Controlled ("Living") Polymerization II

16:160:509 – Polymer Chemistry

Lecture 11 to 12

RUTGERS
School of Arts and Sciences
DEPARTMENT OF CHEMISTRY
AND CHEMICAL BIOLOGY

“Living” Radical Polymerization

Free-radical polymerization also has built-in termination events. Can we achieve “living” radical polymerization?

$$R_p = k_p[P\bullet][M] \qquad R_t = k_t[P\bullet][P\bullet]$$

Propagation is first-order with respect to [P·], while termination is second-order with respect to [P·]. Therefore, decreasing the concentration of radical species should suppress biomolecular termination.

How about we introduce reversible deactivation into free-radical polymerization?

$$PX \rightleftharpoons P\bullet + X \qquad [P\bullet] = K_{act}\frac{[PX]}{[X]}$$

Dormant species — Active species

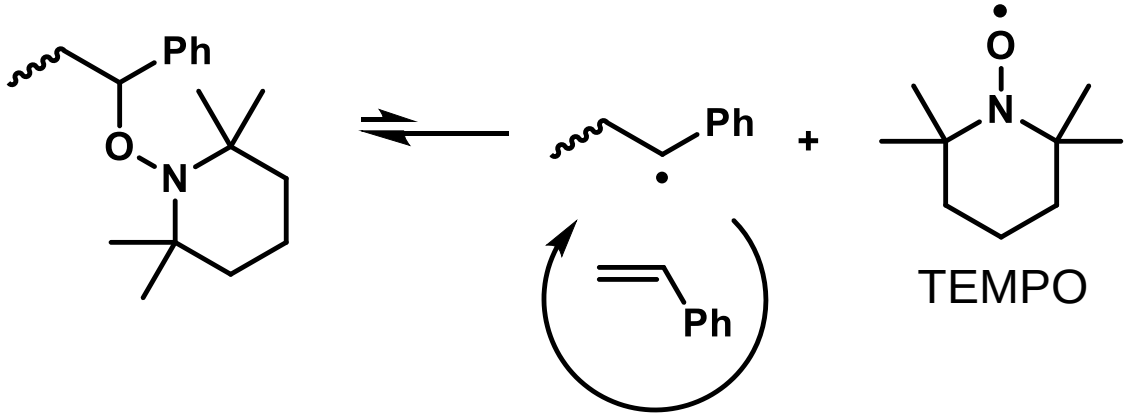
Similar to living cationic polymerization, we need the following:

1. The equilibrium lies far to the left (i.e., K_{act} is small), so the concentration of active radical species remains low to minimize bimolecular termination.
2. The interchange between dormant and active species needs to be fast (faster than k_p) to allows all chains to grow at the same rate on average.

Such polymerization is not truly “living”, as chain termination may still occur. The common terminology used in today’s polymer community is **reversible-deactivation radical polymerization (RDRP)**.

Nitroxide-Mediated Polymerization (NMP)

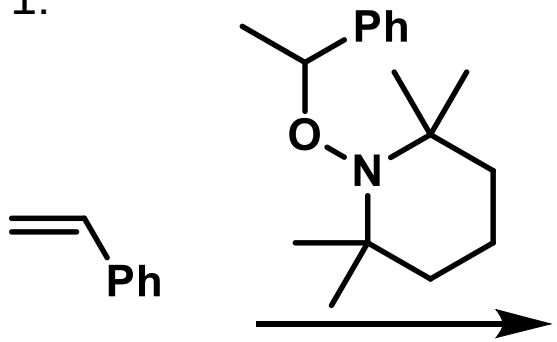
Dormant species Active species



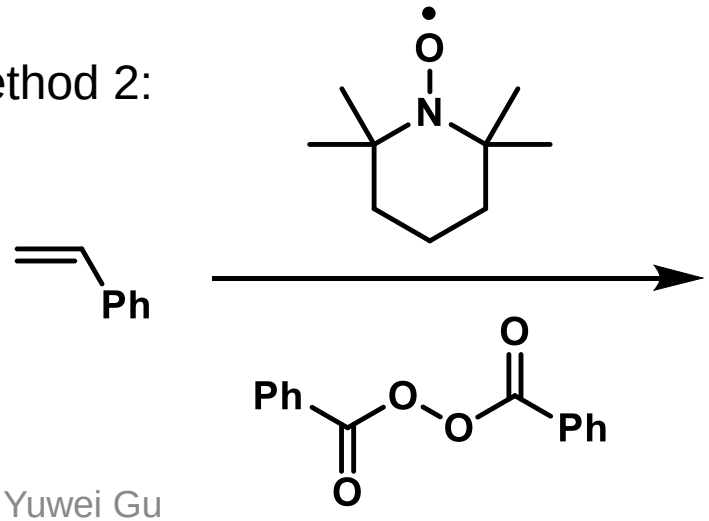
Persistent radical effect: the persistent (long-lived) radical such as TEMPO do not self-terminate

- Discovered by David Solomon from CSIRO in Australia in 1984
- Equilibrium lies far to the left, so the propagating chains spend majority of its time in the dormant state.
- NMP requires high temperatures (125–145 °C) to facilitate rapid reversible activation. It works best for styrene, where narrow dispersity (1.1–1.2) can be achieved.

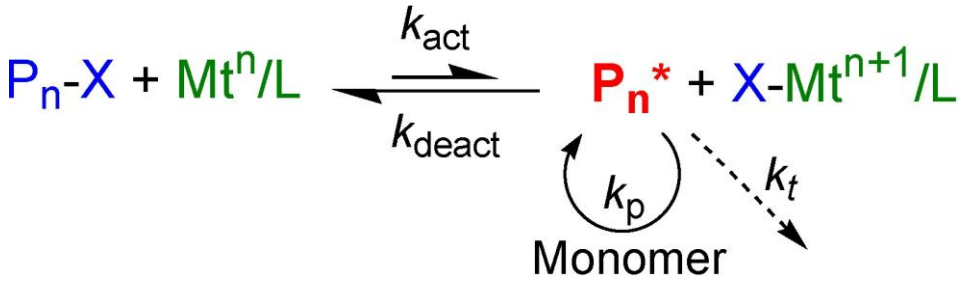
Method 1:

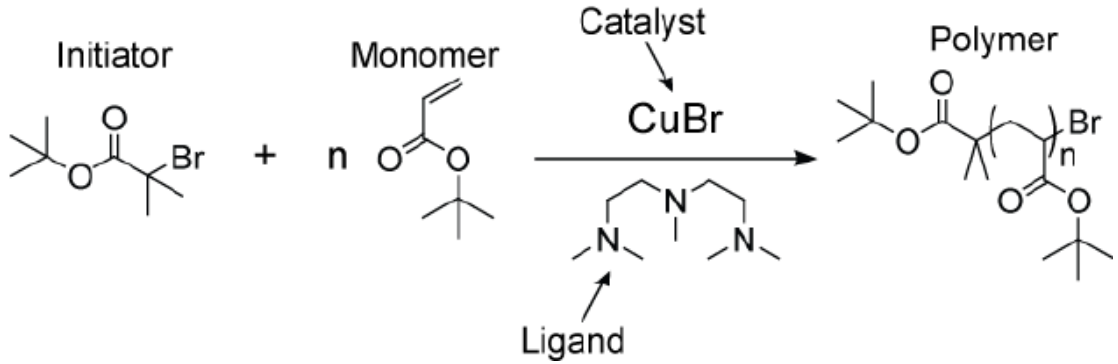


Method 2:



Atom Transfer Radical Polymerization (ATRP)





- Developed by Mitsuo Sawamoto (Kyoto University) and Krzysztof Matyjaszewski (Carnegie Mellon University) independently in 1995.
- Many transition metals have been employed in ATRP, such as Cu, Fe, Ru, Ni, and Os.
- Cu is the most widely used one in today's polymer community.
- ATRP works for a wider range of monomer structures than NMP: styrene, (meth)acrylates, acrylonitrile, acrylamides.
- However, it does not work well for less activated monomers or monomers that may coordinate with the catalyst.

Less activated monomers

Coordinating monomers

Reversible Deactivation in ATRP

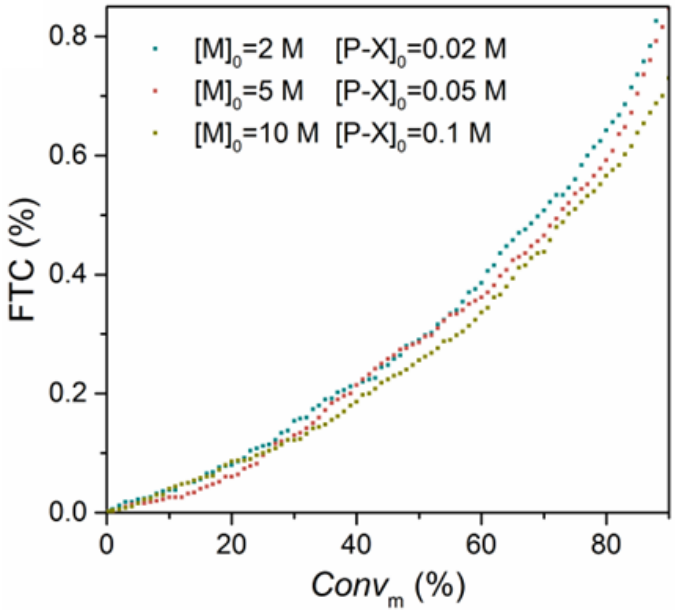
$$P\text{–}X + Cu(I) \underset{k_{deact}}{\overset{k_{act}}{\rightleftharpoons}} P\cdot + Cu(II)\text{–}X \qquad k_{ATRP} = \frac{k_{act}}{k_{deact}}$$

$$k_{ATRP} = \frac{[P\cdot]\cdot[Cu(II)]}{[P\text{–}X]\cdot[Cu(I)]}$$

For a typical ATRP, we have

$k_{ATRP} \sim 10^{-7}$, $\frac{[Cu(II)]}{[Cu(I)]} \sim 0.1$, $[P\text{–}X] \sim [I] \sim 10^{-1}$ M, so $[P\cdot] \sim 10^{-7}$ M

- Hence, the propagating chains spend the majority of their time in the dormant state. Bimolecular termination of radicals still occurs, but to a much lesser extent.
- The simulation here shows FTC (fraction of terminated chains) vs. conversion for an ATRP process, indicating that less than 1% of chains are terminated even when the conversion is above 80%.



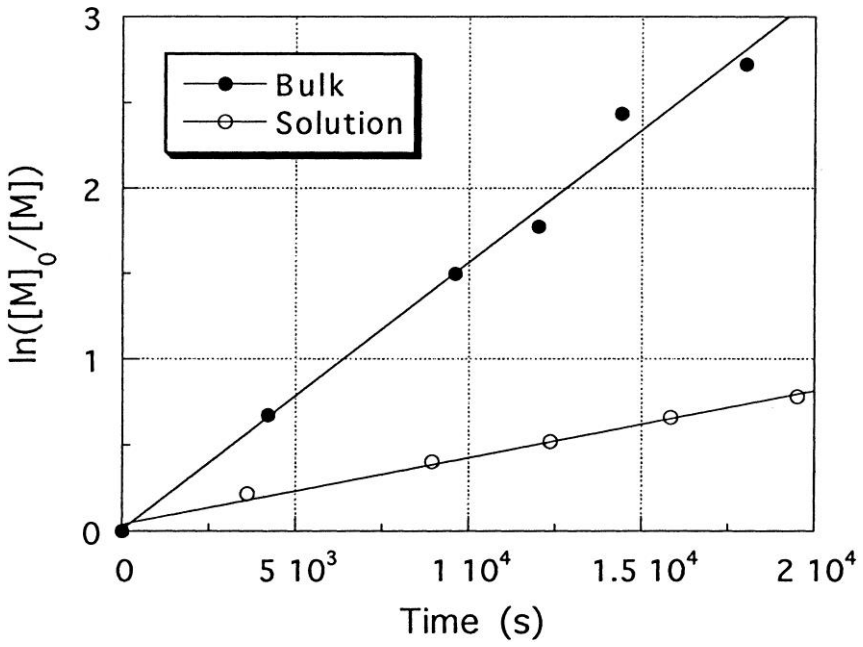
Lyu, J.; Li, Y.; Li, Z.; Johnson, M.; Sosnowski, S.; Szymanski, R.; Matyjaszewski, K.; Wang, W., *Chem. Eng. J.* **2023,** *474*, 145548.

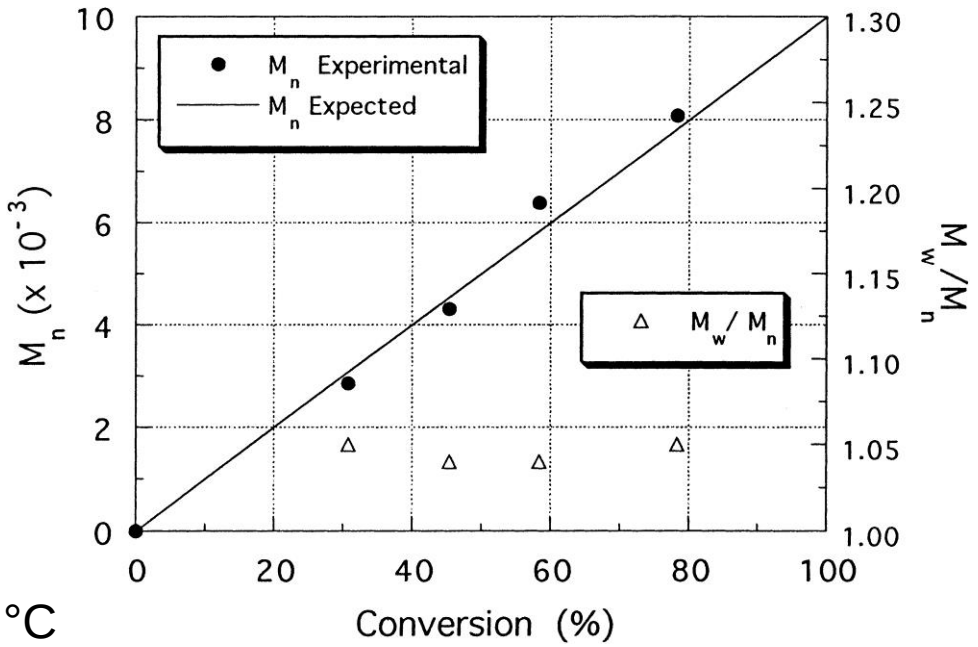
Kinetics of ATRP

To calculate kinetics, $R_p = -\frac{d[M]}{dt} = k_p[P\cdot][M]$

$$\ln\frac{[M]_0}{[M]} = k_p[P\cdot] + = k_p \cdot K_{A\text{-}RP}\cdot[I]\cdot\frac{[Cu(I)]}{[Cu(II)]} \cdot +$$

$$\overline{X_n} = \frac{[M]_0 - [M]}{[I]} = p\cdot\frac{[M]_0}{[I]}$$

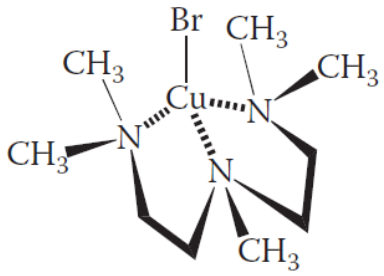


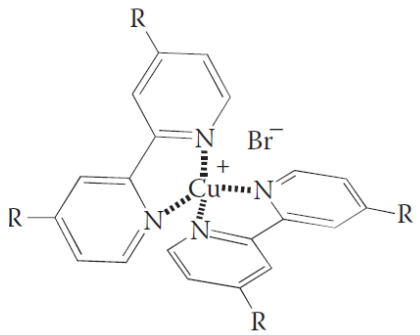


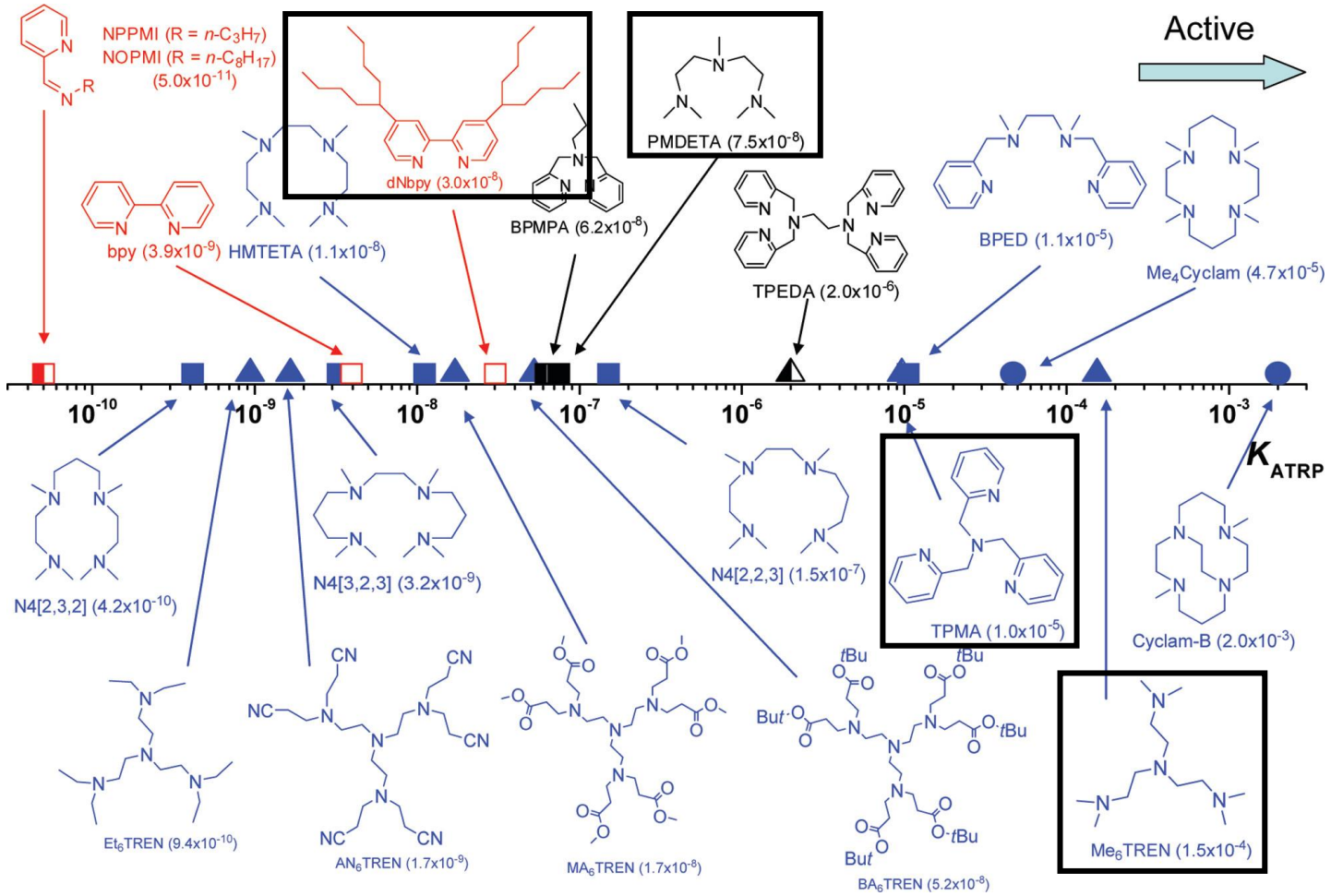
ATRP of styrene at 110 °C

Matyjaszewski, K.; Patten, T. E.; Xia, J., *J. Am. Chem. Soc.* **1997,** *119*, 674-680.

Ligand Structure Dictates Catalyst Activity



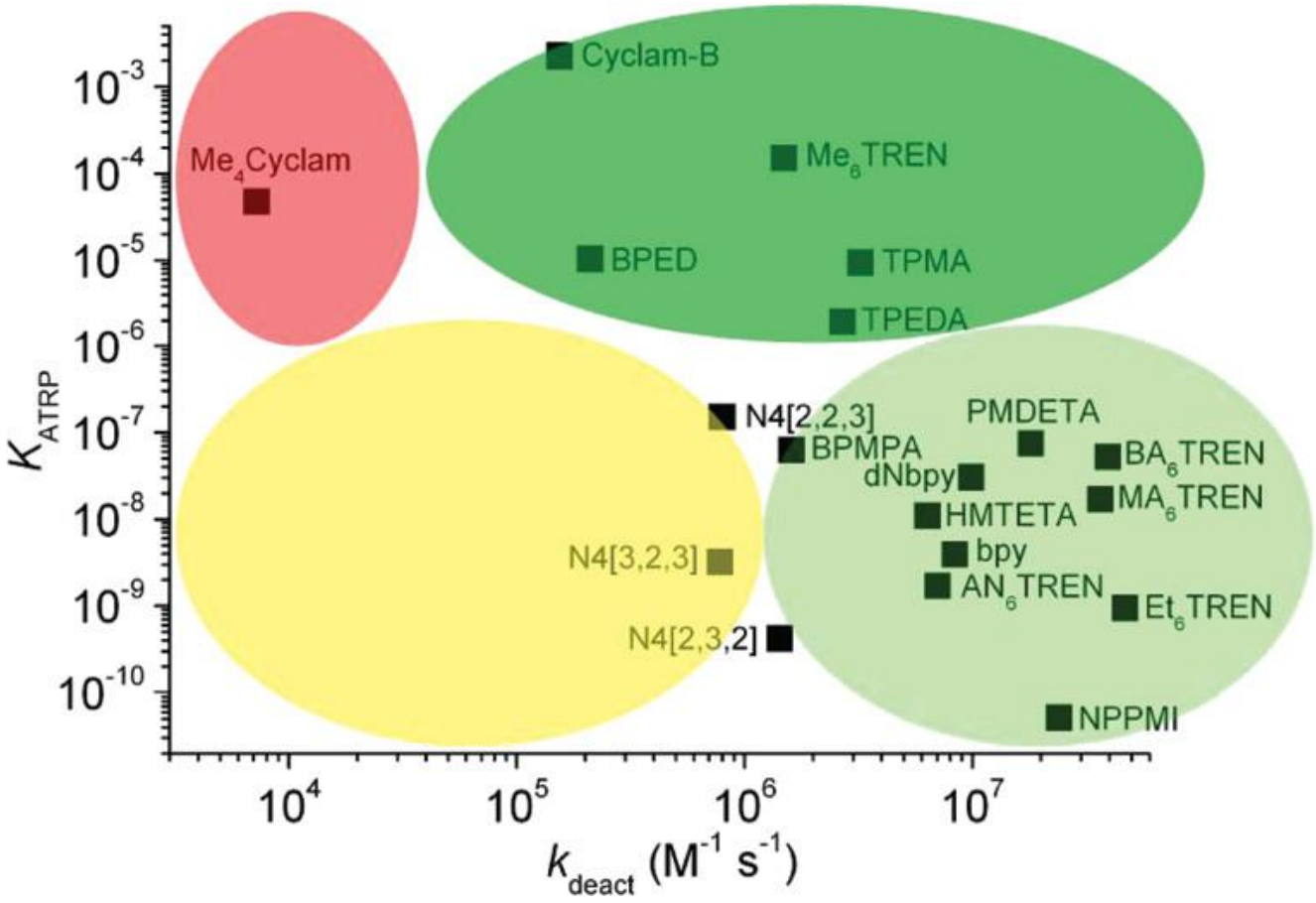




Larger K_{ATRP} suggests a more active catalyst, which can be used at low concentrations to achieve a reasonable polymerization rate.

Tang, W.; Kwak, Y.; Braunecker, W.; Tsarevsky, N. V.; Coote, M. L.; Matyjaszewski, K., *J. Am. Chem. Soc.* **2008,** *130*, 10702-10713.

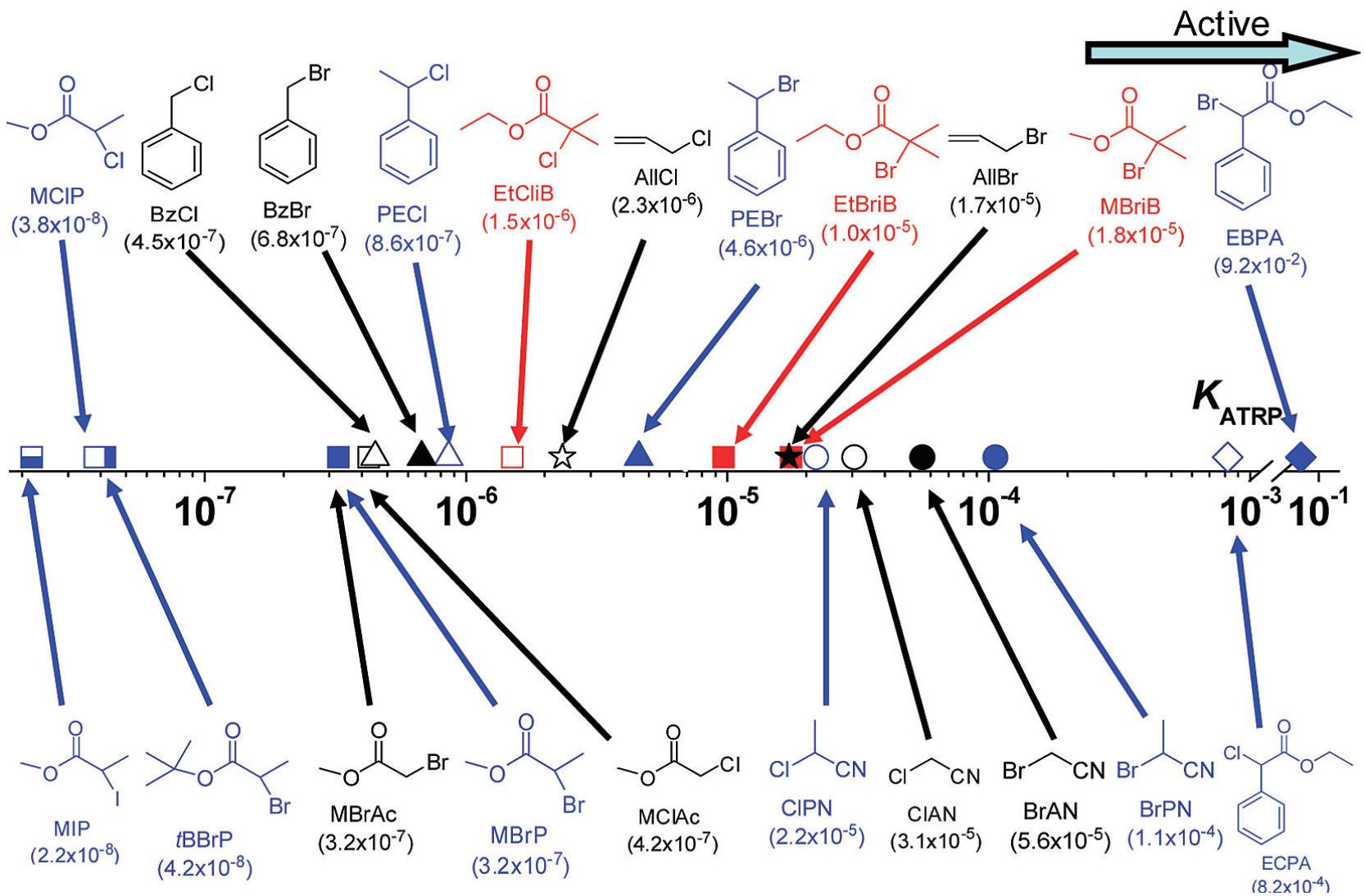
An Ideal Catalyst Should Have a Large Value of k_{deact} for Rapid Deactivation



k_{deact} (~10^6 M^{-1} s^{-1}) is much larger than k_p (~10^3 M^{-1} s^{-1}). Therefore, most active species generated quickly undergo deactivation to dormant species again. Only occasionally do they react with monomer to grow the chain once during the active period. This is very important for achieving good control and narrow dispersity.

Tang, W.; Kwak, Y.; Braunecker, W.; Tsarevsky, N. V.; Coote, M. L.; Matyjaszewski, K., *J. Am. Chem. Soc.* **2008,** *130*, 10702-10713.

Initiator Structure Dictates Rate of Initiation

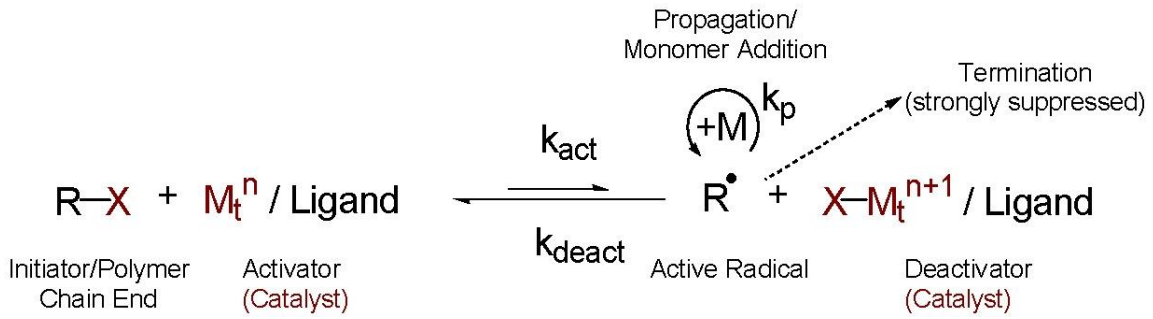


$$\text{R-X} + \text{Cu(I)} \underset{}{\overset{K_{ATRP}}{\rightleftharpoons}} \text{R}\bullet + \text{Cu(II)X}$$

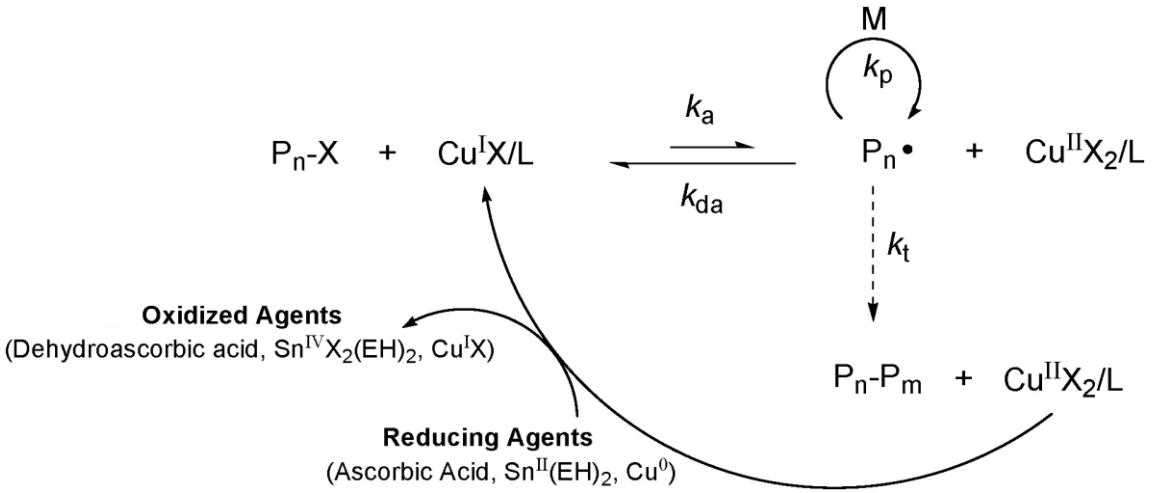
- Larger K_{ATRP} means more active initiators.
- K_{ATRP} is dictated by the strength of R-X bonds and the stability of R· radicals
- In general, we have
  1) Br > Cl
  2) 3° > 2° > 1°
  3) -CN > -Ph > -CO_2R
- To ensure a fast initiation, the most common initiators are those that have some structural similarity to the dormant end-unit of the polymer chains to be produced.

Tang, W.; Kwak, Y.; Braunecker, W.; Tsarevsky, N. V.; Coote, M. L.; Matyjaszewski, K., *J. Am. Chem. Soc.* **2008,** *130*, 10702-10713.

Activator ReGenerated by Electron Transfer (ARGET) ATRP



Normal ATRP



ARGET ATRP

Two problems associated with the normal ATRP process:

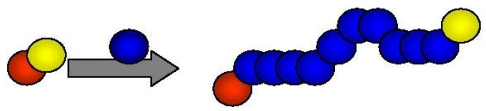
- It takes the initiator and activator (Cu^+) some time to build the dynamic equilibrium. During this period, the production of radicals far outweighs the number of deactivators (Cu^{2+}), resulting in a large number of undesirable bimolecular termination at the initiation stage.
- Even in a perfect world, a fraction of chains still terminate during ATRP, which causes the deactivator concentration (Cu^{2+}) to build up over the course of the reaction.

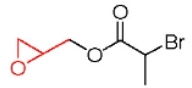
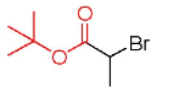
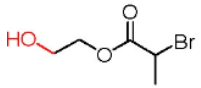
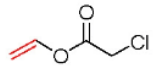
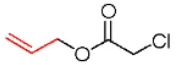
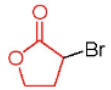
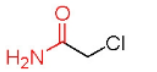
ARGET ATRP solves these problems by performing ATRP using an initiator, Cu(II), and an excess of a reducing agent that reduces Cu(II) to Cu(I) (but does not react with radicals).

Jakubowski, W.; Min, K.; Matyjaszewski, K., *Macromolecules* **2006,** *39*, 39-45.

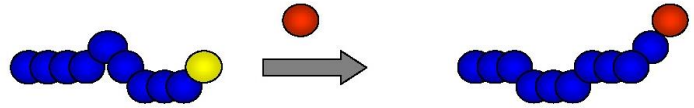
Telechelic (End-Functionalized) Polymers via ATRP

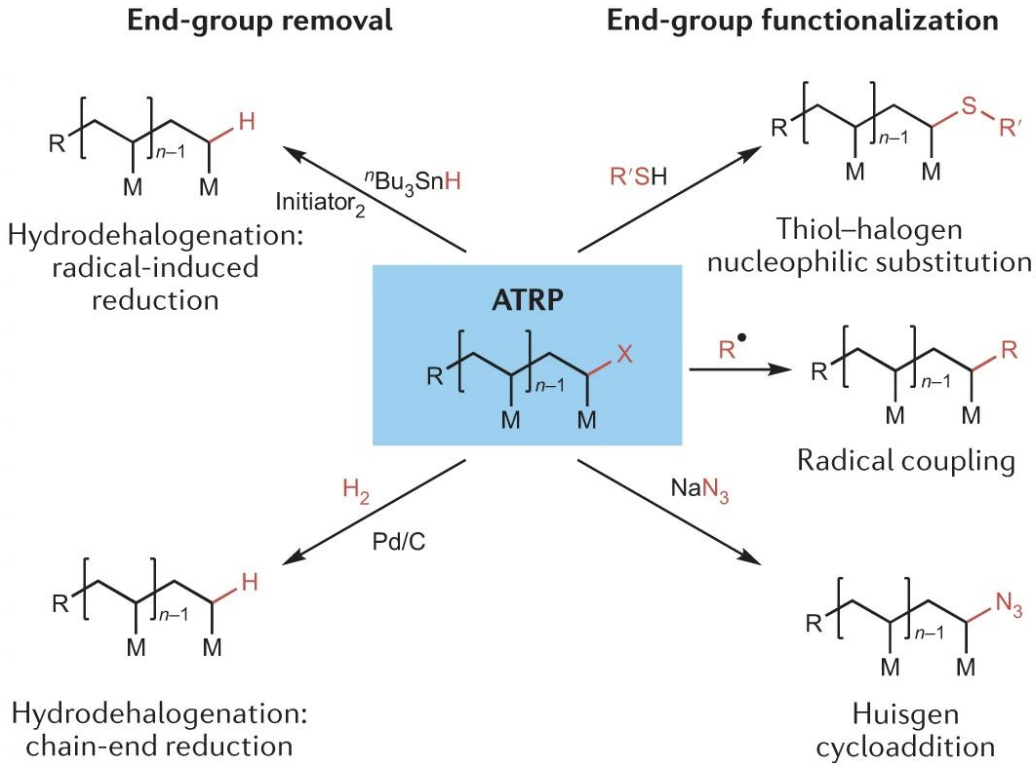
1. Using functional initiator (radical polymerization tolerates a wide range of functional groups)



Initiator	
NC-Ph-CH_2-Br	4-Cyanobenzyl bromide
Br-Ph-CH_2-Br	4-Bromobenzyl bromide
CH_3-CH(CN)-Br	2-Bromopropionitrile
CN-CH_2-Br	Bromoacetonitrile
	Glycidol 2-bromopropionate
	tert-Butyl 2-bromopropionate
	Hydroxyethyl 2-bromopropionate
	Vinyl chloroacetate
	Allyl chloroacetate
	α-Bromo-butyrolactone
	2-Chloroacetamide

2. End-group transformation chemistry



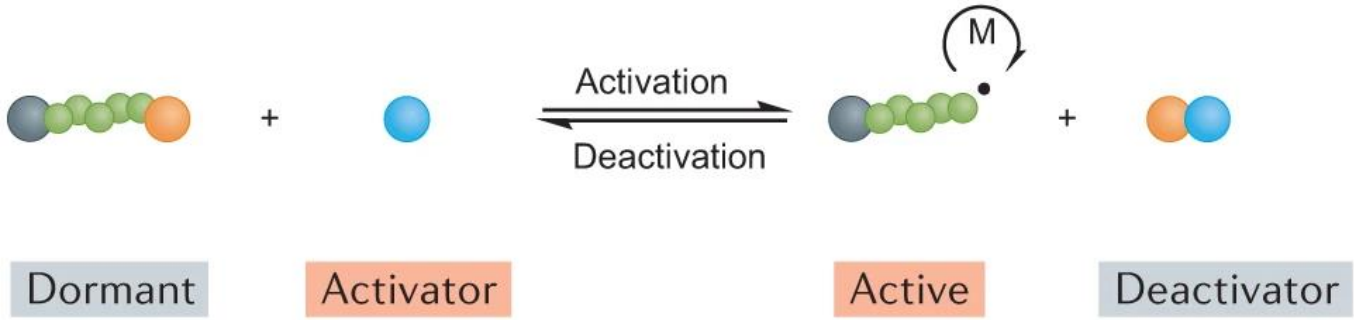


Drawbacks of ATRP: the copper catalysts are hard to remove and might not be desirable for many applications.

Truong, N. P.; Jones, G. R.; Bradford, K. G. E.; Konkolewicz, D.; Anastasaki, A., *Nat. Rev. Chem.* **2021,** *5*, 859-869.

Degenerative Chain Transfer

In ATRP and NMP, reversible deactivation is achieved via reversible chain termination.

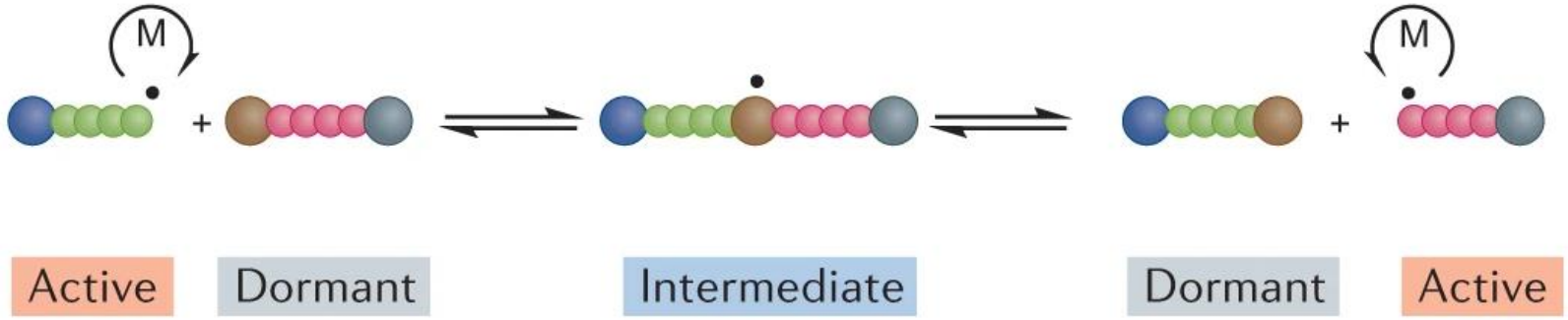


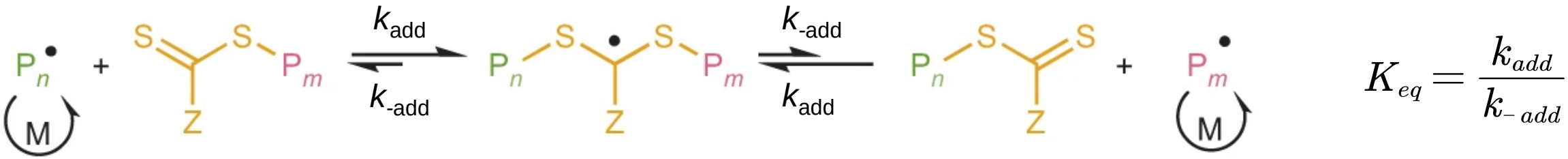
A second way of achieving reversible deactivation: degenerative (reversible) chain transfer.

$$\text{R-P}_n\text{-X} + \text{R-P}_m^{\bullet} \underset{k_{tr}}{\overset{k_{tr}}{\rightleftharpoons}} \text{R-P}_n^{\bullet} + \text{R-P}_m\text{-X}$$

- Most chains need to be maintained in the form of R-P_n-X, which is the dormant state.
- If k_{tr} is larger than k_p (C_{tr} >> 1), we again reach the ideal reversible deactivation scenario, potentially achieving better control and narrower dispersity.

Reversible Addition-Fragmentation Chain Transfer (RAFT) Polymerization





$$K_{eq} = \frac{k_{add}}{k_{-add}}$$

For a typical RAFT polymerization, we might have k_{add} ~ 10^7 (so C_{tr} can be ~10^4), k_{-add} ~ 10^2, K_{eq} ~ 10^5

In a typical RAFT polymerization, most chains exist in the dormant state. For the radical species, most exist as intermediates, while only a small portion exists as active species.

Question: Note that the reversible chain transfer process does not produce new radicals on either side of the equilibrium (i.e., it is degenerative). What is the source of radicals in RAFT?

What Is in a RAFT Polymerization?

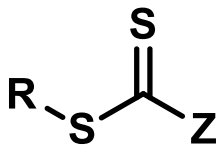
Solution: RAFT polymerization uses a small amount of AIBN to produce radicals throughout the reaction.

- Developed by Graeme Moad, Ezio Rizzardo,and San H. Thang from CSIRO in Australia in 1998.
- The simplest way to think about RAFT polymerization is to consider it as regular free-radical polymerization with a highly active chain transfer agent present.

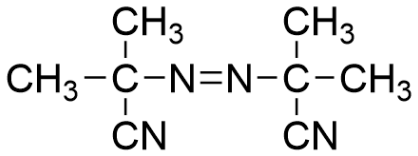
Monomer

Styrene, (meth)acrylates, acrylamides, acrylonitrile, vinyl acetate, etc.

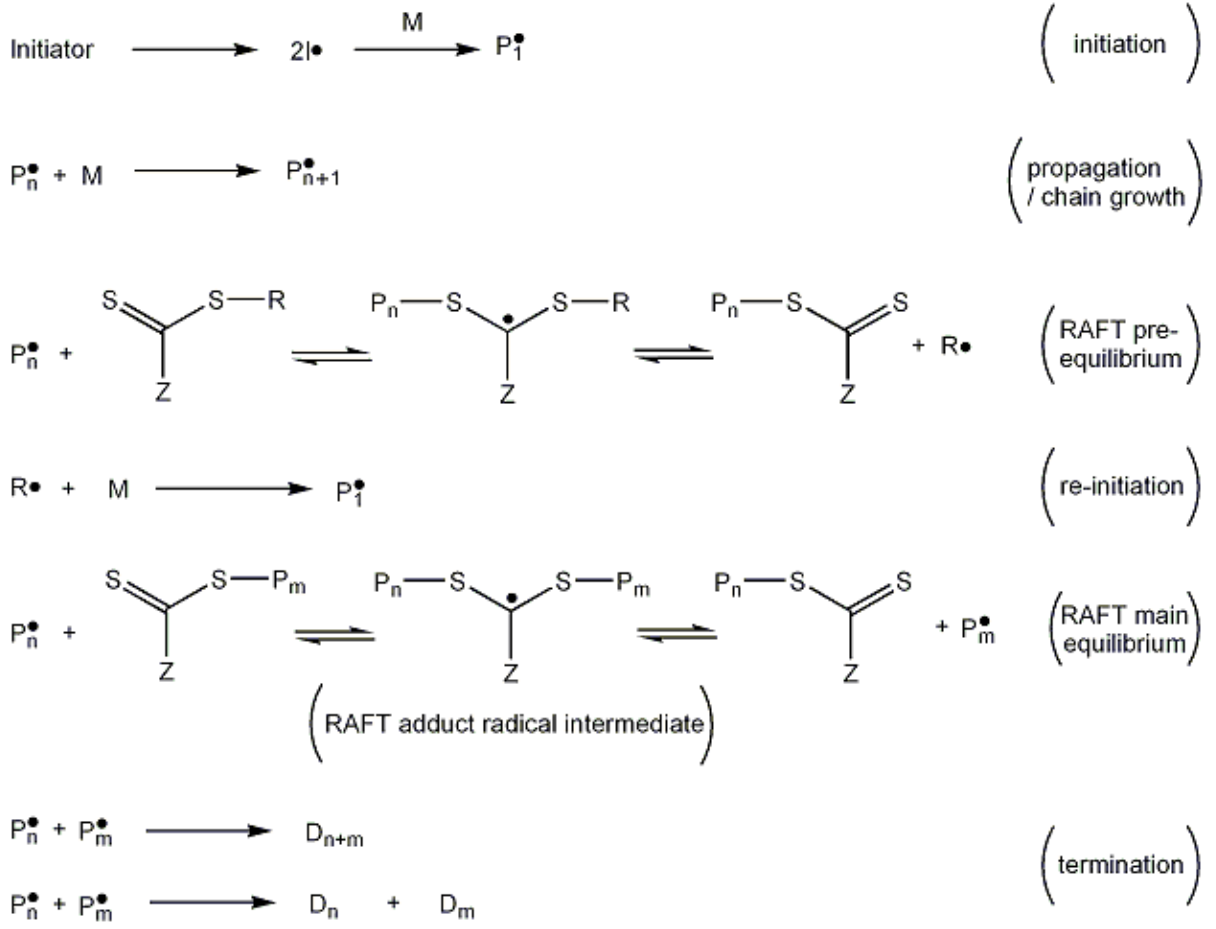
Chain transfer agent (CTA)



Radical initiator



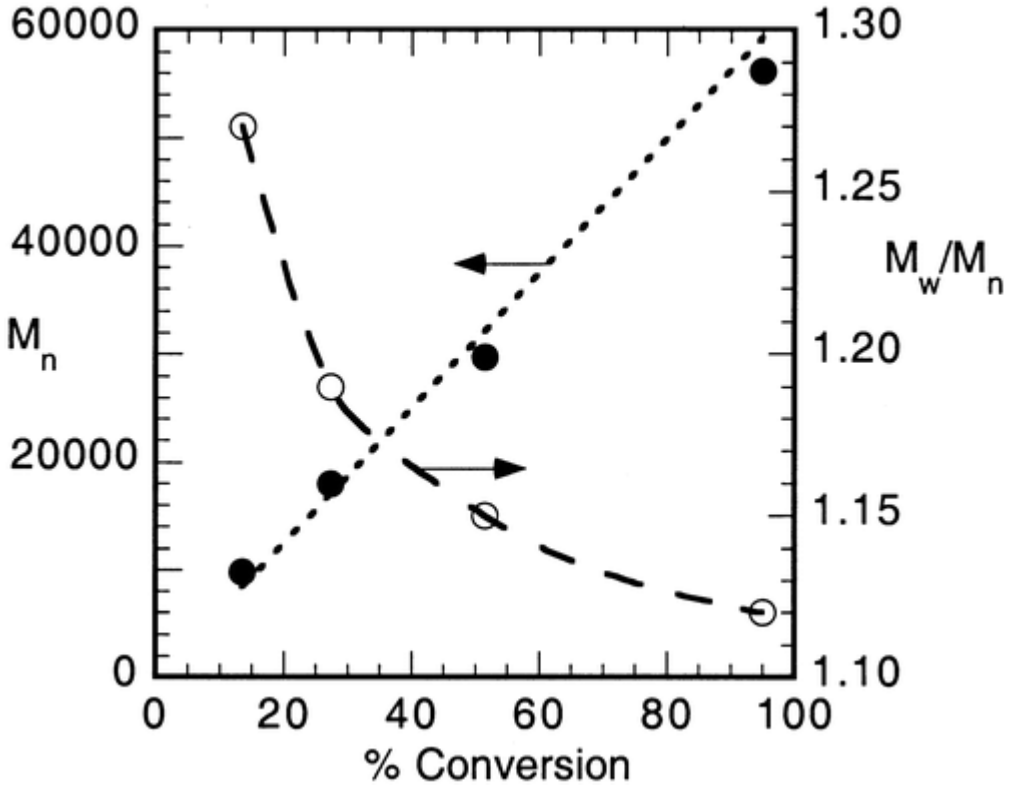
[CTA] : [AIBN] is often larger than 10:1



The “Livingness” of RAFT Polymerization

- Because of the degenerative chain transfer, the total number of chains (i.e., dormant plus active) is equal to the number of CTAs plus the number of the number of radicals introduced from the initiator.

$$N_n = \frac{p[\mathrm{M}]_0}{[\mathrm{CTA}]_0 + 2f([\mathrm{I}]_0 - [\mathrm{I}]_t)}$$



Chiefari, J.; Chong, Y. K.; Ercole, F.; Krstina, J.; Jeffery, J.; Le, T. P. T.; Mayadunne, R. T. A.; Meijs, G. F.; Moad, C. L.; Moad, G.; Rizzardo, E.; Thang, S. H., *Macromolecules* **1998,** *31*, 5559-5562.

The “Livingness” of RAFT Polymerization

- The number of CTAs will dictate the fraction of chains that are maintained in the dormant state (“living chains”). The number of radicals introduced from the initiator will dictate the fraction of chains that will be active—those chains are free radicals that can undergo bimolecular termination (“dead chains”).

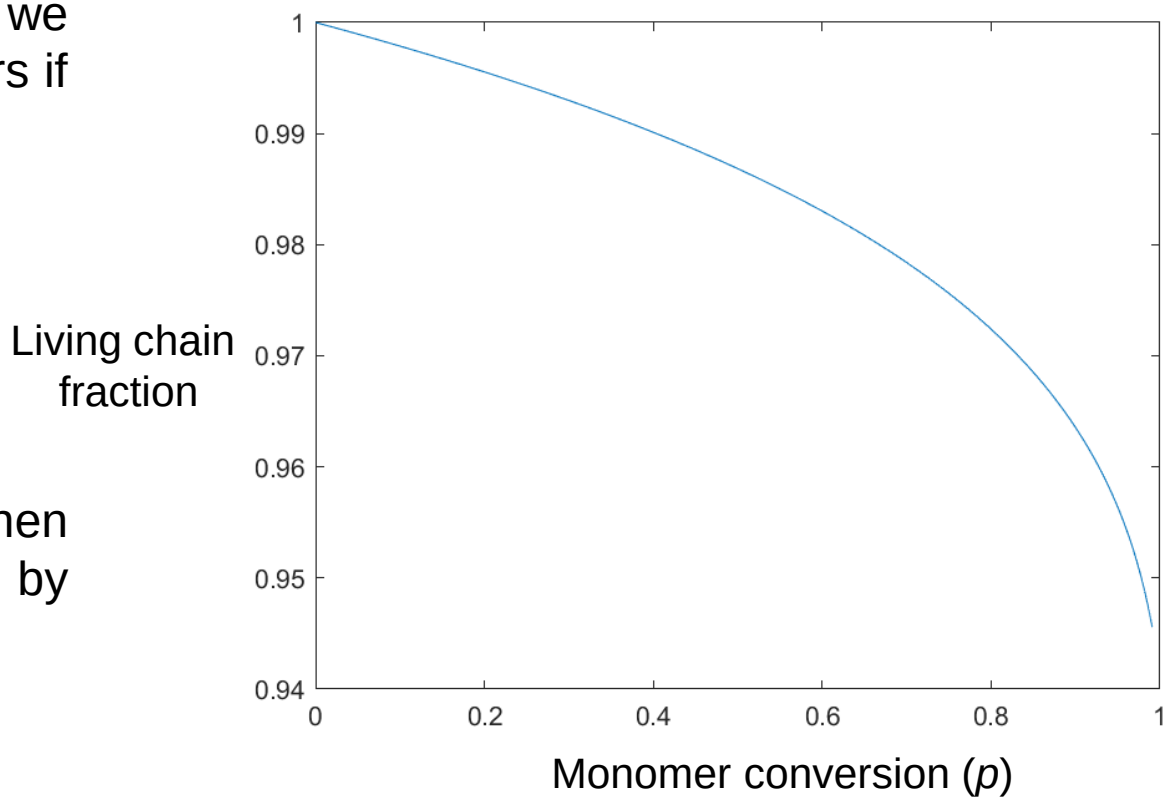
$$\text{living chain fraction} = \frac{[\text{CTA}]_0}{[\text{CTA}]_0 + 2f([\text{I}]_0 - [\text{I}]_t)}$$

For a RAFT polymerization with the following parameters, we can simulate the living chain fraction (come to my office hours if you want to know how to do it)

$k_p = 2.09 \times 10^3$ L mol^{-1} s^{-1} $f = 0.6$

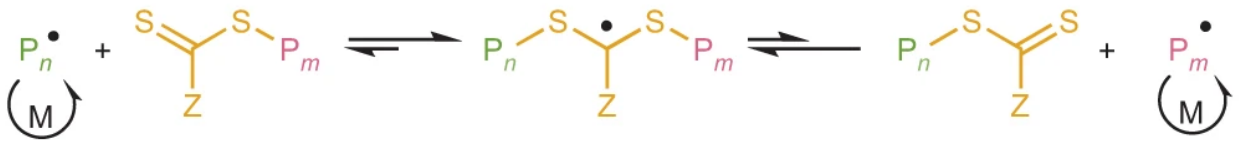
$k_t = 0.95 \times 10^7$ L mol^{-1} s^{-1} [AIBN] = 1.0×10^{-3} mol L^{-1}

$k_d = 3.2 \times 10^{-5}$ s^{-1} [CTA] = 2.0×10^{-2} mol L^{-1}



It shows that less than 3% of chains are terminated even when the conversion is above 80% (this can be improved further by increasing the ratio of [CTA] to [AIBN]).

Monomers in RAFT Polymerization



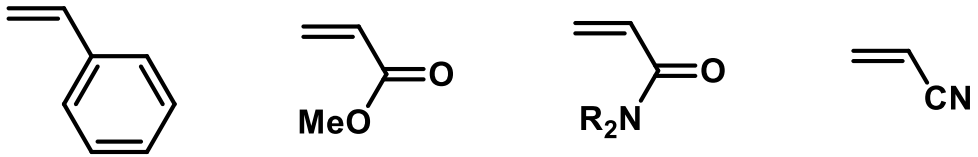
The RAFT equilibrium involves two processes:

- Addition (radical addition to C=S bond)
- Fragmentation (C-S bond broken to form a radical）

Common monomers in RAFT polymerization are divided into two classes:

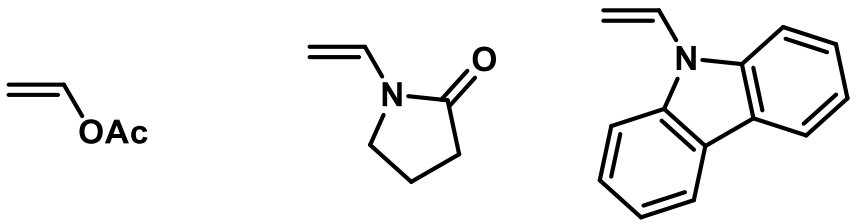
“More activated” monomers (MAMs)

MMA HPAM



St MA AM AN

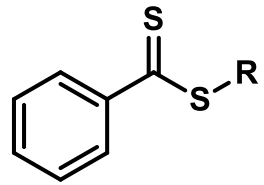
“Less activated” monomers (LAMs)



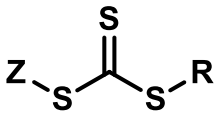
VAc NVP NVC

- MAMs produce relatively more stabilized radicals (fragmentation favored but addition less favored)
- LAMs produce less stabilized but more reactive radicals (addition favored but fragmentation less favored)

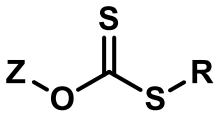
Z Groups in CATs



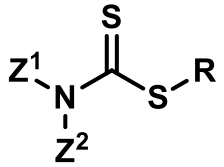
Dithiobenzoates



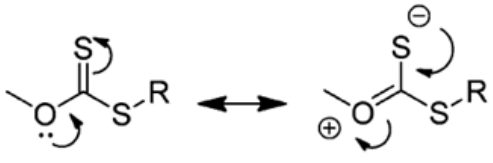
Trithiocarbonates

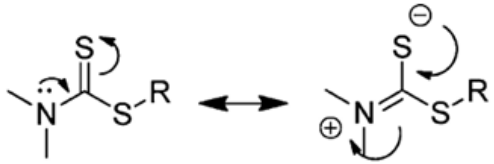


Xanthates

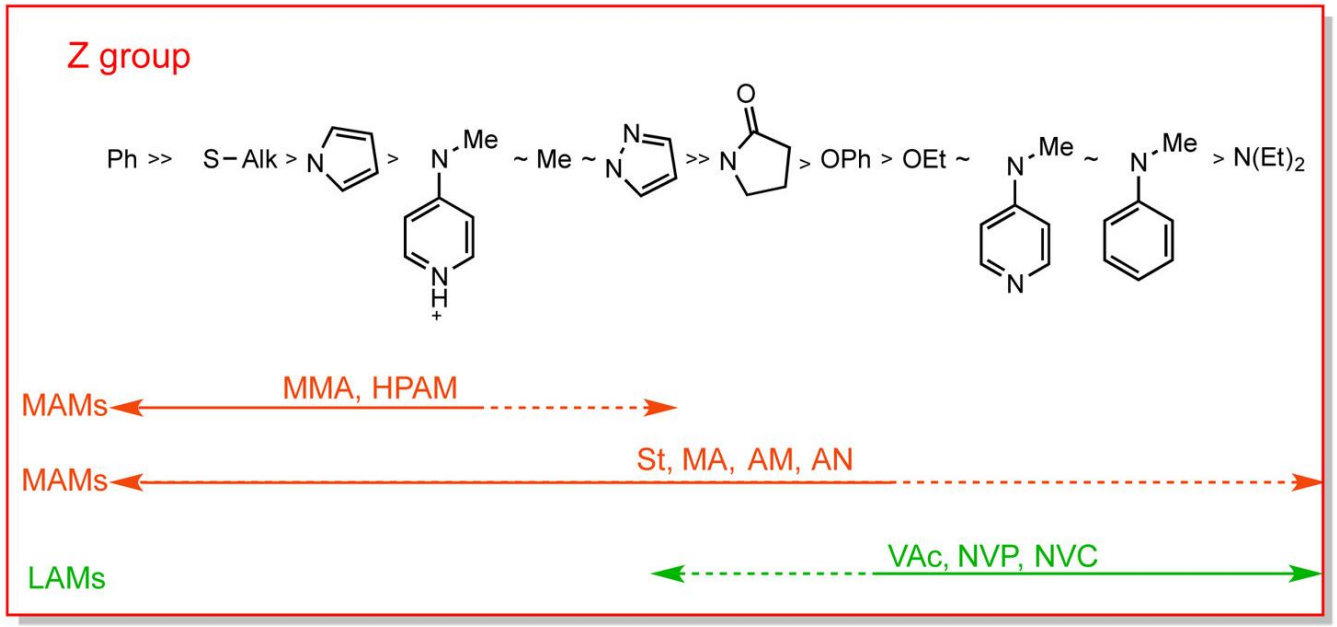


Dithiocarbamates



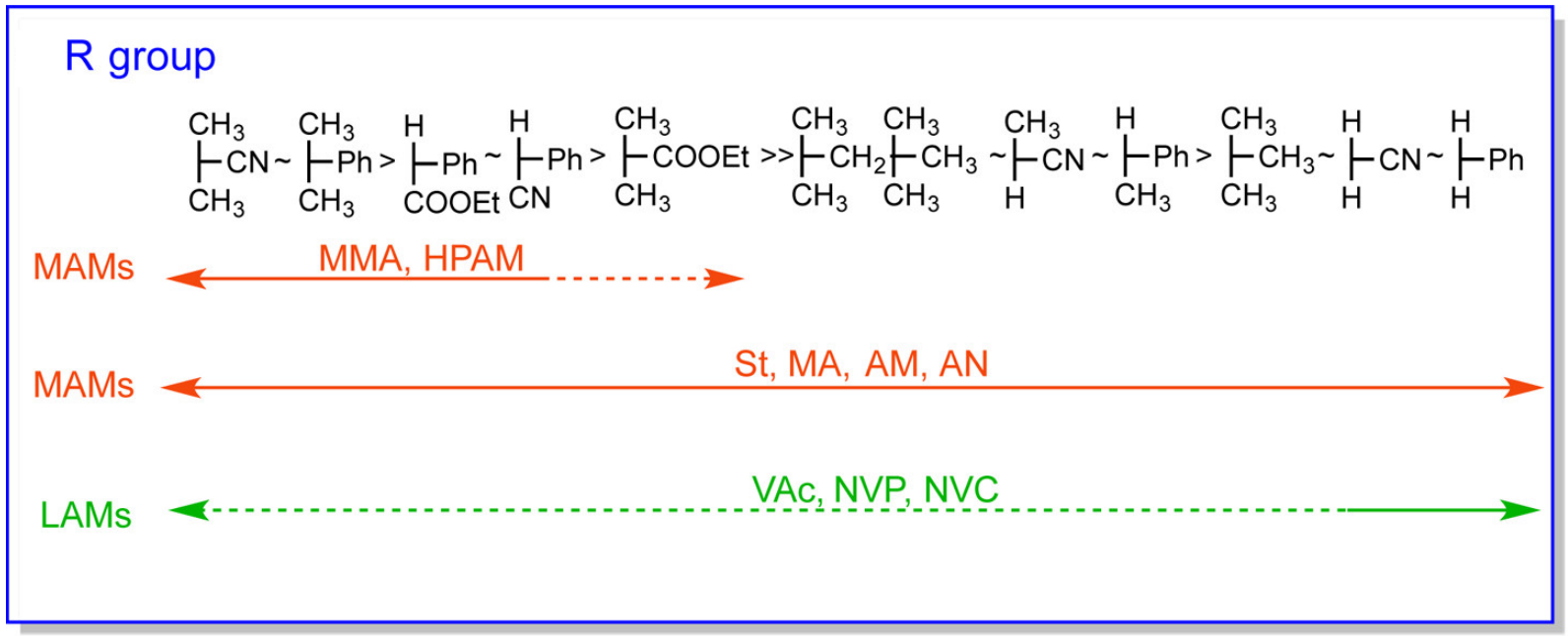


Conjugation to lone pairs stabilizes C=S bonds towards radical addition (but promotes fragmentation once the intermediate is formed)



Keddie, D. J.; Moad, G.; Rizzardo, E.; Thang, S. H., *Macromolecules* **2012,** *45*, 5321-5342.

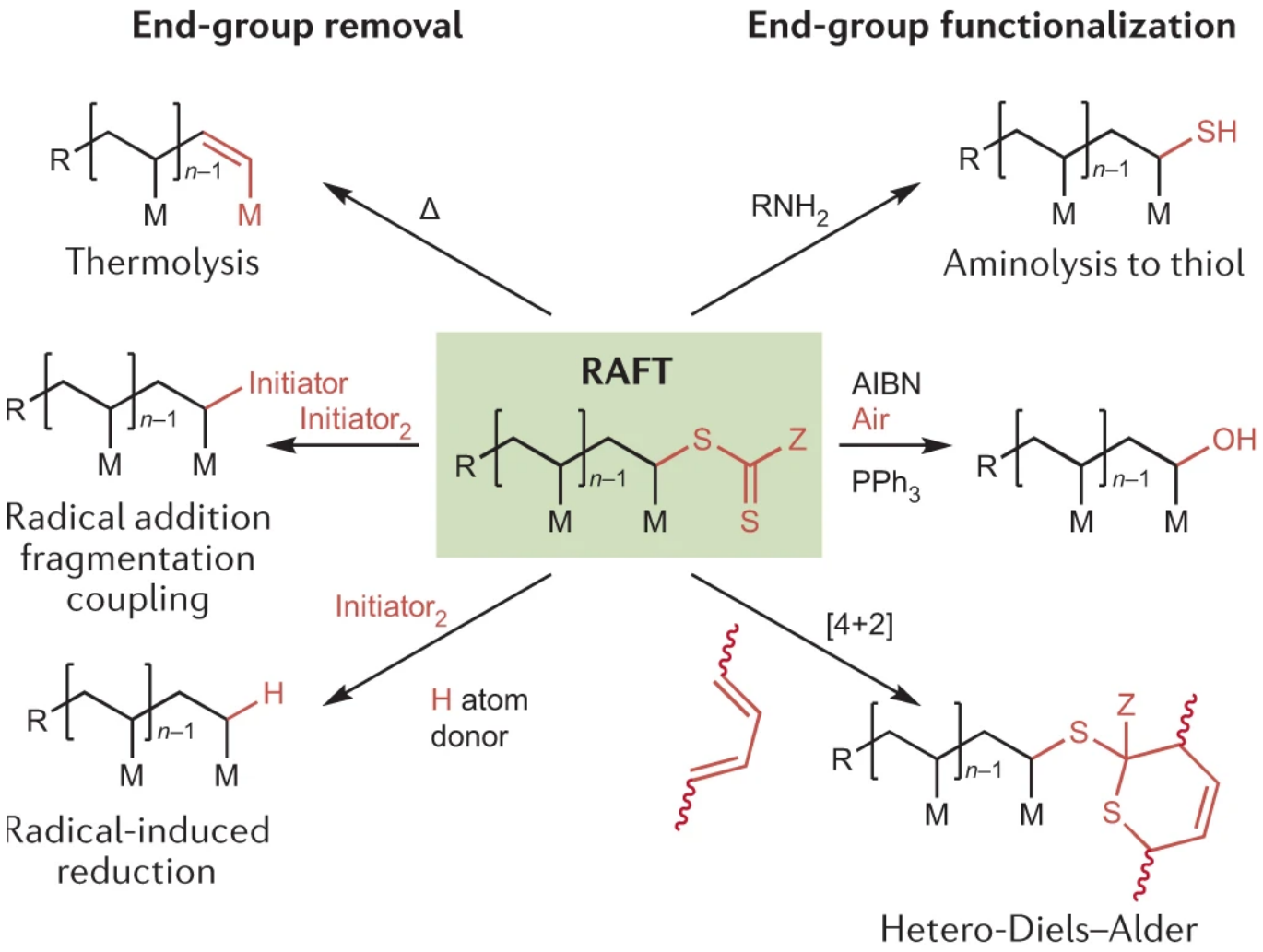
R Groups in CATs



- R groups control the RAFT pre-equilibrium. Most importantly, the R-group has to rapidly reinitiate propagation to ensure all chains are initiated in the same time frame to obtain a narrow distribution.
- Typically, good R groups are groups that mimic monomer radicals.
- The activity of R groups are similar to what is discussed in ATRP (Slide 9). More active monomers require CTAs carrying more active R groups.

Keddie, D. J.; Moad, G.; Rizzardo, E.; Thang, S. H., *Macromolecules* **2012,** *45*, 5321-5342.

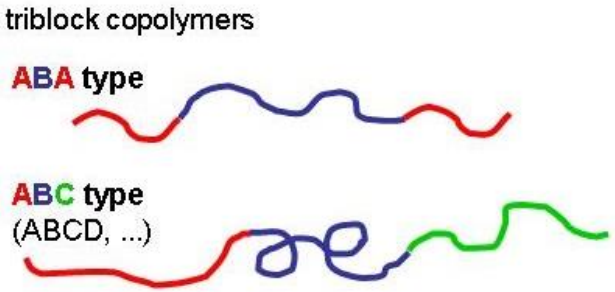
End-Group Modification



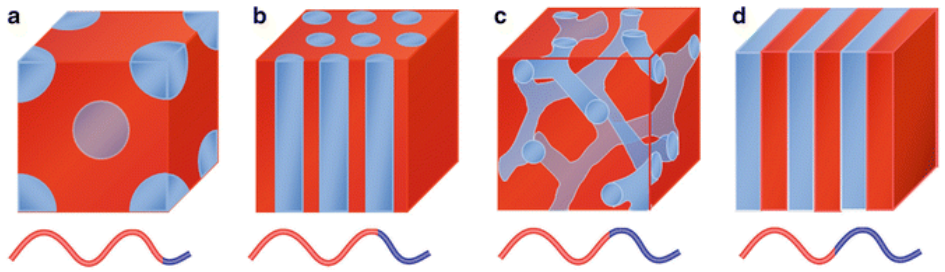
Drawbacks of RTAP: The various sulfur-based CTAs have a yellow color and an unpleasant smell.

Truong, N. P.; Jones, G. R.; Bradford, K. G. E.; Konkolewicz, D.; Anastasaki, A., *Nat. Rev. Chem.* **2021,** *5*, 859-869.

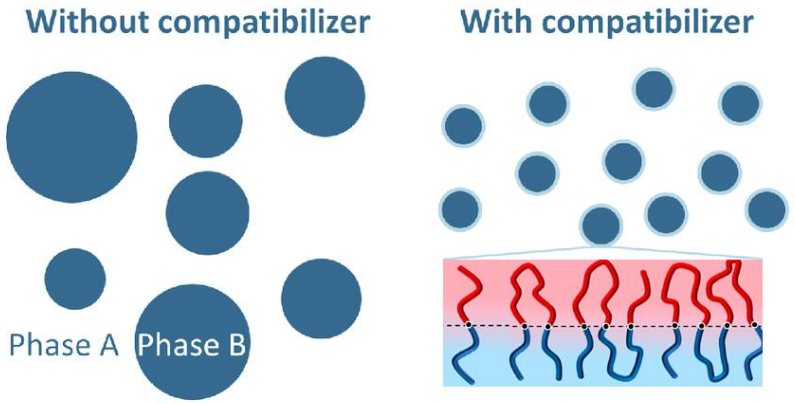
Block Copolymers



Copolymerization does not work well for block copolymer synthesis (recall what we covered in Lecture 8). Instead, we need to make homopolymers of the first block, and then add the second block to it. Living polymerization is thus the ideal method to make block copolymers.



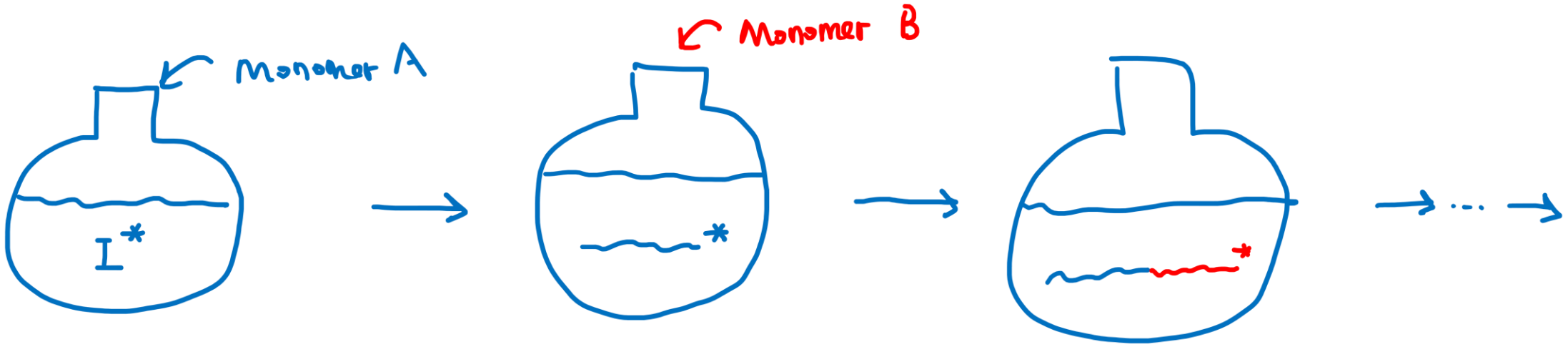
Microphase separation (self-assembled materials)



Compatibilizers (macromolecular surfactants)

Block Copolymer Synthesis

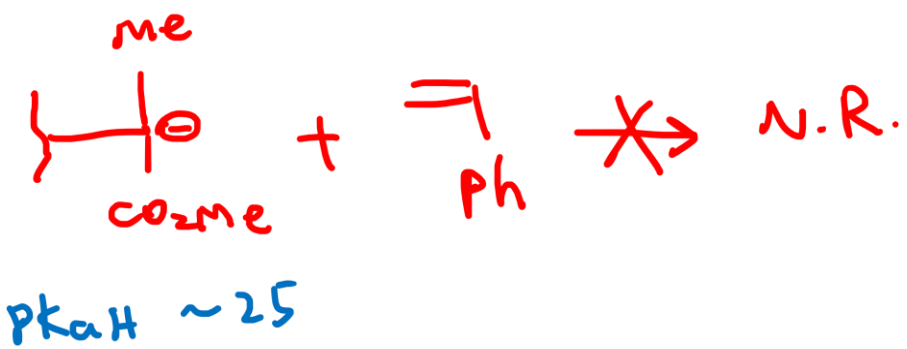
1. Sequential one-pot approach

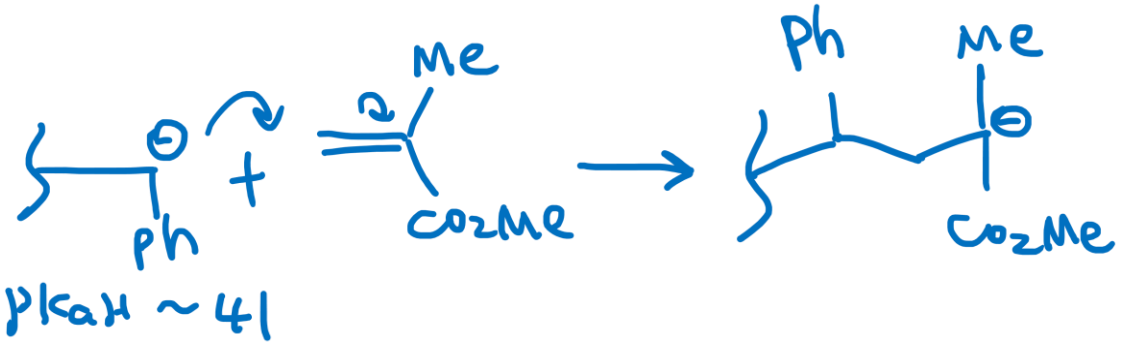


Ideally, monomer A needs to be fully consumed (i.e., 100% conversion) before adding monomer B to ensure perfect "blockness". This approach works best for anionic polymerization, where the reaction can reach 100% conversion with negligible chain transfer or termination.

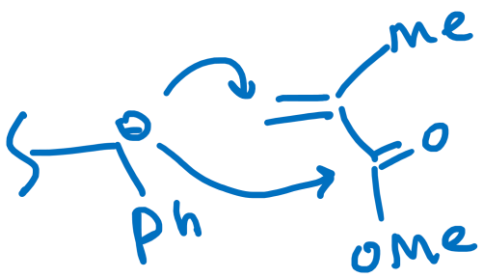
The Order of Addition Should Be Designed Based on the Chain-End Reactivity

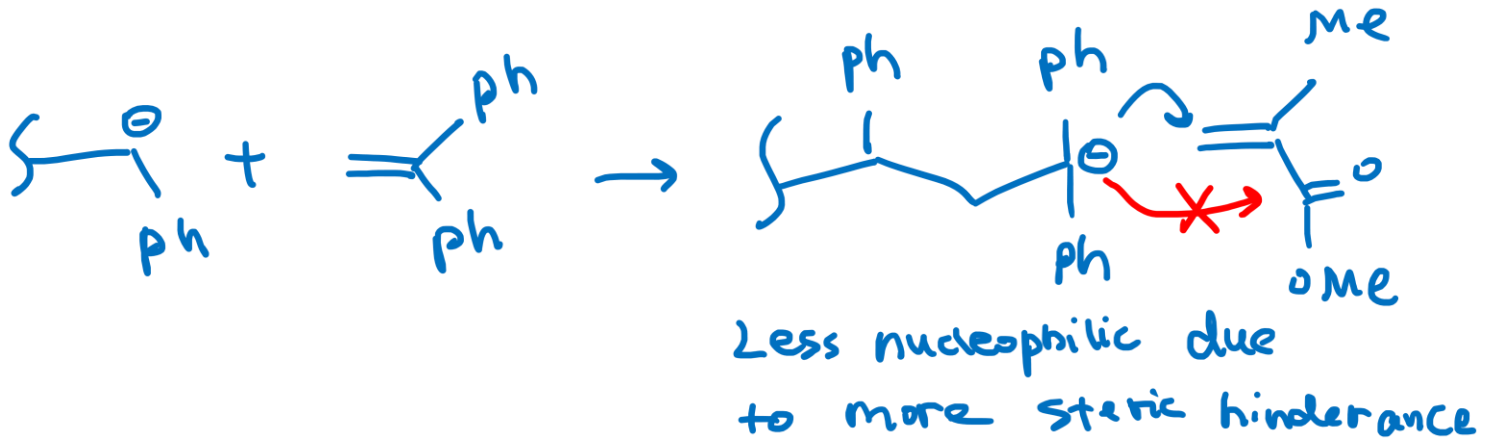
How do we make PMMA-*b*-PS using anionic polymerization?





The carbanion of the first block must be capable of initiating polymerization of the second block.



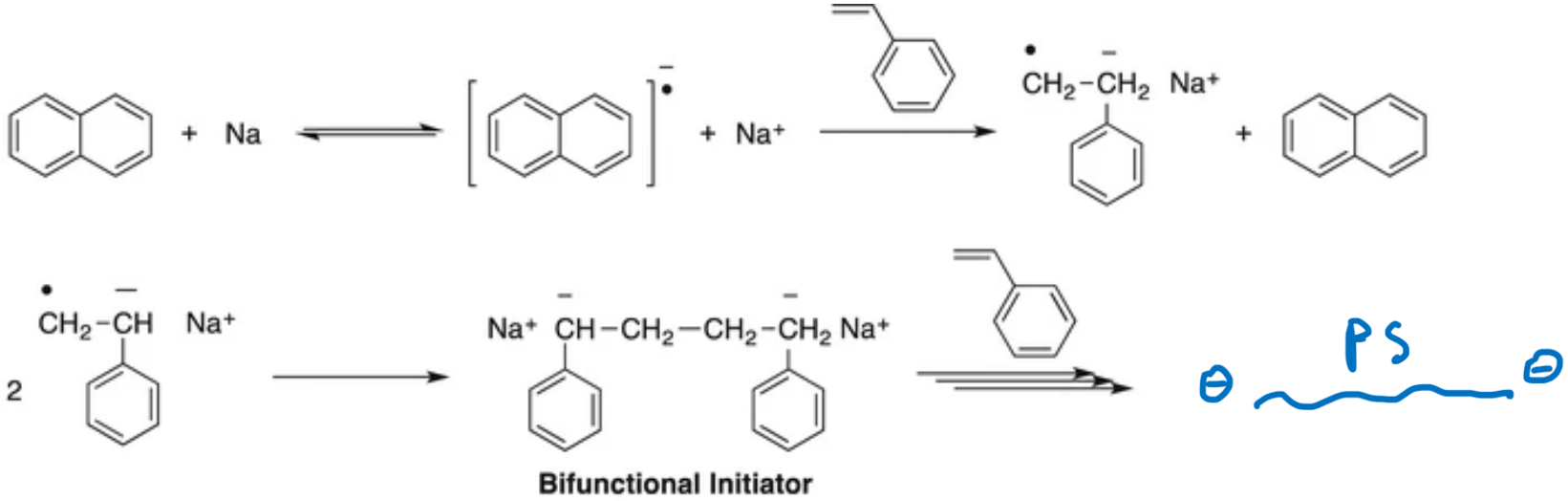


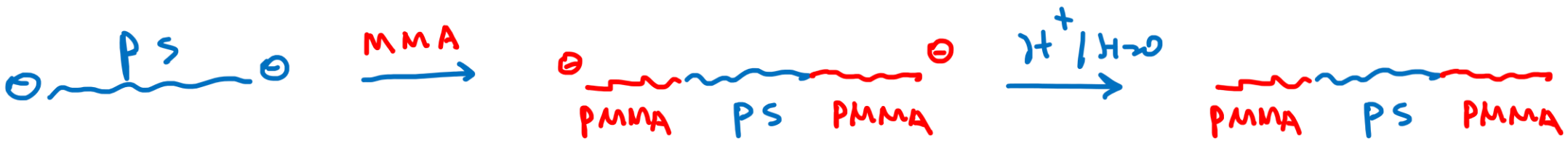
To avoid side reaction, we have a small trick to tame the nucleophilicity of polystyryl carbanion.

Difunctional Initiators Allow Us to Make Triblock Copolymers

How do we make PMMA-*b*-PS-*b*-PMMA using anionic polymerization?

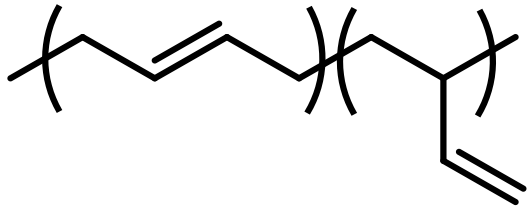
However, we can use a difunctional initiator to make the middle PS block first and then grow the two PMMA blocks from it.



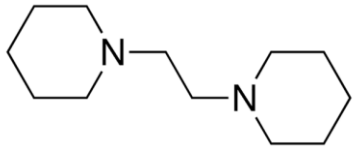


Highly Sophisticated Structures Can Be Made Using This Approach

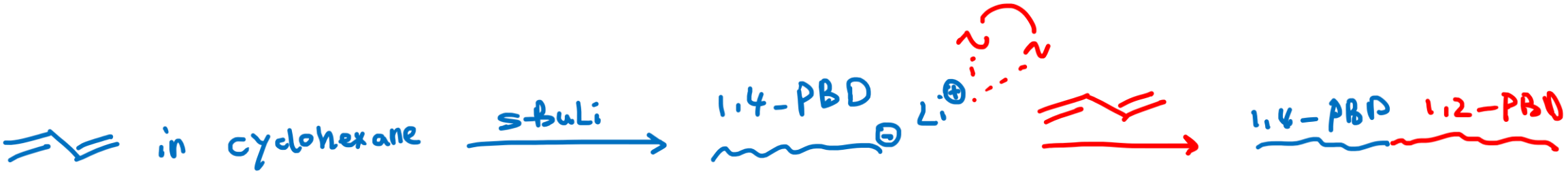
How do we make 1,4-polybutadiene-*b*-1,2-polybutadiene using anionic polymerization?



We have learned that in non-polar solvents, 1,3-diene prefers 1,4-polymerization, while in more polar solvents, 1,3-diene prefers 1,2-polymerization (Slide 17). Hence, such block copolymers can be made by adding an additive such as DIPIP as a “polar modifier” midstream.



DIPIP



Poshyachinda, S.; Edwards, H. G. M.; Johnson, A. F., *Polymer* **1991,** *32*, 334-337.

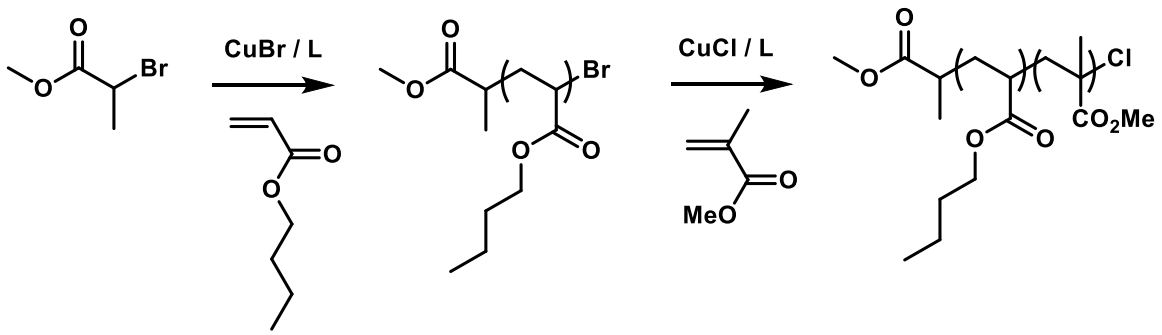
One-Pot Block Copolymer Synthesis Using RDRP

The one-pot approach works less well for RDRP, as a considerable amount of chain termination occurs when conversion is driven close to 100%: at high monomer conversion, the reversible activation/deactivation still occurs but the active species have fewer monomers to react with, so the major pathway for these active species becomes bimolecular termination.

However, it is still possible, although less perfectly.

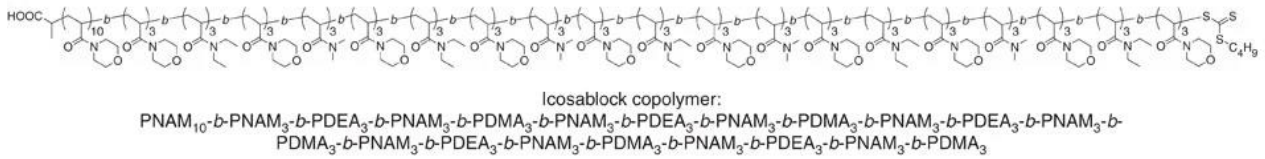
ATRP

The conversion of the first block is driven to ~90% before adding a second monomer to grow the second block. Thus, the second block is not a pure homopolymer. (Notice that CuCl is used to grow the PMMA block—we will discuss this in the following slides)



RAFT

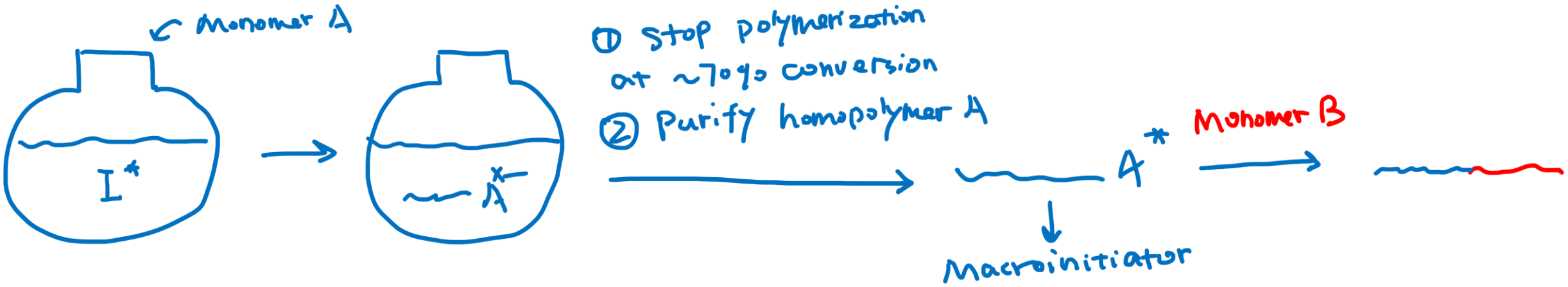
In RAFT, the fraction of living chains is controlled by the [CTA]:[AIBN] ratio. Using less AIBN reduces dead chains, even at near-complete conversion, though it slows polymerization. For example, a remarkable $[CTA]_0$:[initiator] ratio of 1300:1 was used to achieve the following icosablock copolymer.



Matyjaszewski, K.; Shipp, D. A.; McMurtry, G. P.; Gaynor, S. G.; Pakula, T., *J. Polym. Sci. A* **2000,** *38*, 2023-2031.
Gody, G.; Maschmeyer, T.; Zetterlund, P. B.; Perrier, S., *Nat. Commun.* **2013,** *4*, 2505.

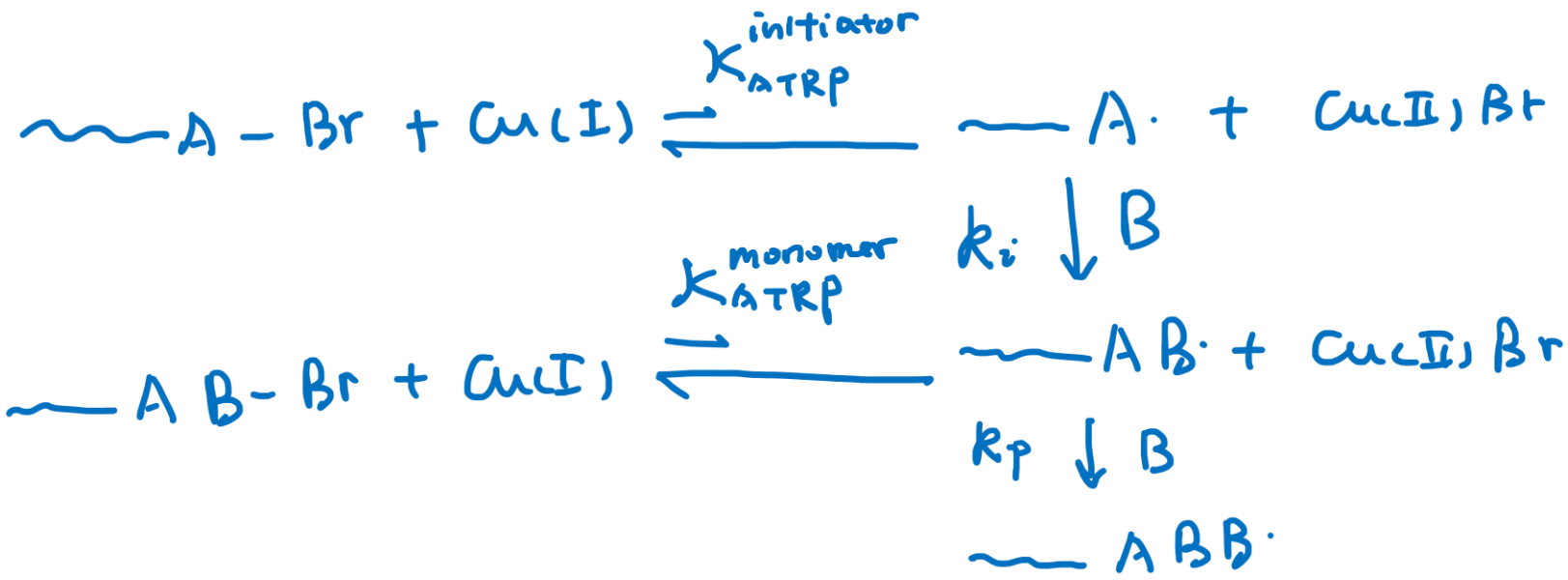
Block Copolymer Synthesis

2. Macroinitiator approach



- It works great for RDRP since the reaction can be stopped at 60% to 70% monomer conversion. The homopolymer is then purified (mostly through precipitation to remove unreacted monomers), characterized, and used as a macroinitiator to grow the second block in a separate pot.
- For a given block copolymer AB, however, we need to consider which block to grow first. This consideration is influenced by the initiation activity of the macroinitiator.

Requirement for Efficient Reinitiation in ATRP

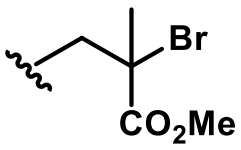


Take ATRP as an example: to maintain the narrow dispersity of the second block, all chains need to be initiated (i.e., A· reacts with monomer B) before chain growth occurs (i.e., B· reacts with monomer B). This requires

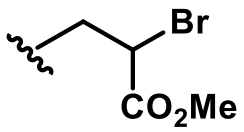
$K_{ATRP}^{initiator} \cdot k_i > K_{ATRP}^{monomer} \cdot k_p$ Since k_i is often close to k_p, we need $K_{ATRP}^{initiator} > K_{ATRP}^{monomer}$

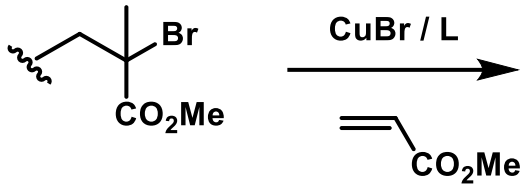
This means the first block (macroinitiator) needs to be a more active initiator (refer to Slide 9 for initiator activity).

How Do We Make PMMA-*b*-PMA Using ATRP?



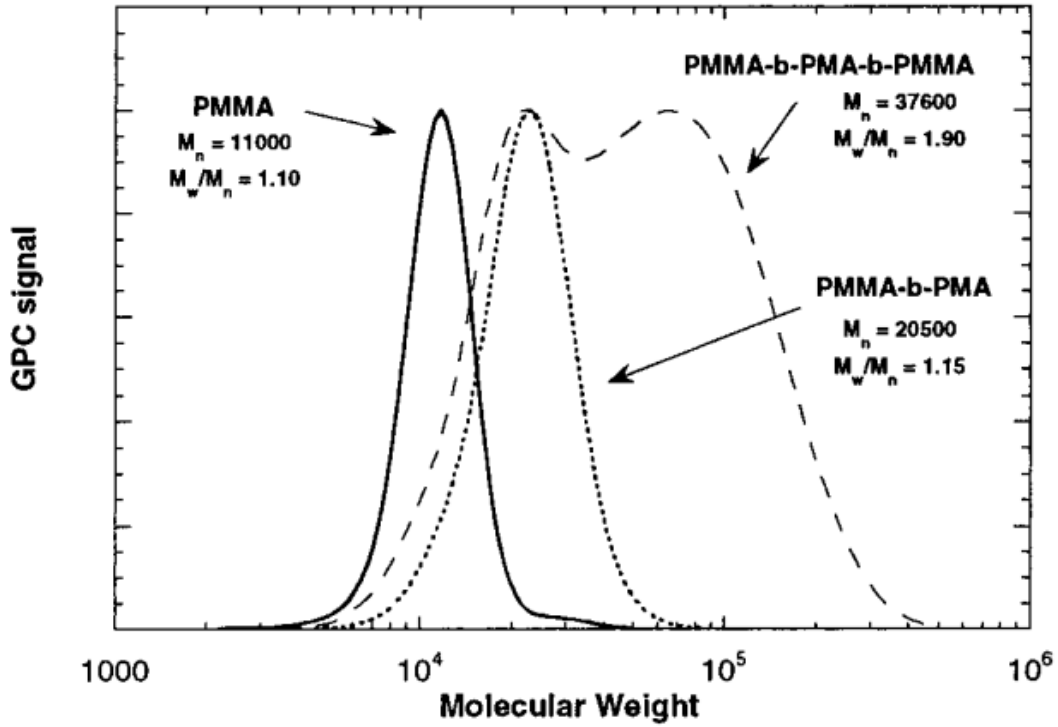
is a more active initiator than





PMMA-*b*-PMA

PMMA macroinitiator

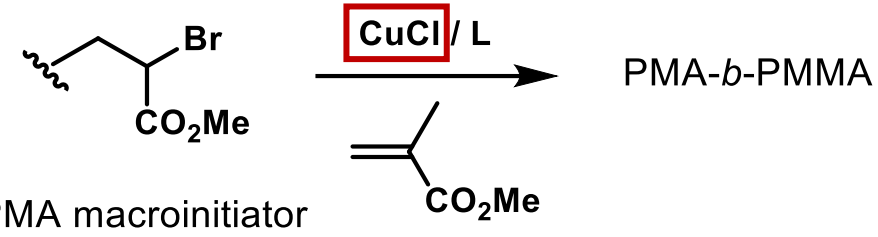


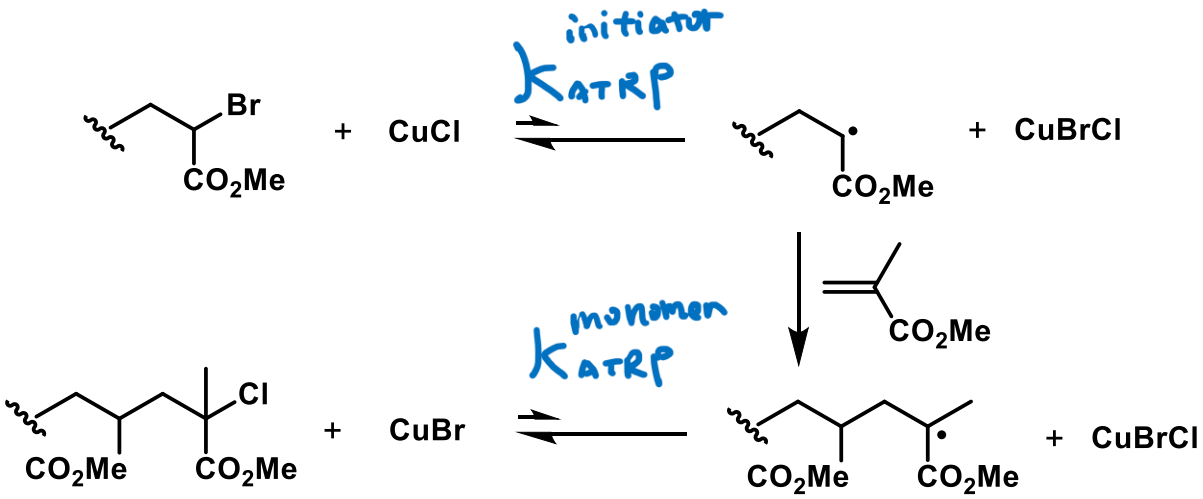
Making the PMMA block first and using it as a macroinitiator provides good control over the growth of the next PMA block. However, when the PMMA-b-PMA was used as a macroinitiator to grow a third PMMA block, a broad distribution resulted.

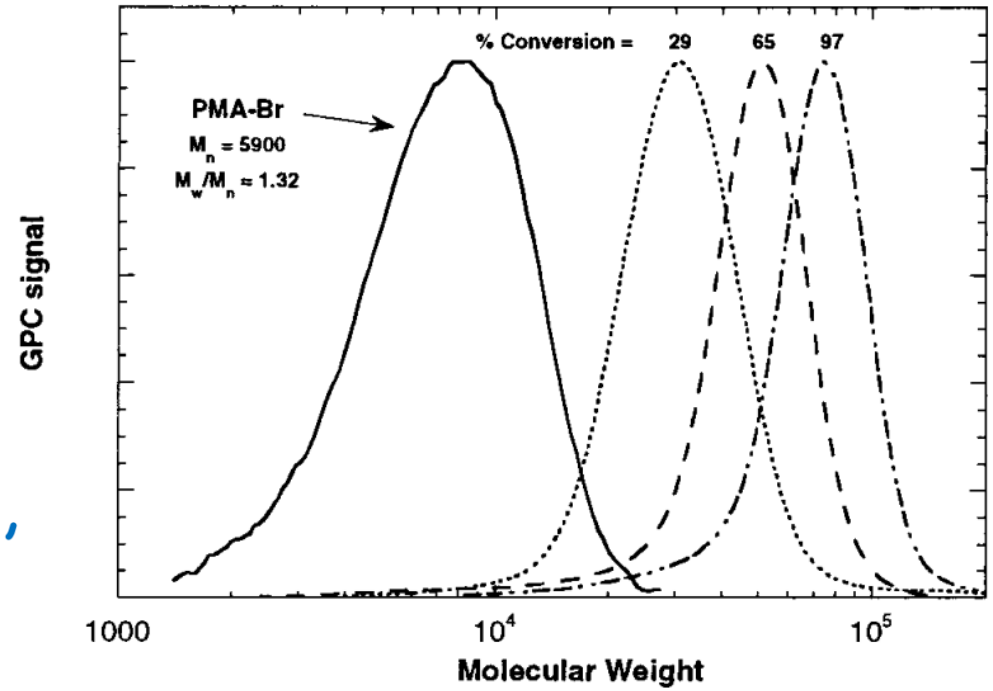
Shipp, D. A.; Wang, J.-L.; Matyjaszewski, K., *Macromolecules* **1998,** *31*, 8005-8008.

How Do We Make PMMA-*b*-PMA Using ATRP?

Starting from a PMA macroinitiator is also possible, but we need to play some trick…





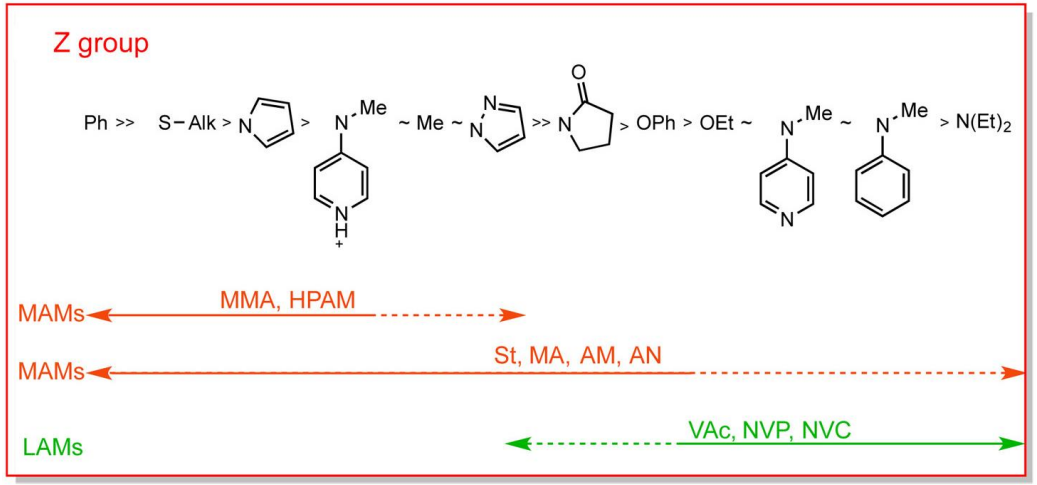


By changing chain end from P–Br to P–Cl,

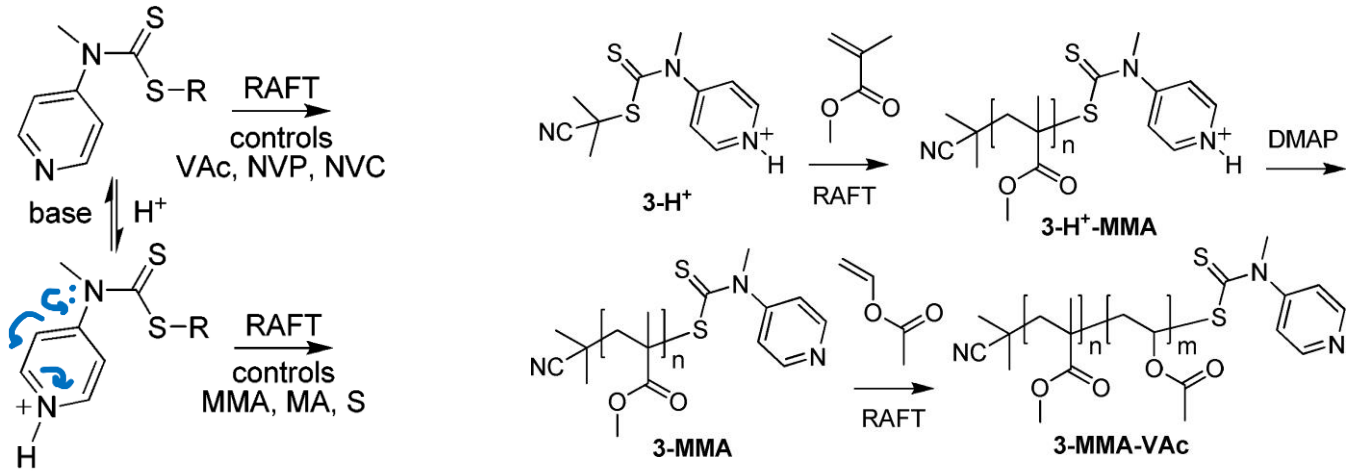
we again have $k_{ATRP}^{initiator} > k_{ATRP}^{monomer}$

Shipp, D. A.; Wang, J.-L.; Matyjaszewski, K., *Macromolecules* **1998,** *31*, 8005-8008.

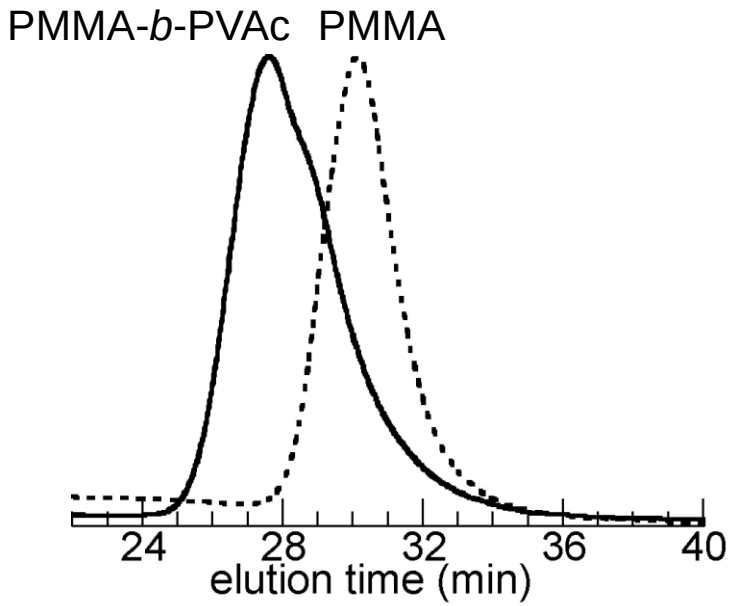
How Do We Make PMMA-*b*-PVAc Using RAFT Polymerization?



- In RAFT polymerization, MAMs and LAMs require different types of Z groups. MMA is a MAM, while PVAc is a LAM—how do we resolve this issue?
- The trick is to design a switchable RAFT agent.



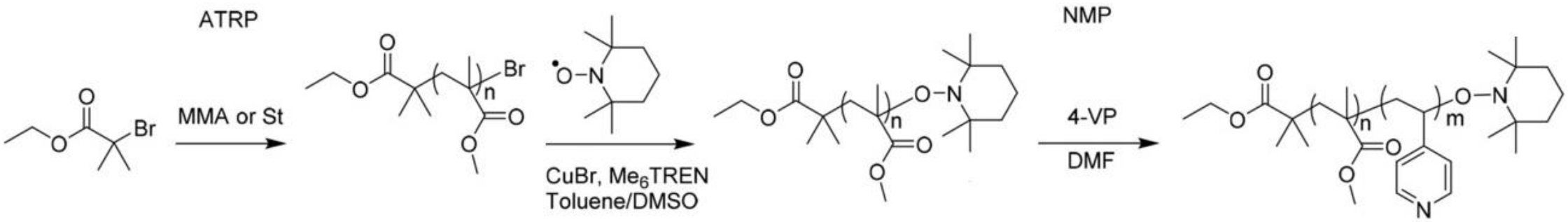
The lone pair on N becomes delocalized after protonation of pyridine, resulting in less conjugation between N and the C=S bond.



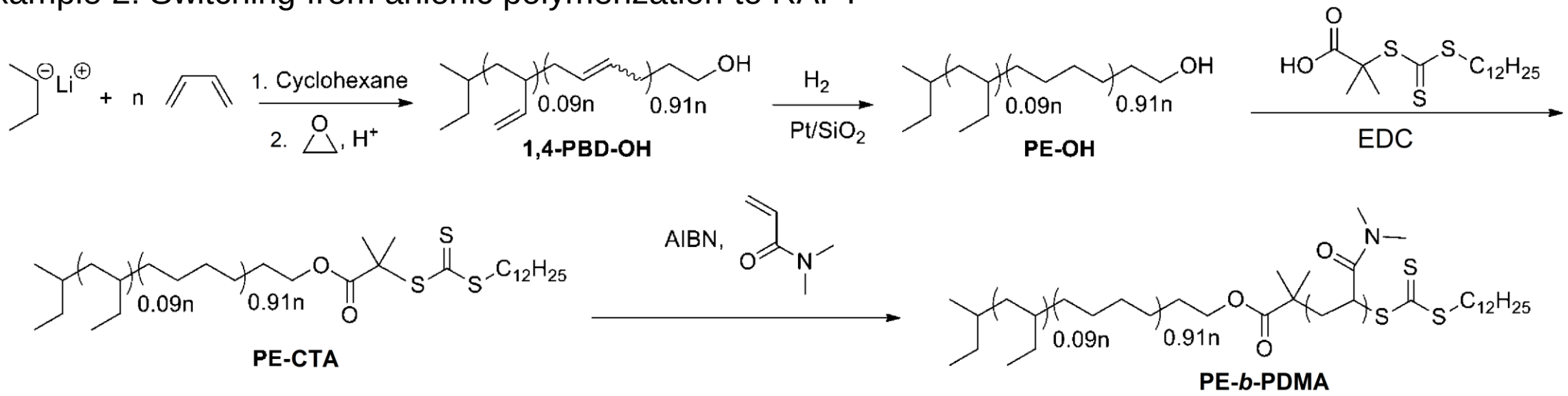
Benaglia, M.; Chiefari, J.; Chong, Y. K.; Moad, G.; Rizzardo, E.; Thang, S. H., *J. Am. Chem. Soc.* **2009,** *131*, 6914-6915.

Macroinitiator Enables Switching Polymerization Methods

Example 1: Switching from ATRP to NMP



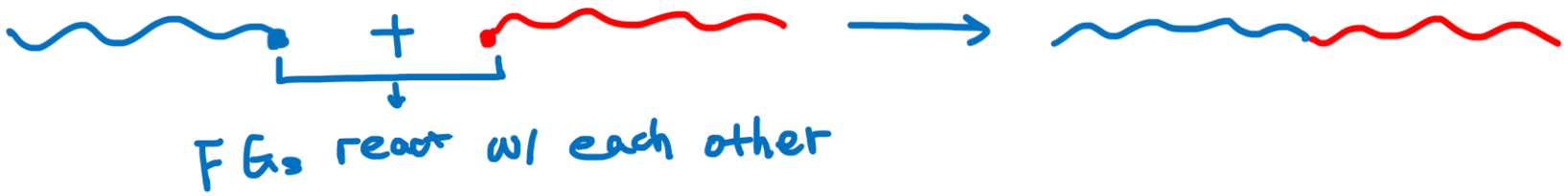
Example 2: Switching from anionic polymerization to RAFT



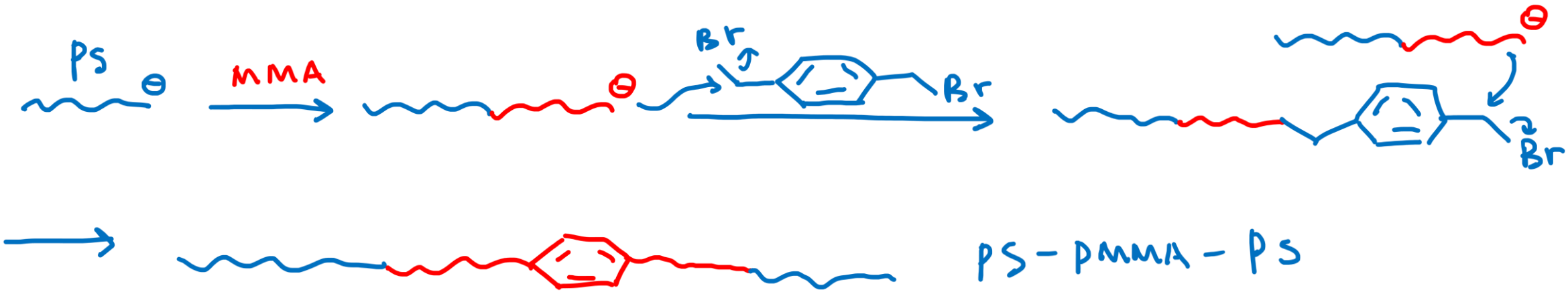
Zhou, Y.-N.; Chen, Z.-C.; Wei, C.; Luo, Z.-H., *Macromol. Chem. Phys.* **2015,** *216*, 329-333.
Yin, L.; Hillmyer, M. A., *Macromolecules* **2011,** *44*, 3021-3028.
Guo, X.; Choi, B.; Feng, A.; Thang, S. H., *Macromol. Rapid Commun.* **2018,** *39*, 1800479.

Block Copolymer Synthesis

3. Coupling approach

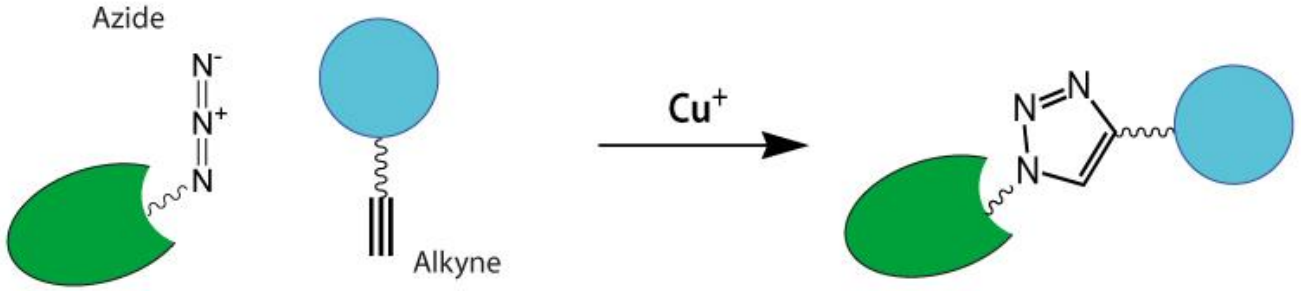


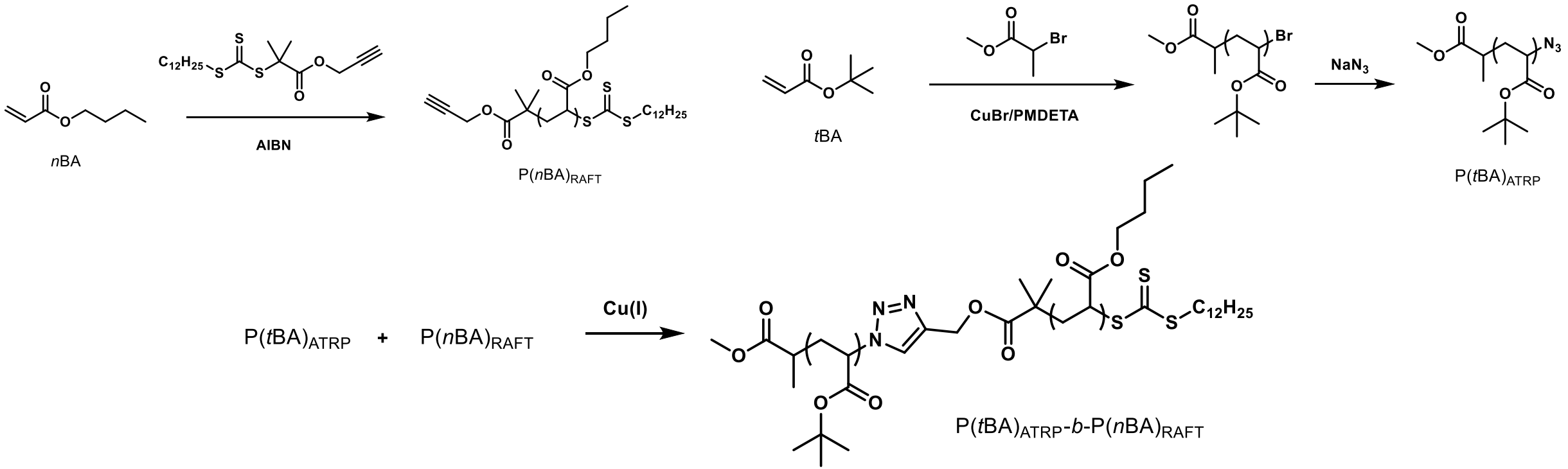
How do we make PS-*b*-PMMA-*b*-PS using anionic polymerization?



Even when run under stoichiometric conditions, incomplete coupling is still probable. Purification is needed to separate the desired triblock copolymer from the unreacted diblock copolymer, which is challenging but possible.

Coupling Of Two Polymers via Click Chemistry



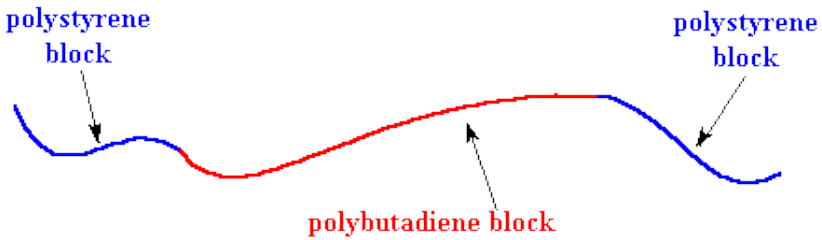


Nasrullah, M. J.; Vora, A.; Webster, D. C., *Macromol. Chem. Phys.* **2011,** *212*, 539-549.

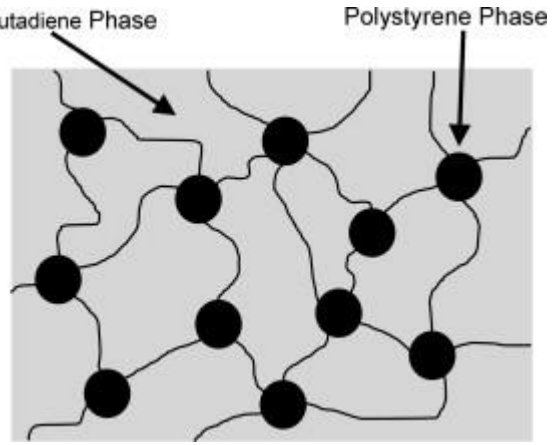
Thermoplastic Elastomers

Polystyrene-*b*-polybutadiene-*b*-polystyrene (SBS)

Polystyrene-*b*-polyisoprene-*b*-polystyrene (SIS)



Soft (rubbery) Hard (glassy)



Ralph Milkovich
(1929-1985)

Developed in 1960s in Shell

It behaves as elastomers at ambient temperatures but are thermoplastic at elevated temperatures where they can be molded and remolded.

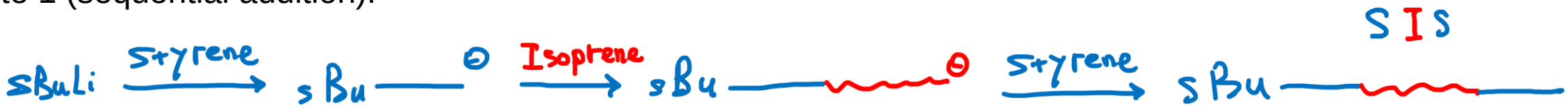
Automobile Bumpers

Elastic Nonwoven

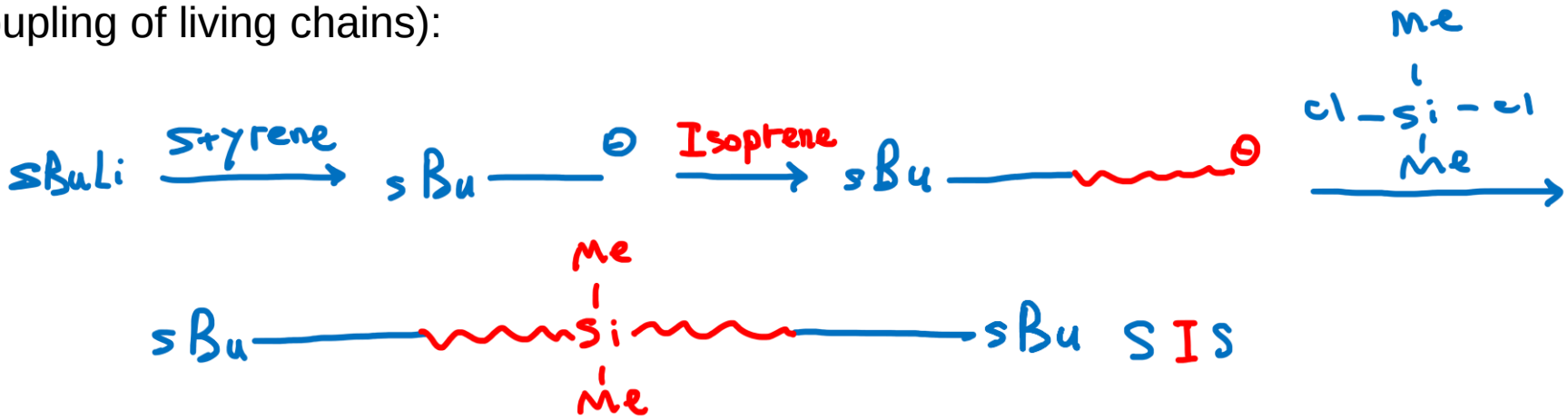
Roofing

Thermoplastic Elastomers

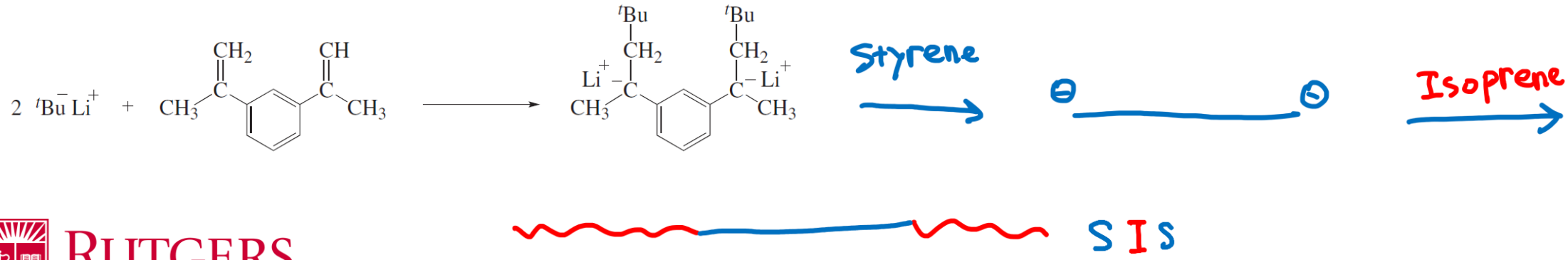
Route 1 (sequential addition):



Route 2 (coupling of living chains):

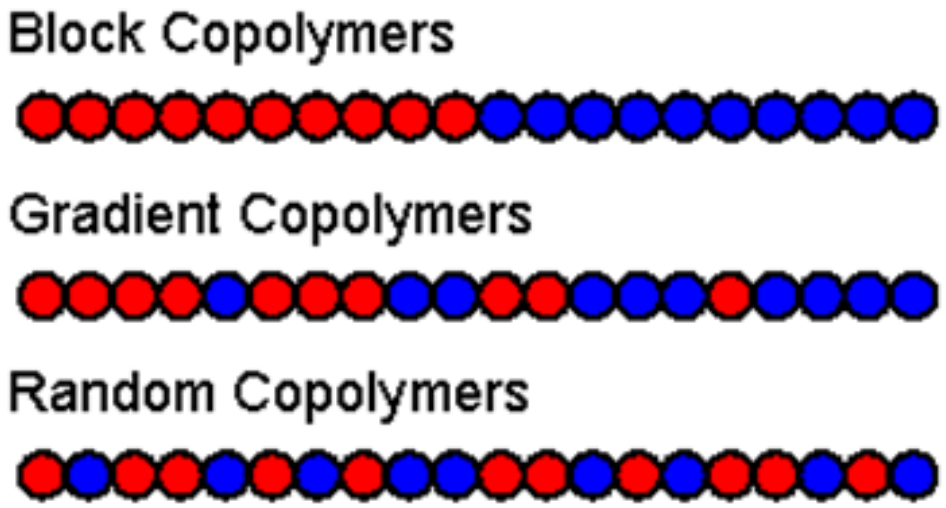


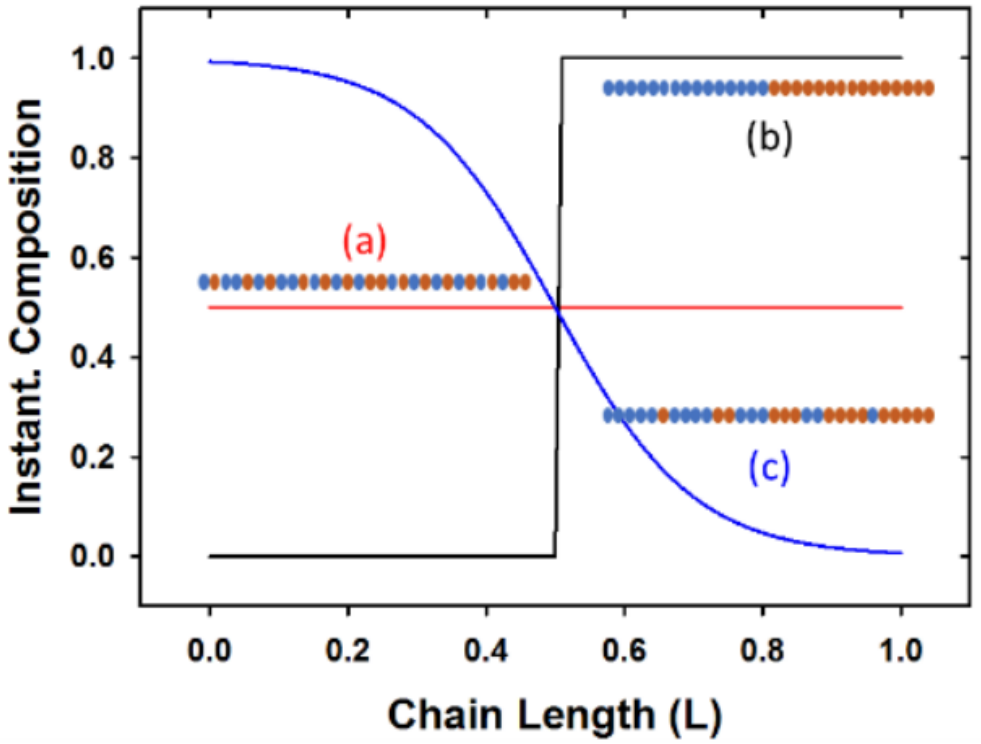
Route 3 (difunctional initiator):



Gradient Copolymers

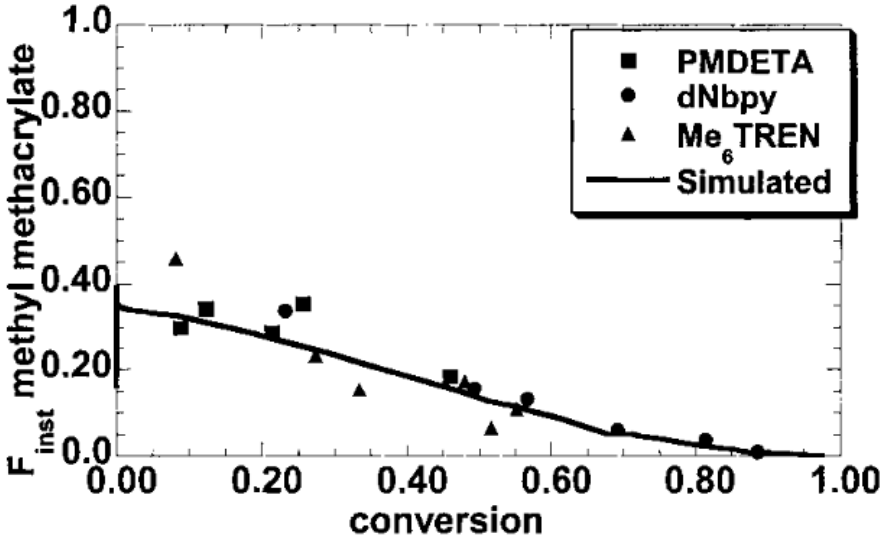
Gradient copolymers are copolymers in which the change in monomer composition is gradual from predominantly one species to predominantly the other.





Gradient Copolymers Synthesized via RDRP

- RDRP is a great way to make gradient copolymers by one-pot copolymerization of a selected mole ratio of monomers with sufficiently different reactivity ratios.
- As the polymerization proceeds, the more slowly reacting monomer is incorporated to a greater extent as a consequence of depletion of the faster reacting monomer at an early stage of polymerization.
- Do not confuse this with the copolymerization discussed in Lecture 8 (Slide 20), where the difference in comonomer reactivity ratios results in the composition of the copolymer formed at the beginning of the copolymerization differing from the composition of copolymers prepared at later stages.
- In contrast, the difference in comonomer reactivity ratios is reflected in the composition along a single chain in RDRP, as each living chain propagates throughout the entire polymerization process.



ATRP copolymerization of methyl methacrylate and *n*-butylacrylate

Matyjaszewski, K.; Ziegler, M. J.; Arehart, S. V.; Greszta, D.; Pakula, T., *J. Phys. Org. Chem.* **2000,** *13*, 775-786.