

## DNA-Templated Reactions with High Catalytic Efficiency Achieved by a Loss-of-Affinity Principle

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### Abstract

Nucleic-acid-templated chemical reactions are currently explored for applications in DNA-encoded drug discovery, nucleic acid diagnostics, and theranostics. Of particular interest are reactions enabling the template to gain catalytic activity, so that enzymatic amplification of low copy targets would no longer be necessary. Herein, we introduce a new reaction design relying on the template-controlled cleavage of PNA-spermine conjugates. With turnover frequencies in the range of 3–10 min<sup>-1</sup> and a  $k_{cat}/K_M = 1.3 \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$ , the loss of affinity upon reaction provides a catalytic efficiency equal to most enzymatic conversions and superior to nucleic-acid-templated reactions reported to date.

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