# Chain-End-Functionalized Polyphosphazenes via a One-Pot Phosphine-Mediated Living Polymerization

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A simple polymerization of trichlorophosphoranimine ($Cl_3P = N–SiMe_3$) mediated by functionalized triphenylphosphines is presented. In situ initiator formation and the subsequent polymerization progress are investigated by ^{31}P NMR spectroscopy, demonstrating a living cationic polymerization mechanism. The polymer chain lengths and molecular weights of the resulting substituted poly(organo)phosphazenes are further studied by ^{1}H NMR spectroscopy and size exclusion chromatography. This strategy facilitates the preparation of polyphosphazenes with controlled molecular weights and specific functional groups at the α-chain end. Such well-defined, mono-end-functionalized polymers have great potential use in bioconjugation, surface modification, and as building blocks for complex macromolecular constructs.
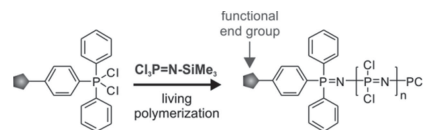
1. Introduction

Poly(organo)phosphazenes are an extremely versatile class of hybrid inorganic–organic polymers whose properties and functionality can be easily tuned by suitable organic side groups attached to the inorganic backbone,[1] and thus can be used to prepare a wide-array of interesting materials, ranging from superhydrophobic polymers[2]

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and high-performance elastomers,[3] to thermoresponsive polymers[4] and biodegradable polymers[5] for a multitude of biomedical applications,[6] such as tissue engineering[7] and advanced drug delivery systems.[8]

Although the precursor polymer, polydichlorophosphazene, is commonly obtained via a thermal ring-opening polymerization[9] with high molecular weights and broad molecular weight distributions, polydichlorophosphazene with controlled molecular weights can also be prepared via the room temperature living cationic polymerization of trichlorophosphoranimine ($Cl_3P = N–SiMe_3$) in solution.[10] Furthermore, tris(organo)phosphoranimines ($R_3P = N–SiMe_3$) can be used as end-groups in the presence of PCl_5 to induce and/or quench the living polymerization of $Cl_3P = N–SiMe_3$, a method which has been used to prepare a number of macromolecular constructs including branched structures,[10a,11] and block copolymers.[12] Other studies, however, have shown that $R_3P = N–SiMe_3$ bearing alkoxy or aryloxy groups did not form a stable cationic species to induce the polymerization of $Cl_3P = N–SiMe_3$, and were only able to quench the polymerization.[13] The preparation of functional organophosphoranimines also often requires multiple step synthesis, for example, via a bromophosphoranimine precursor,[14]

and the repeated vacuum distillations required for purification lead to extensive and time-consuming preparation and extensive handling of toxic phosphoranimines. In an alternative approach, it has been shown that, in the absence of PCl_5, dichlorophosphoranes can also initiate the polymerization of $Cl_3P = N–SiMe_3$[15] and that this could be exploited to prepare organometallic-inorganic block copolymers.[16]

In an attempt to find a simple alternative to incorporate specific reaction sites at polyphosphazene end-groups, the aim of this study was to employ commercially available triphenylphosphines with (protected) functional groups which, after chlorination, could act as initiating species for the cationic polymerization of $Cl_3P = N–SiMe_3$ and thus provide a simple, one-pot method to obtain polyphosphazenes with a (protected) functional group at the α-chain end. Well-defined, mono-end-functionalized polymers have become indispensable building blocks for macromolecular engineering,[17] and thus the methods described here are intended to facilitate the preparation of complex architectures of polyphosphazenes.

2. Experimental Section

2.1. Living Polymerization with PCl_5

PCl_5 (3.58 mg, 17.2 µmol, 1 equiv.) was dissolved in a mixture of anhydrous CH_2Cl_2/$CDCl_3$ (4/1) in an NMR tube sealed with a septum. Then, $Cl_3P = N–SiMe_3$ (53.80 mg, 0.24 mmol, 14 equiv.) in anhydrous CH_2Cl_2/$CDCl_3$ was added via a syringe and the reaction was monitored by $^{31}P\{^1H\}$ NMR spectroscopy until the signal of $Cl_3P = N–SiMe_3$ completely disappeared. The theoretical number of chain length n_{calc} is 28, calculated assuming two initiator molecules are required per chain.[18]

2.2. Polymer 4a

4-(Diphenylphosphino)styrene **1a** (7.50 mg, 26.0 µmol, 1 equiv.) was reacted with C_2Cl_6 (6.77 mg, 28.6 µmol, 1.1 equiv.) in 0.5 mL CD_2Cl_2 for 24 h at room temperature to yield **2a**. The reaction was transferred to an NMR tube and sealed with a septum. First, 1 equiv. of $Cl_3P = N–SiMe_3$ (5.84 mg, 26.0 µmol), then 25 equiv. $Cl_3P = N–SiMe_3$ (0.15 g, 0.65 mmol) were added via a syringe to yield polymer **4a**.

2.3. Polymer 4b

4-Diphenylphosphanyl benzoic acid-2-(trimethylsilyl) ethyl ester **1b** (50 µL of 0.5 M in THF, 10.16 mg, 25.0 µmol, 1 equiv.) and C_2Cl_6 (6.51 mg, 27.5 µmol, 1.1 equiv.) were stirred for 72 h at room temperature. The reaction mixture of **2b** was transferred to an NMR tube followed by the addition of $Cl_3P = N–SiMe_3$ (0.15 g, 0.65 mmol, 26 equiv.).

Both reactions (**4a** and **4b**) were followed with $^{31}P\{^1H\}$ NMR spectroscopy until monomer consumption was complete (up to NMR detection limits). The ratio of the monomer concentration, measured at specific time points during polymerization (M_t), to the initial monomer concentration (M_0) was estimated from the absolute signal intensities in the $^{31}P\{^1H\}$ NMR spectra.

2.4. Poly(organo)phosphazene Series 5b and 6b

n_{calc} was varied from 10, 25, 50, 100, up to 200 by adjusting the ratio of monomer to the chlorinated phosphine **2b** followed by macromolecular substitution. Further experimental details and characterization are included in the Supporting Information.

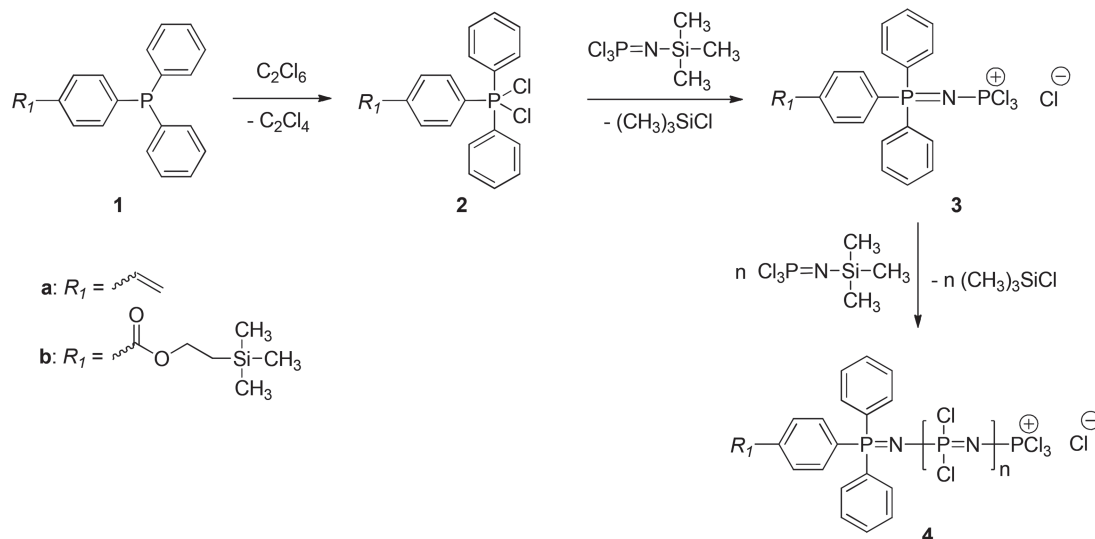## 3. Results and Discussion

3.1. Initiation and Polymerization

Aryl phosphines bearing either a styrene (**1a**) or a trimethylsilyl ester (TMSE) (**1b**) functional group were investigated as potential starting materials for the polymerization of trichlorophosphoranimine ($Cl_3P = N–SiMe_3$) (Figure 1). For this purpose, a small excess of the mild chlorinating agent C_2Cl_6 (1.1 equiv.) was reacted separately with 1 equiv. of the phosphine **1a** and **1b**, respectively, with the reductive dechlorination of C_2Cl_6 yielding the dichlorophosphoranes **2a** and **2b**. $^{31}P\{^1H\}$ NMR spectroscopy showed the disappearance of the phosphine signal at −5.9 ppm of **1a** and an arising signal at 56.4 ppm, indicating the formation of **2a**, with complete conversion of the functional aryl phosphines being observed after 24 h. With **1b**, however, significantly longer chlorination times (up to 72 h) were required until the phosphine signal at −5.1 ppm had disappeared and **2b** was formed as evidenced by the new signal at 56.4 ppm.

The polymerization progress of $Cl_3P = N–SiMe_3$ in the presence of the chlorinated **2a** and **2b**, as polymerization initiators, was monitored via $^{31}P\{^1H\}$ NMR spectroscopy (Figure S1, Supporting Information). After the addition of 1 equiv. of $Cl_3P = N–SiMe_3$, the signal at 64.1 ppm instantly diminished and upon addition of a further 25 equiv. $Cl_3P = N–SiMe_3$, a rapid decrease in the monomer signal at −53.8 ppm was observed, with monomer consumption being complete in 1.5 h. A parallel increase in the signal for the interior $[Cl_2P = N]_n$ groups of the polyphosphazene chain at −16.7 ppm (**4a**) was also observed. Although these results gave a clear indication of the polymerization progress, suggesting a similar mechanism to reported works,[19] details of the precise mechanism are a matter of future investigation.

Monomer conversion over time was monitored via the intensity of the $Cl_3P = N–SiMe_3$ signal at −53.8 ppm in the $^{31}P\{^1H\}$ NMR spectra (Figure 2), with the plots of $\ln(M_t/M_0)$ over time showing pseudo-first-order kinetics. The well-investigated PCl_5-initiated reaction is also shown as a comparison with a similarly linear, living chain growth being observed. In contrast, this phosphine-mediated polymerization results in monodirectional chain growth,

Phosphine-mediated polymerization

a: $R_1 =$ ⌇⌇⌇⟍

b: $R_1 =$ ⌇⌇⌇—C(=O)—O—CH$_2$CH$_2$—Si(CH$_3$)$_2$—CH$_3$

Macromolecular substitution

4b

5b-10: $n_{calc} = 10$	
5b-25: $n_{calc} = 25$	
$R_2 =$ (N-(3'-aminopropyl)-2-pyrrolidone) **5b-50**: $n_{calc} = 50$	
5b-100: $n_{calc} = 100$	
5b-200: $n_{calc} = 200$	

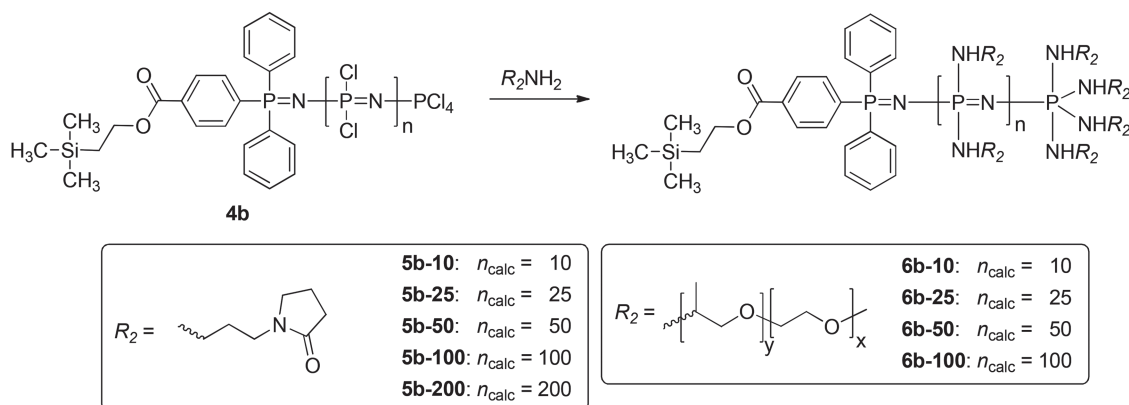|	
6b-10: $n_{calc} = 10$	
6b-25: $n_{calc} = 25$	
$R_2 =$ (Jeffamine) **6b-50**: $n_{calc} = 50$	
6b-100: $n_{calc} = 100$	

Figure 1. Synthetic route to mono-end-group-functionalized polydichlorophosphazenes in a one-pot reaction using a functional phosphine as the initiating species and macromolecular substitution of **4b** with various chain lengths using *N*-(3'-aminopropyl)-2-pyrrolidone (polymers **5b**) and Jeffamine ($x = 19$, $y = 3$) (polymers **6b**), respectively.

as oppose to the bidirectional growth observed with the polymerization of $Cl_3P = N–SiMe_3$ and PCl_5,[18] which otherwise requires $[R_3P = N = PCl_3][PCl_6]$ end-groups for a mono-directional growth to be achieved.[19]

3.2. NMR and SEC Characterization of Polymer Series

A series of polydichlorophosphazenes, with varying ratios of monomer to phosphine-initiator was then prepared, with n_{calc} in the range of 10 to 200, assuming one chlorinated phosphine group per chain. To this end, a solution of **2b** was reacted separately with different amounts of $Cl_3P = N–SiMe_3$ to obtain the respective polydichlorophosphazenes (**4b**) with various polymer chain lengths. ^{31}P NMR spectra of the precursor polymers whereby the monomer:initiator feed ratio (n_{calc}) is 10, 25, and 50 showed narrow signals at -18 ppm and complete

disappearance of the signal at -54 ppm indicating complete consumption of the monomer after 24 h reaction time (Figure 3c). For n_{calc} is 100 and 200, however, polymerization was slow and did not proceed to completion within 24 h. The reaction time had to be increased to 48 h to ensure complete disappearance of the monomer signal in the ^{31}P NMR spectra.

Due to the hydrolytic instability of polydichlorophosphazenes, the chlorine atoms were then substituted in order to give more hydrolytically stable polymers for further characterization (Figure 1). For this purpose, the polydichlorophosphazene series **4b**, with increasing n_{calc}, were substituted with low-molecular-weight *N*-(3'-aminopropyl)-2-pyrrolidone to give the poly(organo)phosphazene series **5b**. ^{1}H NMR spectroscopy confirmed incorporation of the TMSE-phosphine end-group into the polymer chain (Figure 3a) and the experimental
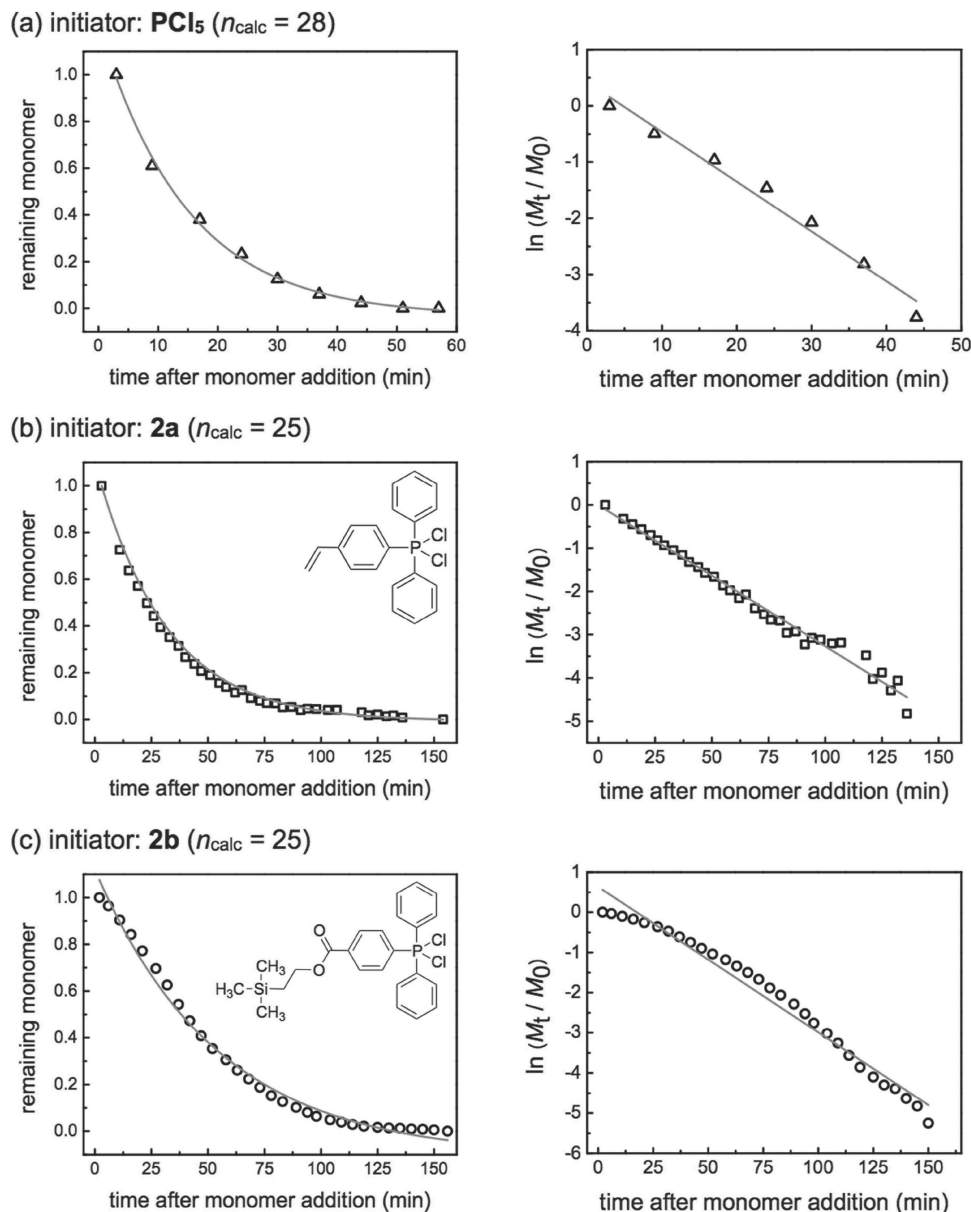
Figure 2. Kinetic study of polymerization initiated with a) PCl$_5$, b) **2a**, and c) **2b** monitored by ^{31}P{^{1}H} NMR spectroscopy. Plots of ln(M_t/M_o) over time show a linear relationship indicating the living nature of the polymerization.

chain length was calculated by integration of the TMSE end-group at 0.01 ppm versus the methylene group at 2.91 ppm of the attached side group (Table 1). For lower values of n, approximate agreement was observed with the expected number of repeat units n_{calc}, thus providing good evidence not only of the phosphine end-group incorporation but also the controlled nature of the polymerization and the ability to regulate the polymer chain length via the initiator to monomer molar feed ratio. However, the polymerization appears to be inhibited, when it comes to higher ratios of monomer to chlorinated phosphine. As can be seen in Figure 3b, an increasing deviation of M_n from the calculated values

was observed. Since complete consumption of the monomer was observed in all ^{31}P NMR spectra of the polydichlorophosphazene precursors, simultaneous side-reactions resulting in a consumption of monomer not participating in chain growth is assumed. As well as the peaks corresponding to the growing polymer chain, ^{31}P NMR spectroscopy showed signals at around 20 ppm (Figures S1 and S2, Supporting Information). Further analysis of this region of the spectrum with HMBC spectroscopy (Figure S3, Supporting Information) shows one peak, which correlates to the phosphine end-group, but also peaks corresponding to the formation of a new species, including a peak at 21.4 ppm, corresponding to
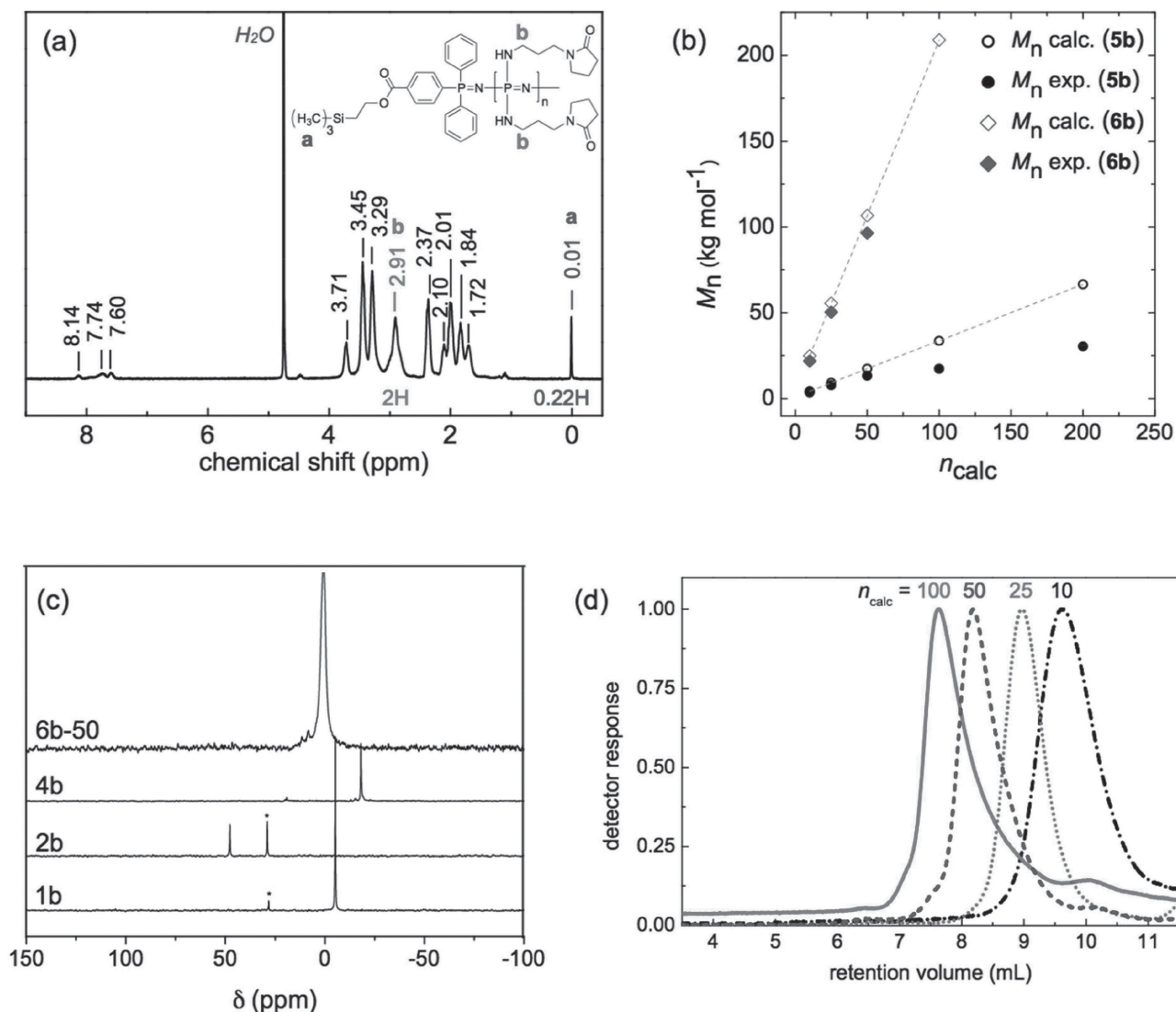
Figure 3. a) Representative ^{1}H NMR spectrum of polymer **5b-25** in D_2O. Values for n_{calc} and thus M_n could be obtained via integration of the protons of the TMSE end-group ($\delta = 0.01$ ppm) versus the $-CH_2$ signals of N-($3'$-aminopropyl)-2-pyrrolidone side groups ($\delta = 2.91$ ppm); b) Plot of M_n versus n_{calc} of polymer series **5b**, M_n calc was calculated from the M:I feed ratio, M_n exp (experimental value) via ^{1}H NMR spectroscopy; c) $^{31}P\{^1H\}$ NMR spectra of the functionalized triphenylphosphine **1b**, the dichlorophosphorane initiator **2b**, dichloropolyphosphazene **4b**, and the macrosubstituted poly(organo)phosphazene **6b**. (* = Phosphine oxide: Since this peak is not present in sample **4b**, but only in the aliquot of **2b** and **1b** taken for NMR spectroscopy, it is assumed that this is formed by hydrolysis and/or oxidation in the NMR sample tube); d) SEC chromatographs of polymer series **6b** with n_{calc} are 10, 25, 50, and 100, respectively.

cyclic by-products.[10a,20] This new species increases with increasing reaction time and represents a competing reaction to the chain growth, particularly chain lengths >50. Interestingly, these peaks were also observed in the ^{31}P NMR spectra of the highly concentrated sample of the PCl_5-initiated polymerization.

In order to achieve higher molecular weight polymers, a further series of poly(organo)phosphazenes was prepared (**6b**) with a significantly larger organic component. The SEC traces of the polymers **6b** are shown in Figure 3d. With the addition of increasing M:I ratio, a clear shift to lower retention volumes is observed. The molecular weights measured are, however, highly underestimated due to the different hydrodynamic behavior of the polystyrene calibration standards (Table 1). In order to confirm that the living chain ends indeed remained active, the precursor of polymer **6b-50** was synthesized with a second, subsequent addition of 25 molar equiv. of $Cl_3P = N-SiMe_3$ after complete consumption of a first portion of 25 molar equiv. of the monomer. ^{31}P NMR spectroscopy of the precursor, as well as SEC of the macrosubstituted polymer (Figure 3d) confirmed complete consumption of the second addition of monomer and thus the living nature of the polymerization.

■ *Table 1.* Size characterization of the polymer series **5b** and **6b.**

Polymer	n_{exp} [b]	$M_{n\,NMR}$ [d] $(M_{n\,calc})$ [c] [kg mol^{-1}]	Polymer	n_{exp} [b]	$M_{n\,NMR}$ [d] $(M_{n\,calc})$ [c] [kg mol^{-1}]	$M_{n\,SEC}$ [e] $(M_{n\,calc})$ [c] [kg mol^{-1}]	M_w/M_n
5b-10 [a]	8	3.6 (4.3)	**6b-10** [a]	9	21.8 (24.9)	8.2 (24.9)	1.2
5b-25 [a]	21	7.7 (9.2)	**6b-25** [a]	23	50.5 (55.6)	14.6 (55.6)	1.1
5b-50 [a]	38	13.3 (17.4)	**6b-50** [f]	45	96.5 (106.7)	26.3 (106.7)	1.1
5b-100 [a]	50	17.4 (33.8)	**6b-100** [a]	—[g]	—[g]	34.6 (208.9)	1.3
5b-200 [a]	90	30.5 (66.5)					

[a] Number indicates n_{calc}, expected degree of polymerization calculated from the molar feed ratio of monomer to initiator; [b] Experimental degree of polymerization, as determined by ^{1}H NMR spectra; [c] Calculated from n_{calc}; [d] Calculated from n_{exp}; [e] Apparent molecular weights measured by SEC using conventional calibration versus linear polystyrene standards; [f] Polymer **6b-50** was synthesized via subsequent addition of two aliquots of 25 molar equiv. of monomer; [g] End-group integral too low for a reliable calculation.

4. Conclusions

The development of a novel approach to synthesize mono-end-functionalized polyphosphazenes via phosphine-based chain initiators has been described. This route yields polydichlorophosphazenes in a one-pot fashion with tunable chain lengths due to the living nature of the polymerization process. Various functional groups can be easily incorporated by careful choice of the phosphine used, thus yielding polyphosphazenes with (protected) functional groups at one chain end that are accessible for subsequent further modifications. Although further investigations into the factors, which could affect the reaction rates of the phosphoranimine polycondensation (e.g., solvent polarity, temperature or concentration) are required, this phosphine-mediated polymerization is shown to be a promising route to prepare controlled, chain-end-functionalized poly(organo)phosphazenes, which could have wide ranging usage, for example, in bioconjugation or as biodegradable building blocks for advanced macromolecular constructs.

Supporting Information

Supporting Information is available from the Wiley Online Library or from the author.

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