

# Oxygen-Enhanced Atom Transfer Radical Polymerization Triggered by a Reactive Copper Superoxido Complex

Kostas Parkatzidis,<sup>a</sup> Nghia P. Truong,<sup>a</sup> Richard Whitfield,<sup>a</sup> Chiara E. Campi,<sup>b</sup> Benjamin Grimm-Lebsanft,<sup>c</sup> Sören Buchenau,<sup>c</sup> Michael A. Rübhausen,<sup>c</sup> Simon Harrisson,<sup>d</sup> Dominik Konkolewicz,<sup>e</sup> Siegfried Schindler,<sup>b</sup> and Athina Anastasaki<sup>a\*</sup>

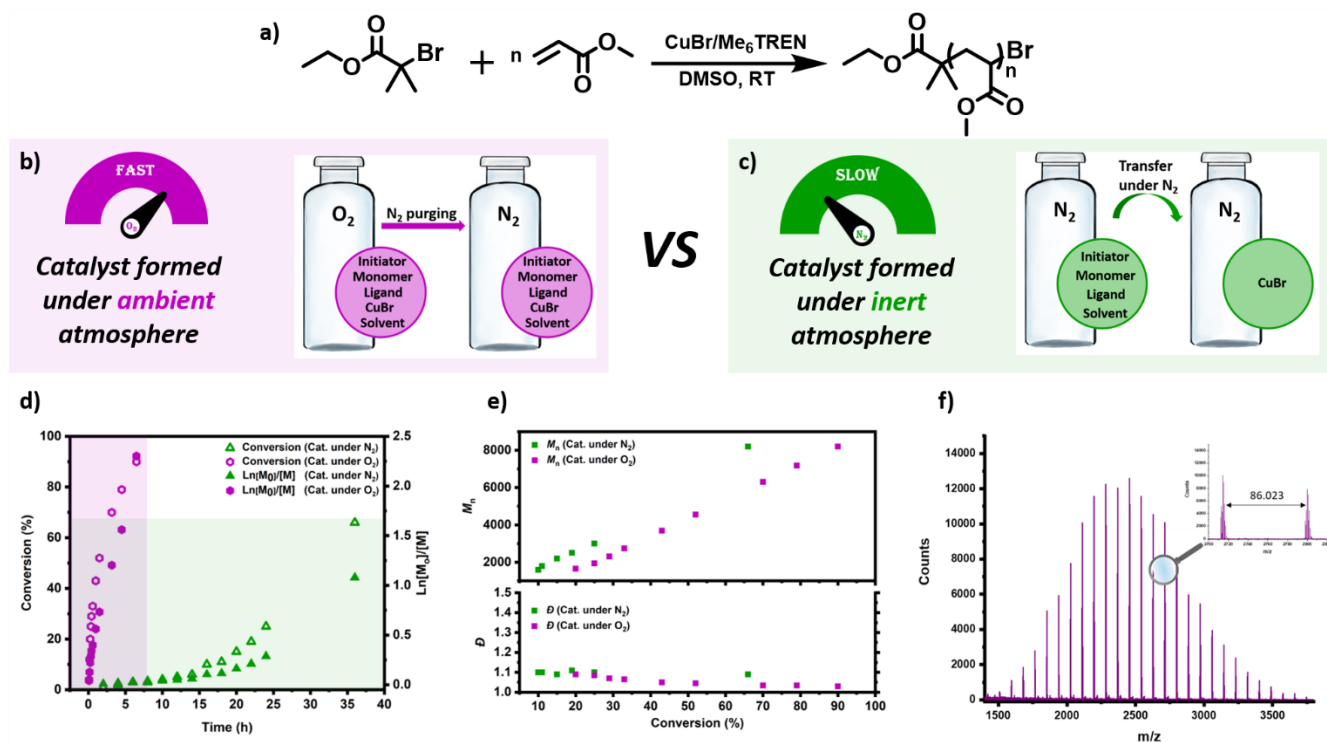
**KEYWORDS:** *Oxygen-enhanced ATRP, ppm Cu ATRP, superoxido copper complex, multiblock copolymers, high end-group fidelity*

**ABSTRACT:** In controlled radical polymerization, oxygen is typically regarded as an undesirable component resulting in terminated polymer chains, deactivated catalysts, and subsequent cessation of the polymerization. Here, we report an unusual atom transfer radical polymerization whereby oxygen favors the polymerization by triggering the *in-situ* transformation of CuBr/L to reactive superoxido species at room temperature. Through a superoxido-catalyzed ATRP mechanism, an order of magnitude faster polymerization rate and a rapid and complete initiator consumption can be achieved as opposed to when unoxidized CuBr/L was instead employed. Exceptional high end-group fidelity has been demonstrated by mass-spectrometry and the one-pot synthesis of block and multiblock copolymers, while pushing the reactions to reach near-quantitative conversions in all steps. A high molecular weight polymer could also be targeted ( $DP_n=6,400$ ) without compromising the control over the molar mass distributions ( $\mathcal{D} < 1.20$ ), even at an extremely low copper concentration (4.5 ppm). The versatility of the technique was demonstrated by the polymerization of various monomer classes in a controlled fashion including acrylates, methacrylates and styrene. Notably, the efficiency of our methodology is unaffected by the purity of the starting CuBr, and even a brown highly-oxidized 15-year-old CuBr reagent enabled a rapid and controlled polymerization with a final dispersity of 1.07, thus not only reducing associated costs but also omitting the need for rigorous catalyst purification prior to polymerization.

During the past 100 years, there have been extraordinary developments in the field of polymer science. Among these, reversible deactivation radical polymerization (RDRP), also referred to as controlled radical polymerization, has received considerable attention and has been recognized by IUPAC as a potentially world-changing technology in chemistry.<sup>1-3</sup> The two most dominant RDRP techniques are reversible addition-fragmentation chain-transfer (RAFT) polymerization,<sup>4,5</sup> and atom transfer radical polymerization (ATRP).<sup>6-8</sup> While both methods rely on an equilibrium between active and dormant species, RAFT operates through a degenerative chain transfer process while ATRP follows a reversible termination pathway.<sup>5,8,9</sup> These methods have enabled access to an enormous scope of polymeric and hybrid materials with excellent control over molecular weight, dispersity, functionality, end-group fidelity, sequence and architecture of the synthesized polymers.<sup>10-23</sup> RDRP methods are more tolerant to functional groups and much simpler to operate than ionic living polymerizations, thanks to their radical nature.

However, it is this radical nature that requires the vast majority of radical polymerizations to be conducted under anaerobic conditions.<sup>24</sup> Oxygen is a radical scavenger which can irreversibly react with propagating radicals formed either through the initiator or the polymer end-group and can

also deactivate the copper catalyst.<sup>25,26</sup> As a result, the presence of oxygen can lead to terminated polymer chains and subsequent cessation of the polymerization.<sup>24</sup> To avoid this, the reaction mixtures must be either rigorously deoxygenated (i.e. by freeze-pump-thaw cycles, nitrogen sparging, etc.) or the polymerization must be performed in a glovebox. To bypass these costly and time-consuming deoxygenation procedures, a number of the so-called “oxygen-tolerant” RDRP approaches have been developed. These make use of a sacrificial reagent (e.g. enzyme, reducing agent, catalyst, etc.) to effectively consume the oxygen prior to the start of the polymerization.<sup>27-29</sup> For example, the enzyme glucose oxidase (GOx) effectively deoxygenates RAFT polymerizations by converting glucose and oxygen to gluconolactone and hydrogen peroxide.<sup>30,31</sup> In an alternative approach, photo-induced electron/energy transfer-RAFT (PET-RAFT) polymerizations could be conducted in an open vessel by either adding a reducing agent or by increasing the amount of the photocatalyst.<sup>32</sup> In the ATRP arena, GOx was utilized as a catalyst to consume oxygen in the presence of glucose and sodium pyruvate while headspace elimination in conjunction with copper catalysis has also been proved suitable to self-deoxygenate ATRP solutions.<sup>33-36</sup> It can thus be concluded that oxygen is thoroughly removed either prior to the polymerization or as the reaction proceeds by



**Figure 1:** (a) Reaction scheme illustrating the polymerization of methyl acrylate under the conditions:  $[MA]/[EBiB]/[CuBr]/[Me_6TREN] = 100:1:0.02:0.12$ . (b) Schematic representation of oxygen-enhanced ATRP in which the formation of the catalyst occurs under ambient atmosphere, (c) Schematic representation of conventional ATRP in which the formation of the catalyst occurs under inert atmosphere, (d, e) Merged kinetic data comparing oxygen-enhanced ATRP (in purple) and conventional ATRP (in green) and (f) SEC kinetic data of oxygen-enhanced ATRP.

introducing enzymes or reducing agents. As such, oxygen is considered an undesirable component and is associated with extensive termination events and side reactions.

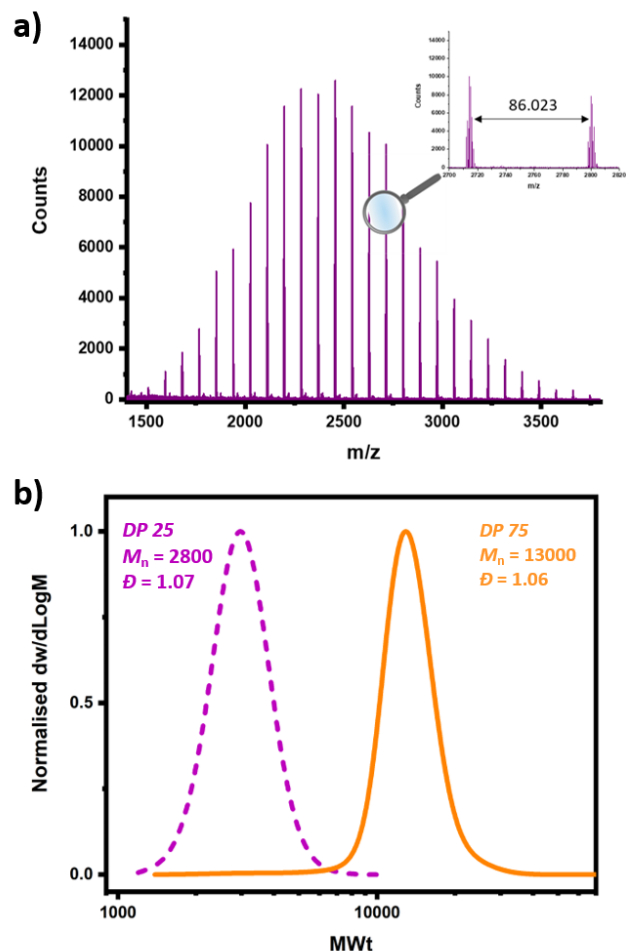
On the contrary, oxygen is rarely employed as a reagent in order to benefit a controlled radical polymerization. An exception to this rule has been recently reported by Boyer and co-workers who utilized oxygen as a co-catalyst (in the presence of trimethylamine and zinc photocatalyst) to activate a RAFT agent, demonstrating remarkable oxygen tolerance.<sup>37</sup> The same group also reported an oxygen-mediated reductive quenching pathway whereby the majority of oxygen was sufficiently eliminated while the remaining catalytic amount of oxygen served as a co-catalyst and triggered a controlled polymerization.<sup>38</sup> In a completely different approach, Matyjaszewski and co-workers employed GOx and horseradish peroxidase alongside copper complexes to report the first example of “oxygen-fueled” ATRP whereby oxygen was continuously fed into the reaction mixture to generate radicals and allow the polymer chains to grow.<sup>39</sup> In all these examples, a range of additional components is required in conjunction with oxygen to trigger a successful polymerization. Notably, the presence of oxygen is less tolerated in ATRP than in RAFT polymerization, as CuBr/L is an oxygen-sensitive catalyst. As such, when conducting a traditional ATRP, CuBr has to be rigorously purified from oxidized contaminants and kept under an inert atmosphere prior to usage, thus significantly adding to the complexity of

the process. Developing more oxygen-tolerant ATRP catalysts would be highly beneficial for a range of practical applications.<sup>40</sup>

In this work, we report the *in-situ* transformation of Cu<sup>I</sup>Br/L to superoxido species Cu<sup>II</sup>O<sub>2</sub>/L in the presence of tris[2-(dimethylamino)ethyl]amine (Me<sub>6</sub>TREN, L) and dimethyl sulfoxide (DMSO). In comparison to the CuBr/L catalyst, the high reactivity of the superoxido species resulted in very fast ATRP activation, full consumption of the initiator (within seconds) and elimination of the induction period. Upon initiation, a much higher rate of polymerization was achieved (i.e. an order of magnitude higher) and the reactions reached quantitative monomer conversions without compromising the control over the molar mass distributions ( $\bar{D} = 1.07$ , **Figure 1**). In addition, exceptional end-group fidelity was confirmed by mass spectrometry allowing for the synthesis of high molecular weight polymers (up to  $DP_n=6,400$ ) as well as the one-pot formation of diblock and multiblock copolymers. The technique was found to be applicable to various monomer families including acrylates, methacrylates and styrene while the purity of the initial CuBr did not affect the integrity of the final materials, thus omitting the catalyst purification step that is often required for traditional ATRP reactions.

### Discovery of oxygen-enhanced atom transfer radical polymerization

Our investigation was conducted using methyl acrylate (MA) as a model monomer, CuBr as a copper source, Me<sub>6</sub>TREN as a ligand, and DMSO as a solvent (**Figure 1a**). In traditional ATRP, a common practice is to protect the oxygen-sensitive CuBr catalyst from oxidation by keeping it under an inert atmosphere followed by the addition of a thoroughly deoxygenated solution containing the remainder of the reaction components (e.g. ligand, solvent, initiator, and monomer) (**Figure 1c**). Interestingly, when this procedure was applied to low catalyst concentrations (i.e. 0.02 equiv. with respect to the ATRP initiator), a very long induction period was observed with only 4% conversion reached within the first 10 h (**Figure 1d and S1a, Table S1a**). Following the induction period, a well-controlled polymerization took place, albeit at a very slow rate reaching 66% conversion in 36 h. The prolonged induction period was attributed to slow initiation, as confirmed by the typical kinetic profile and by <sup>1</sup>H NMR whereby slow initiator consumption was observed (**Figure S2**). These results indicate that CuBr/L is oxidized to CuBr<sub>2</sub>/L through the persistent radical effect.<sup>41</sup> The excess of ligand subsequently acts as a reducing agent and a slow activators regenerated by electron transfer (ARGET) ATRP takes place at room temperature.<sup>42</sup> To explore this scenario, we conducted an additional experiment whereby CuBr was replaced by CuBr<sub>2</sub> under otherwise identical conditions. A very comparable kinetic profile was obtained (**Figure S3, Table S2**), thus validating our initial hypothesis that most CuBr/L is rapidly converted to CuBr<sub>2</sub>/L at the beginning of the reaction. However, when the catalyst was formed under ambient atmosphere (i.e. in the presence of air) by simply mixing ppm concentration of CuBr with DMSO and Me<sub>6</sub>TREN followed by a conventional deoxygenation of the resulting mixture (**Figure 1c**), a completely different kinetic profile was observed (**Figure 1d and S1b, Table S1b**). In particular, the long induction period was eliminated and a very fast initiation took place whereby all the ATRP initiator was completely consumed within a few seconds. Notably, the polymerization rate was much faster and detailed kinetic analysis revealed a short induction period of 3.43 min before the polymerization starts with an initial apparent rate constant of 0.0252 min<sup>-1</sup>. First order kinetics were then observed for 14.5 min (rate constant of 0.069 min<sup>-1</sup>). Following this period, a steady state radical concentration was reached and the polymerization continued with an apparent rate constant of 0.00491 min<sup>-1</sup>. *M<sub>n</sub>* increased linearly with time and good agreement between theoretical and experimental molecular weights was observed. *Đ* values slightly decreased throughout the polymerization, as expected from a controlled process with the final *Đ* being as low as 1.09.<sup>43,44</sup> Importantly, near-quantitative monomer conversions (>99%) could be achieved without compromising the *Đ* value. Additionally, MALDI-ToF-MS and <sup>1</sup>H-NMR spectroscopic analysis was conducted to further investigate the living characteristics of the polymerization with both techniques clearly confirming excellent end-group fidelity (**Figure 2a**). In addition, the high-end group fidelity was further demonstrated by the *in-situ* chain extension of PMA with another aliquot of MA yielding a clear shift in the SEC chromatograms as shown in **Figure 2b**. To summarize, by simply forming the catalyst under ambient atmosphere and

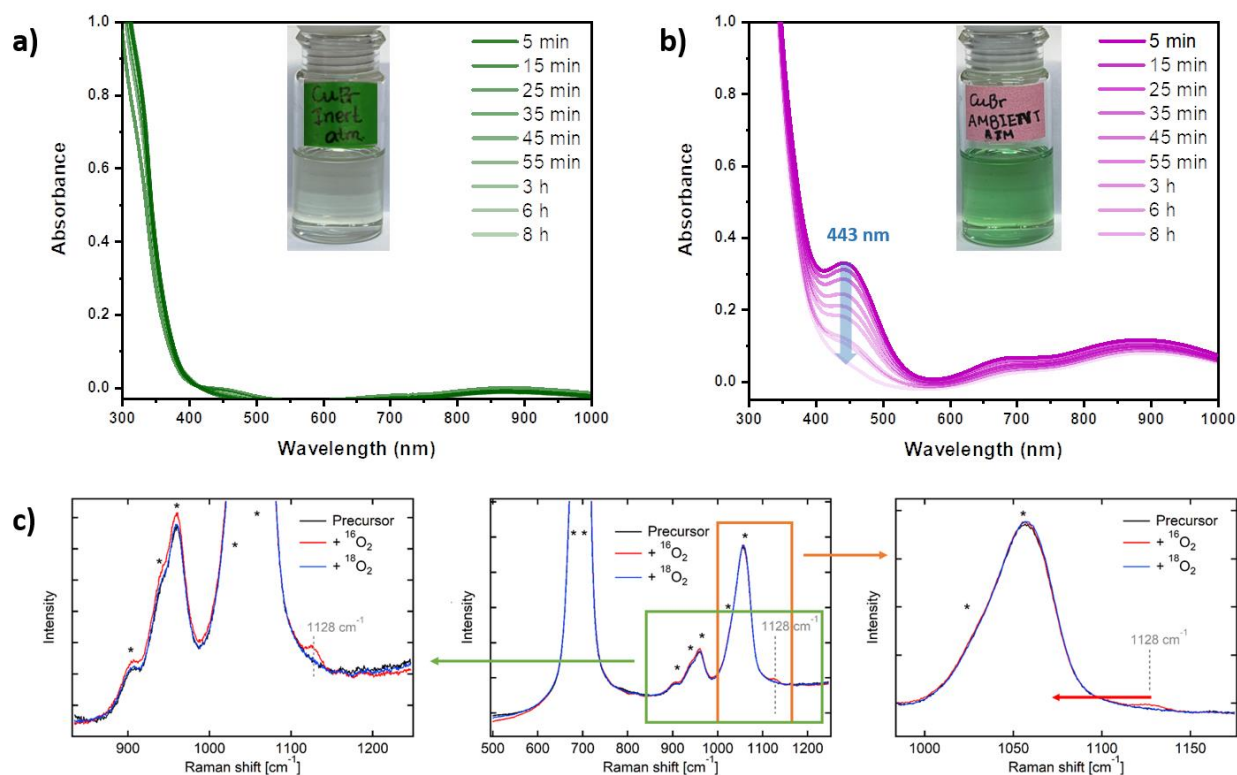


**Figure 2:** (a) MALDI-ToF-MS analysis of PMA<sub>25</sub> synthesized by oxygen-enhanced ATRP and (b) *In-situ* chain extension experiment.

temperature (rather than under inert atmosphere) we were able to trigger a more favorable ATRP reaction with rapid initiator consumption, negligible, if any, induction period, significantly faster polymerization rates and quantitative monomer conversions. This is a very intriguing discovery considering that the literature recommends the thorough deoxygenation of the oxygen-sensitive CuBr/L catalyst prior to commencing the polymerization. Since the two experiments were conducted utilizing identical chemical components and ratios, their remarkable difference indicates fundamentally different mechanistic pathways.

### Mechanistic investigation

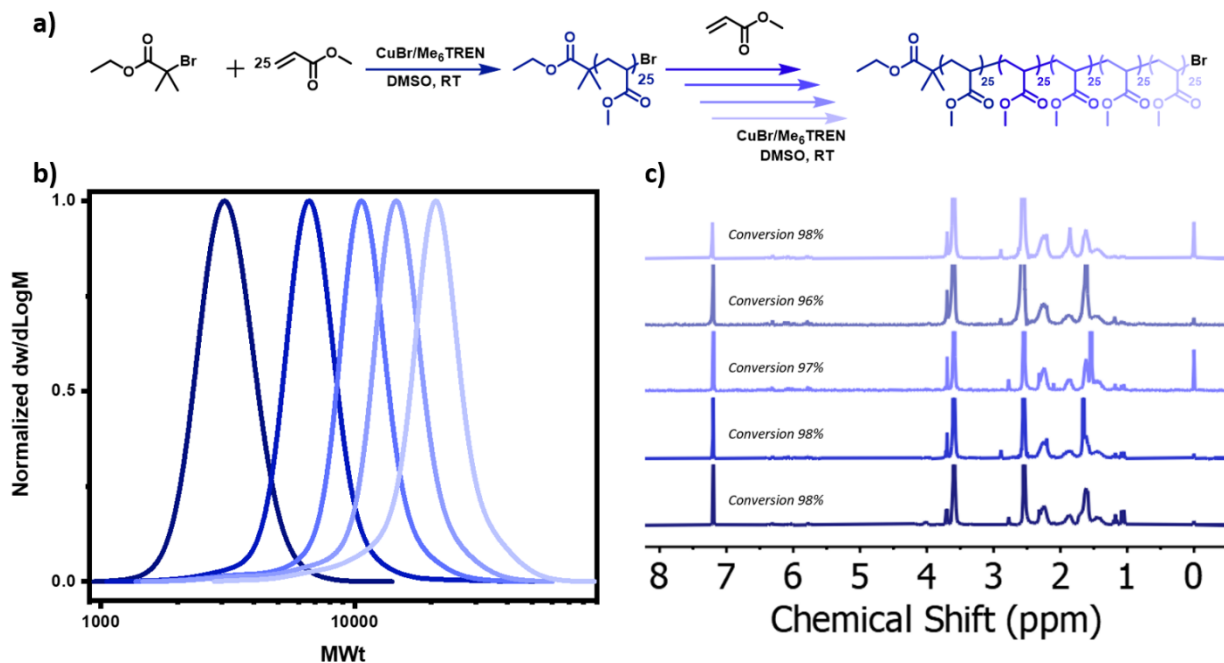
Considering that the only difference between the experiments lies in the formation of the catalyst in the presence of air, we hypothesized that the oxygen may trigger the for-



**Figure 3:** (a) Monitoring of Cu<sup>II</sup> formation by UV-Vis spectroscopy as formed in traditional ATRP (i.e. by mixing CuBr with deoxygenated Me<sub>6</sub>Tren/DMSO under inert atmosphere) (b) Monitoring of Cu<sup>II</sup> superoxido complex decay over time by UV-Vis spectroscopy as formed in oxygen-enhanced ATRP (i.e. by mixing CuBr with Me<sub>6</sub>Tren/DMSO under ambient atmosphere prior to deoxygenation) (c) Raman analysis of the catalyst formed under ambient atmosphere.

mation of very reactive superoxido species under our reaction conditions, thus yielding an enhanced ATRP catalyst.<sup>45,46</sup> To examine this possibility, a solution of DMSO/Me<sub>6</sub>TREN/CuBr (in the absence of ATRP initiator and monomer) was prepared in two different ways in order to resemble the two polymerization protocols and visualize potential color differences. In the first case, a previously deoxygenated solution of DMSO/Me<sub>6</sub>TREN was added to a vessel already containing deoxygenated CuBr (**Figure 3a insert**). Upon mixing, the solution remained colorless, as expected, thus confirming that our thorough deoxygenation procedure prevents CuBr from oxidizing (**Figure S4a**). Instead, in the second case where all the components (i.e. DMSO/Me<sub>6</sub>TREN/CuBr) were pre-mixed under ambient atmosphere prior to deoxygenation (**Figure 3b insert**), a very intense green color could be observed suggesting the oxidation of Cu<sup>I</sup> to Cu<sup>II</sup> (**Figure S4b**). This intense green color has been previously attributed to the formation of superoxido complexes.<sup>47-49 50,51</sup> It is important to note that this is a much more intense green color when compared to mixing CuBr<sub>2</sub>/Me<sub>6</sub>TREN/DMSO under ambient temperature which results in a pale green solution (**Figure S4c**). The aforementioned solutions were subsequently measured by ultraviolet visible (UV-Vis) spectroscopy. In the first case (i.e. formation of CuBr/L catalyst under inert atmosphere), minimal absorption occurred in the range of  $\lambda = 400-1000$

nm, which is typical of Cu<sup>I</sup>(Me<sub>6</sub>TREN)Br complexes in DMSO (**Figure 3a**).<sup>52</sup> Instead, when the catalyst was formed under ambient atmosphere, an unusual UV-Vis spectrum was obtained which did not correspond to typical absorptions for either Cu<sup>I</sup>(Me<sub>6</sub>TREN)Br or Cu<sup>II</sup>(Me<sub>6</sub>TREN)Br<sub>2</sub> species (**Figure 3b**). Specifically, an intense peak at  $\lambda = 443$  nm was observed which decayed over a period of 30-60 minutes. This was accompanied by a broad bimodal absorption at  $\lambda = 600 - 900$  nm. Notably, the initially observed UV-Vis profile matches very well with the spectra of superoxido copper complexes previously reported in the inorganic chemistry literature,<sup>49-51,53</sup> which suggests that the superoxido complexes can be formed with a reasonable lifetime at room temperature in the presence of a commercially available ligand and DMSO. This contrasts with most current reports in which sophisticated ligands and low temperatures (-20 to -180°C) are required to stabilize the formed superoxido complexes.<sup>54-56</sup> Further evidence of the formation of a superoxido complex is provided through reversibility experiments. It is known that superoxido complexes can undergo reversible reaction with oxygen several times prior to observing an unavoidable irreversible decay.<sup>47-49 57</sup>

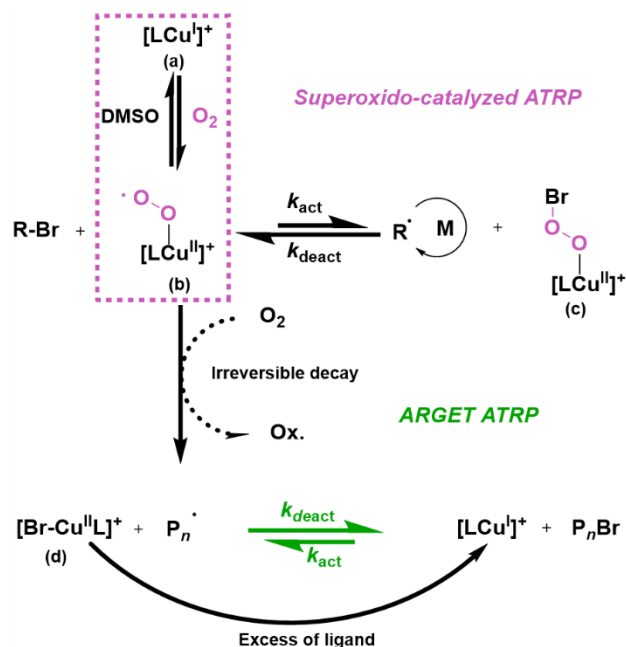


**Figure 4:** Synthesis and characterization of a pseudo multiblock copolymer by oxygen-enhanced ATRP, (a) SEC traces of the molar mass distributions for consecutive cycles during the synthesis of a poly(MA) pentablock copolymer and (b)  $^1\text{H}$  NMR spectra for consecutive cycles whereby very high monomer conversions are reached for each iterative monomer addition step (>97 %).

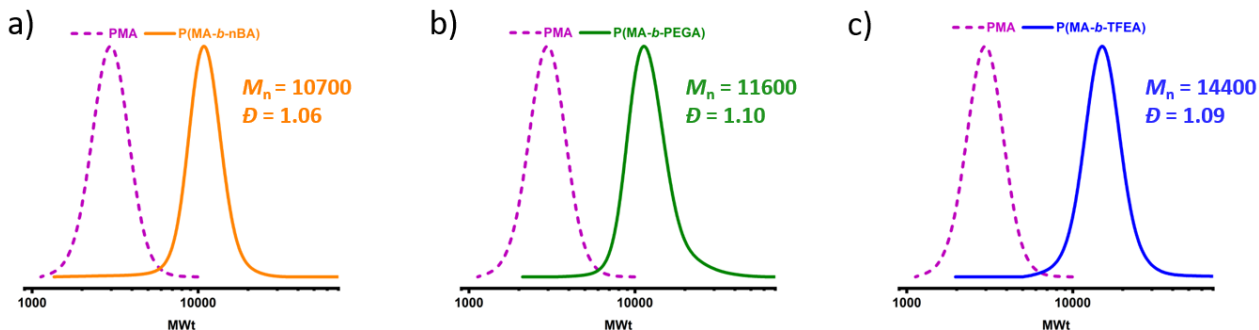
In our system the peak at  $\lambda = 443$  nm undergoes a rapid reduction over time accompanied by a change of color from intense green to yellow/brown suggesting the gradual decay of the superoxido complex. On bubbling the yellow/brown solution with air, the initial green color reappeared and the reformation of the peak at  $\lambda = 443$  nm was observed (**Figure S4d, f**). These cycles could be repeated several times before the brown color dominates the solution and no further reformation of the complex is possible, in line with previous reports.<sup>47,48</sup> Unfortunately, our attempts to isolate the formed complex were unsuccessful, however a mononuclear end-on superoxido copper complex with a TREN related ligand has previously been structurally characterized, so far the only example that could be crystallized.<sup>57</sup> To further support the formation of the postulated superoxido complex Raman spectroscopy was applied. **Figure 3c** shows the characteristic band at  $1128\text{ cm}^{-1}$  of an end-on superoxido copper complex, in perfect agreement with previous measurements.<sup>48,49,51,55</sup> Replacing  $^{16}\text{O}_2$  by  $^{18}\text{O}_2$  led to the disappearance of this band, although the expected band of the  $\text{Cu } ^{18}\text{O}_2$  species was not observed, presumably due to its overlap with the solvent, DMSO. Taken altogether, the characterization methods employed have provided strong evidence for the formation of a copper superoxido complex at room temperature.

**Scheme 1** depicts the proposed ATRP mechanism. In the first part of the polymerization, a superoxido-catalyzed ATRP mechanism dominates whereby the combination of  $\text{CuBr}$  and  $\text{Me}_6\text{TREN}$  in DMSO can efficiently activate dioxygen and produce the superoxido complex which is relatively

stable at room temperature. The formed superoxido complex is then proposed to activate the alkyl halide initiator yielding propagating radicals and  $\text{Cu}^{\text{II}}(\text{Me}_6\text{TREN})\text{O}_2\text{Br}$  acting as activator and deactivator respectively.<sup>58</sup>



**Scheme 1:** Proposed mechanism of ligand of oxygen-enhanced ATRP.



**Figure 5:** SEC analysis for the synthesis of (a) P(MA-b-nBA), (b) P(MA-b-PEGA) and (c) P(MA-b-TFEA) diblock copolymers prepared by oxygen-enhanced ATRP.

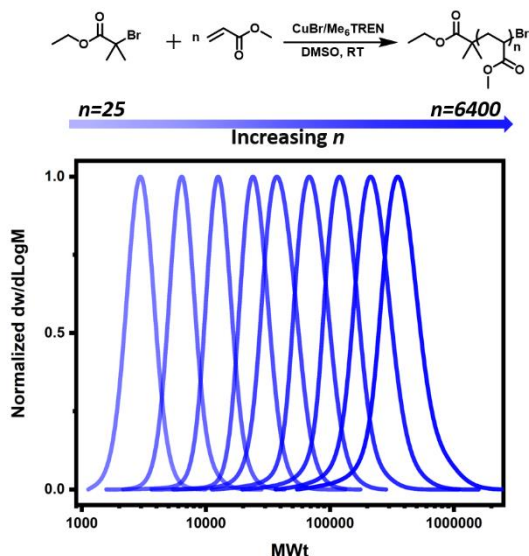
This superoxido copper mediated ATRP equilibrium dominates during the first 20-25 min of the polymerization (first linear kinetic regime) resulting in a very fast initiation due to the rapid reduction of the superoxido complex due to the excess of ligand. The potential of the ligand to act as a reducing agent can be confirmed by a series of polymerization kinetic experiments whereby the more ligand is added, the faster the polymerization rate is while when stoichiometric amounts of ligand and copper are employed, no monomer conversion is observed (**Figure S5**). Direct activation of the vinyl double bond of the monomer by the  $\text{Cu}^{\text{II}}(\text{Me}_6\text{TREN})\text{O}_2\text{Br}$  was excluded as the control experiment in the absence of the ATRP initiator did not yield any polymer formation. After the first 20-25 min, the superoxido complex undergoes irreversible decay and the mechanism switches to a conventional ARGET ATRP mechanism.

#### Investigation into the scope of oxygen-enhanced ATRP

To explore the potential of oxygen-enhanced ATRP, we first investigated the possibility of synthesizing well-defined block copolymers. Our previously acquired MALDI-ToF-MS spectra indicated exceptional end-group fidelity without any sign of side reactions or termination events. To further investigate the livingness of the system, we subsequently chain-extended PMA (Block 1,  $\bar{D} = 1.07$ , 98% conversion) by the *in-situ* injection of a second aliquot of monomer into the polymerization mixture, alongside a fresh solution of  $\text{CuBr}/\text{Me}_6\text{TREN}/\text{DMSO}$  (catalyst formed under ambient atmosphere). It is noted that the additional catalyst was required to enhance the polymerization rate of the second block yielding a pseudo diblock copolymer with a  $\bar{D}$  of 1.09. The process was then repeated three more times resulting in the one-pot synthesis of a pseudo-pentablock copolymer. By looking at the chromatogram of the final pentablock, negligible, if any, coupling is observed despite the very high monomer conversions targeted for each iterative block addition (**Figure 4**, **Table S3**). This is in contrast to the synthesis of an identical pseudo-pentablock copolymer previously obtained by photo-ATRP in which a high molecular weight shoulder was evident by size exclusion chromatography (SEC) thus suggesting significant termination events.<sup>59</sup> In addition, our synthesis appears to have very mi-

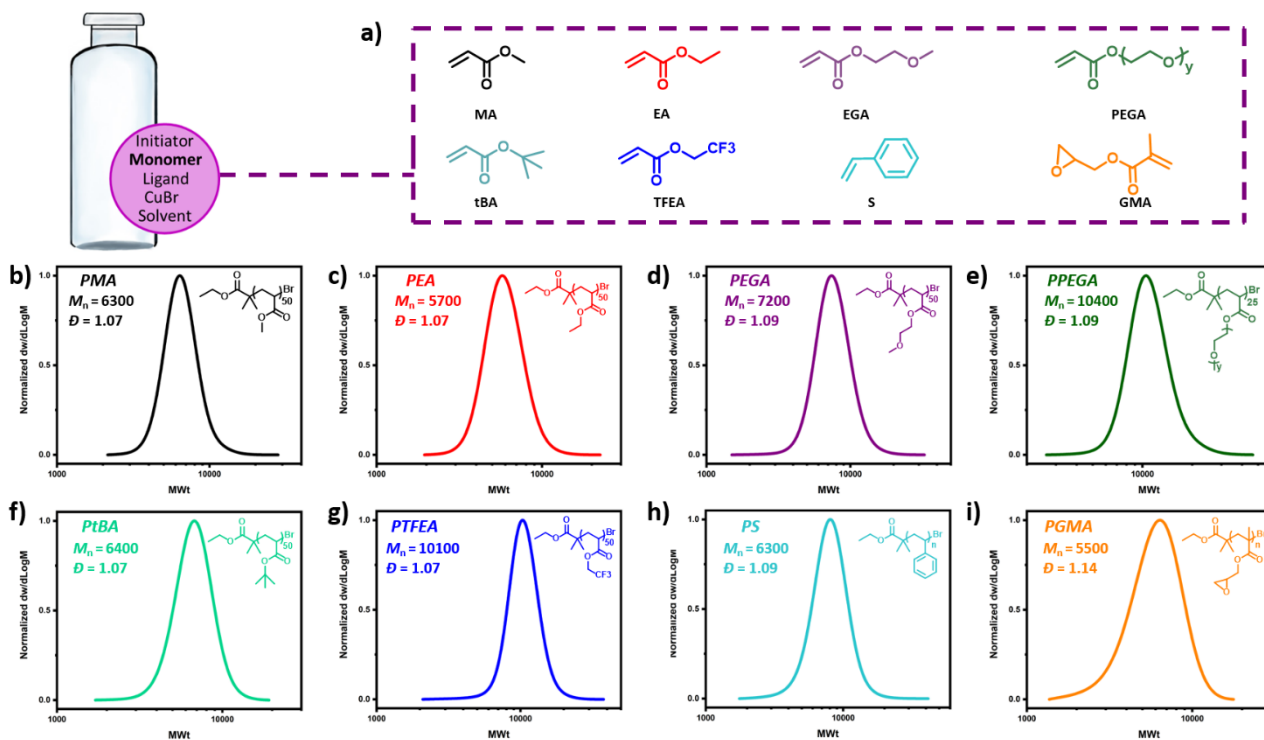
nor low molecular weight tailing in comparison to previously reported  $\text{Cu}(0)$ -RDRP approaches.<sup>60</sup> Collectively, our data suggest that oxygen-enhanced ATRP can be utilized as a versatile platform for the one pot synthesis of multiblock copolymers with minimal termination events.

To further demonstrate the capabilities of the approach, a series of diblock copolymers consisting of hydrophobic, hydrophilic and semi-fluorinated segments were also synthesized as shown in **Figure 5** (**Table S4**). In all cases, the first block reached near-quantitative monomer conversions and



**Figure 6:** SEC analysis of PMA with a range of targeted DPs (25-6400) synthesized via oxygen-enhanced ATRP.

the addition of the second monomer led to well-defined diblock copolymers with the molar mass distribution clearly shifting to higher molecular weights and a final  $\bar{D}$  of 1.10 or below. Another testament of excellent end-group fidelity, is the possibility to synthesize polymers with high molecular weight and such materials can exhibit enhanced properties for various applications.<sup>61</sup>



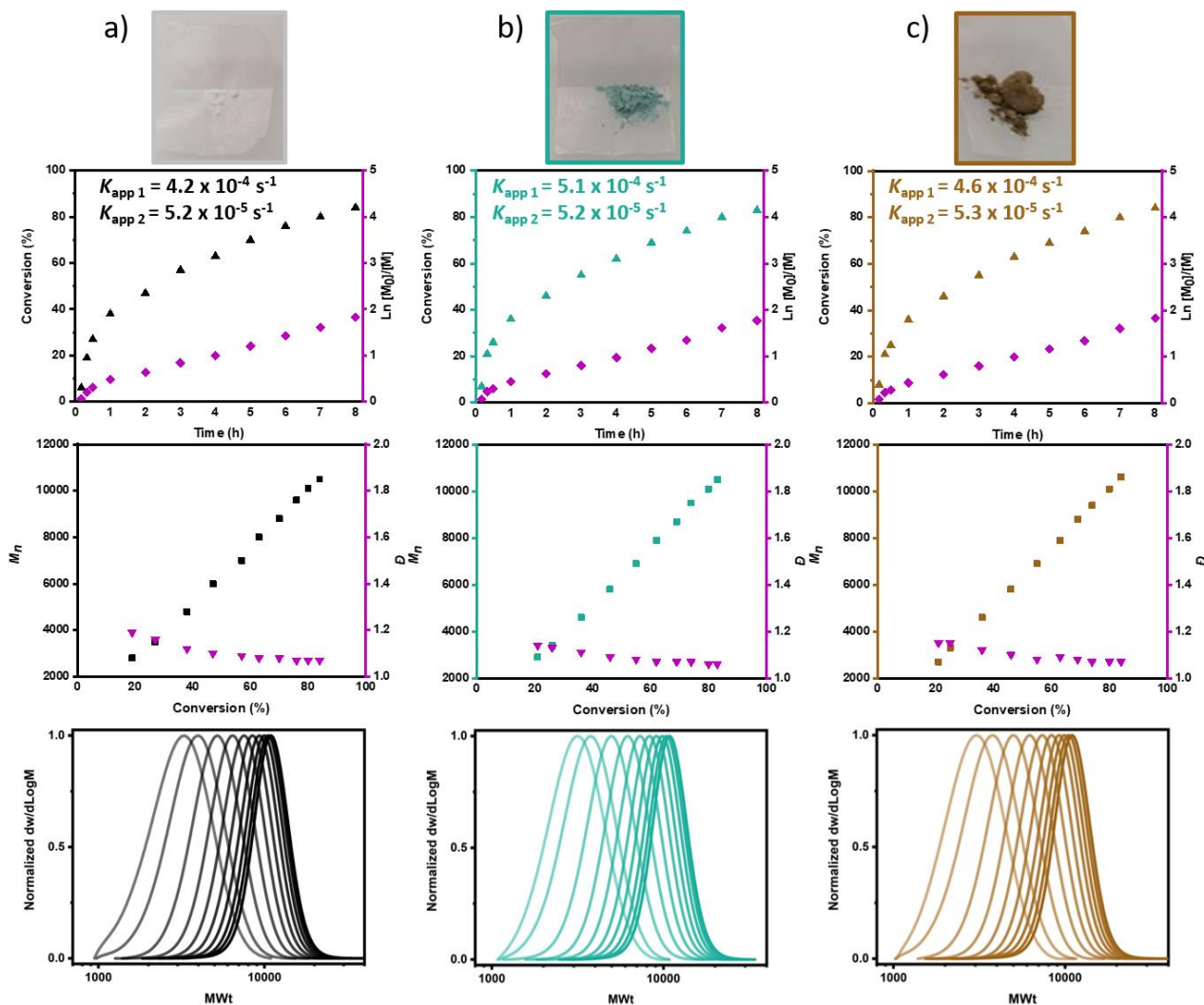
**Figure 7:** Monomer scope of oxygen-enhanced ATRP showing the SEC analysis of the corresponding polymers.

To date, the vast majority of methods available for the synthesis of high molecular weight polymers rely on RAFT polymerization.<sup>62-65</sup> Specifically, for polyacrylates, the vast majority of ATRP reports target  $DP_n$  lower than 800. We envisioned that our system may afford the synthesis of higher molecular weight polymers due to their high livingness. A range of different  $DP_n$  were targeted from 25 to 6,400 (**Figure 6, Table S5**). For instance, using only 9 ppm of Cu, PMA with  $DP_n = 800$  and a  $\bar{D}$  of 1.11 could be easily obtained at 96% of conversion and with very good agreement between theoretical and experimental molecular weights. Notably, we were able to reach an  $M_n$  as high as 340,000 ( $\bar{D} = 1.19$ , targeted  $DP_n = 6400$ ) while using only 4.5 ppm of Cu. The possibility to conduct polymerizations with such low copper content significantly minimizes the issues of polymer discoloration, facilitates purification and expands the compatibility of ATRP materials with various applications. Previous ATRP approaches for higher molecular weight polymers relied on either high pressure or heterogeneous catalysts.<sup>63,66,67</sup> To the best of our knowledge, this is the highest molecular weight polyacrylates synthesized in organic media and by a homogeneous catalytic system.

The scope of the reaction was extended to include a variety of hydrophobic, hydrophilic, semi-fluorinated and functional monomers as depicted in **Figure 7a**. In all cases, near-quantitative conversions could be achieved and well-defined homopolymers with narrow molar mass distributions ( $\bar{D} < 1.09$ ) could be obtained (**Figure 7, Table S6**). Although our initial reaction conditions were not compatible with the polymerization of lower  $k_p$  monomers such as methacrylates and styrene resulting in very slow polymerizations, we

were able to circumvent this by increasing the reaction temperature and catalyst concentration. This allowed the synthesis of poly(glycidyl methacrylate) with a  $\bar{D}$  of 1.14 as well as the synthesis of polystyrene with a  $\bar{D}$  of 1.14, thus significantly increasing the availability of polymeric materials.

Finally, we were interested in exploring the possibility to conduct our experiments without using ultra-pure CuBr. Typically, CuBr can be purchased at different levels of purity and even the purest grade (>99.999%) rarely appears to be a white solid, thus suggesting that some oxidation has already occurred. In addition, CuBr has to be stored under an inert atmosphere to prevent oxidation and even so, it still requires rigorous purification (e.g. by several washings followed by extensive drying under vacuum) prior to usage in traditional ATRP. Since our methodology requires oxygen to form the superoxido complex, we thought that our system may be less affected by oxidation. To investigate this, we conducted three parallel polymerization kinetics using three different grades of CuBr. The first set of kinetics was performed by utilizing CuBr of the highest purity (>99.999%) which visually appears to be a white powder as shown in **Figure 8a (Table S7a)**. The second set of kinetics was designed with a lower purity of CuBr (<98%) that was available in our laboratory (**Figure 8b, Table S7b**) while in the third set of kinetics we employed a 15-year old CuBr with an intense brown color (as it was not kept under inert atmosphere) (**Figure 8c, Table S7c**).



**Figure 8:** Polymerization kinetics of MA via oxygen-enhanced ATRP utilizing: (a) Highly pure CuBr (>99.999%), (b) Less pure CuBr (98% initial purity followed by storage under ambient atmosphere) and (c) Highly oxidized CuBr (90% initial purity followed by storage at ambient atmosphere for 15 years).

Despite the clear difference in the initial purity, all polymerizations followed essentially identical profiles with very similar reaction rates for both polymerization regimes. These experiments highlight the robustness of oxygen-enhanced ATRP as it can efficiently operate regardless of the initial CuBr purity thus not only reducing associated costs but also omitting the need for rigorous purification of CuBr prior to the polymerizations.

## Conclusions

In summary, we have reported an efficient oxygen-enhanced ATRP methodology which relies on the formation of a superoxido complex at room temperature. UV-Vis, and Raman spectroscopy provided unambiguous evidence for the obtained superoxido complex which was subsequently employed for polymerization reactions proceeding through a new ARGET-ATRP mechanism. The versatility of our methodology was demonstrated by the one-pot synthesis of

block and multiblock copolymers, the synthesis of high molecular weight polymers and the extension of the approach to include the polymerization of various monomers. Notably, the polymerization data (e.g. in terms of control over molecular weight, dispersity and polymerization rate) were indistinguishable regardless of the purity of the employed CuBr, thus providing for a robust platform for the synthesis of advanced materials without requiring the purchase of costly catalyst or extensive purification methods.

## ASSOCIATED CONTENT

**Supporting Information.** General information, experimental procedures,  $^1\text{H-NMR}$  spectra, UV-Vis and SEC traces. This material is available free of charge via the Internet at <http://pubs.acs.org>

## AUTHOR INFORMATION



## Corresponding Author

Athina Anastasaki - Laboratory of Polymeric Materials, Department of Materials, ETH Zurich, Vladimir-Prelog-Weg 5, Zurich 8093, Switzerland;

Email: [athina.anasatasaki@mat.ethz.ch](mailto:athina.anasatasaki@mat.ethz.ch)

## Present Addresses

a: Laboratory of Polymeric Materials, Department of Materials, ETH Zurich, Vladimir-Prelog-Weg 5, Zurich 8093, Switzerland;

b: Institute of Inorganic and Analytical Chemistry, Justus-Liebig University of Gießen, Heinrich-Buff Ring 17, D-35392 Gießen, Germany;

c: University of Hamburg, Institut für Nanostruktur und Festkörperphysik, Center For Free Electron Laser Science, Gebäude 99, Luruper Chaussee 149, 22761 Hamburg, Germany

d: Laboratoire de Chimie des Polymères Organiques, University of Bordeaux/ENSCBP/CNRS UMR5629, Pessac, France;

e: Department of Chemistry and Biochemistry, Miami University, Oxford, Ohio 45056, United States;

## Author Contributions

A.A. conceived the initial idea and managed the overall project; K.P., A.A., S.S and N.P.T. designed the experiments; K.P. performed the vast majority of the experiments and analyzed the data. C.C., and S.S., assisted with confirming the formation of superoxido complex and interpreting the initial UV-Vis spectra. B. G-L., S.B., and M.A.R., performed Raman spectroscopy and assisted with the analysis. R.W. performed preliminary experiments and conducted the MALDI-ToF-MS measurement. D.K and S.H. contributed intellectually in the proposed mechanism of ATRP. K.P. wrote the first draft of the manuscript, with all authors involved in the editing of the manuscript. All authors discussed the results and commented on the manuscript.

## ACKNOWLEDGMENT

A.A gratefully acknowledges ETH Zurich for financial support. N.P.T. acknowledges the award of a DECRA Fellowship and DP from the ARC (DE180100076 and DP200100231). KP thanks Onasis Foundation as this scientific paper was partially supported by the Onassis Foundation - Scholarship ID: FZQ051-1/2020-2021.

## REFERENCES

- (1) Corrigan, N.; Jung, K.; Moad, G.; Hawker, C. J.; Matyjaszewski, K.; Boyer, C., Reversible-deactivation radical polymerization (Controlled/living radical polymerization): From discovery to materials design and applications. *Prog. Polym. Sci.* **2020**, *111*, 101311.
- (2) Parkatzidis, K.; Wang, H. S.; Truong, N. P.; Anastasaki, A., Recent developments and future challenges in controlled radical polymerization: a 2020 update. *Chem* **2020**, *6*, 1575.
- (3) Gomollón-Bel, F., Ten Chemical Innovations That Will Change Our World: IUPAC identifies emerging technologies in Chemistry with potential to make our planet more sustainable. *Chem. Internat.* **2019**, *41*, 12.
- (4) Chiefari, J.; Chong, Y.; Ercole, F.; Krstina, J.; Jeffery, J.; Le, T. P.; Mayadunne, R. T.; Meijs, G. F.; Moad, C. L.; Moad, G., Living free-radical polymerization by reversible addition-

fragmentation chain transfer: the RAFT process. *Macromolecules* **1998**, *31*, 5559.

(5) Perrier, S., 50th Anniversary Perspective: RAFT Polymerization-A User Guide. *Macromolecules* **2017**, *50*, 7433.

(6) Kato, M.; Kamigaito, M.; Sawamoto, M.; Higashimura, T., Polymerization of methyl methacrylate with the carbon tetrachloride/dichlorotris-(triphenylphosphine) ruthenium (II)/methylaluminum bis (2, 6-di-tert-butylphenoxide) initiating system: possibility of living radical polymerization. *Macromolecules* **1995**, *28*, 1721.

(7) Wang, J.-S.; Matyjaszewski, K., Controlled/" living" radical polymerization. atom transfer radical polymerization in the presence of transition-metal complexes. *J. Am. Chem. Soc.* **1995**, *117*, 5614.

(8) Lorandi, F.; Fantin, M.; Matyjaszewski, K., Atom Transfer Radical Polymerization: A Mechanistic Perspective. *J. Am. Chem. Soc.* **2022**, *144*, 15413.

(9) Truong, N. P.; Jones, G. R.; Bradford, K. G.; Konkolewicz, D.; Anastasaki, A., A comparison of RAFT and ATRP methods for controlled radical polymerization. *Nat. Rev. Chem.* **2021**, *5*, 859.

(10) Whitfield, R.; Truong, N. P.; Messmer, D.; Parkatzidis, K.; Rolland, M.; Anastasaki, A., Tailoring polymer dispersity and shape of molecular weight distributions: methods and applications. *Chem. Sci.* **2019**, *10*, 8724.

(11) Gentekos, D. T.; Sifri, R. J.; Fors, B. P., Controlling polymer properties through the shape of the molecular-weight distribution. *Nat. Rev. Mat.* **2019**, *4*, 761.

(12) Yin, R.; Wang, Z.; Bockstaller, M. R.; Matyjaszewski, K., Tuning dispersity of linear polymers and polymeric brushes grown from nanoparticles by atom transfer radical polymerization. *Polym. Chem.* **2021**, *12*, 6071.

(13) De Neve, J.; Haven, J. J.; Maes, L.; Junkers, T., Sequence-definition from controlled polymerization: the next generation of materials. *Polym. Chem.* **2018**, *9*, 4692.

(14) Discekici, E. H.; Anastasaki, A.; Kaminker, R.; Willenbacher, J.; Truong, N. P.; Fleischmann, C.; Oschmann, B.; Lunn, D. J.; Read de Alaniz, J.; Davis, T. P., Light-mediated atom transfer radical polymerization of semi-fluorinated (meth) acrylates: facile access to functional materials. *J. Am. Chem. Soc.* **2017**, *139*, 5939.

(15) Anastasaki, A.; Oschmann, B.; Willenbacher, J.; Melker, A.; Van Son, M. H.; Truong, N. P.; Schulze, M. W.; Discekici, E. H.; McGrath, A. J.; Davis, T. P., One-pot synthesis of ABCDE multiblock copolymers with hydrophobic, hydrophilic, and semi-fluorinated segments. *Angew. Chem. Int. Ed.* **2017**, *56*, 14483.

(16) Soeriyadi, A. H.; Boyer, C.; Nyström, F.; Zetterlund, P. B.; Whittaker, M. R., High-order multiblock copolymers via iterative Cu (0)-mediated radical polymerizations (SET-LRP): toward biological precision. *J. Am. Chem. Soc.* **2011**, *133*, 11128.

(17) Boyer, C.; Bulmus, V.; Liu, J.; Davis, T. P.; Stenzel, M. H.; Barner-Kowollik, C., Well-defined protein- polymer conjugates via in situ RAFT polymerization. *J. Am. Chem. Soc.* **2007**, *129*, 7145.

(18) Barner-Kowollik, C.; Davis, T. P.; Heuts, J. P.; Stenzel, M. H.; Vana, P.; Whittaker, M., RAFTing down under: Tales of missing radicals, fancy architectures, and mysterious holes. *J. Polym. Sci., Part A: Polym. Chem.* **2003**, *41*, 365.

(19) Rosen, B. M.; Percec, V., Single-electron transfer and single-electron transfer degenerative chain transfer living radical polymerization. *Chem. Rev.* **2009**, *109*, 5069.

(20) Sumerlin, B.; ACS Macro Lett. **2012**, *1*, 1, 141-145.

- (21) Whitfield, R.; Parkatzidis, K.; Truong, N. P.; Junkers, T.; Anastasaki, A., Tailoring Polymer Dispersity by RAFT Polymerization: A Versatile Approach. *Chem* **2020**, *6*, 1340.
- (22) Parkatzidis, K.; Boner, S.; Wang, H. S.; Anastasaki, A., Photoinduced Iron-Catalyzed ATRP of Renewable Monomers in Low-Toxicity Solvents: A Greener Approach. *ACS Macro Lett.* **2022**, *11*, 841.
- (23) Whitfield, R.; Parkatzidis, K.; Rolland, M.; Truong, N. P.; Anastasaki, A., Tuning Dispersity by Photoinduced Atom Transfer Radical Polymerisation: Monomodal Distributions with ppm Copper Concentration. *Angew. Chem. Int. Ed.* **2019**, *58*, 13323.
- (24) Bhanu, V.; Kishore, K., Role of oxygen in polymerization reactions. *Chem. Rev.* **1991**, *91*, 99.
- (25) Rolland, M.; Whitfield, R.; Messmer, D.; Parkatzidis, K.; Truong, N. P.; Anastasaki, A., Effect of polymerization components on Oxygen-Tolerant Photo-ATRP. *ACS Macro Lett.* **2019**, *8*, 1546.
- (26) Szczepaniak, G.; Jeong, J.; Kapil, K.; Dadashi-Silab, S.; Yerneni, S. S.; Ratajczyk, P.; Lathwal, S.; Schild, D.; Das, S. R.; Matyjaszewski, K., Open-air green-light-driven ATRP enabled by dual photoredox/copper catalysis. *Chem. Sci.* **2022**.
- (27) Szczepaniak, G.; Fu, L.; Jafari, H.; Kapil, K.; Matyjaszewski, K., Making ATRP more practical: oxygen tolerance. *Acc. Chem. Res.* **2021**, *54*, 1779.
- (28) Yeow, J.; Chapman, R.; Gormley, A. J.; Boyer, C., Up in the air: oxygen tolerance in controlled/living radical polymerisation. *Chem. Soc. Rev.* **2018**, *47*, 4357.
- (29) Burrige, K. M.; De Alwis Watuthanthrige, N.; Payne, C.; Page, R. C.; Konkolewicz, D., Simple polymerization through oxygen at reduced volumes using oil and water. *J. Polym. Sci.* **2021**, *59*, 2530.
- (30) Chapman, R.; Gormley, A. J.; Stenzel, M. H.; Stevens, M. M., Combinatorial low-volume synthesis of well-defined polymers by enzyme degassing. *Angew. Chem.* **2016**, *128*, 4576.
- (31) Chapman, R.; Gormley, A. J.; Herpoldt, K.-L.; Stevens, M. M., Highly controlled open vessel RAFT polymerizations by enzyme degassing. *Macromolecules* **2014**, *47*, 8541.
- (32) Xu, J.; Jung, K.; Atme, A.; Shanmugam, S.; Boyer, C., A robust and versatile photoinduced living polymerization of conjugated and unconjugated monomers and its oxygen tolerance. *J. Am. Chem. Soc.* **2014**, *136*, 5508.
- (33) Liarou, E.; Whitfield, R.; Anastasaki, A.; Engelis, N. G.; Jones, G. R.; Velonia, K.; Haddleton, D. M., Copper-mediated polymerization without external deoxygenation or oxygen scavengers. *Angew. Chem.* **2018**, *130*, 9136.
- (34) Theodorou, A.; Liarou, E.; Haddleton, D. M.; Stavrakaki, I. G.; Skordalidis, P.; Whitfield, R.; Anastasaki, A.; Velonia, K., Protein-polymer bioconjugates via a versatile oxygen tolerant photoinduced controlled radical polymerization approach. *Nat. Commun.* **2020**, *11*, 1.
- (35) Enciso, A. E.; Fu, L.; Russell, A. J.; Matyjaszewski, K., A breathing atom-transfer radical polymerization: fully oxygen-tolerant polymerization inspired by aerobic respiration of cells. *Angew. Chem. Int. Ed.* **2018**, *57*, 933.
- (36) Marathianos, A.; Liarou, E.; Anastasaki, A.; Whitfield, R.; Laurel, M.; Wemyss, A. M.; Haddleton, D. M., Photo-induced copper-RDRP in continuous flow without external deoxygenation. *Polym. Chem.* **2019**, *10*, 4402.
- (37) Zhang, L.; Wu, C.; Jung, K.; Ng, Y. H.; Boyer, C., An oxygen paradox: catalytic use of oxygen in radical photopolymerization. *Angew. Chem.* **2019**, *131*, 16967.
- (38) Wu, C.; Jung, K.; Ma, Y.; Liu, W.; Boyer, C., Unravelling an oxygen-mediated reductive quenching pathway for photopolymerisation under long wavelengths. *Nat. Commun.* **2021**, *12*, 1.
- (39) Enciso, A. E.; Fu, L.; Lathwal, S.; Olszewski, M.; Wang, Z.; Das, S. R.; Russell, A. J.; Matyjaszewski, K., Biocatalytic "Oxygen-Fueled" Atom Transfer Radical Polymerization. *Angew. Chem. Int. Ed.* **2018**, *57*, 16157.
- (40) Dworakowska, S.; Lorandi, F.; Gorkczyński, A.; Matyjaszewski, K., Toward Green Atom Transfer Radical Polymerization: Current Status and Future Challenges. *Adv. Sci.* **2022**, 2106076.
- (41) Fischer, H., The persistent radical effect: a principle for selective radical reactions and living radical polymerizations. *Chem. Rev.* **2001**, *101*, 3581.
- (42) Whitfield, R.; Parkatzidis, K.; Bradford, K. G.; Truong, N. P.; Konkolewicz, D.; Anastasaki, A., Low ppm CuBr-triggered atom transfer radical polymerization under mild conditions. *Macromolecules* **2021**, *54*, 3075.
- (43) Kryszewski, P.; Matyjaszewski, K., Kinetics of atom transfer radical polymerization. *Eur. Polym. J.* **2017**, *89*, 482.
- (44) Parkatzidis, K.; Rolland, M.; Truong, N. P.; Anastasaki, A., Tailoring polymer dispersity by mixing ATRP initiators. *Polym. Chem.* **2021**, *12*, 5583.
- (45) Mirica, L. M.; Ottenwaelder, X.; Stack, T. D. P., Structure and spectroscopy of copper-dioxygen complexes. *Chem. Rev.* **2004**, *104*, 1013.
- (46) Elwell, C. E.; Gagnon, N. L.; Neisen, B. D.; Dhar, D.; Spaeth, A. D.; Yee, G. M.; Tolman, W. B., Copper-oxygen complexes revisited: structures, spectroscopy, and reactivity. *Chem. Rev.* **2017**, *117*, 2059.
- (47) Brückmann, T.; Becker, J.; Turke, K.; Smarsly, B.; Weiß, M.; Marschall, R.; Schindler, S., Immobilization of a copper complex based on the tripodal ligand (2-aminoethyl) bis (2-pyridylmethyl) amine (uns-penp). *Z. Anorg. Allg. Chem.* **2021**, *647*, 560.
- (48) Becker, M.; Heinemann, F. W.; Schindler, S., Reversible Binding of Dioxygen by a Copper (I) Complex with Tris (2-dimethylaminoethyl) amine (Me6tren) as a Ligand. *Chem. Eur. J.* **1999**, *5*, 3124.
- (49) Schatz, M.; Raab, V.; Foxon, S. P.; Brehm, G.; Schneider, S.; Reiher, M.; Holthausen, M. C.; Sundermeyer, J.; Schindler, S., Combined Spectroscopic and Theoretical Evidence for a Persistent End-On Copper Superoxo Complex. *Angew. Chem. Int. Ed.* **2004**, *43*, 4360.
- (50) Will, J.; Wuertele, C.; Becker, J.; Walter, O.; Schindler, S., Synthesis, crystal structures and reactivity towards dioxygen of copper (I) complexes with tripodal aliphatic amine ligands. *Polyhedron* **2019**, *171*, 448.
- (51) Komiyama, K.; Furutachi, H.; Nagatomo, S.; Hashimoto, A.; Hayashi, H.; Fujinami, S.; Suzuki, M.; Kitagawa, T., Dioxygen reactivity of copper (I) complexes with tetradentate tripodal ligands having aliphatic nitrogen donors: Synthesis, structures, and properties of peroxo and superoxo complexes. *Bull. Chem. Soc. Jpn.* **2004**, *77*, 59.
- (52) Alsubaie, F.; Anastasaki, A.; Nikolaou, V.; Simula, A.; Nurumbetov, G.; Wilson, P.; Kempe, K.; Haddleton, D. M., Investigating the mechanism of copper (0)-mediated living radical polymerization in organic media. *Macromolecules* **2015**, *48*, 5517.
- (53) Schindler, S., Reactivity of copper (I) complexes towards dioxygen. *Eur. J. Inorg. Chem.* **2000**, *2000*, 2311.

- (54) Brinkmeier, A.; Schulz, R. A.; Buchhorn, M.; Spyra, C.-J.; Dechert, S.; Demeshko, S.; Krewald, V.; Meyer, F., Structurally Characterized  $\mu$ -1, 2-Peroxo/Superoxo Dicopper (II) Pair. *J. Am. Chem. Soc.* **2021**, *143*, 10361.
- (55) Bhadra, M.; Transue, W. J.; Lim, H.; Cowley, R. E.; Lee, J. Y. C.; Siegler, M. A.; Josephs, P.; Henkel, G.; Lerch, M.; Schindler, S., A Thioether-Ligated Cupric Superoxide Model with Hydrogen Atom Abstraction Reactivity. *J. Am. Chem. Soc.* **2021**, *143*, 3707.
- (56) Hoppe, T.; Josephs, P.; Kempf, N.; Wölper, C.; Schindler, S.; Neuba, A.; Henkel, G., An Approach to Model the Active Site of Peptidglycine- $\alpha$ -hydroxylating monooxygenase (PHM). *Z. Anorg. Allg. Chem.* **2013**, *639*, 1504.
- (57) Würtele, C.; Gaoutchenova, E.; Harms, K.; Holthausen, M. C.; Sundermeyer, J.; Schindler, S., Crystallographic characterization of a synthetic 1: 1 end-on copper dioxygen adduct complex. *Angew. Chem. Int. Ed.* **2006**, *45*, 3867.
- (58) Pirovano, P.; Magherusan, A. M.; McGlynn, C.; Ure, A.; Lynes, A.; McDonald, A. R., Nucleophilic reactivity of a copper (II)-superoxide complex. *Angew. Chem.* **2014**, *126*, 6056.
- (59) Anastasaki, A.; Nikolaou, V.; Pappas, G. S.; Zhang, Q.; Wan, C.; Wilson, P.; Davis, T. P.; Whittaker, M. R.; Haddleton, D. M., Photoinduced sequence-control via one pot living radical polymerization of acrylates. *Chem. Sci.* **2014**, *5*, 3536.
- (60) Boyer, C.; Soeriyadi, A. H.; Zetterlund, P. B.; Whittaker, M. R., Synthesis of complex multiblock copolymers via a simple iterative Cu (0)-mediated radical polymerization approach. *Macromolecules* **2011**, *44*, 8028.
- (61) An, Z., 100th anniversary of macromolecular science viewpoint: achieving ultrahigh molecular weights with reversible deactivation radical polymerization. *ACS Macro Lett.* **2020**, *9*, 350.
- (62) Carmean, R. N.; Becker, T. E.; Sims, M. B.; Sumerlin, B. S., Ultra-high molecular weights via aqueous reversible-deactivation radical polymerization. *Chem* **2017**, *2*, 93.
- (63) Allison-Logan, S.; Karimi, F.; Sun, Y.; McKenzie, T. G.; Nothling, M. D.; Bryant, G.; Qiao, G. G., Highly living stars via core-first photo-RAFT polymerization: exploitation for ultrahigh molecular weight star synthesis. *ACS Macro Lett.* **2019**, *8*, 1291.
- (64) Olson, R. A.; Lott, M. E.; Garrison, J. B.; Davidson IV, C. L.; Trachsel, L.; Pedro, D. I.; Sawyer, W. G.; Sumerlin, B. S., Inverse Miniemulsion Photoiniferter Polymerization for the Synthesis of Ultrahigh Molecular Weight Polymers. *Macromolecules* **2022**, *55*, 19, 8451–8460.
- (65) Truong, N. P.; Dussert, M. V.; Whittaker, M. R.; Quinn, J. F.; Davis, T. P., Rapid synthesis of ultrahigh molecular weight and low polydispersity polystyrene diblock copolymers by RAFT-mediated emulsion polymerization. *Polym. Chem.* **2015**, *6*, 3865.
- (66) Wang, Y.; Schroeder, H.; Morick, J.; Buback, M.; Matyjaszewski, K., High-Pressure Atom Transfer Radical Polymerization of n-Butyl Acrylate. *Macromol. Rapid Commun.* **2013**, *34*, 604.
- (67) Percec, V.; Guliashvili, T.; Ladislav, J. S.; Wistrand, A.; Stjern Dahl, A.; Sienkowska, M. J.; Monteiro, M. J.; Sahoo, S., Ultrafast synthesis of ultrahigh molar mass polymers by metal-catalyzed living radical polymerization of acrylates, methacrylates, and vinyl chloride mediated by SET at 25 C. *J. Am. Chem. Soc.* **2006**, *128*, 14156.