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RAFT Polymerization - Investigation of the Initialization Period and Determination of the Transfer Coefficients

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Summary: The rate of activation of the initial RAFT agent is very important with regard to effective control of the polymerization. The initialization period of Benzyl Dithiobenzoate RAFT mediated bulk polymerization of styrene at 120 °C was investigated at different RAFT agent and initiator concentrations. The concentration of the RAFT agent and the monomer concentration in the initial phase of the RAFT polymerization were determined experimentally by Size Exclusion Chromatography (SEC). We characterized the RAFT initialization following the concept of Rizzardo et al.[1,2] by determination of the transfer coefficients. For the determination of the transfer coefficients from the experimental data a Monte Carlo simulation was developed by us.

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

Introduction

Controlled radical polymerization includes a group of polymerization techniques suitable to synthesize narrowly distributed polymeric materials with controlled molecular weights and complex macromolecular architectures. The most prominent of these techniques are Stable Free Radical Polymerization (SFRP),[3] Atom Transfer Radical Polymerization (ATRP)[4] and Reversible Addition Fragmentation Chain Transfer Polymerization (RAFT).[5–7] In all cases, controlled radical polymerization contains a reversible activation process of "dormant" polymer chains.

The RAFT process has proven to be extremely versatile with respect to monomer types and reaction conditions, in contrast to other living polymerization techniques. The RAFT polymerization can be used to synthesize polymers with predetermined molecular weight and narrow molecular weight distribution as well as well-defined polymer architectures, e.g. block, star and brush polymers.

The controlling agents are typically dithioesters with the general structure Z–C(=S)S–R, that have been designed in great structural variety with respect to the leaving group (R-group) and to their stabilizing moiety (Z-group). Both of these groups have a significant effect on degree of control and the kinetics of the RAFT process. The RAFT polymerization proceeds via a degenerative chain transfer mechanism in which two equilibria (see Scheme 1) are superimposed on a conventional radical polymerization (i.e. initiation, propagation and termination). During the pre-equilibrium the initial RAFT agent is consumed and converted into the polymeric dithio-compound. The initialization period was defined as the period in which the employed low molecular RAFT agent is consumed.[9]

In the main equilibrium, the dormant polymer chain is attacked by the propagat-

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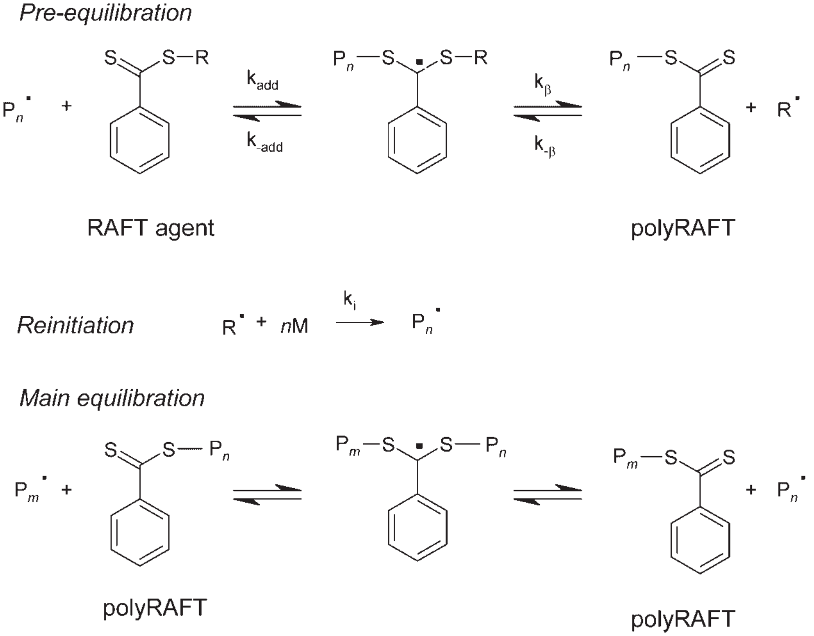


Scheme 1.

Basic reaction steps of the RAFT process.

ing radical. An exchange reaction between propagating chain and dormant chain takes place, which results in the living/controlled nature of the polymerization process.

The rate of activation of the initial RAFT agent is very important with regard to effective control of the polymerization. In situ NMR spectroscopy has been applied for characterization of the RAFT initialization period. Klumpermann et al.[8,9] investigated polymerizations of styrene and methyl acrylate and determined the concentration-time profiles of various low molecular weight species in the reaction mixture. The high initial RAFT agent concentrations necessary for the in situ NMR measurements resulted in a very long initialization period.

We analyzed the reaction mixtures during the initialization period by means of a Size Exclusion Chromatography (SEC) – with a column combination, which provides a good separation within the low-molecular weight range. In an earlier work, we described the activation rate of alkoxyamines and the activating-deactivating equilibrium of nitroxide-controlled radical polymerization using this technique.[10] A very selective photo array detector was used to measure the concentration of the low-molecular weight RAFT agent.

The study presented here reports the initialization behaviour of RAFT-mediated Styrene polymerizations using Benzyl Dithiobenzoate as RAFT agent at 120 °C. The initialization period is the main focus of our investigations in this paper. We characterized the RAFT initialization following the concept of Rizzardo et al.[1,2] 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 leaving group during the initialization period. For the determination of the transfer coefficients from the experimental data a Monte Carlo simulation was developed by us.

Theory and Computational Methods

Following the concept of Rizzardo et al.,[1,2] the consumption of the initial RAFT agent depends on two transfer coefficients (Equation 1, 2):

$$C_{tr} = \frac{k_{tr}}{k_p} \tag{1}$$

$$C_{-tr} = \frac{k_{-tr}}{k_i} \tag{2}$$

$$k_{tr} = k_{add} \cdot \frac{k_\beta}{k_{-add} + k_\beta} \tag{3}$$

$$k_{-tr} = k_{-\beta} \cdot \frac{k_{-add}}{k_{-add} + k_\beta} \tag{4}$$

In the RAFT mechanism (Scheme 1), the rate constants are k_{tr} (Equation 3) for the RAFT agent activation and k_{-tr} (Equation 4) for the reverse reaction between the expelled radical $R^\bullet$ and the polymeric RAFT agent. Following this concept, the conversion of initial RAFT agent and the monomer conversion are summarized in the following reactions:

$$\text{Transfer}: \quad \mathrm{P_n^\bullet} + \mathrm{RAFT} \xrightarrow{k_{tr}} \mathrm{polyRAFT} + \mathrm{R^\bullet} \tag{5}$$

$$\text{Propagation}: \quad \mathrm{P_n^\bullet} + \mathrm{M} \xrightarrow{k_p} \mathrm{P_{n+1}^\bullet} \tag{6}$$

$$\text{Back} - \text{Transfer}: \quad \mathrm{R^\bullet} + \mathrm{polyRAFT} \xrightarrow{k_{-tr}} \mathrm{RAFT} + \mathrm{P_n^\bullet} \tag{7}$$

$$\text{Reinitiation}: \quad \mathrm{R^\bullet} + \mathrm{M} \xrightarrow{k_i} \mathrm{P_{n+1}^\bullet} \tag{8}$$

The determination of the transfer coefficients C_{tr} and C_{-tr} from the experimental data was carried out by means of a Monte Carlo simulation. The applied 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 and RAFT species according to the initial molar composition of the feed (Equation 9–11):

$$n_{Monomer,0} = \frac{[M]_0}{n_{total}} \tag{9}$$

$$n_{RAFT,0} = \frac{[RAFT]_0}{n_{total}} \tag{10}$$

$$n_{polyRAFT,0} = 0 \tag{11}$$

$$P_p = \frac{n_{Monomer}}{n_{Monomer} + C_{tr} \cdot n_{RAFT}} \tag{12}$$

$$P_{Tr} = \frac{C_{tr} \cdot n_{RAFT}}{n_{Monomer} + C_{tr} \cdot n_{RAFT}} = 1 - P_P \tag{13}$$

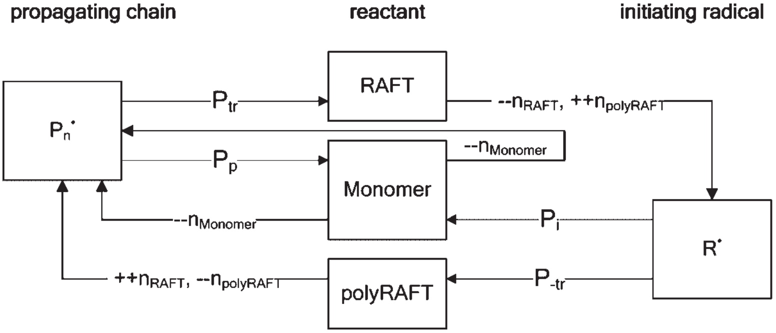
$$P_i = \frac{n_{Monomer}}{n_{Monomer} + C_{-tr} \cdot n_{RAFT}} \tag{14}$$

$$P_{-Tr} = \frac{C_{-tr} \cdot n_{RAFT}}{n_{Monomer} + C_{-tr} \cdot n_{RAFT}} = 1 - P_i \tag{15}$$

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

Every single step in this Monte Carlo simulation represents the execution of exactly one reaction selected from the pool of possible reactions in Equation 5–8. The reaction pathway based upon the effective reaction probabilities for the given reaction conditions is shown in Scheme 2. The reaction probabilities (Equation 12–15) only depend on the current number of molecules (monomer, RAFT and polyRAFT) and the given transfer constants C_{tr} and C_{-tr}.

The Monte Carlo simulation (Scheme 2) is started with a new polymer chain $Pn\bullet$ for which either a propagation step (Equation 6) or a transfer step (Equation 5) can occur. In the case of the propagation step, only one monomer molecule is consumed ($--n_{Monomer}$). If the transfer step takes



Scheme 2.
Monte Carlo simulation of the RAFT initialization.

place, one RAFT molecule is consumed ($--n_{RAFT}$), a new polyRAFT molecule is formed ($++n_{polyRAFT}$) and the active species changes to the reinitiating group $R^\bullet$. Now, either initiation (Equation 8) with consumption of one monomer molecule ($--n_{Monomer}$) or back-transfer (Equation 7) are possible pathways. In the case of the back-transfer step (Equation 7), the RAFT group is transferred from the polyRAFT chain to the low molecular RAFT agent ($--n_{polyRAFT}$, $++n_{RAFT}$). In both reactions, the active species changes from reinitiating group $R^\bullet$ to propagating chain $Pn\bullet$. The initialization as simulated by the Monte Carlo process is a function of monomer conversion and not a function of time.

The results of the simulation are tracked every 5,000 Monte Carlo steps and are analyzed in respect to the composition of the reaction mixture. The number of necessary Monte Carlo steps depends on the initial RAFT agent concentration and the parameters C_{tr} and C_{-tr}. Our Monte Carlo simulation procedure is executed by the mcCopolymer program, programmed in C++ with a Tcl-interface, and employing the Mersenne Twister high-level 623-dimensionally equidistributed uniform pseudo-random number generator.[11] Approximately 0.1 s are needed for the calculation of the RAFT initialization up to complete conversion of the initial RAFT agent on an AMD Opteron 8216 CPU.

The determination of the parameters C_{tr} and C_{-tr} was made by fitting to all experimental data – the time dependent RAFT agent and monomer concentrations, with variation of the initial RAFT agent and initiator concentration. We therefore performed a stochastic scan (100,000 steps) of a parameter space with initial limits selected on the basis of rational considerations and preliminary simulation results.

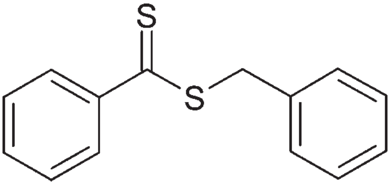
Experimental Part

Materials

The RAFT agent Benzyl Dithiobenzoate (Scheme 3) was synthesized according to the procedure described by Rizzardo et al.[1] 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.

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



Scheme 3.
Benzyl Dithiobenzoate.

nitrogen atmosphere. Samples of one series were taken at different times, cooled down in an ice bath, dissolved in exact 1 mL of THF (1:1). The dissolved reaction solutions were directly injected into the Size Exclusion Chromatography system.

Size Exclusion Chromatography (SEC)

The determination of the RAFT species and the molecular weight distributions were carried out by means of a Size Exclusion Chromatography system with the following components: pump WATERS 510, autosampler WATERS WISP 712, photo array detector Waters PDA 996. The 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 determination of the low-molecular weight species 15 μL of the reaction solutions was injected.

Results and Discussion

Investigation of the Time Dependent RAFT Agent Concentration

The time-dependence of the concentration of the RAFT agent at the beginning of the reaction was determined experimentally by SEC.

For the investigation of the RAFT initialization the reaction solution was examined time dependently during the initial phase of the polymerization by using a SEC column combination, which provides a very good separation of the low-molecular weight species. The measurement of the reaction solutions in the SEC provides a good peak separation of the RAFT agent and the emerging polymer as shown exemplarily in Figure 1 for a RAFT mediated bulk polymerization of styrene at 120 °C after 3 min ($[RN]_0 = 0.05$ mol/L, $[DCP]_0 = 0.006$ mol/L). The elution curves were extracted from the UV spectra of the photo array detector at a wavelength of 500 nm.

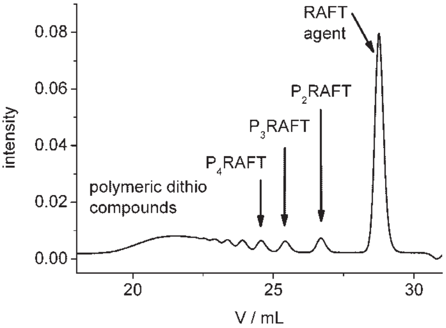


Figure 1.
SEC elution curve (UV, 500 nm) for the reaction solution of a styrene polymerization in bulk at 120 °C after 3 min with $[RAFT]_0 = 0.03$ mol/L, $[DCP]_0 = 0.006$ mol/L.

In the elution curve (Figure 1), the first dominant peak for the elution of the growing polymer as well as the individual, smaller peaks for the oligomers consisting of up to four monomer units can be identified. The species denominated P$_2$RAFT, P$_3$RAFT and P$_4$RAFT in Figure 1 are considered to be oligomers with the RAFT group and two (or three, four) styrene monomer units. The differences in the elution times of the oligomers equal the time differences that occur when calibrating the SEC with styrene standards. The measured oligomers P$_n$RAFT are not used for the kinetic analysis.

The following peak represents the elution of the RAFT agent. The area of this peak decreases with the reaction time (Figure 2-A) and is used by us to determine the kinetics of the RAFT activation. The assignment of this peak was validated by separate SEC measurement of the employed RAFT agent. From this peak we determined the time dependent RAFT agent concentration (Figure 2-B).

Our investigations of the RAFT agent initialization were carried out under real polymerization conditions. In our experiments, initial RAFT agent and the initiator (dicumyl peroxide - DCP) concentrations were varied. The experimental conditions are summarized in Table 1.

At the reaction temperature 120 °C significant thermal initiation of styrene polymerization takes place. This initiation

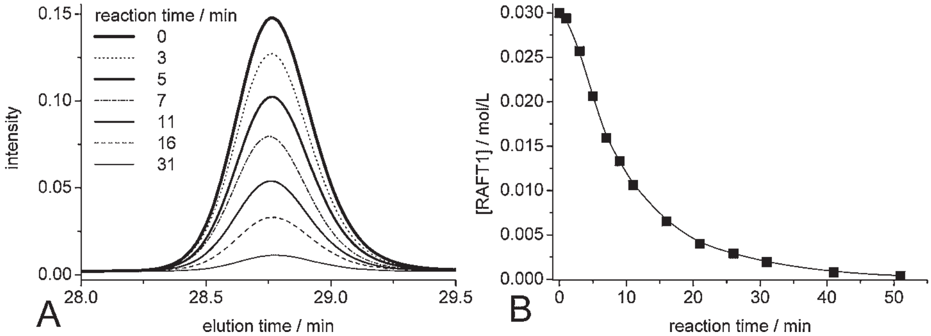


Figure 2.
Time-dependent development of the RAFT peak (A) from the of the SEC elution curve and the resulting RAFT agent concentration (B) with $[RAFT]_0 = 0.03$ mol/L, $[DCP]_0 = 0.006$ mol/L.

appears in addition to the initiation occurs by the initiator DCP. Experiment E2 was carried out considering only this thermal initiation ($[DCP]_0 = 0.0$ mol/L).

For a constant initiator concentration of $[DCP]_0 = 0.003$ mol/L the initialization time decreases with decreasing RAFT agent concentration (E6: $[RAFT]_0 = 0.01$ mol/L vs E3: $[RAFT]_0 = 0.03$ mol/L). In the case of constant RAFT agent concentration $[RAFT]_0 = 0.03$ mol/L, higher initiator concentrations lead to a decrease in initialization time (E5: $[RAFT]_0 = 0.01$ mol/L vs E3: $[RAFT]_0 = 0.01$ mol/L). Both effects can be explained by a shift of the pre-equilibrium (Scheme 1).

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

The determination of the transfer coefficients requires the knowledge of the time dependent RAFT agent and monomer concentrations. Relatively low monomer conversions are reached during RAFT initialization period. The time dependent monomer concentration $[styrene]_t$ can be calculated from the RAFT agent concentration $[RAFT]_t$ and the molecular weight M_n. Equation 16 describes the time dependent concentration of the polymeric dithio compound polyRAFT from the measured $[RAFT]_t$. By means of Equation 17 the number-average degree of polymerization X_n can be calculated from the by SEC determined molecular weight M_n (MM_{RAFT} = molecular weight of the RAFT agent). Using the theoretically expected degree of polymerization X_n (Equation 18) in combination with Equation 16 and 17, the time dependent monomer concentration can be determined (Equation 19).

Table 1.
polymerization experiments.

	$[RAFT]_0$/mol/L	$[DCP]_0$/mol/L
E1	0.05	0.003
E2	0.03	0.000
E3	0.03	0.003
E4	0.03	0.006
E5	0.03	0.018
E6	0.01	0.003

$$[\mathrm{polyRAFT}]_t = [\mathrm{RAFT}]_0 - [\mathrm{RAFT}]_t \quad (16)$$

$$X_n = M_n/104 - MM_{RAFT} \quad (17)$$

$$X_n = \frac{[\mathrm{Styrene}]_0 - [\mathrm{Styrene}]_t}{[\mathrm{polyRAFT}]_t} \quad (18)$$

$$[\mathrm{Styrene}]_t = [\mathrm{Styrene}]_0 - (M_n/104 - MM_{RAFT}) \cdot \left([\mathrm{RAFT}]_0 - [\mathrm{RAFT}]_t\right) \quad (19)$$

Most of experimental points at the examination of the RAFT initialization are located at low monomer conversion. At low monomer conversion, the controlled radical polymerization generates polymers with low molecular weight. Therefore (low conversion, low molecular weight) the gravimetric determination of the monomer conversion is difficult. Our method grants the additional advantage that both concentrations (RAFT agent and monomer) can be determined by one SEC measurement.

The RAFT agent concentration vs. monomer concentration for all experiments is plotted in Figure 4. Both concentrations decrease during the initialization period, the starting point is found on the right side of the plot at $[\text{styrene}]_0 = 8.725$ mol/L. The experimental values for different initiator concentrations are located on one and the same graph (E2, E3, E4 and E5). The RAFT agent concentration proportional to the monomer concentration is independent from the radical concentration.

By means of our stochastic optimization method we determined the transfer coefficients $C_{tr} = 92$ and $C_{-tr} = 1057$. The agreement of the experimental data with the simulation using the determined transfer coefficients was excellent (Figure 4). This result proves that the description of the raft initialization with the two fitted transfer coefficients works over a wide range of experimental conditions (see Table 1).

The proportion between transfer and back-transfer being very low ($C_{tr}/C_{-tr} = 0.09$). Therefore, long times for the RAFT agent initialization period were observed (Figure 3). The expelled leaving group is very reactive and the preferred reaction path of this benzyl radical is not the initialization reaction but rather the back-transfer reaction with the polyRAFT species ($C_{-tr} = k_{-tr}/k_i = 1057$).

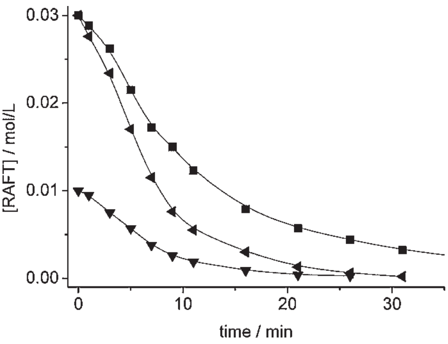


Figure 3.
Time dependent RAFT agent concentration with (■) $[\text{RAFT}]_0 = 0.03$ mol/L, $[\text{DCP}]_0 = 0.003$ mol/L (E3); (◀) $[\text{RAFT}]_0 = 0.03$ mol/L, $[\text{DCP}]_0 = 0.018$ mol/L (E5); (▼)$[\text{RAFT}]_0 = 0.01$ mol/L, $[\text{DCP}]_0 = 0.003$ mol/L (E6).

Due to the large number of experimental data points we can estimate the joint confidence interval of the parameters C_{tr} and C_{-tr}. In the case that error for all the measurements is approximately the same but not exactly known, the determination of this joint confidence interval is performed by a statistical F-test. The probability F-values are used at level 95% probability.

$$\text{deltaRAFT}^2 = \sum_n \left([\text{RAFT}]_{\text{Experiment}} - [\text{RAFT}]_{\text{Simulation}}\right)^2 \tag{20}$$

$$s^2 = \text{deltaRAFT}^2(\text{optC}_{tr}, \text{optC}_{-tr})/(n - p) \tag{21}$$

$$\text{deltaRAFT}^2(C_{tr}, C_{-tr})_{95\%} \le \text{deltaRAFT}^2(\text{optC}_{tr}, \text{optC}_{-tr}) + p \cdot s^2 \cdot F_{95\%}(p, n - p) \tag{22}$$

With Equation 20 we calculate the sum of squares of residuals (deltaRAFT^2) at the minimum ($\text{optC}_{tr} = 92$ and $\text{optC}_{-tr} = 1057$).

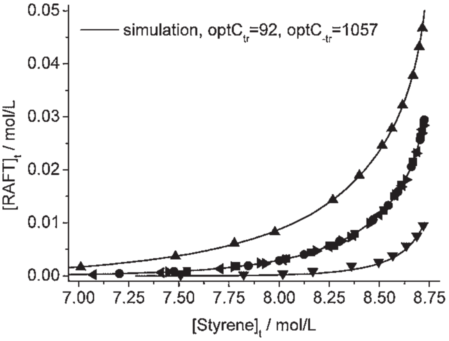


Figure 4.
RAFT agent concentration vs monomer concentration in comparison with the Monte Carlo simulation with (▲) $[\text{RAFT}]_0 = 0.05$ mol/L, $[\text{DCP}]_0 = 0.003$ mol/L (E1); (▶) $[\text{RAFT}]_0 = 0.03$ mol/L, $[\text{DCP}]_0 = 0.0$ mol/L (E2); (■) $[\text{RAFT}]_0 = 0.03$ mol/L, $[\text{DCP}]_0 = 0.003$ mol/L (E3); (●) $[\text{RAFT}]_0 = 0.03$ mol/L, $[\text{DCP}]_0 = 0.006$ mol/L (E4); (◀) $[\text{RAFT}]_0 = 0.03$ mol/L, $[\text{DCP}]_0 = 0.018$ mol/L (E5); (▼)$[\text{RAFT}]_0 = 0.01$ mol/L, $[\text{DCP}]_0 = 0.003$ mol/L (E6).

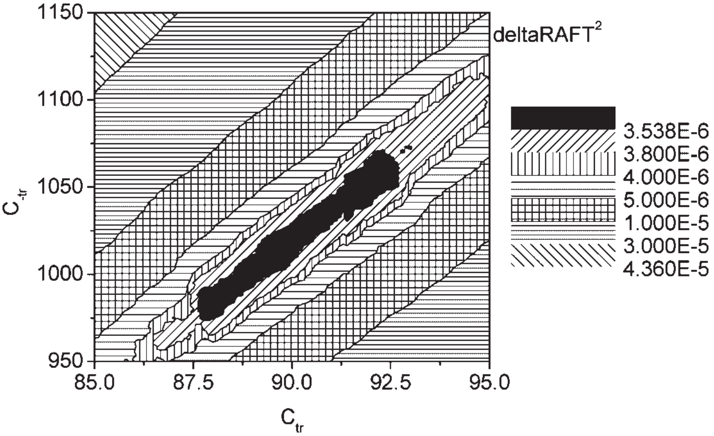


Figure 5.
joint confidence interval (black area) for the parameter C_{tr} and C_{-tr}.

Then the estimation of the variance (s^2) can be obtained (Equation 21) with $n - p$ degrees of freedom. The number of parameters (p) equals two in our case. From our experiments, 70 data points (n) for the parameter estimation were included. With the value from the F-distribution at level 95% ($F_{95\%}(2,70–2)$), all values of the parameters C_{tr} and C_{-tr} were estimated from the stochastic optimization inside the joint confidence interval (Equation 22), presented in Figure 5.

In consideration of the joint confidence interval of the estimated parameters (Figure 5), the relative error in both parameters is approximately the same. The parameters C_{tr} and C_{-tr} are strongly coupled and the proportion between the parameters (C_{tr}/C_{-tr}) is nearly constant over all points inside the joint confidence interval.

As the result of the parameter determination with our Monte Carlo simulation, the parameters C_{tr} and C_{-tr}, as well as the corresponding joint confidence interval, can be obtained.

Conclusion

The initialization period of Benzyl Dithiobenzoate RAFT mediated bulk polymerization of styrene at 120 °C was investigated for different RAFT agent and initiator concentrations. 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 following the concept of Rizzardo et al.[1,2] 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 expelled leaving group during the initialization period. For the determination of the transfer coefficients from the experimental data we developed a Monte Carlo simulation. The resulting transfer coefficients are $C_{tr} = 92$ and $C_{-tr} = 1057$.

With the transfer coefficients the characterization of the initialization period of the RAFT agent Benzyl Dithiobenzoate in agreement with the experimental date is possible. The proportion between transfer and back-transfer is very low ($C_{tr}/C_{-tr} = 0.09$). Therefore, a long time for the RAFT agent initialization period is observed.

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