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Chemical Physics

Surprise From S_N2 Snapshots

Ion velocity measurements unveil additional unforeseen mechanism

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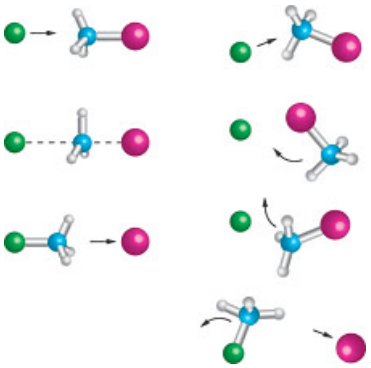
By precisely mapping what happens when individual molecules collide, researchers have uncovered unanticipated details about the mechanism of the bimolecular nucleophilic substitution (S_N2) reaction, a fundamental molecular transformation in organic synthesis (*Science* **2008,** *319*, 183).

In the classic S_N2 mechanism, when a nucleophile such as a chloride anion attacks a compound such as methyl iodide, methyl iodide ejects the iodide "leaving group" and, like a cheap umbrella in high winds, undergoes an inversion of configuration to yield methyl chloride.

Physicist Roland Wester and his team in Matthias Weidemüller's group at the University of Freiburg, in Germany, in collaboration with William L. Hase's group at Texas Tech University, now provide direct evidence for this mechanism in the gas phase. But they also detect an additional, unexpected mechanism. In this new pathway, called the roundabout mechanism, chloride bumps into the methyl group and spins the entire methyl iodide molecule 360° before chloride substitution occurs.



Adapted from *Science*

Unexpected Twist In the classic S_N2 mechanism (left series), chloride attacks methyl iodide, and iodide leaves directly along the axis on which chloride entered. In the newly discovered S_N2 mechanism (right series), chloride smacks into the side of the methyl group. Methyl iodide, reeling from the impact, rotates about its massive iodine atom. After one revolution, chloride displaces iodide.

Wester's team imaged the outcome of an S_N2 reaction at the single-molecule level to reveal these mechanistic details. They crossed a molecular beam of methyl iodide with pulses of chloride ions in an ultra-high-vacuum chamber and detected the S_N2 reaction that occurred at the point where the beams collided. A position-sensitive detector for iodide leaving groups produced images indicating each iodide ion's directional distribution and speed. The team endowed their chloride ions with well-defined velocities, which was crucial for being able to backtrack from those images and understand what was happening at the point of collision.

"This is lovely work," says Benjamin J. Whitaker of the University of Leeds, in England. The imaging technology Wester's team employed had previously been used to study neutral reaction systems, so it's a major advance to apply it to reactions involving ions, he adds.

The team imaged S_N2 reactions at different collision energies, which depend on the speed at which chloride smashes into methyl iodide. Data at lower collision energies support the traditional S_N2 mechanism. However, at higher collision energies, about 10% of the iodide ions fell outside of the expected distribution. "We saw a group of iodide ions with a much slower velocity than the rest," says Wester. "Since energy is conserved, if iodide ions are slow, the energy has to be somewhere else."

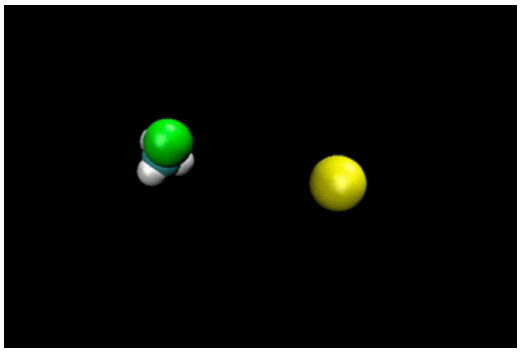
On the basis of calculations performed by their colleagues at Texas Tech, the team concluded that the energy missing from the iodide transfers to the methyl chloride product in the form of rotational excitation, supporting the proposed roundabout mechanism.

The work demonstrates "how the ability to visualize reactions has allowed chemists to quickly identify new reaction channels," says David W. Chandler, senior scientist at Sandia National Laboratories.

"The pictures that are now emerging from these experiments challenge some of our cherished models of elementary reaction mechanism," Whitaker says.

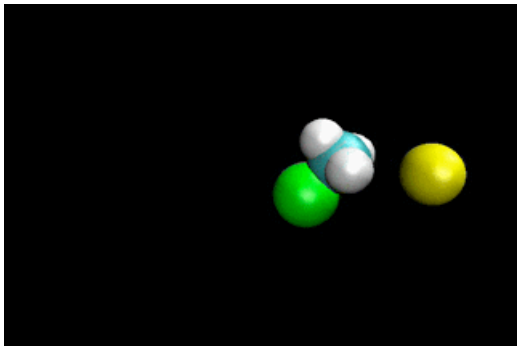
This study examined one S_N2 reaction in the gas phase. Wester's team now hopes to study more-complex reactions between ions and molecules and discern the influence of individual solvent molecules on S_N2 mechanisms.

ROUNDABOUT



Measuring the speed and direction of iodide ion leaving groups reveals an unexpected version of the S_N2 reaction mechanism. An incoming chloride anion bumps the methyl group in methyl iodide on its approach. Methyl iodide spins 360 degrees before chloride substitution and ejection of iodide anion.
Video courtesy of William L. Hase

IN LINE WITH TRADITION



In the classic S_N2 reaction mechanism, chloride attacks methyl iodide from the opposite side of the iodide leaving group. The substrate then undergoes umbrella-like inversion of configuration and ejects iodide out the other side, directly along the axis of chloride's approach.
Video courtesy of William L. Hase