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Previews

Precise and Accelerated Polymer Synthesis via Mixed-Ligand and Mixed-RAFT Agents

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Increasing the rate of polymerization while decreasing the molecular weight distribution and maintaining well-defined chain ends remains one of the most challenging problems of macromolecular synthesis. In this issue of *Chem*, the Anastasaki laboratory demonstrates that mixed-RAFT agents provide a living radical polymerization that makes a very important step toward this goal.

Living radical polymerization provides a synthetic technique to produce polymer chains with well-defined molecular weight distribution, chain length, architecture (e.g., stars and branched) and end-group functionality. Reversible addition-fragmentation chain transfer (RAFT) polymerization is highly versatile to produce polymers in bulk, solution, and dispersed media. This technique was discovered and patented around the same time by two laboratories located across the globe: the Australian CSIRO[1] led by Ezio Rizzardo and the French Rhodia[1] led by Samir Z. Zard. Interestingly, the RAFT discovered by the CSIRO group had a very high chain transfer constant (C_{tr} > 1,000), whereas the French group found a RAFT agent (i.e., named Xanthates) with a C_{tr} ~1 for styrene polymerizations. The high C_{tr} RAFT agents produced a molecular weight distribution that was narrow (M_w/M_n ~1.1) and a number-average molecular weight (M_n) close to the ratio of initial monomer to RAFT concentration ($[M]_0/[RAFT]_0$).[2] For the low C_{tr} agents the M_w/M_n reaches values of about ~2. This value is similar to those of conventional chain transfer dominated free-radical polymerizations, and the M_n at nearly all conversions is close to $[M]_0/[RAFT]_0$. Importantly, the end-group fidelity, with minimum radical-radical termination, is the same at full conversion regardless of the chain transfer agent used. Also, it was found that the C_{tr} was very much dependent upon the monomer. Seminal work by Rizzardo and co-workers[3] demonstrated a universal RAFT agent that could switch its C_{tr} through protonation of the Z-group, allowing one RAFT agent to control the polymerization for a wide variety of monomers.

It was realized that for bulk commodity products, narrow MWD polymers would be difficult to process, and a controlled broader M_w/M_n would be needed. The first attempt to accomplish this with a single RAFT was discovered by Goh and Monteiro.[4] By using a difunctional RAFT agent coupled with kinetic simulations, they could not only control the M_n but produce M_w/M_n between 1 and 2, which are the theoretical limits of using RAFT. An increase in M_w/M_n was accomplished through an increase in the initiator concentration without losing more than one RAFT end-group per chain. The distributions were mostly monomodal with the evolution of an observable shoulder.

In this issue of *Chem*,[5] Anastasaki and co-workers used a mixed-RAFT agent system inspired, most probably, by the SET-LRP mixed-ligand system of the Percec lab[6,7] to control the polymerization kinetics. Here, the authors mixed one highly reactive RAFT agent (C_{tr} > 10) and one low reactive agent (C_{tr} < 10) at varying ratios to control both the M_n and M_w/M_n for a wide variety of monomers (Figure 1). The advantage of this system is that it still provides control over the molecular weight distribution should the monomer be changed (e.g., styrene to vinyl acetate) in which the C_{tr} constants are switched for the two RAFT agents. Obviously, obtaining reproducible and conversions close to 100% are key to successful implementation as observed from this and other work. It is still felt that for this to be highly innovative, M_w/M_n beyond the theoretical range limit and the shape of the molecular weight distribution needs and will be addressed. But this is a simple and elegant first step toward this goal. This research, together with the brief discussion from this preview, takes mixed-ligand and now mixed-RAFT catalysis from cross-coupling[8–10] organic reactions to macromolecular synthesis[6–8] and most probably via other mixed-reagents, back to organic synthesis. Most remarkable, this closed circle between organic and macromolecular synthesis was accomplished by scientists who followed in Hermann Staudinger footsteps at the University of Freiburg[11] and also on the same university campus where Staudinger pioneered 100 years ago, the field of macromolecular chemistry.

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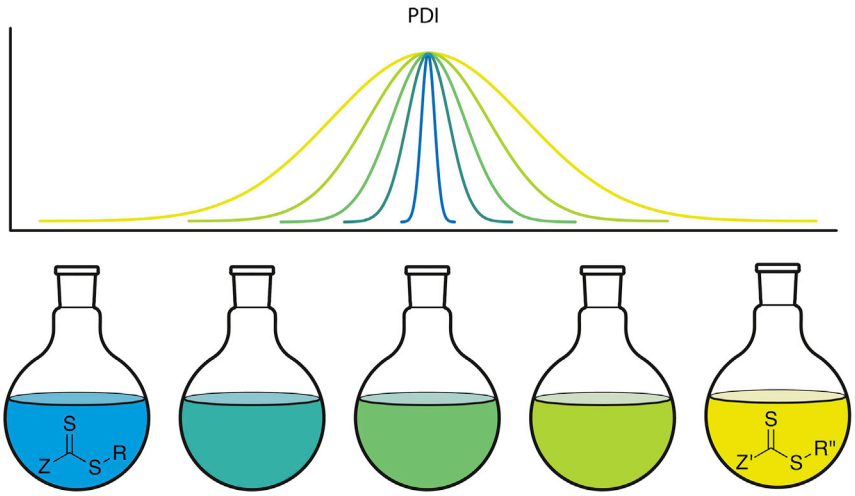

Figure 1. Predicting Molecular Weight Distribution (M_w/M_n or PDI) in Living Radical Polymerization of a Large Diversity of Monomers via Mixed-Raft Agents

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Molecular Representation: Going Long on Fingerprints

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Machine learning for chemistry requires a strategy for representing (featurizing) molecules. In this issue of *Chem*, Sandfort et al. describe an approach that concatenates 24 fingerprint representations into 71,375-dimensional vectors, which are then used for a variety of supervised learning tasks related to chemical reactivity.

There is a tremendous opportunity for computer assistance to augment and, for some problems, surpass human intuition about chemical reactivity to accelerate scientific discovery.[1] Computer-aided chemistry has taken on many forms over the past several decades: synthesis planning, reaction condition optimization, structural elucidation, solubility prediction, etc. A subset of problems relevant to chemical synthesis can be cast as regression tasks where the goal is to predict a scalar property on the basis of one or more molecular structures; this supervised learning formulation is akin to a quantitative structure-activity or structure-property relationship (QSAR or QSPR). The assignment of quantitative metrics of organic reactivity to chemical structures is a cornerstone of physical organic chemistry and dates to the

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