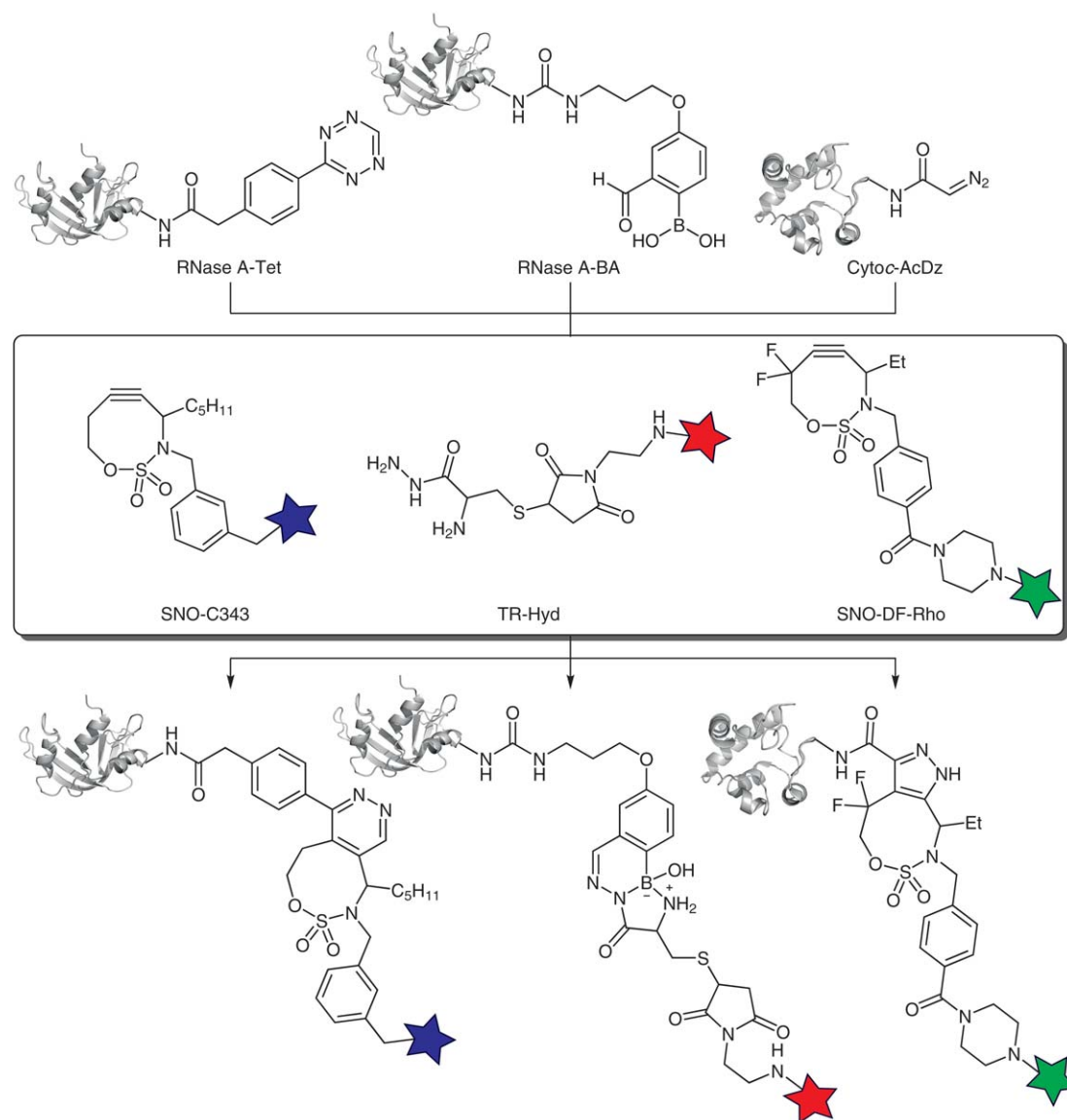


Y. HU, J. M. ROBERTS, H. R. KILGORE, A. S. M. LANI, R. T. RAINES\*, J. M. SCHOMAKER\* (MASSACHUSETTS INSTITUTE OF TECHNOLOGY, CAMBRIDGE AND UNIVERSITY OF WISCONSIN-MADISON, USA)

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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