Acceleration of Diels-Alder Reactions by Mechanical Distortion

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Mechanochemistry (1) involves the use of mechanical energy to activate chemical reactions. Specialized mechanochemical reactors, such as ball mills, planetary mills, or twin-screw extruders have been used to create diverse chemicals and materials, including pharmaceutical ingredients, polymers, nanoparticles, and organometallic compounds. Many aspects of mechanochemical processes reduce usage of organic solvents and can provide regioisomers not obtained solvothermally. Mechanochemical synthesis, however, has not yet been adopted by the synthetic community because many mechanistic aspects of these reactions remain a mystery, and so the outcomes of reactions remain difficult to predict. Here we use arrays of nanoscopic tips to investigate experimentally and computationally the reaction kinetics of mechanically activated [4+2] Diels-Alder cycloaddition reactions between dienophiles and diene monolayers to measure how force affects reaction rates. The experiment (**Figure 1**) uses massively parallel elastomeric arrays containing 900 pyramidal tips4 to bring fluorescently-labelled dienophiles into contact with monolayers of the tethered diene, anthracene, that is immobilized covalently onto the surface of a SiO_2 wafer.

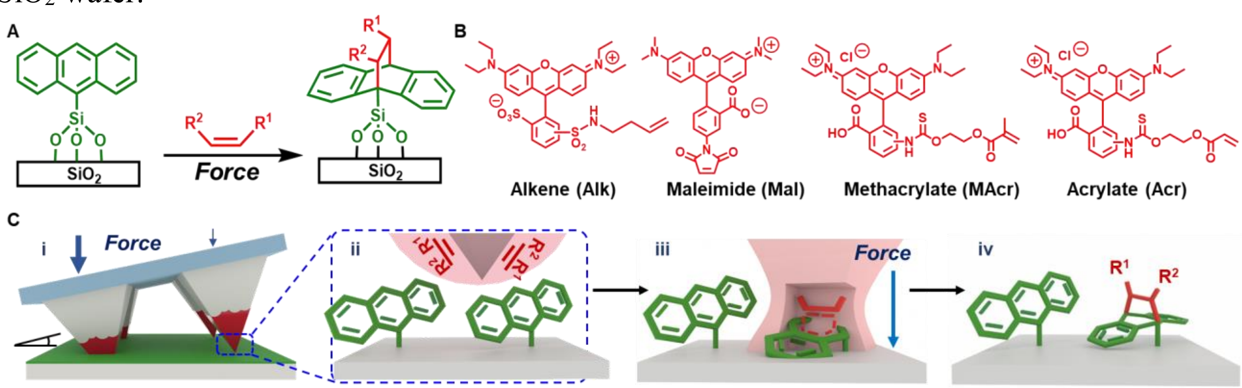

Figure 1. (A) Diels-Alder cycloaddition reaction between anthracenes immobilized onto SiO2 surfaces and dienophiles. (B) Structures of dienophiles **Alk, Mal, MAcr, Acr**. (C) (i) Elastomeric tip array that transfers an ink mixture (red coating) consisting of a dienophile and PEG onto an anthracene-modified surface. (ii) Upon contact with the surface, the tips form nanoreactors, (iii) where forces are applied that accelerate the Diels-Alder cycloaddition reactions. (iv) After washing the surface, only covalently bound molecules remain on the surface.

References: 1. Do, J.-L.; Friščić, T., Mechanochemistry: A Force of Synthesis. *ACS Central Science* **2017,** *3* (1), 13-19.