CATALYST DESIGN

Supra selectivity

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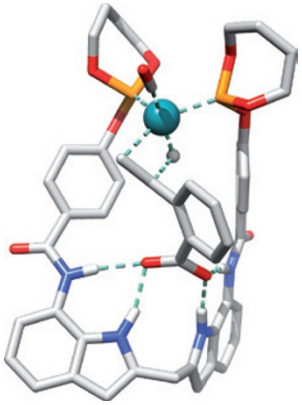
Hydroformylation is an industrially important reaction that converts alkenes into aldehydes by reacting them with a mixture of carbon monoxide and hydrogen. Millions of tonnes of a variety of very useful products are made from relatively cheap alkenes every year through hydroformylation. One particular class of alkene substrate, vinyl arenes, is of great interest. Theoretically, hydroformylation can lead to two possible products — an α-aryl or β-aryl aldehyde — with formation of the branched (α-aryl) product being favoured by interactions of the metal catalyst with the aryl ring. The branched product is chiral and several catalyst systems have been developed to produce this product with both high regio- and stereoselectivity.



Despite being a synthetically useful product, few catalyst systems have been developed that can overcome the natural selectivity of the reaction to produce a linear (β-aryl) aldehyde. Now, Paweł Dydio and Joost Reek from the University of Amsterdam have done just that, by designing a ligand for a rhodium catalyst that dictates the orientation in which a vinyl-2-carboxyarene substrate binds to the catalyst before reaction. The ligand contains two phosphite groups (which coordinate to the rhodium) connected by a diamidodiindolylmethane to form a 'pocket' which binds strongly to the carboxylate group in the substrate. In the key regiochemistry-defining step — migration of a hydride to the alkene (pictured) — it is this strong binding that makes the formation of an α-phenylalkyl rhodium complex (that would ultimately lead to the usual branched product) significantly less favourable. In a control reaction in which the carboxylate group of the substrate is masked as an ester, the natural selectivity (producing 95% of the branched product) is restored.

Dydio and Reek show that the reaction tolerates many other substituents on the aryl ring in addition to the carboxylate directing group, and also demonstrate that the selectivity for the β-aryl aldehyde product is maintained even with additional substituents on the alkene.

HYDROGEN BONDING

Unconventional connections

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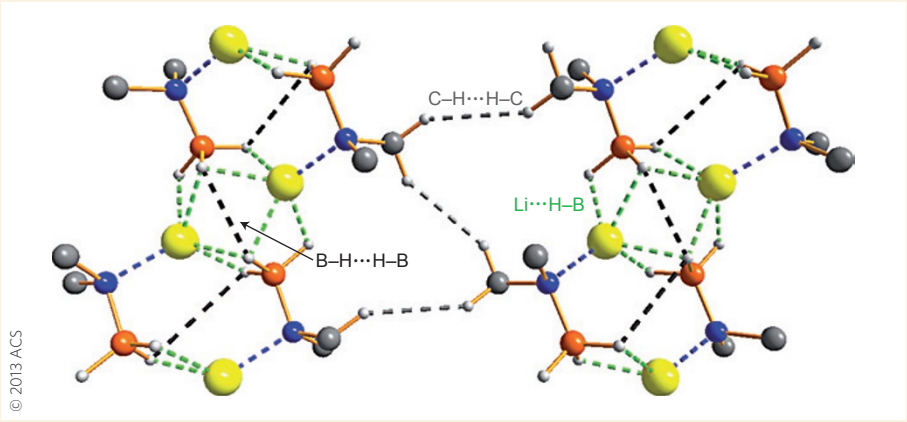
Hydrogen bonding can occur in a variety of situations and is not limited to interactions between polar hydrogens and electronegative atoms of adjacent molecules. Heteropolar dihydrogen interactions (X–H···H–Y) have been observed and, somewhat counter-intuitively, so have homopolar examples, such as between two CH groups. Rather than being governed by electrostatic interactions, these cases arise from attractive van der Waals forces.

By alkylating the NH group of $LiNH_2BH_3$, David J. Wolstenholme, G. Sean McGrady and colleagues from the University of New Brunswick have now suppressed the influence of the conventional proton–hydride N–H···H–B interaction to study in detail the homopolar dihydrogen interactions occurring in solid-state $LiNMe_2BH_3$. The compound was extensively characterized through X-ray crystallography and an analysis of the calculated electron distribution. It was found that $[Li]^+[NMe_2BH_3]^-$ adopts a one-dimensional chain structure (pictured; yellow, Li; orange, B; blue, N; grey, C; white, H) held together by inter-ion Li···N and Li···H–B interactions (shown as blue and green dashed lines, respectively).

Within a given chain, a zigzag arrangement (black dashed lines) of supporting weak B–H···H–B interactions



arising from mutual polarization of the BH groups was found between amidoborane moieties $[NMe_2BH_3]^-$. A significant accumulation of electron density between the two hydrogen atoms confirmed that the BH groups do interact with one another, rather than simply being in close proximity. This conclusion is also supported by the fact that similar B–H···H–B distances were observed in the parent compound $LiNH_2BH_3$. The 1D chains are further connected to each other, albeit loosely, through weaker C–H···H–C dispersion forces (grey dashed lines between the chains) and C–H···H–B interactions (not shown; perpendicular to the plane pictured).

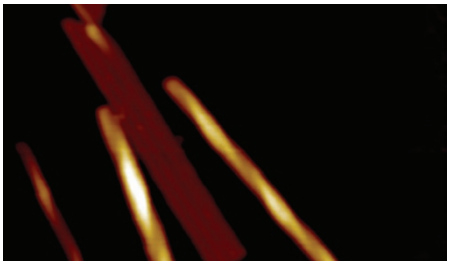
In contrast, the potassium analogue of the compound ($KNMe_2BH_3$) was found to have a sheet-like structure with layers connected to each other through C–H···H–C dispersion forces. This change in topology is caused by subtle differences in the main inter-ion interactions (K···N and K···H–B), which in turn prevent the formation of the weaker B–H···H–B and C–H···H–B bonds. These structural studies underscore the fact that weak homopolar dihydrogen interactions play a substantial supporting role in supramolecular structures, and may contribute to the stability and reactivity of hydrogen-rich compounds. *AP*

In this latter case, a product containing a new stereocentre is formed and the ability to control the selectivity of this process offers a new target for catalyst design and development. *SD*

AMYLOID FIBRILS

Peptides do the twist

Proc. Natl Acad. Sci. USA **110,** 2798–2803 (2013)



In the initial steps of amyloid fibril formation, proteins or peptides self-associate to form small oligomers. The addition of more polypeptide species leads to larger aggregates, termed proto-fibrils, and eventually mature amyloid fibrils. Gathering detailed information on the structure and growth of the intermediate structures could help develop methods to interrupt or reverse the fibrillization process, which could lead to new treatments for a variety of amyloid-related diseases.

Human islet amyloid polypeptide (hIAPP) is found in amyloid deposits in patients with type 2 diabetes. To find out more about what occurs during fibrillization of hIAPP, a team led by Mingdong Dong at Aarhus University, Denmark, investigated the aggregation of a decapeptide ($hIAPP_{20\text{-}29}$). This oligopeptide is thought to be the region of the protein that initiates fibril formation of hIAPP. Dong and co-workers used a combination of atomic force microscopy and microsecond force microscopy to follow the formation and changes in morphology of the peptide nanostructures throughout the aggregation process — from small strands through to helical fibrils. They also measured the rate at which structures thickened, which is a key property for growth and maturation of fibrillar structures.

Initially the decapeptide self-assembled to form thin strands during the so-called lag phase. As aggregation progressed into the elongation phase, the thin ribbons became wider. After a couple of hours, some of the ribbons began to twist and continued to gradually thicken. Multi-strand mature helical fibrils were then formed from the twisted ribbons; however, instead of forming helical fibrils, some of the flat ribbons thickened further and formed large flat ribbons. These larger flat ribbons are still present at the end of the fibrillization process, which proves that the ribbon structures and helical fibrils can co-exist in solution and that not all proto-fibrils transform into mature amyloid fibrils in the case of the hIAPP decapeptide. Dong and co-workers suggest that the thickening of ribbons makes them energetically stable, which enables them to co-exist with the helical fibrils. *RJ*

DNA–PROTEIN INTERACTIONS

Appreciating allostery

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Allostery is the process in which the binding of a ligand to a protein at one site induces conformational changes that affect the subsequent binding of a second ligand at another site. Now, a team of researchers from Peking University and Harvard University, led by Xiao-dong Su, Yujie Sun and X. Sunney Xie, has shown that allostery is not restricted to proteins and can occur through DNA. They probed how the unbinding of a protein from double-stranded (ds) DNA was affected by the presence of another protein attached nearby to the same dsDNA molecule.

dsDNA molecules featuring two protein binding sites a defined distance apart were attached to a surface. A fluorescently labelled protein was then attached to one site before a second protein was flowed over the immobilized dsDNA–protein complexes. During this period, the rate of detachment of the initially bound protein was monitored using single-molecule fluorescence. Su, Sun and Xie saw that, on binding, the second protein could either stabilize or destabilize the attachment of the first protein depending on the proximity of the two binding sites. The dependence oscillated with a period of 10 base pairs, that is, if a protein was able to stabilize a second protein 10 base pairs away, it would destabilize a protein if it was 5 base pairs away. 10 is the number of base pairs it takes for dsDNA to complete one helix turn, and so this allosteric behaviour is linked to the structure of dsDNA.

It is suggested that the allostery results from the mechanical properties of the dsDNA. Protein binding generally takes place in the major groove of dsDNA, and molecular dynamics simulations show that the binding of one protein affects the size of the adjacent major groove, widening it or narrowing it (depending on the protein) — again with a periodicity of 10 base pairs. Su, Sun and Xie also demonstrated allostery in the binding of enzymes relevant to transcription and were able to use the effect to modify gene expression in living bacteria. *GA*

Written by Gavin Armstrong, Stephen Davey, Russell Johnson and Anne Pichon

blogroll

Fighting fear

Changing the tune on chemistry's bad rap

Chemophobia has led manufacturers and proprietors to advertise 'chemical-free' goods and services; it pops up in literature by activist groups like Safer Chemicals, Healthy Families — and has even infected popular media outlets. The rise in the fear of chemicals and chemistry has many chemists, as well as scientists in all fields, asking what can be done to eradicate chemophobia.

One way to counter chemophobia is for scientists and science writers to tackle it head-on. Michelle Francl, a professor of chemistry who blogs at The Culture of Chemistry, responded to a February *New York Times Magazine* article 'The Boy With a Thorn in His Joints' about parents treating their child's arthritis with 'natural' alternatives instead of the recommended methotrexate. Writing in *Slate* (http://go.nature.com/8a9W24), Francl pointed out that the parents' 'natural' alternatives were also chemicals — ones that have their own safety concerns. Stressing that everything is a chemical and all chemicals have risks are tips that Francl gives for fighting a 'chemophobia pandemic'.

ChemBark offers another way to fight chemophobia — by chemists doing outreach. "I think it is important that every chemist spends some time engaging the general public for the purposes of education and promoting the benefits of our field" wrote ChemBark in his post 'Combatting Chemophobia' (http://go.nature.com/IrpfNS). Writing as if he's talking to an outreach naysayer, ChemBark answers typical questions like "What's in it for me?" and charges like "I can't put that on my CV!"

Why fight chemophobia? For one thing, chemistry is "...the amazing and beautiful science of stuff..." as Hank Green puts it in his video on the nucleus (http://go.nature.com/FmjCRo) for Crash Course — a YouTube channel where you can learn about topics from literature to ecology to chemistry (http://go.nature.com/RlbL7W).

Written by DrRubidium, who blogs at http://scientopia.org/blogs/thirtyseven/ and http://www.thejayfk.com/