Chemistry researchers create self-tying knotted molecules in the lab

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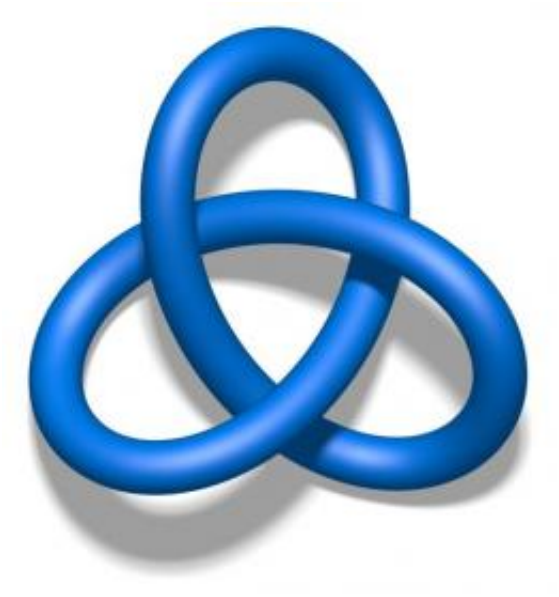

A trefoil knot. Credit: Wikipedia.

(Phys.org)—A group of chemistry researchers working in a lab at Cambridge University have succeeded in causing a group of molecules to form themselves into trefoil knots. The team was working on combinatorial chemistry experiments, they note in their paper describing their achievement in the journal *Science*, when they noticed the spontaneous formation of knots.

As part of an experiment involving creating reaction mixtures, the team was linking naphthalene diimide (NDI) with hydrophilic alanines, which

used cysteine residues as caps. Doing so resulted in the creation of a molecule that displayed both hydrophobic and hydrophilic properties. The caps allowed for reversible disulfide links. The team noted that as longer chains of the molecule were formed, its conflicting reaction to water properties resulted in molecules that twisted themselves together in a solution. When attempting to separate the molecules, researchers noted the presence of a third peak holding them together; repeating the experiment using a higher concentration of salt increased the size of the third peak causing the team to wonder if a knot had been formed. Upon closer inspection using a mass spectrometer, they found that the molecule had spontaneously formed itself into a trefoil knot – one that has three loops and resembles a clover and which cannot be undone without being physically broken apart.

This is the first time a self-forming trefoil knot in a molecule has been caused to come about in the lab; previous attempts to cause such knots to arise have involved trying to force them to occur using a metal ion to serve as a template – allowing them to form on their own is quite naturally much more efficient. Such knots occur quite often in nature however, which has led researchers to believe they could be created in the lab. This new approach shows that not only can such knots be caused to come about on their own, but can be done so in large quantities.

Now that a way has been found to cause spontaneous trefoil knots to come about, the researchers believe there are likely other molecules that can be created that do the same. The trick is in using ingredients that have opposing forces during their creation.

More information: Discovery of an Organic Trefoil Knot, *Science*, 9 November 2012: Vol. 338 no. 6108 pp. 783-785. DOI: 10.1126/science.1227032

ABSTRACT

Molecular knots remain difficult to produce using the current synthetic methods of chemistry because of their topological complexity. We report here the near-quantitative self-assembly of a trefoil knot from a naphthalenediimide-based aqueous disulfide dynamic combinatorial library. The formation of the knot appears to be driven by the hydrophobic effect and leads to a structure in which the aromatic components are buried while the hydrophilic carboxylate groups remain exposed to the solvent. Moreover, the building block chirality constrains the topological conformation of the knot and results in its stereoselective synthesis. This work demonstrates that the hydrophobic effect provides a powerful strategy to direct the synthesis of entwined architectures.