SUPRAMOLECULAR POLYMERS

Chain growth in control

Supramolecular polymerizations typically proceed through stepwise intermolecular mechanisms, concomitant with many side reactions to yield aggregates of unpredictable size, shape and mass. Now, a chain-growth strategy is shown to allow assembly of molecules into supramolecular chain structures endowed with precisely controlled characteristics.

Renren Deng and Xiaogang Liu

Supramolecular polymers are a class of materials characterized by a repetition of monomer units held together by non-covalent forces such as metal coordination, π–π interactions and hydrogen bonding[1–4]. Compared with their covalent counterparts the unique properties of these polymers have attracted considerable attention, for instance, the self-healing ability that arises from the thermodynamic compensation for the formation of defects in materials[3,5]. Yet our understanding of the supramolecular polymerization process remains limited.

In most cases, supramolecular polymerization is governed by thermodynamically controlled growth, arising from the fact that a majority of non-covalent interactions are weak and kinetically labile[6]. For this reason, the polymerization reaction of small molecules typically involves a step-growth mechanism in which large quantities of the precursors are consumed early in the reaction to form oligomers that can further react with each other[7]. At ambient conditions, such events can be extremely complex, and typically result in the formation of macromolecular assemblies with a broad molecular weight distribution.

Writing in *Science*, Daigo Miyajima, Takuzo Aida and colleagues now report small molecules designed to undergo non-covalent chain-growth polymerization and give aggregates with controlled chain length, polydispersity and stereochemical structure[8]. In chain-growth polymerization, monomers become part of the growing polymer chain one at a time; the growth is driven by an initiator molecule and normally only occurs at one end of the polymer chain. In that respect, the key mechanism of chain-growth polymerization is reminiscent of a process called translation in protein synthesis. During translation, ribosomes and transfer RNA (tRNA) work together to decode the sequence of a messenger RNA (mRNA) molecule and produce proteins[9]. The ribosome connects one amino acid at a time and builds a long, sequence-controlled amino acid chain (polypeptide) that eventually becomes part of a protein. Despite considerable recent efforts, however, the design of a synthetic supramolecular system that undergoes chain-growth polymerization has remained challenging.

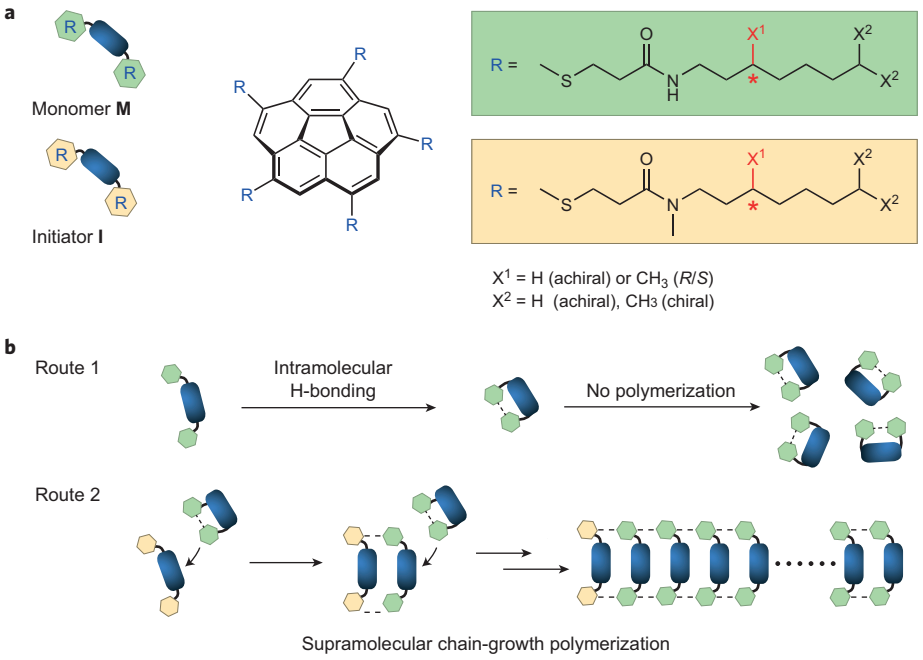

Figure 1 | Schematic representation of the supramolecular chain-growth polymerization process involving bowl-shaped corannulene molecules. **a**, Structure of the monomer **M** and the initiator **I**, prepared by reductive methylamination of **M**. **b**, Route 1: In the absence of initiator **I**, no polymerization occurs as monomer **M** tends to adopt a closed cage conformation owing to strong intramolecular H-bonding. Route 2: Addition of initiator **I** to monomer **M** facilitates chain-growth polymerization through controlled intermolecular H-bonding interactions.

Miyajima, Aida and co-workers have now succeeded in devising such a system by using bowl-shaped corannulene derivatives as monomers that disfavour self-polymerization, yet can be coaxed into it under heating or in the presence of an initiator. In this design, C_5-symmetric non-planar corannulene molecules **M** are functionalized with five amide-appended thioalkyl side chains (Fig. 1a). At ambient temperature, in low-polarity solutions, the monomer **M** does not spontaneously self-assemble into supramolecular polymers[10]. Instead, it adopts a metastable cage-like closed conformation owing to strong intramolecular hydrogen bonding interactions between the NH and CO moieties of the five side-chain amide groups (Fig. 1b, Route 1). Under heating, however, **M** does self-assemble into one-dimensional supramolecular aggregates, which continue to grow when a fresh feed of **M** is added. This shows that **M** does indeed support polymerization, which inspired the researchers to devise an initiator **I** — an *N*-methylated derivative of **M** — that facilitates it.

Compound **I** adopts an open-cage conformation, as its *N*-methylated moieties cannot engage in hydrogen bonding.

For the same reason, it also cannot self-polymerize. Its CO moieties can however serve as proton acceptors for intermolecular hydrogen bonding with the NH amide groups of **M**. The presence of **I** triggers a change in conformation for **M** from closed to open cage — through a reorganization of its hydrogen bonds from intramolecular to intermolecular — and the formation of an **I**–**M** dimer held together by hydrogen bonds between the CO moieties of **I** and the NH groups of **M**. This in turn leaves the CO groups of the **M** monomer of the dimer free to engage in hydrogen bonding with the amido groups of an adjacent, free monomer. This promotes the change of monomer conformation, which then self-assembles with the **I**–**M** dimer to form **I**–**M**–**M**, and so on, so that the process results in the linear growth of supramolecular structures one **M** at a time (Fig. 1b, Route 2). It should be noted that the intermolecular hydrogen bonds formed are only stable in low-polarity media (such as methylcyclohexane), at room temperature. In polar solvents such as $CHCl_3$, the polymer chains would undergo dissociation, even without heating.

The chain-growth process allows precise control over the average length of the supramolecular polymer by simply varying the concentration ratio of monomer to initiator. Adding more initiator molecules to the reaction affects the degree of polymerization, leading to shorter polymers, as directly exemplified by atomic force microscopy of the samples. The resulting supramolecular polymer chains obtained are very uniform, with a polydispersity index (1.2 to 1.3) that is much smaller than polymers prepared without the initiator (typically around 2.0)[7].

A very interesting aspect of this process is that it permits supramolecular polymerization with high stereoselectivity. Having established the chain-growth mechanism, Miyajima, Aida and co-workers went on to prepare a series of optically active monomers and initiators by introducing a chiral centre (*R* or *S*) in the thioalkyl side chain of the corresponding corannulene molecules (Fig. 1a). The team found that the polymerization process occurs only when the monomer and initiator have the same chirality. It is also noteworthy that, in the presence of a chiral initiator and an achiral monomer, a helical chain structure is formed. In this case, monomer **M** can be polymerized into a clockwise- or counter-clockwise-helical chain structure by adding initiators of different chirality (*R* or *S*) without the need for changing the monomer itself. This behaviour shows the extent of control over the polymer topology through stereospecific chain-growth polymerization.

The chain-growth strategy designed by Miyajima, Aida and co-workers is a landmark in supramolecular polymerization, as it enables the construction of nano-sized macromolecular structures with high precision and complex topology. Although the demonstration was performed only on corannulene derivatives, the concept is likely to be scalable across a wide range of rationally designed molecules. A challenging issue remains, namely how applicable this method will be to the preparation of supramolecular polymers with unique optical characteristics and tailored electronic properties. This is a tantalizing prospect for chemists and materials scientists, particularly those interested in manipulating the optical and electronic properties of polymer materials at the molecular level. ❐

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COMPUTATIONAL CHEMISTRY

Making a bad calculation

Computations of the energetics and mechanism of the Morita–Baylis–Hillman reaction are "not even wrong" when compared with experiments. While computational abstinence may be the purest way to calculate challenging reaction mechanisms, taking prophylactic measures to avoid regrettable outcomes may be more realistic.

Arthur Winter

The rise of modern theoretical methods and speedy computers has led to a cheerful exuberance in computing the mechanisms and energetics of chemical reactions. It is now relatively straightforward to calculate transition state geometries and energies for every step in a reaction. Computed transition state geometries give a provocative glimpse of what the highest-energy structures on a reaction trajectory might have looked like for the fraction of a picosecond before a molecular vibration hurtled it over the energetic hilltop and began the reaction tobogganing towards the products. Even more excitingly, the correct computed free energies of all possible transition states for a reaction forecast both the mechanism and the rates for each step, all without stepping into the lab and rinsing out a flask. This is all in principle, of course. Now, Plata and Singleton[1] break up the party by demonstrating that, for a case-study — the Morita–Baylis–Hilman (MBH) reaction — prior computational studies gave wrong predictions for both the reaction energetics and the mechanism of the reaction. This cautionary tale demonstrates that experimental chemists needn't fear being replaced by computational overlords in the immediate future, and also highlights several of the inherent challenges for chemists when modelling complex chemical reactions.

The MBH reaction, is a classic reaction that involves a C–C bond coupling of an activated alkene with an aldehyde by adding a nucleophilic catalyst, usually an amine or phosphine (Fig. 1). In short, the reaction is uncontroversial: the nucleophilic catalyst first attacks the activated alkene to generate a carbanion, providing a new nucleophile that can then direct its attention towards the aldehyde and engage in an aldol-type coupling. The