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Supramolecular Reactor from Self-Assembly of Rod−Coil Molecule in Aqueous Environment

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Rod−coil molecules, consisting of a flexible and a rigid block, represent a unique class of block copolymers, where the anisotropic orientation of the rod segments and the repulsion between the covalently connected segments lead to self-organization into a wide variety of aggregation structures.[1] The supramolecular structures can be tuned by careful selection of the type and relative length of the respective blocks. Another interesting feature of rod−coil molecules is their amphiphilic characteristic that shows a tendency of their lipophilic and lipophobic segments to separate in space into distinct nanodomains.[2] Depending on the solvent content and polarity, rod−coil molecules self-assemble into a wide variety of different aggregation structures through mutual interactions between block segments and solvent.

One can envision that rod−coil amphiphilic molecules based on a hydrophilic poly(ethylene oxide) as a flexible chain self-assembles into micellar aggregates in aqueous environment.[3] The resulting hydrophobic aromatic core of the aggregates would provide a nanoenvironment suitable for the confinement of nonpolar aromatic guest molecules through intermolecular interactions including hydrophobic interactions and $\pi-\pi$ interactions. Accordingly, micellar aggregates of amphiphilic rod−coil molecules based on poly(ethylene oxide) coils raise the possibility of the use as containers for aromatic coupling reactions in aqueous media (Figure 1).

With this in mind, we prepared rod−coil triblock molecule **1** consisting of poly(ethylene oxide) with the number of repeating units of 17 as coil segments and hexa-*p*-phenylene as a rod segment and investigated the Suzuki aromatic coupling reactions in aqueous environment at room temperature. The rod−coil molecule was synthesized using similar procedures reported previously from our laboratory.[4] All of the analytical data, including NMR, GPC, and elemental analysis, are in full agreement with the chemical structure presented. This amphiphilic molecule based on an elongated rod shows aggregation behavior in aqueous media. Dynamic light scattering studies of aqueous solutions showed that the rod−coil molecule self-assembles into micellar aggregates (Figure 2a). The average hydrodynamic radius (R_H) of the aggregate was observed to be approximately 6 nm, suggesting that the micelles consist of hydrophobic disklike rod bundles encapsulated by hydrophilic poly(ethylene oxide) coils, as proposed by rod−coil theories.[5,6] The formation of micellar aggregates of **1** was also confirmed by FE-SEM and TEM experiments, which show spherical entities. As shown in Figure 2, parts b and c, the micrographs show spherical aggregates that are roughly 9−15 nm in diameter and are thus consistent with the results obtained from dynamic light scattering experiments.

The use of the resulting aggregate as a supramolecular reactor for an aromatic coupling reaction in aqueous media was investigated with the Suzuki cross-coupling reaction of aryl halides and aryl boronic acids at ambient temperature.[7] As shown in Table 1, the cross-coupling reactions of iodobenzenes with 1.2 equiv of phenylboronic acids took place in the presence of 0.5 mol % palladium catalyst and 2 equiv of NaOH in a 2.5 × 10^{-3} M aqueous solution of **1** to give the corresponding products with nearly quantitative conversion after 12 h. Under similar conditions, the coupling reactions of a wide range of bromobenzenes including electron-rich and electron-deficient substrates also underwent with quantitative conversion (entries 4−6), clearly demonstrating that the cross-coupling reaction in the presence of **1** is highly effective and allows for the room temperature cross-coupling reaction in aqueous media. Remarkably, the cross-coupling reaction of aryl chloride, which is generally unreactive under the conditions employed to couple aryl bromides and aryl iodides,[8,9] also proceeded under similar room-temperature conditions to afford the corresponding biphenyl in 72% yield (entry 7). It should be noted that, in the presence of conventional non-ionic amphiphile (entry 10) or organic solvent instead of **1** (entry 11), no reactions take place under the aforementioned reaction conditions, indicating that the presence of a bundle-like aromatic core of the aggregate plays a key role in the room-temperature coupling reaction in aqueous environment.

Although the definitive mechanistic details of the reactions still remain to be solved, we believe that these results indicate clearly that the amphiphilic rod−coil system is well-suited as a supra-

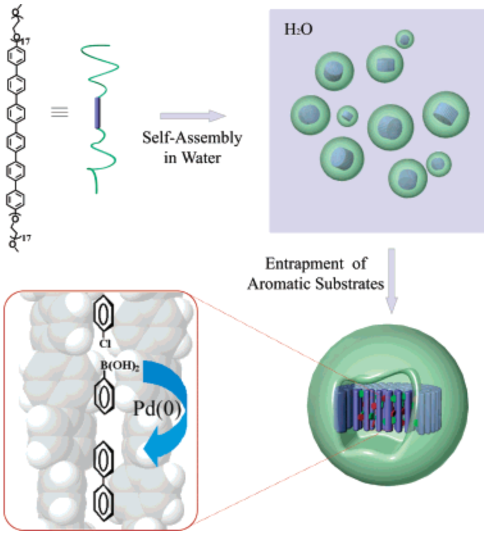

Figure 1. Schematic representation of supramolecular reactor.

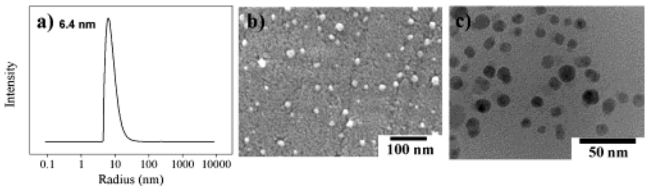

Figure 2. (a) Dynamic laser light scattering. (b) Scanning electron micrograph. (c) Transmission electron micrograph of **1** (2 × 10^{-4} g/mL in H_2O).

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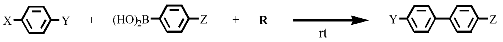
Table 1. Suzuki Cross-Coupling Reaction in Water[a]



entry	X	Y	Z	R	yield (%)[b]
1	I	NO_2	H	1	99
2	I	H	OCH_3	1	99
3	I	OCH_3	H	1	99
4	Br	NO_2	H	1	99
5	Br	H	OCH_3	1	99
6	Br	OCH_3	H	1	99
7	Cl	NO_2	H	1	72
8	Cl	H	OCH_3	1	17
9	Cl	OCH_3	H	1	15
10	Br	OCH_3	H	non-ionic surfactant[c]	no reaction
11	Br	OCH_3	H	THF[d]	no reaction

[a] Reaction conditions: aryl halide (0.1 mmol), aryl boronic acid (0.12 mmol), $Pd(OAc)_2$ (0.5 mol %), PPh_3 (1.0 mol %), NaOH (0.2 mmol), **R** (50 mg, 0.025 mmol), and H_2O (10 mL), stirred at room temperature for 12 h. [b] Percent yields are calculated on the basis of GC analysis using xylene as the internal standard. [c] Polyethylene-*block*-poly(ethylene glycol) ($M_n = 920$, 50 wt % ethylene oxide). [d] THF 5 mL.

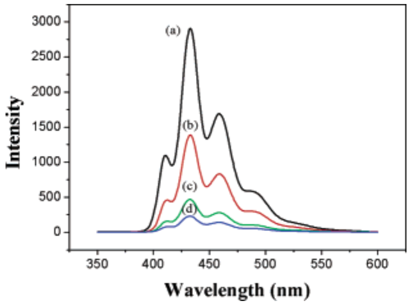


Figure 3. Emission spectra of **1** (2×10^{-4} g/mL in H_2O) by (a) added or (b) no phenyl boronic acid (0.4 mg), (c) triphenyl phosphine (0.4 mg), and (d) 1-bromo-4-nitrobenzene (0.4 mg). Excitation wavelength, 333 nm.

molecular reactor for room-temperature aromatic coupling in aqueous environment. These results can be rationalized by considering the confinement of aromatic substrates by the rod bundles in aqueous environment.[10] With amphiphilic rod−coil molecule in aqueous media, aromatic substrates will be entrapped in the rod bundle that provides a nanoenvironment suitable for the confinement of aromatic substrates through intermolecular interactions, including hydrophobic interactions and $\pi-\pi$ interactions. Within the confined environment of the aromatic core of the micelle, the aromatic substrates might be held in enforced proximity to each other. As a result, this constrained environment would lead to a highly concentrated reaction site that lowers the energy barrier for the Suzuki aromatic coupling reaction.

Entrapment of the aromatic substrates within the aromatic bundles was confirmed with aryl halides, boronic acids, and triphenyl phosphine, respectively, in aqueous solution of **1** by using fluorescence spectroscopy (Figure 3). The emission spectrum of the rod−coil molecule in aqueous solution excited at 333 nm exhibited, in the absence of the aromatic substrates, a strong fluorescence with a maximum at 432 nm. In great contrast, the fluorescence intensities of the aqueous rod−coil solutions containing the aromatic substrates were showed to be significantly suppressed because of fluorescence quenching,[11] demonstrating that they are effectively entrapped within the aromatic bundle of micelle composed of rod−coil building blocks. These results strongly support that the Suzuki coupling reaction occurs within the confined environment of the aromatic bundle of the aggregates. The results described here represent a significant example that self-assembly of amphiphilic rod−coil molecules can provide a useful strategy to construct an efficient supramolecular reactor for aromatic coupling reaction.

In conclusion, we have demonstrated that self-assembly of amphiphilic rod−coil molecules in aqueous solution can be used as a supramolecular reactor for the room temperature Suzuki coupling of a wide range of aryl halides, including even aryl chloride with phenyl boronic acids in the absence of organic solvents, giving rise to an environmentally friendly reaction system. We believe that this supramolecular approach to reactor in aqueous environment will be broadly applicable to a wide variety of catalytic coupling reactions.

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Supporting Information Available: Detailed synthetic procedures, characterization, and UV−vis spectra (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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