Researchers discover chemical reaction that opens new avenues in drug development, protein science

Sulphur-sulphur (S-S) bonds are found in peptides and proteins, drug molecules and polymers such as vulcanised rubber. S-S bonds are essential to the structural stability of proteins, among other purposes.

New Delhi: Researchers have discovered a new chemical reaction, which spontaneously makes and breaks a sulphur-sulphur bond at room temperature, with possible application in drug development, protein science, biotechnology, and chemical and material science.

The bond has so far been difficult to manipulate selectively without using external chemical agents or heat and light.

Researchers including those from Australia's Flinders University used the reaction to modify anti-cancer drugs, among others.

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The 'trisulfide metathesis reaction', described in a paper published in the journal Nature Chemistry, spontaneously makes and breaks S-S bonds without reagents or external stimuli.

The result is a clean, efficient reaction and in some cases, the reaction is complete within seconds, the researchers said.

"It is rare to discover an entirely new reaction, and even more rare for it to be useful in so many fields and applications," senior author Justin Chalker, professor at Flinders University, said.

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Exploratory work for the finding by Chalker and collaborator from the UK's Liverpool University Tom Hasell involved noticing "surprising behaviour of S-S bonds in certain solvents".

With further exploration, a model was developed to account for the new and unusual chemistry, which explains how the bonds break and reform, and under what conditions it might be useful.

The understanding provided the researchers a foundation for applications of the new reaction, including a selective modification of natural products and drug molecules, a rapid synthesis of compound libraries of relevance to medicinal chemistry, and producing fully recyclable polymers.

The team said the reaction is unique because of its extremely high reaction rates, and exquisite selectivity.

Author Harshal Patel, from the Chalker Lab at Flinders University, said the trisulfide metathesis reaction has been successfully used to modify anti-cancer drugs and a chemical library of relevance to drug discovery.

"I'm excited to see how this chemistry is adopted, expanded and applied in ways not yet imagined. Encountering a new reaction is exciting, and we already have demonstrated several meaningful applications in biomolecular and materials chemistry," he said.

"We were also able to make analogs of polyethylene that can be made, used, and then un-made so the plastic can be converted back to the original building blocks. Closed-loop chemical recycling is an important capability in supporting a circular plastics economy," Patel said.

The authors wrote, "When exposed to certain polar aprotic solvents, trisulfides were found to undergo spontaneous metathesis, with the reaction equilibrium established in seconds in some cases. No exogenous reagents, heat, light or other stimuli were required to provoke this reaction."

"Understanding the scope and mechanism of this reaction enabled diverse applications of this chemistry in dynamic combinatorial library synthesis, the covalent modification of complex natural products, and S-S metathesis polymerisation and depolymerisation as a platform for chemically recyclable plastics," they said. PTI

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