Metal-Free ATRP

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Metal-Free Atom Transfer Radical Polymerization

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Perspective

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Evolution and Future Directions of Metal-Free Atom Transfer Radical Polymerization

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Questions

- What are major drawbacks of metal catalyzed ATRP reactions ?
- Other than omitting the need for a metal catalyst, what are further advantages of light-mediated polymerization reactions ?
- What are limitations and possibilities for further improvement of the current protocols that have been established to conduct metal-free ATRP ?

Macromolecular Engineering

Synthesis of polymers with precise control over molecular weight, composition and topology

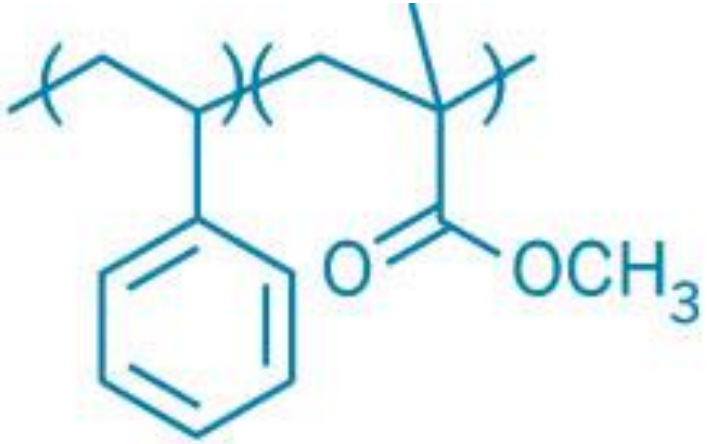
Table 1. Architectural forms of polymers available by living polymerization techniques.

	Polymer	Application
1	OH *Functional ended*	Dispersing agents Synthesis of macromonomers
2	HO OH *α,ω-difunctional*	Elastomers synthesis Chain extension Cross-linking agents
3	*AB Block*	Dispersing agents Compatibilizers for polymer blending
4	*ABA Block*	Thermoplastic elastomers
5	*Graft*	Elastomers Adhesives
6	*Comb*	Elastomers Adhesives
7	*Star*	Rheology control Strengthening agents
8	*Ladder*	High-temperature plastics Membranes Elastomers
9	*Cyclic*	Rheology control
10	*Amphiphilic network*	Biocompatible polymers

Question: Can we achieve this using conventional free radical polymerization ??

O.W. Webster, *Science* **1991**, *251*, 887

Case Study: PS-block-PMMA



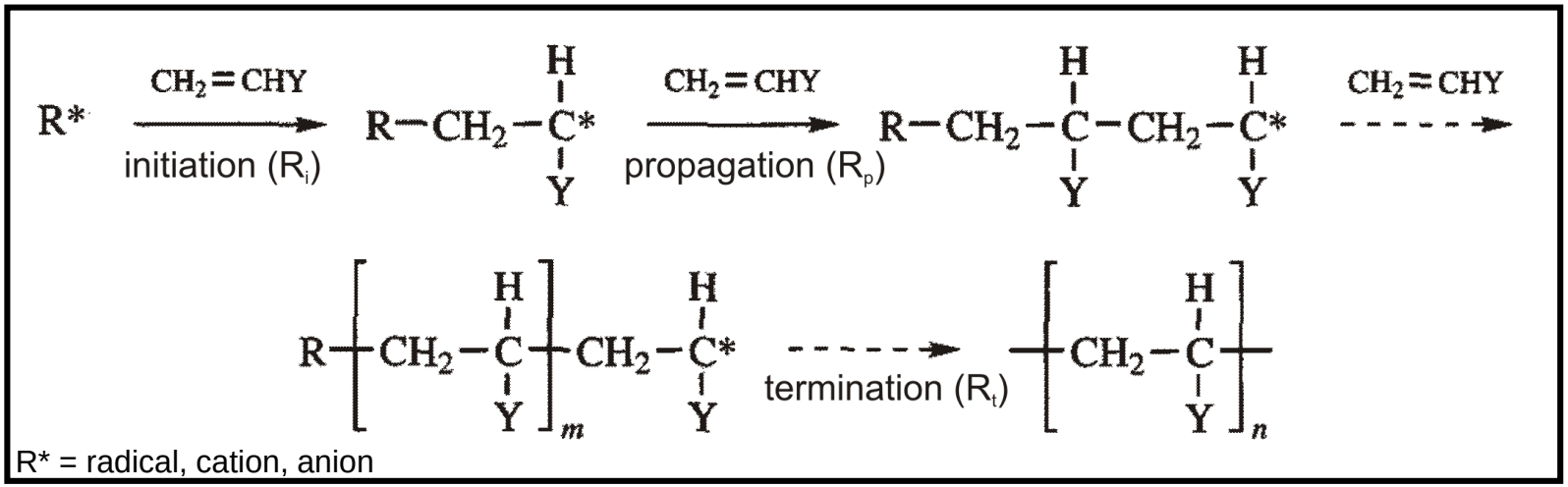
Polystyrene-polymethyl-methacrylate, PS-PMMA

Free radical polymerization

1. Consecutive monomer addition ?

2. Couple PS and PMMA precursors ?

Answer: NO !!



Free radical chain polymerization:

- Initiation is slow compared to propagation and termination ($R_i < R_p, R_t$)
- Chains are very short-lived (< 1 s), due to high chain propagation rates and the existence of termination reactions

As a consequence:

- Relatively broad distribution of chain lengths
- Control over chain length is limited
- Difficult to control polymer composition, functionality and architecture

What Is Needed For Macromolecular Engineering ?

1. Fast and quantitative initiation

All chains start to grow at the same time and $X_n = \Delta[M] / [I]_0$

Consequences:
- Narrow molecular weight distribution
- Precise control of X_n

Since usually X_n = 100 – 1000 and $[M]_0$ = 0.1 – 10 M,
this means $[I]_0 = 1.0 \times 10^{-4}$ – 0.1 M, i.e. relatively high radical concentrations

2. Long-lived polymer chains

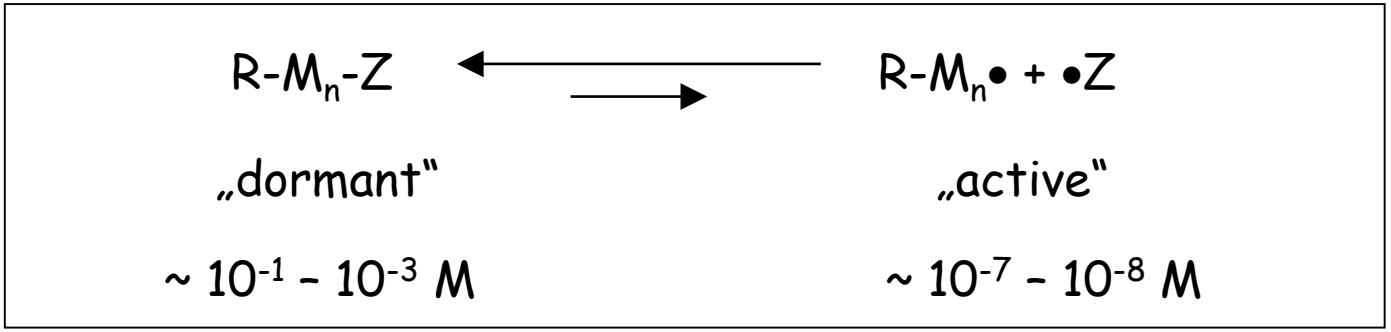
Consequences: Control of end group functionality and polymer architecture

Increasing the lifetime of a polymer chain means reducing the probability for termination to occur.

Since $k_t = 10^6$ L.mol^{-1}.sec^{-1}, this requires $[I]_0 = 10^{-6}$ M,
i.e. relatively small radical concentrations

Fast and quantitative initiation and increasing the lifetime of the growing polymer chains have different demands on $[I]_0$. How can this dilemma be solved?

Polymerization strategies in which a small fraction of active propagating chains is in fast equilibrium with a large fraction of dormant chains, which cannot terminate or propagate



In this way, both requirements can be fulfilled:

1. Low concentration of active radicals prevents termination and increases the lifetime of the growing polymer chains

2. Sufficiently high overall concentration of growing chains allows control of X_n via $\Delta[M]/[I]_0$

-> „Living"/controlled radical polymerization (LRP/CRP)

Living Polymerizations

1. Linear kinetic plot in semilogarithmic coordinates if the reaction is first order with respect to the monomer concentration

2. Linear evolution of MW with conversion.
   MW < $\Delta[M]/[I]_0$ = transfer;
   MW > $\Delta [M/[I]_0$ inefficient initiation or
   chain coupling

3. Polydispersity M_w/M_n close to Poisson distribution ($M_w/M_n \approx 1 + 1/DP_n$)

4. End-functionality is not affected by slow initiation and exchange but is reduced when chain breaking reactions become important

Atom Transfer Radical Polymerization

Radical generation in atom transfer radical polymerization (ATRP) involves an organic halide undergoing a reversible redox process catalyzed by a transition metal compound such as cuprous halide:

$$[R\bullet] = \frac{K[I][Cu^+]}{[Cu^{2+}]}$$

$$R_p = k_p[M\bullet][M]$$

$$R_p = \frac{k_p K[M][I][Cu^+]}{[Cu^{2+}]}$$

$$\ln\frac{[M]_0}{[M]} = \frac{k_p K[I][Cu^+]}{[Cu^{2+}]}\,t$$

$$R{-}Br + CuBr(L) \underset{k_d}{\overset{k_a}{\rightleftharpoons}} R\bullet + CuBr_2(L)$$

activator — deactivator

$$R\bullet \xrightarrow{M} RM_n\bullet$$

$$RM_n\bullet \xrightleftharpoons{CuBr_2(L)} RM_n{-}Br + CuBr(L)$$

$K = k_a/k_d$

$$\bar{X}_n = \frac{[M]_0 - [M]}{[I]_0} = \frac{p[M]_0}{[I]_0}$$

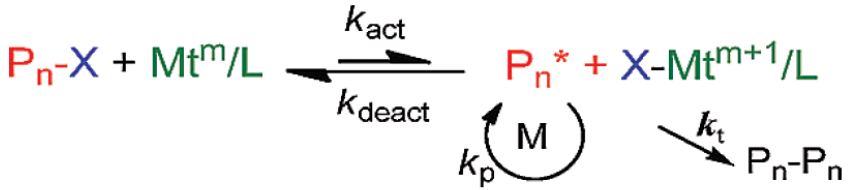
- Fast and quantitative initiation
- Rapid, reversible deactivation

} All propagating chains grow at the same rate and for the same length of time

Atom Transfer Radical Polymerization

ATRP is controlled by an equilibrium between propagating radicals and dormant species, predominately in the form of initiating alkyl halides/macromolecular species (P_nX). The dormant species periodically react with the rate constant of activation (k_{eact}) with transition metal complexes in their lower oxidation state, Mt^m/L, acting as activators (Mt^m represents the transition metal species in oxidation state m and L is a ligand; the charges of ionic species and counterions are omitted here) to intermittently form growing radicals ($P_n^{\bullet}$), and deactivators—transition metal complexes in their higher oxidation state, coordinated with halide ligands $X-Mt^{m+1}/L$ (Scheme 1).

Scheme 1. ATRP Equilibrium



Macromolecules **2012**, *45*, 4015−4039 (dx.doi.org/10.1021/ma3001719)

Removing & Decreasing [Cu]

Removing copper:

Why: Toxic, electronic applications
How: Chromatography (silica, alumina, ion-exchange)

Refining ATRP:

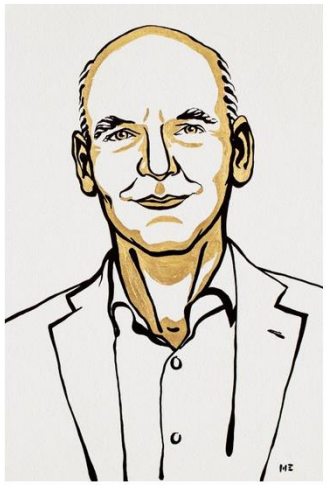
- ICAR-ATRP
- SARA-ATRP
- ARGET-ATRP
- Photo-ATRP

Removal of Copper. As noted above, one limitation of the "early" ATRP procedures was associated with the relatively high concentration of catalyst, often equimolar to initiator. This high concentration of catalyst was required to overcome radical termination reactions.[72,73] Purification methods included passing the polymer solution through silica or neutral alumina columns,[74] stirring with an ion-exchange resin,[75] clay,[76] precipitation of polymers into a nonsolvent,[77] or the use of a heterogeneous catalyst that could be isolated after polymerization.[78] The development of higher activity catalysts and polymerization procedures (ARGET, ICAR, SARA, *e*ATRP) involving continuous regeneration of the deactivator (formed by termination reactions) reduced the amount of copper down to ppm levels.

Macromolecules **2012**, *45*, 4015−4039 (dx.doi.org/10.1021/ma3001719)

Towards Zero Copper

The Nobel Prize in Chemistry 2021



Ill. Niklas Elmehed © Nobel Prize Outreach.

Benjamin List

Prize share: 1/2

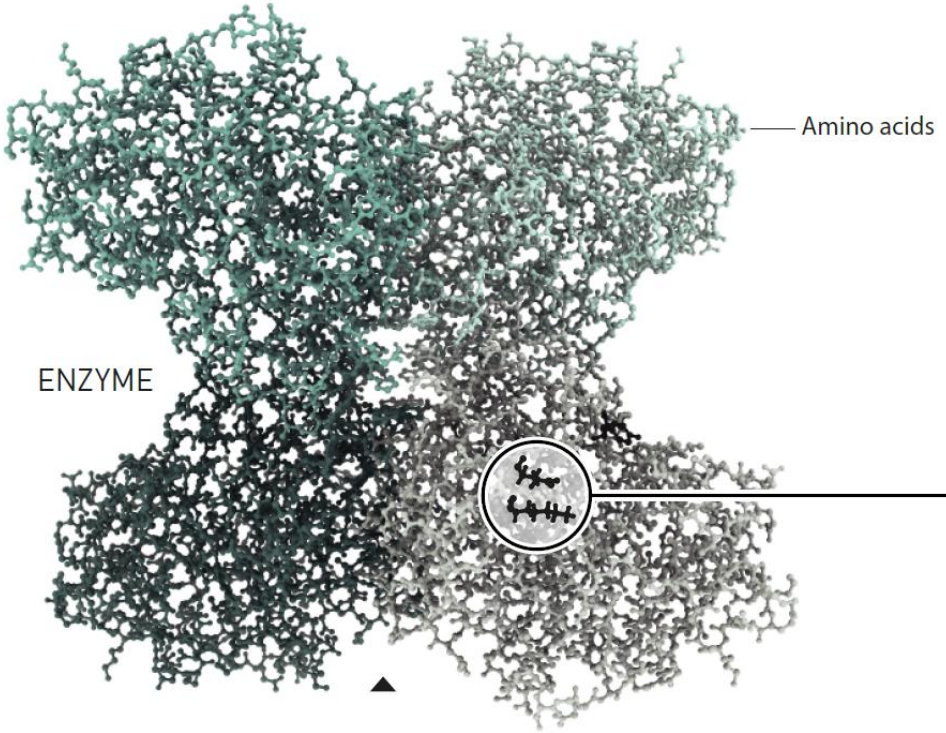
Ill. Niklas Elmehed © Nobel Prize Outreach.

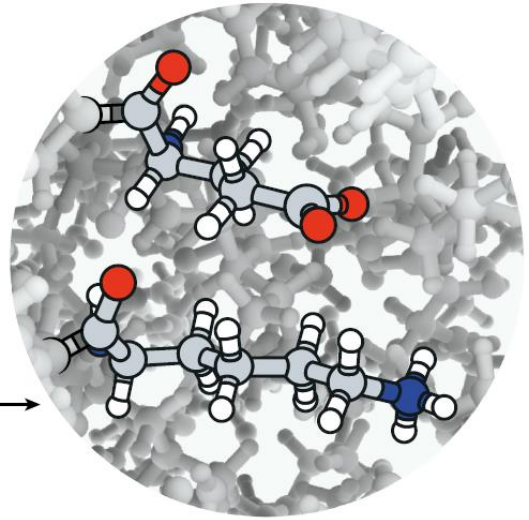
David W.C. MacMillan

Prize share: 1/2

The Nobel Prize in Chemistry 2021 was awarded jointly to Benjamin List and David W.C. MacMillan "for the development of asymmetric organocatalysis."

https://www.nobelprize.org/prizes/chemistry/2021/summary/



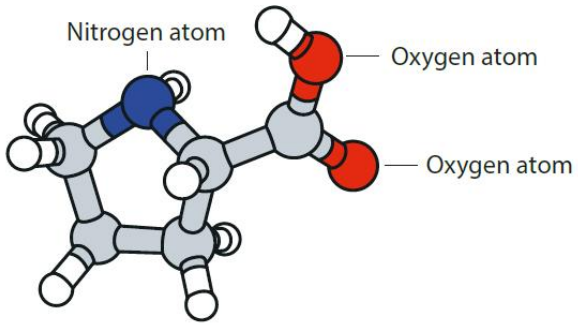


Two of the amino acids that catalyse the chemical reaction.

1 Enzymes consist of hundreds of amino acids, but frequently only a few of these are involved in the chemical reaction. Benjamin List started to wonder whether an entire enzyme was really required to obtain a catalyst.

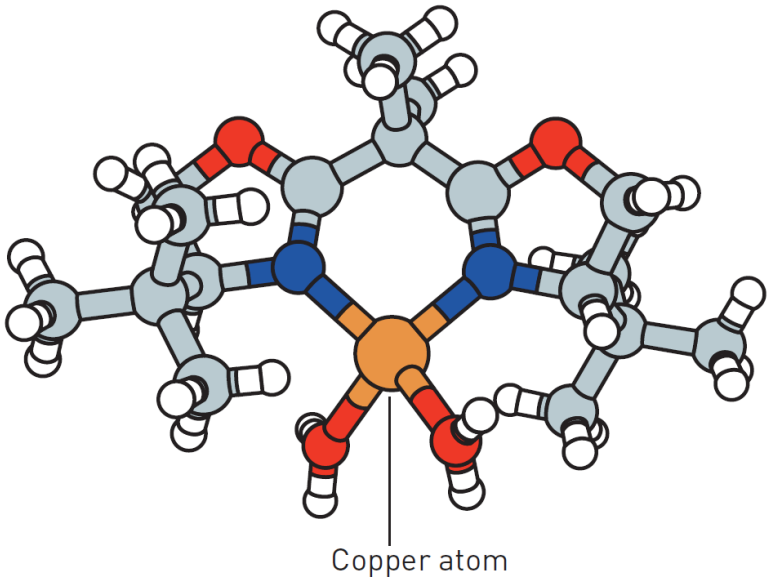
2 Benjamin List tested whether an amino acid called proline – in all its simplicity – could catalyse a chemical reaction. It worked brilliantly. Proline has a nitrogen atom that can provide and accommodate electrons during chemical reactions.

PROLINE



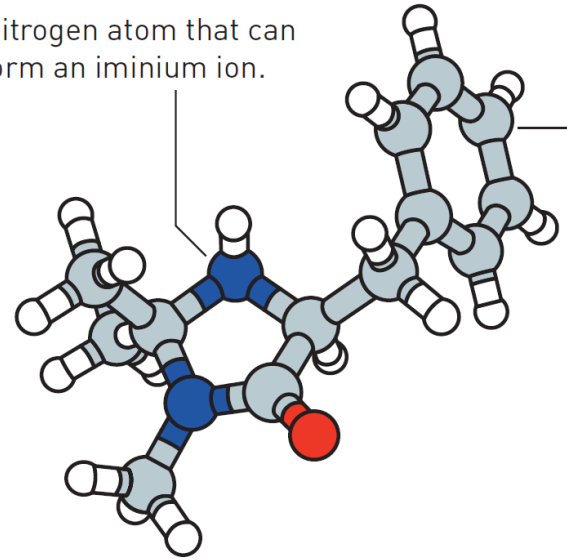
https://www.nobelprize.org/prizes/chemistry/2021/summary/

METAL CATALYST



1 David MacMillan worked with metal catalysts that were easily destroyed by moisture. He therefore started to wonder whether it was possible to develop a more durable type of catalyst.

MACMILLAN'S ORGANOCATALYST

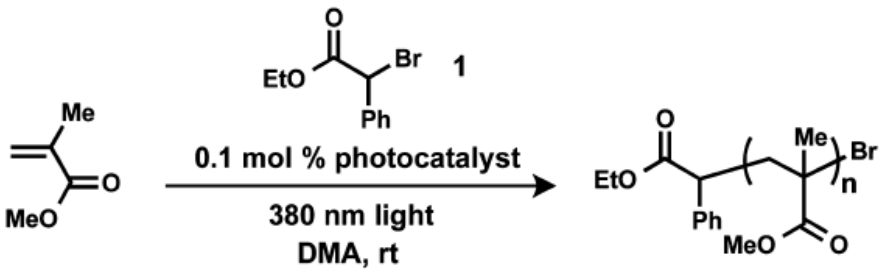


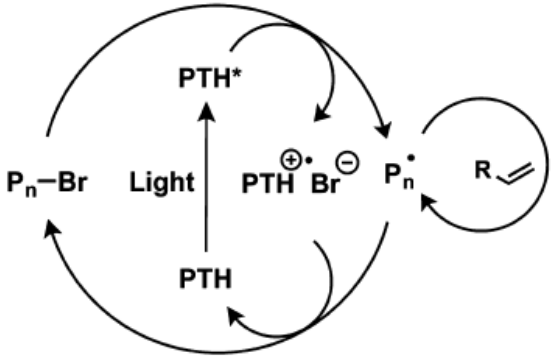
2 He designed some simple molecules that could create iminium ions. One of these proved to be excellent at asymmetric catalysis.

https://www.nobelprize.org/prizes/chemistry/2021/summary/

Metal-Free ATRP

Table 1. Optimization of a Light-Mediated Polymerization of Methyl Methacrylate Using Organic Photoredox Catalysts[a]





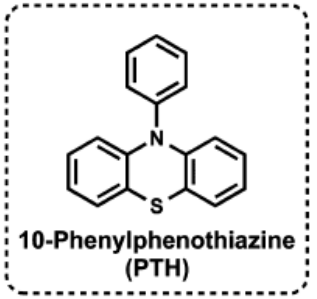
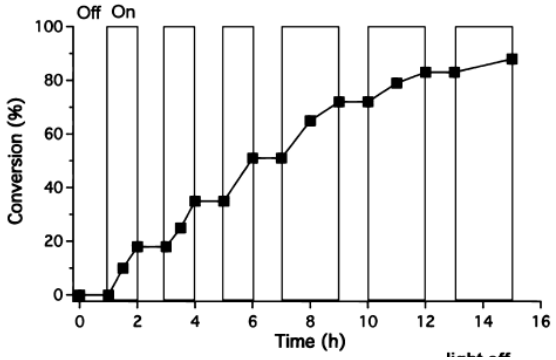
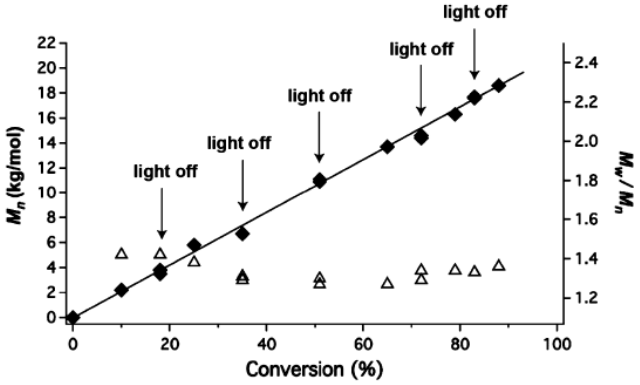
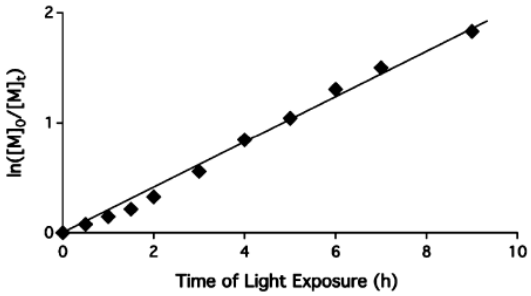


Figure 1. Proposed mechanism of metal-free photomediated ATRP with 10-phenylphenothiazine as the catalyst (P_n = polymer chain).







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Metal-Free Atom Transfer Radical Polymerization

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Metal-Free ATRP

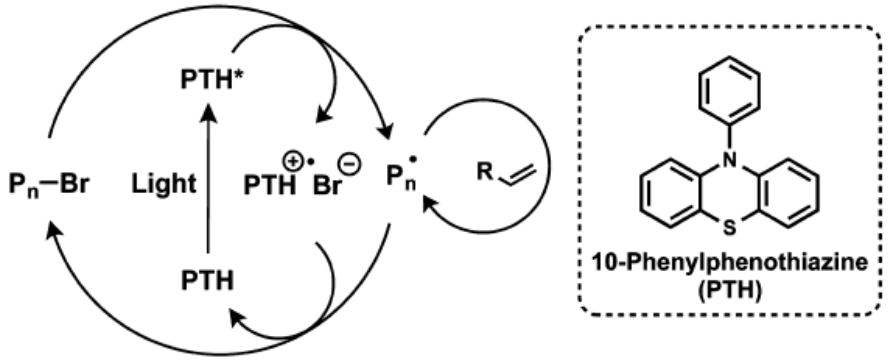


Figure 1. Proposed mechanism of metal-free photomediated ATRP with 10-phenylphenothiazine as the catalyst (P_n = polymer chain).

"Preliminary mechanistic studies suggested that upon excitation with 380 nm light Ph-PTH induces reduction of traditional alkyl bromide-based ATRP initiators via an oxidative quenching cycle. This results in the generation of a propagating radical as well as a deactivating catalyst complex consisting of the radical cation form of the photocatalyst and a bromine anion. This complex subsequently deactivates growing polymer chains through formation of a dormant, bromine-end-capped species and reduction back to the initial ground state Ph-PTH. Significantly, full spectroscopic analysis of the polymer chains formed by Ph-PTH-catalyzed ATRP did not show any differences to polymers prepared by traditional Cu-mediated ATRP, indicating that the products obtained from both processes are chemically and structurally the same."

Taken from: *Macromolecules* **2018**, *51*, 7421−7434

Advantages of Light-Mediated ATRP

Light offers distinct advantages over thermally driven techniques:

(1) exert spatiotemporal control over polymerization
(2) polymerize under ambient temperatures
(3) modulate the stimulus (i.e., wavelength, intensity) for facile modulation of reaction kinetics
(4) exploit multiple wavelengths for orthogonal reactivity/multiple CRP processes in a single reaction vessel

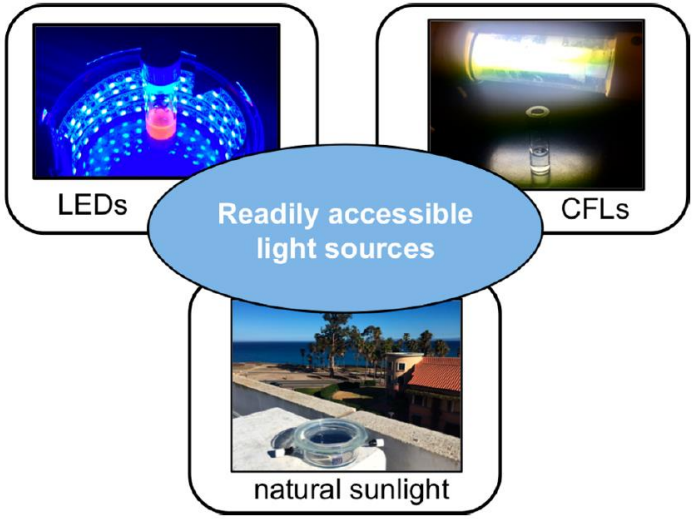
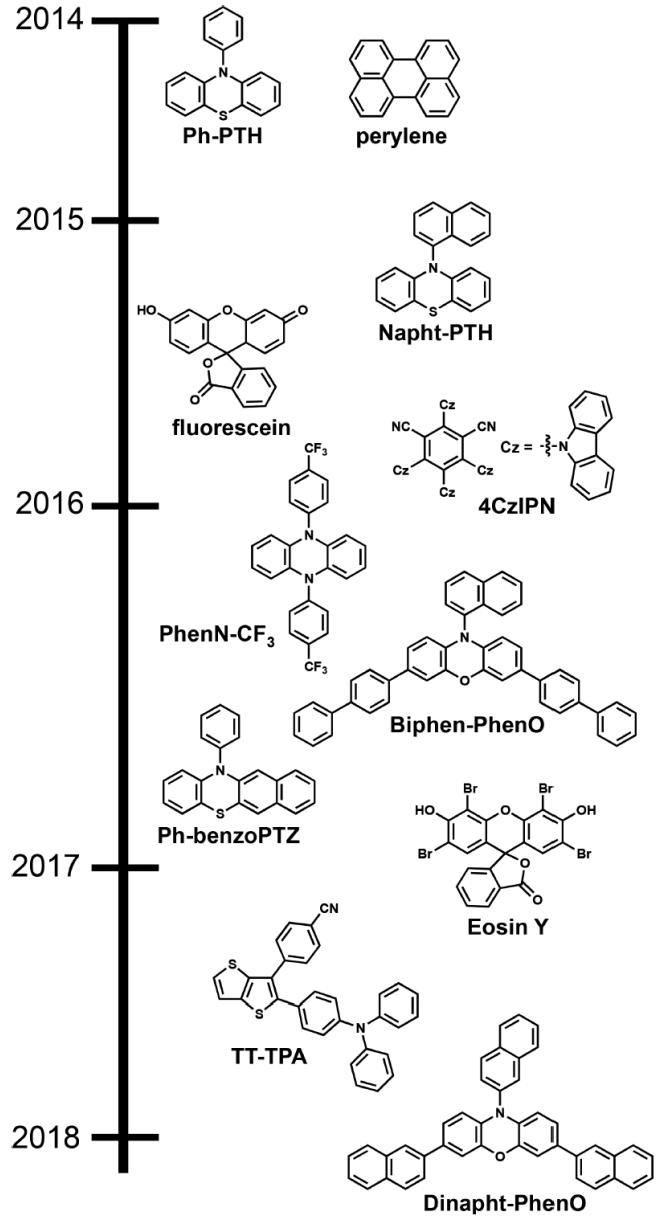


Figure 2. Representative metal-free polymerization setups using light-emitting diodes (LEDs), compact fluorescent lamps (CFLs), and natural sunlight.

Macromolecules **2018**, *51*, 7421−7434

New Dyes

-> More efficient photocatalysts
-> Red and visible light mediated polymerizations



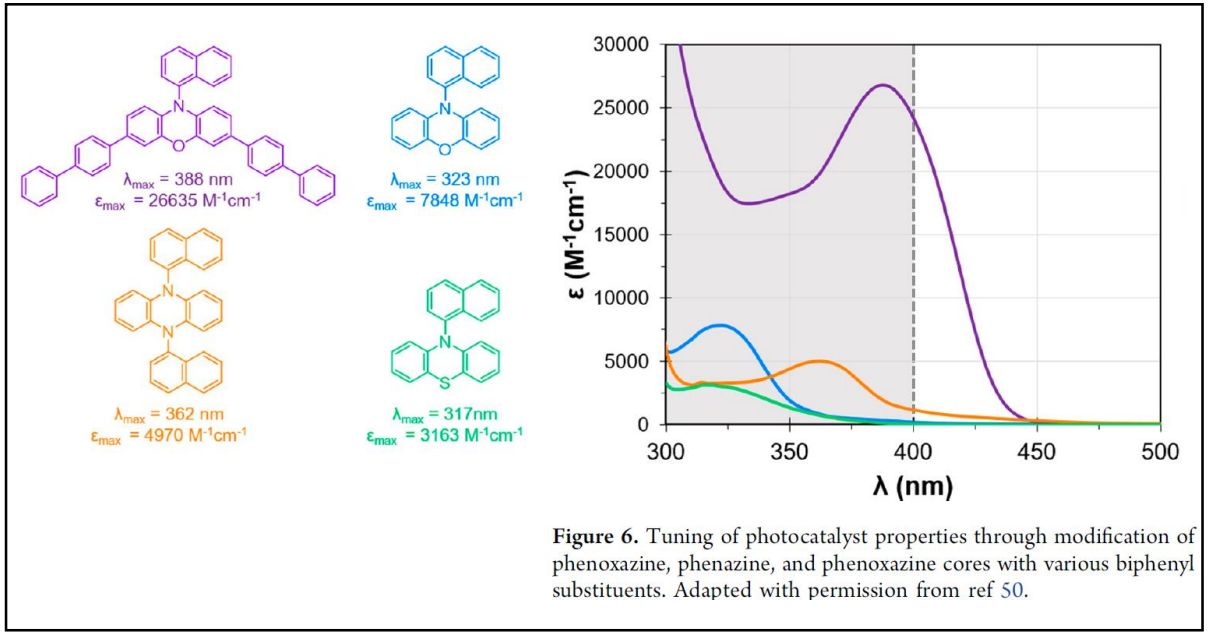


Figure 6. Tuning of photocatalyst properties through modification of phenoxazine, phenazine, and phenoxazine cores with various biphenyl substituents. Adapted with permission from ref 50.

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Solvents and Monomers

"In contrast to this increase in available photocatalysts, a greater understanding of the influence of solvents and initiating species on metal-free ATRP is required to fully benefit from this structural diversity. Interestingly, solvent scope has remained largely unchanged. The initial reports involving Ph-PTH and perylene used N,N-dimethylacetamide (DMA) and N,N-dimethylformamide (DMF) solvents with the rational for these polar aprotic solvents not completely understood."

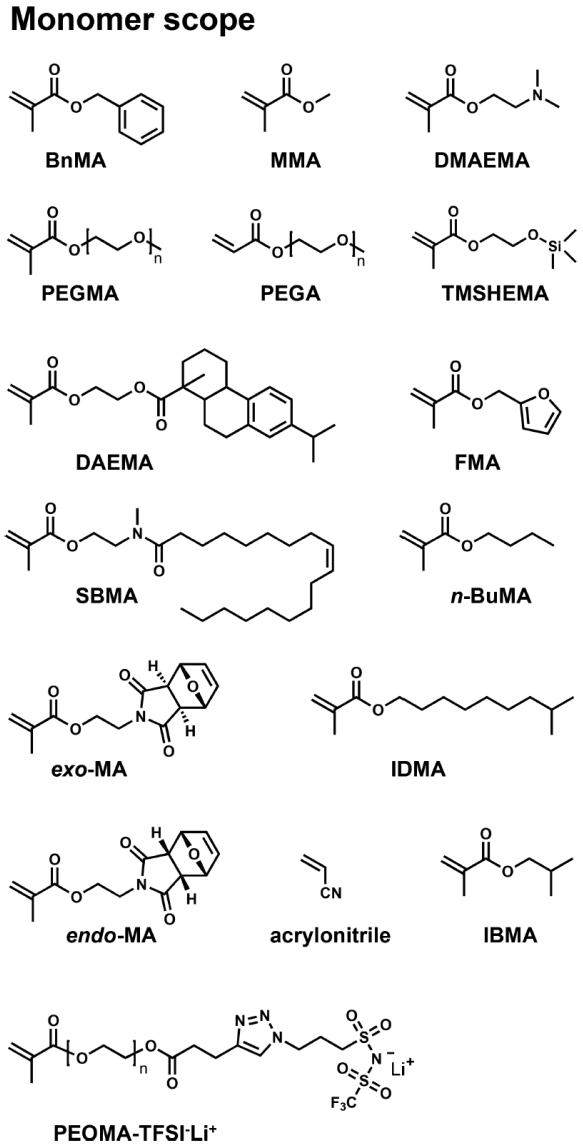
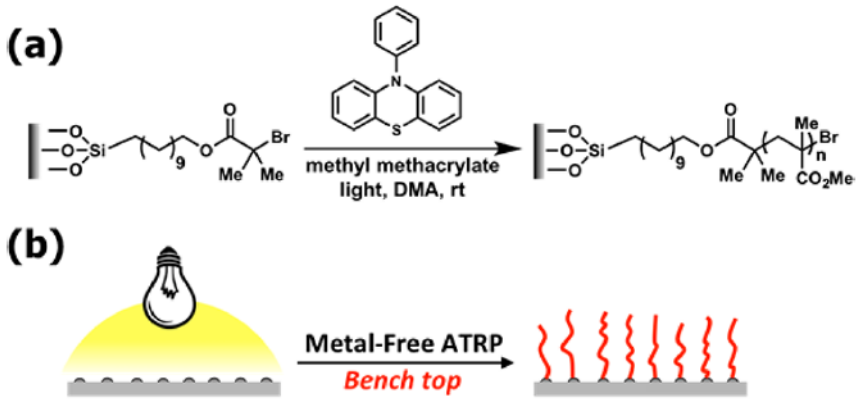


Figure 9. Summary of monomer scope for metal-free ATRP.

Taken from: *Macromolecules* **2018**, *51*, 7421−7434

Surface-Initiated Metal-Free ATRP



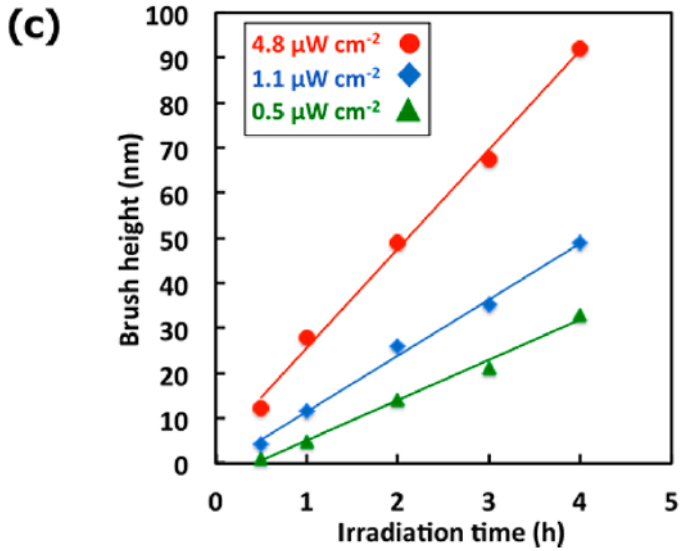


Figure 1. (a) Chemical scheme and conditions for metal-free ATRP using α-bromoisobutyrate-based initiator-functionalized silicon substrates. (b) Illustration of surface-initiated, metal-free ATRP (c) Plot of brush height as a function of irradiation time using varied light intensities in the benchtop chamber.

ACS Macro Lett. **2016**, *5*, 258−262

Surface-Initiated Metal-Free ATRP

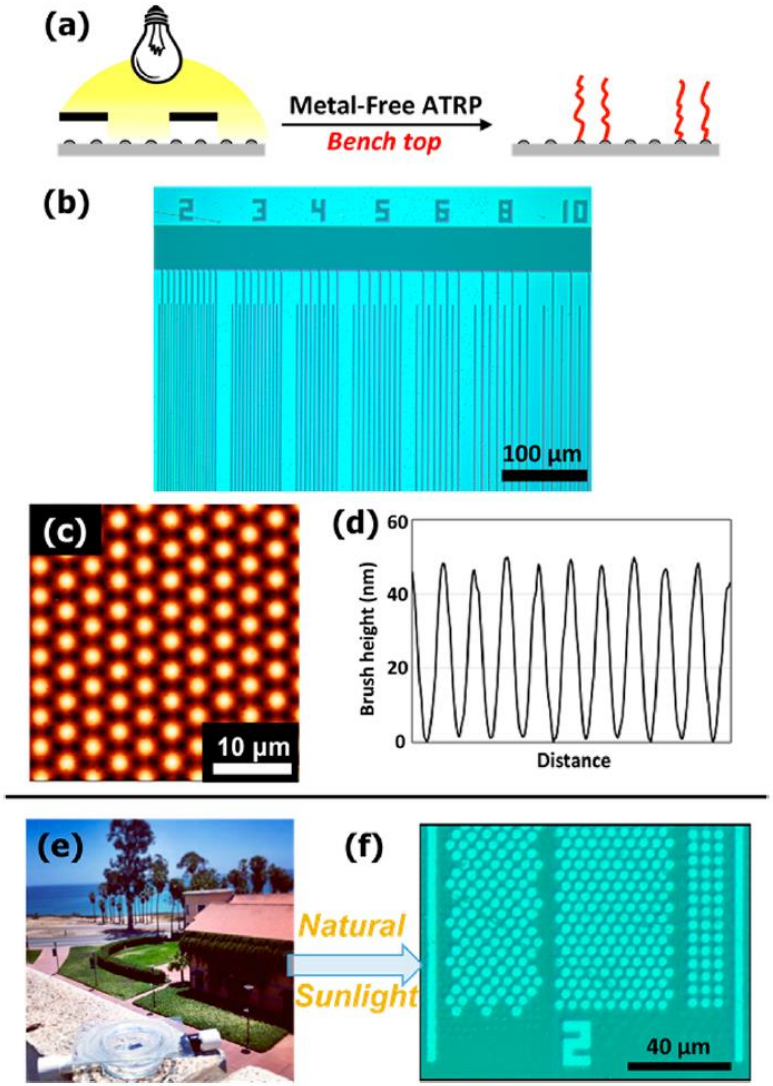


Figure 3. (a) Binary photomasks enable one-step patterning. (b) Optical micrograph of micron-scale line features (2–10 μm). (c) AFM image of 1 μm features and (d) corresponding AFM height profile. (e) Polymerization using sunlight and (f) optical micrograph of patterned 2 μm features (see SI for setup).

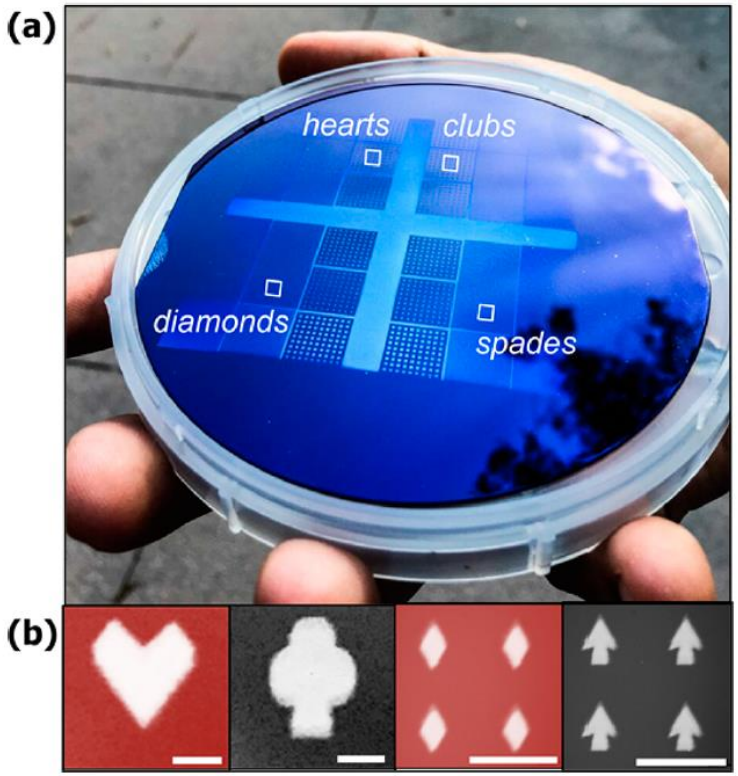


Figure 4. (a) Photograph of large area patterning in a single step of a four-inch wafer using a binary photomask. (b) Optical micrographs of patterned arbitrary features. Scale bars are 200 μm.

ACS Macro Lett. **2016**, *5*, 258−262

Outlook & Challenges

Perspective

Recent Developments and Future Challenges in Controlled Radical Polymerization: A 2020 Update

Kostas Parkatzidis,[1] Hyun Suk Wang,[1] Nghia P. Truong,[1] and Athina Anastasaki[1,*]

Chem 6, 1575–1588, July 9, 2020 © 2020 Elsevier Inc. 1575

However, good control over the polymerization is reported mostly for methacrylates whereas the polymerization of acrylic and styrenic monomers leads to less control over the molecular weight distributions. In a recent promising publication, the controlled metal-free ATRP polymerization of acrylic monomers was reported by Miyake's group.[22] In addition, end-group fidelity is not as high as in the metal-mediated photo-ATRP, encouraging further research in the area. Moreover, the range of currently available catalysts is rather limited, thus, hindering the widespread use of these methodologies. Another remaining challenge in the area is the limited number of solvents reported that, in turn, narrows down the scope of accessible monomers. Last but not least, despite avoiding the use of metals, tedious purification of the organic catalyst is required. It is also unclear whether in the presence of the organic catalyst such materials can be used directly for bio-applications or cases in which intense visible color is not preferred. As such, organic photocatalysts that would yield colorless polymers would also be highly beneficial.

Learning Objectives

- Understand the drawbacks of metal catalyzed ATRP processes.
- Be familiar with the basic concepts of metal-free ATRP.
- Be able to describe the advantages of light mediated polymerization reactions.
- Describe challenges and points for further improvement of the metal-free ATRP protocols that are currently used.