Initialization of RAFT Agents with Different Leaving Groups – Determination of the Transfer Coefficients

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Summary: The leaving group of the initial RAFT agent is one key factor during the initialization period of the RAFT polymerization. Benzyl-, Phenylethyl- and Cumyl Dithiobenzoate RAFT mediated bulk polymerization of styrene at 120 °C was investigated by direct measurement of the concentration of the RAFT agent and determination of the molecular weight in the initial phase of the RAFT polymerization using Size Exclusion Chromatography (SEC). The initialization period can be described by means of two transfer coefficients that are determined by the stability of the free-radical leaving group. By means of a Monte Carlo simulation the RAFT initialization process was characterized and the transfer coefficients from the experimental data were determined.

Keywords: Monte Carlo simulation; radical polymerization; reversible fragmentation chain transfer (RAFT)

Introduction

The reversible addition-fragmentation chain transfer polymerization (RAFT) is one of the living radical polymerization techniques suitable to synthesize polymers of well defined architectures.[1] The RAFT polymerization process contains two equilibria (see Scheme 1): either the initial RAFT agent (pre-equilibrium) or the dormant polymer chain (main equilibrium) is attacked by the propagating radical. During the pre-equilibrium, the initial RAFT agent is consumed and converted into the polymeric dithio-compound. This process was defined as initialization period.[2] In the main equilibrium, an exchange reaction between propagating chain and dormant chain takes place, which results in the controlled nature of the polymerization process.

The selection of the initial RAFT agent is very important with regard to effective control of the polymerization. Our investigated RAFT agents are dithiobenzoates with the general structure Z–C(=S)S–R (Z = phenyl) and structural variety with respect to the leaving group (R-group). The effectiveness of RAFT agents depends on the nature of the R group. For an effective initialization one can formulate two requirements concerning the leaving group: good homolytic cleavage form the intermediate of the pre-equilibrium and effective reinitialization of the free-radical leaving group $R^{\bullet}$.

We analyzed the reaction mixtures during the initialization period of the different dithiobenzoates by means of a Size Exclusion Chromatography (SEC) – with a column combination, which provides a good separation within the low-molecular weight range. The time dependent concentration of the RAFT agents and the molecular weights during the initialization process was determined with SEC using a very selective photo array detector. The study presented here reports the initialization behaviour of Benzyl-, Phenylethyl- and Cumyl Dithiobenzoate RAFT mediated Styrene polymerizations in bulk at 120 °C.

We characterized the RAFT initialization process following the concept of

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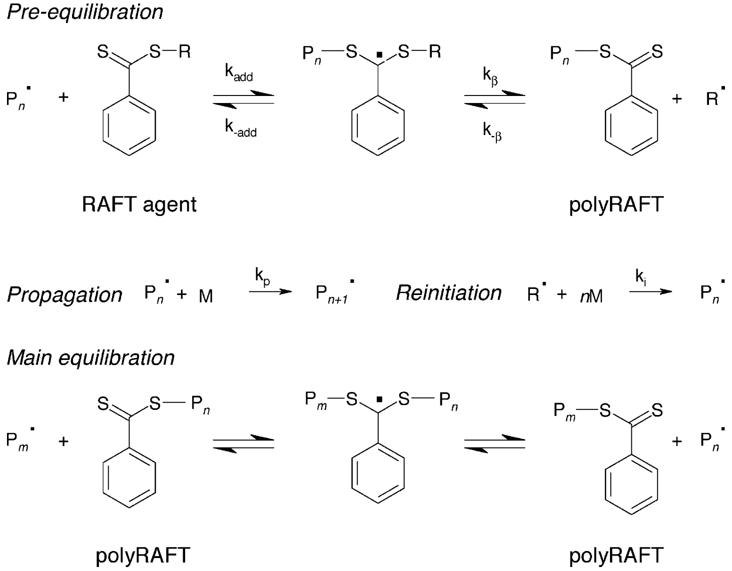


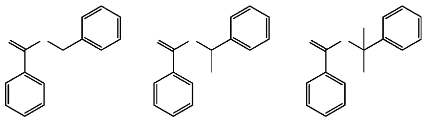
Scheme 1.
reaction steps of the RAFT process.

Rizzardo et al.[3,4] with two transfer coefficients: C_{tr} ($=k_{tr}/k_p$) and C_{-tr} ($=k_{-tr}/k_i$), which describe the reaction path of the propagating radical $P_n^\bullet$ and the free radical leaving group $R^\bullet$. The determination of the two transfer coefficients from the experimental data was carried out by means a Monte Carlo simulation.

Experimental Part

Materials

The RAFT agents Benzyl Dithiobenzoate (Bz-DB), 1-Phenylethyl dithiobenzoate (PhEt-DB) and Cumyl dithiobenzoate (C-DB) (Scheme 2) were synthesized according to the procedure described by Rizzardo et al.[3] The purity of the RAFT agent was more than 98% as verified by ^{1}H-NMR analysis. Styrene (BASF) was distilled under reduced pressure. The initiator dicumyl peroxide - DCP (Fluka) was used without further purification.



Scheme 2.
RAFT agents.

Procedure for the Polymerizations

The polymerizations were carried out in sealed glass ampoules, which were filled with 1 mL reaction solution, at 120 °C under nitrogen atmosphere. Samples of one experiment were taken at different times and cooled down in an ice bath. The reaction solutions were dissolved in exact 1 mL of THF (1:1) and directly injected into the Size Exclusion Chromatography system.

Size Exclusion Chromatography (SEC)

The Size Exclusion Chromatography system consists of the following components: pump WATERS 510, autosampler WATERS WISP 712 and photo array detector Waters PDA 996. With the photo array detector spectra were recorded at a frequency of 1 Hz and a resolution of 4.8 nm. 1 × Ultrastyragel 100 Å and 2 × Ultrastyragel 500 Å were used as columns. THF was used as eluent, with a flow rate of 1.0 mL/min and a temperature of 25 °C. For the analysis 15 μL of the reaction solutions was injected.

Monte Carlo Simulation of the Initialization Process

The concept of transfer coefficients summarized the initialization process of the RAFT polymerization in the following reactions[3,4]:

$$\text{Transfer}: P_n^\bullet + \text{RAFT} \xrightarrow{k_{tr}} \text{polyRAFT} + R^\bullet \tag{1}$$

$$\text{Propagation}: P_n^\bullet + M \xrightarrow{k_p} P_{n+1}^\bullet \tag{2}$$

$$\text{Back-Transfer}: R^\bullet + \text{polyRAFT} \xrightarrow{k_{-tr}} \text{RAFT} + P_n^\bullet \tag{3}$$

$$\text{Reinitiation}: R^\bullet + M \xrightarrow{k_i} P_{n+1}^\bullet \tag{4}$$

In the RAFT mechanism (Scheme 1), the rate constants are k_{tr} (Equation 5) for the conversion of the initial RAFT agent into the polymeric dithio-compound (polyRAFT) and k_{-tr} (Equation 6) for the reverse reaction between the expelled leaving group $R^\bullet$ and the polyRAFT compound.

$$k_{tr} = k_{add} \cdot \frac{k_\beta}{k_{-add} + k_\beta} \tag{5}$$

$$k_{-tr} = k_{-\beta} \cdot \frac{k_{-add}}{k_{-add} + k_\beta} \tag{6}$$

The reaction path of the propagating radical is described by the transfer coefficient C_{tr} ($=k_{tr}/k_p$) and of the expelled leaving group by the back-transfer coefficient C_{-tr} ($=k_{-tr}/k_i$). An effective RAFT agent has a high C_{tr} and low C_{-tr} in the ideal case.

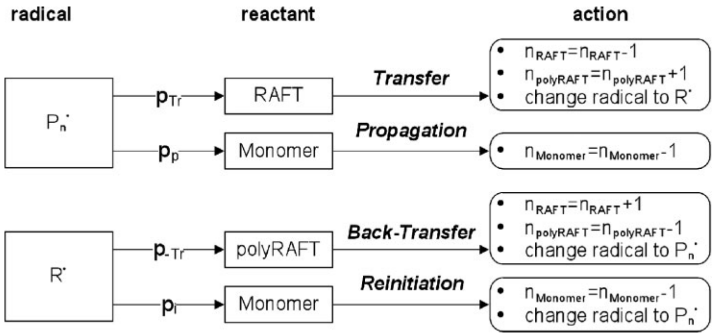
With a Monte Carlo simulation one can describe the RAFT initialization process. Our simulations were initialized with a predetermined total number of monomer and RAFT agent molecules of $n_{total} = 1 \cdot 10^8$ that are distributed among the given monomer ($n_{Monomer,0} = [\text{Monomer}]_0/n_{total}$) and RAFT species ($n_{RAFT,0} = [\text{RAFT}]_0/n_{total}$, $n_{polyRAFT} = 0$) according to the initial molar composition of the feed. One single step in this Monte Carlo simulation represents the execution of exactly one reaction selected from the pool of possible reactions in Equation 1–4. The reaction pathway based upon the effective reaction probabilities for the given reaction conditions is shown in Scheme 3. The reaction probabilities (Equation 7–10) depend only on the current number of molecules ($n_{monomer}$, n_{RAFT} and $n_{polyRAFT}$) and the given transfer constants C_{tr} and C_{-tr}.

$$p_p = \frac{n_{Monomer}}{n_{Monomer} + C_{tr} \cdot n_{RAFT}} \tag{7}$$

$$p_{Tr} = \frac{C_{tr} \cdot n_{RAFT}}{n_{Monomer} + C_{tr} \cdot n_{RAFT}} = 1 - p_P \tag{8}$$

$$p_i = \frac{n_{Monomer}}{n_{Monomer} + C_{-tr} \cdot n_{polyRAFT}} \tag{9}$$

$$p_{-Tr} = \frac{C_{-tr} \cdot n_{polyRAFT}}{n_{Monomer} + C_{-tr} \cdot n_{polyRAFT}} = 1 - p_i \tag{10}$$



Scheme 3.
Monte Carlo simulation of the RAFT initialization .

with:

$n_{Monomer}$	number of monomer molecules
$[M]_0$	monomer concentration in the feed
n_{RAFT}	number of RAFT agent molecules
$[RAFT]_0$	RAFT agent concentration in the feed
$n_{polyRAFT}$	number of polymeric RAFT agent molecules

The Monte Carlo simulation (Scheme 3) starts with a new polymer chain $P_n^\bullet$. Two different steps are feasible, a propagation step (Equation 2) or a transfer step (Equation 1). In the case of the propagation step, only one monomer molecule is consumed. By executing the transfer step, one RAFT molecule is exhausted, a new polyRAFT molecule is generated and the active species changes to the reinitiating group $R^\bullet$. Now, there are once again two possible pathways: on the one hand initiation (Equation 4) with consumption of one monomer molecule, on the other hand back-transfer (Equation 3). Considering the back-transfer step (Equation 3), the RAFT group is transferred from the polyRAFT chain to the low molecular RAFT agent. In both reactions the active species is changed from reinitiating group $R^\bullet$ to propagating chain $P_n^\bullet$.

Every 5,000 Monte Carlo steps the results of the simulation are analyzed in respect to the composition of the reaction mixture. The initial RAFT agent concentration and the parameters C_{tr} and C_{-r} define the number of necessary Monte Carlo steps.

An AMD Opteron 8216 CPU needs approximately 0.1 s for calculating the RAFT initialization up to complete conversion. The procedure of our Monte Carlo simulation procedure is executed by the program "mcCopolymer", which is implemented in C++ with a Tcl-interface utilizing the Mersenne Twister high-level 623-dimensionally equidistributed uniform pseudo-random number generator.[5]

The initialization as simulated by the Monte Carlo process is a function of monomer and RAFT agent conversion and not a function of time. Our model approach contains only two parameters, the transfer coefficients which have to be determined.

A complete kinetic model to be used alternatively leads to a time-dependent solution. This complete model contains all initiation and termination reactions in addition to the shown reactions according to Equation 1–4. It is problematic that the mechanism of the RAFT polymerization is not yet adequately understood with respect to the appearing termination reactions.[6,7] Therefore we prefer the discussed Monte-Carlo simulation compared with the complete kinetic model approach.

The parameters C_{tr} and C_{-tr} were determined by fitting to all experimental data, resulting from time dependent RAFT agent and monomer concentrations, with variation of the initiator concentration. Therefore, we performed a stochastic optimization process ($1 \cdot 10^5$ random sampling steps) of a parameter space with initial limits selected on the basis of rational considerations and preliminary simulation results.

Results and Discussion

Measurement of the Time Dependent RAFT Agent and Monomer Concentration

The time-dependent RAFT agent and monomer concentration was determined by SEC measurements. The employed SEC column combination provides a very good separation of the low-molecular weight species therefore allowing a separation of the RAFT agent peak and the eluation of the oligomers as well as the polymers. Figure 1 exemplarily shows the peak separation for a RAFT mediated (PhEt-DB) bulk polymerization after 6 min.

The eluation curve was extracted from the UV spectra of the photo array detector at a wavelength of 500 nm. In the elution, the first peaks for the oligomers consisting of up to five monomer units (P_5RAFT down to P_2RAFT) can be identified. The

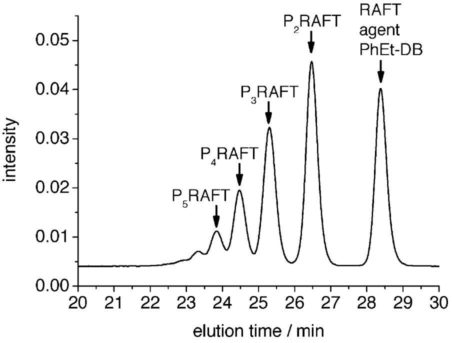


Figure 1.

SEC elution curve (UV, 500 nm) for the reaction solution of a styrene polymerization in bulk at 120 °C after 6 min with $[\text{PhEt-DB}]_0 = 0.03$ mol/L, $[\text{DCP}]_0 = 0.003$ mol/L.

last peak represents the elution of the RAFT agent (PhEt-DB). The assignment of the RAFT peak was validated by separate SEC measurement of the employed RAFT agents.

For the kinetic analysis of the RAFT activation, the time dependent RAFT agent concentration was determined from the decrement of the peak area with the reaction time (Figure 2A). and is used by us to determine the kinetics of the RAFT activation. From this peak we determined the time dependent RAFT agent concentration (Figure 2B). The reliability of the Lambert-Beer law was tested by independent measurements of the RAFT-peak area with different RAFT concentrations.

Additional to the RAFT concentration, the molecular weight of the polymeric dithio compounds (polyRAFT) was determined by the SEC measurements. The knowledge of the degree of polymerization and the concentration of the growing polymers opens an access to the current monomer concentration. By means of Equation 11, the number-average degree of polymerization X_n can be calculated from the molecular weight M_n (MM_{RAFT} = molecular weight of the RAFT agent) and the time dependent concentration of the polymeric dithio compound polyRAFT can be calculated from the measured RAFT concentration $[RAFT]_t$ using Equation 12.

$$X_n = M_n/104 - MM_{RAFT} \qquad (11)$$

$$[polyRAFT]_t = [RAFT]_0 - [RAFT]_t \qquad (12)$$

$$X_n = \frac{[Styrene]_0 - [Styrene]_t}{[polyRAFT]_t} \qquad (13)$$

$$\begin{aligned}[Styrene]_t = {} & [Styrene]_0 \\ & - \left(M_n/104 - MM_{RAFT}\right) \\ & \cdot \left([RAFT]_0 - [RAFT]_t\right)\end{aligned} \qquad (14)$$

With the theoretically expected degree of polymerization X_n during the RAFT initialization (Equation 13) in combination with the number-average degree of polymerization X_n (Equation 11) and the current polyRAFT concentration, the time dependent monomer concentration can be determined (Equation 14). This method for determination of the monomer

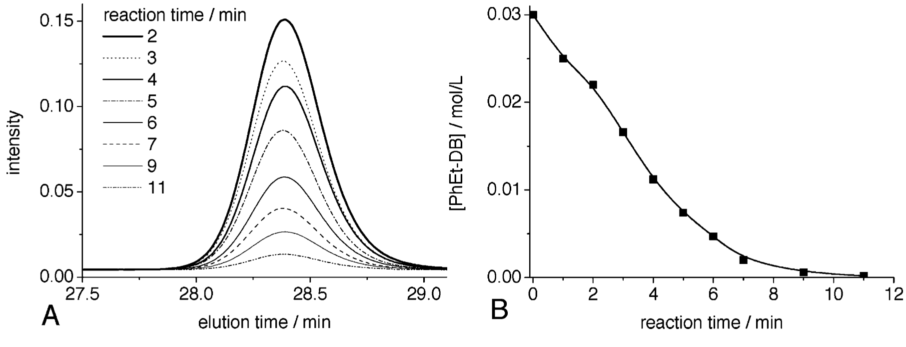


Figure 2.

Time-dependent development of the PhEt-DB peak (A) from the of the SEC elution curve and the resulting PhEt-DB concentration (B) with $[\text{PhEt-DB}]_0 = 0.03$ mol/L, $[\text{DCP}]_0 = 0.003$ mol/L.

concentration is very sensitive which is important due to relatively low monomer conversions reached during the RAFT initialization period. Our method grants the additional advantage that both concentrations (RAFT agent and monomer) can be determined by one SEC measurement.

Table 1.
Polymerization experiments.

	RAFT agent	$[DCP]_0$/mol/L
E1	Bz-DB	0.003
E2	PhEt-DB	0.000
E3	PhEt-DB	0.003
E4	C-DB	0.000
E5	C-DB	0.003

Initialization Rate of the RAFT Agents

The investigations of the initialization of RAFT agents with different leaving groups were carried out under real polymerization conditions. In the experiments, the initiator (dicumyl peroxide - DCP) concentrations were varied in the range from 0.0 mol/L (only thermal initialization) up to 0.003 mol/L DCP. All experimental conditions are summarized in Table 1.

The measurements (Figure 3A) show a strong dependence of the initialization rate of the RAFT agents from the leaving group (C-DB > PhEt-DB > Bz-DB). This effect can be explained by the difference in the fragmentation rate of the intermediate radical (Scheme 1) from the structure of the leaving group. During the initialization phase, differences in the free radical concentrations occur (Figure 3B). If the initialization takes place with the highly reactive benzyl leaving group (Bz-DB), no rate retardation takes place in contrast to the initialization of the other investigated RAFT agents. The rate retardation depends on the reactivity of the free radical leaving group (cymyl < phenylethyl). After the initialization phase, the concentration of the growing free radicals remains constant. The free radical concentrations are calculated from the slope of the ln(M0/Mt) vs. time curve with $k_p = 2038\ s^{-1}$ (120 °C)[8]: initialization of PhEt-DB: $[Pn] = 1.3 \cdot 10^{-8}$ mol/L, C-DB: $[Pn] = 6.5 \cdot 10^{-9}$ mol/L. After the initialization of the RAFT agent and during the initialization of Bz-DB without rate retardation $[Pn] = 2.5 \cdot 10^{-8}$ mol/L.

The retardation effects are currently discussed very divergently in the literature[6] and are not the main focus of this work. The observed retardation during the initialization period was identified in the pre-equilibrium of the RAFT mechanism (Scheme 1).

Determination of the Transfer Coefficients C_{tr} and C_{-tr}

Our Monte Carlo simulation provides RAFT agent and monomer concentration during the initialization process, depending on the initial RAFT and monomer concentration and the parameters Ctr and C-tr. For the determination of the transfer

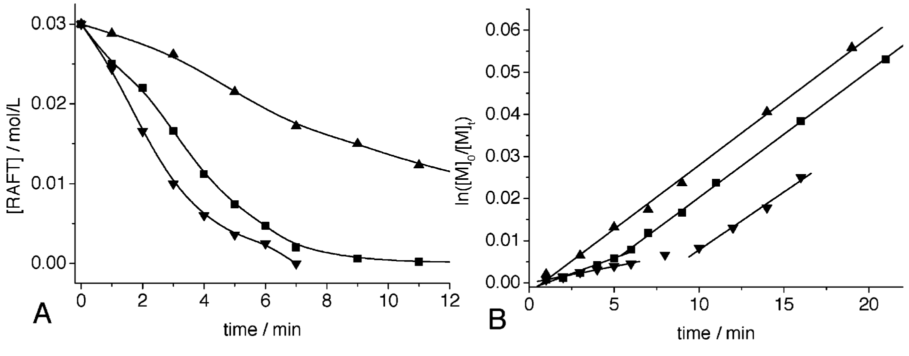


Figure 3.
initialization period of the RAFT agents $[RAFT]_0 = 0.03$ mol/L, $[DCP]_0 = 0.003$ mol/L, A: time dependent RAFT agent concentration, B: rate retardation during RAFT initialization.

coefficients C_{tr} and C_{-tr}, we performed a stochastic scan of a parameter space with initial limits selected on the basis of rational considerations and preliminary simulation results. During the optimization process, the sum of squares of differences between the experimental data [RAFT], [Monomer] and the corresponding simulation data were minimized. The aim of the optimization process was the determination of the global minimum. The stochastic scan over the parameter space is in principle suitable for it if adequate random sampling steps are executed and the limits of C_{tr}(min), C_{tr}(max) and C_{-tr}(min), C_{-tr}(max) are not chosen too closely. Three individual optimization runs with successive reduction of the parameter window size around the optimum results were performed, resulting in an overall number of $1e^5$ random sampling steps. A well defined minimum occurred for all three parameter sets.

The agreement of the experimental data with the simulation using the fitted transfer coefficients was excellent (Figure 4). The RAFT agent as well as the monomer concentrations (obtained from experimental data at different reaction times) are independent from the radical concentration and consequently the thermal polymerizations and the polymerizations with initiator DCP form one single line.

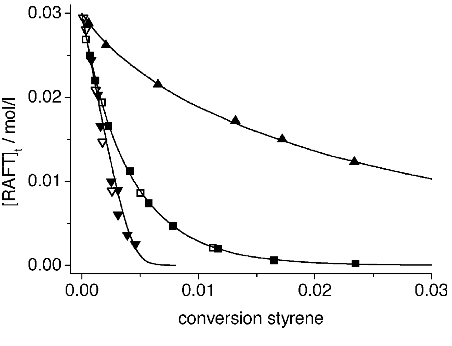


Figure 4.

RAFT agent concentration vs monomer conversion in comparison with the Monte Carlo simulations with (▲) Bz-DB, — $C_{tr} = 92$, $C_{-tr} = 1057$; (■) PhEt-DB, — $C_{tr} = 3331$, $C_{-tr} = 4173$; (▼) C-DB — $C_{tr} = 2037$, $C_{-tr} = 34$; closed symbols $[DCP]_0 = 0.003$ mol/L, open symbols $[DCP]_0 = 0.0$ mol/L.

The determined transfer coefficients reflecting the different reaction pathways depending on the structure and reactivity of the free radical leaving group are Bz-DB: $C_{tr} = 92$, $C_{-tr} = 1057$; PhEt-DB: $C_{tr} = 3331$, $C_{-tr} = 4173$; C-DB: $C_{tr} = 2037$, $C_{-tr} = 34$. If long durations for the RAFT agent initialization period were observed (Bz-DB), the transfer reaction is not very much favored in contrast to the propagation reaction ($C_{tr} = 92$) and the ratio between transfer and back-transfer is very low ($C_{tr}/C_{-tr} = 0.09$). Both RAFT agents PhEt-DB and C-DB initialize with high transfer rates (C_{tr}) and differences are observed in the proportion between transfer and back-transfer C_{tr}/C_{-tr} (PhEt-DB: 0.8, C-DB: 60). It is remarkable that during the initialization of C-DB the back-transfer coefficient of the low reactive cumyl radical is not zero and cannot be neglected.

The differences in the initialization of the RAFT agents has consequences on the polydispersity of the polyRAFT species. After the initialization of the RAFT agent Bz-DB with slow transfer and high back-transfer rate, the polydispersity was nearly 1.2 PDI. In case of the initialization of PhEt-DB and C-DB, the polydispersity was significant lower (<1.1).

Conclusions

The initialization period of Benzyl Dithiobenzoate (Bz-DB), 1-Phenylethyl dithiobenzoate (PhEt-DB) and Cumyl dithiobenzoate (C-DB) RAFT mediated bulk polymerization of styrene at 120 °C was investigated for different initiator concentrations. We observed differences in the duration of the initialization period and retardation effects depending on the structure and reactivity of the free radical leaving group. The concentration of the RAFT agent and the monomer concentration in the initial phase of the RAFT polymerization were determined experimentally by SEC.

We characterized the RAFT initialization of the different RAFT agents by determination of the transfer coefficients

C_{tr} ($=k_{tr}/k_p$) and C_{-tr} ($=k_{-tr}/k_i$). These coefficients describe the reaction path of the propagating radical and the different expelled leaving groups during the initialization period. A Monte Carlo simulation, connected with a stochastic optimization process was used for the determination of the transfer coefficients from the experimental data. The resulting transfer coefficients are Bz-DB: $C_{tr} = 92$, $C_{-tr} = 1057$; PhEt-DB: $C_{tr} = 3331$, $C_{-tr} = 4173$; C-DB: $C_{tr} = 2037$, $C_{-tr} = 34$.

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[1] G. Moad, E. Rizzardo, S. H. Thang, *Aust. J. Chem.* **2005**, *58*, 379.

[2] J. B. McLeary, F. M. Calitz, J. M. McKenzie, M. P. Tonge, R. D. Sanderson, B. Klumperman, *Macromolecules* **2004**, 37. 2383.

[3] Y. K. Cong, J. Krstina, T. P. T. Le, G. Moad, A. Postma, E. Rizzardo, S. H. Thang, *Macromolecules* **2003**, *36*, 2256.

[4] J. Chiefari, R. T. A. Mayadunne, C. L. Moad, G. Moad, E. Rizzardo, A. Postma, M. A. Skidmore, S. H. Thang, *Macromolecules* **2003**, *36*, 2273.

[5] M. Matsumoto, T. Nishimura, *ACM Trans Model Comp Simul.* **1998**, *8*, 3.

[6] C. Barner-Kowollik, M. Buback, B. Charleux, M. L. Coote, M. Drache, T. Fukuda, A. Goto, B. Klumperman, A. B. Lowe, J. B. Mcleary, G. Moad, M. J. Monteiro, R. D. Sanderson, M. P. Tonge, P. Vana, *Journal of Polymer Science, Part: A, Polymer Chemistry* **2006**, *44*, 5809.

[7] M. Buback, P. Vana, *Macromol. Rapid Communications* **2006**, *27*, 1299.

[8] R. G. Gilbert, *Pure & Appl. Chem.* **1996**, *68*, 1491.