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Toward Electrochemically Mediated Reversible Addition−Fragmentation Chain-Transfer (*e*RAFT) Polymerization: Can Propagating Radicals Be Efficiently Electrogenerated from RAFT Agents?

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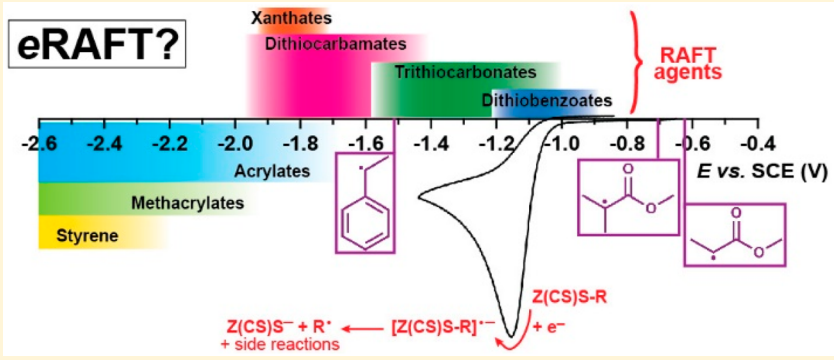
Supporting Information



ABSTRACT: Electrochemistry provides easily tunable parameters for the preparation of well-defined polymers in a spatiotemporal controlled manner under mild conditions. This work discusses the requisites for an electrochemically mediated reversible addition−fragmentation chain-transfer (*e*RAFT) polymerization, in which electrochemical stimuli are used to reduce the RAFT agent, either directly or in the presence of a mediator. The redox properties of several RAFT agents were investigated by cyclic voltammetry and correlated to their structures. The direct electrolysis of RAFT agents in the presence of a monomer caused the loss of RAFT agents, thus leading to uncontrolled polymerizations. These issues could partially be overcome by using a mediator that shuttles the electrons from the electrode to the RAFT agent in solution. Several compounds were tested to define the characteristics of suitable mediators.

INTRODUCTION

Biological systems are capable of precisely and reversibly controlling biopolymerization processes. The observation of natural systems has prompted polymer scientists to develop new techniques for the preparation of high-value polymer-based materials designed for a variety of advanced applications. However, further improvements rely on the ability to exert spatial and temporal control over polymerizations, mirroring natural processes.[1]

Reversible deactivation radical polymerization (RDRP) techniques are based on the intermittent deactivation of polymer chains and allow for the synthesis of (co)polymers with well-defined architectures and precise functionalities. Besides giving access to a wide range of postpolymerization modifications, the preservation of chain-end functionalities is crucial for temporal control. Indeed, if a negligible amount of chain end is lost, external stimuli can be applied to switch the system between "on" and "off" states, thus halting and restarting the polymerization on-demand.[2]

Several external stimuli have been successfully applied to RDRPs, including chemical,[3] photochemical,[4−7] electrochemical,[8−10] and mechanical means.[11−15] These approaches allow for milder reaction conditions and improved control. In particular, the electrochemical regulation offers unique opportunities, such as readily tunable parameters and suitable tools for simultaneously triggering and monitoring the process.[10] In addition, it represents an environmentally friendly approach, which is of increasing industrial interest.[9]

Electrochemically mediated atom transfer radical polymerization (*e*ATRP) was the first technique to effectively combine controlled radical polymerizations with electrochemistry.[8] The ATRP catalyst is a Cu complex; in the Cu^{I} oxidation state it activates the initiator or the dormant chains. The activation step results in the oxidation of the catalyst, thereby generating a Cu^{II} complex that deactivates the propagating radicals.

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Electrochemical tools (i.e., potential and current) were applied to alter the molar ratio of Cu^{I} and Cu^{II} species, thus affecting the polymerization rate and even halting and (re)starting the ATRP on-demand.[8] Moreover, *e*ATRP is a versatile process that has been used for different monomers[16] in water,[17,18] acidic media,[19] ionic liquids,[20] and dispersed media[21,22] and for the modification of surfaces.[23]

Importantly, electrochemical tools provided other advantages to ATRP, including determination of ATRP parameters[24] and in-situ monitoring of the extent of radical termination and stability of the catalysts,[19] allowing for the prediction and rationalization of reaction outcomes. These benefits apply to any process that involves an electron transfer (ET) step, including polymerization techniques based on the use of (organic) photoredox catalysts.[25−27]

A growing interest in electrochemistry[28] has led to the development of electrochemically mediated cationic polymerization,[29] electrochemically switchable ring-opening polymerization,[30] and a few different approaches for electrochemically mediated reversible addition−fragmentation chain-transfer (*e*RAFT) polymerization[31−33] and synergic *e*ATRP/RAFT.[34] However, the role of electrochemistry in these techniques, particularly in RAFT polymerization, is not as straightforward as in the case of ATRP.

The RAFT polymerization is based on the reversible chain transfer of polymer chains, regulated by a chain transfer agent (CTA, or RAFT agent).[35−37] The versatility and success of this technique greatly increased due to the use of external stimuli, primarily light,[38] via either the photoiniferter mechanism[39−41] or the photoinduced electron/energy transfer (PET)-RAFT mechanism.[5,42,43] In contrast, the direct application of electrochemical stimuli to traditional RAFT systems did not yield any polymer.[31] It was proposed that the electrochemical reduction of a CTA formed fragments that were further reduced to anions. To circumvent this issue, the electrochemical stimuli were instead employed to reduce externally added radical sources under mild conditions, obtaining controlled *e*RAFT polymerizations. Alternatively, Cu^{II} complexes were electrochemically reduced to Cu^{I} species that generated radicals by activating a CTA, which acted as an alkyl pseudohalide in an *e*ATRP process.[44]

These initial observations on the electrochemical reactivity of RAFT agents were limited to few CTAs. Still, little is known about the redox properties of RAFT agents. Therefore, this work investigates the feasibility of *e*RAFT via electroreduction of CTAs by defining the requirements and the obstacles of this process. The redox properties of several RAFT agents were analyzed by cyclic voltammetry (CV) and correlated to their structural features. The reduction potentials of CTAs were compared to the reduction potentials of common monomers and their corresponding radicals. This allowed to identify CTA−monomer couples that enabled to apply a potential (E_{app}) that would not affect the propagating radicals.

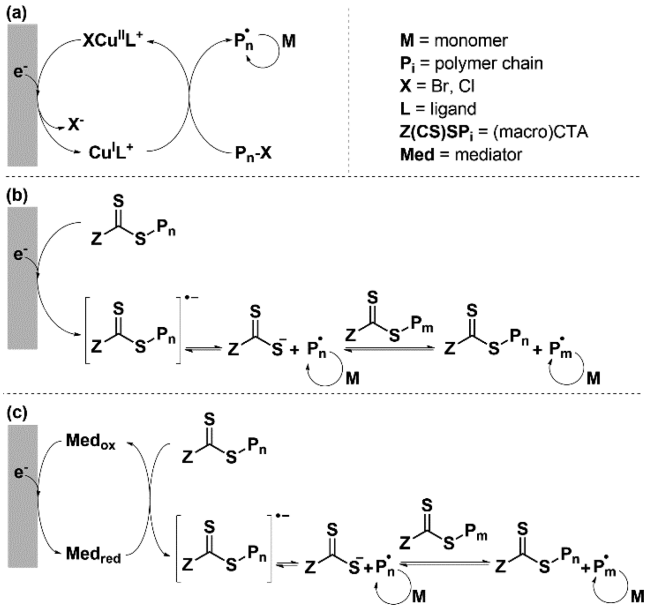
Nevertheless, the electroreduction of the CTAs at the electrode irreversibly consumed the CTAs, and uncontrolled polymerizations were obtained. Therefore, we moved from a direct to a mediated electrolysis by introducing a "mediator" species that was reduced at the electrode and then reacted with the CTAs in solution.[45] The characteristics of suitable mediators for *e*RAFT are discussed in the last part of this work. By employing tetraphenylporphyrin (TPP) as a mediator, the consumption of CTAs during *e*RAFT polymerizations was partially prevented.

CVs recorded before and after electrolysis of RAFT agents and conventional RAFT polymerizations allowed us to assess the stability of the (macro)CTAs. On one hand, this shows that the properties of CTAs and their fate during polymerizations can be assessed by electrochemical tools. On the other hand, these studies confirmed that the CTA is irreversibly consumed when an electrochemical stimulus is applied to the system. The use of a mediator could mitigate the problem. This work provides the foundation for the identification of effective mediators and operating conditions for an *e*RAFT polymerization.

RESULTS AND DISCUSSION

The mechanism of *e*ATRP and two approaches for an *e*RAFT polymerization are compared in Scheme 1. In *e*ATRP, the Cu

Scheme 1. Mechanism of Electrochemically Mediated ATRP (a) and Envisioned Mechanisms of Electrochemically Mediated RAFT via Direct (b) and Mediated (c) Electrolysis of a CTA



catalyst is a "mediator" that shuttles the electron from the electrode to the substrate (i.e., dormant chain) in solution, thus converting a heterogeneous ET to a homogeneous one (Scheme 1a). Importantly, the reduction of Cu catalysts occurs at more positive potentials than the reduction of the other species involved in the process.[24,46] Therefore, when a potential E_{app} is applied to reduce the mediator and start the polymerization, the substrates are electrochemically stable.

In *e*RAFT, conventional radical initiators are replaced with the electrochemical stimulus. Indeed, the electroreduction of a CTA at the electrode surface generates radical anions that further decompose,[31] thereby providing radicals that undergo the classical RAFT process in solution (Scheme 1b). This approach can be described as a direct electrolysis of RAFT agents.

An alternative approach consists in introducing a mediator that is electroreduced at the electrode surface and then reduces the CTA in solution (Scheme 1c). This method can be defined as a mediated electrolysis of a CTA. A more detailed discussion of these approaches is available in the Supporting Information.

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To efficiently apply the electrochemical stimulus, the redox properties of RAFT agents and the other components of a RAFT polymerization need to be investigated. The RAFT agents analyzed in this work are reported in Figure 1.

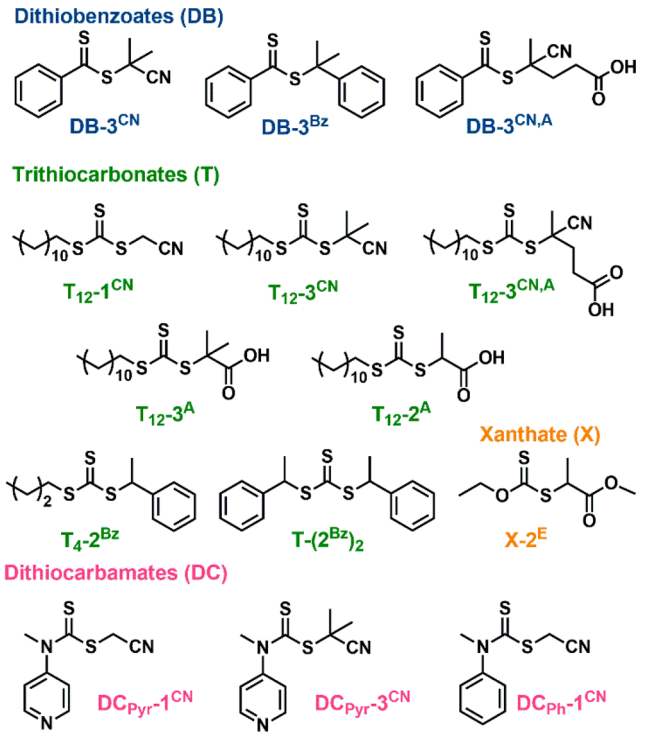

Figure 1. Molecular structures of RAFT agents analyzed in this work.

A unified nomenclature was used to identify the CTAs; considering their general structure as Z(CS)SR, the RAFT agents were written with a first group of characters identifying the Z group, followed by a dash, followed by a second group of characters identifying the R group (i.e., Z-R). The Z groups are subdivided into four categories, namely dithiobenzoates (DB), trithiocarbonates (T), dithiocarbamates (DC), and xanthates (X). For trithiocarbonates, the subscripts T_4 and T_{12} indicate a Z group with a butyl or a dodecyl alkyl chain, respectively. For dithiocarbamates, DC_{Pyr} and DC_{Ph} indicate the presence of a pyridyl or a phenyl ring, respectively. Concerning the R group, the numbers 1, 2, and 3 identify primary, secondary, and tertiary structures. Then, a superscript abbreviation indicates the nature of functional groups present in the R fragment: CN = nitrile, Bz = benzyl, A = acidic carboxyl group, and E = ester.

Redox Properties of RAFT Agents. The literature related to RAFT and PET RAFT polymerizations provides values of the reduction potentials of very few CTAs.[5,43,47] Beyond the field of RAFT polymerization, in-depth studies on the electrochemistry of some dithiobenzoates and trithiocarbonates were conducted by Lund et al.,[48−50] with the aim of defining the mechanism and products of the electroreduction of these compounds. They typically observed the electrochemical generation of short-lived radical anions, which were rapidly subjected to some chemical processes, in an overall complicated series of reactions leading to multiple products.

In this work, we investigated the redox properties of several common RAFT agents (Figure 1), including dithiobenzoates, trithiocarbonates, dithiocarbamates, and a xanthate. DMF was selected as solvent, although some compounds were also studied in CH_3CN for comparison. A glassy carbon (GC) disk was used as working electrode, which showed well-reproducible responses. Conversely, a Pt disk gave irreproducible signals (Figure S1), likely due to the adsorption of some electrogenerated compounds on the Pt surface, as suggested by the decrease in the current recorded over successive scans.

CV of analyzed RAFT agents exhibited the general pattern shown in Figure 2. The main signal of interest is the cathodic

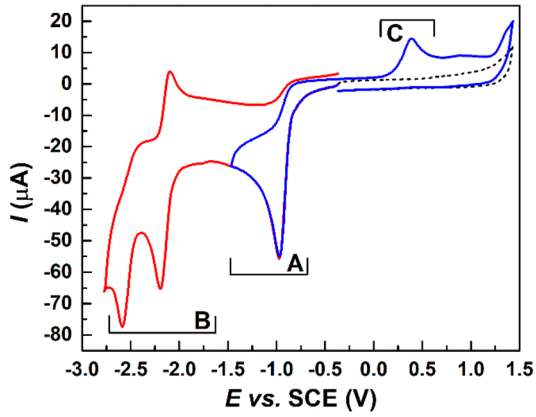

Figure 2. Cyclic voltammetry of 2×10^{-3} M **DB-3^{CN,A}** in DMF + 0.1 M Et_4NBF_4, recorded on a GC disk at scan rate = 0.2 V s^{-1} and T = 25 °C. The letters A, B, and C denote the regions described in the text and common to all RAFT agents. The dashed line represents an oxidative scan not preceded by the reduction of the CTA, i.e., with initial potential −0.5 V vs SCE.

peak in region A, which is ascribed to the reduction of the CTA to the corresponding radical anion (eq 1).

$$Z(CS)SR + e^- \rightleftharpoons [Z(CS)SR]^{\bullet -} \quad (1)$$

By extending the scanned potential range to more negative values, we observed several other voltammetric peaks for all compounds (region B), suggesting that the overall reduction mechanism is complicated and involves various reactions and products.

Figure 3 shows the CV of region A for each CTA. All compounds, with the exception of **T_{12}-2^A** and **T_{12}-3^A**, exhibited one irreversible reduction peak at any tested scan rate (0.02−20 V s^{-1}). The irreversibility of the reduction process indicates that one or more chemical reactions follow the ET process, thereby preventing the observation of the oxidation reaction for $[Z(CS)SR]^{\bullet -}$ when the scan direction is reversed. In other words, the electrogenerated radical anion is not stable in the time scale of the CV, and therefore it cannot be reoxidized to the initial compound.

T_{12}-2^A and **T_{12}-3^A** exhibited two reduction peaks (Figure 3c) that were irreversible at any tested scan rate. The presence of two close peaks is likely due to a "father−son" interaction (i.e., the reaction of an electrogenerated product with the initial compound), specifically a self-protonation reaction.[51] Indeed, the electrogenerated radical anion is rapidly protonated by the carboxylic group of the CTA molecule, and the resulting radical is further reduced at the electrode. Conversely, **DB-3^{CN,A}** and **T_{12}-3^{CN,A}** exhibited only one reduction peak because the carboxylic group was too distant from the Z(CS)S-unit to affect the voltammetric response.

For each RAFT agent, when the scan was reversed and extended to positive potential values, an anodic irreversible

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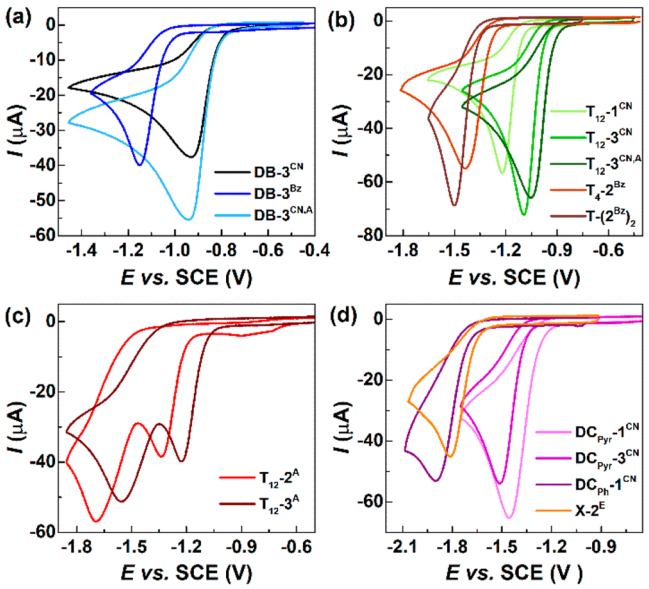

Figure 3. Cyclic voltammetry of analyzed (a) dithiobenzoates, (b, c) trithiocarbonates, and (d) dithiocarbamates and xanthate RAFT agents, recorded in DMF + 0.1 M Et_4NBF_4 on a GC disk, 2×10^{-3} M CTA, scan rate = 0.2 V s^{-1}, and T = 25 °C.

peak was observed, in the potential range 0.3−0.5 V vs SCE (region C in Figure 2). This indicates that one product of the reduction (and following reactions) is stable, and it is oxidized in that potential range. Although it was not possible to clearly identify this species, the oxidation of some thiolates (RS^-) to disulfides was previously reported to occur at a similar potential range.[52] Moreover, Lund et al. identified the presence of thiolates among the products of electrolysis of some dithiobenzoates and trithiocarbonates.[48,49]

Nevertheless, the oxidation peak in region C was observed only if that potential range was scanned after reducing the CTA (Figure 2). Conversely, RAFT agents used for the cationic polymerization of vinyl ethers showed irreversible oxidation peaks at potential values ranging from 0.5 to 1.2 V vs SCE.[27,29]

The irreversibility of the cathodic peak(s) in region A prevents the determination of the standard reduction potential $E^{\ominus}$ (which is generally measured from the semisum of the anodic and cathodic peak potentials). Therefore, the cathodic peak potential, E_{pc}, of each RAFT agent is reported in Table 1. The corresponding onset potentials of reduction, E_{onset}, measured with the tangents method (Figure S2) are listed in Table S1. E_{pc} values depended on the nature of the Z group, with E_{pc} decreasing in the following order: dithiobenzoates > trithiocarbonates > dithiocarbamates ∼ xanthates. For the same Z group, E_{pc} varied with the nature of the leaving group R: more positive E_{pc} values were observed for tertiary R groups, followed by secondary and then primary R groups. This order reflects the stability of generated radicals, with more stabilized radicals facilitating the reduction of the initial compound. Furthermore, electron-withdrawing substituents (e.g., −CN and −COOH) increase the stability of generated radicals, thus shifting E_{pc} to less negative values. A similar behavior was reported for alkyl halides used as ATRP initiators.[53,54]

The presence of a fast chemical reaction following the ET step typically determines a shift in the reduction potential of the substrate toward more positive values as the concentration of substrate increases. For some dithiobenzoates, Lund et al. observed that $dE_{pc}/d\log C = -0.02$ V decade^{-1}, which is compatible with a second-order reaction (most likely a dimerization) following the electron transfer process.[48] Conversely, this trend was not observed for the compounds analyzed in this work, and therefore their radical anions do not appear to decompose via second-order reactions. Instead, some CTAs exhibited a shift of E_{pc} values of 0.01−0.02 V toward more negative potentials when increasing the concentration from 3×10^{-4} to 2×10^{-3} M. In addition, in mixtures of 50 vol % monomer in DMF, E_{pc} values were observed to slightly shift toward more negative values, if compared to pure solvent. Furthermore, E_{pc} shifted to more positive values by increasing the temperature.

E_{pc} values measured in CH_3CN were generally more negative than in DMF (Table 1). In addition, E_{pc} values measured in CH_3CN on a GC disk were generally more positive than on a Pt disk (by considering the first scanning cycle on a clean Pt surface). The reduction of $\mathbf{T_{12}\text{-}1^{CN}}$ in CH_3CN was also studied at both silver and gold working electrodes (Figure S3). E_{pc} of $\mathbf{T_{12}\text{-}1^{CN}}$ became more negative

Table 1. Peak Potential Values for the Reduction of Analyzed RAFT Agents, at T = 25 °C[a]

RAFT agent		E_{pc} (V vs SCE)		
		GC in DMF[b]	GC in CH_3CN[c]	Pt in CH_3CN[c]
dithiobenzoates	$\mathbf{DB\text{-}3^{CN}}$	−1.000	−1.040	−0.87[d]
	$\mathbf{DB\text{-}3^{Bz}}$	−1.150	−1.172	−1.193
	$\mathbf{DB\text{-}3^{CN,A}}$	−0.940	−1.003	−1.192
trithiocarbonates	$\mathbf{T_{12}\text{-}1^{CN}}$	−1.220	−1.293	−1.453
	$\mathbf{T_{12}\text{-}3^{CN}}$	−1.092	−1.279	−1.398
	$\mathbf{T_{12}\text{-}3^{CN,A}}$	−1.050		
	$\mathbf{T_{12}\text{-}2^{A}}$	−1.338 (−1.691)		
	$\mathbf{T_{12}\text{-}3^{A}}$	−1.228 (−1.556)	−1.205 (−1.550)	−1.246 (−1.796)
	$\mathbf{T_4\text{-}2^{Bz}}$	−1.500	−1.585	−1.690
	$\mathbf{T\text{-}(2^{Bz})_2}$	−1.437	−1.548	−1.618
dithiocarbamates	$\mathbf{DC_{Pyr}\text{-}1^{CN}}$	−1.513		
	$\mathbf{DC_{Pyr}\text{-}3^{CN}}$	−1.455		
	$\mathbf{DC_{Ph}\text{-}1^{CN}}$	−1.898		
xanthate	$\mathbf{X\text{-}2^{E}}$	−1.812		

[a]0.1 M Et_4NBF_4 was used as supporting electrolyte; the scan rate was 0.2 V s^{-1}. [b]2×10^{-3} M CTA. [c]1×10^{-3} M CTA. [d]3×10^{-4} M CTA.

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in the order GC > Pt > Au > Ag. This difference is likely due to the interaction of sulfur atoms with Au, Ag, and Pt surfaces.[55] Regardless the electrode material, the cathodic peak was irreversible at the investigated scan rate. It should be noticed that, among the tested electrode materials, only GC was not passivated by the reduction of the CTAs.

The E_{pc} values in Table 1 are in agreement with the values measured by Christmann et al. for similar RAFT agents.[47] However, Xu et al. reported ∼0.8 V more positive potential for **DB-3**^{CN,A} in CH_3CN on a Pt electrode,[5] whereas Sang et al. reported ∼1 and 1.1 V more positive potentials for **DB-3**^{CN} and **DB-3**^{CN,A}, respectively, in CH_3CN on a Pt electrode.[32] Moreover, the CVs showed by Xu et al. and Sang et al. exhibited a quasi-reversible shape.[5,32] These discrepancies may arise from the presence of reducible impurities in the RAFT agents as well as from the poor reproducibility of measurements on the Pt surface.

A complete determination of the mechanism and products of the electroreduction of the analyzed compounds is beyond the scope of this work; however, we attempted to collect some mechanistic insights. The addition of 1−5 equiv of acetic acid to a RAFT agent in DMF generally resulted in increased current for the peak in region A, whereas peaks in region B exhibited more marked changes in terms of both current and potential (Figure S4). In fact, if radical anions or other electrogenerated products react with the initial CTA (i.e., father−son or even grandfather−grandson interactions), the current observed in the presence of the acid is higher than in the case of no added acid.[51,56] This is because the acid protonates all radical anions and/or carbanions, thus preventing their reaction with the original CTA.

Bulk electrolysis of the CTAs can give further information about their reactivity upon reduction. The electrolysis of **DB-3**^{CN}, **DB-3**^{CN,A}, **T**$_{12}$**-1**^{CN}, and **T**$_4$**-2**^{Bz} was performed in DMF, at room temperature, on a GC plate or reticulated vitreous carbon (RVC) electrode with large surface areas. Working and counter electrodes were placed in separated compartments. For each compound, the applied potential was $E_{app} = E_{pc}$ (Table 1). From the charge passed (Q) it was possible to calculate the number of electrons required to reduce one molecule of CTA by using Faraday's law of electrolysis (eq 2):

$$Q = \int_0^t I(t)\,\mathrm{d}t = zFn \tag{2}$$

in which F is the Faraday's constant, n is the number of moles of the substrate, and z is the number of electrons required for the redox process. Q was obtained from the recorded current (I) versus time (t) plot (Figure S5). One electron per molecule was consumed for the electrolysis of the analyzed CTAs. However, two electrons per molecule were consumed for the electrolysis of **DB-3**^{CN,A} in the presence of an excess of acetic acid (Figure S5b), thus supporting the occurrence of father−son reactions.

^{1}H NMR spectra of **T**$_4$**-2**^{Bz} before and after electrolysis showed the disappearance of the signal of the −CH group close to the thiocarbonylthio unit in the R fragment (Figure S6). This indicates that the reductive cleavage occurs at the C−S bond between the Z(CS)S unit and the R group, as proposed by DFT analysis.[57]

Finally, in the CVs recorded before, during, and after the electrolysis of **DB-3**^{CN}, **DB-3**^{CN,A}, and **T**$_4$**-2**^{Bz}, the oxidation peak in region C increased in intensity (Figures S7−S9), indicating that a stable compound was accumulated in solution during the electrolysis.

To summarize, the electrochemical reduction of RAFT agents is characterized by (i) the reductive cleavage of the Z(CS)S−R bond, (ii) a very short lifetime of generated radical anions, (iii) a complex reduction process, with electrogenerated products reacting with the initial compounds, and (iv) the accumulation during electrolysis of a new species with an oxidation potential in the range 0.3−0.5 V vs SCE.

Redox Properties of Common Monomers. Because the reduction of RAFT agents to radical anions occurs at relatively negative potentials (between −0.9 and −1.9 V vs SCE), it was necessary to evaluate the reduction potentials of commonly employed monomers. Cathodic peak and onset potential values for the reduction of acrylonitrile (AN), *n*-butyl acrylate (BA), methyl methacrylate (MMA), and styrene (STY) in DMF are reported in Table 2. E_{onset} was measured under typical polymerization conditions (50 vol % monomer). Other monomers with similar structures are expected to be reduced at similar potential values.

Table 2. Peak and Onset Potential Values for the Reduction of Common Monomers and Standard Reduction Potential of the Corresponding Radicals to Carbanions, in DMF, at T = 25 °C[a]

monomer	E_{pc}[b] (V vs SCE)	E_{onset}[c] (V vs SCE)	$E^{\ominus}_{radical}$[d] (V vs SCE)
AN	−2.17		−0.76
BA	−2.18	−1.74	−0.63[e]
MMA	−2.28	−1.97	−0.91
STY	−2.57	−2.23	−1.53

[a]0.1 M Et_4NBF_4 was used as supporting electrolyte; scan rate = 0.2 V s^{-1}. [b]See Figure S10. [c]50 vol % monomer, calculated through the tangent method. [d]From ref 58. [e]For methyl acrylate radical.

The E_{onset} of a monomer represents the lower limit of the potential window that is available for the *e*RAFT process. In fact, if $E_{app} < E_{onset}$, the monomer will be reduced, which can result in the uncontrolled grafting of polymers/oligomers onto the electrode surface. Therefore, it is required that E_{pc}(CTA) > E_{onset}(monomer) to electrochemically reduce a RAFT agent without affecting the monomer and the electrode surface. According to this criterion, **X-2**^{A} and **DC**$_{Ph}$**-1**^{CN} are not suitable for the *e*RAFT of acrylates via direct electrolysis of the CTA.

Redox Properties of Propagating Radicals. In RDRPs, the radical concentration is typically very low; however, the electrochemical regulation may cause an enhanced radical concentration in the proximity of the working electrode. Propagating radicals can be reduced to their respective carbanions, and this process is generally thermodynamically easier than the reduction of the corresponding monomer. Indeed, standard reduction potentials for relevant radicals ($E^{\ominus}_{radical}$) reported in the literature[53,58] are 1−1.5 V more positive than E_{pc} values of corresponding monomers (Table 2).

Alkyl radicals are typically reduced to carbanions at potentials close to E_{pc} of many RAFT agents. Therefore, this undesired reaction needs to be considered when selecting the CTA-monomer system. It was previously reported that no polymer was obtained when a potential $E_{app} = E_{pc}$(**DB-3**^{CN,A}) or $E_{app} = E_{pc}$(**T**$_{12}$**-3**^{A}) was applied to a mixture of MMA/DMF 1/1 in the presence of **DB-3**^{CN,A} or **T**$_{12}$**-3**^{A}, respectively.[31] In pure DMF, $E^{\ominus}_{radical}$(MMA) ≈ E_{pc}(**DB-3**^{CN,A}) > E_{pc}(**T**$_{12}$**-3**^{A}),

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Table 3. Electrochemically Mediated RAFT via Direct or Mediated Electrochemical Reduction of a RAFT Agent[a]

entry	M	CTA	mediator	[M]/[CTA]/[mediator]	T (°C)	E_{app}[b]	t (h)	conv (%)	$M_n \times 10^{-3}$	$M_{n,th} \times 10^{-3}$	$Đ$
1	STY	**DB-3^{Bz}**		500/1/0	80	$E_{pc,CTA}$	20	30	12.0	13.7	2.85
2	STY	**DB-3^{Bz}**		500/1/0	80	$E_{pc,CTA}$ + 0.06 V	20	45	18.7	20.6	2.43
3	STY	**DB-3^{Bz}**		500/1/0	80	$E_{pc,CTA}$ + 0.12 V	20	25	10.8	11.5	1.75
4	STY	**T$_4$-2^{Bz}**		200/1/0	80	$E_{pc,CTA}$ + 0.06 V	8	17	5.8	3.7	2.82
5	STY	**T-(2^{Bz})$_2$**		200/1/0	80	$E_{pc,CTA}$ + 0.12 V	8	14	1.3	1.6	1.81
6	BA	**T$_{12}$-2^{A}**	TPP	200/1/1	25	$E^{\ominus}_{TPP}$ + 0.06 V	6	17	3.4	3.8	1.22
7	BA	**T$_{12}$-2^{A}**	TPP	200/1/1	25		20				
8	BA	**T$_{12}$-2^{A}**	TPP	200/1/0.1	25	$E^{\ominus}_{TPP}$ + 0.06 V	6	10	2.0	2.4	1.19
9	BA	**T$_{12}$-3^{A}**	TPP	200/1/0.01	25	$E^{\ominus}_{TPP}$ + 0.06 V	6	12	2.1	2.8	1.16
10[c]	BA	**T$_{12}$-2^{A}**	TPP	2000/1/0.06	25	$E^{\ominus}_{TPP}$ − 0.06 V	6	18	46.5	41.9	1.39
11[c]	MA	**T$_{12}$-2^{A}**	TPP	2000/1/0.04	25	$E^{\ominus}_{TPP}$ − 0.06 V	6	13	22.9	17.2	1.27

[a]General conditions: 50 vol % monomer (M) in DMF + 0.1 M Et_4NBF_4, RVC working electrode. [b]Applied potential, measured under polymerization conditions (i.e., temperature and monomer/solvent 1/1 mixture). [c]DMSO was the solvent instead of DMF.

thus suggesting that if radicals were effectively generated in the vicinity of the electrode, they were reduced to carbanions.

According to $E^{\ominus}_{radical}$ values in Table 2, styryl radicals are the most difficult to reduce, and many dithiobenzoates and trithiocarbonates are reduced at more positive potentials. For these reasons, STY was selected as a monomer to attempt an *e*RAFT via direct electroreduction of dithiobenzoates and trithiocarbonates RAFT agents.

Analysis of *e*RAFT via Direct Electroreduction of RAFT Agents. Dithiobenzoates and trithiocarbonates are generally suitable CTAs for the conventional RAFT polymerization of STY.[36,58] Nevertheless, a further requirement for an *e*RAFT polymerization performed by applying a constant potential is that the reduction potential of the CTA does not change significantly after the substitution of the initial R group with a polymer chain. In essence, E_{pc} of the macro(CTA) ≈ E_{pc} of the relative CTA. This requirement is more easily fulfilled if the R group in the RAFT agent and the monomer have identical structures. In particular, RAFT agents with strong electron-withdrawing groups such as −CN and/or −COOH in the α-position to the Z(CS)S unit should be avoided because E_{pc} will significantly shift to more negative values immediately after the addition of a monomer molecule.

Among the analyzed compounds, only **DB-3^{Bz}**, **T$_4$-2^{Bz}**, and **T-(2^{Bz})$_2$** have suitable molecular structure, but E_{pc}(**T$_4$-2^{Bz}**) is very close to $E^{\ominus}_{radical}$(STY). In addition, the low reactivity of STY typically requires high reaction temperatures and long polymerization times.

First, the *e*RAFT polymerization of STY was attempted with **DB-3^{Bz}** as CTA, at T = 80 °C, target degree of polymerization (DP) 500, and three different values of E_{app}: E_{pc}, E_{pc} + 0.06 V, and E_{pc} + 0.12 V (Table 3, entries 1−3). Some polymer was observed at each applied potential, thus indicating that radicals were generated and not immediately electroreduced.

Faster polymerization was obtained at the intermediate potential E_{pc} + 0.06 V. However, the polymerizations were uncontrolled. Kinetic plots were not linear (reaching 25−45% conversion in 20 h), and the obtained polymers exhibited high dispersity ($Đ$) values (Figure S11), although the molecular weights (MWs) matched the theoretical values. The color of the solution became darker over the course of the electrolysis. Similar results were also obtained with **T$_4$-2^{Bz}** and **T-(2^{Bz})$_2$** as CTAs (Table 3, entries 4 and 5).

A control experiment showed that STY was able to self-initiate the polymerization at 80 °C in the absence of applied stimuli. The system reached 29% conversion in 20 h, yielding a polymer with low dispersity ($Đ$ = 1.06), though with a MW much lower than the theoretical value. The different results obtained for the electrochemically mediated polymerizations indicate that radicals were effectively generated through the electrochemical approach.

For comparison, a conventional RAFT polymerization of STY was performed with **T-(2^{Bz})$_2$** as RAFT agent and azobis(isobutyronitrile) (AIBN) as radical initiator; the system was analyzed by CV before and after the polymerization. The process reached 70% conversion in 8 h, with polymer MW matching the theoretical value, and $Đ$ = 1.3 (Figure S12). In contrast, the electrolysis of **T-(2^{Bz})$_2$** gave a polymer with broad MW distribution, and only 14% conversion was observed after 8h (Table 3, entry 5).

After the conventional RAFT polymerization, the reduction peak of **T-(2^{Bz})$_2$** in region A decreased in intensity due to the decrease in the diffusion coefficient of the (macro)CTA because of the attached polymer chain and the increase in solution viscosity (Figure 4a). The peak also slightly shifted to more negative potentials and split in two. In contrast, after the electrolysis of **T-(2^{Bz})$_2$**, no peak was present in region A (Figure 4b), indicating that the CTA was consumed. Moreover, a large anodic peak was observed in region C, in accordance with the electrolysis experiments conducted in the absence of monomer. A similar behavior was observed for each attempted *e*RAFT via direct electroreduction of CTA (Figure S13). This indicates that the application of an electrochemical potential caused the decomposition of CTAs, even for E_{app} > E_{pc}. Therefore, in the attempted *e*RAFT polymerizations radicals were effectively generated, but their propagation could not be controlled because CTAs were consumed during the processes.

Quest for Effective Mediators for the Electroreduction of RAFT Agents. One important advantage of mediated electrolysis versus direct electrolysis is that the reduction (or oxidation) of the mediator avoids possible side reactions occurring at the surface of the working electrode. The first requirement of a suitable mediator is that its standard reduction potential must be more positive than the reduction potential of the substrate (in the case of electroreduction), so that E_{app} can be adjusted to the potential of the mediator, thus leaving the substrate untouched.[45]

At the same time the difference between the potentials of the two species should be small to increase the rate of the homogeneous ET between them. Both the ET between electrode/mediator and mediator/substrate must be fast. A

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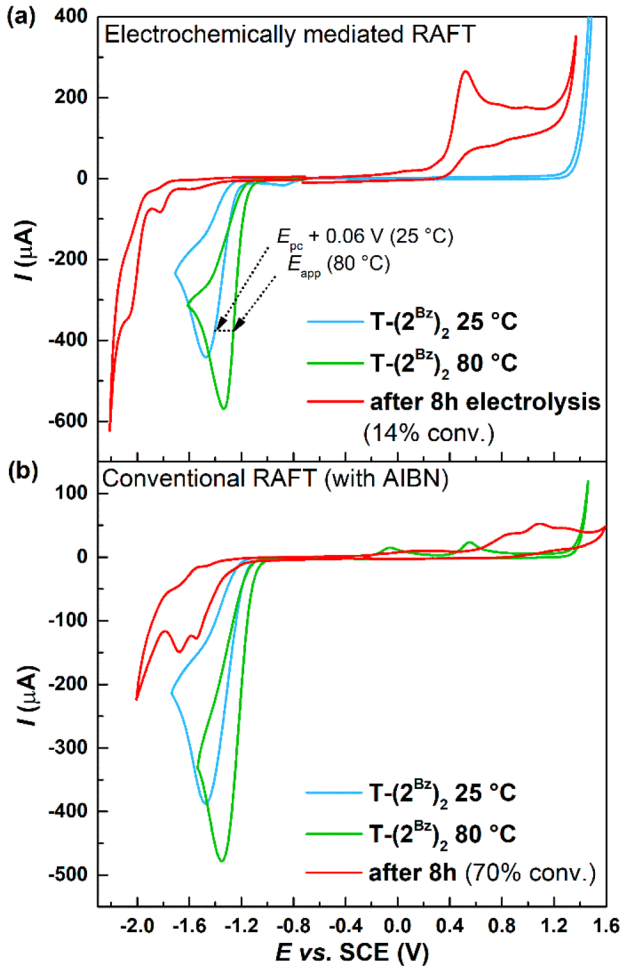

Figure 4. Comparison between CVs of **T-(2^{Bz})$_2$**, recorded before and after 8 h of (a) electrolysis (RVC electrode), and (b) conventional RAFT polymerization initiated by AIBN ([AIBN]/[**T-(2^{Bz})$_2$**] = 0.1). Conditions: 50 vol % STY in DMF + 0.1 M Et_4NBF_4, T = 80 °C, [STY]/[**T-(2^{Bz})$_2$**] = 200/1. CVs were recorded on a GC disk, at scan rate = 0.2 V s^{-1}. Reduction and oxidation were measured separately by changing the direction of the potential scan, starting from (a) −0.8 V vs SCE and (b) −0.3 V vs SCE.

second requirement is that the mediator should be inert to any process other than the ET.

Among the most common mediators for electroreduction reactions are aromatic hydrocarbons and transition metal complexes. Typical Cu complexes used as ATRP catalysts effectively activate dithiocarbamate CTAs, although this reaction proceeds by atom (or group) transfer and not by degenerative chain transfer.[44,60] Herein, we focused on organic mediators.

First, the *e*RAFT of STY (DP = 200, T = 80 °C) was repeated in the presence of an equimolar amount of CTA (**DB-3^{Bz}**) and mediator (3-nitrobenzonitrile, 3-NBN). The mediator showed a reversible voltammetric pattern in 50 vol % STY in DMF, with $E^{\ominus}$ = −0.911 V vs SCE at T = 25 °C. This potential is close to the reduction potential of **DB-3^{Bz}** (E_{pc} = −1.16 V vs SCE under identical conditions). The addition of the RAFT agent enhanced the cathodic peak of 3-NBN, while the anodic peak decreased, indicating that 3-NBN catalytically reduced **DB-3^{Bz}** (Figure S14a). Nevertheless, no polymer was obtained after 8 h of electrolysis at E_{app} = $E^{\ominus}_{3\text{-NBN}}$ + 0.06 V. CVs recorded after electrolysis showed that 3-NBN was preserved, but no catalytic signal was observed. Moreover, the oxidation peak in region C was present again (Figure S14b). Both of these observations point out that the CTA was destroyed during electrolysis, similarly to the case of direct electroreduction.

The process was repeated with **T$_4$-2^{Bz}** as CTA and an equimolar amount of 2-nitro-*m*-xylene as mediator (2-NX, $E^{\ominus}_{2\text{-NX}}$ = −1.275 V vs SCE in 50 vol % STY in DMF, at T = 25 °C, whereas E_{pc}(**T$_4$-2^{Bz}**) = −1.570 V vs SCE). The CV of 2-NX changed as described for 3-NBN after adding the CTA (Figure S15). However, the polymerization was uncontrolled, with almost identical results to the *e*RAFT performed on the same system but in the absence of a mediator.

One possible reason for the poor efficiency of these aromatic hydrocarbons as mediators is the presence of side reactions between mediators and substrates (eqs 3−6, D = mediator). Indeed, the radical anion generated by electroreduction of the aromatic hydrocarbon can couple with a radical fragment (eq 5) or reduce it to a carbanion (eq 6).

$$D + e^- \rightleftharpoons D^{\bullet -} \quad (3)$$

$$D^{\bullet -} + ZSCSR \rightleftharpoons D + ZSCS^- + R^{\bullet} \quad (4)$$

$$D^{\bullet -} + R^{\bullet} \rightarrow DR^- \quad (5)$$

$$D^{\bullet -} + R^{\bullet} \rightleftharpoons D + R^- \quad (6)$$

To minimize these unwanted reactions, one can consider the use of a mediator with a bulky and extensively conjugated structure, which should hamper the coupling reaction (eq 5). Another common strategy to decrease the extent of side reactions is to decrease the operational temperature. Because lower temperatures may dramatically slow down STY polymerization, further experiments were performed with BA, and tetraphenylporphyrin (TPP) was chosen as mediator. Complexes of TPP with transition metals effectively catalyzed PET-RAFT polymerizations.[61] Moreover, an electron donor/acceptor photoredox catalyst for the PET-RAFT of methyl acrylate (MA) was prepared by covalently attaching TPP to trithiocarbonates.[62]

The *e*RAFT of BA (DP = 200, T = 25 °C) was performed with equimolar amounts of TPP and **T$_{12}$-2^{A}**. TPP showed reversible voltammetric behavior, and $E^{\ominus}_{TPP}$ = −1.07 V vs SCE was measured in BA 50 vol % in DMF at T = 25 °C (Figure S16). By applying E_{app} = $E^{\ominus}_{TPP}$ + 0.06 V, a slow but controlled polymerization was obtained. After 6 h, the conversion reached 17% and the polymer showed low dispersity ($Đ$ = 1.22) and MW matching the theoretical value (Table 3, entry 6). It is likely that the high steric hindrance of TPP structure minimized the coupling between the radical anion of TPP and the generated radicals. A control experiment performed in the absence of electrochemical stimuli (Table 3, entry 7) showed no conversion after 20 h, indicating that the electroreduction was necessary to start the polymerization. It should be noted that the carboxylic group of **T$_{12}$-2^{A}** is stable at the selected E_{app} because carboxylic acids are typically reduced at potential values <−1.6 V vs SCE, whereas carboxylates are oxidized at E close to 1.5 V vs SCE.[63]

Typically, mediated electrolysis requires a catalytic amount of mediator because of the continuous (re)generation of the active species at the electrode surface. Indeed, when the amount of TPP was decreased 10 times, the polymerization was only slightly slower (Table 3, entry 8). Similar results were obtained with **T$_{12}$-3^{A}** as CTA and 100 times less TPP (Table 3,

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entry 9). PBA with higher MW and low $Đ$ was obtained by targeting higher DP (DP = 2000) in DMSO; comparable polymerization rate and control were observed for the *e*RAFT of MA under similar conditions (Table 3, entries 10 and 11).

However, CVs recorded for these systems after 6 h of electrolysis exhibited the previously described oxidation peak in region C, although it was much less intense than in the case of direct electrolysis (Figure S16). Importantly, the reduction signal of the CTA (region A) was still present after the electrolysis. Therefore, only partial decomposition of the CTA occurred in the presence of the mediator. In contrast, CVs recorded after a PET-RAFT polymerization of BA with $\mathbf{T_4}$-$\mathbf{2^A}$ as CTA and *fac*-$Ir^{III}(ppy)_3$ as photoredox catalyst (i.e., mediator of the photoinduced polymerization) showed the reduction signal of the macro(CTA) in region A and no peaks in region C (Figure S17). The PET-RAFT polymerization was well-controlled, reaching 90% conversion in 1.5 h (Figure S18).

Although TPP mitigated the negative effect observed in the case of direct electrolysis of CTAs, more effective mediators are necessary to promote faster *e*RAFT polymerizations while completely prevent the CTA decomposition. Based on the presented analysis, compounds with bulky structures and $E^{\ominus} \gtrsim E^{\ominus}_{TPP}$ should be tested, in combination with other trithiocarbonates or dithiobenzoates as RAFT agents. Recently, Sang et al. proposed the use of a redox-active coenzyme, the nicotinamide adenine dinucleotide (NADH), as an electroredox catalyst for RAFT polymerizations.[32] The electrochemical reduction of NADH to NAD^+ was showed to trigger the *e*RAFT of various monomers. However, we could not reproduce these results and systematically obtained no monomer conversion with this approach. One possible explanation is that the NADH molecule is not sufficiently hindered to prevent coupling with generated radicals.

CONCLUSIONS

The electroreduction of several RAFT agents has been studied under various conditions to define the requirements and limitations of an *e*RAFT polymerization. The redox properties of several commonly used CTAs were explored by cyclic voltammetry on a GC electrode. Other electrode materials were passivated after reduction of the RAFT agents.

The reduction of all CTAs to the corresponding radical anions was followed by a series of chemical reactions, including father−son reactions between electrogenerated species and the starting CTA. The cathodic peak potential of the RAFT agents, E_{pc}, decreased in the order dithiobenzoates > trithiocarbonates > dithiocarbamates ≈ xanthate. Keeping constant the Z group, E_{pc} shifted to more positive values with increasing electron-withdrawing and radical-stabilizing power of the R group. The electrolysis of $\mathbf{T_4}$-$\mathbf{2^{Bz}}$ in DMF confirmed the reductive cleavage of the Z(SC)S−R bond.

Propagating radicals were found to be reduced to carbanions at potentials very similar or more positive than those of the CTAs. Monomers instead are generally reduced at more negative potentials than many CTAs. Consequently, for *e*RAFT via direct electroreduction of the CTA, the selection of the CTA−monomer couple and therefore of the E_{app} value should obey two criteria: $E_{pc}(CTA) > E^{\ominus}_{radical}$, and $E_{pc}(CTA) > E_{onset}(monomer)$. In addition, the presence of electron-withdrawing functions in the R group of a CTA determines $E_{pc}(CTA) > E_{pc}(macroCTA)$, thus potentially decreasing the efficiency of the electrochemical stimulus during the polymerization.

Despite taking these aspects into account, low conversion and polymers with broad distribution of MWs were observed for the *e*RAFT of STY via electroreduction of various CTAs. CVs recorded after several hours of electrolysis showed the disappearance of the cathodic peak of the CTA and the accumulation of new species, indicating that the polymerization was not controlled because the RAFT agent was consumed.

The possibility of *e*RAFT via mediated electrolysis of RAFT agents was then explored. Small aromatic hydrocarbons appeared as inefficient mediators, likely because of side reactions involving the electrogenerated radical anion of the mediator and the radicals formed by reductive cleavage of the CTA. Therefore, mediators with highly hindered structures were considered to hamper side reactions such as radical−radical anion coupling. The TPP-mediated *e*RAFT of acrylates at room temperature gave polymers with low dispersity and MWs matching theoretical values, even with low mediator loading [TPP]/[CTA] = 0.01. However, the process was slow, and some decomposition of the CTA was observed by CV.

Based on these results, further work on *e*RAFT should focus on the mediated electrolysis approach, aiming to find more effective mediators and optimize the electrochemical setup. Importantly, the presented characterization of the redox properties of CTAs is relevant for traditional RAFT and PET-RAFT polymerizations, favoring a better mechanistic understanding and facilitating the selection of photoredox catalysts.

ASSOCIATED CONTENT

Supporting Information

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Materials and procedures, additional electrochemical data and discussions, NMR spectra, polymerization kinetics (PDF)

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Notes

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