Electronic Supplementary Material (ESI) for Chemical Communications

Supramolecular Control of Self-Assembling Terthiophene-Peptide Amphiphiles Through the Amino Acid Side Chain

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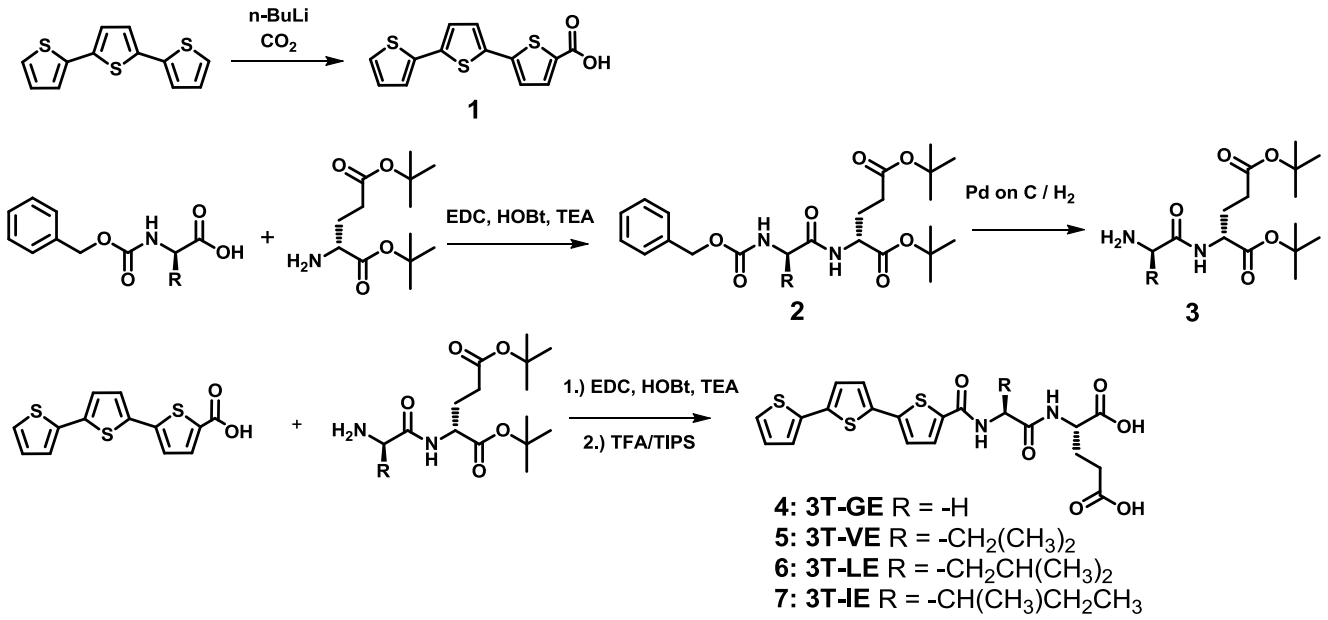
Supporting Information (SI)

Experimental

General. Unless otherwise noted, all reagents were purchased from TCI Chemical, Sigma-Aldrich, and Novabiochem. Mass Spectrometry was obtained using an Agilent 6520 quadrupole time-of-flight (Q-TOF) LC/MS or a Bruker Apex III Matrix-Assisted Laser Desorption Ionization Time-of-Flight mass spectrometer (MALDI-TOF MS), using α-Cyano-4-hydroxycinnamic acid as the matrix. ^{1}H and ^{13}C NMR were recorded on a Varian Inova (500 MHz) or a Bruker AVANCE III (500 MHz, direct cryoprobe) spectrometer, using the residual solvent proton signal as a standard. ^{13}C NMR was recorded at 125 MHz. Reverse-phase high performance liquid chromatography (RP-HPLC) was performed on a Varian ProStar210 Preparative HPLC. Samples for vitreous ice cryo-transmission electron microscopy (cryo-TEM) were prepared by pipetting 8 µL of 0.2 % (w/v) assembled solution onto a plasma cleaned holey carbon TEM grid (Electron Microscopy Sciences), blotted and plunged into liquid ethane using a FEI Vitrobot Mark IV. Samples were kept at -180°C and imaged using a JEOL 1230 TEM. Circular dichroism was performed on a JASCO J-815 instrument using quartz cuvettes with a path length of 0.05 mm. UV-Visible absorption was performed using a Lambda 1050 spectrophotometer and quartz cuvettes with a path length of 0.05 mm. Fourier Transform Infrared Spectroscopy (FT-IR) spectra were recorded in transmission mode using a Thermo Nicolet Nexus 870 spectrometer. Samples were prepared by drop-casting 10 µL of 0.2 % (w/v) assembled solution on to a ZnSe single crystal, and allowed to dry in air into a film. Small angle X-ray scattering (SAXS) was recorded of 0.2 % (w/v) assembled solution in quartz capillaries at the Advanced Photon Source at Argonne National Laboratory, on beamline 5-ID-D.

Synthesis. Unless otherwise noted, all terthiophene-dipeptide derivatives were synthesized via the same general route, described below and shown in Scheme 1.



Scheme S1. Synthesis of terthiophene-dipeptide derivatives.

2,2':5',2"-Terthiophene-5-carboxylic acid (1). 2,2':5',2"-Terthiophene (α-Terthiophene) (0.500 g, 2 mmol) was added to an oven-dried flask degassing under N_2 flow. 25 mL of anhydrous THF was added to the flask via syringe, and the flask was cooled to -78°C in a dry ice/acetone bath. n-Butyllithium (Sigma Aldrich, 2.5 M in hexanes, 0.8 mL) was added dropwise to the flask and the solution was stirred at -78°C for 1 hour. An excess of crushed dry ice was added to the flask and the reaction was left to stir overnight under N_2 flow, while slowly warming to room temperature. The solution was then acidified with 1 M HCl (aq), and the THF was removed by rotary evaporation to afford a yellow precipitate, which was filtered, washed with 1 M HCl, and dried to afford the desired product without further purification (0.562 g, 94%). ^{1}H NMR (500 MHz, d_6-DMSO) δ 13.26 (s, 1H), 7.68 (d, *J*=3.95 Hz, 1H), 7.59 (dd, *J*=0.98 Hz, *J*=5.07 Hz, 1H), 7.48 (d, *J*=3.85 Hz, 1H), 7.40 (d, *J*=3.90 Hz, 1H), 7.34 (d, *J*=3.85 Hz, 1H), 7.13 (dd, *J*=3.65 Hz, *J*=5.05 Hz, 1H); MALDI-MS (m/z): calcd 291.97, found $[M + Na]^+$ 315.666

***N*-Carboxybenzyl-Gly-(L)-Glu(O*t*Bu)-O*t*Bu.** *N*-Carboxybenzyl-Gly carboxylic acid (0.348 g, 1.31 mmol), NH_2-(**L**)-Glu(O*t*Bu)-O*t*Bu (0.300 g, 1.01 mmol), 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDC) (0.222 g, 1.31 mmol), 1-hydroxybenzotriazole (HOBt) (0.201 g, 1.31 mmol), and triethylamine (TEA)

(0.183 mL, 1.31 mmol) were added to a flask and dissolved in 20 mL of dichloromethane. The reaction was allowed to stir overnight at room temperature. The reaction was diluted in dichloromethane, and washed three times with 10% $NaHCO_{3\ (aq)}$, and then washed three times with 5% citric acid $_{(aq)}$. The organic layer was dried over Na_2SO_4, and the solvent was removed by rotary evaporation. The product was purified by flash chromatography (silica gel, 5% methanol in dichloromethane) to afford a clear, colorless oil (0.460 g, 90 %). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35-7.29 (m, 5H), 6.77 (d, *J*=6.55, 1H), 5.53 (s, 1H), 5.12 (s, 2H), 4.48 (td, 1H), 3.90 (s, 2H),2.34-2.20 (m, 2H), 2.14-2.07 (m, 1H), 1.94-1.87 (m, 1H), 1.45 (s, 9H), 1.42 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.35, 170.90, 168.76, 156.55, 136.23, 128.64, 128.31, 128.22, 82.66, 80.96, 67.28, 52.36, 44.48, 31.49, 28.14, 28.06, 27.60 MALDI-MS (m/z): calcd 450.24, found $[M + Na]^+$ 472.839

NH_2-Gly-(L)-Glu(O*t*Bu)-O*t*Bu. *N*-Carboxybenzyl-Gly-(L)-Glu(O*t*Bu)-O*t*Bu (2) (0.460 g, 0.91 mmol) was dissolved in 75:25 dichloromethane : methanol (10 mL). Sufficient Pd on C catalyst was added to the flask so as to provide 10 weight % catalytic loading. The flask was quickly evacuated three times to remove the air, and then placed under a hydrogen atmosphere, and allowed to stir overnight at room temperature. The reaction mixture was diluted in dichloromethane, filtered over Celite, and then washed three times with 10% $NaHCO_{3\ (aq)}$. The solvent was removed by rotary evaporation to afford the product as a clear, colorless oil (0.271 g, 80%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (d, *J*=8.25, 1H), 4.52 (td, *J*=8.29, *J*=4.90, 1H), 3.37 (s, 2H), 2.37-2.21 (m, 2H), 2.19-2.10 (m, 1H), 1.97-1.88 (m, 1H), 1.47 (s, 9H), 1.44 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.82, 172.17, 171.25, 82.32, 80.71, 53.55, 51.73, 44.81, 31.66, 28.14, 28.06 MALDI-MS (m/z): calcd 316.2, found $[M + Na]^+$ 338.759

2,2':5',2"-Terthiophene-5-Gly-(L)-Glu(O*t*Bu)-O*t*Bu. 2,2':5',2"-Terthiophene-5-carboxylic acid (1) (0.117 g, 0.4 mmol), NH_2-Gly-(L)-Glu(O*t*Bu)-O*t*Bu (3) (0.112 g, 0.3 mmol), EDC (0.070 g, 0.4 mmol), HOBt (0.061 g, 0.4 mmol), and TEA (0.056 mL, 0. 4 mmol) were added to a flask and dissolved in 10 mL of N, N-dimethylformamide. The reaction was allowed to stir overnight at room temperature. The solvent was removed by rotary evaporation, and the resulting crude product was dissolved in dichloromethane, washed three times with 10% $NaHCO_{3\ (aq)}$, and then washed three times with 5% citric acid $_{(aq)}$. The organic layer was dried over Na_2SO_4, and the solvent was removed by rotary evaporation. The crude product was purified by flash chromatography (silica gel, 2.5% methanol in dichloromethane) to afford the product as a yellow solid (0.175 g, 90%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 (d, *J*=3.85, 1H), 7.24 (dd, *J*=5.07, *J*=0.725, 1H), 7.18 (d, *J*=2.65, 1H), 7.14 (d, *J*=3.75, 1H), 7.09 (d, *J*=3.85, 1H), 7.08 (d, *J*=3.75, 1H), 7.02 (dd, *J*=4.87, *J*=3.72, 1H), 6.90 (t, *J*=2.27, 1H), 6.84 (d, *J*=7.45, 1H), 4.50 (td, 1H), 4.15 (dd, *J*=4.57,

J=3.07, 2H), 2.38-2.25 (m, 2H), 2.18-2.11 (m, 1H), 1.99-1.92 (m, 1H), 1.47 (s, 9H), 1.43 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.45, 170.62, 168.25, 161.62, 142.16, 137.80, 136.71, 135.97, 134.94, 129.28, 128.01, 125.73, 125.01, 124.51, 124.18, 123.73, 82.70, 81.06, 52.63, 43.16, 31.46, 28.06, 28.00, 27.28 MALDI-MS (m/z): calcd 590.2, found $[M + Na]^+$ 613.060

2,2':5',2"-Terthiophene-5-Gly-(L)-Glu(OH)-OH (4). 2,2':5',2"-Terthiophene-5-Gly-(L)-Glu(O*t*Bu)-O*t*Bu was dissolved in the following solvent mixture: 77.5:20:2.5 dichloromethane: trifluoroacetic acid (TFA): triisopropylsilane (TIPS) and allowed to react at room temperature for six hours. The solvent was removed by rotary evaporation, and the crude product was purified by reverse phase high-pressure liquid chromatography (RP-HPLC) in 0.1% $NH_4OH_{(aq)}$ and methanol. ^{1}H NMR (500 MHz, D_2O) δ 7.50 (d, J=3.90 Hz, 1H), 7.36 (d, J=4.90 Hz, 1H), 7.23 (d, J=3.15 Hz, 1H), 7.20 (d, J=3.80 Hz, 1H), 7.13 (dd, J=6.10 Hz, J=4.00 Hz, 2H), 7.05 (dd, J=4.80 Hz, J=3.80 Hz, 1H), 4.14 (dd, J=8.78 Hz, J=4.53 Hz, 1H), 3.98 (d, J=2.90 Hz, 2H), 2.20-2.17 (m, 2H), 2.07-2.00 (m, 1H), 1.89-1.81 (m, 1H) ^{13}C NMR (125 MHz, D_2O) δ 181.83, 178.50, 170.59, 164.05, 142.32, 137.38, 136.23, 134.35, 134.18, 130.84, 128.23, 126.19, 125.38, 124.51, 124.20, 55.04, 42.62, 33.69, 28.30 MS-ESI (m/z): calcd 478.03, found $[M^+]$ 478.036

2,2':5',2"-Terthiophene-5-(L)-Val-OMe (3) To a round-bottom flask containing 2,2':5',2"-terthiophene-5-carboxylic acid (1, 0.70 g, 2.40 mmol) in DMF (20 mL) was added EDC (0.69 g, 3.60 mmol), HOBt (0.49 g, 3.60 mmol), and triethylamine (1.5 mL). (L)-Valine methyl ester hydrochloride (0.60 g, 3.60 mmol) was added into the solution after 2 minutes. The reaction mixture was stirred for 12 h at room temperature before removing DMF using rotary evaporator at 65 °C. The resultant solid was redissolved in dichloromethane followed by extraction with saturated $NaHCO_{3(aq)}$ × 2 and water × 1. The organic layer was dried over anhydrous $MgSO_4$ and evaporated to dryness under reduced pressure. The crude product was purified by column chromatography on silica gel using dichloromethane and dichloromethane/methanol (v/v 99/1, 98/2) as eluent to afford compound 3 as a yellow solid in 99% yield (0.96 g, 2.40 mmol). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.48 (d, J = 4.0 Hz, 1H), 7.26 (dd, J = 5.0 Hz, 1.0 Hz, 1H), 7.21 (dd, J = 3.5 Hz, 1.0 Hz, 1H), 7.18 (d, J = 4.0 Hz, 1H), 7.14 (d, J = 4.0 Hz, 1H), 7.11 (d, J = 4.0 Hz, 1H), 7.05 (dd, J = 5.0 Hz, 4.0 Hz, 1H), 6.46 (d, J = 8.5 Hz, -NH, 1H), 4.76 (dd, J = 8.5 Hz, 5.0 Hz, -NHCHC(O)O, 1H), 3.80 (s, -OMe, 3H), 2.28 (m, -CHCHMe$_2$, 1H), 1.03 (d, J = 7.0 Hz, 3H), 1.00 (d, J = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 172.54, 161.35, 142.04, 137.80, 136.70, 136.26, 134.93, 129.12,

127.98, 125.70, 125.05, 124.15, 123.90, 123.67, 57.39, 52.33, 31.70, 18.99, 17.95. HRMS-ESI (m / z): $[M + H]^+$ calcd for $C_{19}H_{19}NO_3S_3$, 406.0605; found, 406.0604.

2,2':5',2"-Terthiophene-5-(L)-Val-OH (4) To a flask containing 2,2':5',2"-Terthiophene-5-Val-OMe (3, 0.80 g, 1.97 mmol) in a mixed solvent of THF (40 mL) and methanol (20 mL) was added 1N $NaOH_{(aq)}$ solution (15 mL) slowly. The reaction was stirred for 2 h and checked by TLC regularly. After the starting material was depleted, 1N $HCl_{(aq)}$ solution was slowly titrated into the solution and monitored by pH paper until acidic. THF and methanol was evaporated by rotary evaporator under reduced pressure. The residue was redissolved in dichloromethane followed by extraction with water × 3. The organic layer was collected, dried over anhydrous $MgSO_4$, and evaporated to dryness under reduced pressure to afford compound 4 in 97% yield (0.75 g, 1.92 mmol). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.49 (d, J = 4.0 Hz, 1H), 7.24 (d, J = 4.5 Hz, 1H), 7.19 (d, J = 3.0 Hz, 1H), 7.16 (d, J = 3.5 Hz, 1H), 7.12 (d, J = 4.0 Hz, 1H), 7.09 (d, J = 4.0 Hz, 1H), 7.03 (dd, J = 4.5 Hz, 4.0 Hz, 1H), 6.73 (d, J = 8.5 Hz, -NH, 1H), 4.68 (m, -NHCHC(O)O, 1H), 2.30 (m, $-CHCHMe_2$, 1H), 1.03 (d, J = 7.0 Hz, 3H), 1.01 (d, J = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.90, 161.82, 142.13, 137.83, 136.72, 136.27, 134.90, 129.30, 128.02, 125.75, 125.08, 124.52, 124.18, 123.76, 57.48, 31.45, 19.08, 17.84. HRMS-ESI (m / z): $[M + H]^+$ calcd for $C_{18}H_{17}NO_3S_3$, 392.0443; found, 392.0447.

2,2':5',2"-Terthiophene-5-(L)-Val-(L)-Glu(O*t*Bu)-O*t*Bu (5). To a flask containing 2,2':5',2"-Terthiophene-5-Val-OH (4, 0.45 g, 1.15 mmol) in a mixed solvent of DMF (15 mL) and dichloromethane (5 mL) was added EDC (0.37 g, 1.93 mmol), HOBt (0.26 g, 1.93 mmol), and triethylamine (0.6 mL). l-Glutamic acid di-t-butyl ester hydrochloride (0.51 g, 1.72 mmol) was added into the solution after 2 minutes. The reaction mixture was stirred for 12 h at room temperature before removing DMF under reduced pressure at 65 °C. The resultant solid was redissolved in dichloromethane followed by extraction with saturated $NaHCO_{3(aq)}$ × 2 and water × 1. The organic layer was dried over anhydrous $MgSO_4$ and evaporated to dryness under reduced pressure. The crude product was purified by column chromatography on silica gel using dichloromethane and dichloromethane/methanol (v/v 99/1, 98/2, 95/5) as eluent to afford compound 5 as a yellow solid in 93% yield (0.68 g, 1.07 mmol). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.52 (d, J = 4.5 Hz, 1H), 7.23 (m, 1H), 7.17 (m, 1H), 7.13 (m, 1H), 7.08 (m, 2H), 7.01 (m, 1H), 4.54 (m, 1H), 4.48 (m, 1H), 2.32 (m, 2H), 2.22 (m, 1H), 2.13 (m, 1H), 1.97 (m, 1H), 1.48 (s, 6H), 1.44 (s, 6H), 1.41 (s, 6H), 1.02 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.18, 170.62, 162.55, 161.49, 141.82, 137.57, 136.90, 136.72, 135.13, 129.05, 127.97, 125.53, 124.90, 124.44, 124.06, 123.73, 82.07, 80.71, 58.73, 53.49, 31.45, 31.41, 28.03, 27.09, 19.26, 18.43. HRMS-ESI (m / z): $[M + H]^+$ calcd for $C_{31}H_{40}N_2O_6S_3$, 633.2121; found, 633.2142.

2,2':5',2"-Terthiophene-5-(L)-Val-(L)-Glu(OH)-OH (3T-VE). To a flask containing 2,2':5',2"-Terthiophene-5-Val-Glu(O^{t}Bu)-O^{t}Bu (5, 0.53 g, 0.84 mmol) in a mixed solvent of dichloromethane (29 mL) and triisopropylsilane (1 mL) was added trifluoroacetic acid (10 mL, 25 % v/v) slowly. The deprotection reaction was stirred for 3 h while monitoring by TLC. After starting materials were depleted, solvent was removed by rotary evaporator with a base trap. The crude material was purified by preparation HPLC. ^{1}H NMR (500 MHz, CD_3OD): δ 7.70 (d, J = 4.5 Hz, 1H), 7.35 (d, J = 4.5 Hz, 1H), 7.23-7.20 (m, 3H), 7.13 (m, 1H), 7.04 (dd, J = 7.5 Hz, 3.5 Hz, 1H), 4.53 (m, 1H), 4.37 (m, 1H), 2.48 (m, 2H), 2.22 (m, 2H), 2.01 (m, 1H), 1.06 (m, 6H). ^{1}H NMR (125 MHz, CD_3OD): δ 174.53, 174.01, 163.90, 159.14, 143.39, 139.05, 137.95, 137.77, 136.19, 131.04, 129.14, 126.93, 126.21, 125.60, 125.30, 125.13, 61.06, 55.19, 31.92, 31.07, 27.80, 19.82, 19.06. HRMS-ESI (m / z): $[M + H]^+$ calcd for $C_{23}H_{24}N_2O_6S_3$, 521.0875; found, 521.0877.

***N*-Carboxybenzyl-(L)-Leu-(L)-Glu(O*t*Bu)-O*t*Bu.** *N*-Carboxybenzyl-(L)-Leu carboxylic acid (0.348 g, 1.31 mmol), NH_2-(L)-Glu(O*t*Bu)-O*t*Bu (0.300 g, 1.01 mmol), 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDC) (0.222 g, 1.31 mmol), 1-hydroxybenzotriazole (HOBt) (0.201 g, 1.31 mmol), and triethylamine (TEA) (0.183 mL, 1.31 mmol) were added to a flask and dissolved in 20 mL of dichloromethane. The reaction was allowed to stir overnight at room temperature. The reaction was diluted in dichloromethane, and washed three times with 10% $NaHCO_{3\ (aq)}$, and then washed three times with 5% citric acid $_{(aq)}$. The organic layer was dried over Na_2SO_4, and the solvent was removed by rotary evaporation. The product was purified by flash chromatography (silica gel, 5% methanol in dichloromethane) to afford a clear, colorless oil (0.520 g, 97%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35-7.29 (m,5H), 6.63 (d, *J*=7.55, 1H), 5.20 (d, *J*=8.20, 1H), 5.11 (s, 2H), 4.44 (td, 1H), 4.21 (td, 1H), 2.35-2.21 (m, 2H), 2.15-2.08 (m, 1H), 1.95-1.87 (m, 1H), 1.72-1.59 (m, 2H), 1.54-1.49 (m, 1H), 1.46 (s, 9H), 1.43 (s, 9H), 0.94 (t, *J*=5.95, 6H) ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.55, 172.07, 170.80, 156.26, 136.37, 128.69, 128.33, 128.22, 82.53, 81.01, 67.19, 53.60, 52.51, 42.05, 31.54, 28.22, 28.14, 27.55, 24.78, 23.13, 22.10 MALDI-MS calcd 506.30, found 505.83

NH_2-(L)-Leu-(L)-Glu(O*t*Bu)-O*t*Bu. *N*-Carboxybenzyl-(L)-Leu-(L)-Glu(O*t*Bu)-O*t*Bu (2) (0.480 g, 0.95 mmol) was dissolved in 75:25 dichloromethane: methanol (10 mL). Sufficient Pd on C catalyst was added to the flask so as to provide 10 weight % catalytic loading. The flask was quickly evacuated three times to remove the air, and then placed under a hydrogen atmosphere, and allowed to stir overnight at room temperature. The reaction mixture was diluted in dichloromethane, filtered over Celite, and then

washed three times with 10% $NaHCO_{3\ (aq)}$. The solvent was removed by rotary evaporation to afford the product as a clear, colorless oil (0.343 g, 96%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (d, *J*=8.20, 1H), 4.45 (td, *J*=8.25, *J*=5.00, 1H), 3.38 (dd, *J*=9.92, *J*=3.88, 1H) , 2.33-2.18 (m, 2H), 2.15-2.08 (m, 1H), 1.92-1.85 (m, 1H), 1.77-1.64 (m, 1H), 1.45 (s, 9H), 1.42 (s, 9H), 1.37-1.30 (m, 1H), 0.95 (d, *J*=6.35, 3H), 0.91 (d, *J*=6.35, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.86, 172.30, 171.42, 82.28, 80.78, 53.67, 51.82, 44.30, 31.72, 28.22, 28.15, 28.04, 25.00, 23.60, 21.43 MALDI-MS (m/z): calcd 372.3, found $[M + H]^+$ 373.005.

2,2':5',2"-Terthiophene-5-(L)-Leu-(L)-Glu(O*t*Bu)-O*t*Bu. 2,2':5',2"-Terthiophene-5-carboxylic acid (1) (0.114 g, 0.4 mmol), NH_2-(L)-Leu-(L)-Glu(O*t*Bu)-O*t*Bu (3) (0.112 g, 0.3 mmol), EDC (0.070 g, 0.4 mmol), HOBt (0.061 g, 0.4 mmol), and TEA (0.056 mL, 0. 4 mmol) were added to a flask and dissolved in 10 mL of N, N-dimethylformamide. The reaction was allowed to stir overnight at room temperature. The solvent was removed by rotary evaporation, and the resulting crude product was dissolved in dichloromethane, washed three times with 10% $NaHCO_{3\ (aq)}$, and then washed three times with 5% citric acid $_{(aq)}$. The organic layer was dried over Na_2SO_4, and the solvent was removed by rotary evaporation. The crude product was purified by flash chromatography (silica gel, 2.5% methanol in dichloromethane) to afford the product as a yellow solid (0.110 g, 57%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, *J*=3.90, 1H), 7.25 (dd, *J*=5.20, *J*=1.05, 1H), 7.19 (dd, *J*=3.60, *J*=1.00, 1H), 7.15 (d, *J*=3.75, 1H), 7.11 (d, *J*=3.85, 1H), 7.09 (d, *J*=3.80, 1H), 7.03 (dd, *J*=5.05, *J*=3.60, 1H), 6.74 (d, *J*=7.60, 1H), 6.53 (d, *J*=7.15, 1H), 4.66 (td, *J*=8.45, *J*=5.15, 1H), 4.45 (td, 1H), 2.37-2.20 (m, 2H), 2.16-2.09 (m, 1H), 1.98-1.91 (m, 1H), 1.75-1.71 (m, 2H), 1.69-1.64 (m, 1H), 1.47 (s, 9H), 1.41 (s, 9H), 0.98 (dd, *J*=8.85, *J*=6.05, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.64, 170.74, 170.62, 161.28, 142.06, 137.84, 136.85, 136.65, 135.15, 129.11, 128.12, 125.76, 125.10, 124.62, 124.26, 123.82, 82.56, 81.18, 57.97, 52.82, 38.32, 31.50, 28.18, 27.18, 25.39, 15.38, 11.66 MALDI-MS (m/z): calcd 646.2, found $[M + Na]^+$ 669.110

2,2':5',2"-Terthiophene-5-(L)-Leu-(L)-Glu(OH)-OH (7). 2,2':5',2"-Terthiophene-5-(L)-Leu-(L)-Glu(O*t*Bu)-O*t*Bu was dissolved in the following solvent mixture: 77.5:20:2.5 dichloromethane: trifluoroacetic acid (TFA): triisopropylsilane (TIPS) and allowed to react at room temperature for six (6) hours. The solvent was removed by rotary evaporation, and the crude product was purified by reverse phase high-pressure liquid chromatography (RP-HPLC) in 0.1% $NH_4OH_{(aq)}$ and methanol. ^{1}H NMR (500 MHz, D_2O) δ 7.72 (d, *J*=3.35, 1H), 7.45 (d, *J*=4.80, 1H), 7.38 (s, 2H), 7.34 (d, *J*=3.80, 1H), 7.29 (d, *J*=3.25, 1H), 7.14 (t, *J*=4.20, 1H), 4.63-4.60 (m, 1H), 4.19 (dd, 1H) 2.24 (t, *J*=8.12, 2H), 2.13-2.08 (m, 1H), 1.97-1.89 (m, 1H), 1.83-1.75 (m, 3H), 0.99 (d, *J*=5.75, 3H), 0.96 (d, *J*=5.65, 3H); ^{13}C NMR (125 MHz, CD_3OD) δ 177.85, 177.20, 174.16,

163.97, 143.33, 139.03, 138.04, 137.78, 136.25, 131.12, 129.14, 126.96, 126.24, 125.63, 125.31, 125.14, 55.19, 53.89, 41.77, 32.06, 29.33, 26.17, 23.57, 21.87; MS-ESI calcd 534.10, found $[M^+]$ 534.093

***N*-Carboxybenzyl-(L)-Ile-(L)-Glu(O*t*Bu)-O*t*Bu.** *N*-Carboxybenzyl-(L)-Ile carboxylic acid (0.348 g, 1.31 mmol), NH_2-(L)-Glu(O*t*Bu)-O*t*Bu (0.300 g, 1.01 mmol), 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDC) (0.222 g, 1.31 mmol), 1-hydroxybenzotriazole (HOBt) (0.201 g, 1.31 mmol), and triethylamine (TEA) (0.183 mL, 1.31 mmol) were added to a flask and dissolved in 20 mL of dichloromethane. The reaction was allowed to stir overnight at room temperature. The reaction was diluted in dichloromethane, and washed three times with 10% $NaHCO_{3\ (aq)}$, and then washed three times with 5% citric acid $_{(aq)}$. The organic layer was dried over Na_2SO_4, and the solvent was removed by rotary evaporation. The product was purified by flash chromatography (silica gel, 5% methanol in dichloromethane) to afford a clear, colorless oil (0.460 g, 90 %). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36-7.30 (m, 5H), 6.57 (d, *J*=7.60, 1H), 5.40 (d, *J*=8.60, 1H), 5.10 (s, 2H), 4.45 (td, 1H), 4.06 (dd, *J*=6.13, *J*=7.60, 1H), 2.36-2.22 (m, 2H), 2.14-2.07 (m, 1H), 1.96-1.90 (m, 1H), 1.89-1.82 (m, 1H), 1.53-1.49 (m, 1H), 1.46 (s, 9H), 1.43 (s, 9H), 1.20-1.11 (m, 1H), 0.93 (d, *J*=6.95, 3H), 0.90 (d, *J*=7.35, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172. 42, 170.87, 170.64, 156.18, 136.28, 128.55, 128.17, 128.08, 82.41, 80.93, 67.00, 59.57, 52.47, 37.84, 31.42, 28.07, 27.98, 27.30, 24.82, 15.36, 11.52 MALDI-MS calcd 506.30, found $[M + Na]^+$ 529.149

NH_2-(L)-Ile-(L)-Glu(O*t*Bu)-O*t*Bu. *N*-Carboxybenzyl-(L)-Ile-(L)-Glu(O*t*Bu)-O*t*Bu (2) (0.460 g, 0.91 mmol) was dissolved in 75:25 dichloromethane: methanol (10 mL). Sufficient Pd on C catalyst was added to the flask so as to provide 10 weight % catalytic loading. The flask was quickly evacuated three times to remove the air, and then placed under a hydrogen atmosphere, and allowed to stir overnight at room temperature. The reaction mixture was diluted in dichloromethane, filtered over Celite, and then washed three times with 10% $NaHCO_{3\ (aq)}$. The solvent was removed by rotary evaporation to afford the product as a clear, colorless oil (0.271 g, 80%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, *J*=7.95, 1H), 4.46 (td, *J*=8.00, *J*=5.16, 1H), 3.27 (d, *J*=3.90, 1H), 2.34-2.19 (m, 2H), 2.16-2.07 (m, 1H),1.99-1.87 (m, 2H), 1.46 (s, 9H), 1.43 (s, 9H), 1.40-1.33 (m, 1H), 1.16-1.07 (m, 1H), 0.96 (d, *J*=6.95, 3H), 0.89 (t, *J*=7.30, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.54, 172.22, 171.39, 82.26, 80.74, 60.03, 51.92, 38.12, 31.74, 28.18, 28.09, 28.03, 23.94, 16.26, 12.03 MALDI-MS calcd 372.26, found $[M + Na]^+$ 394.977

2,2':5',2"-Terthiophene-5-(L)-Ile-(L)-Glu(O*t*Bu)-O*t*Bu. 2,2':5',2"-Terthiophene-5-carboxylic acid (1) (0.117 g, 0.4 mmol), NH_2-(L)-Ile-(L)-Glu(O*t*Bu)-O*t*Bu (3) (0.112 g, 0.3 mmol), EDC (0.070 g, 0.4 mmol),

HOBt (0.061 g, 0.4 mmol), and TEA (0.056 mL, 0. 4 mmol) were added to a flask and dissolved in 10 mL of N, N-dimethylformamide. The reaction was allowed to stir overnight at room temperature. The solvent was removed by rotary evaporation, and the resulting crude product was dissolved in dichloromethane, washed three times with 10% $NaHCO_{3\ (aq)}$, and then washed three times with 5% citric acid $_{(aq)}$. The organic layer was dried over Na_2SO_4, and the solvent was removed by rotary evaporation. The crude product was purified by flash chromatography (silica gel, 2.5% methanol in dichloromethane) to afford the product as a yellow solid (0.175 g, 90%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (d, *J*=3.90, 1H), 7.24 (dd, *J*=5.10, *J*=1.10, 1H), 7.19 (dd, *J*=3.49, *J*=0.89, 1H), 7.15 (d, *J*=3.80, 1H), 7.10 (d, *J*=3.85, 1H), 7.09 (d, *J*=3.80, 1H), 7.03 (dd, *J*=5.10, *J*=3.60, 1H), 6.71 (d, *J*=8.40, 1H), 6.67 (d, *J*=7.50, 1H), 4.50-4.44 (m, 2H), 2.37-2.23 (m, 2H), 2.14-2.08 (m, 1H), 1.98-1.91 (m, 2H), 1.47 (s, 9H), 1.41 (s, 9H), 1.30-1.24 (m, 2H), 0.98 (d, *J*=6.80, 3H), 0.95 (t, *J*=7.40, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.64, 170.74, 170.62, 161.28, 142.07, 137.84, 136.85, 136.65, 135.15, 129.11, 128.12, 125.76, 125.10, 124.62, 124.26, 123.82, 82.56, 81.18, 57.97, 52.82, 38.32, 31.50, 28.18, 28.13, 27.18, 25.39, 15.38, 11.66 MALDI-MS calcd 646.22, found [M + Na]$^+$ 669.184

2,2':5',2"-Terthiophene-5-(L)-Ile-(L)-Glu(OH)-OH (8). 2,2':5',2"-Terthiophene-5-(L)-Ile-(L)-Glu(O*t*Bu)-O*t*Bu was dissolved in the following solvent mixture: 77.5:20:2.5 dichloromethane: trifluoroacetic acid (TFA): triisopropylsilane (TIPS) and allowed to react at room temperature for six hours. The solvent was removed by rotary evaporation, and the crude product was purified by reverse phase high-pressure liquid chromatography (RP-HPLC) in 0.1% $NH_4OH_{(aq)}$ and methanol. ^{1}H NMR (500 MHz, D_2O) δ 7.61 (d, J=3.95 Hz, 1H), 7.36 (d, J=5.05 Hz, 1H), 7.27 (d, J=3.70 Hz, 2H), 7.22 (d, J=3.95 Hz, 1H), 7.18 (d, J=3.75 Hz, 1H), 7.05 (dd, J=4.93 Hz, J=3.78 Hz, 1H), 4.34 (d, J=8.45 Hz, 1H), 4.12 (d, J=8.45 Hz, J=4.90 Hz, 1H), 2.20-2.16 (m, 2H), 2.04-1.93 (m, 2H), 1.91-1.83 (m, 1H), 1.56-1.51 (m, 1H), 1.28-1.19 (m, 1H), 0.95 (d, J=6.80 Hz, 3H), 0.87 (t, J=7.38 Hz, 3H) ^{13}C NMR (125 MHz, D_2O) δ 181.99, 178.22, 172.91, 164.01, 142.19, 137.46, 136.13, 134.43, 130.89, 128.24, 126.29, 125.56, 124.71, 124.35, 124.29, 58.90, 55.28, 36.20, 33.87, 30.12, 28.50, 24.70, 14.77, 9.98 MS-ESI calcd 534.10, found [M$^+$] 534.097

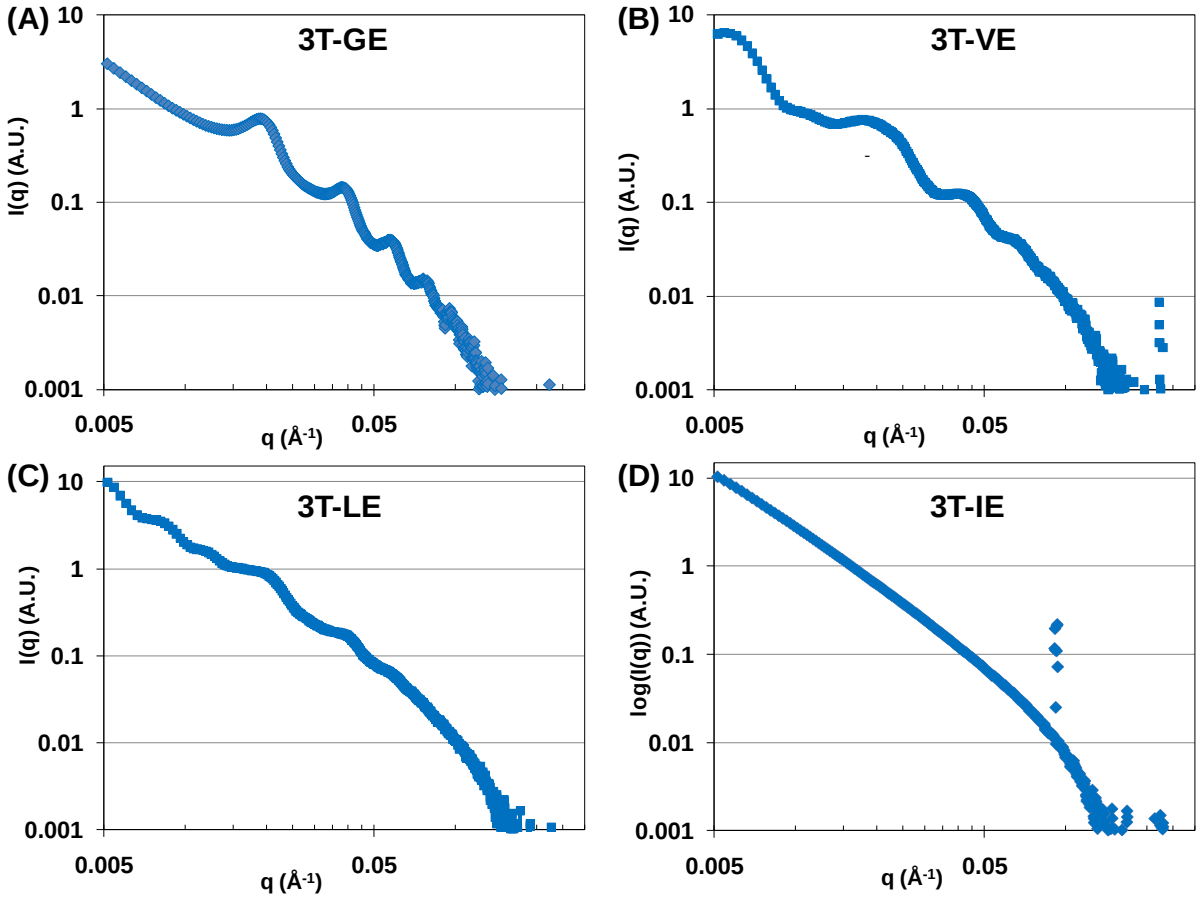


Figure S1. Small Angle X-ray Scattering (SAXS) characterization. (A) The scattering curve for **3T-GE** displays a highly-ordered lamellar pattern, with a periodicity of 347 $Å^{-1}$. (B) The scattering curve for **3T-VE** shows a complex form factor, which likely arises due to scattering from the regular wall-to-wall spacings present in the spiral sheet morphology. (C) **3T-LE** displays a form factor that appears to arise from a mixture of different structures. In the low q regime, the scattering curve has a slope of -3, which is indicative of structures larger than 100 nm. This is consistent with the diameters of the nanotubes observed by cryo-TEM. (D) The scattering curve for **3T-IE** has a slope of -2 in the low q regime, which is consistent with a bilayer-like structure. This scattering curve is consistent with the flat sheet morphology observed by cryo-TEM. In addition, an R_g = 1.8 nm was calculated from the scattering data. This value is consistent with twice the length of the hydrophobic terthiophene core.

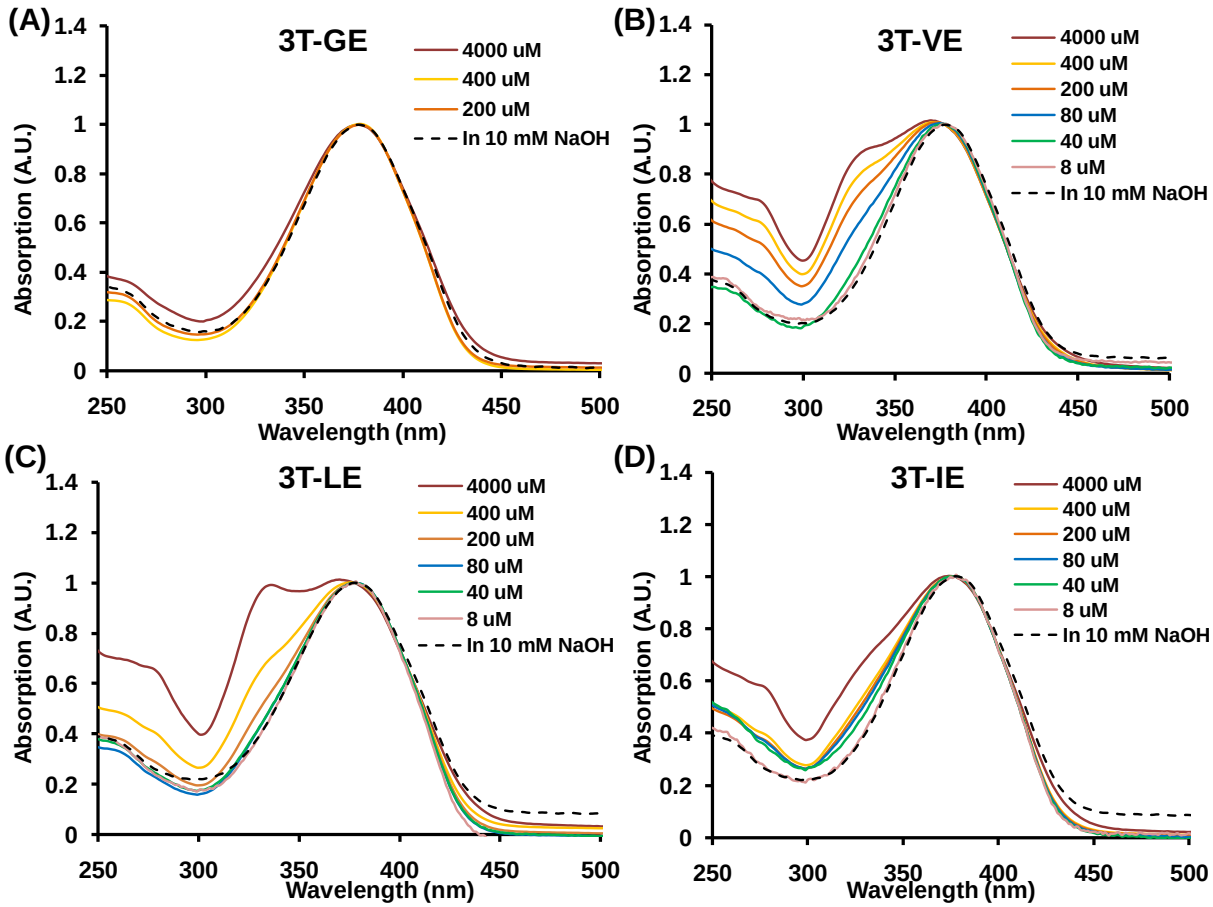


Figure S2. Variable Concentration UV-Visible Spectra. All of the UV-Visible spectra indicate that dilution of each of the assemblies results in disruption of their interactions, as indicated by the loss of the hypsochromically shifted peak. All spectra were compared to that obtained under conditions that do not promote self-assembly by dissolving the sample in excess (10 mM) NaOH (*black, dashed line*), which shows a single absorption maximum at 377 nm. Upon dilution, the hypsochromically shifted shoulder observed for (A) **3T-GE** disappears at concentrations as high as 0.4 mM. However, for assemblies of (B) **3T-VE**, (C) **3T-LE**, and (D) **3T-IE**, the hypsochromically shifted peak only disappears after dilution to concentrations as low as 8 µM. These results suggest that the interactions in assemblies of **3T-GE** are weaker than those in **3T-VE**, **3T-LE**, and **3T-IE**. All spectra have been normalized relative to their absorbance at 377 nm.

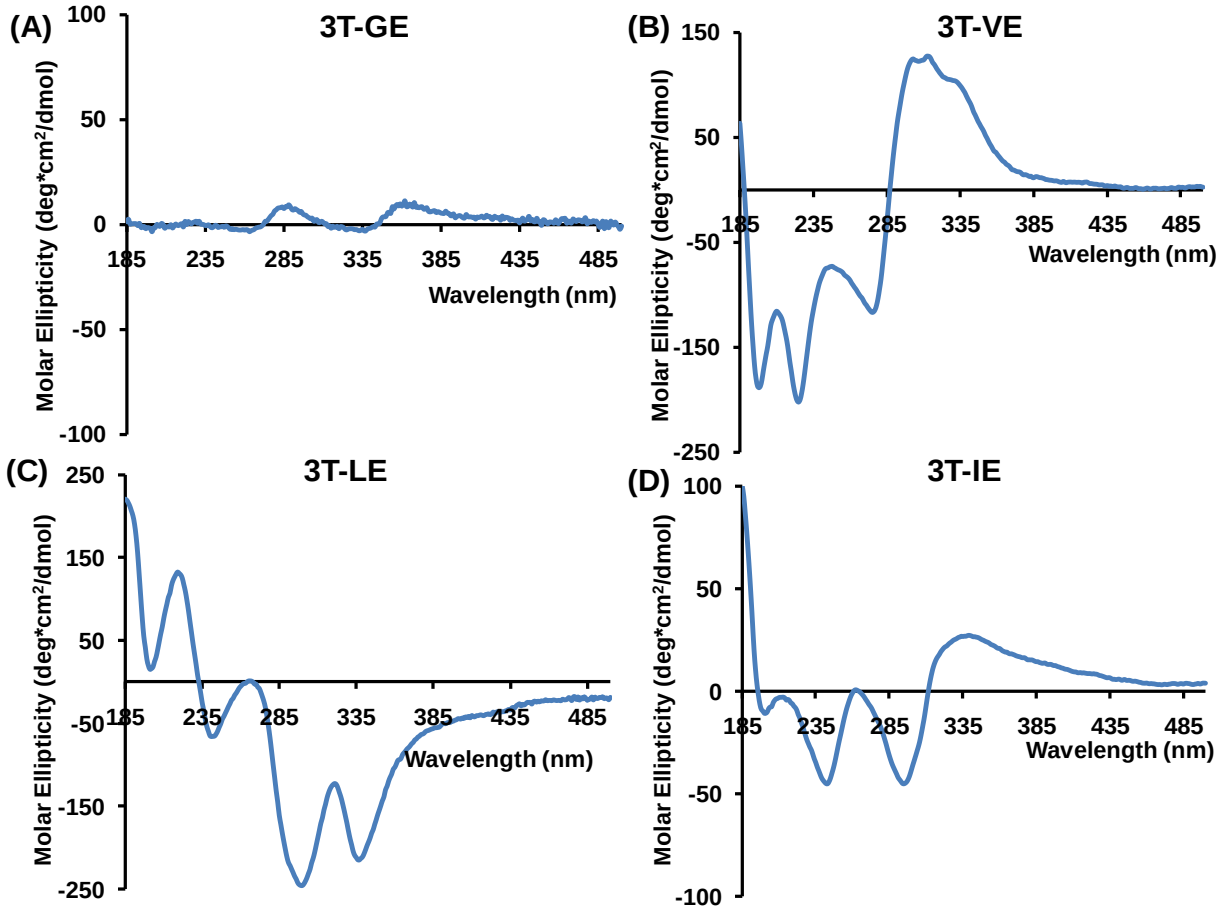


Figure S3. Circular Dichroism (CD) spectra. All of the CD spectra indicate a chiral molecular packing arrangement for each of the assemblies. (A) **3T-GE** shows a relatively weak CD signal. (B) **3T-VE**, (C) **3T-LE**, and (D) **3T-IE** all show monosignate Cotton effects corresponding to the excitonic coupling of terthiophene. Interestingly, **3T-VE** and **3T-IE** display similar spectral patterns, indicating that they may have similar molecular packing arrangements. **3T-LE** displays a CD signal of opposite chirality. Peptide-based signals could not be distinguished in these spectra, likely due to the strong absorbance from the terthiophene moiety.

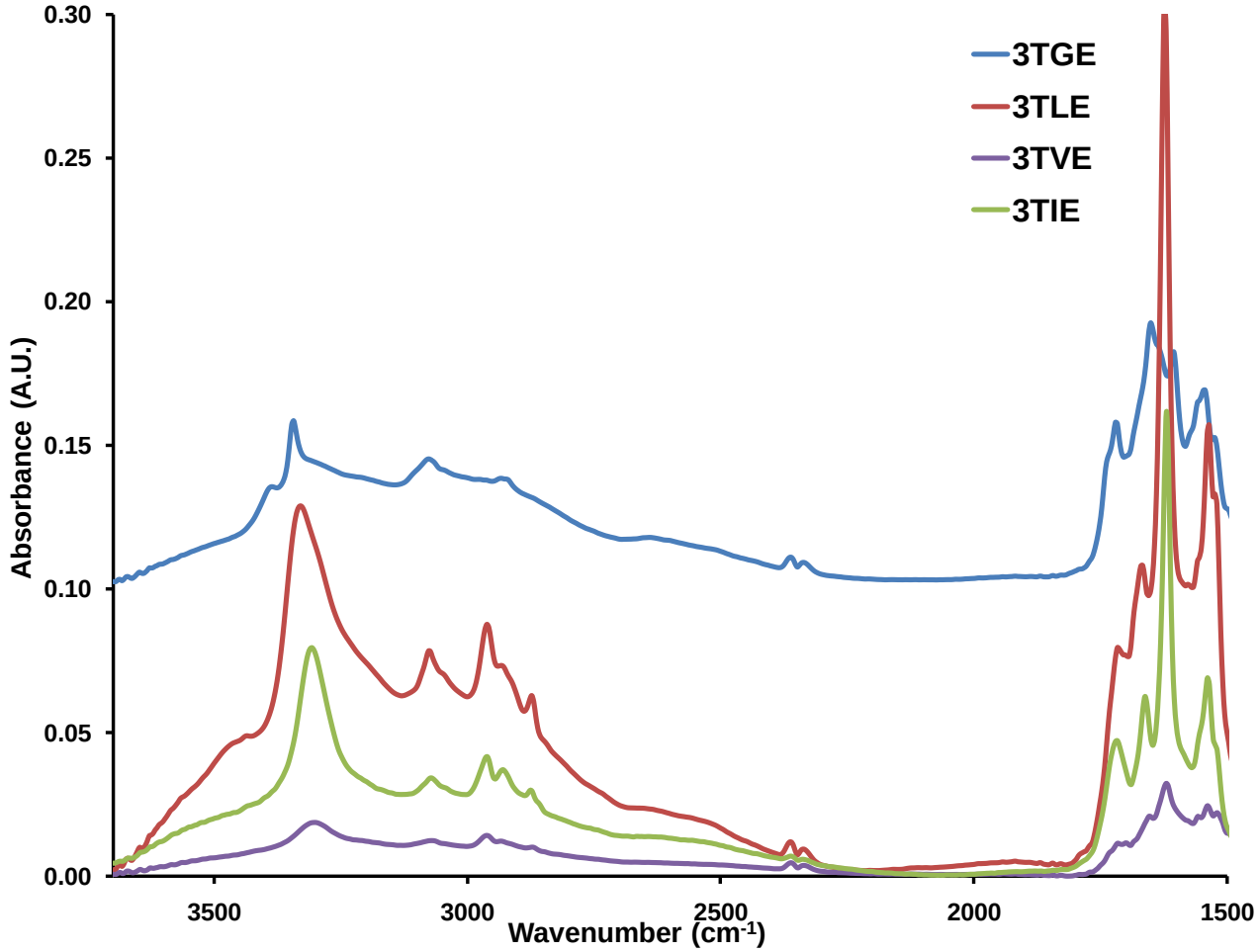


Figure S4. Fourier transform infrared (FT-IR) spectroscopy. The FTIR spectra shown above were taken of assembled solutions of **3T-GE** (*blue*), **3T-LE** (*red*), **3T-IE** (*green*), and **3T-VE** (*purple*). Analysis of the N-H stretching frequency for each of the assemblies is near 3300 cm^{-1}, indicating that hydrogen bonding interactions are occurring. The Amide I peak for each of the assemblies is inconclusive for the presence of any peptide secondary structure. Interestingly, in each of the assemblies, there is a peak at 1712 cm^{-1}, which corresponds to the stretching frequency of the protonated carboxylic acid side chain of glutamic acid. The absorbance values of **3T-GE** were offset along the y-axis for clarity.