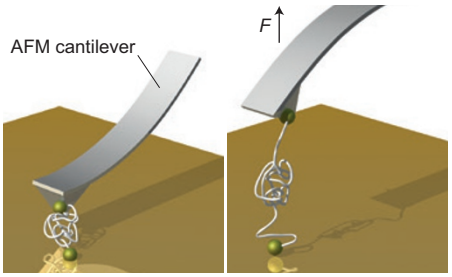
POLYMER FOLDING

A right tangle

J. Am. Chem. Soc. http://doi.org/44f (2015)



Single-chain polymer nanoparticles are globular entities formed by intra-chain crosslinking — either covalent or non-covalent. When supramolecular linkages are used, the resulting nanoparticles can be thought of as crude analogues of folded peptide chains, and have been used to sequester catalytic sites in an effort to mimic enzymes. Unlike peptides, synthetic polymers display inherent variations from chain-to-chain, such as in chain length and the position of their crosslinking groups. This means that the exact nature and strength of their folding can be difficult to ascertain.

Now, Bert Meijer from Eindhoven University of Technology, Zhibin Guan from University of California, Irvine, and colleagues have used single-molecule force spectroscopy to investigate the strength of the intra-chain crosslinks in single-chain polymer nanoparticles. Two different bonding motifs were investigated: 2-ureido-4-[1H]-pyrimidinone (UPy), which contains a self-complementary H-bonding pattern and forms dimers; and benzene-1,3,5-tricarboxamine (BTA), which forms helical stacks of several BTA moieties. The polymer chains were attached at either end to a gold substrate and a gold-coated atomic force microscopy cantilever. Pulling the cantilever away from the substrate unfolded the nanoparticles and statistical analysis of the force-extension curves yielded some surprising insights into the folding of the nanoparticles.

For the nanoparticles held together with UPy dimers, one rupturing event in the force-extension curve for every two UPy functionalities on the chain was expected; however, for higher densities of UPy functionalities, fewer events were observed, suggesting that not all of the UPy groups dimerize during folding. For the BTA stacks, the situation is more complex as multiple BTA units are incorporated into one or more stacks — dependent on the density of BTA functionalities along the chain — within the nanoparticle. Using force spectroscopy analysis, the team were able to extract a dissociation rate constant for the BTA stacks. Interestingly, the stabilities of both UPy dimers and BTA stacks were lower in the polymer nanoparticles than alone in solution, due to the entropic cost of folding the polymer chain or the polarity of the nearby polymer backbone. *CH*

BIOSYNTHESIS

Building a biofactory

Nature Chem. Bio. http://doi.org/4q8 (2015)

Bioengineered microorganisms are able to produce complex metabolites that are difficult to manufacture using traditional synthetic

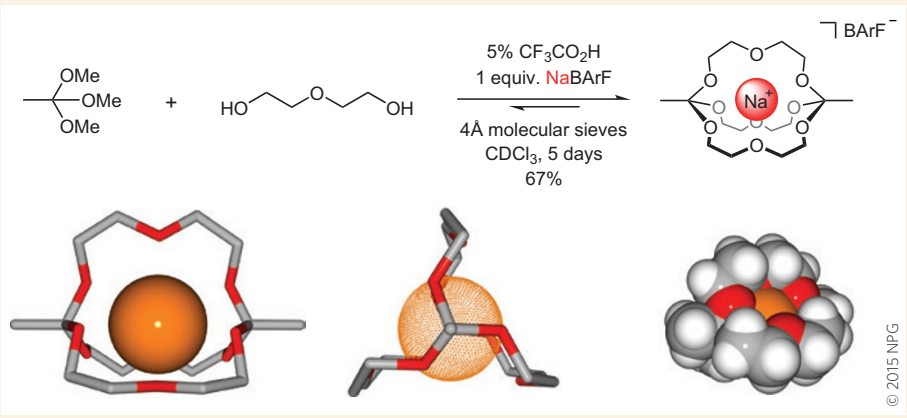
DYNAMIC COVALENT CHEMISTRY

Tales from the cryptates

Nature Commun. **6**, 7129 (2015)

In the early days of host–guest chemistry, researchers would make molecular 'hosts' — typically in the form of rings or cages — and show how they could bind 'guest' species such as metal ions or other small molecules. These iconic molecules, with evocative names such as crown ethers and cryptands, launched a new subfield within chemistry and the award of the 1987 Nobel Prize in Chemistry can be traced back to them. A huge number of host compounds with an incredibly diverse range of structures have been made and studied over the years, some of which require significant synthetic effort to produce.

Now, a team of researchers at Friedrich-Alexander-University Erlangen-Nürnberg in Germany led by Max von Delius has shown how dynamic covalent chemistry can be used to self-assemble cage-like molecules in one step from simple, commercially available compounds. When trimethyl orthoacetate reacts with diethylene glycol in the presence of an acid catalyst and a source of sodium ions, a monometallic complex (known as a cryptate) is formed. This complex features a sodium ion nestled inside an organic



cage built from two orthoacetate caps linked together with three bridging diethylene glycol chains. Molecular sieves are crucial in the reaction to mop up the methanol produced by the orthoester exchange and thus drive the dynamic system to form the cryptate as the major product.

In the absence of a sodium template, the main product of the reaction is the simple eight-membered cyclic orthoester resulting from the 1:1 reaction between trimethyl orthoacetate and diethylene glycol. In the presence of other templates such as lithium or potassium ions, complexes reminiscent of crown ethers are observed, but no cryptates are formed. All of these systems are dynamic in acidic conditions, however, and the addition of an appropriate sodium salt leads to the formation of the sodium cryptate. Although the sodium ion is bound strongly inside the cryptate, it is not trapped there; NMR experiments show that it can move in and out of the cage, albeit relatively slowly. *SC*