Self-assembly from metal-organic vesicles to globular networks: metallogel-mediated phenylation of indole with phenyl boronic acid[†]

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Self-assembly of the conformationally flexible bismethylimidazolyl ligands with Pd(OAc)₂ is described. Depending on whether the ligands provide the hydrogen bonding donor, a switching of metal–organic vesicles to globular networks gelating solvents is achieved. The metallogels exhibit catalytic activity for the cross-coupling of indole with phenyl boronic acid.

The use of coordination chemistry to direct assembly of small component molecules into versatile nanostructures, such as spheres, tubes, rods, and fibers, has opened up exciting opportunities for fabricating materials with potential applications in catalysis, electronic and photophysical materials, host-guest chemistry and biosensing.¹ Morphological transformation of these assemblies has been a hot topic during the past decade accordingly. Imidazole derivatives as building blocks are currently attracting special interest in the creation of metal-organic assemblies.² Recently, the metal ion-mediated self-assembly of conformationally rigid and structurally simple imidazole derivatives such as 1,3-bis(1-imidazolyl)benzene (BIB) with AgNO₃ formed helical nonracemic tubular coordination polymer gelators.³ The reaction of the conformationally rigid 4,4'-bis(1-imidazolyl)biphenyl (BIBP) with Zn(OSO₂CF₃)₂ generated sheet-like coordination polymer microparticles that could be further transformed to nanofibers gelating solvents with sonication.⁴ In this communication, we wish to further explore the self-assembly of the structurally simple and conformationally flexible imidazole derivatives with Pd(OAc)₂, and applications of their assemblies in catalysis (Scheme 1).⁵

Vesicles have achieved prominence due to potential applications in biomimetic models, drug or gene carriers, and nanostructured materials, *etc.* Traditionally, vesicles consist of amphiphilic components, mainly small organic molecules and polymeric materials. However, a design strategy based on coordination chemistry toward metal–organic vesicles has been a challenging field of research, and few examples are known so far.⁶ Herein, we surprisingly found that the self-assembly of Pd(OAc)₂ with the flexible bismethylimidazolyl building units, depending on whether the ligands bear the hydroxyl groups, was capable of creating metal–organic vesicles or globular networks (Fig. 1).

A dimethyl sulfoxide (DMSO) solution of **1** reacted with a DMSO solution of $Pd(OAc)_2$ at a 1:1 molar ratio at room temperature to form a clear yellow solution. Transmission electron microscopy (TEM) studies distinctly revealed that **1** and $Pd(OAc)_2$ spontaneously assembled into spherical particles with a diameter of *ca*. 43 nm (Fig. 2a). The unstained images showed a contrast difference between the periphery and the inner part of the spheres, which is expected from the 2D projection of 3D vesicular structures typically observed by TEM. The structure is clear from a magnified image of a vesicle (Fig. 2b). The wall thickness of vesicles of {[Pd-1](OAc)_2}_n was estimated to be in the range of *ca*. 9–12 nm. A similar observation was obtained for {[Pd-2](OAc)_2}_n (Fig. 2d and e).

Subsequently, the AFM images clearly showed that both 1 and 2 assembled into spherical particles with uniform shape and size in DMSO (Fig. 2c and 2f). The average diameters of the aggregates of $\{[Pd-1](OAc)_2\}_n$ and $\{[Pd-2](OAc)_2\}_n$ estimated from the fitted histograms of the size distribution after subtracting the tip-broadening parameters were 46.5 and 70.0 nm, respectively (Fig. 2g and S1b⁺).⁷ Taking for example $\{[Pd-1](OAc)_2\}_n$, the histogram obtained from the individual diameters of 300 particles shows a Lorentzian distribution $(R^2 = 0.9661)$ with an average size of 46.5 nm and fwhm (full width at half-maximum) of 20.9 nm (Fig. 2g). The ratios of the diameter and height of aggregates generated by $\{[Pd-1](OAc)_2\}_n$ and $\{[Pd-2](OAc)_2\}_n$ were *ca.* 24 and 27, respectively, which illustrated a considerable flattening of the spheres presumably owing to either the high local force exerted by the AFM tip or the removal of the solvent after the transfer of the nanosized assemblies from solution to a mica surface.⁸ Further dynamic light scattering (DLS) experiments



Scheme 1 Chemical structures of ligands BIB, BIBP and 1–7.

^a Key Laboratory of Green Chemistry and Technology of Ministry of Education, College of Chemistry, and State Key Laboratory of Biotherapy, West China Hospital, Sichuan University, Chengdu 610064, People's Republic of China. E-mail: jsyou@scu.edu.cn

^b Department of Chemistry, National Chung Hsing University, Taichung 402, Taiwan

[†] Electronic supplementary information (ESI) available: Synthetic procedures and characterization of **1–7** and **8**; catalytic procedure for 2-phenylation of indole; gelation test; AFM; TEM; DLS; IR spectra; ESI-MS spectra; crystal structure of { $[Pd-3]Cl_2$ ₂ (8). CCDC 759098. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c0cc00112k



Fig. 1 A schematic representation of the self-assembly of ligands 1-7 with Pd(OAc)₂.



Fig. 2 TEM images (unstained) of (a) { $[Pd-1](OAc)_2$ _n, and (d) { $[Pd-2](OAc)_2$ _n in DMSO (1.3 wt%) on a carbon-coated copper grid. (b) and (e) A zoomed-in image marked in (a) and (d), respectively. Tapping-mode AFM height image of aggregates of (c) { $[Pd-1](OAc)_2$ _n, and (f) { $[Pd-2](OAc)_2$ _n in DMSO (0.02 wt%) on a freshly cleaved mica surface after the solvent was evaporated (scale bar: 250 nm). (g) The corresponding histogram (Lorentzian fit) of { $[Pd-1](OAc)_2$ _n. (h) The intensity-weighted distribution of the aggregates obtained from the DLS measurement of the sample of { $[Pd-1](OAc)_2$ _n (1.3 wt%) in DMSO at 25 °C.

with $\{[Pd-1](OAc)_2\}_n$ and $\{[Pd-2](OAc)_2\}_n$ confirmed the formation of supermolecular aggregates with the average diameters of 46.4 and 66.2 nm, respectively, which were in accordance with the AFM and TEM studies. Moreover, the assemblies showed a narrow size distribution indicative of the formation of well-equilibrated structures (Fig. 2h and S1c⁺).

Interestingly, as 1 and 2 with $Pd(OAc)_2$ did not gelate any fluids even upon heating and with sonication, their analogues 3–6 bearing the appended phenolic hydroxyl groups with $Pd(OAc)_2$ induced the formation of remarkably stable metallogels to entrap a variety of organic solvents. When the two hydroxyl groups of 6 were blocked by the methoxymethoxy group to form the ether derivative 7, it resulted in a complete loss of the gelating ability. This observation hinted that the hydroxyl group of 3–6 would be absolutely critical for the formation of gels.

A DMSO solution of **3** was added to a DMSO solution of $Pd(OAc)_2$ at a 1:1 molar ratio at room temperature to spontaneously yield a complete and homogeneous liquid gelation after aging for 3–4 h. Further investigation demonstrated that the gelation also proceeded well in dimethylformamide (DMF), dimethylacetamide (DMA), *N*-methylpyrrolidone (NMP), and a mixture of DMSO and organic solvent (v/v 2:1) (*e.g.*, tetrahydrofuran, 1,4-dioxane, toluene, *m*-xylene, and benzene, *etc.*) (Tables S1 and S2†). The critical

gel concentrations (CGCs) of the { $[Pd-3](OAc)_2$ },, { $[Pd-4](OAc)_2$ }, { $[Pd-5](OAc)_2$ }, and { $[Pd-6](OAc)_2$ }, gelators in DMSO were as low as 0.58 wt%, 0.70 wt%, 0.76 wt% and 0.95 wt%, respectively. All the gelators may be considered as "supergelators" accordingly.⁹ It is notable that transition from one to another could not occur when the gels and vesicles were heated.

The morphology evolution of gelation observed by TEM images provided considerable insight into the formation mechanism of a gel. Taking the aggregation behavior of $\{[Pd-5](OAc)_2\}_n$ as a representative example, the size of the spherical assemblies appeared to be not strongly dependent on the concentrations. At a lower concentration (0.06 wt%, below CGC), $\{[Pd-5](OAc)_2\}_n$ formed nanospherical particles with a diameter of ca. 38-43 nm, which were dispersed in the solution (Fig. 3c). However, at a higher concentration (2.0 wt%, above CGC), the initially formed aggregates (ca. 35-41 nm) unprecedentedly interconnected and further fused to evolve into extended superstructures, which created a threedimensional globular network leading to gelation (Fig. 3a and b). This class of gelation mechanism is unusual, as most previously reported examples are based on self-aggregation of gelator molecules into long, entangled fibrous networks. Similar TEM images were observed for other gelators including $\{[Pd-3](OAc)_2\}_n$ $\{[Pd-4](OAc)_2\}_n$ and $\{[Pd-6](OAc)_2\}_n$ (Fig. S2–S4⁺).

X-Ray diffraction experiments for $\{[Pd-L](OAc)_2\}_n$ proved to be difficult possibly due to their tendency to form amorphous structures. However, the electrosprav ionization time-of-flight (ESI-TOF) mass spectrum studies gave us valuable information. The ESI-TOF spectrum of the complex of 3 and $Pd(OAc)_2$ in a 1:1 molar ratio showed a peak at m/z 1061.7, which corresponds to the species $[Pd_23_2(OAc)_4 \cdot 2H_2O]$ (Fig. S6^{\dagger}). This result suggested the formation of [2 + 2]species of $\{[Pd-3](OAc)_2\}_2$. Instead, we obtained single crystals suitable for X-ray diffraction analysis of {[Pd-3]Cl₂}₂ (8) by slow diffusion of acetone into the mixture of 3 and PdCl₂ in DMSO. The crystallographic studies revealed the discrete dinuclear metallocyclic rectangular unit and the lack of coordination between the hydoxyl group and metal ion (for the crystal structure, see Fig. S5⁺).^{2c,d,10} Therefore, it is reasonable to assume that vesicles and metallogelators might be formed by hierarchical self-assembly of discrete dinuclear macrocyclic units. Although the specific interactions are not



Fig. 3 (a) TEM image (unstained) obtained from the metallogel of $\{[Pd-5](OAc)_2\}_n$ in DMSO (2.0 wt%). (b) A zoomed-in image marked in (a) (scale bar: 50 nm). (c) TEM image (unstained) obtained from the solution of $\{[Pd-5](OAc)_2\}_n$ in DMSO (0.06 wt%).

completely clear at this stage, we speculated that spherical particles might be stabilized by numerous subtle noncovalent interactions of neighboring metallocycles such as van der Waals and π - π stacking interactions. In the case of **3–6**, the extra hydrogen-bonding interactions among the phenolic hydroxyl groups, the OAc⁻ anions and the solvent DMSO molecules might serve as the bridge to connect metallogelators, which leads to fusion of spherical particles to form well-developed three-dimensional networks. The hydrogen-bonding interactions of the hydroxyl groups could be demonstrated by IR studies of free ligands and their corresponding metallogels. For example, in a dry gel of {[Pd-**3**](OAc)₂}_n, the OH-stretching band of **3** was shifted from 3441 cm⁻¹ to 3430 cm⁻¹ (Fig. S7†).



One advantage of metallogels is the possibility to impart collective chemical and physical properties of metal ions that are usually observed in the crystalline and solution state to highly processable gel-phase materials.¹¹ The opaque metallogels formed by 3-6 and $Pd(OAc)_2$ were stable enough to be no longer soluble in other solvents including acetone, dichloromethane, THF, hexane, toluene, methanol, and itself without any visible collapse even over a long period of time (several months). Subsequently, the metallogel of $\{[Pd-3](OAc)_2\}_n$ was used as a medium for the direct phenylation of indole with phenyl boronic acid (eqn (1)). The gel of $\{[Pd-3](OAc)_2\}_n$ afforded the corresponding cross-coupling product in ca. 50% yield. In sharp contrast, both a soluble complex of $\{[Pd-3](OAc)_2\}_n$ and a dry gel of $\{[Pd-3](OAc)_2\}_n$ almost lost the catalytic activity (less than 5% yield). It is reasonable to assume that the enhanced activity of gels might be related to high surface area similar to that of amorphous MOFs.¹² Porous collapse of dry gels might result in a relatively smaller surface area, which leads to hardly delivering the reaction substrates to the metal sites. Despite a moderate yield of cross-coupling product obtained, it would give a clue to exploring a new generation of metallogels exhibiting excellent catalysis in the future.

In summary, we have described the self-assembly of the conformationally flexible bismethylimidazolyl ligands with $Pd(OAc)_2$. The ligands 1–2 that do not contain the hydroxyl group and $Pd(OAc)_2$ self-assemble into a new type of metal-organic vesicles. The ligands 3–6 with the hydroxyl group and $Pd(OAc)_2$ evolve into a three-dimensional globular network thereby resulting in the immobilization of organic fluids after aging. Thus, depending on whether the ligands provide the hydrogen bonding donor, a switching of vesicles to globular networks is achieved. The metallogel materials further show catalytic activity for the cross-coupling of indole with phenyl boronic acid. Efforts are now in progress to investigate the full scope of the transformation to obtain a detailed mechanism

and to apply this strategy to other metallogel systems. The work may open a way for the design of a new generation of vesicles from nontypical amphiphilic architectures.

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Notes and references

- (a) J.-M. Lehn, Supramolecular Chemistry: Concepts and Perspectives, VCH, Weinheim, 1995; (b) S. Kitagawa, R. Kitaura and S. Noro, Angew. Chem., Int. Ed., 2004, 43, 2334; (c) X. Roy and M. J. MacLachlan, Chem.–Eur. J., 2009, 15, 6552; (d) W. Lin, W. J. Rieter and K. M. L. Taylor, Angew. Chem., Int. Ed., 2009, 48, 650.
- (a) M. A. Alam, M. Nethaji and M. Ray, Angew. Chem., Int. Ed., 2003, 42, 1940; (b) X.-C. Huang, J.-P. Zhang and X.-M. Chen, J. Am. Chem. Soc., 2004, 126, 13218; (c) L. Dobrzańska, G. O. Lloyd, H. G. Raubenheimer and L. J. Barbour, J. Am. Chem. Soc., 2005, 127, 13134; (d) L. Dobrzańska, G. O. Lloyd, H. G. Raubenheimer and L. J. Barbour, J. Am. Chem. Soc., 2006, 128, 698; (e) I. Imaz, D. Maspoch, C. Rodríguez-Blanco, J. M. Pérez-Falcón, J. Campo and D. Ruiz-Molina, Angew. Chem., Int. Ed., 2008, 47, 1857; (f) I. Imaz, J. Hernando, D. Ruiz-Molina and D. Maspoch, Angew. Chem., Int. Ed., 2009, 48, 2325.
- 3 S. Zhang, S. Yang, J. Lan, S. Yang and J. You, *Chem. Commun.*, 2008, 6170.
- 4 S. Zhang, S. Yang, J. Lan, Y. Tang, Y. Xue and J. You, J. Am. Chem. Soc., 2009, 131, 1689.
- 5 L. Yan, Y. Xue, G. Gao, J. Lan, F. Yang, X. Su and J. You, *Chem.-Eur. J.*, 2010, **16**, 2250.
- 6 (a) J. H. van Esch, M. Damen, M. C. Feiters and R. J. M. Nolte, *Recl. Trav. Chim. Pays-Bas*, 1994, 113, 186; (b) T. Rispens and J. B. F. N. Engberts, *Org. Lett.*, 2001, 3, 941; (c) D. Li, J. Zhang, K. Landskron and T. Liu, *J. Am. Chem. Soc.*, 2008, 130, 4226; (d) C. P. Pradeep, M. F. Misdrahi, F.-Y. Li, J. Zhang, L. Xu, D.-L. Long, T. Liu and L. Cronin, *Angew. Chem., Int. Ed.*, 2009, 48, 8309.
- 7 (a) P. Samorí, V. Francke, T. Mangel, K. Müllen and J. P. Rabe, *Opt. Mater.*, 1998, 9, 390; (b) A. Ajayaghosh, R. Varghese, S. Mahesh and V. K. Praveen, *Angew. Chem., Int. Ed.*, 2006, 45, 7729.
- 8 (a) M. Yang, W. Wang, F. Yuan, X. Zhang, J. Li, F. Liang, B. He, B. Minch and G. Wegner, J. Am. Chem. Soc., 2005, **127**, 15107; (b) A. Ajayaghosh, R. Varghese, V. K. Praveen and S. Mahesh, Angew. Chem., Int. Ed., 2006, **45**, 3261; (c) C. Schmuck, T. Rehm, K. Klein and F. Gröhn, Angew. Chem., Int. Ed., 2007, **46**, 1693; (d) A. Ajayaghosh, P. Chithra and R. Varghese, Angew. Chem., Int. Ed., 2007, **46**, 230; (e) W. Cai, G.-T. Wang, Y.-X. Xu, X.-K. Jiang and Z.-T. Li, J. Am. Chem. Soc., 2008, **130**, 6936.
- 9 (a) K. Murata, M. Aoki, T. Suzuki, T. Harada, H. Kawabata, T. Komori, F. Ohseto, K. Ueda and S. Shinkai, J. Am. Chem. Soc., 1994, **116**, 6664; (b) T. Klawonn, A. Gansäuer, I. Winkler, T. Lauterbach, D. Franke, R. J. M. Nolte, M. C. Feiters, H. Börner, J. Hentschel and K. H. Dötz, Chem. Commun., 2007, 1894.
- The crystal parameters, data collection and refinement results for CCDC 759098 (8) are summarized in Supporting Information (Table S3[†]).
- 11 For highlights and reviews, see: (a) F. Fages, Angew. Chem., Int. Ed., 2006, 45, 1680; (b) H. Maeda, Chem.-Eur. J., 2008, 14, 11274;
 (c) G. Cravotto and P. Cintas, Chem. Soc. Rev., 2009, 38, 2684;
 (d) M.-O. M. Piepenbrock, G. O. Lloyd, N. Clarke and J. W. Steed, Chem. Rev., 2010, 110, 1960.
- 12 (a) Z. Wang, G. Chen and K. Ding, *Chem. Rev.*, 2009, **109**, 322;
 (b) D. Farrusseng, S. Aguado and C. Pinel, *Angew. Chem., Int. Ed.*, 2009, **48**, 7502; (c) B. Xing, M.-F. Choi and B. Xu, *Chem.–Eur. J.*, 2002, **8**, 5028.