Polymerization

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Cobalt-Catalyzed Carbonylative Copolymerization of *N*-Alkylazetidines and Tetrahydrofuran**

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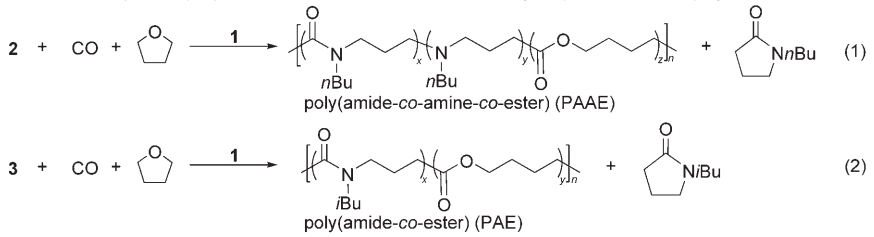
The metal-catalyzed carbonylative polymerization of heterocycles (COPH) has received much attention in the last few years as a novel method for the synthesis of polyamides and polyesters.[1–7] Motivation for these research activities is the practical demand for polymers with heteroatom-containing backbones that are susceptible to hydrolytic and/or enzymatic attack in biological or ecological environments.[8,9] We are interested in the development of COPH using an approach based on single-site catalysts, under the idea that well-defined molecular catalysts would allow rational design and control of the chemical composition, molecular weight, and microstructure of the polymer product.

Herein, we report the carbonylative polymerization of azetidines catalyzed by $[Co(CH_3CO)(CO)_3P(o\text{-tol})_3]$ (**1**; tol = tolyl), and the participation of the tetrahydrofuran (THF) solvent in the polymerization to give ester units in the polymer products. The use of LiI as a cocatalyst eliminates the γ-lactam by-product and influences both the amount and distribution of the ester units in the polymer backbone. The well-controlled distribution of the ester units and the living character of the polymerization have allowed the synthesis of polymers with alternating amide blocks and ester segments, which undergo two-stage degradation.[10]

Herein, *N*-*n*-butylazetidine (**2**) and *N*-isobutylazetidine (**3**) are used as representative monomers. The polymerization was carried out in THF under CO (1000 psi) at 60–80 °C (Table 1). For **2**, in addition to the major carbonylative enchainment that resulted in the amide units, a simple ring-opening enchainment without carbonylation was also observed, which resulted in amine units in the polymer chain (entries 1 and 2).[7c] For the sterically bulkier and less nucleophilic **3**, selective carbonylative enchainment occurred, as assessed by NMR spectroscopy (entries 3–8).[11] Somewhat surprisingly, carbonylative enchainment of THF also took place and resulted in δ-oxyvaleroyl ester units in the polymer products.[12] Thus, the reactions of **2** and **3** in THF produced poly(amide-*co*-amine-*co*-ester)s (PAAEs) and poly(amide-*co*-ester)s (PAEs), respectively [Table 1, Eqs. (1) and (2)].

Table 1: Carbonylative polymerization of azetidine and THF (CO pressure 1000 psi).[a]



Entry	THF [mL]	Azetidine	Azetidine/**1** (molar ratio)	Cocatalyst	Selectivity[b]	Ester abundance [%]	$M_n \times 10^{-3}$ (PDI)[c]
1[d,e]	20	**2**	8:1	–	(81:9)[f]:10	8.3	2.16 (1.47)
2[d,e]	20	**2**	16:1	–	(84:8)[f]:8	4.7	3.78 (1.55)
3[d,e]	20	**3**	8:1	–	75:25	16	1.43 (1.18)
4[d,e]	20	**3**	16:1	–	82:18	9.4	2.68 (1.20)
5[d,e]	20	**3**	32:1	–	86:14	6.7	5.43 (1.20)
6[d,e]	30	**3**	48:1	–	83:17	4.3	7.42 (1.23)
7[d,g]	35	**3**	80:1	–	85:15	3.3	13.3 (1.22)
8[d,g]	40	**3**	100:1	–	82:18	2.4	15.5(1.25)
9[d,e]	30	**3**	18:1	LiI	>99:1	16.7	4.38 (1.12)
10[d,e]	30	**3**	18:1	$LiBPh_4$	84:16	8.5	2.63 (1.35)
11[d,e]	30	**3**	18:1	nBu_4NI	>99[h]:1	0	–
12[i]	65	**3**	(18×2):1	LiI	>99:1	15	7.51 (1.18)
13[i]	70	**3**	(18×3):1	LiI	>99:1	9.1	11.65 (1.21)
14[i]	75	**3**	(18×4):1	LiI	>99:1	8.7	14.92 (1.23)

[a] Catalyst **1** (0.12 mmol) used in all runs; cocatalyst (0.24 mmol) used for entries 9–14. Quantitative total conversion was achieved, except for entry 11. [b] Molar ratio of azetidine converted to polymer and γ-LA. [c] Determined by GPC with a refractive index detector against polystyrene standards with $CHCl_3$ as the eluent. [d] Oil-bath temperature 70 °C. [e] Reaction time 48 h. [f] Molar ratio of amide and amine units estimated by ^1H NMR spectroscopy. [g] Reaction time 72 h. [h] Monomer conversion 58 %. [i] Autoclave interior temperature 62 °C; 18 equiv of **3** added 10 h after the previously added **3** was exhausted.

The extent of THF carbonylative enchainment differed when **2** and **3** were used as the monomer: twofold as many ester units were incorporated with **3** than with **2** (entries 1 vs. 3, and 2 vs. 4).

The ester abundance, which is defined as the number of ester units divided by the total number of all monomer units, was also a function of the initial monomer-to-catalyst ratio. Higher monomer loadings resulted in a lower degree of ester incorporation (entries 3–8), which suggests that the reaction of THF was favored when the azetidine concentration was low. Directly monitoring the amide and ester growth by in situ IR spectroscopy confirmed that the ester abundance in the

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Supporting information for this article (polymerization procedures, plots of M_n versus conversion, NMR spectra of polymer products, and mechanistic hypotheses on γ-lactam formation) is available on the WWW under http://www.angewandte.org or from the author.

polymer increased as the reaction proceeded (Figure 1). The polymerization has a living character, as evidenced by the narrow polydispersity (Table 1, entries 3–8) and the linear

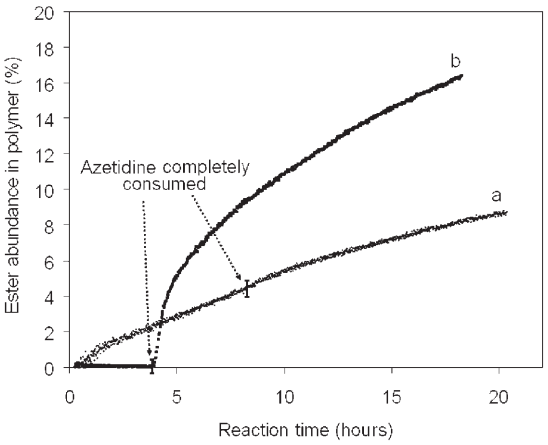
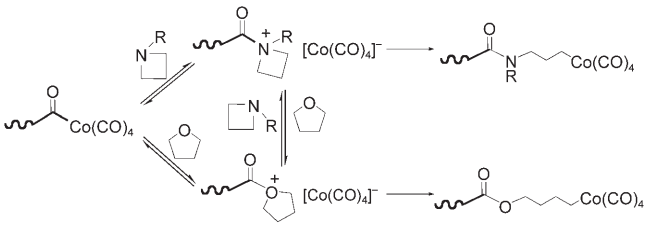


Figure 1. Change of ester abundance in the polymer chain as a function of reaction time. Line a: reaction in the absence of LiI; line b: reaction in the presence of LiI.

increase of molecular weight (M_n) with increasing monomer conversion,[11] and hence the ester units must populate the polymer chain in a gradient fashion that increases from the head to the tail. The gradient ester distribution and the variation in the ester abundance can likely be attributed to competition for the acyl site by THF, azetidine, and $[Co(CO)_4]^-$ ions and the relative ring-opening rates of azetidine and THF (Scheme 1).[12] Note that although the incorporation of THF was observed by Osakada and co-workers in the carbonylative polymerization of oxiranes,[5] we have never observed such reactivity in the carbonylative polymerization of aziridines.[7]



Scheme 1. Plausible mechanistic scenario affecting THF enchainment.

The selectivity of the polymerization of both **2** and **3** suffered from the ring-expanding side reaction that produced the γ-lactam (γ-LA). The selectivity did not deteriorate over a 12-fold increase in monomer loading (entries 3–8). The total conversions to the polymer and γ-LA were quantitative in all runs (entries 1–8). The formation of γ-LA did not annihilate the living character of the polymerization. Therefore, we tentatively attribute the formation of γ-LA to a process intrinsically coupled to the polymerization, most likely "back-biting"[6] as opposed to catalyst decomposition.[7a] We further hypothesize that back-biting happens at the stage of the acylazetidinium intermediate rather than that of the acyl-$Co(CO)_4$ intermediate.[13] Based on this hypothesis, one could formulate that the addition of nucleophiles, such as I^- ions, capable of opening the azetidium ring would bias the reaction toward polymerization. Indeed, the γ-LA by-product was eliminated with the addition of two equivalents of LiI relative to **1** (entry 9). The role of I^- in suppressing the formation of γ-LA was corroborated by the fact that the amount of **3** converted to γ-LA was hardly affected by the addition of $LiBPh_4$ (entry 10). Furthermore, nBu$_4$NI was also effective in suppressing the formation of γ-LA, although the polymerization was slower, and converted only 58% of **3** in 48 h under otherwise identical conditions (entries 9 vs. 11). The latter observation suggests that the Li^+ cation must also play a role in the polymerization.

In addition, LiI exerted an unexpected effect on the distribution and abundance of ester units in PAE. In situ IR spectroscopic monitoring of the polymerization revealed that in the presence of LiI, ester units did not form until complete consumption of **3** (Figure 1). The formation of the ester units began once the growth of the amide units stopped, and the final ester abundance was appreciably higher with LiI than without LiI for the same reaction time (entries 4 vs. 9). Thus, the PAEs produced in the presence of LiI are best characterized as consisting of an amide block followed by a very short ester segment. Note that again, Li^+ cations must play a role in the reaction of THF, as no ester units were formed in the presence of nBu$_4$NI (entry 11).

The combination of the segmental ester distribution and the living character of the polymerization provides an opportunity for the synthesis of PAEs with multiple, alternating amide blocks and ester segments. This was achieved by periodically feeding **3** into the reaction 10 hours after the previously added **3** was exhausted. The multiple additions under high pressure preserved the living polymerization, as demonstrated by the relatively narrow polydispersity indices (PDI; entries 12–14 in Table 1) and the linear increase of M_n with increasing number of monomer additions (Figure 2). Methanolysis of the PAEs at room temperature under acidic conditions completely eroded the ester linkages in the

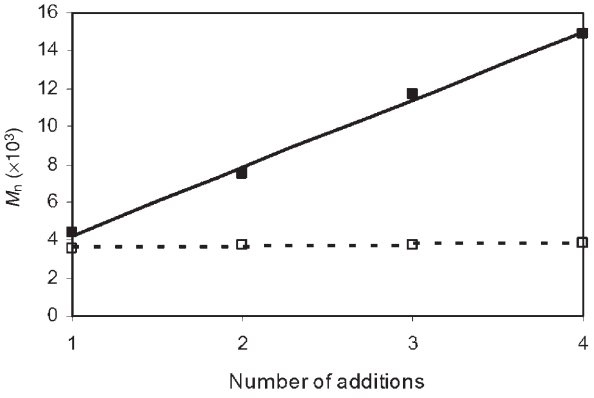


Figure 2. The linear increase of M_n values of PAEs with increasing number of additions of **3** (——; PAEs from entries 9, 12–14, Table 1). The dashed line shows the nearly constant M_n values of the methanolysis products independent of the M_n values of the original PAEs.

backbone in 12 hours. The M_n values of the resulting polyamides were significantly reduced to the narrow range of 3570–3880 g mol^{-1}, and their PDI values were rather small in the range of 1.11–1.30. The uniform M_n and the narrow PDI of the methanolysis products are consistent with the anticipated microstructure of the PAEs, that is, amide blocks with uniform block length separated by segments of ester units. In comparison, the polyamides from the degradation of PAEs synthesized in the absence of LiI under otherwise identical conditions by multiple additions of **3** displayed a much broader molecular weight distribution.[11] Finally, the polyamides that resulted from methanolysis at room temperature can be completely degraded in refluxing water in one day under acidic conditions. Thus, the chemical compositions and their distributions in the above PAEs dictate that they would undergo two-stage degradation.

The Co-catalyzed living carbonylative polymerization of *N*-alkylazetidines provides a method that circumvents the thermodynamic problem for the synthesis of poly(γ-lactam)s via the ring-opening polymerization of γ-LAs.[13] The participation of THF in the polymerization is an interesting feature of this reaction. The ability of LiI to control the selectivity of the reaction and the microstructure of the polymer product is likely not limited to azetidines, but may also be applicable to other heterocyclic monomers. Combination of the above attributes has allowed the synthesis of PAEs with controlled molecular weight and microstructure that impart unique chemical degradation properties.

Experimental Section

Azetidine monomers were synthesized with modified methods from the literature,[14] and were dried with Bu_2Mg at room temperature. The synthesis of catalyst **1** was previously reported.[6] THF was refluxed over Na/benzophenone and freshly distilled.

The polymerizations were carried out in 300-mL stainless-steel reactors equipped with a stainless-steel tube as the reservoir for addition of azetidines. The tube was connected to the reactor by a stainless-steel ball-valve fitting. The reactor was located in a well-ventilated hood, around which CO detectors were placed. Catalyst **1** was dissolved in a small amount of THF and added to the stainless-steel tube with a syringe under a gentle flow of CO. After being charged with the solvent, the reactor was immediately pressurized with CO (1000 psi) and was heated with either an oil bath or a heating jacket. The stainless-steel tube holding the monomer was slightly overpressurized to allow the addition of azetidine. Multiple additions of monomer under high pressure could be performed in the same way. After the reaction was complete, the reactor was cooled to ambient temperature and the pressure was released into the fume hood. The polymer product was isolated by removal of solvent under vacuum, washing with ether/hexane (1:3 v/v), and drying under vacuum at room temperature.

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