Depolymerization Kinetics of Self-Immolative Polymers

**Significance:** Self-immolative polymers are materials that degrade into small molecules by an intramolecular cascade reaction upon removal of an end-capping group. Due to their backbones primed for degradation, self-immolative polymers require strategic design and synthesis. Here, Gillies and co-workers have synthesized two new self-immolative polymers with different degradation rates by altering the nucleophilicity and electrophilicity of the functional groups participating in the intramolecular cascade reaction.

**Comment:** Previously reported self-immolative polymer 1 depolymerizes through a cyclization–1,6-elimination pathway with the cyclization being the rate-determining step. By increasing the electrophilicity of the carbonyl by changing it from a carbamate to a carbonate, as seen in polymer 2, the rate of depolymerization was increased 500-fold. A further increase in depolymerization was achieved when the nucleophile was changed from an amine to a thiol (polymer 3). Polymer 3 is of particular interest due to its redox-sensitive depolymerization, which could be used for cytosolic drug delivery.

**Previous work (J. Am. Chem. Soc. 2009, 131, 18327):**

**This work:**

Overall depolymerization rates: polymer 3 \((7.8 \times 10^{-2} \text{ min}^{-1}) > \text{polymer 2 (2.6} \times 10^{-2} \text{ min}^{-1}) > \text{polymer 1 (6.8} \times 10^{-2} \text{ h}^{-1})