

Enlightening the Mechanism of Copper Mediated PhotoRDRP via High-Resolution Mass Spectrometry

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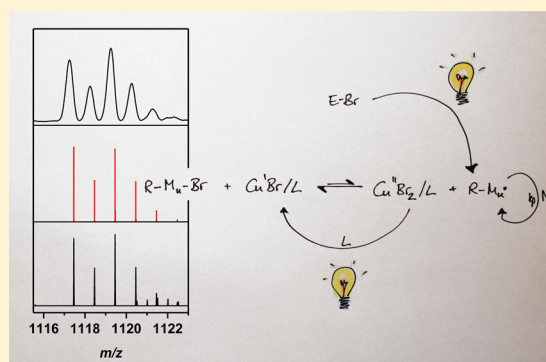
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S Supporting Information

ABSTRACT: The initiation mechanism of photochemically mediated Cu-based reversible-deactivation radical polymerization (photoRDRP) was investigated using pulsed-laser polymerization (PLP) and high-resolution mass spectrometry. The variation of the catalyst composition and ESI-MS analysis of the resulting products provided information on how initiator, ligand, copper species, and monomer are interacting upon irradiation with UV light. A discussion of the results allows for a new postulation of the mechanism of photoRDRP and—for the first time—the unambiguous identification of the initiating species and their interactions within the reaction mixture. One pathway for radical generation proceeds via UV light-induced C–Br bond scission of the initiator, giving rise to propagating radicals. The generation of copper(I) species from copper(II) can occur via several pathways, including, among others, via reduction by free amine ligand in its excited as well as from its ground state via the irradiation with UV light. The amine ligand serves as a strong reducing agent and is likely the main participant in the generation of copper(I) species.



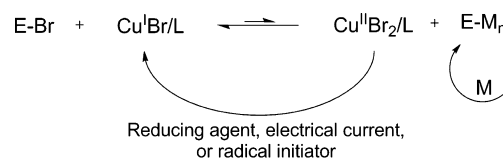
INTRODUCTION

The development of reversible-deactivation radical polymerization (RDRP) techniques set a milestone in polymer chemistry research.^{1–3} It enables the synthesis of well-controlled polymers with defined end groups, molecular weight, and architecture, combined with the benefits of radical polymerization, i.e., high tolerance toward a wide range of monomer functionalities under mild reaction conditions. Among several efficient techniques in the field of RDRP, atom-transfer radical polymerization (ATRP)¹ and single-electron transfer living radical polymerization (SET-LRP)^{4,5} are two of the most popular methods. In both techniques, the nearly full elimination of chain termination events is a result of a redox equilibrium in which a transition metal complex ($M^n X/L$) activates an alkyl halide (P_n-X) generating alkyl radicals and the metal complex in a higher oxidation state ($M^{n+1} X_2/L$). In most cases, copper complexes $Cu^I X/L$ (the activator) and $Cu^{II} X_2/L$ (the deactivator) are employed as catalysts and bromine is the transferred halogen. For the distinct differences of the techniques, the reader is referred to the literature.^{6–8} In the past decade, significant improvements have been achieved in minimizing the amount of catalyst,^{9,10} leading to potential applications in biological fields,¹¹ as well as in considerably decreasing the sensitivity toward oxygen. For instance, the use of reducing agents that continuously regenerate Cu^I species throughout the reaction process (ARGET ATRP) has been a

major step toward a higher control over the polymer structure and a facile handling of the reaction mixture, due to its increased tolerance to oxygen.

Recently, the influence of external stimuli on the redox equilibrium of the transition metal complex has been subject of further investigation (Scheme 1). To continuously regenerate

Scheme 1. Mechanism of ATRP with Activator Regeneration (M = Monomer)



the catalyst to its lower oxidation state ($Cu^I X/L$), an electrochemical stimulus can be applied during the polymerization (eATRP),^{12,13} or an additional source of radicals from a standard radical initiator can be employed (ICAR ATRP).¹⁴

The application of light has also been investigated as a possible external stimulus on the redox equilibrium, leading to the introduction of photoRDRP (herein, photoATRP as well as

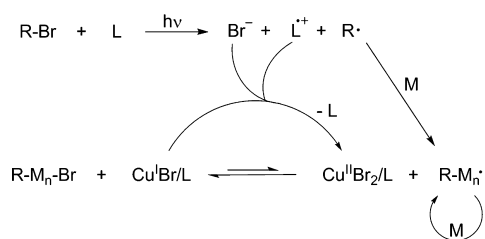
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photoLRP are included)^{15–21} as the latest advancement in ATRP and SET-LRP technology. The positive influence of light on ATRP has been discovered for the first time by Guan and Smart,¹⁸ reporting increased polymerization rates, higher final conversions, and an enhanced living character for an ATRP conducted under visible light, compared to an ATRP carried out in the dark. Tasdelen et al.¹⁶ reported the initiation of an ATRP by light, starting from the highest oxidation state of the catalyst ($\text{Cu}^{\text{II}}\text{X}_2/\text{L}$) and therefore indicating that the formation of $\text{Cu}^{\text{I}}\text{X}/\text{L}$ can be triggered by photochemical means. The successful photochemically initiated iridium-based ATRP was reported by Hawker and co-workers.^{22,23} Furthermore, the iridium-based photoinitiation was combined with the reversible addition–fragmentation chain transfer (RAFT) polymerization by Boyer et al.^{24,25} In addition to iridium-based photoinitiation processes, a wide range of other photoredox catalyst systems have been investigated such as ruthenium-, chlorophyll-, and organo dye-based systems.^{26–29} Mosnáček and Ilčíková¹⁵ as well as Konkolewicz et al.¹⁹ expanded the scope of photoATRP particularly toward low copper catalyst concentrations, down to 50–100 ppm, the employment of visible light and sunlight, as well as to aqueous systems. Mosnáček et al. successfully carried out a photoRDRP under a limited amount of air without the loss of control.³⁰ For the first time, photoRDRP was carried out in a continuous flow reactor by Junkers and co-workers,³¹ underpinning the versatility of the reaction protocol. Photo-ATRP and photoLRP represent the elegant combination of RDRP techniques, bearing structural control over molecular weight and dispersities, with the benefits of light-triggered reactions, i.e., giving temporal and spatial control over the reaction process. The fast-growing exploitation of photoRDRP testifies these benefits.

Lately, attempts^{17,20} were made to elucidate the mechanism of photoRDRP, i.e., to clarify how the reduction of the $\text{Cu}^{\text{II}}\text{X}_2/\text{L}$ complex (the only one initially present) can be triggered by light and which roles the ligand (L) and the initiator (R–X) are playing. Anastasaki et al.¹⁷ carried out several experiments, varying the composition as well as systematically omitting components of the RDRP mixture, in order to evaluate their individual role in the complete photo process. Their experiments with acrylates and tris[2-(dimethylamino)ethyl]amine (Me_6TREN) as the ligand showed that, next to a suitable alkyl halide as initiator, the presence of an aliphatic tertiary amine σ -donor ligand in excess (relative to Cu^{II}) is required to successfully start and maintain a well-controlled polymerization. Their proposed mechanism (Scheme 2) involves the photo-activation of free Me_6TREN with a subsequent outer-sphere single-electron transfer (OSET) from the excited ligand to the alkyl halide initiator, leading to a C–Br bond scission. The resulting radical was proposed to initiate the well-controlled

Scheme 2. Mechanism of PhotoRDRP Proposed by Anastasaki et al.¹⁷

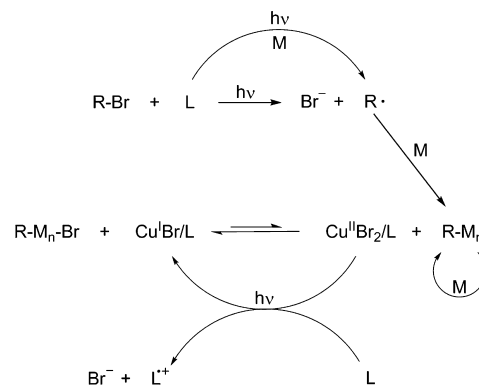


monomer propagation, based on the deactivation reaction with $\text{Cu}^{\text{II}}\text{Br}_2/\text{Me}_6\text{TREN}$ species that is present in the reaction from the start. Next to the initiator radical, the OSET reaction was proposed to form Me_6TREN radical cations and bromide anions that are involved in the oxidation of $\text{Cu}^{\text{I}}\text{Br}/\text{Me}_6\text{TREN}$, formed during the deactivation reaction of propagating radicals, into $\text{Cu}^{\text{II}}\text{Br}/\text{Me}_6\text{TREN}$. However, the question arises whether, with such high amounts of $\text{Cu}^{\text{I}}\text{Br}_2/\text{Me}_6\text{TREN}$ present from the beginning, the deactivation process as the exclusive pathway to form $\text{Cu}^{\text{I}}\text{Br}/\text{Me}_6\text{TREN}$ is sufficient to maintain a high polymerization rate.

Matyjaszewski and co-workers²⁰ subsequently carried out a similar set of experiments. The kinetics of several possible reaction pathways were studied experimentally and in conjunction with simulation techniques. Rate coefficients were derived via rate/conversion fitting for various reactions that could be relevant for photoRDRP. Subsequently, the experimentally determined rate coefficients, derived via the analysis of global kinetic data, were employed for simulations in order to investigate the mechanism of $\text{Cu}^{\text{I}}\text{Br}/\text{Me}_6\text{TREN}$ and radical generation.

As illustrated in Scheme 3, it is proposed that the main pathway to generate $\text{Cu}^{\text{I}}\text{Br}/\text{Me}_6\text{TREN}$ is the photochemically

Scheme 3. Mechanism of PhotoRDRP Proposed by Matyjaszewski et al.²⁰



mediated reduction of Cu^{II} complexes by free ligand, in particular by tertiary amines, and the formation of the corresponding radical cation. The formation of radicals that can initiate a polymerization is proposed to occur via a synergistic reaction between alkyl halides and ligand. However, this process is only assigned a small contribution and is 1 order of magnitude slower than the formation of $\text{Cu}^{\text{I}}\text{Br}/\text{Me}_6\text{TREN}$. Therefore, as in the case of Anastasaki et al., it was not sufficiently demonstrated how an adequate amount of initiator radicals can be generated under irradiation in order to rapidly start the polymerization process. Considering all studies carried out to unravel the mechanism of photoRDRP, it can be assumed that Cu^{II} species are being reduced to Cu^{I} species via a photochemical process. There is some evidence that the initiator and/or the ligand are involved in the reduction process of the Cu^{II} species. However, none of the proposed mechanisms were verified on a molecular level, i.e., by nuclear magnetic resonance spectroscopy (NMR), mass spectrometry, or similar techniques. Therefore, the proposed pathways can only be considered as best guesses.

Herein, we present an elucidation of the mechanism of photoRDRP based on pulsed-laser polymerization (PLP)^{32–34}

and electrospray-ionization mass spectrometry (ESI-MS).³⁵ The benefit of employing PLP as the polymerization method is that, with its high-frequency pulsed laser, it generates relatively short polymer chains while still performing photoinitiated free-radical polymerization (FRP). The control over chain length is achieved through very short time intervals between the consecutive laser pulses, allowing only very short growth periods for the polymer chains. In the present work, we employed methyl methacrylate (MMA) as the monomer, as its molecular weight can be readily controlled by PLP even at intermediate laser frequencies. However, previous studies focused on methyl acrylate (MA) as well as MMA. The relatively short polymers were analyzed by ESI-MS, providing insight into the exact structure of the polymer and its end groups and consequently on the nature of the initiating species. In analogy to the reports of Anastasaki et al.¹⁷ and Matyjaszewski and co-workers,²⁰ we varied the composition of a typical photoRDRP mixture containing ethyl α -bromoisobutyrate (EBiB, initiator), copper(II) bromide, tris-[2-(dimethylamino)ethyl]amine (Me₆TREN, ligand), methyl methacrylate (MMA), and dimethyl sulfoxide (DMSO, solvent). DMSO was chosen as the solvent, due to its positive influence on the monomer conversion.¹⁷ To understand the behavior of initiator, ligand, and copper(II) bromide under UV irradiation, each of these components was independently irradiated in a solution of MMA and DMSO and in different combinations, respectively. A careful discussion and summary of the results allows for a deeper understanding of the chemical processes at play in photoRDRP and the postulation of a new mechanism of this process.

RESULTS AND DISCUSSION

To provide a well-structured overview of the results of the current work, we singled out each combination of reagents that was polymerized by PLP and analyzed by quadrupole ESI-MS and high-resolution orbitrap ESI-MS. These combinations are summarized in Table 1. All species that were detected by mass spectrometry are depicted in Scheme 4. To obtain complete evidence regarding the detected species, all samples were additionally measured by high-resolution orbitrap mass spectrometry, confirming the proposed structures.

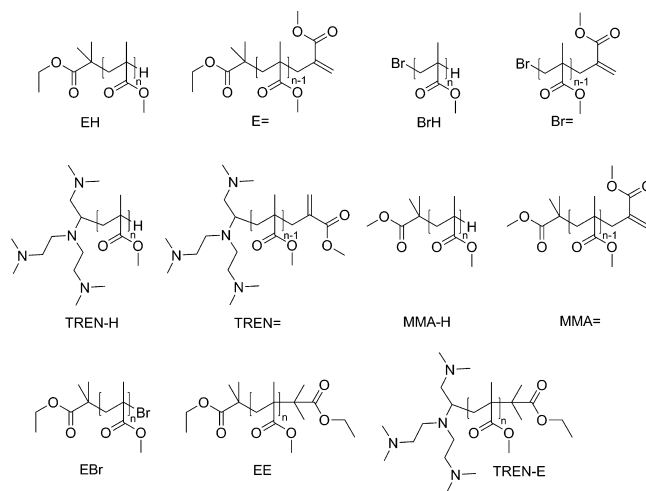
Pulsed-Laser Irradiation of EBiB/MMA. Photoactivated polymerization of MMA was observed in a DMSO solution

Table 1. Summary of All Pulsed-Laser RDRP Experiments Carried out with Variable Composition

entry	[M]:[I]:[CuBr ₂]:[L] ^{a,b,c}	conversion (%) ^d	M _n (g·mol ⁻¹) ^e	D ^e
1	50: -: -: -	-	-	-
2	50:1: -: -	3.1	18000	1.56
3	50: -: -: 0.06	0.6	20000	5.00
4	50: -: 0.02: -	-	-	-
5	50: -: 0.02:0.06	3.3	14400	2.93
6	50:1: -: 0.06	1.6	14000	2.21
7	50:1: 0.02: -	-	-	-
8	50:1: 0.02:0.02	2.1	1900	1.28
9	50:1: 0.02:0.03	3.8	2100	1.29
10	50:1: 0.02:0.04	3.8	2100	1.28
11	50:1: 0.02:0.08	5.3 ^f	2600	1.24

^aI = EBiB. ^bL = Me₆TREN. ^cDMSO (30 vol %). ^dAfter 90 000 pulses, determined by gravimetry. ^eSee SEC data in Supporting Information Figure S1. ^fAfter 60 000 pulses.

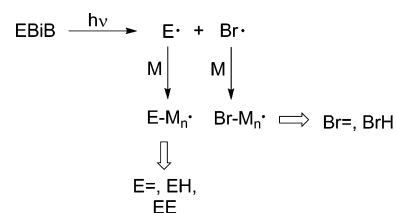
Scheme 4. Chemical Structures Found in ESI-MS, Derived from Variations in the Composition



without the presence of copper or ligand, initiated by the widely used initiator EBiB. Typically, EBiB undergoes a C–Br bond scission in the presence of Cu^IBr species, resulting in the formation of an ethyl isobutyrate tertiary radical that initiates propagation, if monomer is present, and the oxidation of Cu^IBr species to the corresponding Cu^{II}Br₂ complex. However, without the presence of copper species EBiB, or any other ATRP initiator, it is in general not expected to form radicals easily or to act as a radical photoinitiator.

Yet, in our experiments we find unambiguous evidence for a radical cleavage of EBiB into an ethyl isobutyrate radical and a bromine radical under irradiation and the initiation of MMA polymerization by both radical species, as illustrated in Scheme 5. ESI-MS analysis (see Figure 1A and Scheme 4) of

Scheme 5. Reaction Pathway of EBiB after Irradiation



poly(methyl methacrylate) (pMMA) that was formed in the presence of the sole EBiB shows the presence of ethyl isobutyrate-initiated chains (visualized by the disproportionation peaks E= and EH and the termination peak EE) as well as bromine-initiated chains (the disproportion peaks Br= and BrH). Thus, EBiB seems to act as a conventional photoinitiator at 351 nm.

Pulsed-Laser Irradiation of Me₆TREN/MMA. The photoinitiation ability of Me₆TREN was analyzed in a PLP experiment containing Me₆TREN, the monomer MMA, and DMSO as the solvent. We found Me₆TREN-initiated as well as MMA-initiated polymer chains in the mass spectra (see Figure 1B, the disproportionation peaks TREN= and TRENH, ionized by either sodium ions or protons, and MMA= and MMAH). This finding confirms that the aliphatic tertiary amines are able to produce radicals upon UV irradiation which can initiate MMA propagation. Additionally, to a high extent, we find chains carrying MMA as the initiating fragment. MMA

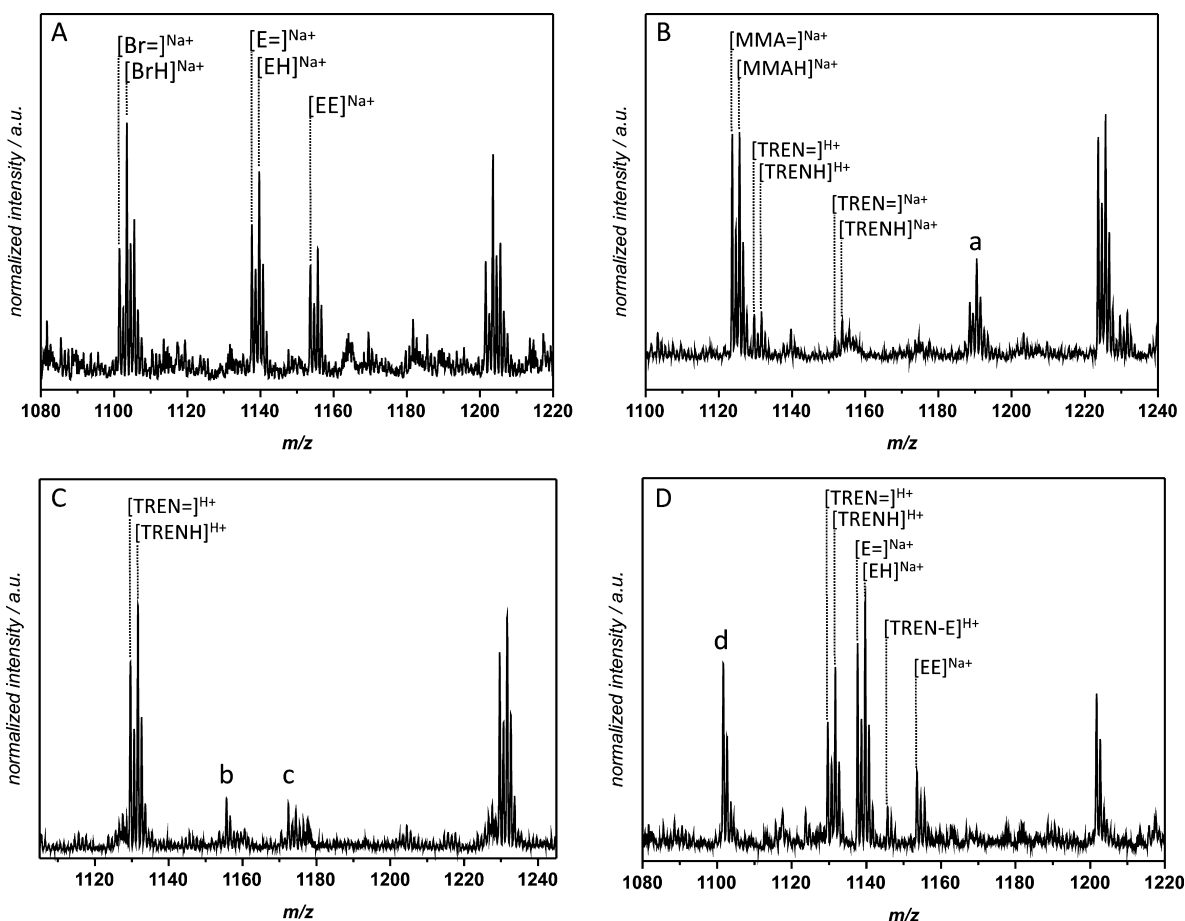
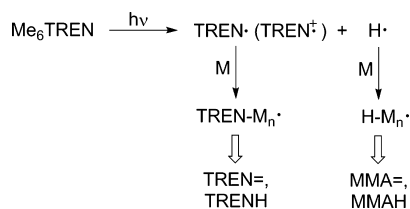


Figure 1. Mass spectra of pMMA synthesized from different combinations of the photoRDRP composition. (A) [MMA]:[EBiB]:[CuBr₂]:[Me₆TREN] = 50:1:0:0; (B) [MMA]:[EBiB]:[CuBr₂]:[Me₆TREN] = 50:0:0:0.12; (C) [MMA]:[EBiB]:[CuBr₂]:[Me₆TREN] = 50:0:0.2:0.12; (D) [MMA]:[EBiB]:[CuBr₂]:[Me₆TREN] = 50:1:0:0.12. Peaks a, b, c, and d where investigated by collision-induced dissociation (CID) experiments. While it was possible to find amine- and ethyl oxide-based fragments, an unambiguous assignment of the peaks revealed impossible. It must be noted that signal d does not appear in orbitrap ESI-MS measurements. It can therefore be assumed that the species is formed during the ionization process.

itself is not known to form radicals upon UV irradiation, instead it needs a radical source to start a propagation reaction. In our PLP experiments with MMA and DMSO alone no polymer was obtained (see entry 1, Table 1) The initiation of chain growth by MMA as the initiating species can be explained by the light-induced formation of an excited Me₆TREN species and the subsequent abstraction of a hydrogen radical in α -position of one of the amine groups of the ligand.

We assume that an abstraction of a hydrogen atom occurs by MMA, forming a perfectly suited radical initiator for MMA propagation. However, amines are known to form radical cations upon irradiation.³⁶ Therefore, the radical cations are depicted in Scheme 6 in brackets. A more detailed discussion about the role of the radical cation in the photoRDRP process

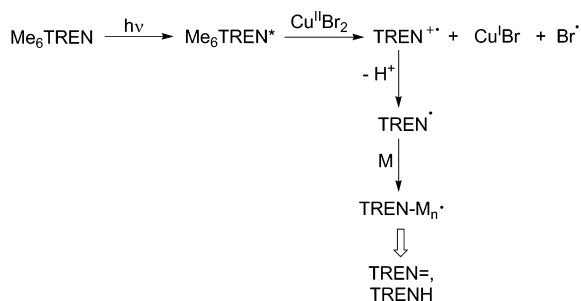
Scheme 6. Reaction Pathway of the Ligand Me₆TREN upon Irradiation



is given in the further course of this work. To simplify matters, in chemical schemes and peak assignments the short version TREN is used for the ligand Me₆TREN.

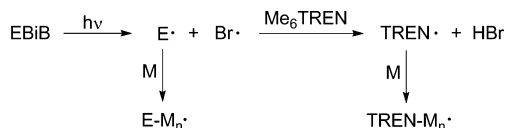
Pulsed-Laser Irradiation of Me₆TREN/CuBr₂/MMA. The behavior of the Cu^{II}Br₂/Me₆TREN complex under photopolymerization conditions was studied, revealing relatively high monomer conversions of up to 3.3%. Interestingly, the initially green-colored reaction solution (d⁹ Cu(II)) turned colorless on visual observation after the irradiation process. A reduction of the Cu^{II}Br₂/Me₆TREN toward the corresponding Cu^I species is therefore highly probable. The ESI-MS analysis of the obtained polymer (see Figure 1C) shows almost exclusively Me₆TREN-initiated chains. MMA-initiated chains, as observed in the polymerization mixture Me₆TREN/MMA, are absent. A connection between these two observations, the visible reduction of Cu^{II}Br₂ during the irradiation and the absence of MMA-initiated polymer, is likely.

We suggest that, instead of the hydrogen atom abstraction by the MMA double bond, the amine ligand is excited by UV light, subsequently reducing Cu(II) species to Cu(I) species as illustrated in Scheme 7. The resulting amine radical cation (aminium radical) preferably forms α -aminoalkyl radicals, via deprotonation at an α -carbon, which can subsequently react with the monomer and initiate polymerization. Bromine radicals formed during the process can, as described in the

Scheme 7. Reaction Pathway of Me₆TREN in the Presence of Copper(II) Bromide

further course of this work (see Scheme 9), again contribute to the formation of Cu(I) species.

Pulsed-Laser Irradiation of EBiB/Me₆TREN/MMA. Photopolymerization experiments of a mixture of the initiator, ligand, monomer, and solvent (thereby only lacking copper) and its subsequent ESI-MS analysis revealed the formation of ethyl isobutyrate-initiated (E= and EH) as well as Me₆TREN-initiated chains (TREN= and TRENH) as demonstrated in Figure 1D. No bromine- or MMA-initiated polymer could be detected in the ESI-MS. An altered reaction pathway for bromine radicals can therefore be assumed, as illustrated in Scheme 8. The highly reactive radical Br[·] could either abstract a

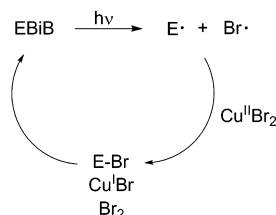
Scheme 8. Reaction Pathway of EBiB in the Presence of Me₆TREN upon Irradiation

hydrogen atom from excited Me₆TREN (which subsequently forms radicals that can initiate a polymerization), or Br[·] could undergo a termination reaction. Furthermore, the formation of a bromide of the radical cation ligand (TREN⁺ Br⁻), as previously reported for aromatic amines in metal-free ATRP,²⁸ could be possible. However, such ion pairs are possibly less stable in the case of aliphatic amines and therefore are expected to decompose toward amine radicals which can initiate polymerization.

Pulsed-Laser Irradiation of EBiB/CuBr₂/MMA. PLP experiments involving the initiator, copper(II) bromide, monomer, and solvent but no ligand did not yield any polymer formation. Although the initiator alone is capable of forming two initiating radicals upon irradiation, no polymer was found.

The copper(II) bromide is most likely acting as a radical quencher for ethyl isobutyrate and bromine radicals. The visual observation of a change of color of the solution from initially green toward being pale yellow after the irradiation is an indication for the reduction of Cu^{II} species. The yellow color could possibly be due to the formation of small amounts of elemental bromine. Therefore, we propose that both, ethyl isobutyrate and bromine radicals, are formed during irradiation, but are rapidly captured by copper(II) bromide, forming copper(I) bromide (d¹⁰), EBiB (which could form radicals again) and elemental bromine (Br₂), as illustrated in Scheme 9. Since only 0.2 equiv of copper(II) bromide are present compared to the initiator, one could assume that a long irradiation time is needed to achieve a full consumption of

Scheme 9. Reaction Pathway of EBiB in the Presence of Copper(II) Bromide after Irradiation



copper(II) bromide and eventually the successful initiation of monomer by ethyl isobutyrate and bromine radicals.

However, it is highly probable that elemental bromine, formed during the quenching reaction of bromine radicals by copper(II) bromide, can again react with copper(I) bromide and form the oxidized state of the latter. Furthermore, the very low extinction coefficient of EBiB at 351 nm suggests the formation of very small amounts of radicals during irradiation. We assume that less than 20% of the added EBiB performs a C–Br bond scission in the time frame of the irradiation and that therefore the amount of copper(II) bromide (0.2 equiv compared to EBiB) is sufficient to quench radicals that are formed by EBiB.

Pulsed-Laser Irradiation of EBiB/CuBr₂/Me₆TREN/MMA (PhotoDRP). Photopolymerization experiments with a reaction solution containing all classical reagents of a photoDRP, i.e., initiator, ligand, copper(II) bromide, monomer, and solvent showed a controlled-living polymerization behavior with lower molecular weight polymer and lower dispersities ($\mathcal{D} \leq 1.3$) and a linear correlation between molecular weight and monomer conversion or applied pulse number, respectively (see Supporting Information Figures S2 and S3), unlike all other previously described combinations which showed typical free-radical polymerization characteristics with high molecular weights and dispersity indices above $\mathcal{D} = 2$. ESI-MS analysis of the generated polymer (see Figure 2) reveals the presence of ethyl isobutyrate-initiated polymer carrying a bromine end group (EBr) and thus represents an unambiguous proof for the successful atom-transfer reaction

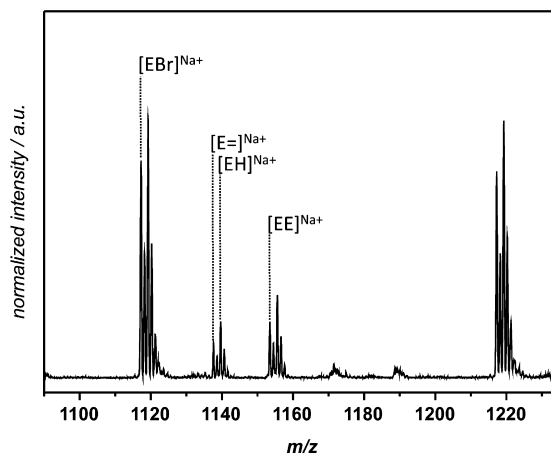


Figure 2. Mass spectrum of poly(methyl methacrylate) formed in photopolymerization experiments with EBiB/Me₆TREN/CuBr₂/MMA/DMSO with the ratio of Me₆TREN/CuBr₂ = 4/1. Ethyl isobutyrate-initiated chains with a bromine end group (EBr) are detected as well as ethyl isobutyrate-initiated chains with disproportionated (E= and EH) or terminated (EE) with a second chain.

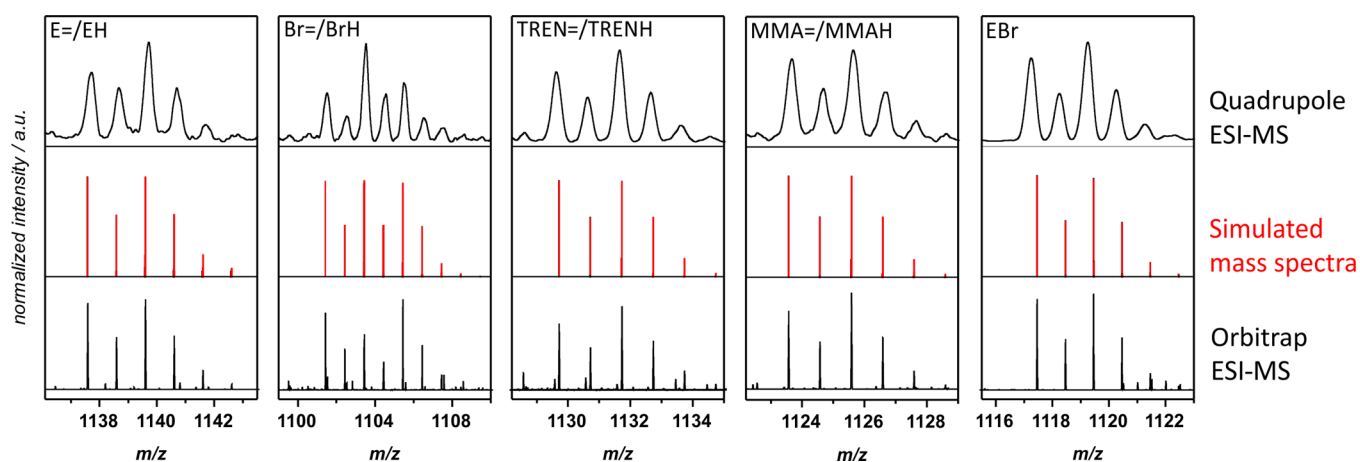


Figure 3. Comparison of quadrupole ESI-MS (top row) and high-resolution orbitrap ESI-MS measurements (bottom row) with the simulated mass spectra (middle row) of the significant chemical structures found for various reagent compositions.

during the polymerization. In addition, next to bromine end-capped chains we also found ethyl isobutyrate-initiated chains that underwent termination, either by disproportionation (E= and EH) or by combination with an ethyl isobutyrate radical (EE). ESI-MS analysis reveals no presence of Me₆TREN-, bromine radical-, or MMA-initiated chains. We assume that our technique based on PLP and ESI-MS gives insight into the very early stages of the polymerization mechanism due to the very low monomer conversions (<3.8%) that can be produced and analyzed. We can detect which species are formed at the beginning of the polymerization. Therefore, the absence of bromine- and monomer-initiated chains underlines the high capability of Br· and excited Me₆TREN species to reduce Cu^{II} species toward Cu^I, i.e., their rate coefficient for the reducing reaction being significantly higher than for the monomer initiation reaction. To undoubtedly identify the various structures illustrated in Scheme 4, for all samples high-resolution orbitrap ESI-MS was performed. The orbitrap mass spectrometer operates by radially trapping ions about a central spindle electrode. An outer barrel-like electrode is coaxial to the inner spindle-like electrode and mass/charge values are measured from the frequency of harmonic ion oscillations, along the axis of the electric field, experienced by the orbitally trapped ions. Thereby, high mass resolutions (up to 140 000) can be achieved.³⁷ A direct comparison of the orbitrap mass spectra with the calculated masses confirms the proposed structures (see Figure 3 and Table 2).

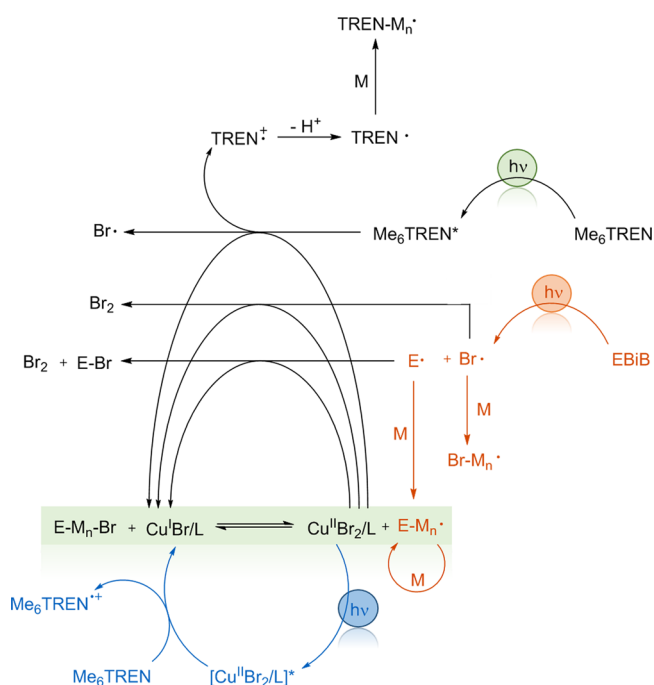
The Mechanism of PhotoRDRP. Merging the information concerning how the polymerization ingredients—initiator, ligand, and copper bromide—interact during the exposure to light gives insight into a complex mechanistic system, as illustrated in Scheme 10. After the UV-induced C–Br bond scission of the initiator into alkyl and bromine radicals (in orange, Scheme 10), the alkyl radical initiates the polymerization, whereas bromine radicals interact with copper(II) bromide, forming the activator copper(I) bromide and bromine. The latter is highly reactive and therefore, with high probability, continues to react. It is important to note that already in this first step copper(I) bromide is formed, which can subsequently perform an atom transfer reaction with the initiator and thus generate radicals. The atom transfer process between alkyl bromides and Cu(I) species remains the main pathway for the generation of initiating radicals. The UV-induced C–Br scission of the initiator serves solely as a support

Table 2. Comparison of Theoretical and Experimentally Determined Molecular Mass for the Significant Structures Found for Various Reagent Compositions

structure	elemental formula	(<i>m/z</i>) _{theo} ^a	(<i>m/z</i>) _{exp} ^b	Δ <i>m/z</i>
E=	C ₅₆ H ₉₀ NaO ₂₂ ⁺	1137.5816	1137.5881	0.0065
EH	C ₅₆ H ₉₂ NaO ₂₂ ⁺	1139.5973	1139.6031	0.0058
Br=	C ₅₀ H ₇₉ BrNaO ₂₀ ⁺	1101.4240	1101.4305	0.0065
BrH	C ₅₀ H ₈₁ BrNaO ₂₀ ⁺	1103.4397	1103.4466	0.0069
TREN=	C ₅₇ H ₁₀₁ N ₄ O ₁₈ ⁺	1129.7105	1129.7163	0.0058
TRENH	C ₅₇ H ₁₀₃ N ₄ O ₁₈ ⁺	1131.7262	1131.7313	0.0051
MMA=	C ₅₅ H ₈₈ NaO ₂₂ ⁺	1123.5660	1123.5701	0.0041
MMAH	C ₅₅ H ₉₀ NaO ₂₂ ⁺	1125.5816	1125.5840	0.0024
EBr	C ₅₁ H ₈₃ BrNaO ₂₀ ⁺	1117.4553	1117.4622	0.0069

^aCalculated exact mass. ^bMeasured by high-resolution orbitrap ESI-MS. ^cIonized with H⁺.

Scheme 10. Proposed Mechanism of PhotoRDRP, Based on Structures Found in ESI-MS for Varied Combinations of EBiB, Me₆TREN, CuBr₂, Monomer, and Solvent



for reducing Cu(II) species as well as for generating initiating radicals. From our experiments (see Scheme 9), we know that initiator-based radicals can reduce copper(II) bromide. In that case bromine-terminated initiator species are formed, which have the same structure as the actual initiator that was added at the beginning. However, we assume that this step only plays a minor role and that the propagation reaction starting from an initiator radical is more favored. The ligand plays an important role for the efficient reduction of copper(II) bromide throughout the reaction. We assume the coexistence of two processes associated with the amine ligand that both contribute to the reduction of copper(II). First, due to its high extinction coefficient for the employed wavelength, the CuBr₂/Me₆TREN complex could be excited upon irradiation and subsequently quenched by free amine ligand, forming CuBr/Me₆TREN and the radical cation of the amine ligand (in blue, Scheme 10). A similar mechanism was recently shown by Lalevée and co-workers³⁸ for a Cu(phen)₂⁺ complex and triethylamine. The second process involving the ligand is the light-induced excitation of Me₆TREN and the subsequent reduction of Cu(II)Br₂ toward the corresponding Cu(I) species. In general, the ligand contributes to a continuous (re)generation of the activator species and thus averts the accumulation of deactivator species in the reaction, preventing the persistent radical effect.^{39,40} The ligand supports the rapid adjustment of the RDRP equilibrium, confirmed by the observation that higher concentrations of ligand lead to higher rates of polymerization, as seen in previous studies.^{17,20} A legitimate question is why no ligand-initiated polymer chains (TREN= and TRENH) are found in the mass spectra of the polymer generated from the complete RDRP reaction mixture (Figure 2). At present we cannot answer that question with high certainty. However, we assume that the initiation ability of Me₆TREN radicals is limited and that Me₆TREN preferably serves as reducing agents. The principal role of the ligand seems to be the reduction of Cu(II) species, but not the initiation of new chains.

Photoinduced Electron Transfer of the Ligand. Our experiments evidence that in a photoRDRP the amines serve as electron donors, i.e., enabling reduction of Cu(II) toward Cu(I). Yet, it is known that photoexcitation of electron donors as well as acceptors changes their redox properties, and they act as sensitizers (as illustrated in Supporting Information Figure S4).^{36,41–43} Excitation of a sensitizer molecule transfers an electron from the highest occupied molecular orbital (HOMO) into the lowest unoccupied molecular orbital (LUMO). The electron transfer from the LUMO requires less energy than from the HOMO. Therefore, a sensitizer in its excited state is a far better reducing agent than in its ground state,^{36,42,43} explaining why amines can serve as reducing agents for Cu(II) toward Cu(I) and therefore accelerate the polymerization under irradiation with light. It is known that amines and their derivatives undergo photoinduced electron transfer reactions.^{29,36,41–43} This process results in the formation of aminium radicals (cation radicals of amines), that preferably form α -aminoalkyl radicals, via deprotonation at an α -carbon, which can subsequently react, for instance, with olefinic substrates. The preference for hydrogen abstraction follows the order of tertiary > secondary > primary > aromatic amines, provided no steric hindrance is involved.^{44,45} The low preference of aromatic amines to abstract a hydrogen in α -position thus explains why all attempts to carry out a photoRDRP with aromatic ligands such as 2,2'-bipyridine

remained unsuccessful.¹⁷ It has been previously reported that esters can act as electron acceptors with amines as electron donors to form ion pairs when irradiated in the presence of each other. Interactions between tertiary amines and carbonyl compounds in the ground state can lead to formation of unstable complexes.⁴⁶ It is noted that similar interactions cannot be excluded in the present case. It is also possible that excitation of the CuBr₂/Me₆TREN complex can result in reduction with subsequent activation of alkyl bromide. This alternative mechanism, as suggested by a referee, is also consistent with some of the data.

UV–Vis Measurements during PhotoRDRP. In the recent publications of Anastasaki et al.¹⁷ and Matyjaszewski and co-workers,²⁰ UV–vis spectroscopic analysis of the photoRDRP reaction mixture before and after irradiation served as key supporting data for the mechanistic investigations. Thereby, the decreasing absorption of the CuBr₂/Me₆TREN complex in the range of 600–1000 nm after the irradiation was interpreted as an evidence for its reduction toward CuBr/Me₆TREN. However, the absorption spectrum of CuBr/Me₆TREN in DMSO was not reported. We carried out similar UV–vis measurements (see Supporting Information Figure S5) for a complete photoRDRP mixture, prior to and after laser irradiation, and indeed, we found a decrease in the absorption in the range of 600–800 nm arising from the d⁹ d–d transition of Cu(II). For the solution from mixing the lower oxidation state CuBr with Me₆TREN, we observe three absorption maxima: one in the 600–800 nm range as well as two for shorter wavelengths (250–350 and 400–500 nm). Compared to CuBr₂/Me₆TREN, the absorption maxima in the ranges of 600–800 and 250–350 nm are shifted toward shorter wavelengths. The absorption maximum of CuBr/Me₆TREN at 400–500 nm does not appear for CuBr₂/Me₆TREN and could therefore be employed for the detection of the lower oxidation state complex. However, in the work of Matyjaszewski and co-workers,²⁰ this absorption band is not visible for samples irradiated for different times. Yet, in the studies of Anastasaki et al.,¹⁷ the increase of the absorption in the 400–500 nm range for irradiated samples is detected. Therefore, due to apparent experimental inconsistencies which possibly arise from different low level impurities between laboratories, the absorption of the photoRDRP solution before and after the irradiation has certain limitations for conclusive mechanistic investigations. Since the CuBr/Me₆TREN species is highly sensitive toward oxygen, demonstrated by the change in UV–vis absorption of CuBr₂/Me₆TREN after a short time period (see Supporting Information Figure S5), the procedure of the UV–vis measurement appears to be somewhat unreliable and needs to be supported by additional information.

CONCLUSIONS

We have investigated the mechanism of photoRDRP via pulsed-laser polymerization and high resolution mass spectrometry, an approach that, in comparison to previous reports, allows for the unambiguous identification of the initiating species and their interaction within the reaction mixture. We found that the initiation of the polymerization proceeds via the UV light-induced C–Br bond scission of the initiator, providing radicals that can propagate as well as react with copper(II) species that were present at the beginning. The generation of copper(I) species occurs via the electron transfer reaction between (UV light-) excited amine ligand species and copper(II) moieties. In addition, the copper(II) complex,

excited by UV light, is expected to be quenched by free ligand forming the corresponding copper(I) complex and the ligand as an amine radical cation. The ligand therefore plays an important role as a reducing agent. However, next to the ligand, other species promote the generation of copper(I) species as well, such as alkyl and bromine radicals. In conclusion, the mechanism of photoRDRP is a complex interaction between UV light and the typical reagents used including initiator, ligand, and copper(II) bromide.

■ ASSOCIATED CONTENT

Supporting Information

Detailed descriptions of experimental and analytical procedures and supplementary figures. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.5b03048.

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Notes

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■ REFERENCES

- (1) Matyjaszewski, K. *Macromolecules* **2012**, *45*, 4015.
- (2) Nicolas, J.; Guillauneuf, Y.; Lefay, C.; Bertin, D.; Gignes, D.; Charleux, B. *Prog. Polym. Sci.* **2013**, *38*, 63.
- (3) Barner-Kowollik, C. In *Handbook of RAFT Polymerization*; Wiley-VCH Verlag GmbH & Co. KGaA: Weinheim, 2008; p 1.
- (4) Percec, V.; Guliashev, T.; Ladislav, J. S.; Wistrand, A.; Stjernedahl, A.; Sienkowska, M. J.; Monteiro, M. J.; Sahoo, S. *J. Am. Chem. Soc.* **2006**, *128*, 14156.
- (5) Percec, V.; Popov, A. V.; Ramirez-Castillo, E.; Monteiro, M.; Barboiu, B.; Weichold, O.; Asandei, A. D.; Mitchell, C. M. *J. Am. Chem. Soc.* **2002**, *124*, 4940.
- (6) Haehnel, A. P.; Fleischmann, S.; Hesse, P.; Hungenberg, K.-D.; Barner-Kowollik, C. *Makromol. React. Eng.* **2013**, *7*, 8.
- (7) Anastasaki, A.; Waldron, C.; Wilson, P.; McHale, R.; Haddleton, D. M. *Polym. Chem.* **2013**, *4*, 2672.
- (8) Konkolewicz, D.; Wang, Y.; Zhong, M.; Kryszewski, P.; Isse, A. A.; Gennaro, A.; Matyjaszewski, K. *Macromolecules* **2013**, *46*, 8749.
- (9) Jakubowski, W.; Matyjaszewski, K. *Angew. Chem., Int. Ed.* **2006**, *45*, 4482.
- (10) Pintauer, T.; Matyjaszewski, K. *Chem. Soc. Rev.* **2008**, *37*, 1087.
- (11) Siegwart, D. J.; Oh, J. K.; Matyjaszewski, K. *Prog. Polym. Sci.* **2012**, *37*, 18.
- (12) Magenau, A. J. D.; Strandwitz, N. C.; Gennaro, A.; Matyjaszewski, K. *Science* **2011**, *332*, 81.
- (13) Magenau, A. J. D.; Bortolamei, N.; Frick, E.; Park, S.; Gennaro, A.; Matyjaszewski, K. *Macromolecules* **2013**, *46*, 4346.
- (14) Konkolewicz, D.; Magenau, A. J. D.; Averick, S. E.; Simakova, A.; He, H.; Matyjaszewski, K. *Macromolecules* **2012**, *45*, 4461.
- (15) Mosnáček, J.; Ilčíková, M. *Macromolecules* **2012**, *45*, 5859.
- (16) Tasdelen, M. A.; Uygun, M.; Yagci, Y. *Makromol. Rapid Commun.* **2011**, *32*, 58.
- (17) Anastasaki, A.; Nikolaou, V.; Zhang, Q.; Burns, J.; Samanta, S. R.; Waldron, C.; Haddleton, A. J.; McHale, R.; Fox, D.; Percec, V.; Wilson, P.; Haddleton, D. M. *J. Am. Chem. Soc.* **2013**, *136*, 1141.
- (18) Guan, Z.; Smart, B. *Macromolecules* **2000**, *33*, 6904.
- (19) Konkolewicz, D.; Schröder, K.; Buback, J.; Bernhard, S.; Matyjaszewski, K. *ACS Macro Lett.* **2012**, *1*, 1219.
- (20) Ribelli, T. G.; Konkolewicz, D.; Bernhard, S.; Matyjaszewski, K. *J. Am. Chem. Soc.* **2014**, *136*, 13303.
- (21) Dadashi-Silab, S.; Atilla Tasdelen, M.; Yagci, Y. *J. Polym. Sci., Part A: Polym. Chem.* **2014**, *52*, 2878.
- (22) Fors, B. P.; Hawker, C. J. *Angew. Chem., Int. Ed.* **2012**, *51*, 8850.
- (23) Treat, N. J.; Fors, B. P.; Kramer, J. W.; Christianson, M.; Chiu, C.-Y.; Alaniz, J. R. d.; Hawker, C. J. *ACS Macro Lett.* **2014**, *3*, 580.
- (24) Xu, J.; Jung, K.; Atme, A.; Shanmugam, S.; Boyer, C. *J. Am. Chem. Soc.* **2014**, *136*, 5508.
- (25) Shanmugam, S.; Xu, J.; Boyer, C. *Macromolecules* **2014**, *47*, 4930.
- (26) Xu, J.; Jung, K.; Boyer, C. *Macromolecules* **2014**, *47*, 4217.
- (27) Shanmugam, S.; Xu, J.; Boyer, C. *Chem. Sci.* **2015**, *6*, 1341.
- (28) Treat, N. J.; Sprafke, H.; Kramer, J. W.; Clark, P. G.; Barton, B. E.; Read de Alaniz, J.; Fors, B. P.; Hawker, C. J. *J. Am. Chem. Soc.* **2014**, *136*, 16096.
- (29) Xu, J.; Shanmugam, S.; Duong, H. T.; Boyer, C. *Polym. Chem.* **2015**, DOI: 10.1039/c4py01317d.
- (30) Mosnacek, J.; Eckstein-Andicsova, A.; Borska, K. *Polym. Chem.* **2015**, *6*, 2523.
- (31) Wenn, B.; Conradi, M.; Carreiras, A. D.; Haddleton, D. M.; Junkers, T. *Polym. Chem.* **2014**, *5*, 3053.
- (32) Olaj, O. F.; Bitai, I.; Hinkelmann, F. *Makromol. Chem.* **1987**, *188*, 1689.
- (33) Voll, D.; Junkers, T.; Barner-Kowollik, C. *J. Polym. Sci., Part A: Polym. Chem.* **2012**, *50*, 2739.
- (34) Frick, E.; Ernst, H. A.; Voll, D.; Wolf, T. J. A.; Unterreiner, A.-N.; Barner-Kowollik, C. *Polym. Chem.* **2014**, *5*, 5053.
- (35) Gies, A. P. In *Mass Spectrometry in Polymer Chemistry*; Wiley-VCH Verlag GmbH & Co. KGaA: Weinheim, 2011; p 33.
- (36) Kumar, J. S. D.; Das, S. *Res. Chem. Intermed.* **1997**, *23*, 755.
- (37) Hu, Q.; Noll, R. J.; Li, H.; Makarov, A.; Hardman, M.; Graham Cooks, R. *J. Mass Spectrom.* **2005**, *40*, 430.
- (38) Yang, Q.; Dumur, F.; Morlet-Savary, F.; Poly, J.; Lalevée, J. *Macromolecules* **2015**, *48*, 1972.
- (39) Fischer, H. *Macromolecules* **1997**, *30*, 5666.
- (40) Fischer, H. *Chem. Rev.* **2001**, *101*, 3581.
- (41) Das, S.; Suresh, V. In *Electron Transfer in Chemistry*; Wiley-VCH Verlag GmbH: Weinheim, 2008; p 379.
- (42) Julliard, M.; Chanon, M. *Chem. Rev.* **1983**, *83*, 425.
- (43) Kavarnos, G. J.; Turro, N. J. *Chem. Rev.* **1986**, *86*, 401.
- (44) Chow, Y. L.; Danen, W. C.; Nelsen, S. F.; Rosenblatt, D. H. *Chem. Rev.* **1978**, *78*, 243.
- (45) Lewis, F. D.; Crompton, E. M. In *CRC Handbook of Organic Photochemistry and Photobiology*, 2nd ed.; CRC Press: Boca Raton, FL, 2003; Vols. 1 & 2.
- (46) Wheeler, O. H.; Levy, E. M. *Can. J. Chem.* **1959**, *37*, 1727.