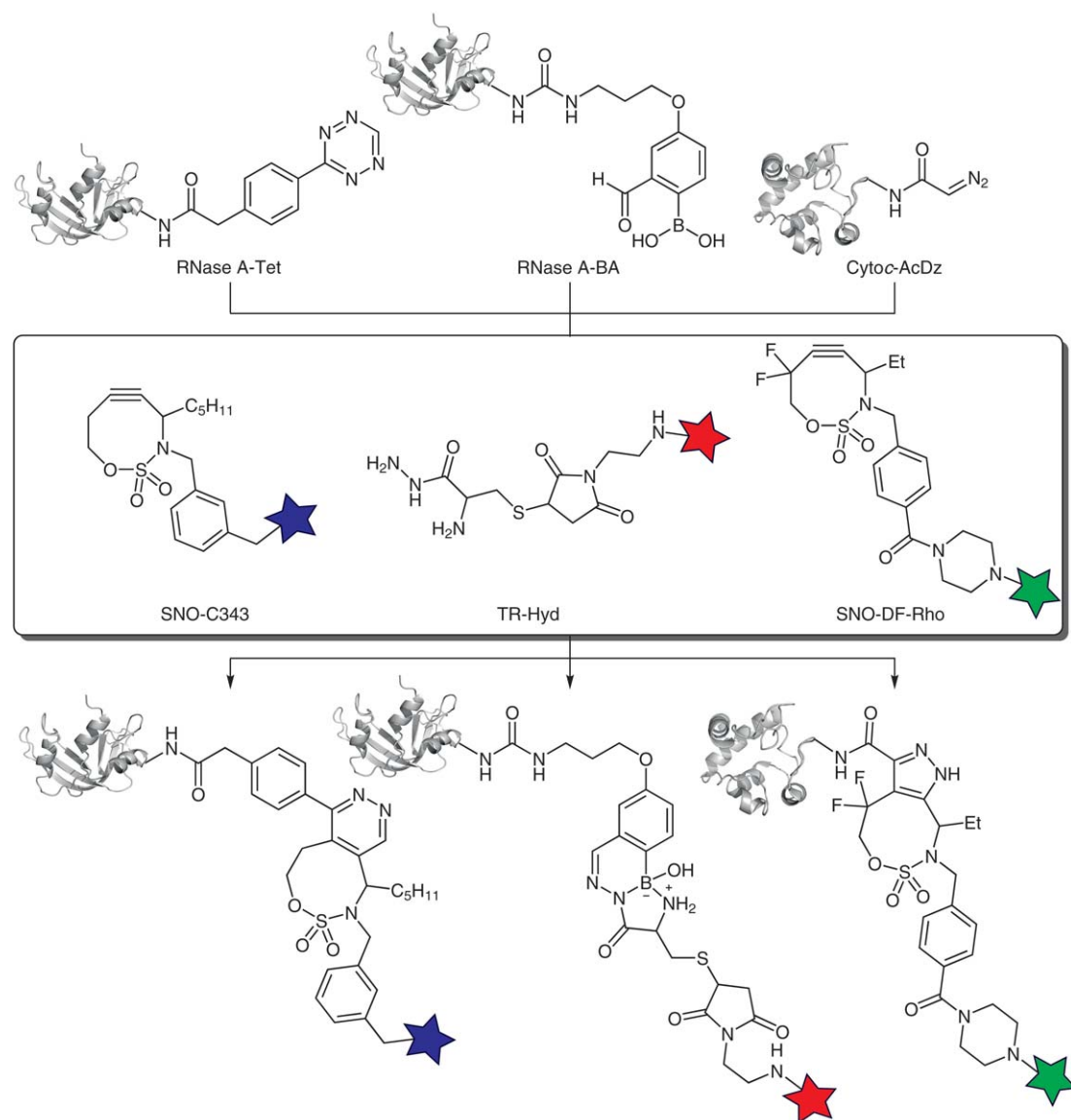


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Triple, Mutually Orthogonal Bioorthogonal Pairs through the Design of Electronically Activated Sulfamate-Containing Cycloalkynes

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Teaching Old Clicks New Tricks



Significance: The introduction of bioorthogonal reactions has enabled tremendous advances in chemical biology. The authors designed two new, mutually orthogonal pairs by electronic tuning of S-, N-, and O-containing cyclooctynes (SNO-OCTs). The reported system should prove to be a useful tool for future *in cellulo* investigations.

Comment: Using computational and experimental studies, the authors were able to design cyclooctynes with orthogonal reactivities. By including a previously reported boronic acid/hydrazine pair, the authors were able to obtain a triple ligation system and demonstrated its utility through protein and cellular labeling assays.

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