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Published in: Macromolecules

DOI: 10.1021/acs.macromol.8b01150

Link to publication

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Aqueous Phase Separation Behavior of Highly Syndiotactic, High Molecular Weight Polymers with Densely Packed Hydroxy-Containing Side Groups

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Supporting Information

ABSTRACT: Herein we describe the Rh-catalyzed C1 polymerization of silyl-protected diazoacetates of the general formula HC(N=N)(C(==O)O(CH2)x)OSiR3, where x = 2–5. After polymerization and subsequent desilylation, syndiotactic polymers bearing a hydroxy-containing side group on every backbone carbon are obtained. The molecular weight of the desired polymers can be controlled via chain transfer with methanol during the polymerization. The produced polymers are compared to atactic analogues formed by [(η5-C5H5)PdCl]-catalyzed polymerization of silyl-protected diazoacetates with the same general formula. While the polymers produced by the Rh and Pd catalysts have the same hydrophilic/hydrophobic balance, the stereoregularity of the polymers formed by the Rh catalyst was found to be of influence on the thermoresponsive behavior of the polymer. The effect of this stereoregularity on the thermoresponsive phase separation behavior of the produced polymers in aqueous solution was investigated.

INTRODUCTION

Stimuli-responsive polymers are polymers that show changes in their chemical and/or physical properties in response to changes of their environment (stimuli), e.g. change in pH, temperature, or exposure to light. One can imagine a myriad of applications for these polymers, and indeed they gained increasing attention in the biomedical (e.g. biosensing, controlled drug delivery, and imaging contrast agents), bioengineering, and chemical fields (e.g. stabilization of colloids, oil-displacing agents, and catalyst supports). Most polymers used in those fields are thermoresponsive polymers, which undergo a reversible phase transition when subjected to temperature changes. The temperature at which the phase transition in solution occurs is called the critical solution temperature. Polymers that become soluble as the temperature transition in solution occurs is called the critical solution temperature changes. The temperature at which the phase transition of the polymer. The effect of this stereoregularity on the thermoresponsive phase separation behavior of the produced polymers in aqueous solution was investigated.

the polymers. Transition metal (TM) catalyzed polymerization is known to give access to highly stereoregular polymers, but many polar functional groups on the monomers are not compatible with existing catalysts in TM polymerization. This makes the preparation of well-defined, stereoregular, high molecular weight (Mn) polymers from polar functionalized C2 monomers very difficult. A new strategy for the synthesis of stereoregular, high molecular weight polymers is TM-catalyzed C1 (methylene or carbene) polymerization. This approach allows for the synthesis of stereoregular polymers that are functionalized with polar groups on every backbone carbon and is also a powerful tool to obtain polymers with a large structural diversity. Cu- and Pd-catalyzed C1 polymerization reactions of diazoesters and diazoketones have been reported, but the low molecular weight and atacticity of the obtained polymers as well as the often observed random incorporation of azo groups are limitations of these catalyst systems. Rh-catalyzed C1 polymerization is more selective and gives access to high molecular weight and highly syndiotactic polymers with polar ester functionalities at every carbon atom of the polymer backbone. Recently, Ishara and co-workers published the synthesis of C1 analogues of PHEMA, PHEA (poly(2-hydroxyethyl acrylate)), and oligo(ethylene glycols) (OEGs) via palladium-
catalyzed C1 polymerization of hydroxyl-containing diazoacetates.\textsuperscript{42,43} The resulting polymers were expected to have unique properties such as high hydrophilicity and superior thermal and mechanical properties due to the denser packing of the substituents around the polymer chain. Indeed, the resulting polymers are soluble in water and show thermoresponsive behavior in aqueous media. However, the polymers have low $M_w$ and atactic structures. This work inspired us to investigate the polymerization of silyl-protected hydroxyl-containing diazoacetates using the stereospecific Rh catalyst I (Scheme 1).\textsuperscript{37,41} We wondered in particular what would be the effect of the stereoregularity (syndiotactic instead of atactic) of these type of polymers on their LCST behavior. We have previously shown that the active species in the Rh-catalyzed polymerization of diazoacetates is the $\left[\left(\text{C}_8\text{H}_{11}\right)\text{Rh}^{\text{III}}-\text{OH}\right]^+$ species II, formed in situ from precatalyst I. This active species II gives the highest stereocontrol as well as the highest initiation efficiency known in the polymerization of diazoacetates.\textsuperscript{41} Herein we describe the Rh-catalyzed polymerization of silyl-protected diazoacetates, using complex I, and subsequent deprotection of these functionalized polymers to yield the desired polymers, functionalized with a hydroxyl-containing side chain at every carbon atom of the polymer backbone. On the basis of our previous results,\textsuperscript{41} we expected that polymers with a stereoregular and dense packing of hydroxyl groups in the polymer chain would be obtained. We show that indeed syndiotactic polymers are formed and that their tactility and the length and the type of side chains affect the behavior of these polymers in aqueous media. Those polymers with the proper hydrophilic/hydrophobic balance show thermoresponsive behavior in aqueous solution. The influence of the tactility, $M_w$ (controlled by alcohol-mediated chain transfer\textsuperscript{40}), and the concentration of the polymer solutions on their thermoresponsive behavior is demonstrated.

### Scheme 1. Rh Precatalyst I (\\[\left(\text{Allyl}-\beta-\text{Alkyl Hydroxide})\text{Rh(N}_3\right)] ) and the Active (\\[\left(\text{Allyl–Ene})\text{Rh}^{\text{III}}-\text{OH}\right]^+$ Species II

![Scheme 1](image)

### RESULTS AND DISCUSSION

#### Rh-Catalyzed Synthesis of Hydroxy-Containing Polymers from Diazooacetates. The silyl-protected monomers $^x\text{M}_x$ with different spacer lengths ($x = 2–5$) were synthesized following a protocol similar to that reported by Ihara and co-workers.\textsuperscript{43} To synthesize the highly functionalized and stereoregular polymers, we used the allyl-$\beta$-alkyl hydroxide Rh catalyst precursor I (Scheme 1) instead of the $\left[\left(\eta^3-\text{C}_3\text{H}_5\right)\text{PdCl}\right]$ catalyst used by Ihara and co-workers. \textsuperscript{43} Subsequent deprotection of polymers $^x\text{P}_x$ ($x = 2–5$) with HCl in a THF/MeOH mixture produced the hydroxyl-containing polymers $^x\text{M}_x$ ($x = 2–5$) in high yields (Scheme 2).

The polymerization of the silyl-protected monomers was performed in CH$_2$Cl$_2$ with a monomer/catalyst ratio of 50:1. To this solution the monomer was added at 0 °C, after which the reaction mixture was allowed to warm up to room temperature and stirred over a period of 16 h. The thus formed polymers were isolated and separated from co-produced oligomers by precipitation with methanol. The results of the polymerization reactions are summarized in Table 1.

In entry 3, polymerization of $^x\text{M}_x$ was performed using $\left[\left(\eta^3-\text{C}_3\text{H}_5\right)\text{PdCl}\right]$ as catalyst, also used by Ihara and co-workers,\textsuperscript{43} to compare the Pd and Rh complexes as catalysts in the polymerization of these diazoacetates. The use of $\left[\left(\eta^3-\text{C}_3\text{H}_5\right)\text{PdCl}\right]$ causes a decrease of both yield and $M_w$ but produces polymers with a narrower polydispersity than rhodium catalyst I (see Table 1, entries 2 and 3).

By changing the monomer/catalyst ratio to 25:1 (Table 1, entry 6), we were able to synthesize polymers with a molecular weight almost half of the $M_w$ obtained when using a 50:1 ratio (Table 1, entry 5). Our group\textsuperscript{40} and the group of Ihara\textsuperscript{26} have independently reported that in the presence of alcohols or water Rh- and Pd-catalyzed polymerization of diazoacetates proceeds to give polymers. Ihara showed that when using $\left[\left(\eta^3-\text{C}_3\text{H}_5\right)\text{PdCl}\right]$ as the catalyst, direct polymerization of the unprotected hydroxyl-containing diazocate $^x\text{M}_x$ is possible and forms the same polymers as when using the protected monomer $^x\text{M}_x$.\textsuperscript{43} Therefore, to avoid time-consuming protection–deprotection processes, we attempted to polymerize the unprotected monomer $^x\text{M}_x$ with precatalyst I, but unfortunately only dimers were formed in this case. So this approach was discarded.

As alcohols are known to act as chain-transfer agents in Rh-mediated carbene polymerization,\textsuperscript{40} we investigated the effect of alcohol on the polymerization of the silyl-protected monomer $^x\text{M}_x$ to control the chain length of the resulting polymer $^x\text{P}_x$. As such, monomer $^x\text{M}_x$ was polymerized in the presence of different amounts of methanol (Table 1, entries 7–9). As expected, increasing the amount of methanol led to

![Scheme 2](image)
Table 1. Polymerization Results Using Monomers *M*<sub>2</sub>–*M*<sub>5</sub><sup>a</sup>

<table>
<thead>
<tr>
<th>entry</th>
<th>monomer</th>
<th>solvent (CH&lt;sub&gt;2&lt;/sub&gt;Cl&lt;sub&gt;2&lt;/sub&gt;:MeOH)</th>
<th>catalyst</th>
<th>yield (%)</th>
<th><em>M</em>&lt;sub&gt;n&lt;/sub&gt; (kDa)</th>
<th><em>M</em>&lt;sub&gt;n&lt;/sub&gt; (kDa)</th>
<th><em>M</em>&lt;sub&gt;n&lt;/sub&gt;/<em>M</em>&lt;sub&gt;n&lt;/sub&gt;</th>
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<tr>
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<td>(η&lt;sup&gt;3&lt;/sup&gt;-C&lt;sub&gt;3&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;)PdCl</td>
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<td>I&lt;sup&gt;b&lt;/sup&gt;</td>
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<td>I</td>
<td>24</td>
<td>18</td>
<td>12</td>
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<sup>a</sup>Reaction conditions: monomer/[Rh] = 50:1; solvent CH<sub>2</sub>Cl<sub>2</sub> or a mixture of CH<sub>2</sub>Cl<sub>2</sub> and MeOH; addition of monomer at 0 °C followed by warming up to room temperature and stirring for 16 h. <sup>b</sup>Monomer/[Rh] = 25:1.

Figure 1. Variable temperature <sup>1</sup>H NMR experiment of p*M*<sub>3</sub> and p*M*<sub>4</sub> in benzene-<sup>d</sup><sub>6</sub> and toluene-<sup>d</sup><sub>8</sub>, respectively.

Figure 2. <sup>1</sup>H NMR spectrum (methanol-<sup>d</sup><sub>4</sub>) of p*M*<sub>5</sub> obtained by polymerization of *M*<sub>5</sub> catalyzed by Rh-catalyst I (left) and <sup>1</sup>H NMR spectrum taken from Ihara and co-workers<sup>43</sup> (DMSO-<sup>d</sup><sub>6</sub>) of poly-S<sub>5</sub>' formed by polymerization of S<sub>5</sub> with [(η<sup>3</sup>-C<sub>3</sub>H<sub>5</sub>)PdCl] (right). Signals marked with an asterisk correspond to the solvent and traces of water.
shorter polymers without affecting the polymer yield much, even up to a CH2Cl2:MeOH ratio of 1:1.5 (Table 1, entries 7 and 8). A huge decrease of $M_w$ and $M_n$ was observed when polymerization was attempted in 100% MeOH, but in this case also the yield is compromised (Table 1, entry 9). This is most likely caused by increased formation of (very) short oligomers, which remain soluble in the methanol solvent, which was used to wash and separate the polymer fraction from the oligomer and dimer fractions. Nonetheless, the $M_w$ and $M_n$ of the polymers can be tuned, both by varying the monomer/catalyst feed ratio and by the addition of varying amounts of MeOH to the reaction mixture.

The hydroxy-containing polymers pM$_x$ (x = 2–5) required for solubility studies in water were obtained in high yields by deprotection of the corresponding silyl-protected polymers pM$_x^s$ (x = 2–5), using HCl in a THF/MeOH mixture (Scheme 2).

To investigate the stereoregularity of the polymers formed by Rh catalyst I, we characterized the polymers by NMR. First, a variable temperature $^1$H NMR experiment with pM$_3$ and pM$_4$ formed by Rh catalyst I showed a sharpening of all $^1$H NMR peaks upon heating to 100 °C (Figure 1), which confirms the expected highly syndiotactic nature of pM$_3$ and pM$_4$. Second, comparison of the $^1$H NMR spectra of deprotected syndiotactic pM$_5$ prepared by using complex I and atactic pM$_5$ prepared by Ihara and co-workers using [($\eta^3$-C$_3$H$_5$)PdCl]$_4$ showed that the signal for the polymer backbone (peak a in Figure 2) is considerably sharper for syndiotactic pM$_5$, indicative for the formation of highly syndiotactic polymers using Rh complex I, while [($\eta^3$-C$_3$H$_5$)PdCl] produces essentially atactic polymers.

Figure 3. $^{13}$C NMR spectrum (methanol-$d_4$) of pM$_5$. Signals marked with an asterisk correspond to the solvent.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Yield (%)</th>
<th>$M_w$ (kDa)</th>
<th>$M_n$ (kDa)</th>
<th>$M_w/M_n$</th>
<th>Yield pM$_5$ (%)</th>
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<td>1</td>
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<td>460</td>
<td>125</td>
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<tr>
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<td>155</td>
<td>70</td>
<td>2.2</td>
<td>~100</td>
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<td>18</td>
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<td>1.6</td>
<td>86</td>
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Table 2. Solubility Studies of Polymer pM$_x$ in Aqueous Solution

<table>
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<tr>
<th>Entry</th>
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<th>Yield (%)</th>
<th>$M_w$ (kDa)</th>
<th>$M_n$ (kDa)</th>
<th>$M_w/M_n$</th>
<th>Yield pM$_5$ (%)</th>
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</table>

Aqueous solutions of pM$_5$ were prepared by adding demineralized water to the polymers. At room temperature pM$_5$ is insoluble in water, but upon cooling to 4 °C most of the polymer dissolved. A small part of the polymer formed a swollen gel-like material, which largely dissolved upon sonication of the mixture in a 4 °C room. Separating the solution from the gel and warming the solution to room temperature produced an opaque aggregate. Concentrations of these solutions were determined after the UV–vis measurements by freeze-drying the aqueous solutions and weighing the polymer residue.
Third, the sharp signals in the $^{13}$C NMR spectrum of $pM_5$ and the resemblance to the NMR signature of our previously reported syndiotactic polymers unequivocally show that a syndiotactic polymer is formed by catalyst I (Figure 3).

**Solubility Studies of the Hydroxyl-Containing Polymer $pM_5$ in Aqueous Media.** It is known that hydroxyl-containing polymers with an appropriate hydrophilic/hydrophobic balance can undergo a temperature-dependent phase separation in aqueous solution.14−19,42,43

The critical solution temperature (CST) at which phase transition occurs depends among others on the ratio of hydrophilic and hydrophobic moieties in the polymer side chains. For instance, Ihara and co-workers recently showed that atactic $pM_5$ (Scheme 2) show a lower critical solution temperature (LCST)-type phase separation in aqueous solutions, whereas polymers with shorter side chain spacers ($x = 2−4$) and thus less hydrophobic units in the side chain spacer show no thermoresponsivity.43 When the temperature of aqueous solutions of the thermoresponsive polymer ($x = 5$) increases above the LCST, the solutions become cloudy, indicating that insoluble aggregates are formed. Parameters that might be of influence on the thermoresponsive phase separation behavior of a polymer are its tacticity, molecular weight, and concentration. We were particularly curious to see whether there would be any in aqueous solutions, whereas polymers with shorter side chain spacers ($x = 2−4$) and thus less hydrophobic units in the side chain spacer show no thermoresponsivity. When the temperature of aqueous solutions of the thermoresponsive polymer ($x = 5$) increases above the LCST, the solutions become cloudy, indicating that insoluble aggregates are formed. Parameters that might be of influence on the thermoresponsive phase separation behavior of a polymer are its tacticity, molecular weight, and concentration. We were particularly curious to see whether there would be any influence among others on the ratio of hydrophilic/hydrophobic moieties in the polymer side chains. Therefore, we investigated the thermoresponsive behavior of syndiotactic polymer $pM_5$ in aqueous solution in comparison to the thermoresponsive behavior of its atactic analogue. The results are summarized in Table 2.

The aqueous $pM_5$ solutions were examined with UV–vis spectroscopy to determine the LCST for these polymer solutions (Table 2, Figures 4 and 5). The LCST for these polymers is defined as the temperature at which the transmittance of 700 nm light is reduced by 50%.

**Figure 4.** Temperature dependence of the transmittance at 700 nm (heating curves) for aqueous solutions of $pM_5$. Influence of the concentration of $pM_5$ ($M_w/460 \text{kDa} \; M_n = 125 \text{kDa}$) on the LCST.

![Figure 4](image-url)

**Figure 5.** Temperature dependence of the transmittance at 700 nm (heating curves) for 0.5 wt % aqueous solutions of $pM_5$. Influence of the $M_w$ on the LCST and comparison to the atactic analogue of $pM_5$. Curves from the atactic polymers are taken from ref 43.

![Figure 5](image-url)

Measurement of the transmittance through aqueous solutions of syndiotactic $pM_5$ ($M_w = 460 \text{kDa} \; M_n = 125 \text{kDa}$) of different concentrations (0.03–0.5 wt %) showed that the LCST of the syndiotactic polymer increases with decreasing concentration (Figure 4 and Table 2, entries 1a–1f).

To investigate how the polymer tacticity influences the LCST, we compared atactic $pM_5$, reported by Ihara33 (0.5 wt % in aqueous solution, $M_w = 13.7 \text{kDa} \; M_n = 1.60$, LCST = 20 °C) with one of our syndiotactic $pM_5$ samples of roughly the same molecular weight and PD1 and the same concentration in aqueous solution (Table 2, entry 4a: $M_w = 12 \text{kDa}, M_n/M_w = 1.60$, LCST = 7.2 °C). In this direct comparison, the tacticity of the polymer proved to have a large influence on the thermoresponsive behavior of the polymers. There is a difference of ~13 °C between the LCST of the atactic and syndiotactic polymers, with the syndiotactic polymers consistently having lower LCST values than the atactic polymers (Figure 5). Similar differences have been observed for aqueous solutions of poly(N-isopropylacrylamide) polymers with different tacticities, where a higher percentage of $meso$ diad content also resulted in a lower LCST.44−46

The lower LCST of syndiotactic $pM_5$, compared to its atactic analogue can perhaps be explained by a different type of aggregates formed by the syndiotactic polymers. Thermotropic and lyotropic LC behavior of these type of polymers was demonstrated (DSC, POM, X-ray diffraction, SAXS, WAXS, and solid-state NMR), and scanning tunneling microscopy (STM) revealed that syndiotactic poly(ethylene acetate) (PEA) self-assembles into triple helices (Figure 6, top).47 Subsequent studies by Tokita, Shikinaka, Ihara, and co-workers confirmed that PEA and related syndiotactic polymers of diazoacetates show thermotropic liquid crystalline behavior due to a rod-like helical conformation in the polymer backbone.48−50 The syndiotactic polymer $pM_5$ is likely to form similar triple helices, and the forces keeping the aggregates together are likely to be stronger in such triple-helix aggregates than in the atactic material, leading to a lower LCST for the syndiotactic polymer than for the atactic material (Figure 6, bottom). Solvation into individual polymer chains in solution is enthalpy-driven, while formation of aggregates at higher temperature is an entropy-driven process, releasing water solvent molecules upon aggregation of the individual solvated polymer chains. The syndiotactic $pM_5$ polymers most likely form more densely packed aggregates than their atactic analogues, as they prefer to aggregate first into tightly packed triple helices before aggregating/crystallizing further. As a result, entropy effects are stronger for syndiotactic $pM_5$ than...
The results are also in contrast with those obtained for the LCST to clearly decrease with increasing molecular weight. LCST-type phase separation behavior, as it is common for the behavior contrasts with most other polymer solutions showing kDa) sample breaks this trend (Table 2, entry 1a). This samples measured at 0.5 wt % concentrations (pM5 syndiotactic molecules involved in solvation of individual polymer chains upon aggregate formation, leading to larger entropy contributions. for atactic pM5 so that aggregation takes place already at a lower temperature (lower LCST).

The LCST values of the syndiotactic pM5 polymers with various molecular weights measured at 0.5 wt % concentrations are remarkably similar. The 12−70 kDa samples seem to indicate a slight decrease in LCST in water occurring at lower temperature than aggregation of its atactic analogue due to formation of more densely packed aggregates, thus releasing more water molecules involved in solvation of individual polymer chains upon aggregate formation, leading to larger entropy contributions. The LCST values of the syndiotactic pM5 polymers with various molecular weights measured at 0.5 wt % concentrations (Table 2, entries 2a, 3a, and 4a), but the di anomalously lower temperature (lower LCST). The behavior observed for atactic pM5 (in contrast to syndiotactic pM5) is the expected behavior and can attributed to increased entropy of mixing with decreasing M_w. The behavior contrasts with most other polymer solutions showing LCST-type phase separation behavior, as it is common for the LCST to clearly decrease with increasing molecular weight. The results are also in contrast with those obtained for the earlier reported atactic analogue of pM5 for which the LCST also clearly decreases with increasing molecular weight for samples measured at 0.5 wt % concentrations (M_w = 13.7 kDa, LCST = 20 °C and M_w = 8.1 kDa, LCST = 25 °C, see Figure 5). The behavior observed for atactic pM5 (in contrast to syndiotactic pM5) is the expected behavior and can attributed to increased entropy of mixing with decreasing M_w.

Because of these facts, the LCST at 0.5 wt % concentrations are only very small and rather irregular despite large changes in M_w, we suspected that the concentrations of the syndiotactic pM5 polymers measured at 0.5 wt % were actually too high because of possible “saturation effects” in the LCST behavior. Similar “saturation” of the LCST values over wide concentration ranges has been observed also for other polymers.51−53 Within such saturation domains, the measured LCST values typically lie too close (i.e. within the margin of error) to draw any reliable conclusions. Indeed, also for syndiotactic pM5 this proved to be the case. When the LCST is plotted as a function of both concentration and molecular weight (Figure 7), it becomes clear that the LCST values of the three higher molecular weight polymers (40, 70, and 125 kDa) levels off at concentrations higher than 0.1 wt %. Above a concentration of 0.1 wt %, the LCST values of the three polymers become more or less equal, independent of the molecular weight and PDI and become only slightly lower upon increasing the concentration further. The onset of this “saturation effect” seems to occur the earliest for the highest molecular weight polymer (125 kDa).

Interestingly, at much lower concentrations (0.05 wt %), the higher molecular weight polymers (40−125 kDa) clearly show an “abnormal” LCST behavior, in which the LCST increases as molecular weight increases. For the higher M_w polymers (40−125 kDa), this behavior seems unaffected by differences in the PDI (for lower weight polymers measured at low concentrations there may be an influence). Similar “abnormal” dependence of the LCST on M_w was also found in aqueous solutions of poly(N-isopropylacrylamide) by Tong and co-workers.51,57

As described above, for the shorter (less entangled) polymer chains, association into triple helix preaggregates is probably easier than for the longer (more entangled) ones, thus explaining the observed “abnormal dependence” of the LCST on the molecular weight of pM5 (Figure 6).

However, below a critical molecular weight this behavior may deviate, since we found that the lowest molecular weight polymer (12 kDa) behaves completely different from the higher molecular weight polymers (40−125 kDa) (Figure 7). For this short polymer, the LCST “saturation effect” starts at much higher concentrations and proceeds with a much steeper slope. Furthermore, the LCST of this polymer is considerably higher than that of the other polymers at 0.05 wt % concentration and clearly does not follow the same “abnormal” LCST behavior as was observed for the higher molecular weight polymers. This deviant behavior could originate from several causes. Perhaps the 12 kDa polymer is too short to form the same aggregates as the higher molecular weight polymers (Figure 6). Alternatively, for this short polymer the Flory−Huggins interaction parameter may become dominant,52,53 thereby overruling the “abnormal” LCST behavior. A third possible cause for its normal LCST behavior may be the
methoxy chain-end groups, which are introduced by using methanol as a chain-transfer agent to synthesize these short polymers. Lastly, we cannot exclude an influence of the polydispersity of the 12 kDa polymer, which is narrower than the PDI values of the heavier polymers (40–125 kDa).

The results described above and related studies with poly(ethylene glycol), poly(HEMA), poly(vinyl ether)-s, and polycrystalline have revealed that separation behavior of these polymers, providing backbone and/or side chains can cause significant changes in the phase separation behavior. This prompted us to also synthesize a syndiotactic polymer containing ethylene glycol side chains. See the Supporting Information for details.

However, the thus obtained polymer turned out to be a rare example of a syndiotactic high-$M_w$ polymer that is fully water-soluble. It does not undergo any phase separation over a temperature range between 0 and 70 °C.

**CONCLUSIONS**

Overall, this study has clarified that Rh-catalyzed carbene polymerization enables the synthesis of thermoresponsive, syndiotactic, high molecular weight polymers. The molecular weight of these polymers can be tuned by changing the monomer/catalyst ratio or by using methanol-mediated chain transfer. Polymer $pM_5$ was found to have an appropriate hydrophilic/hydrophobic balance to undergo a temperature-dependent phase separation in aqueous solution. The LCST of $pM_5$ was demonstrated to be drastically influenced by tacticity; the LCST of syndiotactic $pM_5$ is much lower than that of its atactic analogue with the same molecular weight, and in contrast to atactic $pM_5$, syndiotactic $pM_5$ reveals an "abnormal dependence" of the LCST on the molecular weight of the polymer. By changing the molecular weight and the concentration of these polymers, we can fine-tune the LCST of an aqueous solution of $pM_5$. Modification of the polymer backbone and/or side chains can cause significant changes in the phase separation behavior of these polymers, providing future opportunities for designing novel thermoresponsive polymers for a broad scope of applications.

**EXPERIMENTAL SECTION**

**General.** The silyl-protected diazoacetates $pM_5$ were prepared according to the literature, except that for the synthesis of the monomers anhydrous solvents were used during the reaction and non-dried solvents during work-up. N,N′-Ditosylhydrazine (TsNH$_2$) was necessary for the monomer synthesis was prepared according to the method published by Fukuyama and co-workers. Rh precatalyst I was synthesized according to previously published methods. Further details can be found in the Supporting Information.

**Polymerization of the Diazoacetates:** Formation of Polymers $pM_5$–$pM_5$. As an example, the synthesis of $pM_5$ is described. In a dry Schlenk flask equipped with a stir bar and septum, $M_5$ (1.28 g, 4.47 mmol) was dissolved in 5 mL of dry dichloromethane (DCM). In another dried Schlenk flask 38.6 mg (0.09 mmol) of Rh catalyst I (monomer:catalyst ratio 50:1) was dissolved in 2 mL of dry DCM and cooled to 0 °C. The solution of $M_5$ was added in a dropwise manner to the solution of Rh catalyst, using a syringe. Evolution of $N_2$ was observed. After the addition of $M_5$, the reaction mixture was allowed to warm up to room temperature and stirred overnight. The reaction mixture was concentrated until a volume of ca. 1 mL was left, after which dry MeOH was added to precipitate the polymer. The polymer was separated from the supernatant by centrifugation and three washing steps with dry MeOH. This yielded $pM_5$ as an off-white solid (0.69 g, 59%). $^1$H NMR (CDCl$_3$, 300.1 MHz), δ (ppm): 3.95 (br, 2H, -OCH$_2$-), 3.59 (br, 2H, CH$_2$OSi-), 3.13 (br, 1H, -[CH$_2$]-), 1.62 (br, 2H, -CH$_2$CH$_2$CH$_2$CH$_2$-), 1.53 (br, 2H, -CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$-), 1.36 (br, 2H, -CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$-), 0.90 (s, 9H, -SiBu), 0.05 (s, 6H, -Si(CH$_3$)$_2$-).

$pM_5$: Yield: 47%. $^1$H NMR (CDCl$_3$, 300.1 MHz), δ (ppm): 4.25 (br, 2H, -OCH$_2$-), 3.69 (br, 2H, -CH$_2$OSi-), 3.39 (br, 1H, -[CH$_2$]-), 0.93 (s, 9H, -SiBu), 0.25 (s, 6H, -Si(CH$_3$)$_2$-).

$pM_5$: Yield: 52%. $^1$H NMR (CDCl$_3$, 300.1 MHz), δ (ppm): 4.11 (br, 2H, -OCH$_2$-), 3.71 (br, 2H, -CH$_2$OSi-), 3.12 (br, 1H, -[CH$_2$]-), 1.85 (br, 2H, -CH$_2$CH$_2$CH$_2$-), 0.93 (s, 9H, -SiBu), 0.10 (s, 6H, -Si(CH$_3$)$_2$-).

PolymORIZATION of $M_5$ via MeOH-Mediated Chain Transfer. The procedure followed is the same as for polymerization without chain transfer, except for the use of a solvent mixture of DCM and MeOH (total reaction volume between 5 and 7 mL). Three chain-transfer polymizations were performed with $M_5$, with DCM:MeOH ratios of 4:1, 1:1.5, and 0:1. The formed polymers ($pM_5$) were isolated according to the procedure described above.

**Deprotection of the Silylated Polymers.** Deprotection of the polymers was done with HCl in a THF/MeOH mixture. After completion of the deprotection, all volatiles were evaporated, the crude solid was dissolved in as little as possible MeOH, and the polymers were precipitated from the reaction mixture by addition of THF. The desilylated polymers were isolated in high yield (>90%). The deprotection of $pM_5$ is described as an example. In 5 mL of THF was dissolved 200 mg (0.77 mmol) of $pM_5$ and MeOH (1 mL) was added to enhance the solubility of the formed desilylated polymer. Subsequently 1 mL of concentrated HCl (37%) was added in a dropwise manner. As soon as precipitation of solid was observed, a few extra drops of MeOH were added. A stir for 1–2 h the solvents were evaporated on a rotavap until a volume of ca. 1 mL was left, and then more MeOH was added, after which solvents were again evaporated until a volume of ca. 1 mL was left. This step was repeated twice, after which the mixture was concentrated for the last time to ca. 0.5–1 mL. Addition of THF (~10 mL) resulted in precipitation of the deprotected polymer, which was collected using centrifugation.

Washing with THF yielded $pM_5$ as an off-white sticky solid (0.10 g, 90%). $^1$H NMR (DMSO-$d_6$, 300.1 MHz), δ (ppm): 4.40 (b, 1H, OH), 3.89 (b, 2H, -OCH$_2$-), 3.40 (b, 2H, -CH$_2$OH), 3.06 (b, 1H, -[CH$_2$]-), 1.57 (b, 2H, -CH$_2$CH$_2$CH$_2$CH$_2$-), 1.44 (b, 2H, -CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$-), 1.32 (b, 2H, -CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$-).

$^1$C NMR (methanol-$d_4$, 75.4 MHz), δ (ppm): 172.6 (C==O), 66.3 (OCH$_3$), 63.0 (CH$_2$OH), 46.5 (-[CH$_2$]-), 33.6 (-CH$_2$CH$_2$CH$_2$CH$_2$-), 29.5 (-CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$-), 23.6 (-CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$-).

**ASSOCIATED CONTENT**

$^3$ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.macromol.8b01150.

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ACKNOWLEDGMENTS

The work described in this paper was financially supported by The Netherlands Organization for Scientific Research (NWO TOP-Grant 716.015.001) and the Research Priority Area Sustainable Chemistry of the University of Amsterdam.

REFERENCES


(54) Relationships between concentration and Mw and LCST have been described in other reports. Usually, the polymers that are compared have very similar PDI values. Whereas in some papers the PDI is not taken into consideration as a parameter which could be of influence on the LCST, others observed an influence of the PDI on the LCST behavior or found a minor role of the PDI on the LCST for polymers with high molecular weight.


