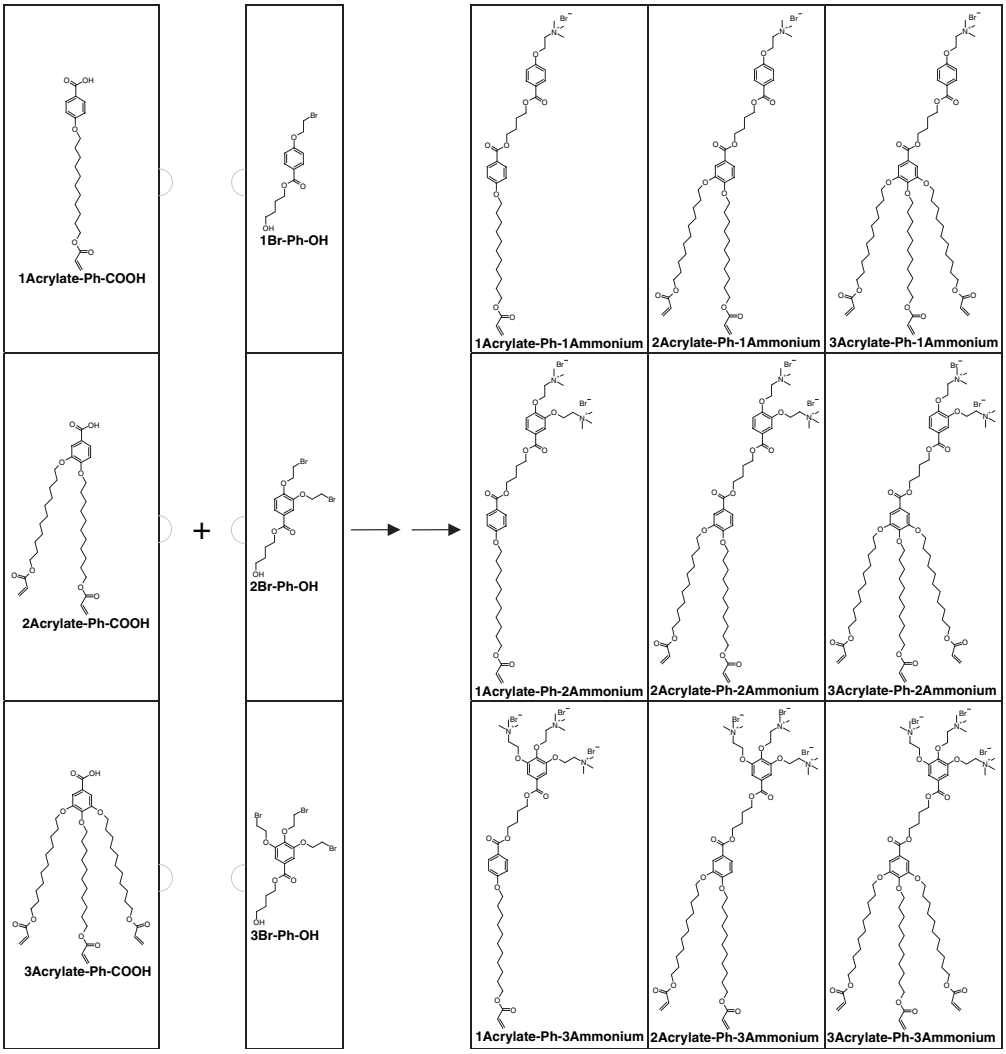


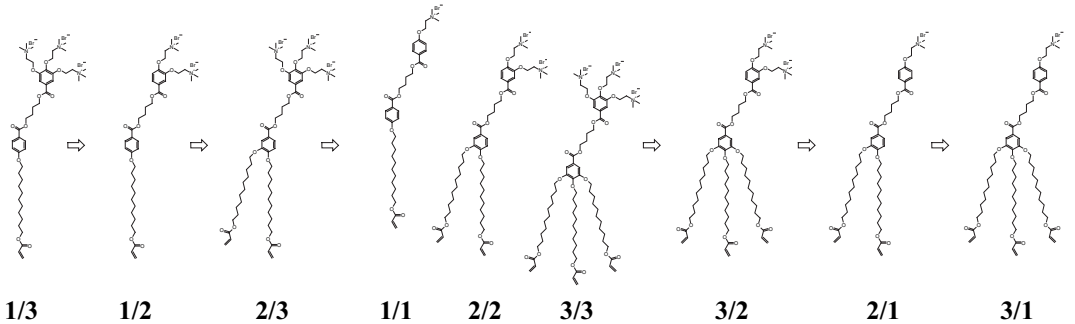
Scheme 1. Nine polymerizable amphiphiles assembled from three hydrophobic modules and three hydrophilic modules.

of ammonium head groups and the number of polymerizable tails as in Scheme 2. The head/tail number ratios could be viewed as approximate equivalents of the CPPs. The generic synthetic procedure is summarized in Scheme 3. The typical ^{1}H-NMR spectra of the polymerizable amphiphiles are shown in Fig. 1.

Molecular design

The molecular design of the polymerizable amphiphiles was based on three points:

(1) The hydrophobic part and the hydrophilic part are separated with a spacer. This makes it more practical to estimate the relative size of the two different parts. And the properties of the amphiphiles could be better predicted with the concept of CPP.
(2) The spacer between the hydrophobic part and the hydrophilic part is replacable. The properties of the polymerizable amphiphiles could be altered via inserting a special spacer group, e.g. a chromophore group, a stiff rod group, chiral group or a group promoting H-bonding formation.



Scheme 2. Nine polymerizable amphiphiles in a sequence from high to low head/tail number ratios.

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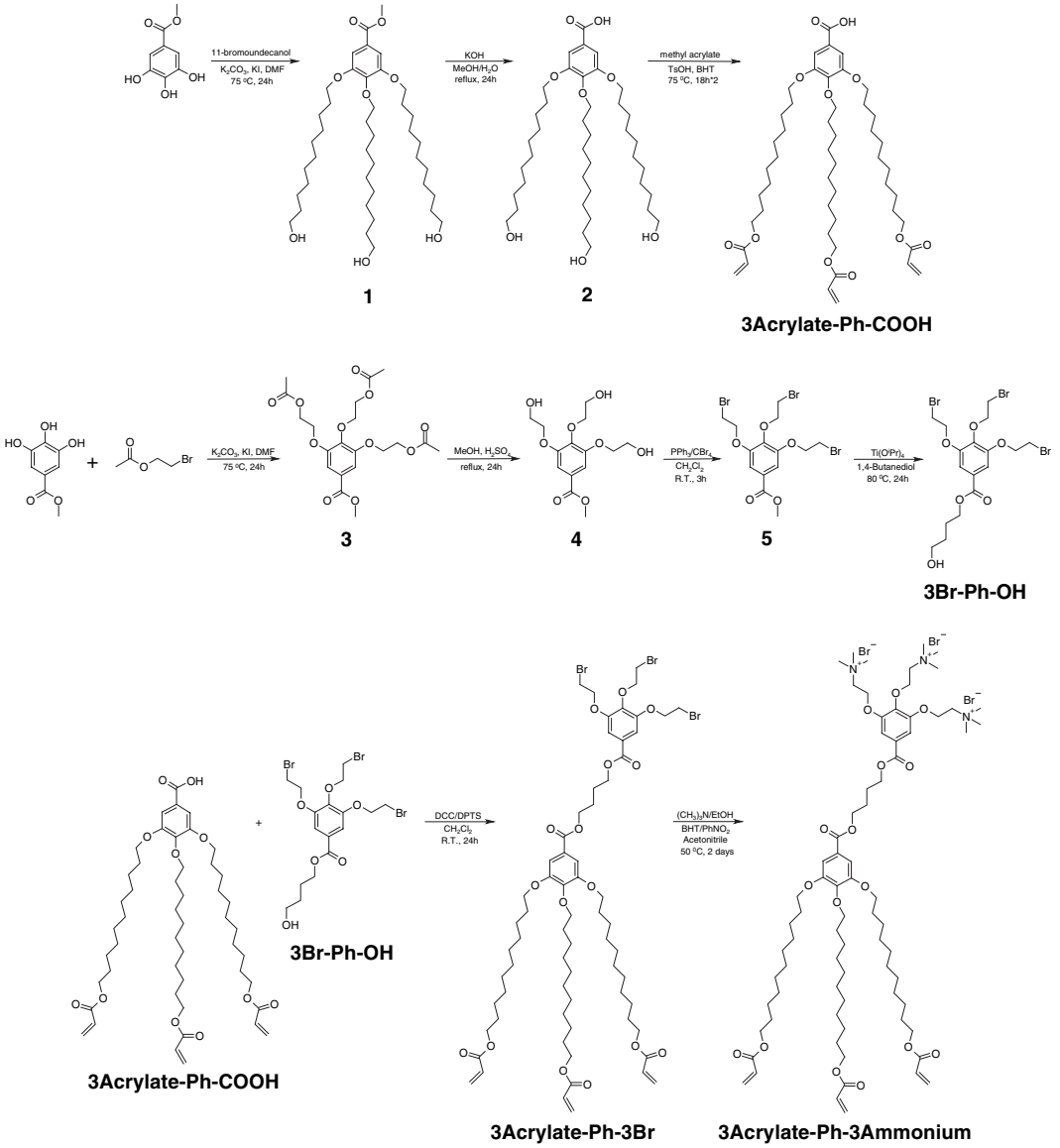

Scheme 3. The generic synthetic procedure of the polymerizable amphiphiles.

(3) The molecular scale of the amphiphiles could be enlarged via simplely replacing the aromatic connectors with larger ones. For example, methyl gallate (A in Scheme 4), a connector used in the current procedure, could be replaced with molecules B and C shown in Scheme 4. The resulting hierarchy molecular structures were common in dendrimer chemistry.

Synthesis

Two features of the synthetic procedure are noteworthy:

(1) Three steps of transesterification were used: one to remove the protecting acetyl group from **3**, one to connect the spacer group with the brominated module to assemble the hydrophilic part (3Br-Ph-OH), and the other one to acrylate the multi-hydroxy carboxylic acid (**2**). All of these transesterification steps, catalyzed by *p*-toluenesulfonic acid or titanium tetraisopropoxide [$Ti(O^i\ Pr)_4$], go smoothly under mild conditions with high yields. In the acrylation of the multi-hydroxy carboxylic acid (**2**), an acylation procedure with acryloyl chloride, suffered by the side reaction of forming anhydride, only lead to impure product with low yield. With the transesterification procedure the multi-hydroxy carboxylic acid was treated in methyl acrylate with *p*-toluenesulfonic acid as the catalyst. After chromatographic removal of the by-product (methyl ester, <10 wt%) formed by reaction of the acid group in the substrate, the product of high purity could be produced with a yield higher than 80%.

(2) All of the amphiphiles are purified with a general procedure of recrystallization at low temperature (ca. $-22^{\circ}C$) and in N_2 atmosphere. Most of the amphiphiles (Scheme 1), with one or more ammonium groups, are very hygroscopic. This complicated the purification process. The solution is based on a modified version (Figure 2) of the assembly introduced by the class guidebook.[11] The modified assembly is convenient for initial filtration and repetitive recrystallization. For most of the polymerizable amphiphiles the recrystallization procedure includes a step of recrystallization in the reaction mixture

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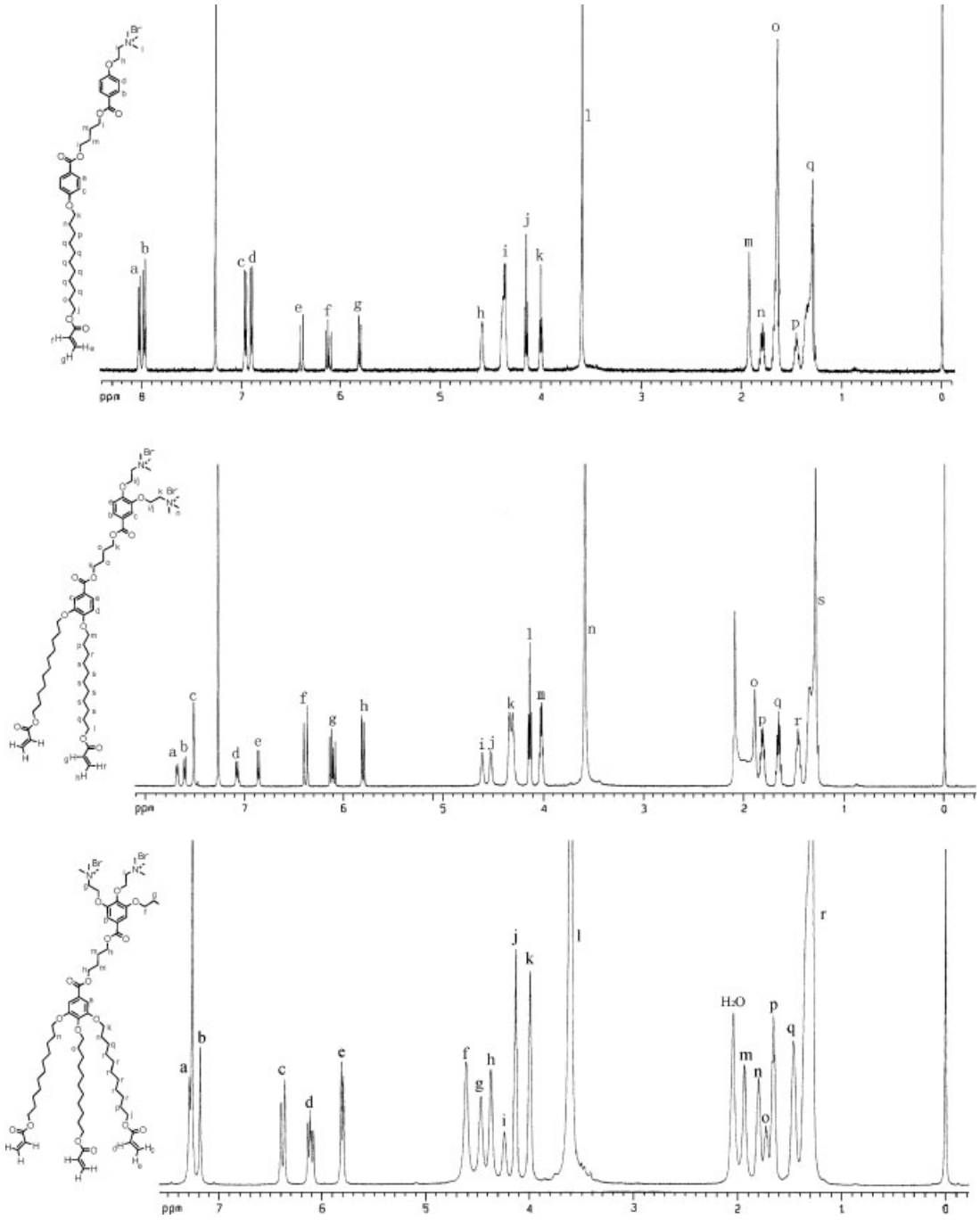
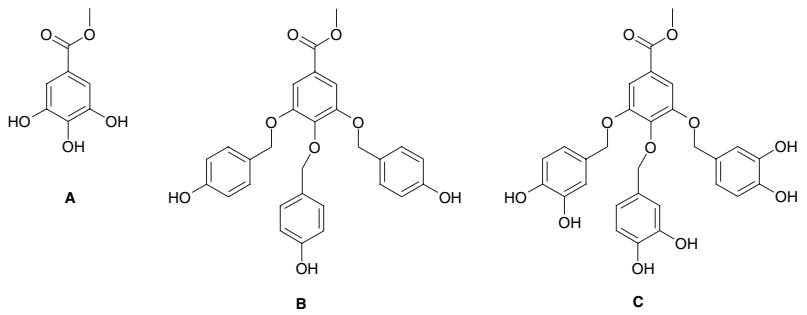


Figure 1. Typical ^{1}H-NMR spectra of the polymerizable amphiphiles.



Scheme 4. Replaceable structures of the aromatic connector in Scheme 3.

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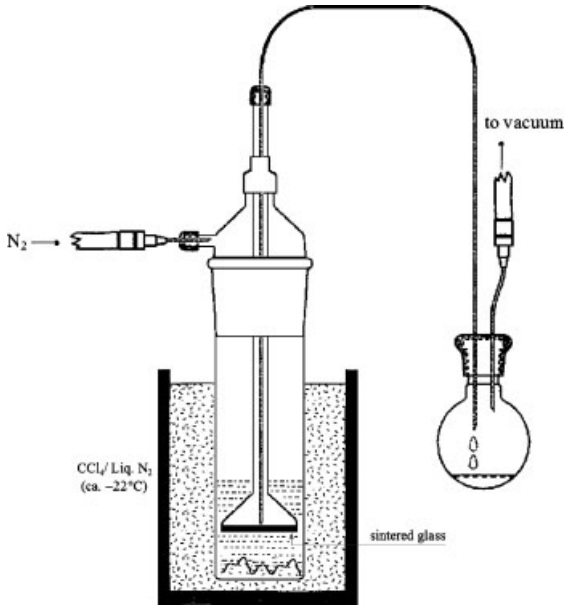

Figure 2. The general assembly for recrystallization of the polymerizable amphiphiles at low temperature and in nitrogen atmosphere.

and two to three steps of recrystallization in 20 times dry acetonitrile. But for some polymerizable amphiphiles (2Acrylate-Ph-3Ammonim and 1Acrylate-Ph-3Ammonium) the solubility is very sensitive to the presence of alcohol and then the reaction should be evaporated to dryness before recrystallization mixture. But for recrystallization steps with the product of low solubility the recrystallization mixture could be sonicated thoroughly and heat should not be applied to avoid occurrence of polymerization. One point is critical for smooth filtration: the recrystallization mixture should be cooled slowly in the refrigerator and then filtered in the CCl_4/N_2(liquid) bath. Sudden cooling in the cold bath often lead to a stiff cake impossible for filteration. Generally the combined yields for the last two steps (esterification and amination) of the procedure could be optimized to be higher than 70% with careful operation.

CONCLUSION

A group of nine polymerizable amphiphiles are designed, synthesized and characterized. Their CPPs are systematically varied. The synthetic procedures developed for them were optimized and could be extended to prepare polymerizable amphiphiles of larger scale. The work as a whole provides access to a new category of polymerizable amphiphiles with systematic structural variation, which are useful in manufacturing nanostructured polymeric materials via immobilization of surfactant phases.

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