

The Janus-faced role of external forces in mechanochemical disulfide bond cleavage.

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Rok wydania

2013

Czasopismo

Nature Chemistry

Numer woluminu

5

Strony

685-691

DOI

10.1038/NCHEM.1676

Kolekcja

Naukowa

Język

Angielski

Typ publikacji

Artykuł

Streszczenie

Recent force microscopy measurements on the mechanically activated cleavage of a protein disulfide bond through reaction with hydroxide ions revealed that for forces greater than 0.5 nN, the acceleration of the reaction rate is substantially reduced. Here, using *ab initio* simulations, we trace this 'reactivity switch' back to a dual role played by the mechanical force, which leads to antagonistic effects. On the one hand, the force performs work on the system, and thereby accelerates the reaction. On the other hand, the force also induces a conformational distortion that involves the S–S–C–C dihedral angle, which drives the disulfide into a conformation that is shielded against nucleophilic attack because of steric hindrance. The discovery of force-induced conformational changes that steer chemical reactivity provides a new key concept that is expected to be relevant beyond this specific case, for example in understanding how 'disulfide switches' regulate protein function and for the rational design of mechanoresponsive materials.

Adres publiczny

<http://dx.doi.org/10.1038/NCHEM.1676>