

Young Career Focus: Dr. Duncan Browne (Cardiff University, UK)

Background and Purpose. SYNFORM regularly meets young up-and-coming researchers who are performing exceptionally well in the arena of organic chemistry and related fields of research, in order to introduce them to the readership. This Young Career Focus presents Dr. Duncan Browne (Cardiff University, UK).

Biographical Sketch



Dr. D. Browne

Duncan Browne was born in Dunstable (UK). He graduated with an MChem degree in Chemistry with study in industry from the University of Sheffield (UK) during which time he spent one year as an intern at GSK, Stevenage (UK). In 2009, he was awarded a PhD in Organic Synthesis under the supervision of Professor Joseph P. A. Harrity. During this time, he spent 3 months at Syngenta, Jealotts Hill (UK). Following his PhD, he was awarded a one-year Doctoral Prize Fellowship from the EPSRC before moving in 2010 to the ITC and Whiffen Laboratories at the University of Cambridge (UK) as a Post-doctoral Research Associate with Professor Steven V. Ley FRS CBE. There he enjoyed developing new flow chemistry tools, techniques and synthetic methods as well as applying them to industrially relevant processing problems. In 2012, Duncan was appointed as a Fellow in Natural Sciences at Sidney Sussex College (University of Cambridge) and, in 2013, he was made Director of Studies in Natural Sciences. In September 2014, Duncan established his independent research group and became Lecturer in Organic Synthesis & Medicinal Chemistry at Cardiff University (UK). In 2017, he was recognized by both the RSC journals Green Chemistry and Reaction Chemistry and Engineering as an 'Emerging Investigator' and he was a recipient of a Thieme Chemistry Journals Award.

INTERVIEW

SYNFORM *What is the focus of your current research activity?*

Dr. D. Browne My research group is focused on the design and development of new concepts in organic synthesis with specific emphasis on the incorporation of enabling tools and technologies to deliver efficient synthetic processes.

Many of the principles of green chemistry and sustainability can be met by embracing new technologies that are inherently cleaner when compared to the current status quo. By designing new synthetic methods that take full advantage of the capabilities of different enabling technologies, one will end up automatically with greener, cleaner processes. Part of our goal is to explore what the true capabilities of these methods are, both as individual tools and as more complex hybrid designs.

Currently we have a strong focus on mechanochemistry, specifically solvent-free or solvent-minimized processes that take place in high-speed ball mills. We are in search of reactivity or selectivity that is not accessible by other means. Along the way we hope to also gain a better understanding of how reactions can be optimized under these conditions.

SYNFORM *When did you get interested in synthesis?*

Dr. D. Browne I was interested in chemistry from a young age, stimulated by an enthusiastic and encouraging teacher at high-school. I was privileged to have two chemistry teachers at that time. One of my teachers was a former worker at the Ministry of Defense. I remember in one lab practical session we prepared dinitrotoluene! Or at least he led us to believe that's what we were doing; we had to go to a lab at the far end of the science block and work in this strange thing called a fume-cupboard. Looking back, I would like to have seen the NMRs and analytical data for the starting materials and products, as I don't have any evidence that we actually prepared DNT. I remember he stressed that we should keep the reaction very cold to avoid a 3rd nitration reaction leading to TNT; we

were made to neutralize the reaction mixture at low temperature! I enjoyed the excitement of that practical class. It was later on at university, when I spent a year at GSK (Stevenage, UK) and received some encouraging comments (I lacked confidence) about my abilities, that I realized I was capable and really enjoying the subject. My enjoyment still continues today. I like to see a range of chemistry and projects.

SYNFORM *What do you think about the modern role and prospects of organic synthesis?*

Dr. D. Browne I think that it is true to say that the breadth of applications of organic chemistry continues to increase and the subject is becoming ever more diverse. Organic chemists

tend to be very creative in their problem solving. The fact that some industrial sectors are shifting (or have already shifted) towards exploring biochemical opportunities has almost certainly caused a spike in creativity in the field; it is a very exciting time. There still exists much excellent work on fundamental synthesis and the design and development of new reactions, but there is also a move towards interdisciplinary applications that align with engineering, sustainability and artificial intelligence. Organic chemists have an excellent ability to keep their science under critical analysis and this helps it to move forward at a rapid pace. Simply look at the rapid growth in photochemistry, electrochemistry and earth-abundant or metal-free catalysis: the capabilities that these methods have delivered already are quite remarkable.



Figure 1

SYNFORM Your research group is active in the area of organic synthesis and new methodology. Could you tell us more about your research and its aims?

Dr. D. Browne Currently we are particularly focused on the area of mechanochemistry. It is becoming more widespread as a technique for molecular synthesis with new mechanochemical reactions being discovered at an increasing frequency. Whilst mechanochemical methods are solvent-free and can therefore lead to improved sustainability metrics, it is more likely that the significant differences between reaction outcomes, reaction selectivities and reduced reaction times will make it a technique of interest to the wider synthetic

community. However, predicting these outcomes *a priori* is a challenge. My research group and I have started out by trying to put together a conceptual framework and understanding of the current state of play of this research area (based on the existing literature) whilst experimentally trying to understand what is required and what the important factors or variables are. My organic chemistry and flow processing training taught me that intuition for reaction optimization comes from a hands-on experience and seeing how product distribution and yields respond to changes in the system. Only then can you get a feeling for the potential phenomena at play. Already we have been on an exciting journey thinking about solid state form, Young's modulus of materials and grinding auxiliaries.

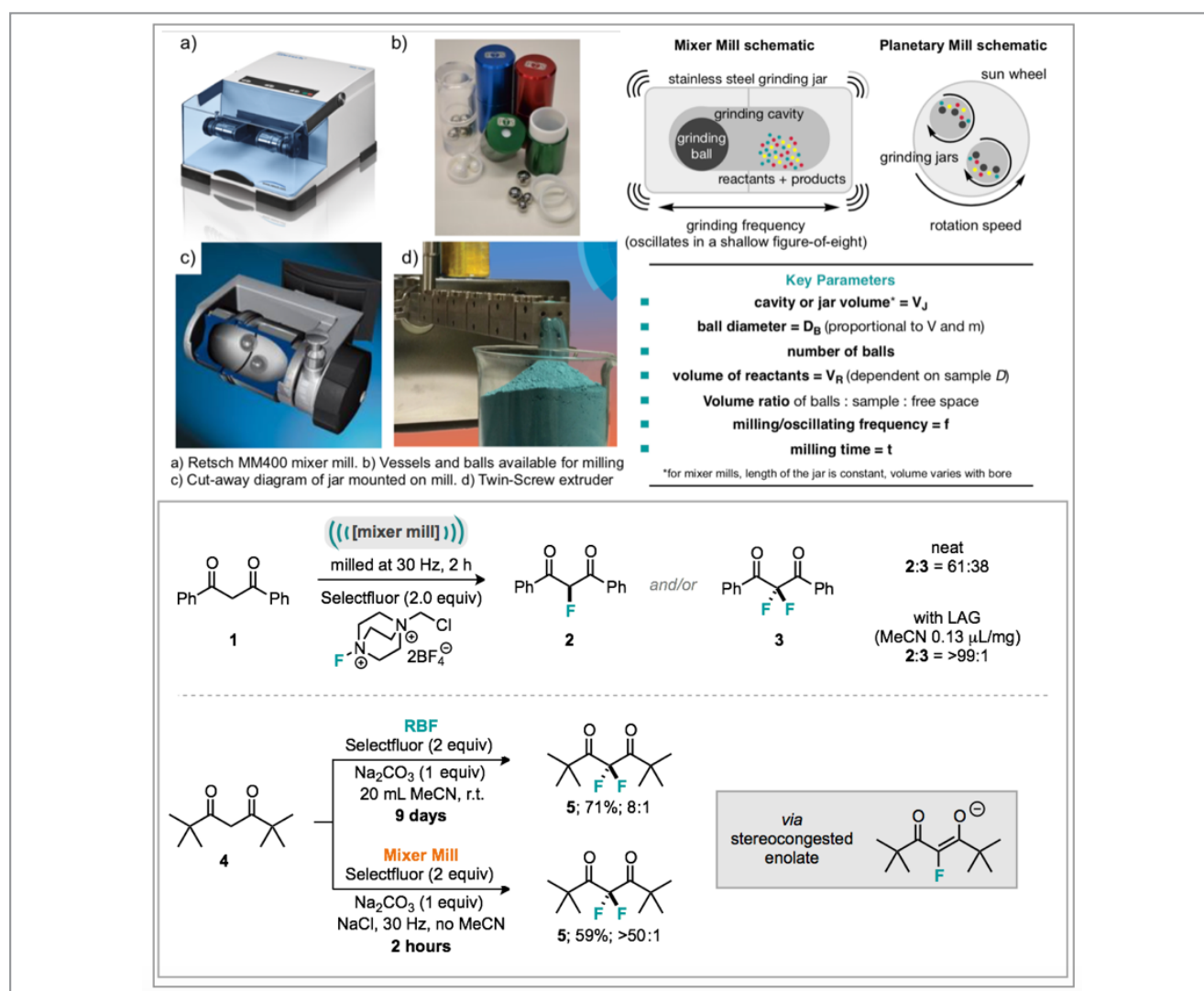


Figure 2

None of which are things I expected or associated with organic chemistry five years ago. It's not to say that organic chemistry has never been conducted using milling devices; it has, and there are many examples. However, the branch of chemistry that has mostly explored the action of milling on product formation is that done by solid-state chemists and those interested in polymorphism, co-crystallization and crystal engineering. We have run several different classes of reactions under milling conditions and have found in at least 50% of cases that there are interesting (unpredictable) outcomes. We aim to get to a point where we understand the process enough to pre-design reactions, reactivity or selectivity only available in the solid state.

SYNFORM *What is your most important scientific achievement to date and why?*

Dr. D. Browne I take pleasure in the fact that many of the Masters students and visitors that have been part of the research team have gone on to study for PhDs in the UK, Europe and the USA; it pleases me to see them still enthusiastic when they leave! I consider this an important scientific achievement.

Our most exciting lab results are happening right now and are unreported, but have derived from our earlier work on developing an understanding of the technique within the research team. One of our projects started out by simply exploring the mechanochemical fluorination of 1,3-dicarbonyls using Selectfluor. This was initially meant as a prelude or warm-up exercise to the 'real idea', but instead proved interesting at the early stage and developed into its own project (*Green Chem.* **2017**, *19*, 2798). It was observed that upon neat grinding of two equivalents of Selectfluor with dibenzoylmethane, a 61:38 ratio (95% total isolated yield) of monofluorinated to difluorinated dicarbonyls could be isolated. However, upon the addition of acetonitrile (3 equiv or 0.125 mL), the selectivity changed to 100:0 (98% isolated yield) in favor of the monofluorinated product. This was/is a known phenomenon in the area of polymorphism and co-crystallization, that the addition of a liquid can change the outcome of the non-covalently bonded product distribution. The phenomenon is known as Liquid Assisted Grinding (LAG). As an organic chemist, I was skeptical of adding solvent to a reaction that is claimed to be solvent-free! However, the effect is specific to acetonitrile and is real. It appears to slow down the rate of formation of the monofluorinated product, stabilize it once it is reached and prevent it from further fluorination and conversion to the difluorinated product. This observation was explored and held true across a small range of sub-

strates. In this same body of work, we also explored difluorination and noted that the mechanochemical difluorination of 2,2,6,6-tetramethyl-3,5-heptanedione occurred within two hours, whereas the analogous reaction in solvent required nine days to run to completion. I think that this is our most important mechanochemistry work to date. It is one of the first demonstrations that LAG techniques can also have an impact on covalent bond-forming product distributions but it has also served as an inspiration to us to explore this science further.

