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Detailed Structural Analysis of a Self-Assembled Vesicular Amphiphilic NCN-Pincer Palladium Complex by Using Wide-Angle X-Ray Scattering and Molecular Dynamics Calculations

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Abstract: Wide-angle X-ray scattering experiments and allatomistic molecular dynamics calculations were performed to elucidate the detailed structure of bilayer vesicles constructed by self-assembly of an amphiphilic palladium NCNpincer complex. We found an excellent agreement between the experimental and calculated X-ray spectra, and between the membrane thickness determined from a TEM image and that calculated from an electron-density profile, which indicated that the calculated structure was highly reliable. The analysis of the simulated bilayer structure showed that in general the membrane was softer than other phospholipid bilayer membranes. In this bilayer assemblage, the degree of alignment of complex molecules in the bilayer membrane was quite low. An analysis of the electron-density profile shows that the bilayer assemblage contains a space through which organic molecules can exit. Furthermore, the catalytically active center is near this space and is easily accessible by organic molecules, which permits the bilayer membrane to act as a nanoreactor. The free energy of permeation of water through the bilayer membrane of the amphiphilic complex was 12 kJ mol⁻¹, which is much lower than that for phospholipid bilayer membranes in general. Organic molecules are expected to pass though the bilayer membrane. The self-assembled vesicles were shown to be catalytically active in a Miyaura–Michael reaction in water.

Introduction

As nanomaterials, bilayer vesicles constructed by the self-assembly of amphiphilic molecules have received much attention from a wide range of scientists.^[1] In particular, it has been re-

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ported that amphiphilic molecules that contain a catalytically active site self-assemble to form catalytically active self-assembled vesicles that can be used to induce organic reactions in water.^[2-4] We recently reported the formation of self-assembled vesicles of amphiphilic palladium pincer complexes and their use in the catalysis of reactions in water (Figure 1).^[5-7] The formation of bilayer vesicles was shown to be essential for the efficient promotion of reactions in water. The promotion of the



Figure 1. Self-assembly of amphiphilic palladium NCN-pincer complex 1.

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reaction through the formation of a vesicular structure is explained in terms of the spontaneous concentration of organic substrates in the hydrophobic region as a result of hydrophobic interactions, and the subsequent approach of the substrate to the catalytic center (Figure 2). The organic transformation



Figure 2. Schematic diagram of the catalytic system.

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proceeds rapidly as a result of the presence of high concentrations of the organic substrate near the catalytic center. To the best of our knowledge, this study was the one of the earliest successful examples of catalysis by using a self-assembled architecture. Although microscopic analyses (transmission electron microscopy (TEM), scanning electron microscopy (SEM), atomic-force microscopy, fluorescence microscopy, and confocal laser scanning microscopy) of the vesicles showed that these vesicles were spherical hollow structures, the detailed molecular structure of the bilayer membrane remained unclear. If the detailed bilayer structure could be clarified, we would be able to discuss how organic transformations take place in bilayer membranes.

In the structural analysis of liposomes, solid-state ²H NMR spectroscopy is a powerful tool for understanding the fluidity of the membrane and the packing of the lipid molecules in the membrane, among other aspects. Furthermore, molecular-dynamics (MD) calculations for liposomes have shown a high degree of consistency with the results of solid-state ²H NMR spectroscopy on liposomes.^[8]

MD calculations are also a powerful tool for estimating the structure of membranes. In the last decade, as a result of the increase in computational power and the development of sophisticated software, MD calculations have become a useful tool for investigation of the properties of biomembranes. Furthermore, the use of all-atomistic force-field parameters has greatly improved the reliability of MD calculations in comparison with NMR spectroscopy measurements. Although many MD calculation studies on phospholipid bilayers have been reported, no study of the application of MD calculations to determine the self-assembled bilayer structure of amphiphilic transition-metal complexes has been reported.

A detailed structural analysis of self-assembled architectures is important to elucidate their function. Wide-angle X-ray scattering (WAXS) and MD calculation have been used in the structural analyses of self-assembled architectures (such as bilayer vesicles or nanotubes).^[9,10] In these reports, the structures of assemblages at the molecular level were confirmed. A combination of WAXS and MD calculations is one of the most useful techniques for performing detailed structural analyses of selfassembled nanoarchitectures.

Here we report a detailed analysis of the bilayer structure generated by the self-assembly of a palladium NCN-pincer complex conducted by means of WAXS experiments and MD calculations. A good agreement between the experimental and calculated X-ray spectra and between the membrane thickness as determined from TEM images and that calculated from the electron-density profile was obtained, and indicated that the results of MD calculations are highly reliable. The calculation showed that the alignment order of the complex molecules in the bilayer structure was much lower than in pure phospholipid bilayer membranes. In addition, the MD calculations showed that water molecules can enter the hydrophobic region of the bilayer membrane. The calculation results also showed that organic substrates can be incorporated into the membranes, so that bilayer vesicles can act as nanoreactors.

Experimental Section

General information

Commercially available chemicals (purchased from Aldrich, TCI, Kanto, Wako, Nakalai, or Alfa Aesar) were used without further purification, unless otherwise noted. NMR spectra were recorded by using a JNM-A500 spectrometer (500 MHz for ¹H, 125 MHz for ¹³C). Chemical shifts for ¹H NMR spectra are reported in δ [ppm] referenced to an internal tetramethylsilane standard. Chemical shifts for ¹³C NMR spectra are given relative to CDCI₃ as an internal standard (δ = 77.0 ppm). ¹H and ¹³C NMR spectra were recorded in CDCI₃ at 25 °C unless otherwise noted. El mass spectra were recorded by using an Agilent 5973N spectrometer attached to an Agilent 6890N gas chromatograph. Millipore water was obtained from a Millipore Milli-Q Biocel A10 purification unit. Complex 1 and vesicular 1_{vscl} were prepared by using the reported methods.^[5a,b]

Grazing-incidence-angle wide-angle X-ray scattering

The sample for grazing-incidence-angle WAXS (GIWAXS) measurements was prepared as follows. A suspension of 1_{vscl} in H₂O was dropped onto a silicon wafer and then air dried. High-resolution Xray scattering experiments were carried out at 25 °C by using a synchrotron radiation X-ray beam with a wavelength of 0.80 Å on beamline BL44B2^[11] at SPring-8 (Hyogo, Japan). An angle of incidence of 0.04° was used in the measurements. A large Debye– Scherrer camera, 286.48 mm in length, was used with an imaging plate as a detector and all diffraction patterns were obtained in 0.01° steps (2 θ). The duration of exposure to the X-ray beam was 60 min for 1 and 15 min for background.

Catalytic reaction with 1_{vscl} in water

An aqueous suspension of 1_{vscl} (1 mL, 2.6 mg, 2.4×10^{-3} mmol), cyclohex-2-ene-1-one (**2**, 11.5 mg, 0.12 mmol), and sodium tetraphenylborate (**3**, 61.6 mg, 0.18 mmol) were placed in a vial, and the mixture was agitated by shaking at 25 °C for 12 h. The reaction was quenched with sodium chloride, then the mixture was extracted with methyl *tert*-butyl ether (MTBE; 4×1.5 mL). The extracts were combined, dried over Na₂SO₄, and filtered through silica gel with MTBE as an eluent. After removal of the solvent, the product

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was dissolved in CDCl₃ that contained 1,1,2,2-tetrachloroethane as an internal standard. The chemical yield was determined by using 1 H NMR spectroscopy.

Data for 3-phenylcyclohexanone (4) [CAS: 20795-53-3]

¹H NMR (500 MHz, CDCl₃): δ = 7.31–7.34 (m, 2H, Ph*H*), 7.21–7.25 (m, 3H, Ph*H*), 2.98–3.04 (m, 1H, C*H*-Ph), 2.57–2.62 (m, 1H, C*H*₂), 2.50–2.55 (m, 1H, C*H*₂), 2.43–2.48 (m, 1H, C*H*₂), 2.34–2.41 (m, 1H, C*H*₂), 2.12–2.17 (m, 1H, C*H*₂), 2.06–2.10 (m, 1H, C*H*₂), 1.73–1.89 ppm (m, 2H, C*H*₂); ¹³C NMR (125 MHz, CDCl₃): δ = 210.9 (C=O), 144.3 (Ph-C attached to cyclohexanone), 128.6 (PhC), 126.6 (PhC), 126.5 (PhC), 48.9 (CH attached to Ph), 44.7 (CH₂), 41.1 (CH₂), 32.7 (CH₂), 25.5 ppm (CH₃); MS: *m/z*: 174 [*M*]⁺.

Computational methods

Parameterizations for pincer complex 1

The all-atomistic CHARMM general force field (CGenFF)^[12] was used for pincer complex **1**. Complex **1** was formed by connecting the pincer unit (PINC), dodecane (DODE), and triethylene glycol (TEG) residues (Figure 3). For the DODE and TEG residues, we used the



Figure 3. The molecular structure of complex 1. Right: A model drawn by using VMD^[18] (C: cyan, H: white, O: red, N: blue, Cl: yellow, Pd: pink).

CGenEF parameters for hexane (HEXA) and poly(ethylene glycol) monomer (PEGM) residues, respectively, as presented in the standard top_all36_cgenff.rtf and par_all36_cgenff.prm files. The parameters for the PINC residue were determined by noting that this residue is constructed from the pincer backbone of complex 1 and a benzene (BENZ) residue. The rigid TIP3P^[13] model was used for water molecules. The initial structure of the pincer backbone of 1 was constructed on the basis of the crystal structure of an NCNpincer complex.^[14] The atom types of the PINC residue were transferred from BENZ, SCH2, and CLET residues in the CGenFF parameters without palladium. The atom type of Pd was determined according to the reported method.^[15] The bond lengths, bond angles, and dihedral angles of the PINC residue were determined on the basis of these atom types and the optimized geometry. The lengths of the chemical bonds (C-Pd, Pd-N1, Pd-N2, Pd-Cl) and the dummy bonds (C-N1, N1-Cl, Cl-N2, N2-C) were fixed by using the SHAKE/RATTLE algorithm.^[16] Consequently, Pd atoms were fixed on the rigid rhomboidal plane formed by the C-N1-Cl-N2 atoms.

This planar structure is consistent with the structure of palladium NCN-pincer complexes in the solid state.^[14] The charges on the PINC residue were transferred from the pincer backbone and BENZ, with charge adjustment of the linking atoms according to

the reported method.^[17] The PINC, DODE, and TEG moieties were connected by deleting extra hydrogen atoms, and the charges were also transferred with charge adjustment of the connecting atoms^[17] to obtain pincer complex **1**.

MD calculation of the bilayer structure of complex 1

An MD calculation for the self-assembled amphiphilic NCN-pincer palladium complex bilayer membrane was performed to investigate its detailed structure. The system investigated herein is summarized in Table 1. In the bilayer membrane of the palladium NCN-

Table 1. Details of the system investigated in the present calculations.					
<i>T</i> [K]	298.15				
<i>P</i> [atm]	1.0				
No. of complex molecules	128				
No. of water molecules	15532				
Total number of atoms	67972				

pincer complex, the number of complex molecules per leaflet was 64 and the number of water molecules was 15532.^[19] The Lennard–Jones interaction was cut off at 1.2 nm by applying a switching function from 0.8 to 1.2 nm. The electrostatic interaction was calculated by using the particle mesh Ewald (PME) method.^[20] The temperature (*T*) and the hydrostatic pressure (*P*) were held at 298.15 K and 1 atm, respectively, by using a combination of the Nosé–Hoover chain and Parrinello–Rahman methods.^[21] The equations of motion were numerically solved by using integrators based on the RESPA^[22,23] with a single time step of 2 fs. The lengths of all chemical bonds relative to hydrogen atoms and of the chemical and dummy bonds around the Pd atoms described above were constrained by using the SHAKE/RATTLE/ROLL method.^[23] An MD calculation 130 ns long was performed by using the PME version of our originally developed software MODYLAS.^[24]

Convergence to the equilibrium state may be monitored by using the membrane area per molecule. As shown in the Supporting Information (Figure S2), it converged well within 60 ns. Trajectories for the last 70 ns run have been used for detailed analyses.

Results and Discussion

Comparison of the experimental and simulated WAXS spectra of 1_{vscl}

To demonstrate the validity of our simulation result, we first compared the experimental WAXS spectrum of $\mathbf{1}_{vscl}$ with the computed spectrum of the calculated bilayer assemblage of complex **1**. The GIWAXS experiment for $\mathbf{1}_{vscl}$ gave an amorphous pattern spectrum (Figure 4, blue line). A simulated WAXS spectrum was calculated by using a reported method.^[9a] The X-ray scattering intensity in the Born approximation can be written as follows [Eq. (1)]:

$$I(\mathbf{q}) \propto \overline{\left\langle \left| \sum_{j,m} f_j(\mathbf{q}) \mathbf{e}^{i\mathbf{q}\cdot \mathbf{r}_{j,m}} \right|^2 \right\rangle}$$
(1)

in which $\mathbf{r}_{j,m}$ is the position of the *j*th atom on the *m*th molecule and the symbols $\langle \cdots \rangle$ indicate an ensemble average. The overbar indicates an average over all possible relative orientations of the wave vector \mathbf{q} with respect to the simulation cell, to take into account the fact that the experimental samples consist of vesicles,

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Figure 4. Comparison of the experimental and simulated XRD spectra (blue line: experimental XRD spectrum; red line: simulated XRD spectrum). The error bars represent the standard deviations estimated from one 70 ns interval average.

which we approximated as nonoriented bilayers. The number of wave vectors was over 10⁶, which enabled us to calculate *l*(**q**) up to **q** = 8.5 Å⁻¹ with very high accuracy.

The quantity $f_j(\mathbf{q})$ is the form factor of atom *j* and it is computed by using the formula in Equation (2):

$$f(\mathbf{q}) = c + \sum_{i=1}^{4} a_i \exp\left[-b_i \left(\frac{\mathbf{q}}{4\pi}\right)^2\right]$$
(2)

in which c, a_{ii} and b_i are the Cromer–Mann coefficients for the given atomic species.

The resulting spectrum consisted of the spectrum of the bilayer assemblage of complex 1 and the spectrum of the water molecules. To obtain the calculated spectrum of the bilayer assemblage of complex 1, it was necessary to subtract the spectrum of water molecules from the spectrum of the MD calculation result for the total system.^[9a] An MD calculation for the bulk water system (52 080 water molecules) was also carried out under identical conditions to those used for the bilayer membrane assemblage of complex 1 with water molecules. This gave a calculated X-ray spectrum for the water molecules, which we subtracted from the calculated spectrum for the total system to give the desired spectrum for the bilayer membrane of complex 1 (Figure 4, red line).

The simulated WAXS spectrum (Figure 4, red line) shows excellent agreement with the experimental WAXS spectrum of $1_{\rm vscl}$. This indicates that the simulated bilayer structure is highly reliable.

Structural properties of membranes of 1_{vscl}

Next, we analyzed the structural properties of the membrane in detail. Table 2 lists the geometric properties of the MD unit cell and the lipid bilayer averaged over the final 70 ns. S is the membrane area, *a* is the area per complex molecule, and *h* and *V* are the height and volume of the unit cell, respectively. The error given in Table 2 corresponds to the standard deviation over an average of seven 10 ns intervals. The calculated membrane area per complex molecule is (85.6 ± 1.9) Å², which is much greater than that of phospholipid bilayers in the liquid-crystalline state (60–65 Å²).^[25]

The fluctuation in S gives the isothermal area compressibility (χ_7^5) of the bilayers by applying the expression in Equation (3).

Table 2. Calculated structural and thermodynamic properties of the bilayer structure of complex 1, and the experimental membrane area per lipid^[25] and isothermal area compressibility of DPPC, POPC, and DMPC bilayers in the liquid-crystalline state.^[26-28]

	S×10 ³ [Å ²]	a [Ų]	h [Å]	V×10 ⁵ [Å ³]	$\chi_T^{\rm S}~[{ m m}^2{ m J}^{-1}]$
1 ^[a] DPPC	5.48±0.12 -	85.6±1.9 63.1	120±2 -	6.56±0.01 -	5.57±0.04 4.0
POPC	_	(323.15 K) ^[25] 64.3	_	_	(323.15 K) ^[26] 3.0–5.5
	_	(303.15 K) ^[25]	_	_	(298.15 K) ^[27]
DIVIFC	-	(303.15 K) ^[25]	-	-	(302.15 K) ^[28]

[a] Errors in the first five quantities correspond to the standard deviation over the average of seven 10 ns intervals. Errors for the last quantity represent the propagation error of the standard deviation of the variance, $<(S-<S)^2>$, and the standard deviation of the average, <S>, over one 70 ns interval average.

$$\chi_{T}^{S} = \frac{1}{k_{B}T} \frac{<(S - < S >)^{2} >}{~~}~~$$
(3)

in which < ... > represents the time average over the final 70 ns. Table 2 also lists the calculated values of χ_T^5 . In membrane 1, the calculated value of χ_T^5 was 5.57 m²J⁻¹ at 298.15 K. This value is greater than that of experimental pure bilayer membranes of dipalmitoylphosphatidylcholine (DPPC), 1-palmitoyl-2-oleoylphosphatidylcholine (DPPC), and 1,2-dimyristoylphosphatidylcholine (DMPC) in their liquid-crystalline states (Table 2).^[26-28] This result indicates that the complex bilayer is laterally softer than the pure lipid bilayers.^[29]

To check the structure of the calculated bilayer membrane, a snapshot of the simulated bilayer structure is shown in Figure 5. The order of alignment of the complex molecule was low.



Figure 5. Snapshot of the equilibrated bilayer membrane structure of palladium NCN-pincer complex 1 (C: cyan, H: white, O: red, N: blue, CI: yellow, Pd: pink), drawn by using VMD.^[18]

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Electron-density profile

To check the position of the atoms in the bilayer membrane, the distribution of atoms along the bilayer normal (*z* axis) and the resultant electron-density profile were investigated. Figure 6 shows the electron-density profile along the *z* axis ($\rho_e(z)$) averaged over the final 70 ns, in which the origin of *z* is taken to be the center of mass of the bilayer. The distribution was almost symmetric with respect to z=0 Å for this system.



Figure 6. Calculated electron-density profiles (black line: total, orange line: complex, aqua-blue line: water, red line: pincer backbone, blue line: dodecyl group, green line: TEG group, pink line: palladium atom, purple line: chlorine atom). The point at z=0 is the center of mass of the bilayer. Error bars represent the standard deviations estimated from the average of seven 10 ns intervals.

The distribution of the complex ranged from -30 to +30 Å, which shows that the thickness of the membrane was about 60 Å (Figure 6, orange line). This calculated membrane thickness is consistent with the TEM observations (Figure 1). The pincer backbone (Figure 6, red line) was located between the hydrophobic dodecyl group region (Figure 6, blue line) and the hydrophilic TEG group region (Figure 6, green line). Interestingly, palladium (Figure 6, pink line) faced both the hydrophilic and hydrophobic regions. Furthermore, a number of water molecules were observed in the inner hydrophobic region of the bilayer membrane (Figure 6, aqua-blue line). Therefore, hydrophobic organic molecules also can exist in the inner region of the bilayer assemblage. If external organic molecules are present in the hydrophilic or hydrophobic regions in the bilayer, these molecules can easily reach the palladium atoms. Organic transformations can, therefore, be catalyzed by our vesicular nanocomposite $(\mathbf{1}_{vscl})$ in water.

Order Parameter of the C–H Vector in the Dodecyl and TEG Chains

The order parameter of the C–H vector (S_{CH}) is a measure of the order of the dodecyl and TEG chains. In general, the ²H NMR spectroscopy experiment with deuterium-substituted acyl tails permits the determination of the order parameter of the C–D vector (S_{CD}) from the width of the quadrupole splitting of the target C–D bonds. In the MD calculations, the order parameter was calculated by using the expression in Equation (4).

$$S_{\rm CH} = \left\langle \frac{1}{2} (3\cos^2\theta - 1) \right\rangle \tag{4}$$

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in which θ is the angle between the C–H vector and the *z* axis. The quantities S_{CD} and S_{CH} are essentially the same. Figure 7 shows the calculated value of S_{CH} as a function of the carbon number of the dodecyl and TEG chains. The values of S_{CH} for dodecyl and TEG chains are very small compared with the corresponding values for the acyl tails of phospholipids that form bilayers in the liquid-crystalline state (0.20–0.25 in the middle of acyl chains; <0.05 at the chain terminal).^[8]



Figure 7. The calculated order parameter of C–H vectors of the dodecyl chains (top right) and TEG chains (bottom right). The error bars represent the standard deviations estimated from the average of seven 10 ns intervals.

To elucidate the origin of the low value of S_{CH} , we also estimated the order parameter for Pd–C bonds (S_{PdC}) as a measure of the alignment order of the central pincer framework. The calculated value of S_{PdC} was (0.32 \pm 0.01), which is much smaller than the order parameter for the long axes of DPPC molecules in a fluid phospholipid bilayer (0.7 to 0.8).^[8] That is, the order of alignment in the central pincer framework in the bilayers of the amphiphilic complex is quite low. Therefore, the very small values of S_{CH} in the side chains derive from low-order alignment of complex molecules in the bilayers. This observation is consistent with the snapshot of the bilayer structure (Figure 5). However, the S_{CH} values for C9, C10, C11, and C12 in the dodecyl chains were relatively high. These results show that the bilayer membrane is weakly supported by a relatively high-order alignment of the terminal 1-methyl group and the three methylene groups near the terminus of the dodecyl chains (Figure 8).

Radial distribution function between palladium atoms

Intermolecular metallophilic interactions are known to be one of the driving forces for the construction of supramolecular structures. $^{\scriptscriptstyle [30]}$

Intermolecular Pd–Pd interactions (typical Pd–Pd contact length = 3.16–3.37 Å) have been observed in solid-state planar Pd complexes.^[31] To check for the presence of Pd–Pd interactions in self-assembled bilayer assemblage 1_{vsclr} we investigated the radial distribution function between the palladium atoms (Figure 9). The first peak was observed at 7.7 Å, which is much longer than the





Figure 8. Membrane model (red: four terminal C atoms in the dodecyl chain, blue: remaining eight C atoms in the dodecyl chain; pink rectangle: pincer framework, green: TEG chain).



Figure 9. Radial distribution function between the palladium atoms. Error bars represent the standard deviations estimated from the average of seven 10 ns intervals.

typical range for Pd^{II} - Pd^{II} contact lengths (3.16–3.37 Å), which indicates that Pd-Pd interactions do not occur in this bilayer assemblage.

Electrostatic potential of the membrane

To discuss the effect of the electrostatic properties on the permeability of the bilayer membrane toward organic molecules, we analyzed the electrostatic potential of the membrane by the reported method.^[32] Figure 10 shows the electrostatic potentials of the membrane along the *z* axis. The electrostatic potential at the center of the membrane was 0.7 V. The potential value of the bilayer membrane of complex **1** is similar to that of bilayer membranes of pure DPPC or POPC.^[33] From the viewpoint of the electrostatic properties of the membrane, the permeability of our bilayer assemblage is, therefore, similar to that of bilayer membranes of DPPC or POPC.



Figure 10. Electrostatic potentials (blue line: total; red line: complex; green line: water). The potential was set to zero at the edge of the simulation box. The point at z=0 is the center of mass of the bilayer. Error bars represent the standard deviations estimated from the average of seven 10 ns intervals.

Membrane permeation free-energy profile of water

Figure 11 shows the membrane permeation free-energy profile of water along the *z* axis, $\Delta G(z)$, obtained from the number-density profile of water molecules along the *z* axis, $\rho_w(z)$, by using Equation (5).

$$\Delta G(z) = -k_{\rm B}T \ln\left(\frac{\rho_{\rm w}(z)}{\rho_{\rm w,0}}\right) \tag{5}$$

in which the basis of $\Delta G(z)$ was chosen for the bulk region of water with a number density of $\rho_{w,0}$. The free-energy barrier to water permeation through our bilayer membrane was 12 kJ mol^{-1} . In contrast, the free-energy barrier to permeation of water through pure phospholipid bilayer membranes in the liquid-crystalline state is over $25 \text{ kJ mol}^{-1,[34]}$ The free energy of permeation of water through our bilayer membrane is, therefore, much lower than for permeation through pure phospholipid bilayer membranes. At 298.15 K, $\exp((-11 \text{ kJ mol}^{-1})/k_{\text{B}}T) \approx 0.012$, which is much greater than $\exp((-25 \text{ kJ mol}^{-1})/k_{\text{B}}T) \approx 0.0004$. Therefore, water molecules tend to permeate through the bilayer membrane of complex 1. The reason for this lower energy barrier is still unclear. We speculate that the quite low order of alignment of the complexes in the bilayer membrane (see above) might provide space for the perme-

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Figure 11. Membrane permeation free-energy profile of water. The point at z=0 is the center of mass of the bilayer. Error bars represent the standard deviations estimated from the average of seven 10 ns intervals.

ation of water molecules through the bilayer membrane. From this analytical result, it is expected that organic molecules can pass through the bilayer membrane of complex 1 and diffuse to the catalytically active center.

The Miyaura-Michael reaction of cyclohex-2-en-1-one with sodium tetraphenylborate

To demonstrate the catalytic activity of self-assembled vesicular 1_{vscl} we performed the Miyaura–Michael reaction^[35] for cyclohex-2en-1-one (2) with sodium tetraphenylborate (3) in the presence of self-assembled vesicular $\mathbf{1}_{vscl}$ in water (Table 3). The reaction proceeded smoothly to give 3-phenylcyclohexanone (4) in 83% yield (Table 3, entry 1). Conversely, when non-self-assembled complex 1_{amps} was used as the catalyst, product 4 was obtained in only 7% yield (Table 3, entry 2). The formation of the self-assembled architecture is, therefore, essential for efficient promotion of the reaction. We also carried out the reaction in various organic solvents, and the yield of 3-phenylcyclohexanone (4) was 6% or less even



(Cl₂CHCHCl₂).

when vesicular $\mathbf{1}_{vscl}$ was used as the catalyst (Table 3, entries 3–8). These results indicate that vesicular $\mathbf{1}_{vscl}$ disassembles or dissolves in organic solvents to give catalytically less active monomeric 1, whereas in water, vesicular $\mathbf{1}_{\text{vscl}}$ is present and operates as an efficient catalyst.

Conclusion

We performed a GIWAXS experiment and all-atomistic MD calculation for a self-assembled vesicular palladium NCN-pincer complex. We found an excellent agreement between the experimental and calculated X-ray spectra and between the membrane thickness determined from a TEM image and that calculated from an electrondensity profile, which indicated that the simulated structure was reliable. An analysis of the simulated bilayer structure showed that the membrane was relatively softer than phospholipid bilayer membranes in general. In this bilayer assemblage, the alignment order of complex molecules in the bilayer assemblages was quite low. The analysis of the electron-density profile showed that the bilayer assemblage contained a space through which organic molecules could exit. The catalytically active center is close to this space and easily accessible by organic molecules. The bilayer membrane structure can, therefore, act as a nanoreactor. In relation to the electrostatic properties of bilayer membrane complex 1, the potential of the bilayer membrane of complex 1 is similar to that of bilayer membranes of pure phospholipids. In contrast, the freeenergy barrier to permeation of water through the bilayer membrane of complex 1 is much lower than that for pure phospholipid bilayer membranes. Therefore, water molecules tend to permeate through the bilayer membrane of complex 1. This analytical result suggests that organic molecules can also pass through the bilayer membrane of complex 1 and diffuse to the catalytically active center. Finally, we demonstrated the catalytic activity of self-assembled vesicular 1_{vscl}. Vesicular 1_{vscl} catalyzed the Miyaura-Michael reaction of cyclohex-2-en-1-one with sodium tetraphenylborate in water to give 3-phenylcyclohexanone in 83% yield. In contrast, when non-self-assembled $\mathbf{1}_{\text{amps}}$ was used as the catalyst, the product was obtained in only 7% yield. The formation of a bilayer structure is, therefore, essential for the efficient promotion of the reaction in water.

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