Supporting Information for

Substrate-Driven Transient Self-Assembly and Spontaneous Disassembly Directed by Chemical Reaction with Product Release

Huaxin Wang, Yanyan Wang, Bowen Shen, Xin Liu and Myongsoo Lee*

State Key Lab for Supramolecular Structure and Materials, College of Chemistry, Jilin University, Changchun 130012, China

E-mail: mslee@jlu.edu.cn
1. General Methods.
All reactions were performed in oven-dried glassware under dry argon atmosphere. Toluene was
dried by distillation from sodium-benzophenone immediately prior to use. Dichloromethane (DCM)
and acetonitrile (ACN) were dried by distillation from CaH$_2$. Distilled water was polished by ion
exchange and filtration. Other solvents and organic reagents were purchased from commercial
vendors and used without further purification unless otherwise mentioned. The reactions were
monitored by thin-layer chromatography (TLC; Merck, silica gel 60 F254 0.25 mm) with
visualization under UV light (254 nm) or treating iodine, phosphomolybdic acid. The products were
purified by flash column chromatography on silica gel (230-400 mesh). Recycling preparative high-
pressure chromatography (HPLC) was performed for further purification of the final desired
molecules by using Prominence LC-20AP (SHIMADZU) and YMC C8 reverse phase column (250
x 4.6 mm I.D., S-5 μm, 12 nm & 250 x 20.0 mm I.D., S-5 μm, 12 nm). $^1$H-NMR and $^{13}$C-NMR
spectra were recorded on Bruker AVANCE III 500. All compounds were subjected to $^1$H NMR
analysis to confirm ≥ 98% sample purity. Chemical shifts were reported in ppm relative to the
residual solvent peak (CDCl$_3$: $^1$H, 7.26; $^{13}$C, 77.23) or tetramethylsilane (TMS) peak. Multiplicity
was indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), quin (quintet), m (multiplet),
dd (doublet of doublets), dt (doublet of triplets), td (triplet of doublets), br s (broad singlet). Coupling
constants are reported in Hertz (Hz). Matrix-Assisted Laser Desorption/ Ionization Time of Flight
Mass Spectrometry (MALDI-TOF-MS) was performed on a Bruker Microflex LRF20 using trans-
2-[3-(4-tert-butylphenyl)-2-methyl-2-propenyli-dene]malononitrile (DCTB) as a matrix. UV/Vis
spectra were obtained from a Hitachi U-2900 Spectrophotometer. Fluorescence spectra were
obtained from a Hitachi F7000 Fluorescence Spectrophotometer. Dynamic Light Scattering (DLS)
measurement was performed using an ALV/CGS-3. X-ray diffraction (XRD) patterns were obtained
using a Rigaku D/max 2550 diffractometer (Rigaku Co.). Fourier transform infrared (FT-IR) spectra
were collected on a Brucker VERTEX 80V at ambient temperature.

TEM experiments. To investigate the self-assembled structures in aqueous solution, a drop of each
sample solution was placed on a carbon-coated copper grid (Carbon Type B (15-25 nm) on 200
mesh, with Formvar; Ted Pella, Inc.) and the solution was allowed to evaporate under ambient
conditions. These samples were stained by depositing a drop of uranyl acetate aqueous solution
(0.4-1.0 wt %) onto the surface of the sample-loaded grid. The dried specimen was observed by a
JEOL-JEM HR2100 operated at 120 kV. The cryogenic transmission electron microscopy (cryo-
TEM) experiments were performed with a thin film of aqueous solution of amphiphiles (3 μl)
transferred to a lacey supported grid. The thin aqueous films were prepared under controlled
temperature and humidity conditions (97-99 %) within a custom-built environmental chamber in
order to prevent evaporation of water from sample solution. The excess liquid was blotted with filter
paper for 2-3 seconds, and the thin aqueous films were rapidly vitrified by plunging them into liquid
ethane (cooled by liquid nitrogen) at its freezing point. The grid was transferred, on a Gatan 626
cryo holder, using a cryo-transfer device and transferred to the JEOL-JEM HR2100 TEM. Direct
imaging was carried out at a temperature of approximately -175 °C and with a 120 kV accelerating
voltage, using the images acquired with a Dual vision 300 W and SC 1000 CCD camera (Gatan,
Inc.; Warrendale, PA). The data were analyzed using Digital Micrograph software.
XRD experiments. To prepare the powder sample, aqueous solution containing 1 and R1 was treated with freeze-drying. The freeze-dried sample was then transferred to the holder and investigated by a Rigaku D/max 2550 diffractometer (Rigaku Co.).

FT-IR experiments. To prepare R1 sample for FT-IR, a thin and transparent KBr pellet was prepared and R1 was dropped onto the pellet then checked at ambient temperature. To prepare 1 or 2, 5 mg of solid was mixed with KBr then subsequently grind the mixture for 5 minutes. The pellet of mixture with KBr was made and then checked at ambient temperature. To prepare 1 or 2 with R1 sample, first aqueous solution of 1 or 2 with R1 was made, then aqueous solution was freeze-dried. The freeze-dried sample was mixed with KBr then subsequently grind the mixture for 5 minutes. The pellet of mixture with KBr was made and then checked at ambient temperature.

DLS experiments. The dynamic light scattering experiments were performed by ALV/CFS-3 using He-Ne laser operating at 632.8 nm. The scattering was kept at 90° during the whole experiment at 25 °C. The hydrodynamic diameter was determined from autocorrelation functions by the time interval method of photon correlation and the CONTIN method using the software provided by the manufacturer. To avoid the influence of dust, all solutions were filtered through a 0.45-μm membrane filter.

Sampling method. All sample solutions were prepared by evaporation of a CHCl₃ mixture of 1 or 2 (75.3 μM) and R1 (a mole ratio R1/1 of 5:1), then K₂CO₃ (72 μM) aqueous solution was added to the dry film and the solution was sonicated for 30 min in ice bath. The solution was stand at least 8 hr at room temperature.

Determination of conversion. ACN/CHCl₃ (4/1, v/v) was added to the film evaporated from reaction solution, and the solution was injected into the HPLC. The conversion was confirmed by analytical-C8 column (mobile phase: ACN with 0.1% Formic Acid, flow rate: 0.7 ml/min, λ = 254 nm). The qualitative analysis was determined by the retention time compared with the pure product after purification and characterization, which is as following: tᵣ = 15.3 min (R1); tᵣ = 14.3 min (P1); tᵣ = 19.2 min (P2).

SₕAr reaction in the presence of 1. The aqueous solution of 1 and R1 followed by above-mentioned method was added into the dry thin film of R2 (or R3, a mole ratio R2 or R3/1 of 5:1). After addition, sonication in ice bath for 1 min was necessary and the reaction solution was stirred for 2 hr at room temperature.

Control experiment for SₕAr reaction in the presence of 2. The aqueous solution of 2 and R1 followed by above-mentioned method was added into the dry thin film of R2 (or R3, a mole ratio R2 or R3/1 of 5:1). After sonication in ice bath for 1 min, the reaction solution was stirred for 2 hr at room temperature.

Control experiment for SₕAr reaction without self-assembling molecules. The reaction solution was prepared by R1 and R2 (or R3) dry film and pyridine (75.3 μM) CHCl₃ solution was added then stirred for 2 hr at room temperature.
\textbf{\textsuperscript{1}H-NMR experiments for \textit{S\textsubscript{N}Ar} reaction.} A solution of methanol-\textit{d}/D\textsubscript{2}O (1/1, v/v, 500 μl) was added into the dry film of \textit{1} (4.52 mM) and \textit{R1} (a mole ratio \textit{R1}/\textit{1} of 5:1). The solution was sonicated for 30 min in ice bath and standing 8 hr at room temperature. Then the solution was added into the dry film of \textit{R2} (a mole ratio \textit{R1}/\textit{R2} of 1:1) and sonicated for 1 min in ice bath. \textsuperscript{1}H-NMR spectra was performed every 20 min.

\textbf{The next cycles of the \textit{S\textsubscript{N}Ar} reaction.} After completion of the reaction, filtration of the solution by membrane filter (PTFE, pore size, 0.45 μm) was carried out, then K\textsubscript{2}CO\textsubscript{3} (a mole ratio K\textsubscript{2}CO\textsubscript{3}/\textit{R1} of 1:1) was added to the solution. Next cycle reaction was followed by same procedure above-mentioned.
2. Synthetic method.

1) Synthesis of 1 and 2.

Reagents and conditions: (a) ROTs, 4-hydroxy-4′-iodobiphenyl, Cs$_2$CO$_3$, ACN, reflux, overnight, yield, 60%; (b) 1,3-Benzenediboronic Acid Bis(pinacol) Ester, sat. NaHCO$_3$ (aq), Pd(PPh$_3$)$_4$, ethanol, toluene, reflux, overnight, yield, 25%; (c) 2 M Na$_2$CO$_3$ (aq), Pd(PPh$_3$)$_4$, ethanol, toluene, reflux, overnight, yield, 32%; (d) 2 M Na$_2$CO$_3$ (aq), Pd(PPh$_3$)$_4$, ethanol, toluene, reflux, overnight, yield, 63%.

Compound 3. 4-hydroxy-4′-iodobiphenyl (350.0 mg, 1.18 mmol), ROT$_{S1}$ (543.1 mg, 0.98 mmol) and Cs$_2$CO$_3$ (1596.5 mg, 4.90 mmol) were dissolved in anhydrous CH$_3$CN (11.8 ml). The mixture was refluxed overnight under Ar atmosphere. After completion of the reaction as monitored by TLC, the reaction mixture was cooled down to room temperature. The resulting mixture was condensed under reduced pressure, and dissolved in ethyl acetate. The organic layer was washed with brine and dried over MgSO$_4$ (s). The organic phase was filtered with Celite and the filtrate was condensed in a rotary evaporator. The crude product was purified by flash silica gel chromatography (eluent condition: methanol: ethyl acetate = 1: 10 v/v) to provide 60% yield as a colorless oil.

$^1$H NMR (500 MHz, Chloroform-$d$) $\delta$ 7.75 (d, $J = 8.5$ Hz, 2H), 7.48 (d, $J = 8.8$ Hz, 2H), 7.31 (d, $J = 8.4$ Hz, 2H), 6.99 (d, $J = 8.7$ Hz, 2H), 4.10 (d, $J = 5.6$ Hz, 2H), 3.65 (ddd, $J = 10.2$, 5.5, 2.7 Hz, 2H), 3.59 – 3.51 (m, 4H), 3.39 (s, 6H), 2.45 (p, $J = 6.2$ Hz, 1H). MALDI-TOF mass: m/z calcd. for C$_{30}$H$_{45}$INaO$_9$ [M + Na]$^+$, 699.20; found, 699.71.

Compound 4. 1,3-Benzenediboronic Acid Bis(pinacol) Ester (1200.0 mg, 3.636 mmol), 1,3-dibromobenzene (215.4 mg, 0.909 mmol), Pd(PPh$_3$)$_4$ (104.0mg, 0.09 mmol) were refluxed in mixture of saturated aqueous NaHCO$_3$ (7.5 ml), ethanol (11.0 ml) and toluene (19.0 ml) for
overnight under Ar atmosphere. After completion of the reaction as monitored by TLC, the reaction mixture was cooled down to room temperature. The resulting mixture was condensed under reduced pressure, and dissolve in ethyl acetate. The organic layer was washed with brine and dried over MgSO₄ (s). The organic phase was filtered with Celite and the filtrate was condensed in a rotary evaporator. The crude product was purified by flash silica gel chromatography (eluent condition: ethyl acetate: hexane 1: 3 v/v) to provide 25% yield as a white solid.

\[ ^1H \text{ NMR (500 MHz, Chloroform-}d\text{)} \delta 8.84 \text{ (s, 2H), 8.24 (s, 1H), 8.08 (s, 2H), 7.90 (d, J = 7.5 Hz, 2H), 7.74 (dt, J = 7.6, 1.6 Hz, 2H), 7.53 (t, J = 7.5 Hz, 2H), 1.38 (s, 24H).} \]

**Compound 1.** Compound 3 (174.9 mg, 0.259 mmol), compound 4 (50.0 mg, 0.103 mmol) and Pd(PPh₃)₄ (1.2 mg, 0.001 mmol) were refluxed in mixture of 2 M aqueous Na₂CO₃ (0.7 ml), ethanol (1.3 ml) and toluene (2.6 ml) for overnight under Ar atmosphere. After completion of the reaction as monitored by TLC, the reaction mixture was cooled down to room temperature. The resulting mixture was condensed under reduced pressure, and dissolve in ethyl acetate. The organic layer was washed with brine and dried over MgSO₄ (s). The organic phase was filtered with Celite and the filtrate was condensed in a rotary evaporator. The crude product was purified by flash silica gel chromatography (eluent condition: methanol: ethyl acetate = 1: 10 v/v). Finally, the purified product was further purified by prep-HPLC (C8 column ACN: H₂O= 85: 15 v/v, with 0.1% Formic Acid) to provide 32% yield as white waxy solid.

\[ ^1H \text{ NMR (500 MHz, Chloroform-}d\text{)} \delta 8.92 \text{ (d, J = 2.2 Hz, 2H), 8.17 (s, 1H), 7.90 (t, J = 1.8 Hz, 2H), 7.71 (td, J = 7.5, 7.0, 1.7 Hz, 6H), 7.69 – 7.63 (m, 6H), 7.63 – 7.55 (m, 6H), 7.03 – 6.98 (m, 4H), 4.10 (d, J = 5.6 Hz, 4H), 3.70 – 3.59 (m, 50H), 3.56 – 3.51 (m, 8H), 3.36 (s, 12H), 2.44 (hept, J = 6.0 Hz, 2H).} \]

\[ ^{13}C \text{ NMR (126 MHz, Chloroform-}d\text{)} \delta 158.99, 147.38, 141.96, 140.34, 139.04, 138.50, 136.86, 133.27, 133.05, 129.76, 128.12, 127.69, 127.26, 127.05, 126.32, 126.15, 115.05, 72.06, 70.78, 70.77, 70.75, 70.66, 70.62, 69.49, 66.28, 59.15, 40.08, 27.04. \]

MALDI-TOF mass: m/z calcd. for C₇₇H₁₀₁NNaO₁₈ [M + Na]⁺, 1350.69; found, 1351.87.

**Compound 2.** Compound 2 was prepared by the synthetic method of compound 1 with compound 3 (154.2 mg, 0.228 mmol) and compound 5 (50.0 mg, 0.104 mmol). The crude product was purified by flash silica gel chromatography (eluent condition: methanol: ethyl acetate = 1: 8 v/v). Finally, the purified product was further purified by prep-HPLC (C8 column ACN: H₂O= 85: 15 v/v) to provide 63% yield as white waxy solid.

\[ ^1H \text{ NMR (500 MHz, Chloroform-}d\text{)} \delta 7.92 \text{ (s, 1H), 7.91 (s, 2H), 7.72 (d, J = 8.2 Hz, 4H), 7.69 – 7.63 (m, 10H), 7.59 – 7.53 (m, 7H), 7.00 (d, J = 8.7 Hz, 4H), 4.09 (d, J = 5.7 Hz, 4H), 3.68 – 3.59 (m, 50H), 3.53 (dd, J = 5.8, 3.6 Hz, 8H), 3.36 (s, 12H), 2.44 (hept, J = 6.0 Hz, 2H).} \]

\[ ^{13}C \text{ NMR (126 MHz, Chloroform-}d\text{)} \delta 158.81, 141.88, 141.78, 141.44, 139.98, 139.33, 133.04, 129.30, 127.99, 127.58, 127.06, 126.41, 126.38, 126.24, 126.14, 126.08, 114.90, 71.94, 70.66, 70.64, 70.54, 70.51, 69.37, 66.15, 59.04, 39.96. \]

MALDI-TOF mass: m/z calcd. for C₇₈H₁₀₂NaO₁₈ [M + Na]⁺, 1349.70; found, 1350.27.
2) Synthesis of P1 and P2 at a conventional reaction condition.

Scheme 2: Synthetic method of P1 and P2.

Reagents and conditions: (e) K$_2$CO$_3$, ACN, DCM, 80 °C, overnight, yield, 50%; (f) K$_2$CO$_3$, DMSO, DCM, 70 °C, overnight, yield, 55%.

**P1.** 1-Chloro-2,4-dinitronaphthalene$^{52}$ (100.0 mg, 0.397 mmol) and 2-hexyldecane-1-thiol (153.7 mg, 0.595 mmol) were dissolved in ACN (4.0 ml) and DCM (1.0 ml). K$_2$CO$_3$ (164.2 mg, 1.191 mmol) was added and stirred overnight at 80 °C under Ar atmosphere. After completion of the reaction as monitored by TLC, the reaction mixture was cooled down to room temperature. The resulting mixture was condensed under reduced pressure, and dissolve in DCM. The organic layer was washed with brine and dried over MgSO$_4$ (s). The organic phase was filtered with Celite and the filtrate was condensed in a rotary evaporator. The crude product was purified by flash silica gel chromatography (eluent condition: DCM: hexane 1: 1 v/v) to provide 50% yield as yellow oil.

$^1$H NMR (500 MHz, Chloroform-$d$) $\delta$ 8.91 – 8.86 (m, 1H), 8.62 – 8.58 (m, 1H), 8.40 (s, 1H), 7.93 - 7.85 (m, 2H), 2.93 (d, $J = 6.0$ Hz, 2H), 1.40 – 1.13 (m, 25H), 0.87 (td, $J = 7.0$, 5.6 Hz, 6H). $^{13}$C NMR (126 MHz, Chloroform-$d$) $\delta$ 150.61, 146.42, 136.31, 135.59, 131.60, 129.74, 128.84, 125.66, 124.08, 117.56, 43.09, 38.74, 32.96, 31.87, 31.76, 29.76, 29.70, 29.51, 29.42, 29.26, 26.47, 26.43, 22.67, 22.61, 14.11, 14.07.

**P2.** 4-Methylbenzyle bromide (R$_3$, 17.8 mg, 0.097 mmol) and 2-hexyldecane-1-thiol (30.0 mg, 0.116 mmol) were dissolved in DMSO (1.0 ml) and DCM (0.5 ml). K$_2$CO$_3$ (40.1 mg, 0.290 mmol) was added and stirred at 70 °C overnight under Ar atmosphere. After completion of the reaction as monitored by TLC, the reaction mixture was cooled down to room temperature. The resulting mixture was condensed under reduced pressure, and dissolve in DCM. The organic layer was washed with brine and dried over MgSO$_4$ (s). The organic phase was filtered with Celite and the filtrate was condensed in a rotary evaporator. The crude product was purified by flash silica gel chromatography (eluent condition: ethyl acetate: hexane 1: 20 v/v) to provide 55% yield as a colorless oil.

$^1$H NMR (500 MHz, Chloroform-$d$) $\delta$ 7.19 (d, $J = 8.0$ Hz, 2H), 7.10 (d, $J = 7.8$ Hz, 2H), 3.64 (s, 2H), 2.38 (d, $J = 6.2$ Hz, 2H), 2.32 (s, 3H), 1.49 (p, $J = 6.2$ Hz, 1H), 1.25 (dddd, $J = 26.3$, 20.1, 13.4, 6.8 Hz, 26H), 0.88 (td, $J = 7.0$, 1.8 Hz, 6H). $^{13}$C NMR (126 MHz, Chloroform-$d$) $\delta$ 136.39, 135.67, 129.06, 128.76, 77.27, 77.01, 76.76, 37.57, 36.59, 36.31, 33.22, 31.93, 31.88, 29.95, 29.61, 29.34, 26.60, 26.56, 22.70, 22.68, 21.08, 14.13.
Figure S1. $^1$H and $^{13}$C-NMR spectra of 1 in CDCl$_3$ (with 2 μl triethylamine).
Figure S2. $^1$H and $^{13}$C-NMR spectra of 2 in CDCl$_3$. 
Figure S3. MALDI-TOF-MS spectra of 1 and 2.
Figure S4. $^1$H and $^{13}$C-NMR spectra of P1 in CDCl$_3$. 
Figure S5. $^1$H and $^{13}$C-NMR spectra of P2 in CDCl$_3$. 
Figure S6. UV spectra of 1 (75.3 μM) before (blue dash line) and after (red solid line) addition of R1 (a mole ratio R1/1 of 5:1) in aqueous solution. UV spectra of supernatant after completion of reaction (green solid line) and then neutralization (blue solid line).

Figure S7. FL spectra of 1 (75.3 μM) before (blue line) and after (red line) addition of R1 (a mole ratio R1/1 of 5:1) in aqueous solution. Excitation wavelength: 275 nm.
**Figure S8.** Fluorescence intensity trend at 372 nm of 1 (75.3 μM) addition different mole ratio of R1 in aqueous solution. Excitation wavelength: 275 nm.

**Figure S9.** FT-IR spectra of R1 (grey line), 1 (red dash line), 2 (green dash line), 1 with R1 (red solid line, in a mole ratio R1/1 of 5:1), 2 with R1 (green solid line, in a mole ratio R1/2 of 5:1) in bulky state.
Figure S10. (a) Negatively-stained TEM and (b) cryo-TEM images of 2 (75.3 μM) with addition of R1 (a mole ratio R1/2 of 5:1) in aqueous solution.

Thio-etherification of R1 with 4-methylbenzyl bromide in the presence of 1

Figure S11. (a) Thio-etherification of R1 with 4-methylbenzyl bromide. (b) HPLC chromatograms of reaction product and R1 with time variation. (c) The conversion (●) and disappearance of R1 (▲) as a function of time.
**Figure S12.** Conversion of R1 in the presence of 1 (●) and 2 (▲) for thio-etherification reaction.

**Figure S13.** ¹H-NMR of P1 obtained from the precipitates after completing the reaction (80 min) before purification (up) and after purification (down). This result demonstrates that the precipitated product is not contaminated by 1.
Figure S14. (a) The 2nd cycle HPLC chromatograms for the $S_N$Ar reaction of R1 and R2 in the presence of 1 (inset: R1) with time variation. (b) The conversion (●) and disappearance of R1 (▲) as a function of time.

When added pre-synthesized P1 directly into 1 solution (a mole ratio P1/1 of 5:1) which induced micellar aggregates. Then HCl is added to disassemble with precipitation. The precipitate shows to be pure P1.

Figure S15. $^1$H-NMR of P1 obtained from the aqueous solution of 1 with pre-synthesized P1 after addition HCl. This result shows the potential capability that the reaction, which cannot produce protonic acid, can release the product autonomously.
$S_N\text{Ar}$ reaction with different ratios of the substrates in the presence of 1

**Figure S16.** (a) The conversion of R1 (inset: HPLC chromatograms of reaction) as a function of time. (b) Negatively-stained TEM image after $S_N\text{Ar}$ reaction completion in the presence of 1 (75.3 μM, a mole ratio substrates/1 of 2:1) in aqueous solution. This result demonstrates that the reaction undergoes with less amount of substrates but the structure cannot disassemble after the completion of reaction.

**Figure S17.** (a) The conversion of R1 as a function of time. (b) HPLC chromatograms of reaction product with time variation. (c) $^1\text{H}$-NMR of precipitates obtained from the aqueous reaction solution of 1 with substrates (a mole ratio substrates/1 of 20:1). This result demonstrates that the reaction cannot fully converse with larger ratio of substrate. The precipitate shows mixture of substrates and product.
References