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Solventless reaction dramatically accelerates supramolecular self-assembly†

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Received (in Cambridge, UK) 16th April 2002, Accepted 17th May 2002
First published as an Advance Article on the web 6th June 2002

It has been disclosed that the supramolecular self-assembly is dramatically accelerated under solvent-free conditions leading to higher-order fabrications of two- or three-dimensional topology and even double helicates.

Self-assembly plays a pivotal role in supramolecular chemistry.[1–6] Hydrogen bonding is of prime importance in biological systems such as in the double helix formation of DNA. Another important protocol is brought about by metal complexation which leads to artificial supramolecular systems. So far these assembling events have been conducted in solution. Recently, the usefulness of solvent-free reaction has been fully recognized, yet the reactions employed are mostly limited to making and breaking covalent bonds.[7–9] Virtually, no supramolecular chemistry has been involved although the formation of inclusion compounds in the solid state[7,9] may be classified in this category. Self-assembly through metal complexation requires unstrained movements of both ligands and metal ions resulting in the most thermodynamically stable higher-order structures. It has been accepted now that molecules are able to move even in the solid with considerable freedom.[8,9] In this context, we expected that the self-assembly would be driven by metal–ligand interactions without solvent. This has proved to be indeed the case. We report herein that the solventless reaction not only gives rise to supramolecular self-assembly in a similar way as the solution reaction, but also accelerates the reaction rate dramatically. This protocol effects facile fabrication of various supramolecules with two- or three-dimensional topology as well as double helical structure.[10–12]

Fujita *et al.* reported that (en)M$(NO_3)_2$ (en = ethylenediamine), **1a** (M = Pd) and **1b** (M = Pt), upon mixing with 4,4′-bipyridine (**2**) in ethanol–methanol–water, furnished molecular squares **3** (Scheme 1).[13,14] Although the reaction of the palladium complex was complete in 10 min at room temperature, it took more than 4 weeks even at 100 °C for the reaction of the platinum complex in D_2O to be completed affording **3b** in *ca.* 80% yield. In striking contrast, we found that this reaction was brought to completion within 10 min at room temperature simply by mixing **1b** and **2** without solvent. A powdered mixture of **1b** and **2** in a 1 : 1 ratio was ground in a mortar with a pestle in the ambient atmosphere. The mixture became gummy immediately. After 10 min, the ^{1}H NMR spectrum of the mixture in D_2O exhibited complete consumption of the starting materials and formation of **3b** together with a small amount of other species that could be attributed to linearly assembled oligomers. Reprecipitation of the mixture from water–ethanol furnished a 76% yield of **3b** whose spectral data were fully consistent with that reported. On the basis of the extremely slow reaction rate in solution, obviously no supplementary assembly had proceeded during the recrystallization of the crude product. The process of the solventless assembling was monitored by ^{1}H NMR in D_2O. As depicted in Fig. 1, the profiles are completely the same as reported for the assembling in solution, that is, initial formation of linear oligomeric intermediates followed by conversion to **3b** (refer to Fig. 1 in ref. 14). The neat mixture after 3 min grinding at room temperature corresponded to that obtained by the solution reaction after 1 week at room temperature, then 1 week at 100 °C. After 10 min, the solventless reaction was complete, and remarkably, ^{1}H NMR exhibited formation of **3b** together with the same byproduct in a comparable amount as observed in the solution process. It follows from these results that the assembling under solvent-free conditions proceeded in the same manner as in solution.

Our next choice was bowl-shaped molecule **5** that had been obtained by heating a suspension containing **1a** and triazine-based ligand, **4**, in water at 70 °C (Scheme 2).[15,16] After grinding a powdered mixture of these two components for 10

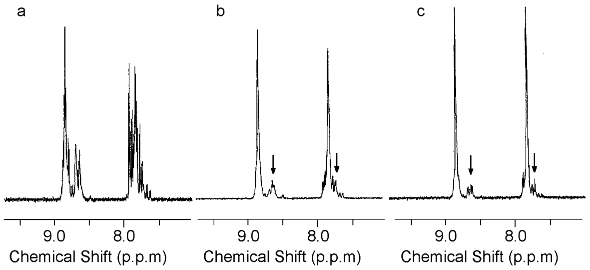
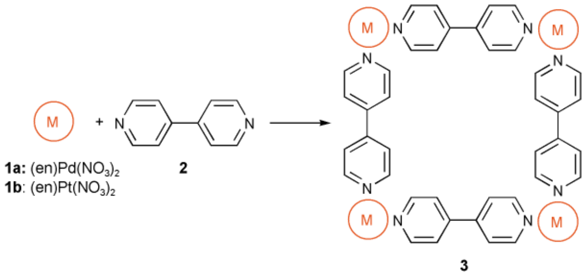
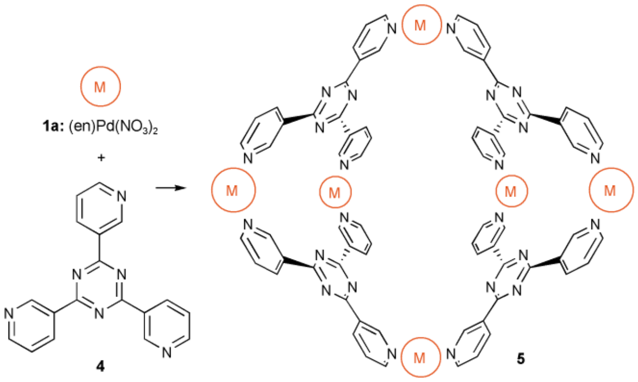


Fig. 1 ^{1}H NMR spectra (500 MHz, D_2O) of products obtained by grinding **1b** and **2** at room temp: (a) after 1 min grinding, (b) after 3 min grinding, (c) after 10 min grinding. Arrrowed peaks correspond to by-products.



Scheme 1



Scheme 2

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† Electronic supplementary information (ESI) available: experimental details and CD spectra. See http://www.rsc.org/suppdata/cc/b2/b203651g/

DOI: 10.1039/b203651g

min at room temperature, the mixture was dissolved in water and addition of methanol caused precipitation of **5** in 90% yield within 5 min. The reprecipitation was performed as quickly as possible to minimize the possible further propagation of the self-assembly during the manipulation. In order to confirm that this had not been the case actually, we monitored the reaction in D_2O at 20 °C. ^{1}H NMR spectra with a dioxane internal standard indicated that the yield of **5** was 11% after 10 min, 13% after 20 min, 17 % after 1 h, and 56 % after 4 h, respectively. As such, it is reasonable to conclude that the achievement of the 90% yield resulted virtually from the solventless reaction. The facileness of this reaction is apparent from the high yield at room temperature while the solution reaction required a higher reaction temperature.

Finally, double helix formation under solvent-free conditions was realized by use of chiral oligo(bipyridine)copper complexes **8** that had been originally reported by Siegel, Cozzi and coworkers (Scheme 3).[17,18] They obtained double helicates upon treatment of chiral oligo(bipyridine) ligands **6** with copper triflate or trifluoroacetate in acetonitrile. Because these copper salts are unstable in air, $[(CH_3CN)_4Cu]PF_6$ (**7**) was employed instead in our reaction. The authentic helicates **8** were prepared by treating **6** with **7** in chloroform–acetonitrile at room temp. for 5 h according to the original procedure. These compounds were confirmed spectroscopically and by elemental analyses. The helicates gave large $[\alpha]_D$ values with opposite sign to **6** (see Scheme 3). The CD spectra of these compounds exhibited similar profiles to those of the Siegel–Cozzi compounds.[17] The solventless assembly was performed by grinding a powdered mixture of **6** and **7** with appropriate stoichiometry at room temperature. The mixture immediately changed from faintly pale yellow to wine red. The progress of the assembling event could be qualitatively monitored by the solid-state CD spectra. As shown in Fig. 2, the helicates exhibit a Cotton effect with zero-point at 287 nm intervened by two peaks with nearly equal intensities at 253 and 314 nm. On the other hand, the patterns of the free ligands **6** are different giving rise to a single peak at 254 nm. Thus, the peaks at 253 and 314 nm should appreciably differ in intensity if **8** were contaminated by **6**. After grinding for 5 min, the solid-state CD spectra of the mixture exhibited virtually the same profiles as those of the helicates obtained in solution, indicative of completion of the assembling. Then, the mixture was washed with benzene to remove the unreacted free ligand if any. The residue was passed through a short column on alumina (eluent, 95:5 dichloromethane–methanol) to give quantitative yields of **8**.

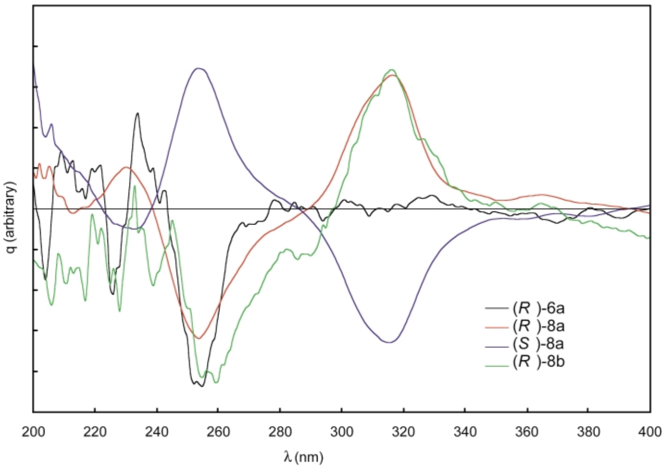
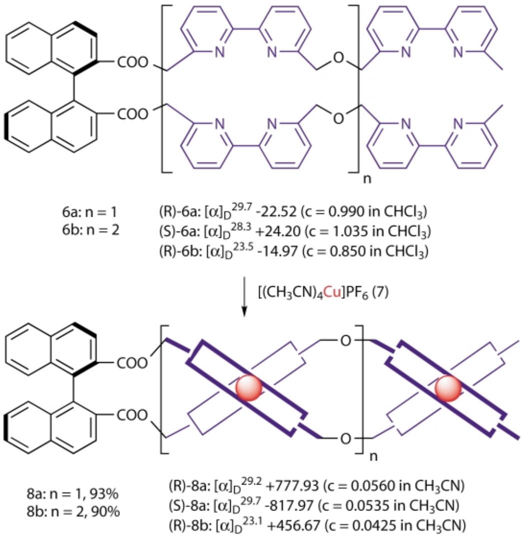


Fig. 2 CD spectra of **6** and **8** prepared without solvent. CD spectra were measured in Nujol mull at room temperature.



Scheme 3

It is apparent from the above results that supramolecular self-assembly is dramatically accelerated under solvent-free conditions leading to higher-order fabrications of two- or three-dimensional topology and even double helicates. Such shortening of the reaction time together with solvent-free operation is promising from the standpoint of process chemistry. The solventless assembly may possibly develop into new technology for simplified synthesis of supramolecular devices.[19–21]

We are grateful to Professor F. Toda (Okayama University of Science) for helpful discussion, and Professor M. Sisido (Okayama University) and Professor K. Tanaka (Ehime University) for CD spectra.

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