Chemistry Update

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Calendar of Events

Easter Celebration
Date: Thursday 6 April
Time: 11am-12pm
Location: C/B/102

ABCR Tabletop Exhibition
Date: Wednesday 12 April
Time: 9.30am-3pm
Location: Chemistry A Block Foyer

Research Seminar
Title: "From palladium to iodine - towards sustainable catalysis for late-stage functionalisation" and "New functional groups for synthetic and discovery chemistry"
Speaker: Dr Miriam O'Duill, University of Nottingham and Prof Mike Willis, University of Oxford
Date: Wednesday 12 April
Time: 1pm-2.30pm
Location: C/B/101

Research Seminar
Speaker: Prof. Reinhard Maurer, University of Warwick
Date: Wednesday 19 April
Time: 1pm-2pm
Location: C/A/101

Research Seminar
Speaker: Basile Curchord, University of Bristol, RSC Awards Lecture
Date: Wednesday 26 April
Time: 1pm-2pm
Location: C/A/101

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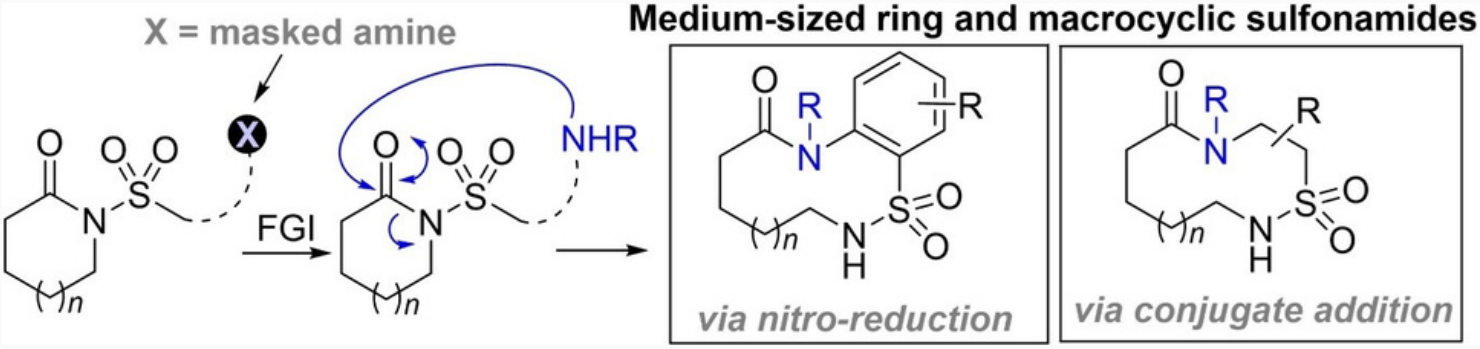
Expanding Sulfonamide Chemistry

A new synthetic method developed in York that enables the simple synthesis of a wide range of biologically important cyclic sulfur-containing molecules has been discovered.



These molecules – known as 'sulfonamides' – are common components found in small molecule drugs, used to treat cancer, HIV and various viral and bacterial infectious diseases. Molecules arranged in large rings – also known as 'macrocycles' – are also very important compounds in medicines. However, synthetic methods able to install sulfonamide groups into macrocycles are scarce, thus limiting the ability to use this potentially valuable combination to discover new treatments for disease.

Dr Will Unsworth and his research team have great interest in the development of new and improved synthetic routes to macrocycles and set out to use their expertise to make macrocyclic sulfonamides.

They combined two distinct synthetic strategies, both of which are based on cascade reactions – processes which combine multiple reaction steps into a single operation (see Figure). Cascade reactions bring several benefits in terms of making synthesis quick and easy, and avoiding the need to handle or isolate potentially toxic intermediates. The team made use of nitro groups or alkenes as masked amines that could be unmasked via reduction or conjugate addition respectively. This allows a diverse range of componds to be simply and efficiently turned into cyclic sulfonamides. These two new reactions allow access to families of previous inaccessible molecules, enabling their biological potential to be properly explored.

The teamwork on this project exemplifies the collaborative and international ethos in much of the research carried out in the Department of Chemistry at the University of York. The work to develop one of the two new synthetic methods was led by Chinese PhD Zhongzhen Yang. The second was led by Ukrainian PhD student Illya Zalessky, who deserves huge credit for driving this research whilst also working to support refugees escaping the war in his homeland. The project was also supported by predictive computational chemistry, conducted by PhD student Ryan Epton and Prof Jason Lynam.

Speaking about the research Dr Unsworth said: "Although we have worked on ring expansion reaction, we have never explored sulfonamides before. With the discovery of these two new reaction classes, we can now make macrocyclic sulfonamides remarkably easily, which will enable the exploration of their pharmaceutical properties.'

The research is published in *Angewandte Chemie*

Oak National Academy award to develop science in schools

Researchers at the University of York have been awarded £1.4 million to develop online science materials for schools.

The Centre for Industry Education Collaboration (CIEC), part of the Department of Chemistry and the University of York Science Education Group (UYSEG), will work together to develop lesson resources for teachers and pupils covering the primary and secondary science curriculum in England, age 5-16.

Working with the Oak National Academy, the curriculum resources will draw on the expertise and work of both groups and will be developed by members of UYSEG's Best Evidence Science Teaching (BEST) project team and CIEC, working with expert science teachers across the country.

The materials will support teachers to engage in evidence-informed practice, to improve and develop resources, a current key Government initiative in education.

Joy Parvin, Director of CIEC said: "As well as developing a full suite of resources for Key Stages 1 and 2, we will be collaborating with our secondary colleagues to smooth transition from Key Stage 2 to 3, thus building on the knowledge and skills children have gained during their primary years."

The CIEC team of six primary science specialists and dedicated science education researchers, engage in a wide range of primary science initiatives, nationally and internationally, focusing on the development of primary science resources and the delivery of continuing professional development.

Matt Hood, Chief Executive of Oak National Academy, said: "Every part of the education sector – from trusts to publishers to subject associations – are part of this collaboration, forming a coalition of top-tier expertise. It means teachers will have access to some of the smartest curriculum thinking and resource design on tap, something they have told us they want."

CIEC is a collaborative organisation, with current partnerships with many STEM companies across the UK to run Children Challenging Industry, Science Oxford's Thinking Doing Talking Science, Teacher Assessment in Primary Science, National STEM Learning, and the Association for Science Education (ASE BEST Bites, an online Continuing Professional Development resource for teachers, in partnership with ASE and UYSEG, and funded by Wellcome).

For more information about the CIEC visit the web pages.

University launches renewable chemistry institute

The University of York has partnered with renewable chemicals company, Circa Group, to launch the Circa Renewable Chemistry Institute (CRCI).

The new Institute aims to produce and promote bio-based products that are safer and more sustainable for the chemical industry. The partnership also means that students will be able to work on real-world projects in renewable chemistry to support their future careers in the industry.

A significant breakthrough of the partnership so far has been the creation of Cyrene™ - a multipurpose green solvent that often outperforms the toxic petroleum-based materials. Its application extends across pharmaceuticals, paints and coatings, textile recycling, agrichemicals and many more.

Professor James Clark, Director of the CRCI at the University of York, said: “We have worked with Circa now for nearly a decade, and the strength of the relationship lies in the shared belief that the chemical industry can and will be environmentally responsible and able to transition from fossil-based chemicals to commercially viable bio-based products.

As part of the partnership, Circa and its key customers will have access to all of the latest research from the University’s Green Chemistry Centre of Excellence (GCCE), as well as the use of laboratories, equipped with the latest technologies. In addition to developing commercial applications for Cyrene™, the team will be looking for the next breakthrough in renewable chemistry.

Nick Smith, Head of Development and Commercialisation for Circa, said: “This partnership provides the skills and expertise of both the Green Chemistry Centre of Excellence and the Biorenewables Development Centre to support application and process development with market leaders who are moving their manufacturing processes to safer and more sustainable products, such as Cyrene™.”

The launch event included a panel discussion with chemical industry leaders including Croda, Synthomer and the Chemical Industries Association, and explored the barriers and critical success factors in the adoption of renewable chemistry. Professor Boelo Schuur from the University of Twente and Dr Jane Murray from Sigma-Merck also gave guest lectures.

The CRCI will serve as a contact point for international and local chemical industry networks, as well as funders, future customers, academics, and government officials.

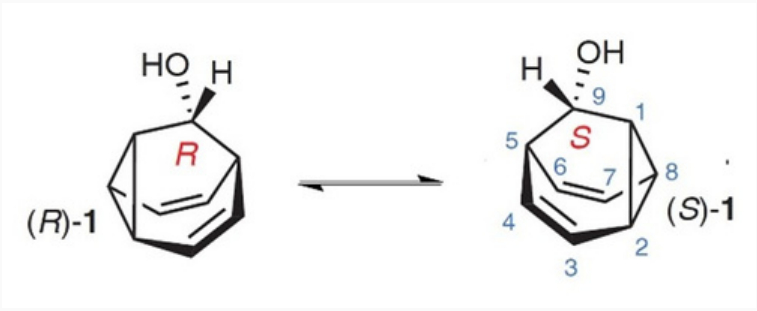
For more information about the Institute, visit the web pages.

Interconverting Mirror-Image Molecules

Recent research from scientists at the Universities of York and Durham has developed new concepts about the shape and dynamic nature of molecules.

When a carbon atom forms four bonds to different groups, the molecule can exist in two mirror image forms. These mirror image forms are vital in medicine because they have different biological activities. Usually, it is impossible to interconvert between these 'enantiomers' because to do so would require a bond to be broken, a process that needs too much energy.

The team of researchers, led by Dr Paul McGonigal, who recently joined the Department of Chemistry in York as a Reader in the Molecular Materials Group, demonstrated that if the chiral centre was part of a dynamic molecular cage structure, then a simple rearrangement of the cage could lead to inversion of the mirror image form of the molecule. In this way, carbon-based stereochemistry, which is normally considered to be fixed and rigid, became dynamic, fluxional and responsive – a new paradigm in carbon-centred chirality.



One isomer of the cage, the R form, shown on lefthand side, spontaneously changes into its mirror-image S form and then back again

The molecular cage has nine carbons atoms in its structure, which are held together by a pair of carbon–carbon double bonds and a three-membered cyclopropane ring (see Figure). This combination of bonds allows some of the bonds in the structure to trade places with one another spontaneously.

Dr Aisha Bismillah, a postdoctoral researcher in the McGonigal Group and the lead investigator of the project, commented: "Our dynamic carbon cages change their shape extremely quickly. They hop back and forth between their mirror image structures millions of times a second. Seeing them adapt to match changes in their environment is truly remarkable."

Further to uncovering this unique dynamic form of stereochemical interconversion, the researchers demonstrated that the preferences of the cage could be transmitted to nearby metal centres, opening the possibility that this type of responsive chirality might find uses in catalysis, and the synthesis of chiral molecules for biomedical applications.

Reflecting on the way in which these results overturn established ideas, Dr McGonigal said: "The way our dynamic carbon cage interacts with other molecules and ions is fascinating. The cage adapts, giving the mirror-image structure with the 'best fit'. We hope, in due course that this intriguing bonding concept will be found to apply in other contexts, and potentially used to underpin new applications for more dynamic molecular materials."

This research has been published in the journal *Nature Chemistry*. It was funded by the EPSRC and Leverhulme Trust.

Twisting Chemical Bonds Beyond their Limits

Recent research from scientists at the Universities of York and Durham twists molecules to their breaking point in order to challenge the understanding of chemical bonds.

Chemical bonding in aromatic molecules is key to the structure, stability and function of chemicals such as drugs and plastics. For a molecule to be termed ‘aromatic’, some of its electrons must flow freely around a ring in its structure. A classic example is benzene. Six of its electrons are shared around a ring of six carbon atoms.

Aromatic rings prefer to be flat. However, recent research has shown this isn’t always the case. When aromatic rings are strained, they become twisted. But how far can a ring be twisted before its aromatic bonding breaks?

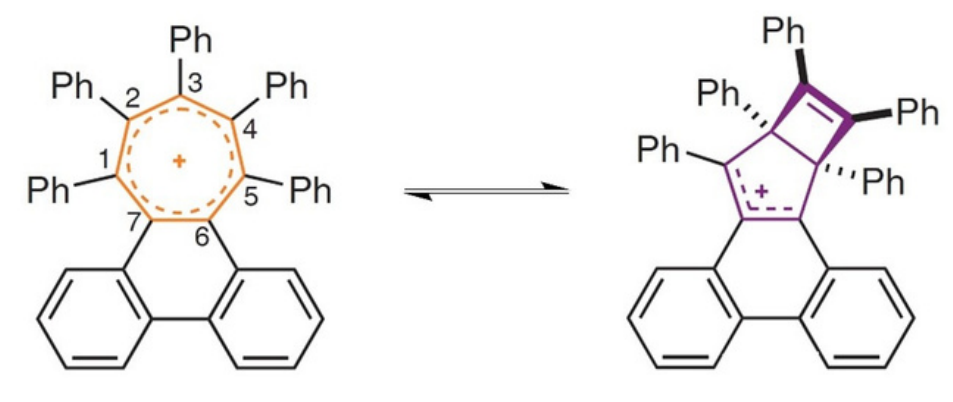
The team working on this research have found an elegant way to answer this fundamental question. They achieved this by making overcrowded aromatic rings. Rather than benzene, they used tropylium, which shares electrons around a ring of seven carbon atoms. Each of these carbon atoms can be functionalised, and having seven attachment points in the ring rather than six allowed the researchers to cram more groups around the edge of the aromatic ring, causing more strain.

They found that low levels of overcrowding made the ring twist, but without breaking its aromatic bonding. Remarkably, the molecule could be twisted by 45° from one end to the other.

“In these overcrowded molecules, strain and aromatic bonding are delicately balanced,” said Dr Paul McGonigal. “The structure, properties, and potential applications of a material are ultimately determined by this balance.”

By adding progressively larger groups around the edge of the ring, the team twisted the ring further, eventually causing the aromatic bonding to break. The electrons no longer circle the seven carbon atoms and instead, the ring pinches across its middle to form two smaller flat rings (see Figure).

Surprisingly, the researchers found there is a balance point, where the ring jumps back and forth between aromatic structure and the two smaller rings. One molecule made in this study spends 90% of its time as the pinched structure and 10% of its time as a larger aromatic ring.



The 7-membered ring (left) becomes so crowded around its periphery that it rearranges by pinching across the middle (right), with the molecule alternating between the two structures

“The reversible pinching and reopening of an aromatic ring are truly remarkable,” said Promeet Saha, a PhD student in the McGonigal group and the lead investigator of this project. “Aromatic bonding is such a powerful stabilising force that we usually think of it being a constant presence. However, our findings demonstrate that it can be surprisingly dynamic.”

“The precise control over the twisting of our molecules is unprecedented,” added Dr McGonigal. “We were not only able to twist an aromatic molecule up to the maximum amount of strain it can tolerate, but also to discover what happens when we push beyond that limit. We hope this investigation is a step towards us being able to more routinely turn aromatic bonding ‘off’ and ‘on’ in a controlled manner.”

Dr Paul McGonigal works as part of the Molecular Materials Group in the Department of Chemistry at The University of York.

This research has been published in the journal *Nature Chemistry* The work was funded by the EPSRC.

In memory of Zongheng Li

Zongheng Li joined the department in 2019 as a student on the Green Chemistry and Sustainable Industrial Technology MSc course, and then enrolled as a PhD student under the supervision of Martin Bates and James Sherwood. Halfway through his PhD project, aged just 26, Zongheng tragically died on 23rd May 2022 after a short, unexpected illness. During his time in the department, Zongheng made a lasting impact on his fellow students. He is remembered as a sociable, friendly, and supportive friend. Zongheng liked to travel, and entertained friends from the UK at his family home in China in the holidays. It is with sadness, but also pride, that we install the new bench in the Chemistry quad in honour of Zongheng. It will serve as a permanent reminder of the talented individual who we have lost, as will our continuation of Zongheng’s research on the understanding of polymer solubility and design of greener solvents.

A moment of reflection is planned for Tuesday 23rd May, to commemorate a year since Zongheng’s passing. Further details will follow.