Supporting information

for

Theoretical study on substituent and solvent effects for nanocube formed with gear-shaped amphiphile molecules

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1. The value of the GAFF and RESP charge for 1

The parameters of General Amber Force Field (GAFF)[8] and Restrained Electrostatic Potential (RESP) charge[9] for each atom of methylated gear-shaped amphiphile molecule (**1**) are shown in Table S1, where the numbers of atom are in Fig. S1. In the case of demethylated gear-shaped amphiphile molecule (**2**), the methyl groups are replaced to the hydrogen atoms where the GAFF parameters are set to "ha".
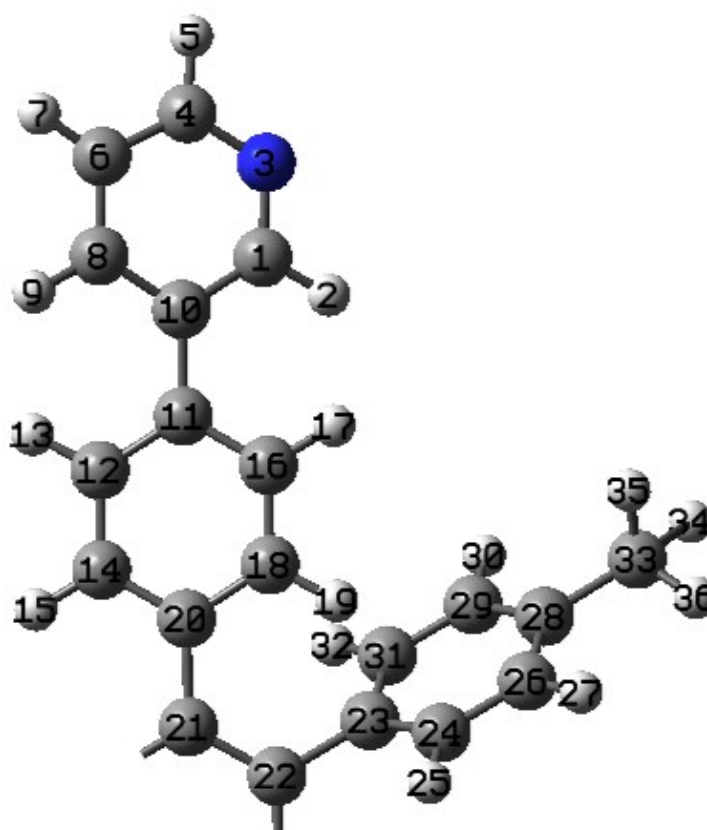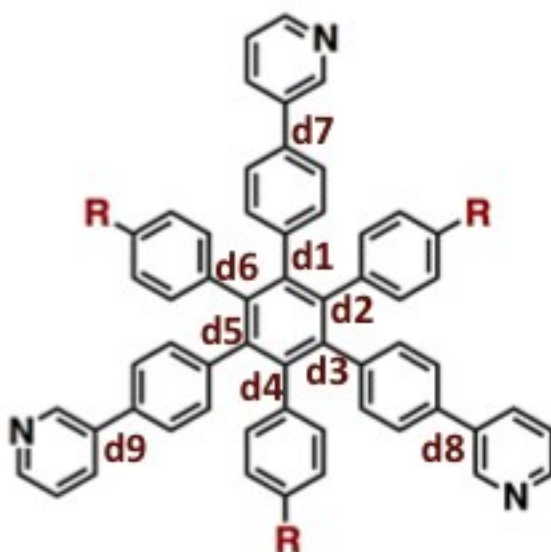

Figure S1 The label of a part of gear-shaped amphiphile molecule for **1**.

Table S1 The value of GAFF and charges of a part of for **1**.

	GAFF	RESP	Mulliken	ESP
1	ca	0.2716	0.057	0.440
2	h4	0.0739	0.200	0.038
3	nb	-0.5861	-0.518	-0.636
4	ca	0.2900	0.064	0.454
5	h4	0.0731	0.201	0.042
6	ca	-0.3305	-0.259	-0.545
7	ha	0.1535	0.210	0.205
8	ca	-0.0229	-0.150	0.178
9	ha	0.1386	0.219	0.097
10	ca	-0.0120	-0.058	-0.237
11	ca	-0.0513	0.017	-0.014
12	ca	-0.1647	-0.216	-0.122
13	ha	0.1263	0.206	0.136
14	ca	-0.0762	-0.183	-0.277
15	ha	0.1166	0.205	0.156
16	ca	-0.1647	-0.216	-0.085
17	ha	0.1263	0.210	0.124
18	ca	-0.0762	-0.183	-0.294
19	ha	0.1160	0.205	0.162
20	ca	0.0237	0.002	0.344
21	ca	-0.0158	-0.034	-0.170
22	ca	-0.0102	-0.025	-0.008
23	ca	0.0048	-0.009	0.075
24	ca	-0.1223	0.179	-0.114
25	ha	0.1263	0.200	0.133
26	ca	-0.2206	-0.226	-0.355
27	ha	0.1468	0.195	0.178
28	ca	0.1278	0.044	0.354
29	ca	-0.2206	-0.226	-0.383
30	ha	0.1468	0.195	0.183
31	ca	-0.1223	-0.179	-0.071
32	ha	0.1263	0.044	0.123
33	c3	-0.1668	-0.507	-0.400
34	h3	0.0580	0.182	0.106
35	h3	0.0580	0.174	0.108
36	h3	0.0580	0.174	0.113

2. The values of the dihedral angles between benzene-pyridine ring

We have also performed the geometry optimization of a hexamer of gear-shaped amphiphile molecules with the density functional theory (DFT) at the ωb97xd/cep-4g* level[9] with the constraint of S_6 symmetry. The optimized structure calculated by GAFF is quite similar to those by HF and DFT. However, a small difference was found at the dihedral angle value between benzene-pyridine rings. The dihedral angles as shown in Fig. S2 for minimized structure of molecule **1** by GAFF, DFT, and the X-ray experimental crystal straucture[2] are shown in Table S2. We note here that these values by GAFF are in reasonable agreement with those by DFT and the experimental structure, although the dihedral angles of benzene-pyridine rings (d7, d8, and d9) with GAFF are smaller than those values.

Figure S2   The label of dihedral angle for gear shaped amphiphile molecule.

Table S2　The values of dihedral angle between **Py** and benzene for gear shaped amphiphile molecule **1** (degree).

|	d1	d2	d3	d4	d5	d6	d7	d8	d9
GAFF	57.2	56.4	54.9	53.2	55.6	55.3	16.7	0.8	2.1
DFT	72.3	89.8	47.6	63.5	66.7	87.6	32.9	30.2	40.4
exptl.[2]	78.8	72.5	75.7	89.6	87.1	89.0	44.2	42.8	39.5

The Coulomb interaction energy between all atoms and all methyl groups of nanocube $\mathbf{1}_6$ is also shown in Table S3. These Coulomb interactions are almost the same values around -14 (kcal/mol). We note here that our minimized structures of the nanocubes $\mathbf{1}_6$ and $\mathbf{2}_6$ are not complete cubic and, hence, do not keep a C_3 symmetry.

Table S3   The values of partial Coulomb interaction energy for all methyl groups which received from all atoms (kcal/mol).

| No. of molecule	No. of substituents	Energy (kcal/mol)
1	1	-14.5
1	2	-14.2
1	3	-14.3
2	1	-14.4
2	2	-14.3
2	3	-14.4
3	1	-14.4
3	2	-14.2
3	3	-14.4
4	1	-14.4
4	2	-14.2
4	3	-14.4
5	1	-14.5
5	2	-14.2
5	3	-14.4
6	1	-14.5
6	2	-14.2
6	3	-14.5

3. The results for all RMS*d*

In order to quantify the overall fluctuations of nanocube 1_6 structure, we analyzed the root mean square deviation (RMS*d*). The RMS*d* measures the deviation of a target set of nanocube structure to a reference set of the average nanocube 1_6 structure. We have employed the independent 60 production runs for both substituents (1_6 and 2_6) in each solvent (pure water, aqueous methanol, and pure methanol). One RMS*d* in each solvents is shown in Figure 2. Other nine RMS*d*s in pure water (Figure S3(a)), aqueous methanol (b), and pure methanol (c). The structures of 1_6 were maintained in all trajectories during 2 nsec.
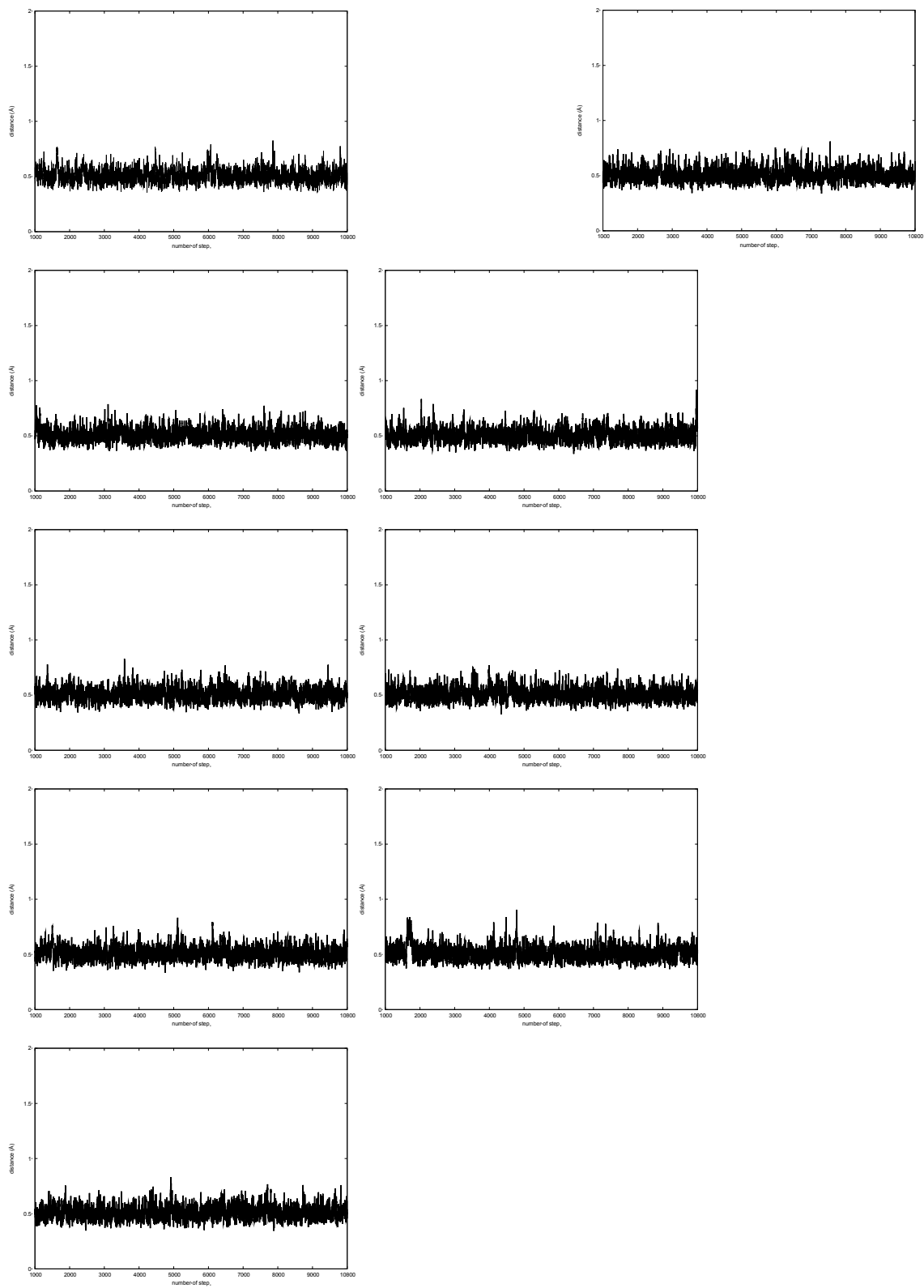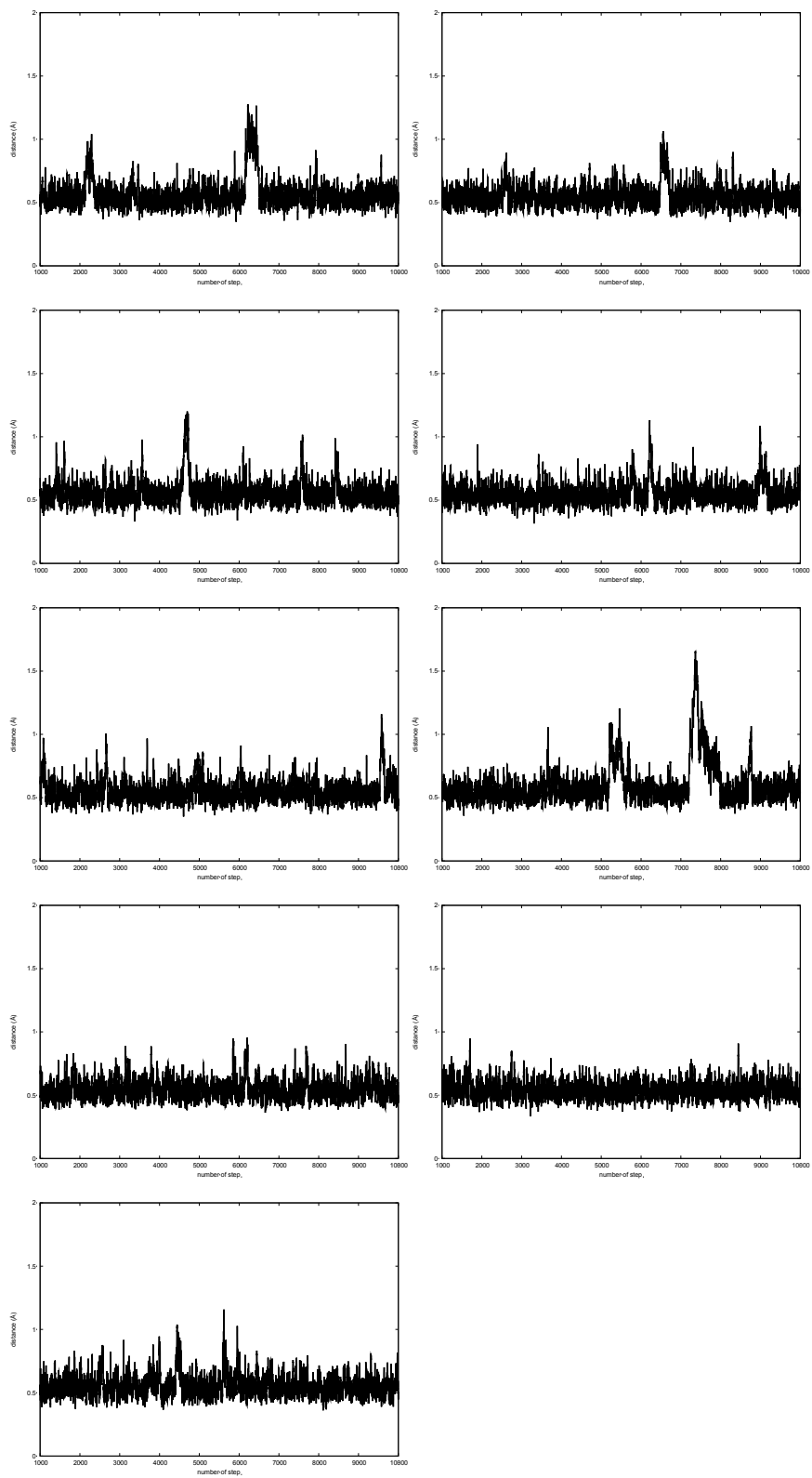
Figure S3(a)   The RMS*d*s for nine trajectories of **1**$_6$ in pure water.
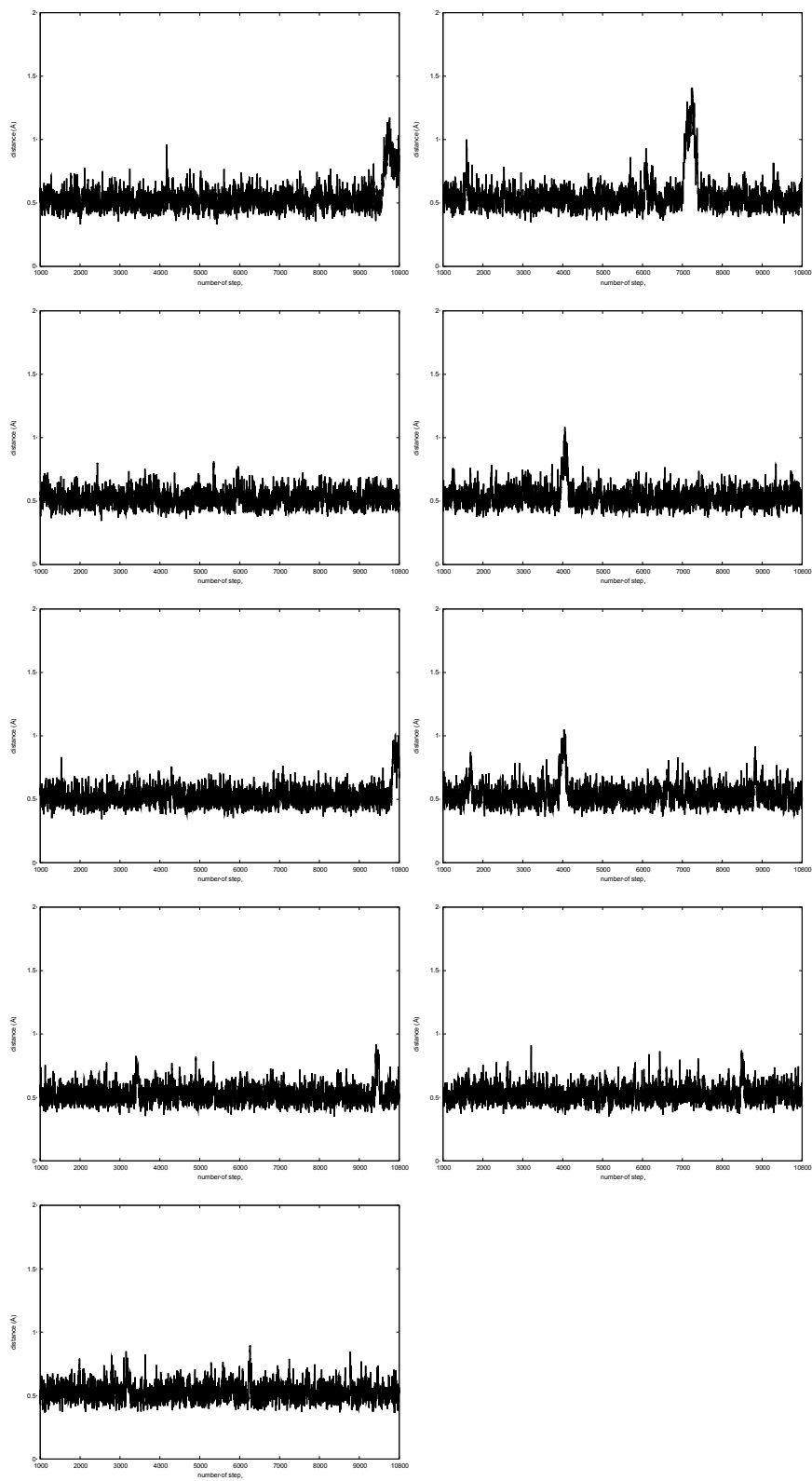
**Figure S3(b)** The RMS*d*s for nine trajectories of 1_6 in aqueous methanol.

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Figure S3(c) The RMS*d*s for nine trajectories of **1**$_6$ in pure methanol.

4. The PCA for 1_6

In order to separate the overall motion into uncorrelated characteristic components, we carried out the principal components analysis (PCA). The PCA modes with low frequency have intermolecular motions representing a distortion of the nanocube. Previous studies in the gas phase[5(b)], pure water[6(a)] and pure methanol[6(b)] solvents indicated that the nanocube 2_6 was fluctuated more than the nanocube 1_6. In order to pick out the independent principal components from the trajectory, we have carried out the PCA. To explain substituent effect, we have already carried out the PCA in pure water[6(a)].

The most dominant PCA mode for 1_6 in all the solvents are fluctuating around averaged distance for example all center of distance between **Py-Py** or **Py**-Me. And then structure 1_6 is maintained cube shape. The difference between 1_6 and 2_6 for all solvent is also same tendency for previous work in pure water[6(a)]. For low-frequency PCA modes in all solvents, there are three quasi-degenerated intermolecular stretching modes along the C_3 axis (Figure S4(a)) and two quasi-degenerated intermolecular rotational modes (Figure S4(b)). The lowest and second lowest frequency modes for 1_6 are quasi-degenerated, which are the intermolecular stretching mode. The lowest frequency for 2_6 only has the rotational mode. Molecule **2**, which is the component of 2_6, is connected with **Py**1 of 2_6 only. So all the **2**s can rotate in 2_6. On the other hands, CH-π chain restricts the intermolecular rotational motion of each molecule **1**. Therefore, these intermolecular interactions are indispensable for the stability of the nanocube.
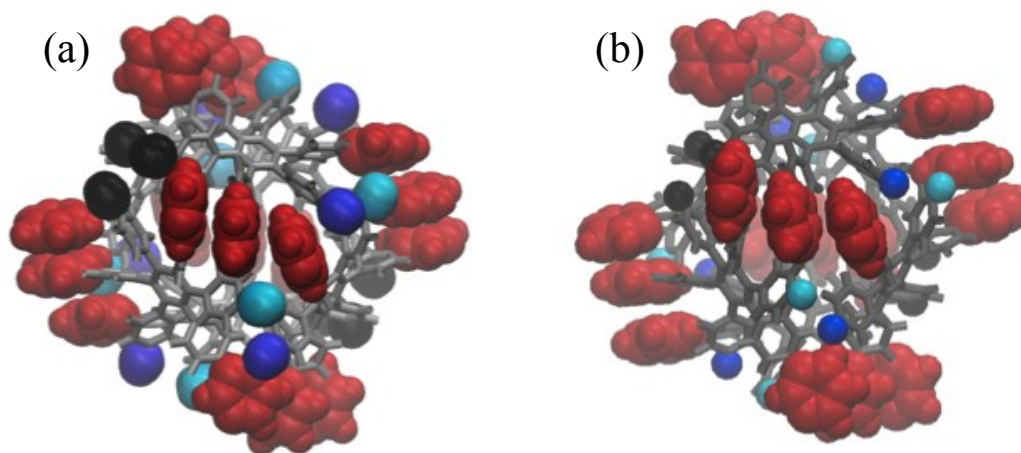
Figure S4   Structural fluctuation of lowest frequency mode for 1_6 and 2_6 around substituent groups by principal components analysis (PCA). Red moieties represent 3-pyridyl groups. Blue, black, and cyan moieties represent R1, R2, and R3 for the substituent groups (= CH_3 and H), respectively.

5. The RDFs for all solvents

In Figure S5(a), three RDFs of N1-Ow, N2-Ow, and N3-Ow with the solid, dashed, and dotted lines, respectively, for ten trajectories. The distances for the first and second peaks of Nn-Ow (n = 1, 2, and 3) are found to be at 2.85 and 4.85 Å, respectively. The Nn in 1_6 has direct hydrogen bonding with water molecules, which forms solvation shell. The intensity of the first peak of N1-Ow is lower than those of N2-Ow and N3-Ow. Next, we focus on the more detailed solvent distribution around methyl groups. Figure S5(b) indicates the three RDFs of Men-Ow (n = 1, 2, and 3) with the solid, dashed, and dotted lines, respectively, for ten trajectories. The shapes of these RDFs are quite similar to that of our previous work[6(a)]. The 1st peaks for three RDFs are at the same position of 3.95 Å in pure water, while experimentally three methyl groups of 1_6 are chemically inequivalent by ^{1}H-NMR in aqueous methanol[4(a), (b)].
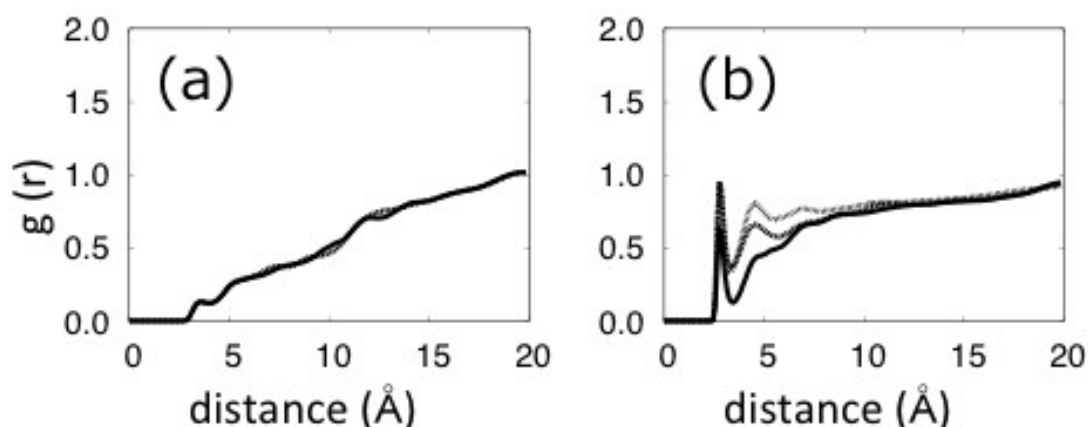
Figure S5 The radial distribution functions (RDFs) of intermolecular nanocube 1_6-water in pure water for (a) C1-Ow and C2-Ow, (b) N1-Ow, N2-Ow, and N3-Ow, where Ow is oxygen atom in water molecule. The labels of C1 (solid line) and C2 (dashed line) are for carbons on the hydrophobic surface of nanocube 1_6, N1 (solid line), N2 (dashed line), and N3 (dashed spaced line) for nitrogen atoms of **Py**s. The details for these labels are shown in Figure 1.
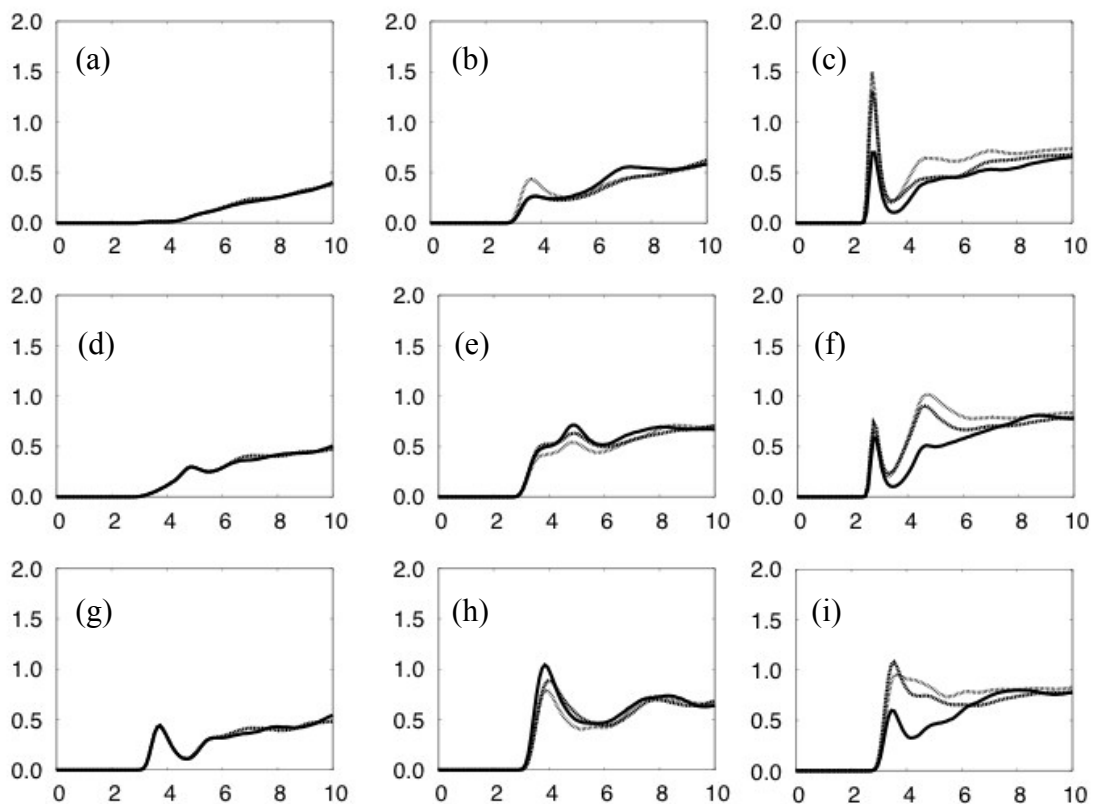
Figure S6 The RDFs of intermolecular nanocube 1_6 in aqueous methanol of (a)-(c) water, (d)-(f) methanol oxygen, and (g)-(h) methanol carbon. The details for these labels are shown in Figure 1. The RDFs of intermolecular nanocube 1_6 -water for (a) C1-Ow and C2-Ow, (b) N1-Ow, N2-Ow, and N3-Ow, and (c) Me1-Ow, Me2-Ow, Me3-Ow, where Ow is oxygen atom in water molecule. The RDFs of intermolecular nanocube 1_6-methanol for (d) C1-O and C2-O, (e) N1-O, N2-O, and N3-O, and (r) Me1-O, Me2-O, Me3-O, where O is oxygen atom in methanol molecule. The labels of C1 (solid line) and C2 (dashed line) are for carbons on the hydrophobic surface of nanocube 1_6. The RDFs of intermolecular nanocube 1_6-methanol for (g) C1-C and C2-C, (h) N1-C, N2-C, and N3-C, and (i) Me1-C, Me2-C, Me3-C, where C is carbon atom in methanol molecule. The labels of C1 (solid line) and C2 (dashed line) are for carbons on the hydrophobic surface of nanocube 1_6, N1 (solid line), N2 (dashed line), and N3 (dashed spaced line) for nitrogen atoms of 3-pyridyl groups, Me1 (solid line), Me2 (dashed line), and Me3 (dashed spaced line) for carbon atoms of substituents. The details for these labels are shown in Figure 1.

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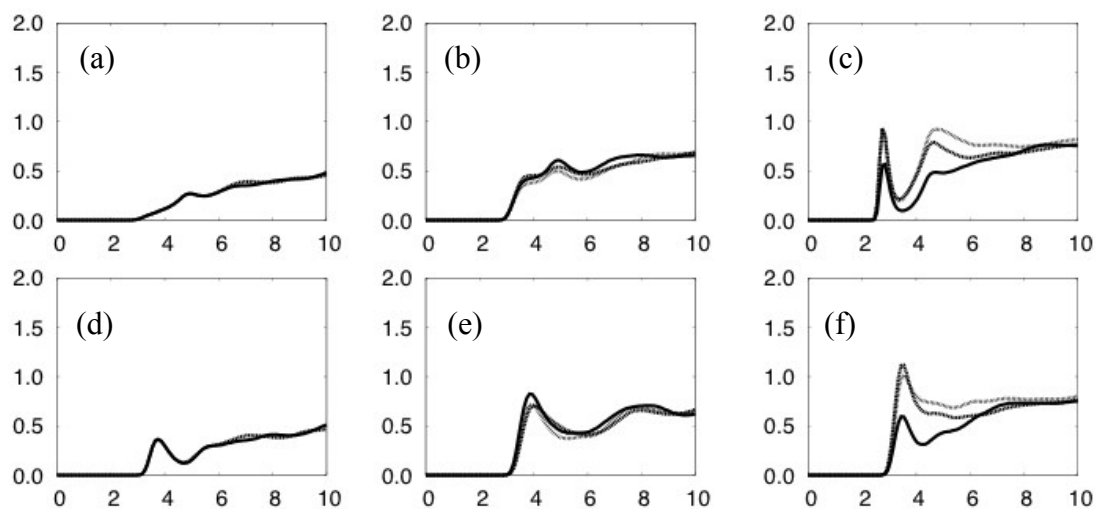
Figure S7 The RDFs of intermolecular nanocube 1_6 in pure methanol of (a)-(c) methanol oxygen, and (d)-(f) methanol carbon; (a) Cn-Om, (b)Men-Om, (c)Nn-Om, (d)Cn-Cm, (e)Men-Cm and (f)Nn-Cm. The details for these labels are shown in Figure 1.

6. The average distances (standard deviation) for π-π stacking and CH-π

Tables S4 and S5 show the average distances (standard deviation) of **Py**1-**Py**2 and **Py**1-**Py**3 for the π-π stacking and these of **Py**3-Me1 and **Py**3-Me3 for the CH-π interaction, respectively, in pure water, aqueous methanol, and pure methanol solvents.

First, we discuss the distances of **Py**1-**Py**2 and **Py**1-**Py**3. In all solvents, both the average distance and standard deviation of **Py**1-**Py**3 distance are greater than those of **Py**1-**Py**2 one. Strictly speaking, the distance **Py**1-**Py**3 becomes longer, as the methanol solvent molecules are increased among three solvents.

Next, we discuss the distances of **Py**3-Me3 and **Py**3-Me1. The largest average distance value of **Py**3-Me3 was found in pure methanol solvent, followed in pure water, and in aqueous methanol, clearly indicating that the distance becomes longer by the concentration of methanol molecules. On the other hand, the average distance of **Py**3-Me1 does not change by the amount of methanol molecules among three solvents. Such trend is consistent with the discussion in the previous subsection, where we showed that the distance of **Py**3-Me3 in the rare event structure **B** becomes longer than that of the average structure **A** due to the effect of nearest neighboring methanol solvent molecule.

Table S4 The average distances between **Py**s in water, aqueous methanol, and methanol solvent. The standard deviations are also in parentheses. The distance for the **Py**1 (the middle of the triple π stacking)-**Py**2 (near the C_3 axis side) and **Py**1-**Py**3 (near the vertices in the C_3 axis). The centroid is calculated the coordinate for **Py**. The labels are shown in Figure 1

	Py1-**Py**2	**Py**1-**Py**3
pure water	3.84 (0.24)	4.40 (0.32)
aqueous methanol	3.84 (0.26)	4.51 (0.35)
pure methanol	3.85 (0.28)	4.56 (0.37)

Table S5 The **Py**3-Me1 and **Py**3-Me3 distances during MD simulation for 1_6 in water, aqueous methanol, and methanol solvents. The labels are shown in Figure 1.

	Py3-Me1	**Py**3-Me3
pure water	4.29 (0.38)	4.41 (0.31)
aqueous methanol	4.27 (0.44)	4.41 (0.32)
pure methanol	4.31 (0.51)	4.42 (0.34)

7. The SDF for 1 in aqueous methanol

Figure S8 shows the SDFs in aqueous methanol solvent of (a) carbon atoms of methanol molecules, Cm, (b) oxygen atoms of methanol molecule, Om, and (c) oxygen atoms of water molecules, Ow, for monomer molecule **1**, for simplicity. Figure S8(1) shows that the Cm distributes around the hydrophobic surface for **1**, while Figure S8(2) shows that the Om distributes outside of the Cm. These figures clearly show that hydroxy group of methanol molecules directly coordinate to water molecule, and methanol molecules cover the hydrophobic surface. In Figure S8(3), Ow distributes around the Nn and near the Om. From these Figures S8(1)-(3), the molecule **1** can get a hydrophilic character due to the existence of methanol molecules between molecule **1** and water molecules. The results for SDF clearly show that the nanocube has the ability of the solvation in water solvent via methanol molecules.
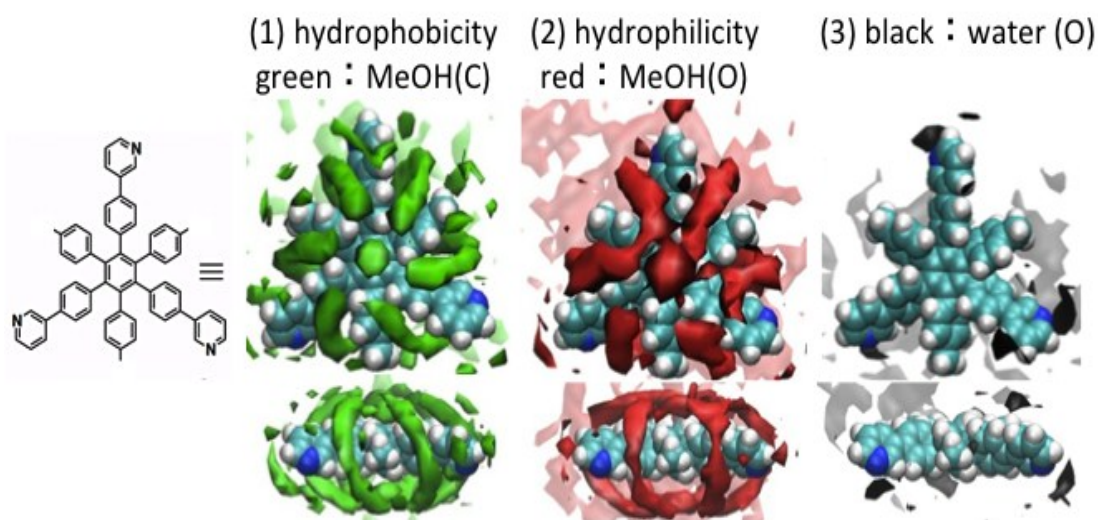
Figure S8 The SDFs of (1) carbon, (2) oxygen of methanol molecule, and (3) oxygen of water molecule in aqueous methanol solvent for **1**. The colors of cyan, blue, and white are carbon, nitrogen, and hydrogen atoms, respectively.