BEYOND CATENANES: SYNTHETIC MOLECULAR KNOTS

Reported by Sarah Bonson December 4th, 2018

BACKGROUND

What are Molecular Knots?

Molecular knots are observed in polymers, circular DNA, and protein structures, and have provided a tremendous synthetic challenge for chemists.[1] A molecular knot is a closed-loop, interwoven macrocyclic structure that can be described by the number of crossings, the number of discrete components, and the order of the knot as determined from knot tables.[1] Non-trivial knots have more than two crossings, with the trefoil knot being the simplest non-trivial knot structure.[2] A variety of characterization techniques are used to study molecular knots, including nuclear magnetic resonance spectroscopy (^{1}H, NOESY, DOSY), mass spectrometry (ESI-MS, MS/MS), and x-ray crystallography.

Catenanes: Early Milestones in Molecular Link Synthesis

The first synthetic catenane was reported by Edel Wasserman in 1960, although in low yield.[3] This achievement challenged synthetic chemists to find creative methods to assemble such molecules more efficiently. In 1983, the Sauvage group reported the copper-templated assembly of a synthetic catenane,[1] which provided a generalizable synthetic approach to mechanically bonded structures. Sauvage shared the 2016 Nobel Prize in Chemistry for this transformative advancement.[1]

FROM CATENANES TO KNOTS: SYNTHETIC STRATEGIES

Supramolecular Interactions

Since the first catenane synthesis, several knots have been synthesized. One synthetic method uses supramolecular interactions, such as solvophobic effects and π-stacking, to pre-organize susbtrates.[4,5] Though early attempts to employ this strategy were largely unsuccessful,[2] the Frontera group exploited hydrophobic interactions to synthesize two different catenanes and a trefoil knot from generalizable building blocks.[4] In another supramolecular approach, the Chi group recently employed π-π interactions in a coordination-driven assembly to form a composite knot with eight crossings.[5]

Metal Helicate-Templated Synthesis

Following their success producing a catenane by metal-templation, the Sauvage group used a linear double helicate to synthesize the first trefoil knot.[2] Apart from successes in small knots, attempts to synthesize larger knots from linear helicates were hindered because of increased distance between the two

loose ends.[2] A solution to this problem came as Lehn reported the self-assembly of an iron circular helicate in 1996.[2] This advance sparked the development of a circular helicate-templated approach, which has been used to synthesize various catenane and knot structures.[6-8]

Interwoven Molecular Grids

A third strategy for the assembly of molecular knots, which has been largely pioneered by the Leigh group, is the construction of a grid pattern via metal coordination followed by adjoining loose ends to construct a loop(s). The formation of metal-templated *n* x *n* grid structures has been used to produce a catenane with twisted rings as well as various knot structures.[9]

THE FUTURE OF MOLECULAR KNOTS

In addition to providing a synthetic challenge, molecular knot structures have been studied for applications in host-guest chemistry, molecular motors, and catalysis.[2,10] Nonetheless, the utilization of knots in these fields is still in early stages of investigation. Further development of switchable helicates may allow for stereodivergent synthesis of knots, which could enhance their catalytic potential. The study of molecular knots might provide a deeper awareness of the function and properties of naturally occurring knot structures while advancing fundamentals of synthetic organic chemistry.

SUMMARY

Molecular knot synthesis has rapidly progressed over the past two years, but to date less than ten knot topologies of more than six billion theoretical knot structures have been synthesized. Though current methods have successfully produced impressive knot structures, stereoselectivity and scalability remain as outstanding challenges in the field. Continued efforts to conquer the synthetic challenge of molecular knots while gaining a deeper understanding of structure – function relationships could allow for optimization of polymer properties, a better understanding of DNA and enzymes, additional uses in molecular machines, and advances in catalysis.

REFERENCES

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