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COMMUNICATION

L-Lactide Polymerization Studied by ^1H NMR with Diffusion Ordered Spectroscopy (DOSY). “One NMR Tube Experiment” Providing: Conversion, Polymer Structure, M_n and M_w .

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L-lactide polymerization has been studied by “One NMR Tube Experiment”. Traditional ^1H NMR, providing structure, conversion and number average molar mass (M_n) has been combined with Diffusion Ordered Spectroscopy (DOSY), yielding mass averaged molar mass (M_w). Thus, complete kinetic experiment could be performed without sampling, in one NMR tube.

Diffusion Ordered Spectroscopy (DOSY) has been elaborated above fifty years ago and today every NMR spectrophotometer has capability to conduct DOSY experiments. DOSY gives the dependence of the intensity of the peak ascribed to the given nuclei on its diffusion coefficient (D) and magnetic field gradient.¹ The physical principle of DOSY has been explained clearly in literature and various aspects of experimental set-up have been discussed.²⁻⁴ An exhaustive review of original papers devoted to the method and its applications in various areas of organic chemistry, including polymer chemistry, has also been published.⁵ In polymer chemistry DOSY has mostly been used in determination of M_w . This method has also been applied in our present work on L-lactide polymerization, to complement our kinetic work.

The detailed description of the theoretical bases of the method, eventually related to the Stokes-Einstein relation-ship (1) of the size of molecules and their diffusion coefficients has been given in several papers.⁶⁻⁹

$$D = \frac{Tk_B}{6\pi\eta R_H} \quad (1)$$

Where T is the absolute temperature, k_B is the Boltzmann constant, η is viscosity of the medium, and R_H is hydrodynamic radius of the studied molecule.

On the basis of the mean field theory molar mass M is related to R_H and leads to the dependence of M on D according to the simple equation (2), resembling the Mark-Houwink-Sakurada equation.¹⁰

$$R_H = KM^\nu \quad (2)$$

K is proportionality constant and ν is scaling exponent.

Finally, the relation between M and diffusion coefficient has a relatively simple form (3).

$$D = K'M^{-\nu} \quad (3)$$

The K' and ν coefficients have been determined for a few polymer-solvent systems.^{7,11-13}

Recently Grubbs et al. in a paper entitled “Application of ^1H DOSY for Facile Measurement of Polymer Molecular Weights” applied DOSY for the first time in studies of controlled polymerization of styrene and of 1,5-cyclooctadiene (ROMP).¹³ The conversion and mass average molar mass (M_w) data have been determined in the Grubbs’ paper by sampling the reaction mixture.

We decided to follow the Grubbs’ approach and study the L-lactide (LA) polymerization in this way, although in place of sampling the reaction mixture we performed polymerization in a sealed NMR tube, acquiring all the information “on-line” without taking samples. This was possible because the rate of the studied process is sufficiently slow at the measurement temperature, assuring that neither the measurements nor the polymerization were disturbed.

This work is divided into three parts. In the first one the dependence of diffusion coefficient on M_w for poly(L-Lactide) (PLA) is given. In the second this dependence is verified in a kinetic experiment with sampling the polymerization mixture. The third is devoted to the actual “One NMR Tube Kinetic Experiment”.

All experimental details, analytical procedures, results of characterization of the synthesized samples are described in the Electronic Supplementary Information (ESI).

Five samples of PLA were prepared (polymerization with $\text{Sn}(2\text{-ethylhexanoate})_2$ ($\text{Sn}(\text{Oct})_2$)/benzyl alcohol (BzOH) catalytic system) and precipitated from the polymerization solution. M_w were measured by SEC and D using DOSY. In addition, number average molar masses M_n were determined by ^1H NMR and SEC and compared with M_n calculated from the conditions of polymerization. The tabulated (Table 1) data were used to determine the analytical dependence of D on M_w (Figure 1). Then the relative difference (called “error”) between M_w determined by SEC and M_w calculated from D , using the established analytical dependence is given in the last column of Table 1.

Table 1 Characteristics of PLA samples

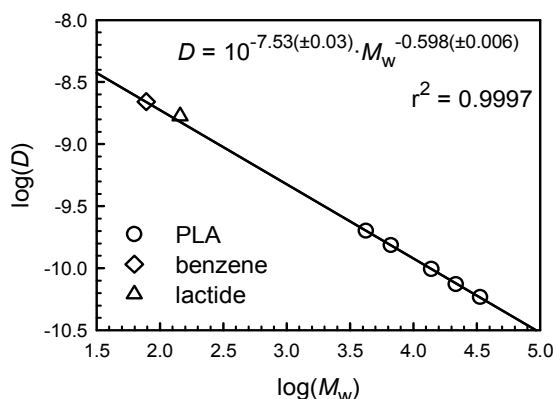
id	M_n (th) ^a	M_n ^b	M_n ^c	M_w ^c	\bar{D} ^c	$10^{11} \cdot D^d$ (m ² ·s ⁻¹)	M_w ^d	error ^e (%)
A	3 200	4 000	4 100	4 200	1.03	20.301	4 207	-0.6
B	4 660	6 450	6 300	6 700	1.05	14.977	6 601	3.5
C	10 500	13 100	13 500	13 900	1.03	9.857	13 861	0.2
D	20 100	20 100	21 000	21 600	1.03	7.301	22 065	6.3
E	29 700	30 100	31 000	33 700	1.09	5.838	33 056	-1.1

^a Based on stoichiometry and conversion. ^b Integration of ¹H NMR spectra. ^c SEC with MALLS detection. ^d DOSY NMR in C₆D₆. ^e $(M_w(\text{SEC}) - M_w(\text{DOSY})) \cdot 100 / M_w(\text{SEC})$.

As seen from the data collected in Table 1, the M_n determined by SEC with MALLS detector and from integrations of signals in the ¹H NMR spectra are consistent with the theoretical ones, based on the ratio $144.13x[\text{LA}]_0/[\text{BzOH}]_0$. Differences noted for the calculated and measured smallest masses could be ascribed to the fractionation-removal of the lower mass molecules during precipitation of the crude samples. Low dispersities (\bar{D}) (ranging from 1.03 to 1.09), indicate controlled behaviour of the applied polymerization process.

The DOSY spectra for PLA solutions were acquired according to the protocol used by Grubbs et al. (details given in ESI).¹³ A novel ITAMeD algorithm and the Matlab® script provided recently by Urbańczyk et al. have been used for extraction of D values from attenuation decay curves.⁶ Comparing with other methods, ITAMeD does not require any assumptions on composition of the analysed sample.

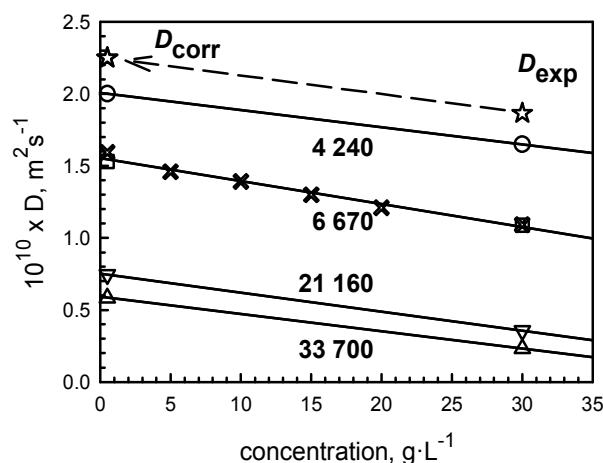
The NMR signal decay curves and obtained diffusion coefficient distributions are presented in the ESI. The numerical values of D and M_w are given in Table 1.

**Fig. 1** Weight-averaged molecular mass (M_w) vs. diffusion coefficient (D) log-log plot for PLA in benzene-d₆.

In Figure 1 the dependence of the diffusion coefficients on the corresponding mass average molar masses is given. A straight line fits the experimental data with correlation coefficient $r^2 = 0.9997$ and passes closely to points obtained for benzene and LA. The proportionality constant K' is equal to $10^{-7.53(\pm 0.03)}$ and value of the scaling exponent $\nu = 0.598(\pm 0.006)$. The value of the scaling exponent indicates that benzene is a good solvent for PLA, as it was established earlier on the basis of viscosity measurements.¹⁴ The D values extracted from DOSY spectra using the T1/T2 TopSpin module yield nearly identical result as the ITAMeD method: $K' = 10^{-7.53(\pm 0.03)}$ and $\nu = 0.597(\pm 0.006)$ (cf. Figure S5 in ESI).

The M_w values, calculated from analytical relationship (cf. Figure 1), were then compared with M_w determined by SEC. The highest noticed difference was equal to 6.3%.

Even though the established dependence is valid only for the polymer concentration of $0.5 \text{ g} \cdot \text{L}^{-1}$, after determining correction factors it has been successfully applied in studies of polymerization kinetics with changing concentration of the formed polymer. Polymer concentration's changes may also influence the diffusion coefficient by aggregation phenomena or simply by increasing solution viscosity. In order to correctly analyse the experimental data the dependence of D on polymer concentration (from 0.5 to $30 \text{ g} \cdot \text{L}^{-1}$) has been determined and plotted as in Figure 2.

**Fig. 2** Dependence of the D on M_w and concentration of polymer. Open marks: data used for determining of plot slopes. Crosses: data used for confirmation of linearity of the concentration dependence. Stars illustrate a correction introduced by equation 4. Numbers indicate M_w of samples.

The dependencies are linear and slopes do not depend on molar masses. It follows that the mean value of the slope (S) is equal to $(1.3 \pm 0.2) \cdot 10^{-12} \text{ m}^2 \cdot \text{l} \cdot \text{g}^{-1} \cdot \text{s}^{-1}$ and it is common for all molar masses within the studied range. Thus, the corrected value of the diffusion coefficient can be calculated from equation (4):

$$D_{\text{corr}} = D_{\text{exp}} - S(c_{\text{exp}} - c_{\text{corr}}) \quad (4)$$

Where: c is concentration; indices “exp” and “corr” mean experimental and corrected value, respectively.

Finally the M_w values were calculated from the D_{corr} using equation given in Fig. 1.

After having established the dependence of D on M_w and polymer concentration, it had been necessary to verify the correctness of this relationship before performing the “One NMR

Tube Experiment". Therefore a kinetic experiment on L-lactide polymerization was first performed with sampling of the polymerization mixture (protocol and conditions of experiments are given in ESI). The determined molar masses are given in Table 2.

Table 2 M_n , M_w , \bar{D} and D as determined by SEC, ^1H NMR and DOSY measurements in the kinetic experiment with sampling

id	M_n^a	M_w^a	\bar{D}^a	M_n^b	M_w^c	\bar{D}^d	$10^{11} \cdot D^c$ ($\text{m}^2 \cdot \text{s}^{-1}$)
1	6 500	6 800	1.03	6 800	6 780	1.00	1 5042
2	8 450	8 600	1.02	8 600	8 620	1.01	1 3048
3	9 400	9 700	1.04	9 800	10 100	1.03	1.1846
4	10 200	10 600	1.03	9 400	10 100	1.07	1.1840

^a SEC with MALLS detection. ^b Integration of ^1H NMR spectra. ^c From DOSY. ^d $M_n(^1\text{H NMR})/M_w(\text{DOSY})$

Data collected in Table 2 (as well as Figure S8 in ESI) show, that for the dead macromolecules both the DOSY and SEC methods give almost identical M_n and M_w . This additionally indicate that the relationship between M_w and D has been correctly determined. Moreover, \bar{D} of polymer samples range from 1.00 to 1.07, as expected for chains formed in the controlled-living polymerization.

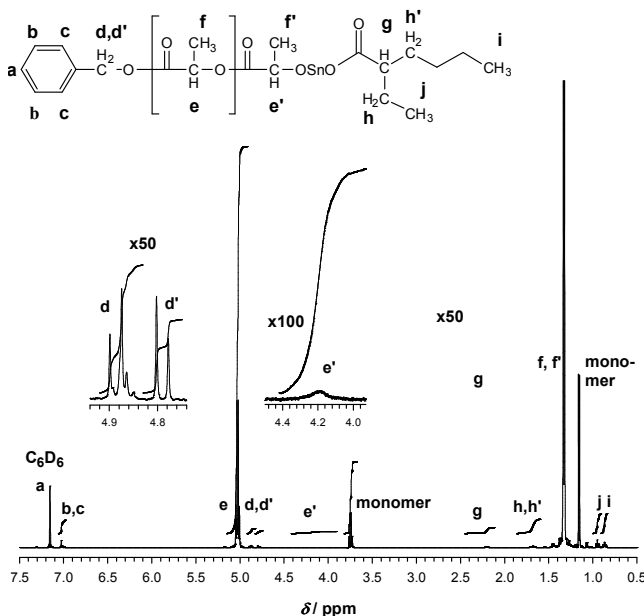


Fig. 3 ^1H NMR 500 MHz spectrum of the living PLA in C_6D_6 initiated by $\text{Sn}(\text{Oct})_2/\text{BzOH}$ system. Temperature 353 K, reaction time 12 h, $[\text{LA}]_0 = 0.226 \text{ mol} \cdot \text{l}^{-1}$, $[\text{BzOH}]_0 = 2.99 \cdot 10^{-3} \text{ mol} \cdot \text{l}^{-1}$, $[\text{Sn}(\text{Oct})_2]_0/[\text{BzOH}]_0 \approx 1.0$. Integrations (proton number): $d' = 1.0$, $e = 134.0$, monomer = 25.0.

Application of DOSY for studies of the polymerization kinetics of L-Lactide using the "One NMR Tube Experiment" approach is illustrated by polymerization conducted in sealed NMR tubes (experimental details are given in ESI). Polymerization mixture, containing C_6D_6 , LA, and initiating-catalytic system $\text{Sn}(\text{Oct})_2/\text{BzOH}$, was prepared and transferred into NMR tube under vacuum. The tube was then sealed-off and kept in a thermostat at 353 K. At predetermined time intervals the tube was cooled and ^1H NMR as well as DOSY spectra of the polymerizing mixture were acquired at 298 K. At this temperature, during the time of measurements (20 min), polymerization practically does not take place.

Table 3 Conversion, P_n , M_n , D , M_w and \bar{D} determined from ^1H NMR and DOSY measurements for the "One NMR Tube Experiment"

time s	conv.	P_n^a	M_n^b	$10^{10} \cdot D$ $\text{m}^2 \cdot \text{s}^{-1}$	M_w	\bar{D}^c
3 600	0.115	11.5	2 030	2.780	2 430	1.20
7 200	0.296	21.6	3 490	1.947	4 410	1.26
10 800	0.413	30.9	4 820	1.494	6 870	1.43
21 600	0.650	47.2	7 200	1.144	10 700	1.49
32 400	0.777	61.0	9 200	1.007	13 300	1.45
43 200	0.844	65.8	9 900	0.9972	13 500	1.36
129 600	0.924	72.9	10 900	0.9017	16 000	1.47
129 600 ^d	0.918	71.5	10 700	1.072	12 000	1.12

^a number of LA units. ^b BzOH and $-\text{SnOct}$ end groups. ^c M_n/M_w ^d quenched

The monomer conversion and degree of polymerization P_n have been determined from integrations of the standard ^1H NMR spectrum (Figure 3). The spectrum shows the structure of active macromolecules being in equilibrium with the temporarily inactive chains with $-\text{OH}$ end groups, in agreement with ref. 15. The monomer conversion was calculated from the ratio of integration of the methine protons of the lactoyl units e signal (overlapped quartets at $\delta = 5.0 - 5.1$ ppm) to integration of the monomer signal (quartet centred at $\delta = 3.75$ ppm). Signals e' and g are broadened due to equilibrium between active and inactive chains and therefore cannot be used for calculations of P_n of living macromolecules. P_n and M_n were calculated from the ratio of integrations of signals e and d' (the latter at $\delta = 4.89$ ppm).

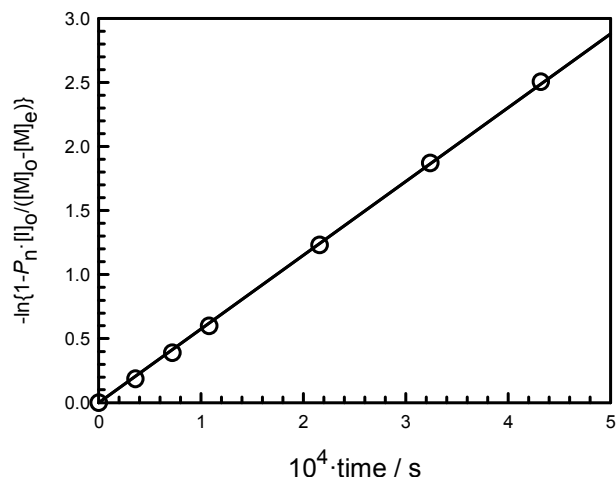


Fig. 4 Kinetic plot of the polymerization of LA in C_6D_6 initiated by $\text{Sn}(\text{Oct})_2/\text{BzOH}$ system. Temperature 353 K, $[\text{LA}]_0 = 0.226 \text{ mol} \cdot \text{l}^{-1}$, $[\text{BzOH}]_0 = 2.99 \cdot 10^{-3} \text{ mol} \cdot \text{l}^{-1}$, $[\text{Sn}(\text{Oct})_2]_0/[\text{BzOH}]_0 \approx 1.0$.

Figure 4 presents the experimental plot of the left hand side of equation 5 as function of time.

$$-\ln\left(1 - \frac{[I]_0 P_n}{[M]_0 - [M]_e}\right) = k_p [I]_0 t \quad (5)$$

The corresponding equation has been derived for living irreversible polymerization in one of our previous works by combining $\ln([M]_0/[M]_t) = -k_p [I]_0 t$ and $P_n = ([M]_0 - [M]_t)/[I]_0$.¹⁶ Equation 5, after introduction of $[M]_e$, is valid for the reversible

polymerization and can be used for determination of the propagation rate constant. The linearity of the plot (as in Figure 4) means that termination and irreversible transfer are simultaneously absent. $[I]_0$ in Equation 5 is equal to the invariant concentration of the living growing chains. However, in the system studied in this work, the concentration of the growing chains, being invariant, is neither equal to $[\text{Sn}(\text{Oct})_2]_0$ nor to $[\text{BzOH}]_0$. As the major aim of this work is demonstration of the “One NMR Tube Experiment”, it suffices to estimate the $[I]_0$ value using an approach presented in the work from our laboratory as well as the kinetic studies by Morbidelli.^{17,18}

It has been determined in our work, that the instantaneous concentration of the active centres is a function of $[\text{ROH}]$ for an invariant $[\text{Sn}(\text{Oct})_2]_0$.¹⁷ For the conditions used in the present work $[\text{P}^*] \approx [\text{ROH}]/3$ (where $[\text{P}^*]$ is the concentration of the momentarily active species. This results from formation of active species in the reversible reaction of $\text{Sn}(\text{Oct})_2$ and BzOH , followed by the propagation step with reversible inter-conversion of active chains into the temporarily inactive ones.

The slope in Figure 4 ($k_p[I]_0$) is equal to $5.76 \cdot 10^{-5} \text{ s}^{-1}$ and it follows that $k_p \sim 0.058 \text{ l} \cdot \text{mol}^{-1} \cdot \text{s}^{-1}$ ($[I]_0 = 1.134 \cdot 10^{-2} \text{ mol} \cdot \text{l}^{-1}$) which is close to $0.091 \text{ l} \cdot \text{mol}^{-1} \cdot \text{s}^{-1}$, calculated taking into account the temperature coefficient for k_p as determined by Morbidelli in bulk for the temperature range from 403 to 483 K.¹⁸

The values of diffusion coefficients for the instantaneous polymer concentrations were extracted from the on-line acquired DOSY spectra and corrected to the proper concentration (eq. (4)). M_w values were obtained from equation given in Figure 1.

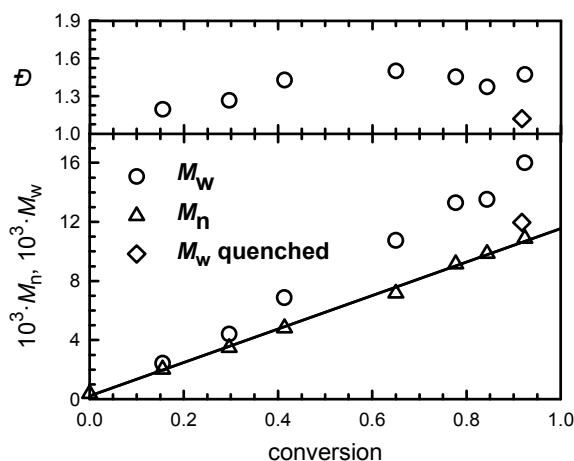


Fig. 5 Dependence of M_n , M_w and D on conversion in living polymerization of LA in C_6D_6 at 353 K, initiated by $\text{Sn}(\text{Oct})_2/\text{BzOH}$. $[\text{LA}]_0 = 0.226 \text{ mol} \cdot \text{l}^{-1}$, $[\text{BzOH}]_0 = 2.99 \cdot 10^{-3} \text{ mol} \cdot \text{l}^{-1}$, $[\text{Sn}(\text{Oct})_2]_0/[\text{BzOH}]_0 \approx 1.0$. Solid line is the least square fit to the M_n data. Numerical data in Table 3.

In Figure 5 the dependences of M_n and M_w on conversion are given. D values shown in the figure were calculated as equal to the ratio M_w/M_n .

The determined values of M_w (and therefore also D) are higher than expected for controlled-living polymerization. There are several possible reasons: aggregation of the living chains, reversibility of propagation, particularly important at higher conversion, and inter-conversion of the active and temporarily inactive chains. All these phenomena vanish for quenched samples. Indeed, M_w (and therefore also D) drop to the level characteristic for macromolecules formed in the controlled-living conditions. Corresponding results obtained from ^1H NMR/DOSY and SEC analyses of the “killed” polymers are shown in Table 2. A decrease of M_w and D was noticed also after

quenching the polymerization in the “One NMR Tube Experiment” (cf. Table 3 and Figure 5). Hence, the described methodology gives also an insight into the subtle phenomena in the polymerizing systems.

Conclusions

It has been shown, in the controlled polymerization of L-lactide, that combination of different NMR techniques (standard and DOSY) allows studying on-line the kinetics of polymerization together with determination of M_n , M_w and D . Moreover, in the same experiment carried out in a single NMR tube, the poly(L-lactide) structure analysis has been possible.

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Notes and references

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Electronic Supplementary Information (ESI) available: experimental procedures, NMR and SEC data. See DOI: 10.1039/c000000x/

- 1 E. O. Stejskal, J.E. Tanner, *J. Chem. Phys.*, 1965, **42**, 288.
- 2 J. N. Maki, N. M. Loening In *Modern NMR Spectroscopy in Education*, Eds.: D. Rovnyak, R. Stockland, American Chemical Society, 2007, ch. 12.
- 3 W. S. Price, *Concepts Magnetic Res.*, 1997, **9**, 299.
- 4 W. S. Price, *Concepts Magnetic Res.*, 1998, **10**, 197.
- 5 C. S. Johnson Jr., *Prog. NMR Spectrosc.*, 1999, **34**, 203.
- 6 M. Urbańczyk, D. Bernin, W. Koźmiński, K. Kazimierzczuk, *Anal. Chem.*, 2013, **85**, 1828.
- 7 A. Chen, D. Wu, C. S. Johnson Jr., *J. Am. Chem. Soc.*, 1995, **117**, 7965.
- 8 A. Jerschow, N. Müller, *Macromolecules*, 1998, **31**, 6573.
- 9 K. F. Morris, C. S. Johnson Jr., *J. Am. Chem. Soc.*, 1993, **115**, 4291.
- 10 M. Doi, S. F. Edwards, *The Theory of Polymer Dynamics*, Oxford University Press, 1994, ch. 2.
- 11 S. Augé, P.-O. Schmit, C. A. Crutchfield, M. T. Islam, D. J. Harris, E. Durand, M. Clemancey, A.-A. Quoineaud, J.-M. Lancelin, Y. Prigent, F. Taulelle, M.-A. Delsuc, *J. Phys. Chem. B*, 2009, **113**, 1914.
- 12 R. Plummer, D. J. T. Hill, A. K. Whittaker, *Macromolecules*, 2006, **39**, 3878.
- 13 W. Li, H. Chung, C. Daeffler, J. A. Johnson, R. H. Grubbs, *Macromolecules*, 2012, **45**, 9595.

Journal Name

- 14 A. Schindler, D. Harper, *J. Polym. Sci.: Polym. Chem. Ed.*, 1979, **17**, 2593.
- 15 A. Kowalski, A. Duda, S. Penczek, *Macromolecules*, 2000, **33**, 7359.
- 16 S. Penczek, P. Kubisa, R. Szymanski, *Macromol. Chem. Rapid. Commun.*, 1991, **12**, 77.
- 17 A. Kowalski, A. Duda, S. Penczek, *Macromolecules*, 2000, **33**, 689.
- 18 Y. Yu, G. Storti, M. Morbidelli, *Ind. Eng. Chem. Res.*, 2011, **50**, 7927.