Design and Synthesis of Ladder-Shaped Tetracyclic, Heptacyclic, and Decacyclic Ethers and Evaluation of the Interaction with Transmembrane Proteins

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Ladder-shaped polyether (LSP) toxins produced by marine phytoplankton are often implicated in food poisoning, causing a serious threat to human health. Their toxicity is generally accounted for by interaction with transmembrane (TM) proteins. To elucidate these interactions, we have designed and synthesized artificial ladder-shaped polyethers (ALPs) comprising 6/7/6/6 tetracyclic, 6/7/6/6/7/6/6 heptacyclic, and 6/7/6/6/7/6/6/7/6/6 decacyclic systems (A series: both sides were functionalized as diols, B series: one side remained as diol and the other side was protected as benzyl ethers, see Fig. 2). The ALPs possessing the simple iterative structure with a different number of rings helped understand the structure-activity relationship with respect to the molecular length, which is supposed to be important when naturally occurring LSPs elicit their toxicity. The interaction of these ALPs with TM proteins was evaluated by using glycophorin A (GpA), which was known to form homo-dimers in the lipid bilayer membranes and dissociate in the presence of LSPs. The heptacyclic ether (ALP7B) revealed the most potent activity in the presence of 2% SDS buffer, whereas, under the low concentration of SDS (0.03%), the decacyclic ether (ALP10A) exhibited intriguing phenomenon to induce precipitation of GpA in a dose-dependent manner. The different activities among the ALPs can be accounted for by the concept of 'hydrophobic matching' i.e. the length of the hydrophobic region including the side chains of ALP7B and ALP10A is ca. 25Å, which matches well with that of the hydrophobic region of α-helical TM proteins, as well as the hydrophobic thickness of lipid bilayer membranes. The concept of the 'hydrophobic matching' would be a clue to understanding the interaction between LSPs and TM proteins as well as the mechanism of their potent toxicity, and also a guiding principle to design ALPs possessing higher affinity to TM proteins.

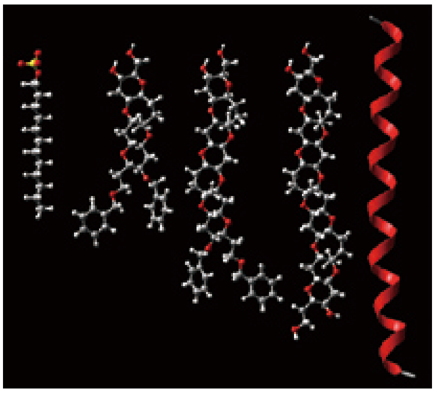

Fig. 1 3D structures of SDS, ALP4B, ALP7B, ALP10A, and GpA-TM (from left).

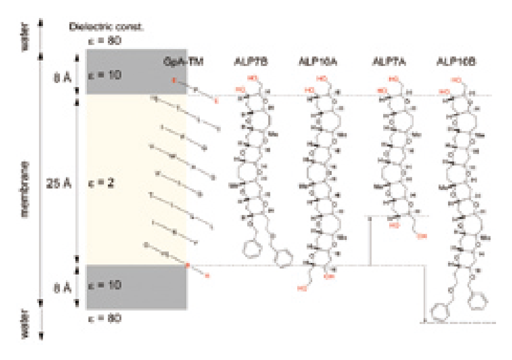

Fig. 2 Hydrophobic matching model.

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Rhodium Nanoparticle Encapsulated in a Porous Carbon Shell as an Active Heterogeneous Catalyst for Aromatic Hydrogenation

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Metal nanoparticles (MNPs) are active and important catalytic materials because of their large surface area and size-dependent unique properties. These MNP-based catalysts are usually preserved by organic ligands to prevent agglomeration to the thermodynamically favored bulk metal and are used in homogeneous systems. However, because their active metal surface is covered by organic ligand, their intrinsic high catalytic activity is therefore inhibited. We considered that a "rattle-type" nanostructure, a core MNP encapsulated by a hollow porous shell, would be a promising structure because this nanostructure enables stabilization of the naked core MNP. The titled paper described fabrication of Rh nanoparticle core encapsulated in the mesoporous carbon shell (Rh/hmC) and its catalytic activity for aromatic ring hydrogenation in water.

From the result of TEM observation, Rh/hmC was revealed to consist of a hollow carbon cage (70 nm in diameter with a shell thickness of 15 nm) and a central Rh nanoparticle with an average particles size of 4.0 nm. FT-IR spectrum of Rh/hmC showed that the Rh metal was naked in the carbon shell without covered by PVP. Analyzing the N_2 adsorption isotherm of Rh/hmC revealed a bimodal pore structure with a small mesopore system centered at 2.9 nm and a micropore system of <1.0 nm in diameter.

The activity of Rh/hmC was tested in the aromatic ring hydrogenation of t-butylbenzene. Hydrogenation of t-butylbenzene was performed in various solvents (methanol, octane, acetone and water) under 0.5 MPa H_2 atmospheres at 333 K for 2 h. The highest conversion of 68% was obtained when water was used. In the Rh/hmC nanostructure, the lateral porous carbon shell provides the medial Rh nanoparticle with a hydrophobic microenvironment. When Rh/hmC was dispersed in water containing t-butylbenzene, therefore, the non-polar substrate could be accumulated in the hollow spaces. Moreover, the core Rh nanoparticle is free from any ligands and thus has a large effective metal surface to induce the catalytic reaction. These specific characteristics of Rh/hmC resulted in the high levels of catalytic activity in water.