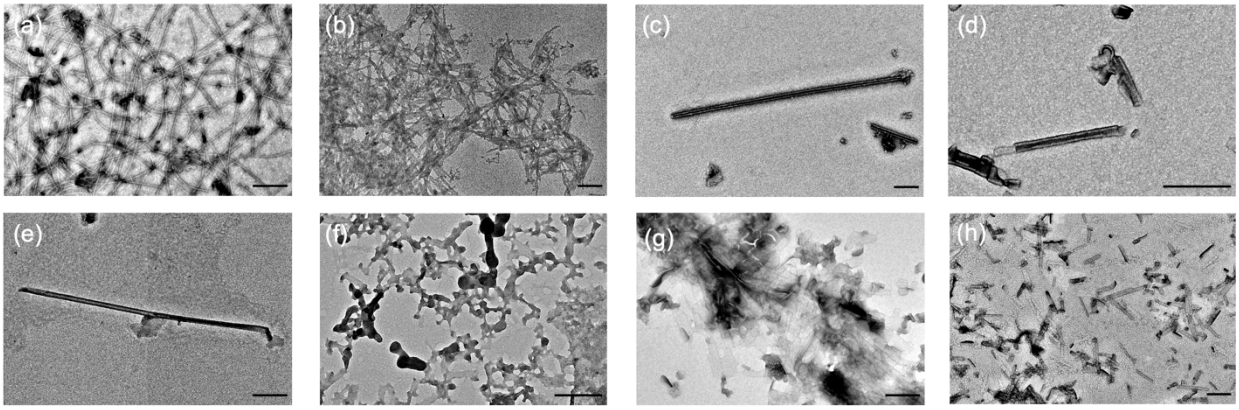
Supplementary Information

Effects of molecular flexibility and head group repulsion on aramid amphiphile self-assembly

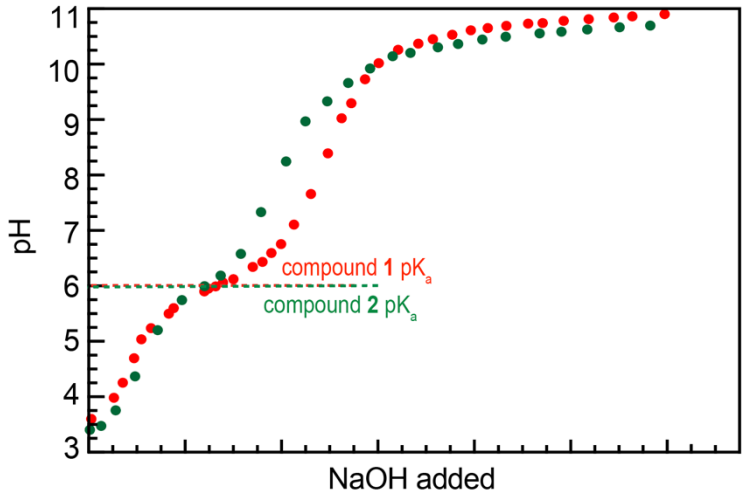
Samuel J. Kaser†, Andrew J. Lew†, Dae-Yoon Kim, Ty Christoff-Tempesta, Yukio Cho, and Julia H. Ortony

†These authors contributed equally to this work.

Supplementary Figures



Supplementary Figure 1 | TEM images of compounds **1-3** after sonication for 24 hours. Scale bars = 200 nm. (a) Compound **1**, pH 7; (b) Compound **1**, pH 11; (c) Compound **2**, pH 3; (d) Compound **2**, pH 7; (e) Compound **2**, pH 11; (f) Compound **3**, pH 3; (c) Compound **2**, pH 7; (c) Compound **2**, pH 11.

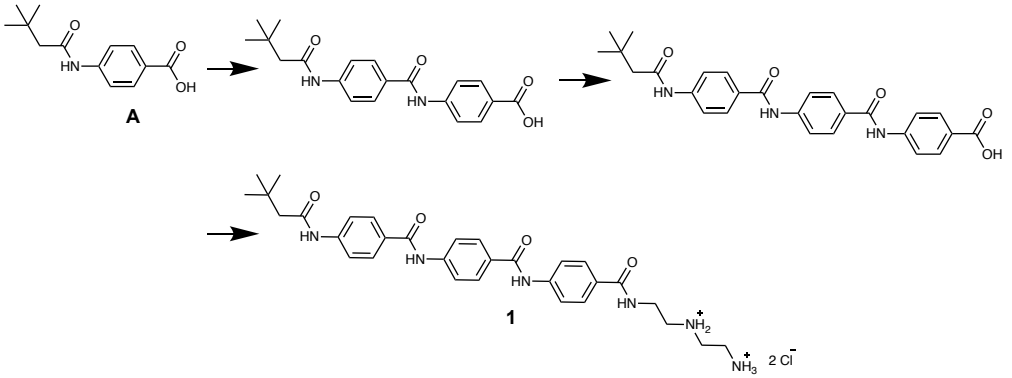


Supplementary Figure 2 | Replicate titrations of acidified suspensions of compounds **1** (red) and **2** (green).

Syntheses and Characterization

All reagents were purchased from MilliporeSigma and used without further purification. Solvents were purified before use. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance III DPX 400 in deuterated dimethyl sulfoxide (DMSO-d_6) at room temperature. Chemical shifts were quoted in parts per million (ppm) and referenced to tetramethylsilane (TMS).

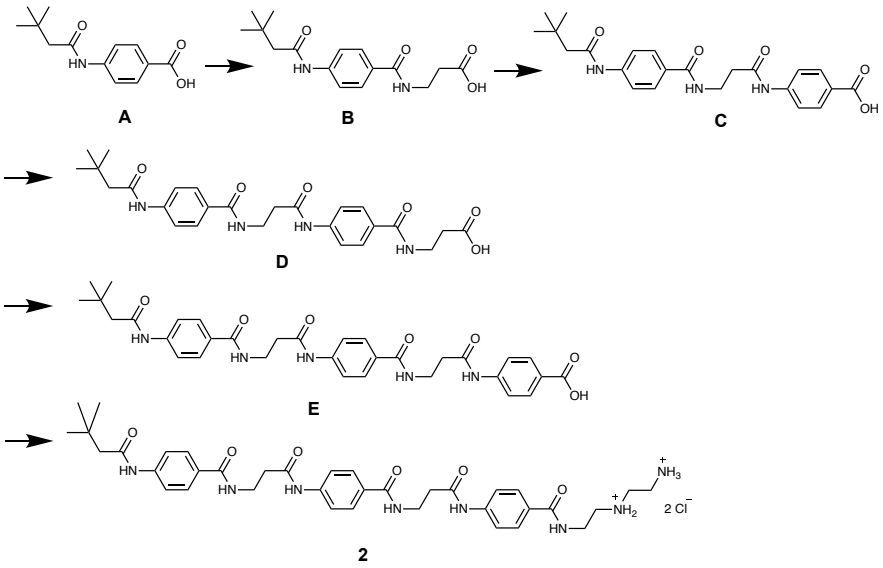
Compound 1



Scheme 1

An aramid amphiphile with a triaramid structural domain and cationic head group was synthesized as previously described (Scheme 1).[1] Briefly, a solution of 4-(4-(4-(3,3-dimethylbutanamido)benzamido)benzamido)benzoic acid (0.85 mmol), 1,4-bis-Boc-1,4,7-triazaheptane (BBT, 2.55 mmol), *N*-(3-(dimethylamino)propyl)-*N'*-ethylcarbodiimide hydrochloride (EDC, 2.55 mmol), and 4-dimethylaminopyridine (DMAP, 2.55 mmol) in dimethylformamide (DMF, 20 mL) was stirred at room temperature for 24 h. After reaction, the solvent was removed *in vacuo,* the remaining residue was washed with water and methanol several times, and the precipitate was captured by filtration. The solid product was stirred in dichloromethane/trifluoroacetic acid (DCM 25 mL/TFA 5mL) for 24 h. This solution was evaporated under reduced pressure and the off-white solid product was precipitated with 1M NaCl (aq). The precipitate was filtered, washed with water and then diethyl ether, and dried *in vacuo*. Yield: 65%. ^{1}H NMR (400 MHz, DMSO-*d6*): δ = 7.97 (m, 10H), 7.77 (d, 2H), 3.59 (m, 2H), 3.39 (m, 2H), 3.12 (m, 4H), 2.25 (s, 2H), 1.04 (s, 9H) ppm. ^{13}C NMR (400 MHz, DMSO-*d6*): δ = 171.1, 167.1, 165.6, 142.7, 129.1, 128.8, 128.5, 120.2, 119.4, 118.6, 50.1, 47.5, 44.5, 35.7, 31.4, 30.1 ppm.

Compound 2



Scheme 2

Synthesis of B. 4-(3,3-Dimethylbutanamido)benzoic acid (3.4 mmol), EDC (10.2 mmol), DMAP (10.2 mmol), and methyl 3-aminopropionate hydrochloride were dissolved in DMF (20 mL). The mixture was stirred at room temperature for 24 h. The solvent was removed *in vacuo* and the residue was washed with water and then $CHCl_3$ several times and captured by filtration. The resultant solid was refluxed in tetrahydrofuran/ethanol (THF 15 mL/EtOH 5 mL) and 10 M LiOH (aq) for 6 h. An off-white precipitate was obtained by addition of hydrochloric acid (HCl) solution (5 M), which was collected by filtration, purified with water, and dried under vacuum to afford the final product. Yield: 89%. ^{1}H NMR (400 MHz, DMSO-*d6*): δ = 7.77 (d, 2H), 7.67 (d, 2H), 3.45 (m, 2H), 2.45 (m, 2H), 2.22 (s, 2H), 1.03 (s, 9H) ppm.

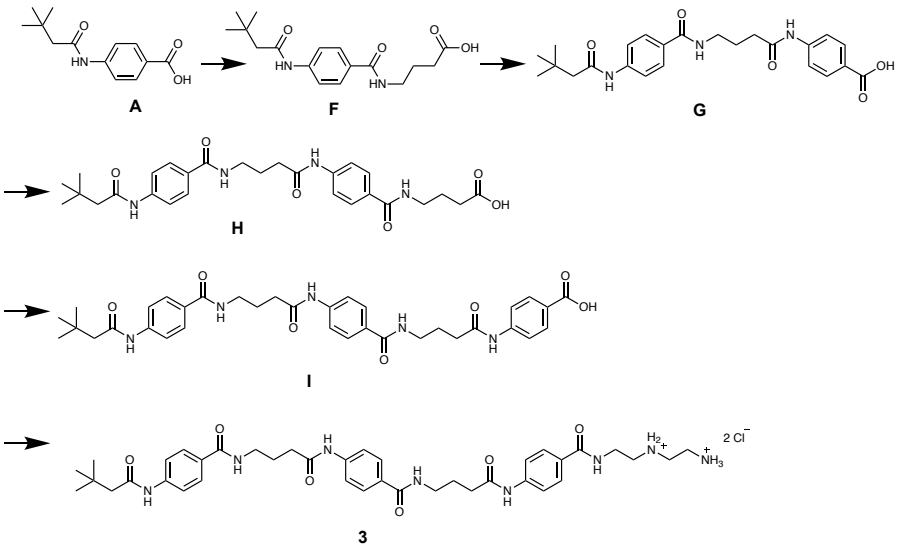
Synthesis of C. A solution of **B** (1.0 mmol), methyl 4-aminobenzoate (3.0 mmol), EDC (3.0 mmol), and DMAP (3.0 mmol) in DMF (20 mL) was stirred at room temperature for 24 h. After reaction, the solvent was removed *in vacuo* and the remaining residue was washed with water and acetonitrile several times, and the precipitate was obtained by filtration. The resultant solid was refluxed in THF/EtOH (15 mL/ 5 mL) and LiOH (aq) (10 M) for 12 h. An off-white precipitate was obtained by addition of HCl solution (5 M), which was collected by filtration, purified with water, and dried under vacuum to afford the final product. Yield: 91%. ^{1}H NMR (400 MHz, DMSO-*d6*): δ = 7.87 (d, 2H), 7.78 (d, 2H), 7.73 (d, 2H), 7.66 (d, 2H), 3.55 (m, 2H), 2.66 (m, 2H), 2.21 (s, 2H), 1.03 (s, 9H) ppm.

Synthesis of D. As in **B**, except with **C** replacing **A** as a starting material. Yield: 75%. ^{1}H NMR (400 MHz, DMSO-*d6*): δ = 7.78 (d, 4H), 7.66 (d, 4H), 3.56 (m, 2H), 3.43 (m, 2H), 2.65 (m, 2H), 2.48 (m, 2H), 2.21 (s, 2H), 1.04 (s, 9H) ppm.

Synthesis of E. As in **C**, except with **D** replacing **B** as a starting material. Yield: 86%. ^{1}H NMR (400 MHz, DMSO-*d6*): δ = 7.89 (d, 2H), 7.80 (d, 4H), 7.71 (d, 2H), 7.67 (d, 4H), 3.55 (m, 4H), 2.66 (m, 4H), 2.21 (s, 2H), 1.03 (s, 9H) ppm.

Synthesis of 2. A solution of E (0.4 mmol) was added to a solution of EDC (1.6 mmol) and DMAP (1.6 mmol) in DMF (15 mL). After stirring at room temperature for 30 min, bis-Boc-triazaheptane (0.8 mmol) was added and the solution was sonicated in an ultrasonic bath for 30 min. The mixture was then stirred for 24 h. After reaction, the solvent was removed *in vacuo*, the remaining residue was washed with water and then methanol three times. The precipitate was captured by filtration. The solid product was stirred in DCM/TFA (25 mL/5 mL) for 12 h. This solution was evaporated under reduced pressure and the product was precipitated with 1M NaCl (aq). The precipitate was filtered, washed with water and then diethyl ether, and dried *in vacuo* to yield an off-white powder. Yield: 72%. ^{1}H NMR (400 MHz, DMSO-*d6*): δ = 7.85 (d, 2H), 7.80 (d, 4H), 7.72 (d, 2H), 7.67 (d, 4H), 3.55 (m, 6H), 3.22 (m, 2H), 3.18 (m, 2H), 3.13 (m, 2H), 2.65 (m, 4H), 2.21 (s, 2H), 1.03 (s, 9H) ppm. ^{13}C NMR (400 MHz, DMSO-*d*): δ = 170.8, 170.4, 166.9, 166.3, 142.2, 129.2, 128.4, 118.7, 50.1, 47.4, 44.6, 36.9, 36.2, 35.7, 31.3, 30.1 ppm.

Compound 3



Scheme 3

Synthesis of F. As in **B**, except with methyl 4-aminobutyrate hydrochloride replacing methyl 3-aminopropionate hydrochloride. Yield: 84%. ^{1}H NMR (400 MHz, DMSO-*d6*): δ = 7.78 (d, 2H), 7.65 (d, 2H), 3.25 (m, 2H), 2.27 (m, 2H), 2.22 (s, 2H), 1.74 (m, 2H), 1.03 (s, 9H) ppm.

Synthesis of G. As in **C**, except with **F** replacing **B** as a starting material. Yield: 87%. ^{1}H NMR (400 MHz, DMSO-*d6*): δ = 7.89 (d, 2H), 7.81 (d, 2H), 7.72 (d, 2H), 7.67 (d, 2H), 3.29 (m, 2H), 2.42 (m, 2H), 2.22 (s, 2H), 1.85 (m, 2H), 1.03 (s, 9H) ppm.

Synthesis of H. As in **D**, except with **G** replacing **C** as a starting material. Yield: 71%. ^{1}H NMR (400 MHz, DMSO-*d6*): δ = 7.80 (d, 4H), 7.67 (d, 4H), 3.27 (m, 4H), 2.40 (m, 2H), 2.27 (m, 2H), 2.22 (s, 2H), 1.85 (m, 2H), 1.76 (m, 2H), 1.03 (s, 9H) ppm.

Synthesis of I. As in **E**, except with **H** replacing **D** as a starting material. Yield: 82%. ^{1}H NMR (400 MHz, DMSO-*d6*): δ = 7.87 (d, 2H), 7.81 (d, 4H), 7.72 (d, 2H), 7.67 (d, 4H), 3.28 (m, 4H), 2.41 (m, 4H), 2.22 (s, 2H), 1.87 (m, 4H) 1.03 (s, 9H) ppm.

Synthesis of 3. As in **2**, except with **I** replacing **E** as a starting material. Product is an off-white powder. Yield: 69%. ^{1}H NMR (400 MHz, DMSO-*d6*): δ = 7.85 (d, 2H), 7.79 (d, 4H), 7.71 (d, 2H), 7.67 (d, 4H), 3.54 (m, 2H), 3.28 (m, 4H), 3.20 (m, 2H), 3.17 (m, 2H), 3.09 (m, 2H), 2.41 (m, 4H), 2.22 (s, 2H), 1.85 (m, 4H) 1.03 (s, 9H) ppm. ^{13}C NMR (400 MHz, DMSO-*d*): δ = 171.9, 170.8, 166.7, 166.2, 142.2, 129.3, 128.4, 118.7, 50.1, 47.1, 44.6, 36.3, 35.7, 34.4, 31.3, 30.1, 25.5 ppm.