

**Figure 2** | Topologically distinct entanglements of hexagonal layers. Two different modes of polycatenation are shown, which both result in an increase in dimensionality, versus interpenetration in which the dimensionality remains the same.

By way of example,  $[n]$ -catenanes are the simplest example of polycatenation ( $0D + 0D \rightarrow 1D$ ), whereas the structure of  $\text{Cd}(\text{imidazolate})_2$  is an example of a twofold interpenetrated<sup>6</sup> diamondoid (called **dia**) network ( $3D + 3D \rightarrow 3D$ ) (see Figs 1 and 2). A further criterion for polycatenation is that, unlike interpenetration, each distinct building block is never interlaced with all the others in the array. So, in structures such as  $\text{Cd}(\text{imidazolate})_2$ , we can define a degree of interpenetration, because there is always a finite number of interpenetrated components. This is impossible for polycatenated arrays where there are an infinite number of entangled components, as shown in Fig. 2 for hexagonal layers<sup>3</sup>.

Starting from simple rings, it is perfectly possible to imagine structures more complex than the  $[n]$ -catenane chains — in which each

ring is linked to just two adjacent rings — and obtain something two-dimensional (2D) akin to medieval chain-mail<sup>2,3</sup>. If the finite building block is a 3D cage it is possible to extend the catenation in three directions, as in the compound reported by Lu and co-workers.

Here, each cage links to six other equivalent cages, giving rise to a type of octahedral six-coordination that is the basic node of the primitive cubic net (called **pcu** according to the modern nomenclature for nets)<sup>8</sup> (Fig. 1). It is important to keep in mind that — as is usual in solid-state chemistry — such descriptions depend on the types of interaction that are being considered. If we take into account only the strongest interactions, such as covalent bonds, we describe the polycatenated and interpenetrated array as above. In general, topological descriptions may consider

supramolecular interactions — in particular hydrogen bonding — as important building factors of solid-state architectures. Here, if we also consider secondary weak interactions, then the independent motifs become connected and a different entanglement arises.

How can such complex topologies be detected? In the past, the crystallographer needed great experience in 3D visualization and the help of ball-and-stick models to explain these complicated arrangements. Thankfully, modern tailored software allows us to compute, detect and classify entanglements in periodic structures<sup>9,10</sup>. Such computer methods give us much better design capabilities for new extended architectures.

The results of Lu and co-workers demonstrate that, provided it is theoretically possible, almost any — even bizarre — entanglement can be realized in nature. First, however, it is important to thoroughly explore the relationships between the intricate sub-architectures to identify possible pathways for their synthesis. □

*Davide M. Proserpio is in the Department of Structural Chemistry DCSSI, Università degli Studi di Milano, Via Venezian 21, 20133 Milano, Italy. e-mail: davide.proserpio@unimi.it*

#### References

1. Long, J. R. & Yaghi, O. M. *Chem. Soc. Rev.* **38**, 1213–1214 (2009).
2. Fang, L. *et al. Chem. Soc. Rev.* **39**, 17–29 (2010).
3. Carlucci, L., Ciani, G. & Proserpio, D. M. *Coord. Chem. Rev.* **246**, 247–289 (2003).
4. Jin, C. M., Lu, H., Wu, L. Y. & Huang, J. *Chem. Commun.* 5039–5041 (2006).
5. Kuang, X. *et al. Nature Chem.* **2**, 461–465 (2010).
6. Blatov, V. A., Carlucci, L., Ciani, G. & Proserpio, D. M. *CrystEngComm* **6**, 377–395 (2004).
7. Franci, M. *Nature Chem.* **1**, 334–335 (2009).
8. O’Keeffe, M., Peskov, M. A., Ramsden, S. J. & Yaghi, O. M. *Acc. Chem. Res.* **30**, 1782–1789 (2008).
9. Blatov, V. A. *IUCr CompComm Newsletter* **7**, 4–38 (2006).
10. [www.topos.ssu.samara.ru/starting.html](http://www.topos.ssu.samara.ru/starting.html)

## MECHANOCHEMISTRY

# Forcing a molecule’s hand

Ultrasound can be used to control molecular processes as delicate as rotation around a single carbon–carbon bond.

S. Karthikeyan and Rint P. Sijbesma

**T**ug of War’ is a game that tests the strength of two teams pulling on a rope in opposite directions. If it is being played on a molecular scale, the game is known as polymer mechanochemistry, and the interest is not so much in the muscle power of the contestants as in the strength of the rope and its fate under stress. Writing in the *Journal of the American Chemical*

*Society*, Bielawski and co-workers<sup>1</sup> have brought this increasingly popular game to a higher level of sophistication by showing that pulling on molecular ropes may be used to promote racemization of chiral molecules.

In the past, chemists have focused almost exclusively on the use of light or heat to bring about chemical reactions. Promoting reactions with force is an alternative that is

much less popular, although the principle is well established, particularly when the transformation is simply a matter of breaking bonds in the main chain of a polymer — mastication of rubber to reduce its molecular weight is an example of a bond breaking reaction that is widely used in industry.

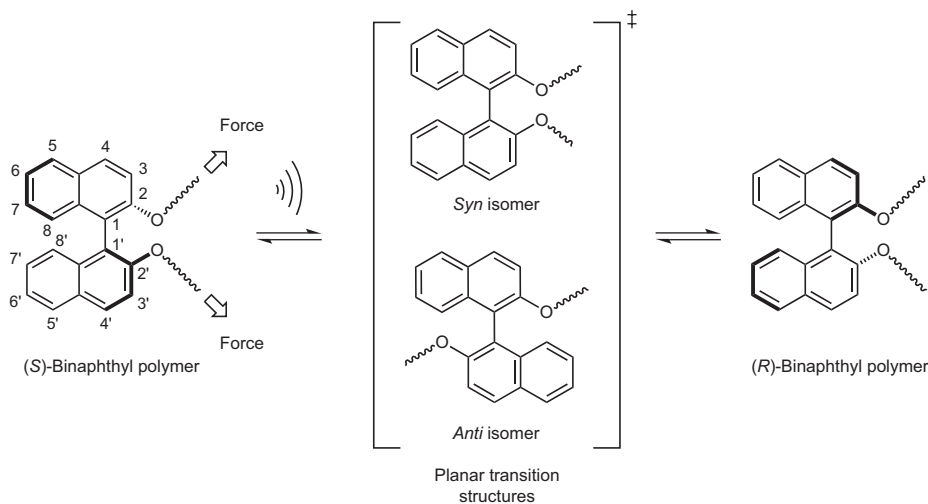
Recently there has been a flurry of reports that show how mechanical forces applied

to polymer chains can be used for far more subtle manipulation of chemical bonds. Polymer mechanochemistry has become a burgeoning field that uses mechanical forces to bias reaction pathways<sup>2</sup>, to change the colour of materials<sup>3</sup>, to trigger multiple reactions in a single polymer chain<sup>4</sup>, and to selectively break weak coordinate bonds to activate dormant catalysts<sup>5</sup>. Recent theoretical work has helped to create a much better understanding of mechanical force as a unique stimulus for chemical reactions<sup>3,6</sup>. Chemists have begun to work in this area with renewed effort because of its potential applications in self-healing polymers, molecular strain gauges and controlled drug release, and because they recognize the possibility that it will provide greater understanding of the mechanochemical transduction mechanisms in biological systems.

Bielawski and co-workers have now elegantly shown that mechanical force can be used to surmount the high energy barrier associated with rotation about the C–C single bond in binaphthyl derivatives and thus convert one mirror image of this molecule to the other (Fig. 1). These mirror-image molecules are called atropisomers — stereoisomers resulting from the hindered rotation around a C–C single bond. The barrier for C–C bond rotation in binaphthyl derivatives is high (~30 kcal mol<sup>-1</sup>), which makes their racemization at ambient temperatures extremely slow. In fact, even at 195 °C, the half-life ( $t_{1/2}$ ) of the parent binaphthol molecule is as long as 4.5 hours (ref. 7).

How did the team, led by Texas-based chemist Chris Bielawski, manage to isomerize these stable chiral molecules? One of the most efficient ways to exert pulling forces on a molecule is to use the intense flow fields around collapsing cavitation bubbles in sonicated solutions. For effective transfer of the mechanical force to the reactive unit, it is essential to functionalize it with polymer chains. Therefore, Bielawski and co-workers appended poly(methyl acrylate) chains with total molecular weights between 10 and 100 kDa to binaphthyl derivatives. When the polymeric (*S*)-binaphthyl derivative (with  $M_n = 98.7$  kDa) was sonicated in acetonitrile solution, circular dichroism spectroscopy showed that more than 95% of the derivative had racemized after 24 hours. As a measure of the relative efficiency of the mechanical force, heating of the same (*S*)-binaphthyl-functionalized polymer was also investigated, but heating at 250 °C for 72 hours gave no change in the intensity of the circular dichroism signal.

The mechanical action of ultrasonication is always accompanied by thermal effects, and the heating effect of collapsing cavitation



**Figure 1** | Racemization of binaphthyl-based polymers with ultrasound. Starting with the (*S*)-configured binaphthyl polymer, ultrasonic irradiation leads to rapid racemization, which may occur through one of the planar transition structures shown.

bubbles can be strong. Therefore, control experiments that establish the contribution of heating are important. To this end, ultrasonication experiments were performed on binaphthyl derivatives without the attached polymer chains. In these experiments, no racemization was observed. Further convincing evidence for the mechanochemical origin of the racemization comes from the molecular-weight dependence of the racemization rate observed for binaphthyl derivatives attached to polymer chains with  $M_n$  varying from 10 to 100 kDa. The ultrasound-induced isomerization shows a limiting molecular weight (between 25 and 50 kDa), below which no change was observed.

The present work raises interesting questions concerning the pathway by which the stereoisomers are interconverted. The two stereoisomers are stable because the steric bulk of the substituents adjacent to the biaryl bond prevents free rotation. Isomerization of the binaphthyl may therefore proceed by passage of 2,8'- and 2',8 substituents (the so-called *anti* route) or 2,2'- and 8,8' substituents (the so-called *syn* route)<sup>7,8</sup> (Fig. 1). Detailed theoretical studies on thermal racemization pathways of 1,1'-binaphthyl analogues suggest that the most favourable pathway proceeds through the centrosymmetric *anti* transition state, but this is favoured over the *syn* route by only 4 kcal mol<sup>-1</sup>. Does the mechanically facilitated reaction follow the preferred thermal reaction pathway, as the authors propose? Investigating this question may reveal unexpected complexities. It is, for instance, imaginable that the favoured pathway has several transition states and includes mechanically as well as thermally surmounted barriers. Given the fact that

applied mechanical forces change the potential energy surface in a direction-dependent manner, the question can be answered conclusively only with detailed calculations using methods specifically developed to study mechanochemical reactions<sup>2,6</sup>.

The importance of the work lies in showing the path to selectivity to others who consider entering the fascinating field of mechanochemistry. Although polymer scission using ultrasound has been used for many decades, the use of mechanical forces to perform useful transformations and applications is still in its infancy. In the near future, efforts to use mechanochemistry productively will undoubtedly increase, and selectivity will be the focus of attention. Bielawski and co-workers have shown that the seemingly untamed force of ultrasound can be used to control a process as simple and fundamental as rotation about a C–C single bond. □

S. Karthikeyan and Rint P. Sijbesma are in the Laboratory of Macromolecular and Organic Chemistry, Eindhoven University of Technology, P.O. Box 513, 5600 MB Eindhoven, The Netherlands. e-mail: k.sivasubramanian@tue.nl; r.p.sijbesma@tue.nl

## References

- Wiggins, K. M. *et al.* *J. Am. Chem. Soc.* **132**, 3256–3257 (2010).
- Hickenboth, C. R. *et al.* *Nature* **446**, 423–427 (2007).
- Davis, D. A. *et al.* *Nature* **459**, 68–72 (2009).
- Lenhardt, J. M., Black, A. L. & Craig, S. L. *J. Am. Chem. Soc.* **131**, 10818–10819 (2009).
- Piermattei, A., Karthikeyan, S. & Sijbesma, R. P. *Nature Chem.* **1**, 133–137 (2009).
- Ribas-Arino, J., Shiga, M. & Marx, D. *Angew. Chem. Int. Ed.* **48**, 4190–4193 (2009).
- Meca, L., Reha, D. & Havlas, Z. *J. Org. Chem.* **68**, 5677–5680 (2003).
- Kranz, M., Clark, T. & von Rague Schleyer, P. J. *Org. Chem.* **58**, 3317–3325 (1993).