Experimental Section

Materials

4,4’-Methylene bis(4-phenyl isocyanate), 3-aminopropionic acid, 7-aminoheptanoic acid, 12-aminododecanic Acid, 4-(2-aminoethyl)benzoic acid, 4,4’-methylenebis (cyclohexyl isocyanate), 1,5-naphthalene diisocyanate, hexamethylene diisocyanate, 1-dodecylamine, 4-(2-aminoethyl) benzenesulfonamide, 4,4'-methylene-diphenol, 12-bromododecanoic acid, pyrene, thioindigo and other conventional reagents/solvents were obtained from commercial sources and used as received unless otherwise mentioned.

Characterization

Transmission electron microscopy (TEM) images were taken using an FEI TECNAI 12 transmission electron microscope operating at 120 kV. High-resolution TEM (HRTEM) and selected area electron diffraction (SAED) images were taken using a JEOL JEM-2200FS transmission electron microscope. TEM grids were purchased from Electron Microscopy Sciences (FCF400-Cu, 10-nm formvar coated grids, stabilized with evaporated 1-nm carbon film). Scanning electron microscopy (SEM) images were taken using an FEI Magellan 400 FESEM in SE imaging mode. The substrate for SEM measurement was plain glass microscope slide (Fisherfinest™). The gold-coated samples were pretreated with 30-s gold sputtering (Cressington Sputter Coater 108). Atomic force microscopy (AFM) images were taken using a Brucker Dimensions 3000 Scanning Probe Microscope under tapping mode. Silicon wafers [Cemat Silicon S.A., (111)-oriented] were pre-cleaned by sonication in ethanol and acetone for 20 min, respectively. Then the wafers were dried with Ar flow and treated with UV-O_3 for 15 min. For TEM, SEM, and AFM measurement, the 2D material at a concentration of 0.2 $mg \cdot mL^{-1}$ was drop-cast onto the corresponding substrate. Confocal microscopy images were taken using a Nikon A1 confocal microscope. Powder X-ray diffraction (XRD) was performed on a PANalytical X'Pert Material Research Diffractometer with a copper source. Small/wide angle X-ray scattering data was collected with a GANESHA 300 XL SAXS system.

General Synthesis Procedure

A solution containing 1 equivalent (1 mM) of diisocyanate in anhydrous DMSO (5 mL) was added to a DMSO solution (5 mL) containing 2.5 equivalents (2.5 mM) of corresponding amino acid at room temperature. After addition, the mixture was stirred at room temperature under Ar for 24~48 hours. Then the solid raw product was collected after precipitation in water and filtration. The raw product was washed with 0.5 M HCl solution (20 mL), DI water (20 mL), methanol (20 mL), and ethyl acetate (20 mL) 3 times, respectively. The residue was purified by recrystallization in ethyl acetate (30 mL) to afford white or light-brown powder as desired product.

AUCO$_2$-2: The General Procedure was applied to 4,4'-methylene bis(4-phenyl isocyanate) and 3-aminopropionic acid. The procedure afforded the product (0.312 g, 73%) as white powder. ^{1}H NMR (400 MHz, DMSO-*d*$_6$), δ: 8.52 (s, 2H), 7.30 (d, *J* = 9.6 Hz, 4H), 7.09 (d, *J* = 8.4 Hz, 4H), 6.16 (t, *J* = 9.6 Hz, 2H), 3.80 (s, 4H), 3.32 (s, 4H), 2.40 (s, 4H).

AUCO$_2$-6: The General Procedure was applied to 4,4'-methylene bis(4-phenyl isocyanate) and 7-aminoheptanoic acid. The procedure afforded the product (0.405 g, 75%) as white powder. ^{1}H NMR (400 MHz, DMSO-*d*$_6$), δ: 8.51 (s, 5H), 7.32 (d, *J* = 8.4 Hz, 4H), 7.08 (d, *J* = 8.4 Hz, 4H), 6.02 (t, *J* = 9.6 Hz, 2H), 3.80 (s, 4H), 3.29 (d, *J* = 9.2 Hz, 4H), 2.18 (t, *J* = 7.2 Hz, 2H), 1.27-1.50 (m, 16H).

AUCO$_2$-11: The General Procedure was performed with 4,4'-methylene bis(4-phenyl isocyanate) and 12-aminododecanic acid. The procedure afforded the product (0.537 g, 79%) as white powder. ^{1}H NMR (400 MHz, DMSO-*d*$_6$), δ: 8.28 (s, 2H), 7.24 (d, *J* = 9.2 Hz, 4H), 7.05 (d, *J* = 9.2 Hz, 4H), 6.03 (t, *J* = 5.6 Hz, 2H), 3.73 (s, 4H), 3.01 (t, *J* = 5.6 Hz, 4H), 2.16 (t, *J* = 7.2 Hz, 4H), 1.24-1.47 (m, 24H).

AUbCO$_2$: The General Procedure was applied to 4,4'-methylene bis(4-phenyl isocyanate) and 4-(2-aminoethyl)benzoic acid. The procedure afforded the product (0.487 g, 84%) as light gray powder. ^{1}H NMR (400 MHz, DMSO-*d*$_6$), δ: 8.80 (s, 2H), 7.84 (d, *J* = 8.8 Hz, 4H), 7.61 (d, *J* = 8.4 Hz, 4H), 7.37 (dd, *J* = 2.0 Hz, *J* = 2.4 Hz, 4H), 7.09 (dd, *J* = 4.8 Hz, *J* = 4.4 Hz, 4H), 6.11 (t, *J* = 5.2 Hz, 4H), 3.81 (s, 4H), 3.46 (t, *J* = 6.4 Hz, 4H), 2.73 (s, 4H).

AcUCO$_2$: The General Procedure was applied to 4,4'-methylene bis(cyclohexyl isocyanate) and 12-aminododecanic acid. The procedure afforded the product (0.554g, 80%) as white powder. ^{1}H NMR (400 MHz, DMSO-*d*$_6$), δ: 5.85 (s, 4H), 3.80 (m, 4H), 3.94 (s, 4H), 2.16 (d, *J* = 7.6 Hz, 4H), 1.24-1.48 (m, 56H).

AnUCO$_2$: The General Procedure was performed with 1,5-naphthalene diisocyanate and 12-aminododecanic acid. The procedure afforded the product (0.429g, 67%) as purple powder. ^{1}H NMR (400 MHz, DMSO-*d*$_6$), δ: 8.57 (s, 2H), 8.00 (dd, *J* = 7.6 Hz, *J* = 7.6 Hz, 2H), 7.64 (dd, *J* = 7.6 Hz, *J* = 7.2 Hz, 2H), 7.37 (ddd, *J* = 7.6 Hz, 2H), 6.12 (t, *J* = 9.6 Hz, 2H), 3.10 (s, 4H), 2.17 (d, *J* = 7.2 Hz, 4H), 1.27-1.92 (m, 40H).

AlUCO$_2$: The General Procedure was applied to hexamethylene diisocyanate and 12-aminododecanic acid. The procedure afforded the product (0.425g, 71%)

as white powder. ^{1}H NMR (400 MHz, DMSO-d_6), δ: 7.68 (s, 2H), 5.75 (s, 2H), 2.94 (s, 8H), 2.17 (t, J = 7.6 Hz, 4H), 1.25-1.92 (s, 52H).

AUA: The General Procedure was performed with 4,4'-methylene bis(4-phenyl isocyanate) and 1-dodecylamine. The procedure afforded the product (0.546 g, 88%) as white powder. ^{1}H NMR (400 MHz, DMSO-d_6), δ: 8.27 (s, 2H), 7.27 (d, J = 26.8 Hz, 4H), 7.03 (d, J = 24.0 Hz, 4H), 5.61 (s, 2H), 3.77 (s, 4H), 2.68 (s, 4H), 1.64 (s, 4H), 1.25-1.92 (s, 42H).

AUE: The General Procedure was applied to 4,4'-methylene bis(4-phenyl isocyanate) and 12-amino-1-dodecanoic acid methyl ester. The procedure afforded the product (0.592 g, 87%) as white powder. ^{1}H NMR (400 MHz, DMSO-d_6), δ: 8.26 (s, 2H), 7.25 (d, J = 8.4 Hz, 4H), 7.01 (d, J = 8.4 Hz, 4H), 6.02 (s, 2H), 3.88 (s, 2H), 3.66 (s, 6H), 3.03(s, 4H), 1.24-1.50 (m, 36H).

AUbsA: The General Procedure was performed with 4,4'-methylene bis(4-phenyl isocyanate) and 4-(2-aminoethyl)benzoic acid. The procedure afforded the product (0.520 g, 80%) as white powder. ^{1}H NMR (400 MHz, DMSO-d_6), δ: 8.52 (s, 2H), 7.74 (d, J = 8.4 Hz, 4H), 7.41 (d, J = 8.4 Hz, 4H), 7.25 (dd, J = 8.4 Hz, J = 9.3 Hz, 4H), 7.01 (dd, J = 8.4 Hz, J = 8.4 Hz, 4H), 6.06(t, J = 5.2 Hz, 4H), 3.79 (s, 4H), 2.80 (t, J = 6.8 Hz, 4H).

AECO$_2$: The synthesis of AECO$_2$ was performed from one step reaction between 4,4'-methylene-diphenol and 12-bromododecanoic acid following a previous report[1]. A mixture of 4,4'-methylenediphenol (0.1 mmol), 12-bromododecanoic acid (0.3 mmol), and K_2CO_3 (1 mmol) in anhydrous DMSO (10 mL) was stirred at 60 °C for 24 h and then cooled to room temperature. The precipitated product was filtered and recrystallizated from *n*-hexanes to yield the derivatives as white powder. The procedure afforded the product (0.511 g, 89%) as white powder. ^{1}H NMR (400 MHz, DMSO-d_6), δ: 6.94 (d, J = 4.4 Hz, 4H), 6.65 (d, J = 2.0 Hz, 4H), 3.87 (t, J = 6.4 Hz, 4H), 3.90 (s, 2H), 2.16 (t, J = 6.4 Hz, 4H), 1.65 (t, J = 7.6 Hz, 4H), 1.38-1.63 (m, 28H).

AUtCO$_2$: The General Procedure was performed with 4,4'-methylene bis(4-phenyl isocyanate) and 12-hydroxydodecanoic acid. The procedure afforded the product (0.581 g, 85%) as white powder. ^{1}H NMR (400 MHz, DMSO-d_6), δ: 9.47 (s, 2H), 7.32 (t, J = 6.8 Hz, 4H), 7.07 (t, J = 8.4 Hz, 4H), 4.02 (t, J = 6.8 Hz, 4H), 3.78 (s, 2H), 2.16 (t, J = 7.2 Hz, 4H), 1.25-1.61 (m, 36H).

Preparation of 2D sheets

AU molecules (1 mg) were added to DMSO (200 µL) and further dispersed using an ultrasonic bath. The sonication was performed on a Branson 3510 ultrasonic cleaner (42 kHz frequency) for 15 min at 100 W. Then the mixture was injected to the bottom of a 20-mL glass vial containing DI water (5 mL) to make a turbid suspension. The obtained suspensions were kept without stirring for at least 12 hours before further characterization. Other molecules in the analog (Scheme 2) were utilized following the same procedure.

Preparation of 2D sheet in powder form

The 2D materials formed in aqueous media was filtered and dried under vacuum. The obtained solid was grinded into powder form with mortar and pestle.

Pyrene loading for 2D sheets

To a 150-μL DMSO solution containing 1 mg of AU molecules, 0.1 mg of pyrene in 50 μL of DMSO was added and sonicated for 15 minutes. Then the same method for regular 2D sheets preparation (as described above) was applied.

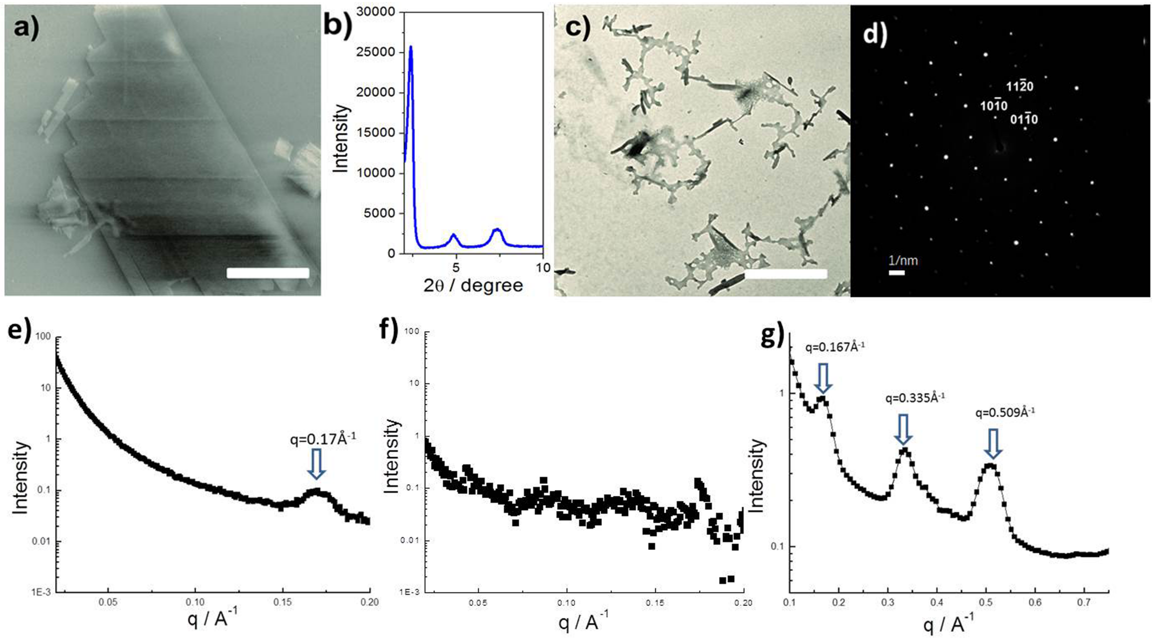

Figure S1. a) SEM image of uncoated 2D sheets. b) XRD spectra for AuCO$_2$-11 2D sheets. The peak at 2θ = 2.37°, 4.78°, and 7.28° indicates *d*-spacing of 37 Å, 18 Å, and 12 Å, respectively. c) Self-assembly of AUCO$_2$-11 in DMSO after sonicating for 15 min. d) Diffraction pattern of selected area electron diffraction (SAED) for 2D sheets. The corresponding distance for $(10\bar{1}0)$, $(01\bar{1}0)$ plains are 3.81 Å, which in accordance with the distance of the visible lattice fringes (0.376 Å). e) Small angle X-ray scattering (SAXS) spectra of the 2D material in powder form. The peak at *q* = 0.17 Å indicates a *d*-spacing of 37 Å. f) SAXS spectra of the 2D sheets in solution. No significant peak was observed. g) Wide angle X-ray scattering (WAXS) spectra of the 2D material in powder form. Scale bar in (a) = 5 μm, (c) =1 μm.

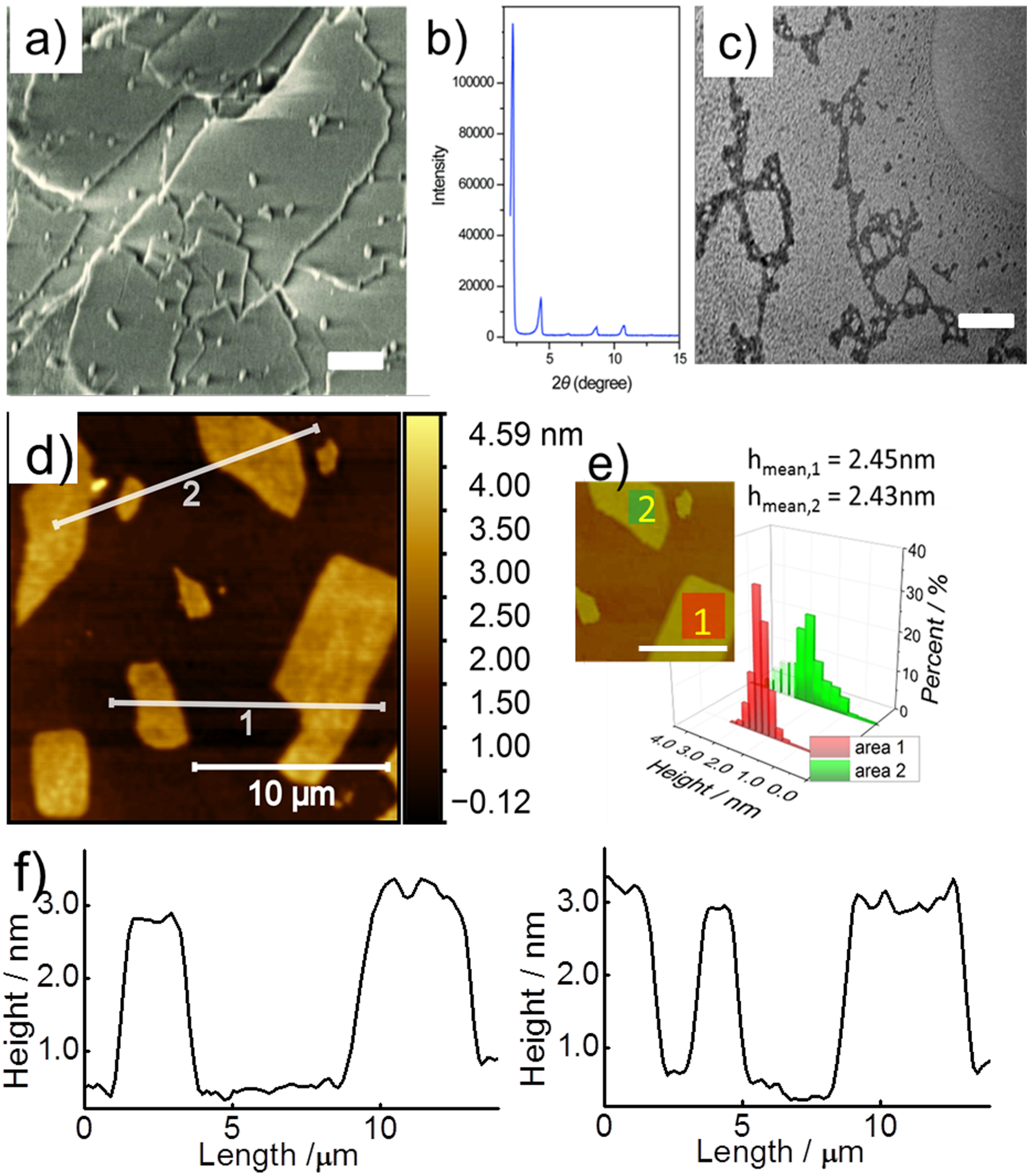

Figure S2 a) SEM image of AUbsA 2D sheet in water. b) XRD spectra of AUbsA 2D sheet shows a peak at $2\theta = 4.38°$, indicating a *d*-spacing of 22 Å. c) AUbsA in DMSO after sonication. No significant amount of 2D structure was observed. d) AFM image of 2D sheets. e) Histogram of height distribution in selected area of 2D sheets. f) Height profiles along selected cross sections on AFM image. Average height was 2.4 nm based on the difference between average top and trough attitude. Scale bar in (a) = 5 µm, (c) = 1 µm, (e)=5 µm.

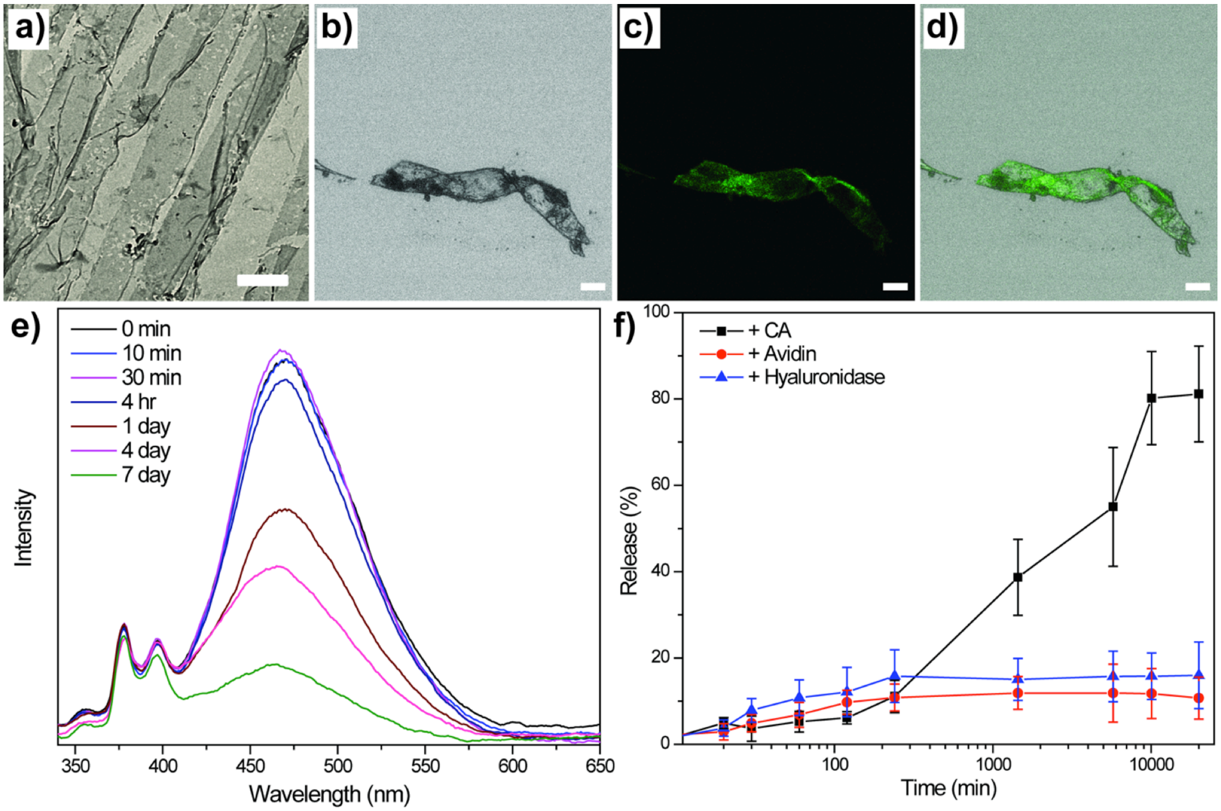

Figure S3. Color illustration of **Figure 4** in the manuscript**.** TEM images of AUbsA a) after loading of the pyrene. Confocal images of the 2D sheet, b) bright field, c) pyrene, d) merged image of (b) and (c). e) Pyrene release from 2D sheet in the presence of BCA. f) Plot of % release with time and comparison with controls. Scale bar (a)=5 μm, (b-d)=10 μm.

Reference

[1] D. T. Jayaram, S, Ramos-Romero, B. H. Shankar, C. Garrido, N. Rubio, L. Sanchez-Cid, S, Gómez, J, Blanco, D. Ramaiah, *ACS Chem. Biol.*, **2016**, *11*, 104–112.