

# Kinetic Study upon the Thermal Degradation of Poly(N-isopropylacrylamide-co-5,6-benzo-2-methylene-1,3-dioxepane) Statistical Copolymers

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*Statistical copolymers N-isopropylacrylamide (NIPAM) – 5,6-benzo-2-methylene-1,3-dioxepane (BMDO) with different compositions were prepared by RAFT polymerization and characterized by <sup>1</sup>H NMR, GPC and DSC analyses. Their solid-state thermal degradation was investigated for the first time by TGA, showing that the presence of the BMDO units within the PNIPAM chain decreased the thermal stability of the copolymer. In the case of higher BMDO content copolymers the onset decomposition temperature was lower even than that of PBMDO, and also a multistep decomposition process was noticed. The evolution of the global activation energy of the degradation process as a function of degradation conversion was determined by means of the Kissinger-Akahira-Sunose isoconversional method.*

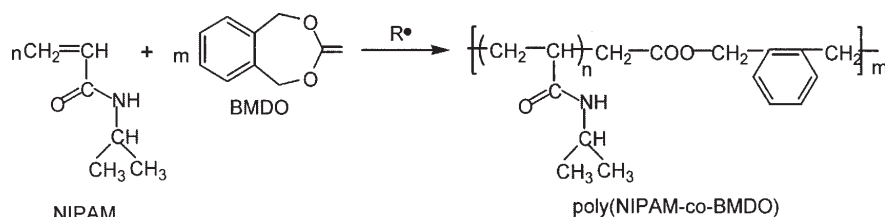
**Keywords:** N-isopropylacrylamide; 5,6-benzo-2-methylene-1,3-dioxepane; copolymer; thermosensitive; thermal degradation; Kissinger-Akahira-Sunose isoconversional method

Thermosensitive water-soluble polymers have been intensely researched within the last decades due to both their biomedical and industrial applications, based on their temperature-triggered hydrophilic-hydrophobic transition in aqueous solutions [1-8]. Amongst them, poly(N-isopropylacrylamide) (PNIPAM) is maybe the most well known, largely involved in biomedical research due to its lower critical solution temperature (LCST  $\approx$  32°C) close to body temperature and abrupt thermal response [9,10]. However, PNIPAM is a non-biodegradable polymer because of the backbone being made up only of C-C bonds and therefore, difficult to be removed from the body, which seriously limits its biomedical applications. To overcome this, degradable PNIPAM polymers containing hydrolysable ester groups within the backbone have been prepared recently by free-radically copolymerizing NIPAM with cyclic ketene acetals, like for example 5,6-benzo-2-methylene-1,3-dioxepane (BMDO, scheme 1) [11,12] or 2-methylene-1,3-dioxepane (MDO) [13,14]. After the hydrolysis of these in-chain ester groups, the polymer molecule is broken in smaller segments that should be both soluble and easy to remove from the body because of their lower MW.

Both crosslinked [12] and linear [11,12] NIPAM – BMDO statistical copolymers were prepared by free radical polymerization, either conventional [11] or living/controlled

(ATRP and RAFT) [12], and the synthesized copolymers were evaluated from the point of view of molecular structure [11,12], comonomer reactivity ratios [11], phase transition temperature in aqueous solution [11,12], glass transition temperature [11], hydrolytic degradability [11,12] and cytotoxicity [12]. However, no information concerning the thermal degradation of these copolymers was provided neither within these papers, nor somewhere else, although the stability of several other PNIPAM copolymers was reported in literature [15-17].

The present paper aims at investigating the solid-state thermal degradation of the NIPAM-BMDO statistical copolymers, which may be important to know when the fabrication of a certain object involves copolymer processing by various techniques requiring higher temperatures like for example injection molding or extrusion. We will show within this paper that the presence of the BMDO units inside the PNIPAM chain decreased the thermal stability of PNIPAM, and very interesting, at higher BMDO content, the stability of the copolymers was lower even than that of PBMDO. The evolution of the global activation energy of the degradation process as a function of degradation conversion was determined by means of an isoconversional method.



Scheme 1. Copolymerization of NIPAM and BMDO and structure of the resulting statistical copolymers

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Sample code	NIPAM/BMDO mol/mol	monomer(s)/RAFT agent/initiator mol/mol/mol	monomer(s)/solvent ratio g/ml	reaction time h
PNIPAM	100/0	88/1/0.1	3/10	24
PNB1	80/20	88/1/0.1	3.4/10	48
PNB2	40/60	100/1/0.4	5.1/10	72
PNB3	20/80	100/1/0.4	5.5/10	72
PBMDO	0/100	100/-/2.5	-**	27

\* solvent – DCB, initiator – DTBP; RAFT agent – TTC; temperature - 120°C;

\*\* bulk polymerization.

## Experimental part

### Materials and methods

N-Isopropylacrylamide (NIPAM, Aldrich, 97%) was recrystallized from hexane. 5,6-Benzo-2-methylene-1,3-dioxepane (BMDO) was synthesized according to the procedure of Wickel and Agarwal [18] and stored under nitrogen. The RAFT agent 2-dodecylsulfanylthiocarbonylsulfanyl-2-methylpropionic acid (S-1-dodecil-S'-( $\alpha,\alpha'$ -dimethyl- $\alpha''$ -acetic acid) trithiocarbonate, TTC) was synthesized as described in literature [19] and stored in the refrigerator. 1,2-Dichlorobenzene (Sigma-Aldrich, anhydrous, 99%, DCB) and di-*t*-butyl peroxide (Chimopar S.A., 98%, DTBP) were used as received.

### Synthesis of (co)polymers

A dried 10 mL Schlenk flask was charged with 0.6 – 0.8 g monomer(s) and the appropriate amount of TTC, and sealed by a rubber septum. The flask content was cycled 6 times between vacuum and nitrogen, and finally filled with nitrogen. Separately, the appropriate volume of solvent was bubbled with nitrogen in a 5 mL flask for 25 min, the calculated amount of DTBP was added and nitrogen was passed through the mixture for 5 more min. The initiator solution was then transferred via a degassed syringe to the polymerization flask, and the reaction mixture was allowed to polymerize under stirring at 120°C for various time intervals. In the case of PBMDO synthesis, the initiator was added directly to the Schlenk flask via a degassed microsyringe. The experimental conditions employed are displayed in table 1. At the end of the reaction time, the reaction mixture was cooled down, diluted with chloroform and precipitated in cold diethyl ether (PNIPAM, PNB1) or hexane (PNB2, PNB3, PBMDO). The precipitate was isolated by filtration or decantation and dried under vacuum at room temperature to constant weight. The amount of precipitate obtained was employed for the calculation of the overall monomer conversion (table 2). The polymer was purified one more time by dissolution in chloroform, filtration through a 0.45 $\mu$ m microfilter, precipitation in

diethyl ether or hexane, isolation by filtration or decantation and drying under vacuum.

### Characterization

The molecular weights and molecular weight distributions of the synthesized polymers were determined by gel permeation chromatography (GPC), carried out on an Agilent Technologies 1200 series instrument, with a PolarGel M (300x7.5 mm) column and an Agilent 1200 differential refractometer, in DMF, at 30°C and a flow rate of 1 mL/min. Calibration was made with polystyrene standards.

<sup>1</sup>H NMR spectra were recorded on a 300 MHz Varian Gemini 300 BB spectrometer, using deuterated chloroform as the solvent.

The glass transition temperature ( $T_g$ ) of the synthesized polymers was determined by differential scanning calorimetry (DSC) measurements carried out on a NETZSCH DSC 204 F1 Phoenix instrument operating under nitrogen flow at 10°C/min heating rate. Samples weighing about 5 mg were cycled between -60 and 200°C, and  $T_g$  was determined by means of the instrument software from the inflexion point obtained during the second heating cycle.

The thermogravimetric analyses (TGA) were carried out on a Thermal Analysis Q500 instrument by heating samples of about 2.1  $\pm$  0.1 mg from room temperature to 650°C under nitrogen flow. In order to use isoconversional methods, each sample was scanned at four different heating rates (2, 5, 10, 20°C/min).

## Results and discussions

### (Co)polymer synthesis and characterization

The copolymerization reactivity ratios of NIPAM and BMDO are very different, i.e.  $r_{\text{NIPAM}} = 7.31$  and  $r_{\text{BMDO}} = 0.11$  [11], which means that NIPAM is consumed much faster than BMDO during the copolymerization process. As a consequence, in a conventional free radical copolymerization process the composition of the macromolecules

Sample	Overall monomer conversion %	(NIPAM/BMDO) <sub>copolymer</sub> mol/mol	$M_n$	PDI	$T_g$ °C
PNIPAM	90	100/0	6300	1.39	127
PNB1	67	82/18	6600	1.46	111
PNB2	65	49/51	3180	1.95	51
PNB3	60	23/77	2860	1.91	25
PBMDO	36	0/100	3600	2.65	17

**Table 2**  
CHARACTERISTICS OF THE  
(CO)POLYMERS PREPARED

formed at different reaction times is different, i.e. those formed at the beginning of the process are rich in NIPAM units, while those formed at higher conversions have an increased BMDO unit content [20]. Such a copolymer composition drift does not occur in a living polymerization process, where the copolymer is made up of macromolecules having all the same composition, although a composition drift can be noticed along the macromolecular chain instead [21]. Therefore, in order to avoid the formation of macromolecules of different composition that could have affected the reproducibility of the thermal degradation process, we employed a living/controlled free radical polymerization technique, namely reversible addition-fragmentation chain transfer (RAFT) polymerization, which was already used for the preparation of some NIPAM-BMDO statistical copolymers with a lower BMDO units content [12]. The same RAFT procedure was applied for the preparation of the PNIPAM homopolymer, while PBMDO was synthesized by bulk conventional radical polymerization [22] because the RAFT polymerization led to very low conversions under the experimental conditions employed within this work. As BMDO strongly slows down the copolymerization rate [11], different experimental conditions were used for the RAFT synthesis of PNIPAM and NIPAM-BMDO copolymers (table 1) in order to obtain higher conversions (table 2).

The (co)polymers prepared were characterized from the point of view of their composition, molecular weight and polydispersity and glass transition temperature. The structure and composition of the polymers were determined by <sup>1</sup>H NMR. Figure 1 shows that the copolymer spectra contained the characteristic proton signals of both NIPAM and BMDO units. All of them displayed a broad peak corresponding to the methylene ester units of the opened acetal cycle BMDO units at 4.6-5.4 ppm [11,18, 23]. The area of this peak and of the one at 3.9 ppm belonging to the methine proton in the isopropyl group of NIPAM were used to calculate the copolymer composition (table 2). The NIPAM/BMDO mole ratio in the copolymers was always higher than that in the feed due to the higher reactivity of NIPAM, in agreement with the published data [11,12].

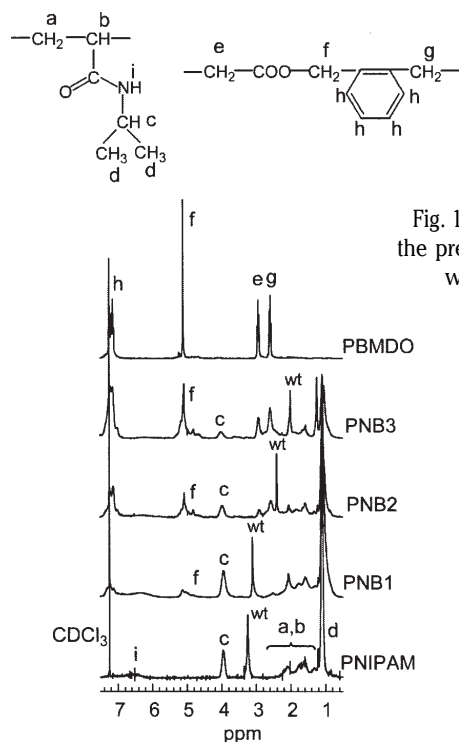


Fig. 1. <sup>1</sup>H NMR spectra of the prepared (co)polymers. wt = water traces

The molecular weights and molecular weight distributions of the polymers prepared were determined by GPC in DMF (table 2). The  $M_n$ s obtained seem to be underestimated, very likely due to the calibration with polystyrene standard. The measured polydispersities indicated a good control of the polymerization process for PNIPAM and PNB1, but at higher BMDO concentrations the polymerization control was lost, as indicated by the PDI values being around 2.

Besides <sup>1</sup>H NMR, the DSC measurements (table 2, fig. 2) confirmed the copolymer formation, the  $T_g$  values determined for the P(NIPAM-co-BMDO) copolymers falling in-between those of PNIPAM and PBMDO, and increasing with NIPAM unit concentration. The  $T_g$  values determined for PNIPAM and PBMDO, i.e. 127°C and 17°C, respectively, were around those reported in literature, i.e. 132°C [17], 140°C [15] or 143°C [11] for PNIPAM and 15°C [15] or 20°C [11] for BMDO, a little smaller in the case of PNIPAM very likely because of the lower molecular weight.

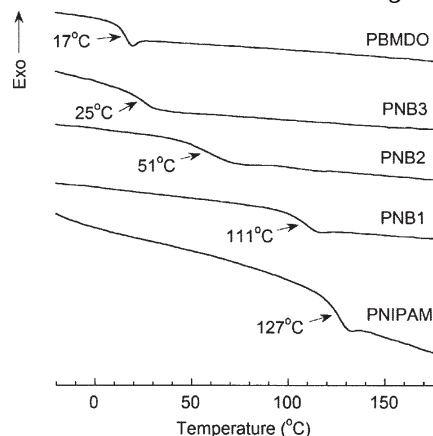


Fig. 2. DSC traces for the prepared (co)polymers. Second heating cycle

### Thermal degradation

The thermal degradation of the synthesized (co)polymers was investigated by TGA (fig. 3). The results showed that the presence of the BMDO units within the PNIPAM chain decreased the thermal stability of the copolymers, the onset decomposition temperature in the case of higher BMDO content copolymers being even lower than that for PBMDO. Also, a multistep decomposition was noticed for the copolymers containing larger amounts of BMDO units (fig. 3B).

The thermal degradation process of the (co)polymers prepared was more in depth investigated by performing a computational kinetic analysis. Thus, the global activation energy of the degradation process as a function of conversion was calculated based on four TGA experimental data sets acquired at different heating rates (2, 5, 10, 20°C/min) by applying the Kissinger-Akahira-Sunose iso-conversional method [24,25].

The isoconversional methods allow the computation of the global activation energy for each given conversion without any arbitrary assumption of a model function ("model-free methods"). The theory behind these methods is based on the kinetics of polymer degradation (considered as reactions in solids), usually described by eq. (1):

$$\frac{d\alpha}{dt} = k(T)f(\alpha) \quad (1)$$

where:

$\alpha$  = conversion degree,  $t$  = time,  $d\alpha/dt$  = reaction rate,  $k(T)$  = temperature-dependent rate constant,  $f(\alpha)$  =

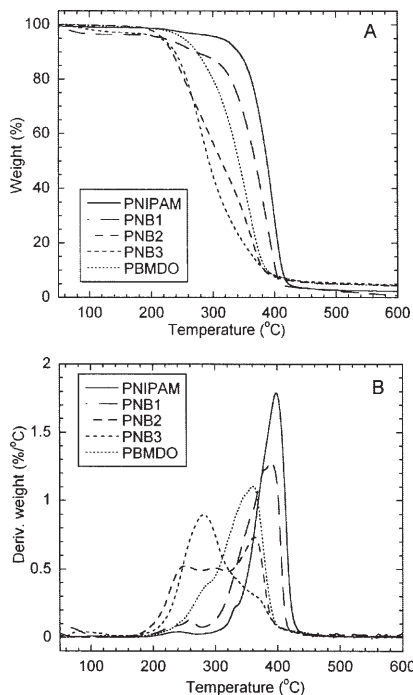


Fig. 3. TGA (A) and DTG (B) traces for the prepared (co)polymers. Heating rate = 10°C/min

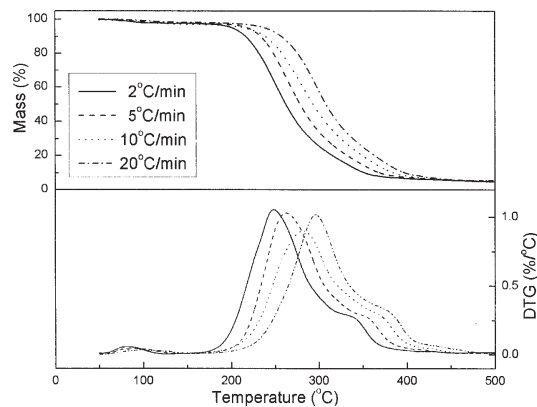


Fig. 4. TGA and DTG curves for the PNB3 sample at different heating rates

reaction mathematical model. The temperature dependence of  $k(T)$  obeys an Arrhenius-type expression, and, therefore, eq. (1) yields:

$$\frac{d\alpha}{dt} = A \exp\left(-\frac{E}{RT}\right) f(\alpha) \quad (2)$$

where:

$A$  = the preexponential factor,  $E$  = the activation energy,  $R$  = the gas constant.

By logarithmation and differentiation versus  $T^{-1}$ , eq. (2) can be written as:

$$\frac{d \ln(d\alpha / dt)_\alpha}{dT^{-1}} = -\frac{E_\alpha}{R} \quad (3)$$

According to eq. (3), it becomes clear that the reaction rate is a function only of the temperature at a specific conversion degree (subscript  $\alpha$  in  $E_\alpha$  denotes the value of activation energy for the conversion  $\alpha$ ). Several isoconversional methods have been proposed to solve this equation by Kissinger-Akahira-Sunose [24,25], Ozawa-Flynn-Wall [26,27], Friedman [28], Vyazovkin [29,30], Cai and Chen [31]. Among them, the Kissinger, Akahira and Sunose (KAS) method (eq. 4) was recommended by the ICTAC Kinetics Committee as providing more accurate results [32].

$$\ln\left(\frac{\beta_i}{T_{\alpha,i}^2}\right) = \ln\left(\frac{AR}{E_\alpha}\right) - \ln[g(\alpha)] - \frac{E_\alpha}{RT_{\alpha,i}} = ct. - \frac{E_\alpha}{R} \cdot \frac{1}{T_{\alpha,i}} \quad (4)$$

where:

$i$  is the number of the experiment,  $\beta_i = dT_i/dt$  - heating rates,  $T_{\alpha,i}$  - temperature corresponding to conversion  $\alpha$  for the experiment  $i$ , and  $g(\alpha)$  is definite by the relation (5):

$$g(\alpha) = \int_0^\alpha \frac{d\alpha}{f(\alpha)} \quad (5)$$

The activation energy  $E_\alpha$  is determined from the plot of  $\ln(\beta_i/T_{\alpha,i}^2)$  (left side of eq. 4) versus  $1/T_{\alpha,i}$  at constant conversion degree  $\alpha$ , for  $i$  heating rates. This is considered a typical plot for the KAS isoconversional method and the graph consists in series of collinear points corresponding at the same conversion  $\alpha$ . The activation energy  $E_\alpha$  is determined from the slope of these lines.

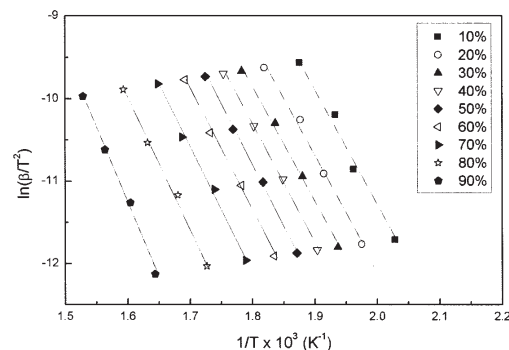


Fig. 5.  $\ln(\beta/T^2)$  vs.  $1/T$  plot according to KAS method, at different degradation extent. PNB3 sample

From TGA experimental data, the conversion degree  $\alpha$  was determined as the fraction of the mass loss:

$$\alpha = \frac{m_0 - m_t}{m_0 - m_\infty} \quad (6)$$

where:

$m_0$  and  $m_\infty$  are the initial and final sample weights and  $m_t$  - the sample weight at time  $t$ .

Figure 4 shows the TGA/DTG curves for all heating rates for the PNB3 sample. As expected, the curves were translated to higher temperatures when the heating rate increased, due to thermal inertia (a shift of approximately 15°C could be observed by doubling the heating rate) [32].

The TGA experimental data series for each of our samples were further used to compute the activation energy  $E_\alpha$  as a function of conversion degree of the degradation process  $\alpha$ . The characteristic  $\ln(\beta_i/T_{\alpha,i}^2)$  vs.  $1/T_{\alpha,i}$  plots of the KAS isoconversional method displayed good collinearity of the points for all the samples (fig. 5).

The dependence of the global activation energy of the degradation process, calculated from the slope of plots similar to those displayed in figure 5, on conversion for the polymers prepared is shown in figure 6.

It is interesting to note that the activation energy showed variations in all cases, even for the homopolymers, which indicated that the degradation process occurred in more steps (processes occurring simultaneously or successively). This finding was in agreement with the shape of the TGA and DTG curves (fig. 3), where more or less evident "shoulders" corresponding to processes of reduced intensity could be seen.

In agreement with the DTG traces, the most important variation of  $E_\alpha$  was noticed for the PNB2 sample, which displayed three degradation steps (three maxima on the DTG curve, fig. 3B). In this case, one can notice a plateau for  $E_\alpha \sim 102$  kJ/mol up to a conversion of about 0.25



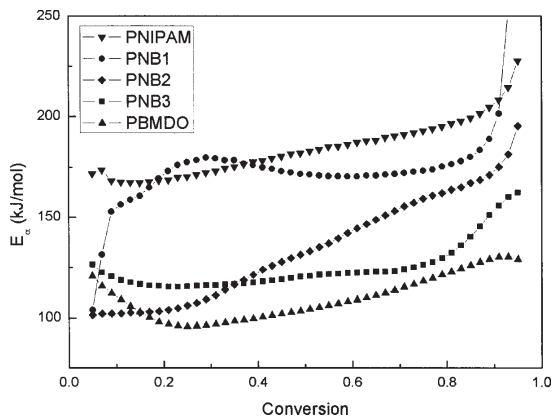


Fig. 6. Activation energy  $E_{\alpha}$  as a function of degradation conversion for the prepared (co)polymers

(ascribed to the first peak on the DTG curve), followed by a continuous increase of  $E_{\alpha}$  due to the overlapping of the processes. An inflexion point could be observed on the  $E_{\alpha}$  curve at a conversion value of about 0.54, which can be looked as the passing point from the second to the third degradation step.

Very interestingly, it should be noted that, above a conversion of 0.4, the activation energy values obeyed the monomer content order, i.e. they increased as the NIPAM units content increased. However, below this conversion value, the composition order was not observed, because of the copolymers with a higher NIPAM units content. Similar effects, when the activation energy evolution was not in agreement with the monomer content, was previously reported as well [33,34].

## Conclusions

The solid-state thermal degradation of some NIPAM – BMDO statistical copolymers of various compositions was investigated by TGA. The results showed that the presence of the BMDO units within the PNIPAM chain decreased the thermal stability of the copolymers, the onset decomposition temperature in the case of higher BMDO content copolymers being lower even than that of PBMD0. Also, a multistep decomposition was noticed for the copolymers containing larger amounts of BMDO units. The evolution of the global activation energy of the degradation process as a function of degradation conversion was determined by means of the Kissinger-Akahira-Sunose isoconversional method. It was shown that above a conversion of 0.4, the activation energy values obeyed the monomer content order, i.e. they increased as the NIPAM units content increased. However, below this conversion value, the composition order was not observed, because of the copolymers with a higher NIPAM units content.

*Acknowledgements:* This work was supported by a grant of the Ministry of National Education, CNCS – UEFISCDI, project number PN-II-ID-PCE-2012-4-0082. GT acknowledges the financial support of the Sectorial Operational Programme Human Resources Development, financed from the European Social Fund and by the Romanian Government under the contract number POSDRU/156/1.2/G/135764

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Manuscript received: 21.11.2014