CHIRAL SEPARATION

Molecular doormen

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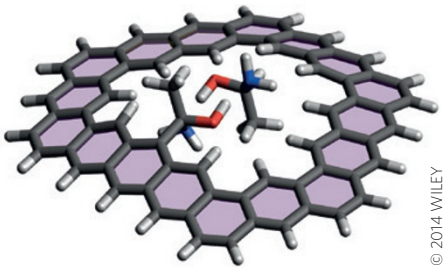

When enantioselective syntheses of drug molecules or natural products are impossible, impractical or prohibitively expensive, chiral separation of a racemic product or intermediate offers a viable alternative. Many chiral separations are chromatography-based, and rely on a series of interactions between the racemate and a chiral stationary phase. The net result is separation of the two enantiomers, but the process can be time-consuming and wasteful of the mobile phase.

Now, a team led by Andreas Hauser and Peter Schwerdtfeger from the University of California, Berkeley and Massey University, respectively, have shown that it is theoretically possible to use a nanoporous membrane instead of a stationary phase to achieve chiral separation. This means that, for each molecule, only one event — either passing through a pore or not — would be needed to achieve macroscopic separation, rather than the multiple interactions with the stationary phase that occur in chiral chromatography. However, a chiral pore alone cannot discriminate between enantiomers because the molecules can approach from either 'above' or 'below' the pore.

To overcome this problem, the team modelled a nanopore in graphene with an added out-of-plane single-enantiomer 'gatekeeper' molecule attached to the pore rim. They show that the gatekeeper molecule (1-aminoethanol) forms dimers with free *R*- or *S*-1-aminoethanol — with a difference in binding energy that would be too small to achieve chiral separation by itself. However, the small differences in size and orientation of the dimers are enough to greatly amplify the difference in free energy required to pass through the nanopore. The net result is that one enantiomer 'fits' through the pore, and one is blocked due to the size of the dimer formed with the gatekeeper molecule. Although the system modelled is based upon a single pore in a graphene sheet, the approach could be extended to other nanoporous membranes and other gatekeeper molecules, provided the pore size is carefully chosen and controlled. If this approach proves experimentally viable, then it could be a useful alternative to preparative chromatography for chiral separations. *CH*

ANTIBIOTICS

Resistance is restored

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The highly adaptable nature of bacteria has led to the evolution of strains that are resistant to common antibiotics. Agents that work through a different mechanism of action are required to overcome this resistance — such as ceftaroline approved by the FDA in 2010, which can treat methicillin-resistant *Staphylococcus aureus* (MRSA).

CARBOBORATION

Addition to alkynoates

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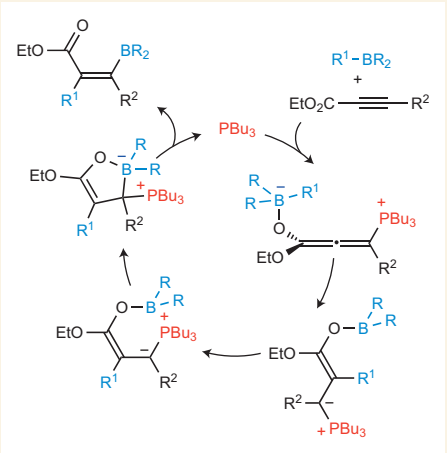
Alkenyl boron derivatives are potentially useful synthetic intermediates that can, through subsequent cross-coupling reactions, be used to prepare highly substituted alkenes. Nickel- and palladium-catalysed additions of alkynyl or cyanoboron derivatives to alkynes have been described, but these methods have not been extended to more commonly available organoboranes. Now, Masaya Sawamura, Hirohisa Ohmiya and Kazunori Nagao from Hokkaido University, Japan, have reported a phosphine-catalysed addition of alkyl-, alkenyl- and arylboranes across the triple bond of alkynoates to produce β-borylalkenoates.

While investigating metal-catalysed reactions of organoboron compounds, they observed that, in the presence of a catalytic quantity of phosphine, an alkylborane reacted with an alkynoate. The addition occurred with the less electronegative boron adding to the more positively charged alkynoate carbon and with the overall carboboration occurring with anti-stereoselectivity — a mode of addition not previously observed using metal catalysis. The proposed mechanism of the reaction begins with conjugate addition of the phosphine catalyst assisted by the Lewis-acidic borane to form an allenolate intermediate. An alkyl group from the borane then migrates to the central carbon of the allenolate to produce a phosphonium ylide.



Several bond rotations allow the formation of a cyclic borate that can then form the product — transferring the boryl group to the β-carbon of the formed alkene and eliminating the phosphine catalyst.

The scope of the reaction was investigated using a series of organoboranes and alkynoates. Sterically hindered aryl-, as well as alkenyl- and alkyl-alkynoates were successfully reacted, albeit with lower yields. A series of alkylboranes — prepared *in situ* by hydroboration of terminal alkenes and used without purification — were also found to react smoothly, as did aryl boranes. So far, simple trialkylphosphines are the only suitable catalysts with triarylphosphines, amines and N-heterocyclic carbenes all failing to provide any product. Attempts to cross-couple the β-borylalkenoates using palladium catalysis were presumably hampered by the sensitivity of the ester to aqueous base, though conversion to an amide first alleviated this issue, providing access to a stereodefined tetrasubstituted alkene. *SD*