Electronic Supplementary Material (ESI) for Polymer Chemistry.

Supporting Information

Concentration-Directed Morphological Evolution of Boronate Ester-Based Dynamic Covalent Nanoparticles: A Facile Approach for Size and Shape Control

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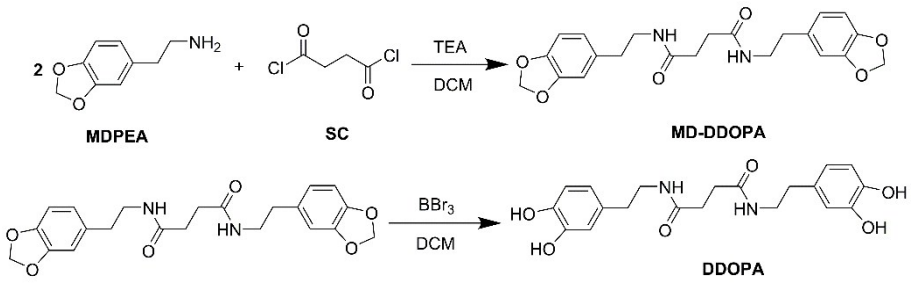
I. Materials

Succinyl Chloride (SC), 3,4-methylenedioxyphenethylamine (MDPEA) and borontribromide (BBr_3) were purchased from Aladdin Industrial Corporation (Shanghai, China). 3-Aminophenylboronic acid monohydrate (3APBA) was purchased from Accela ChemBio Co., Ltd (Shanghai, China). Solvents and inorganic salts were all purchased from Jiangtian Chemical Technology Co., Ltd (Tianjin, China). Dichloromethane (DCM), tetrahydrofuran (THF) and dimethyl sulfoxide (DMSO) were dried by distilling over CaH_2 before used. Other reagents were used without further purification.

II. Experiments

Synthesis of DDOPA

The synthesis of double dopamine monomer (named as DDOPA) referred to Snow's work[1] with a little change. As shown in the **Scheme S1**, there were two steps.



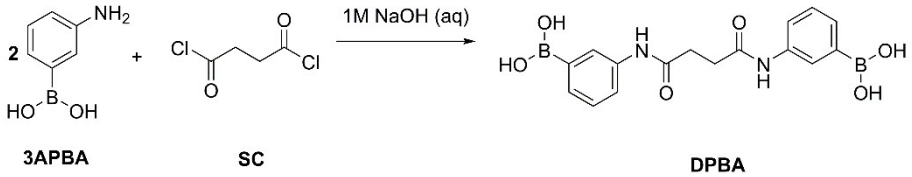
Scheme S1. Synthetic route of DDOPA

The first step was to synthesize protected dicatechols (MD-DDOPA). 3,4-Methylenedioxyphenethylamine (MDPEA, 2.81 g, 17 mmol) and triethylamine (TEA, 2.06 g, 20.4 mmol) were dissolved in dry DCM. Succinyl chloride (SC, 0.75 mL, 6.8 mmol) diluted by dry DCM was added dropwise to the above-mentioned solution at 0 ºC. Then, the mixture was recovered to room temperature and stirred overnight. The crude product was collected by filter and resuspended in ethyl acetate. After washed by dilute hydrochloric acid, saturated sodium bicarbonate solution and distilled water, white solids were obtained (2.08 g, 74%). ^{1}H-NMR spectrum (DMSO-d_6) was shown in **Fig. S2A**.

The second step was deprotection. MD-DDOPA (825 mg, 2 mmol) was suspended in dry DCM, and 5 equiv. of BBr_3 was added slowly in it. After stirred for 6 h, 20 mL HCl (1 M) was added to stop the reaction and the mixture was diluted by 200 mL distilled water. Ethyl acetate was used to extract the product from aqueous solution, concentrated to about 20 mL and precipitated into hexane. The white powders were collected after dried under vacuum (273 mg, 35%).

^{1}H-NMR spectrum (DMSO-d_6) was shown in **Fig. S2B**. ^{13}C-NMR spectrum (CD_3OD) was shown in **Fig. S3**. ESI-MS was shown in **Fig. S4**.

Synthesis of DPBA



Scheme S2. Synthetic route of DPBA

The synthetic route of new double phenylboronic acid monomer (referred to as DPBA) was shown in **Scheme S2**. Simply, 3-Aminophenylboronic acid monohydrate (3APBA, 1.86 g, 12 mmol) was dissolved in 1 M NaOH aqueous solution and cooled down to 0 ºC. Succinyl chloride (SC, 0.33 mL, 3 mmol) was added into the previous solution dropwise with dry THF. The mixture was stirred overnight at room temperature. 1 M HCl was used to adjust solution to pH 2.0 when the crude products were precipitated. Lightly brown crystals were collected after filtered, washed with brine, and recrystallized from deionized water (668 mg, 61%).

^{1}H-NMR spectrum (DMSO-d_6) was given in **Fig. S5**. ^{13}C-NMR spectrum (DMSO-d_6) was shown in **Fig. S6**. ESI-MS was shown in **Fig. S7**.

Synthesis of BDNPs

For easy to control the reaction time, DDOPA and DPBA powders were dissolved separately in dry DMSO as given concentration (1.0 mM, 2.5 mM, 5.0 mM and 10.0 mM), and 10 equiv. of TEA was added in DPBA solution as catalyst. The two kinds of solution were mixed by 1:1 *v/v* and kept in thermostatic bath at predesigned temperature.

NMR Experiment

All ^{1}H-NMR, ^{13}C-NMR and ^{11}B-NMR spectra were recorded on Bruker Avance III 400 (400 MHz, SUI). ^{13}C-NMR spectrum of DDOPA was measured with deuterated methanol (CD_3OD) while other NMR spectra were all measured with deuterated dimethyl sulfoxide (DMSO-d_6).

^{1}H-NMR and ^{13}C-NMR spectra were used to characterize the structure of monomers.

^{11}B-NMR spectra were measured to confirm the formation of boronate ester bonds

under 1.0 mM equimolar initial concentrations after 24 h. DPBA solution (with TEA) under same concentration was measured as control.

^{1}H-NMR experiment was also used to track the reaction process of BDNPs under 2.5 mM equimolar initial concentrations. NMR spectra were recorded at 1 h, 2 h and 12 h after precursor solutions mixed. DDOPA and DPBA solutions were added TEA and measured as control.

ESI-MS Experiment

Electrospray ionization mass spectrometry (ESI-MS) was record on miorOTOF-QII (Bruker Daltonics, US). All data were obtained in positive-ion mode. The flow of drying gas (N_2) was 6 L/min with the temperature of 180 °C. The elution program of HPLC began with a mixture of acetonitrile/methanol, 1:1 (*v*/*v*), at a flow rate of 10 mL/min. Sodium formate (0.024 mM) was added to the solvent to enhance the electrospray ion current.

***In situ* DLS Measurement**

In situ DLS experiments were performed on Zetasizer (Nano ZS, Malvern, UK). Normally, DMSO was filtered with a 220 nm hydrophobic filter before use. Monomer solutions with a certain concentration were mixed in a cuvette and placed into the sample chamber at predesigned temperature. The measurement was conducted at the appointed time with a scattering angle of 173°.

TEM Observation

The morphologies of BDNPs were observed by transmission electron microscopy (TEM, JEM100CXII, JP). TEM samples were prepared by dropping the solution of BDNPs on the carbon coated grids and excessed solvent was absorbed by filter paper. Then, the samples were dried in vacuum at room temperature. The sampling time coordinated with the DLS results and shown in figures. Size distributions were analyzed by counting 50 particles from TEM images.

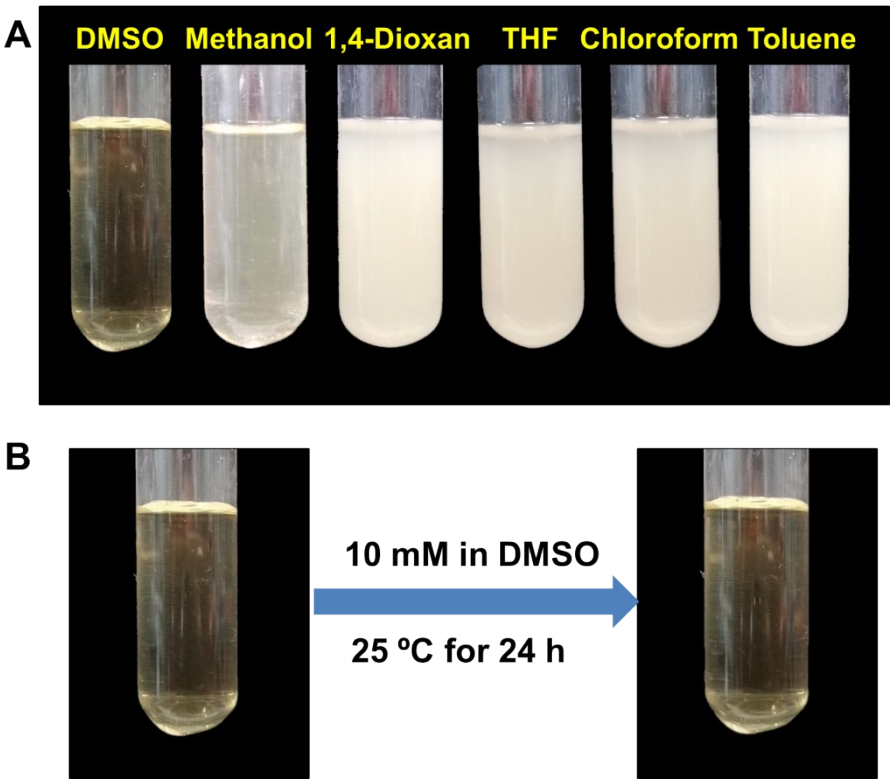


Fig. S1. Photos of precursor monomers (**A**) dissolved in different solvents and (**B**) before and after reacted for 24 h in DMSO. (The initial concentrations of precursor monomers were 10.0 mM with 10 equiv. of TEA as catalyst).

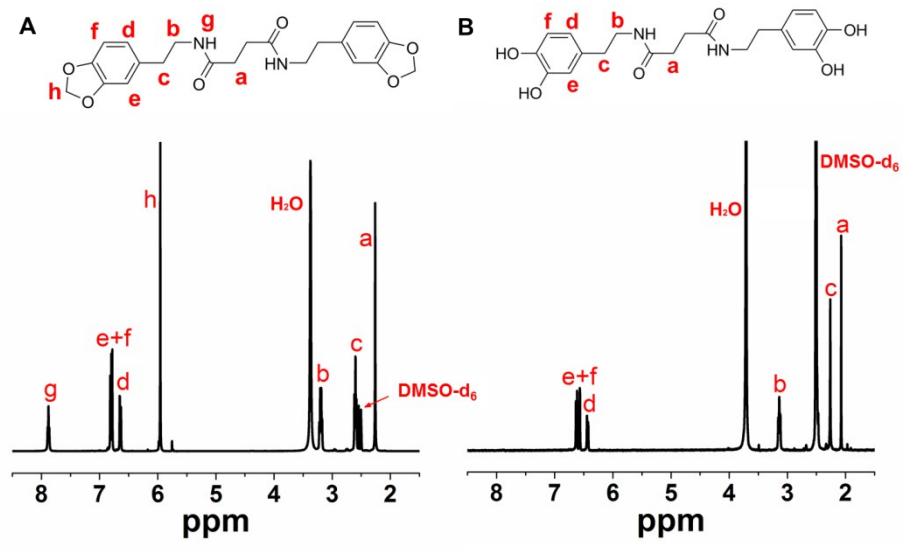


Fig. S2. ^{1}H-NMR spectra of MD-DDOPA (**A**) and DDOPA (**B**) in DMSO-d_6.

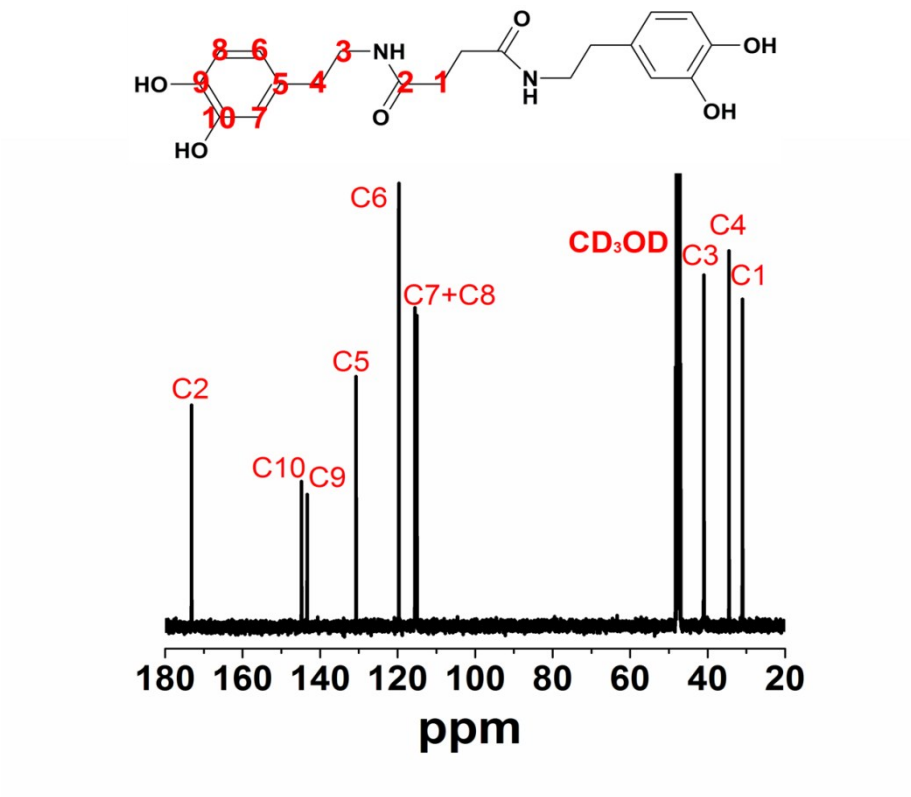


Fig. S3. ^{13}C-NMR spectrum of DDOPA in CD_3OD.

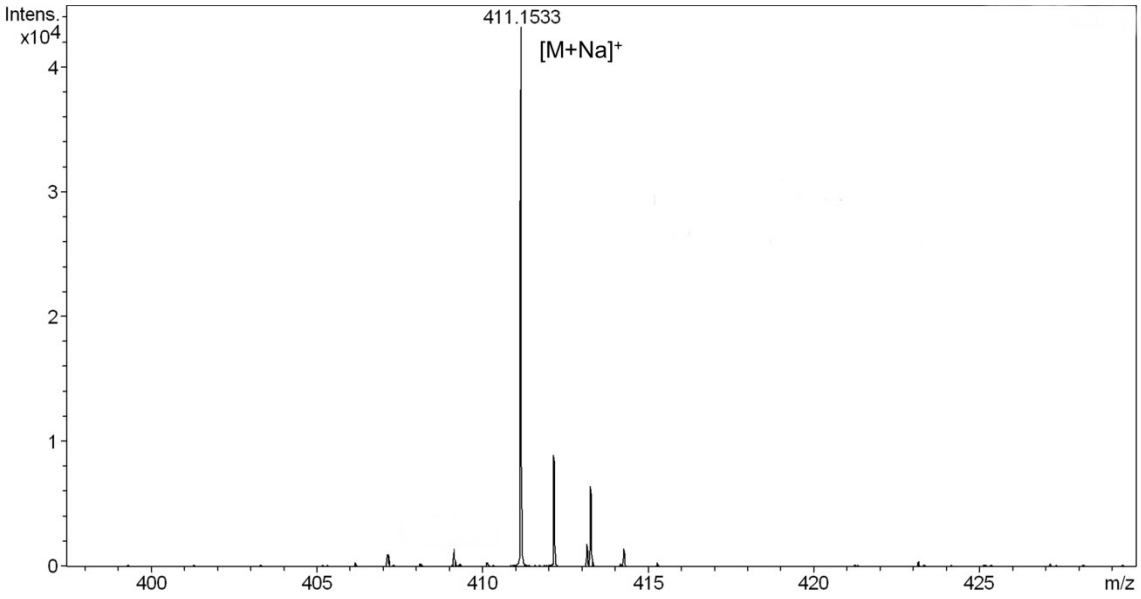


Fig. S4. ESI-MS data of DDOPA. The m/z 411.1533 ions stand for $[M+Na]^+$.

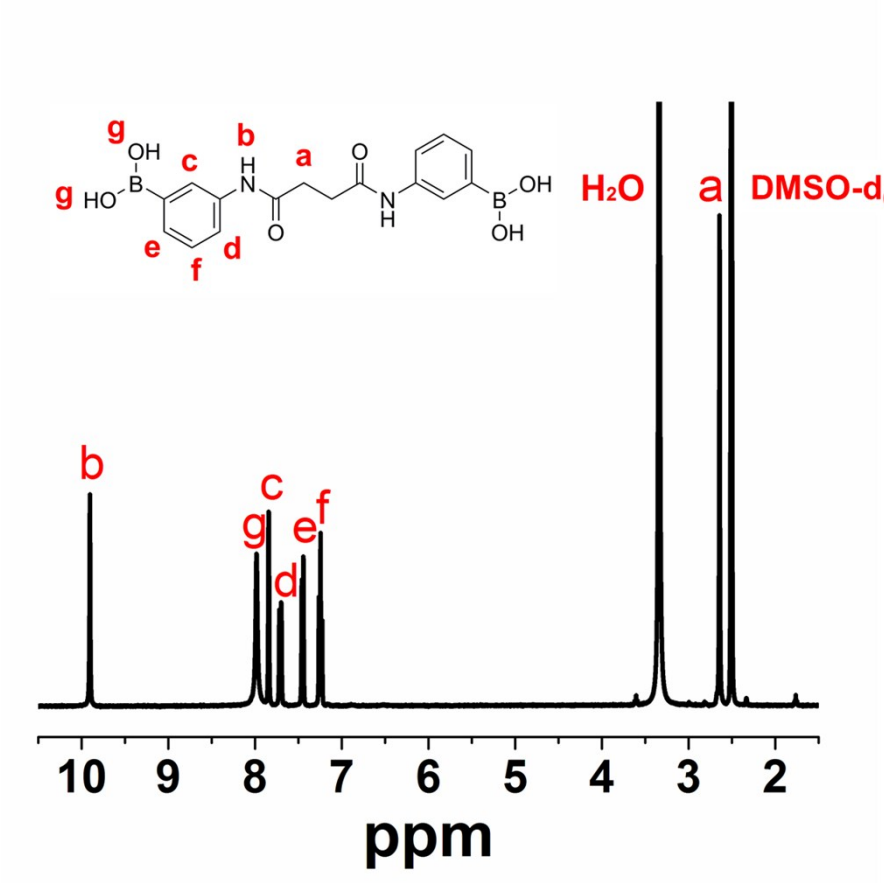


Fig. S5. ^{1}H-NMR spectrum of DPBA in DMSO-d_6.

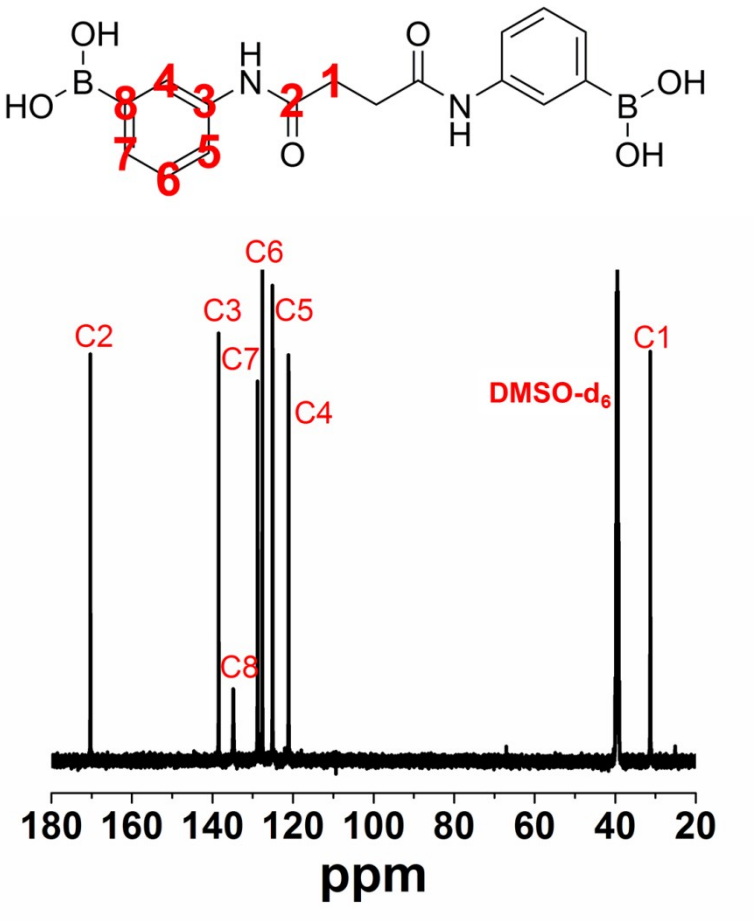


Fig. S6. ^{13}C-NMR spectrum of DPBA in DMSO-d_6.

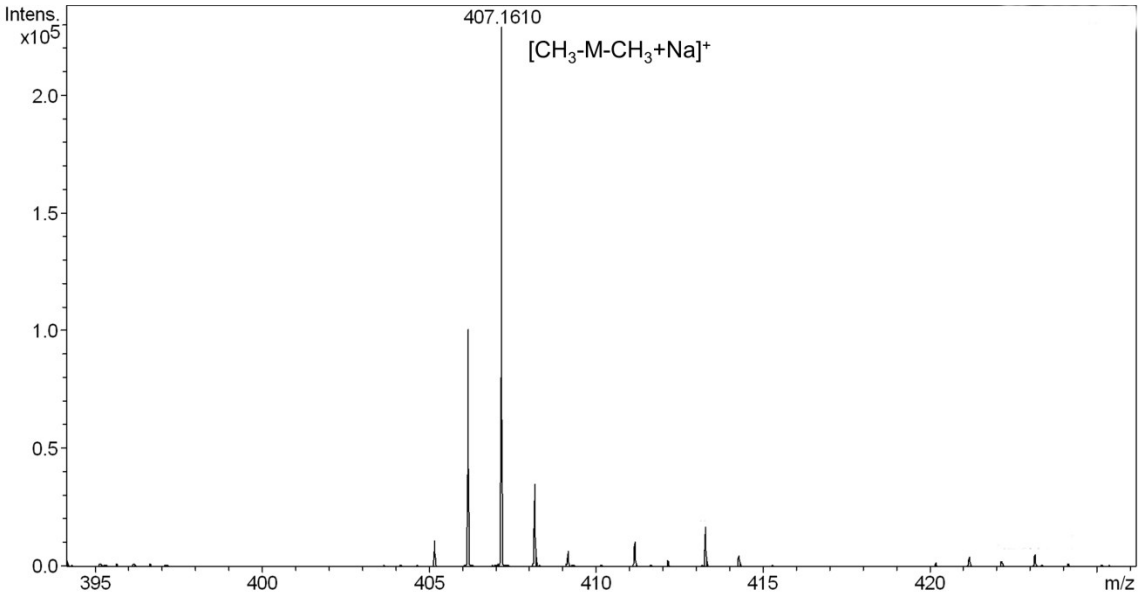


Fig. S7. ESI-MS data of DPBA. The m/z 407.1610 ions stand for $[CH_3\text{-M-}CH_3+Na]^+$. Boronic acid monomers can combine with the methanol in the eluent in the production of ionic vaporization (180 °C).

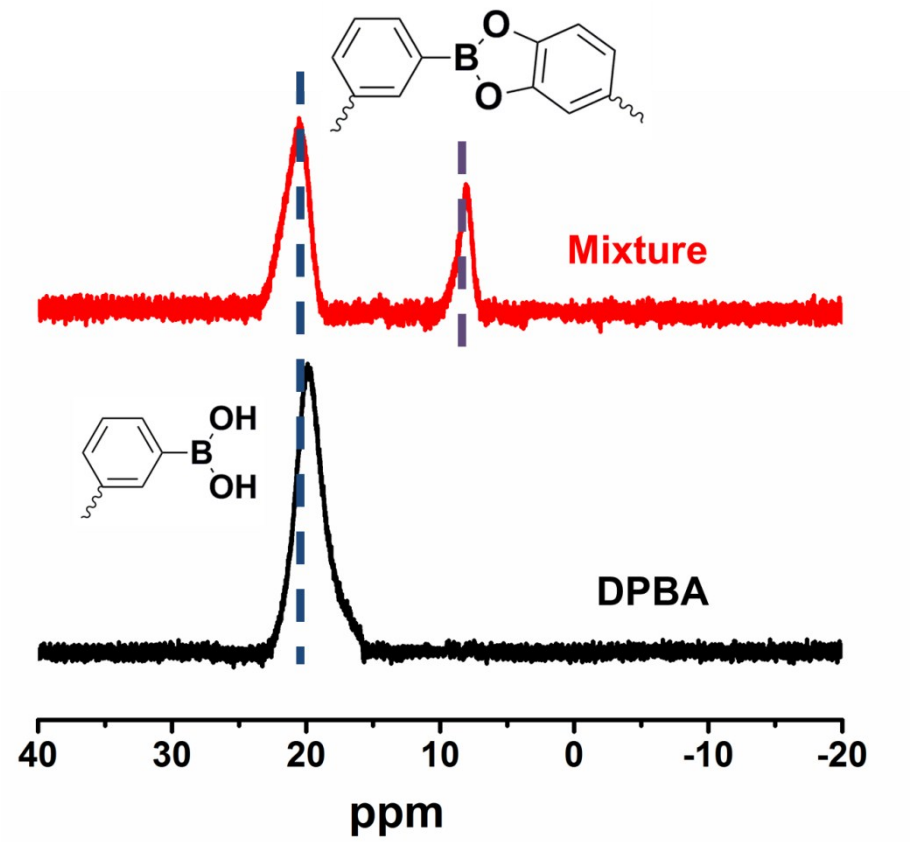


Fig. S8. ^{11}B-NMR spectra of DPBA and reaction mixture incubated for 24 h in DMSO-d_6 under 1.0 mM equimolar initial concentrations

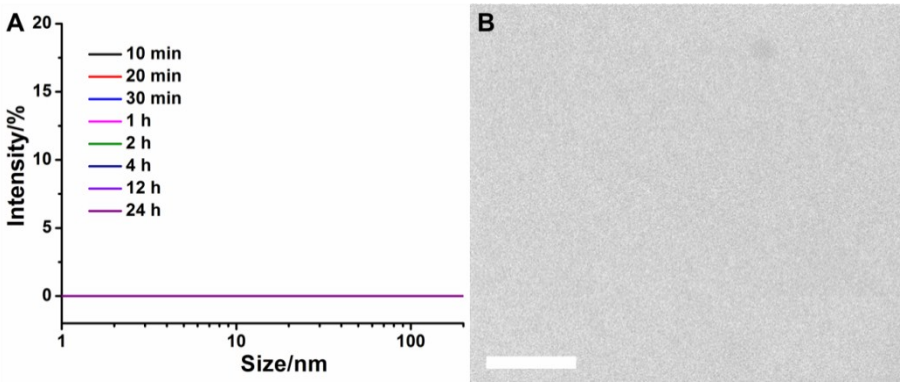


Fig. S9. *In situ* DLS measurements of BDNPs formation under 1.0 mM equimolar initial concentrations (**A**) and TEM detection at 24 h (**B**). The scale bar is 0.5 μm.

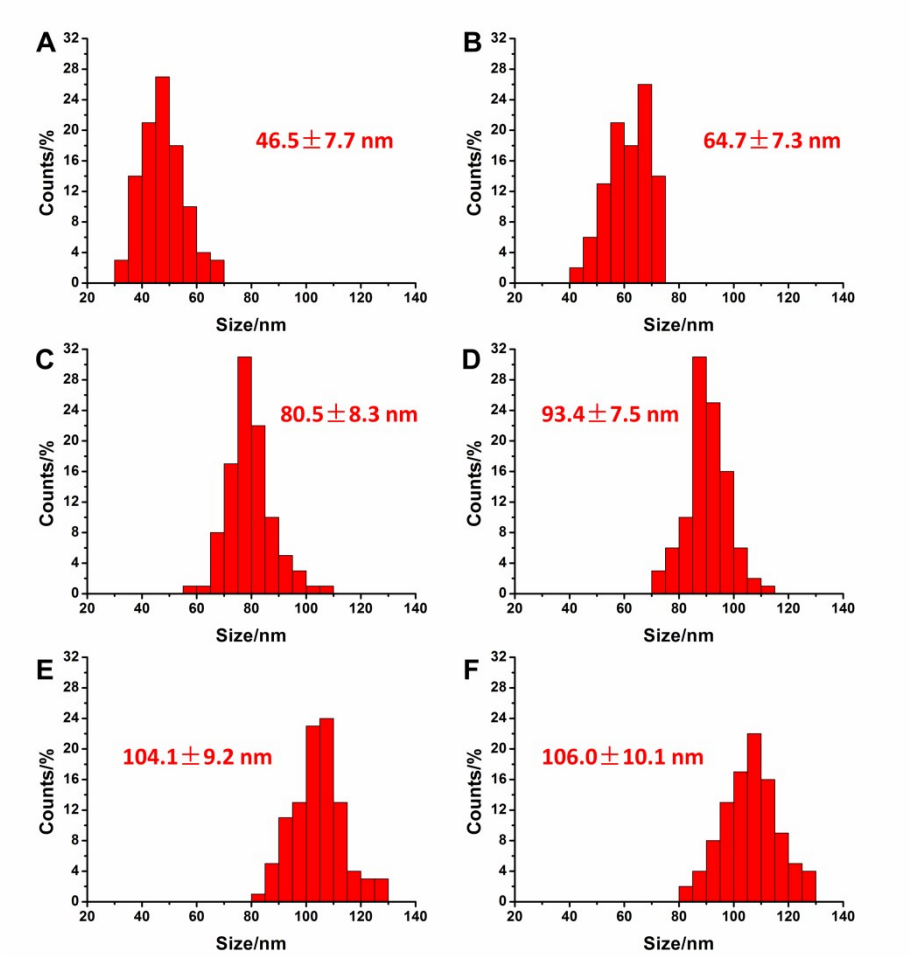


Fig. S10. Histograms of the size distributions of BDNPs from TEM images under 2.5 mM equimolar initial concentrations with different time: (**A**) 2 h; (**B**) 4 h; (**C**) 8 h; (**D**) 10 h; (**E**) 12 h; (**F**) 24 h.

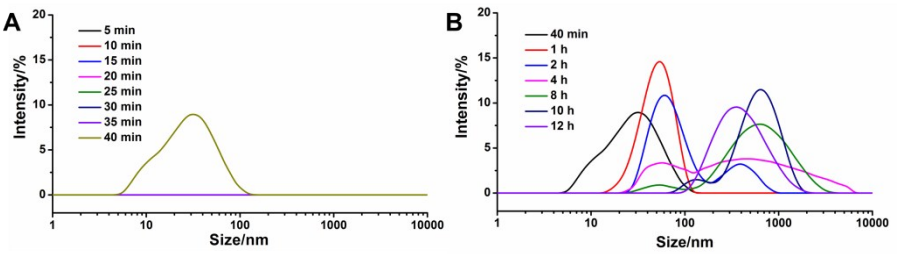


Fig. S11. *In situ* DLS measurements of BDNPs formation process before (**A**) and after nucleation (**B**) under 10.0 mM equimolar initial concentrations.

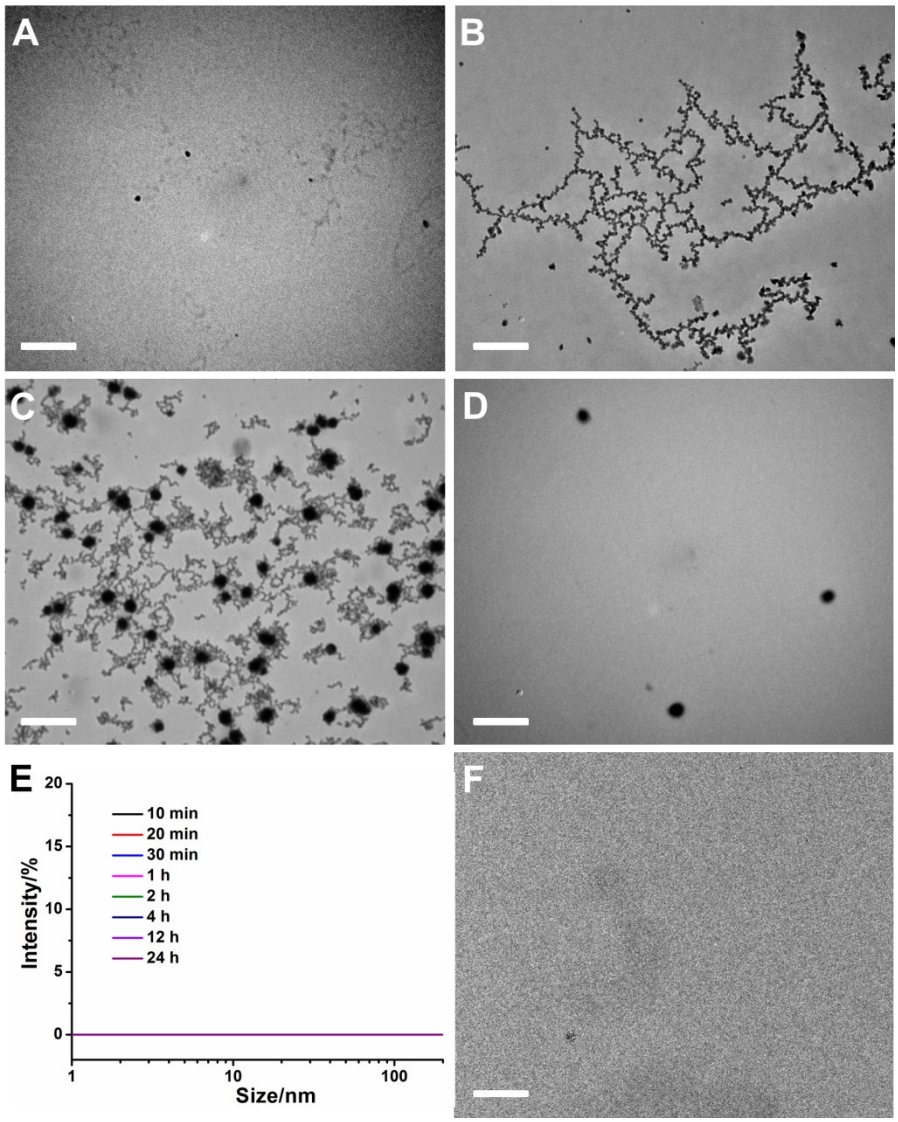


Fig. S12. Typical TEM images of BDNPs collected at 1 h (**A**), 8 h (**B**), 10 h (**C**) and 12 h (**D**) at 35 ºC; *In situ* DLS measurements of BDNPs formation process at 50 ºC (**E**); TEM image (**F**) of BDNPs formed at 50 ºC after 24 h. The initial concentrations of precursor monomers were 5.0 mM. The scale bars are all 0.5 μm.

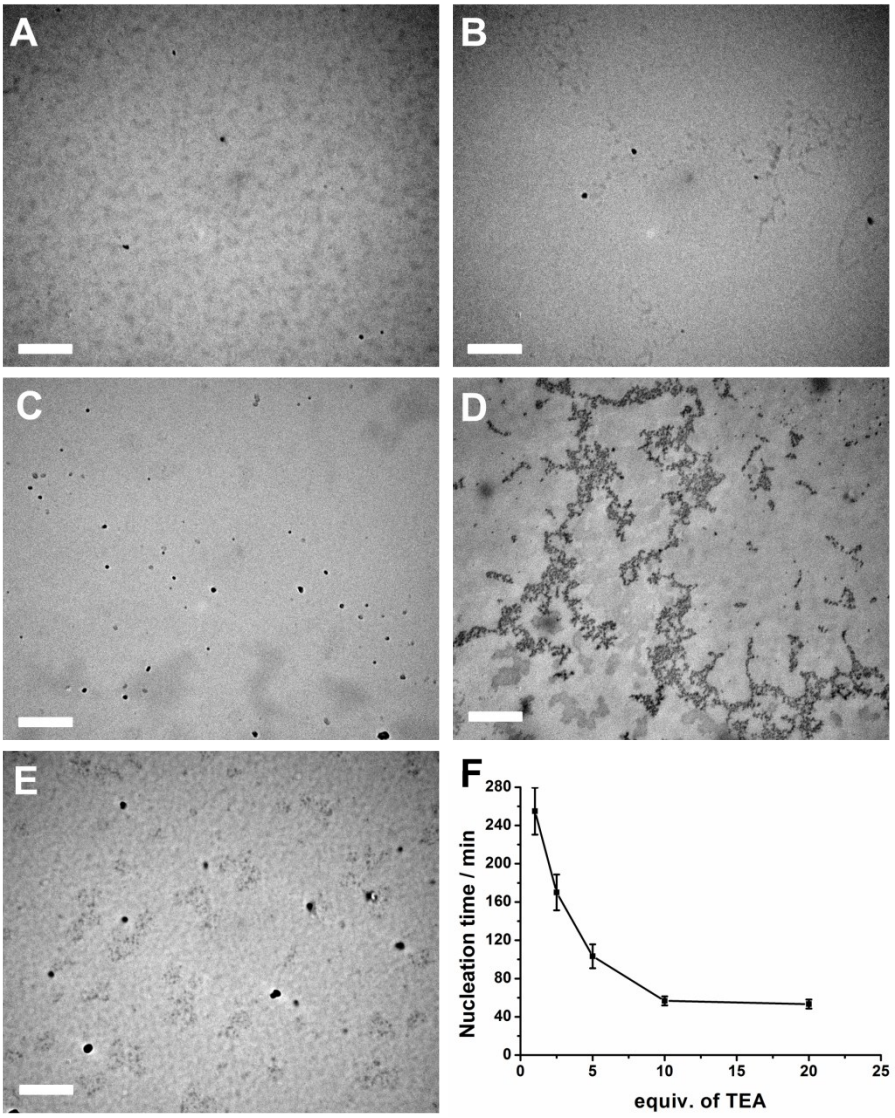


Fig. S13. Typical TEM images of BDNPs formed with 5 equiv. of TEA collected at 2 h (**A**), 4 h (**B**), 8 h (**C**), 12 h (**D**) and 24 h (**E**), which were similar to those formed with 10 equiv. of TEA but with a little lag. The scale bars are all 0.5 μm. Impact of TEA concentration on nucleation time (**F**). All the initial concentrations of precursor monomers were 5.0 mM.

III. References

1. *U.S. Pat*., 7514583, 2009.