

Acceleration of Diels–Alder Reactions by Mechanical Distortion

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This paper, authored by the group of Professor Adam Braunschweig at the City University of New York (USA), addresses one of the biggest challenges that has stood in the way of the ‘greening’ of organic chemistry, which is the heavy reliance of the chemical industry on solvents. According to Professor Braunschweig, organic solvents currently account for ~90% of chemical waste, and heating and cooling them is one of the reasons why chemical manufacturing uses ~37% of all manufacturing energy. “Mechanochemical reactions, where force is used to drive the reaction under solvent-free conditions, can eliminate a substantial amount of waste and energy usage in chemical manufacturing,” said Professor Braunschweig, adding: “Mechanochemistry, however, has not been widely adopted because the chemical community does not understand how force acts upon the transition state and why different products are observed under mechanochemical conditions vs. solvothermal conditions.” He explained: “The reason this has been so difficult to investigate is because it’s really hard to measure the force being applied to reactants, so no one really understood what happens to molecules. The few theories that existed couldn’t really explain different selectivities – why different products were sometimes observed under mechanochemical conditions – so they were incomplete. Here, we did some really complicated experiments using modified surfaces, nanoscopic tip-arrays, kinetics, etc., but the conclusions are really simple to understand: what we found is that pushing on molecules bends them. That’s it. But what’s really cool about that is that the bent molecules tend to follow a different reaction path than their unbent counterparts, because these new pathways may have lower activation barriers for the bent molecules but not the unbent molecules. In a nutshell, the consequences of this work are: chemists can now start investigating computationally how bending molecules may affect reactivity or they can understand previously unexplainable selectivities with this new paradigm.”

This research paper is a result of collaboration between an interdisciplinary team composed of experimental and computational chemists and mechanical engineers that are all part of the National Science Foundation’s Center for Mechanical Control of Chemistry (CMCC). The authors of this work believe that mechanochemistry has the chance to completely change how organic chemistry is carried out in the next twenty years, but it is currently in its infancy, and so it requires experts in both chemistry and mechanics to answer very basic questions

that have not yet been answered. “This paper is really answering the most basic question in mechanochemistry, what happens when you push on molecules with directional force?” said Professor Braunschweig. He continued: “As evidence of how much we have to learn about mechanochemical reactions, this most basic of questions had not yet been addressed adequately.”

To perform these studies, the authors used a modified Park Systems atomic force microscopy platform in the Braunschweig lab to control precisely the force and time applied between molecules on surfaces and molecules on the tips of polymer-pen arrays, which are elastomeric arrays with hundreds of individual tips. Professor Braunschweig explained: “Upon bringing the tips into contact with the surfaces, a nanoreactor is formed between the tips and the surfaces that confines the reactants under an applied force. The computer-controlled movement of the piezoactuators that hold the array provide precise control over force and reaction time. With these parallel arrays, we can test the effects of many values of force and time in a single printing experiment, which allows us to explore the effects of hundreds of different experimental conditions on reaction rates of Diels–Alder reactions in a single afternoon. As a result, we could test a series of Diels–Alder reactions and extract structure–activity relationships under applied load.”

Professor Braunschweig explained that the authors investigated the reaction kinetics of [4+2] Diels–Alder cycloaddition reactions between dienophiles and surface-confined diene monolayers to measure how force affects reaction rates. They chose pericyclic reactions because they proceed in concerted fashion without intermediates, which minimizes challenges in analyzing their kinetics. “The first and primary goal was to induce chemical reaction using mechanical compression and confirm the bond formation by characterizing the reaction outcome in different ways,” remarked Professor Braunschweig. He went on: “After establishing this method, we selected reactants that had a well-established order in reactivity in solution-based chemistry. The dienophiles were modified with fluorophores, so the reaction was analyzed by simply taking fluorescent images of the printed surfaces. Experiments were complemented with density-functional theory (DFT) calculations and finite element analysis modeling of the forces exerted between the tips and the surfaces.”

Professor Braunschweig told SYNFORM of two unexpected results that helped the authors understand what was really occurring in this system, and in mechanochemical reactions more generally. He explained: “The first surprise came when we were able to determine the activation volumes of these reactions. The activation volume is the dependence of the reaction rates on pressure. The activation volumes of Diels–Alder reactions under hydrostatic pressure – pressure applied in solution which presses on reactants from all sides equally – have been known for ~50 years. The activation volumes under uniaxial forces – where pressure is applied from one direction, as occurs in our system and other mechanochemical reactors – were approximately 1000 greater than in solution, which told us something unique was occurring under uniaxial stress.” This helped guide the authors’ calculations, which revealed another big surprise, which is that force acts by bending the molecules, and only a tiny amount of bending is needed to substantially accelerate the reaction. Professor Braunschweig said: “For example, to get a reduction in the activation barrier of ~4 kJ/mol under hydrostatic conditions requires ~150 MPa of pressure, whereas under mechanochemical conditions (uniaxial stress) the same 4 kJ/mol lowering of the activation barrier can be achieved at <1 MPa. This is like the force of gently pressing two fingers together.” Professor Braunschweig

concluded: “That was an incredible result to us, and it’s when we realized that we had discovered something profound.”

Mattes Fank

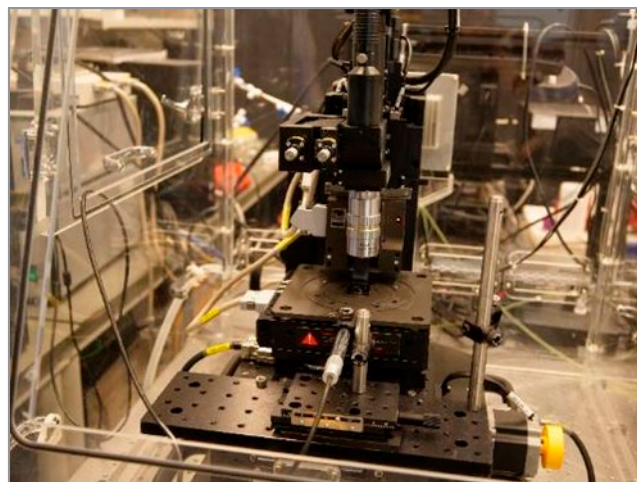


Figure 1 The printing platform is based on a customized atomic-force microscope equipped with a tilting stage, humidity chamber, and holder to accommodate massively parallel polymer pen arrays

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