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Phosphorus-Containing Polymers

Poly(phosphorodiamidate)s by Olefin Metathesis Polymerization with Precise Degradation

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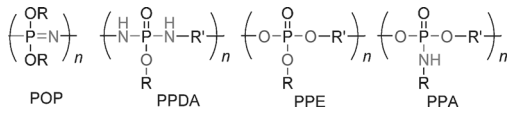
Abstract: Degradable polymers are a currently growing field of research for biomedical and materials science applications. The majority of such compounds are based on polyesters and polyamides. In contrast, their phosphorus-containing counterparts are much less studied, in spite of their potential precise degradation profile and biocompatibility. Herein, the first library of poly(phosphorodiamidate)s (PPDAs) with two P–N bonds forming the polymer backbone and a pendant P–OR group is prepared through acyclic diene metathesis polymerization. They are designed to vary in their hydrophilicity and are compared with the structural analogues poly(phosphoester)s (PPEs) with respect to their thermal properties and degradation profiles. The degradation of PPDAs can be controlled precisely by the pH: under acidic conditions the P–N linkages in the polymer backbone are cleaved, whereas under basic conditions the pendant ester is cleaved selectively and almost no backbone degradation occurs. The PPDAs exhibit distinctively higher thermal stability (from thermogravimetric analysis (TGA)) and higher glass transition and/or melting temperatures (from differential scanning calorimetry (DSC)) compared with analogous PPEs. This renders this exotic class of phosphorus-containing polymers as highly promising for the development of future drug carriers or tissue engineering scaffolds.

Introduction

P–N linkages in polymers have been only scarcely investigated to date. The typical example of such compounds are poly(organophosphazene)s (POPs, **1**), going back to pioneering works from the 1960s.[1] Their general structure $(N=PR_2)_n$, with R as a halogen, organic, or organometallic unit, is usually prepared by the thermal ring-opening polymerization of hexachlorocyclotriphosphazene.[1] POPs with different properties such as hydrophilicity or crystallinity depending on the nature of the side group have been reported.[2–4] POPs have been discussed as potential alternatives to conventional polymers and have become probably one of the most famous "inorganic polymers" to date.[3a]

However, the structural versatility of the main chain is limited with only P=N bonds forming the backbone. Herein, we prepare the first poly(phosphorodiamidate)s (PPDAs, **2**) with two P–N linkages and different alkyl chains in the backbone to vary their hydrophilicity and crystallinity. In recent works, we and other research groups have studied poly(phosphoester)s (PPEs, **3**) as a promising class of materials for applications from bio to materials science.[5] Our group introduced the functional group tolerant olefin metathesis polymerization to the preparation kit of PPEs.[6] Together with the chemical versatility of the phosphotriester repeat units, linear or branched polymers with a wide range of functional groups can be prepared.[5a,7] Wooley and co-workers reported recently acid-labile poly(phosphoramidate)s (PPAs, **4**): PPA and PPE share the same polyphosphodiester backbone (Scheme 1), but PPAs have an acid-labile phosphoramidate bond as a side group.[8]



Scheme 1. General structures of poly(organophosphazene)s (POP, **1**), poly(phosphorodiamidate)s (PPDA, **2**), poly(phosphoester)s (PPE, **3**), and poly(phosphoramidates) (PPA, **4**).

One aspect that has been scarcely studied is polymers with phosphoramidate linkages in the main chain,[9] the so-called main chain poly(phosphorodiamidate)s (PPDAs), which have mostly been reported as aromatic flame-retardant oligomers.[10] Phosphorus-containing flame retardants show attractive properties compared with the previously used halogenated flame retardants as they prevent toxic gases being released during combustion and bioaccumulation[11] or in general exhibit low toxicity, which opens future possibilities for novel polymers with P–N linkages.[12]

The acyclic diene metathesis polycondensation was used to prepare a library of novel PPDAs with variable hydrophilicity. These new compounds have been characterized and compared with structurally analogous (also novel) PPEs with respect to their thermal stability and hydrolysis. Monomers and polymers were investigated by ^{1}H NMR, ^{13}C NMR, ^{31}P NMR, ^{1}H

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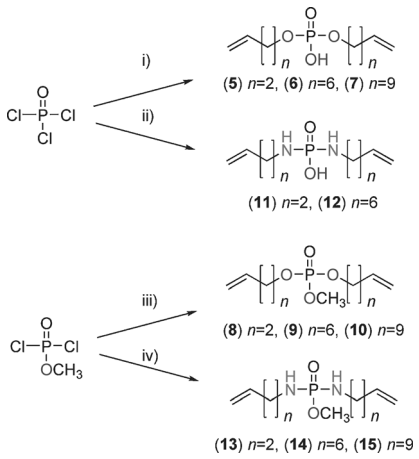
DOSY spectroscopy, and ESI-MS (only monomers). The thermal properties reveal glass transition temperatures and/or melting points depending on the microstructure. The degradation of the water-soluble monomers and polymers was investigated by variation of the pH. Under basic conditions, the pendant P–O bond is cleaved selectively, whereas under acidic conditions the backbone of PPDAs is degraded. In contrast, PPEs show a statistical cleavage of the side or main chain under these conditions.

These PPDAs broaden the scope of P-containing polymers as future biodegradable materials with adjustable hydrophilicity and precise degradation profile, and have additional potential for flame-retardant polymer additives.



Scheme 2. Synthetic strategy for phosphate and phosphorodiamidate monomers for the ADMET polymerization: (i) a) alcohol, pyridine, b) water; (ii) a) amine, pyridine, b) water; (iii) alcohol, pyridine; (iv) amine, pyridine.

Results and Discussion

Monomer synthesis

For the comparison between PPEs and PPDAs, a library of different monomers was prepared (Scheme 2): the phosphate monomers **5**–**10** carry either a P–OH or a P–OCH_3 side group with two unsaturated alkyl chains of different length attached by P–O bonds. Monomers **11**–**15** have analogous structures, but instead of phosphoesters, two phosphoramidate linkages attach the polymerizable groups.

The reasoning for choosing these monomer structures is their expected stability profiles: it is well known that phosphodiesters are resilient to hydrolysis, whereas phosphotriesters can be cleaved hydrolytically. Such structures are compared with our novel PDAs.

The monomers with P–OH functionality are accessible by esterification or amidation with 3-butene-1-amine, 3-butene-1-ol, 7-octene-1-amine, 7-octene-1-ol, 10-undecene-1-amine, and 10-decene-1-ol, followed by careful hydrolysis (Scheme 2). The phosphate monomers carrying a methyl ester side chain (**8**, **9**, **10**) can be prepared either by the direct coupling of methyl dichlorophosphate with the respective unsaturated alcohol or by treating $POCl_3$ with two equivalents of the respective alcohol, followed by hydrolysis. The intermediate monomer (i.e., with the pendant hydroxyl group) is then reacted with trimethyl orthoacetate as previously reported.[13]

^{1}H NMR and ^{13}C{H} NMR spectroscopy, along with elemental analysis and ESI-MS confirmed the successful synthesis of the monomers (see the Supporting Information). Monomer **5** is the only water-soluble one of the phosphate-based monomers, whereas for the phosphorodiamidates both "butenyl" monomers (**11** and **13**) are water-soluble owing to the hydrophilic phosphoramidate. Figure 1 shows the NMR spectra of monomers **11** and **13**. The ^{1}H NMR spectrum of **13** exhibits the characteristic doublet of a methoxy phosphoester at approximately $\delta = 3.6$ ppm ($J = 11.2$ Hz), due to coupling with the NMR-active phosphorus. The ^{31}P{H} NMR spectra exhibit single resonances at approximately $\delta = 8.7$ ppm for **11** and $\delta = 17.0$ ppm for **13**, which are consistent with the ^{31}P NMR chemical shifts of other reported phosphorodiamidates.[8]

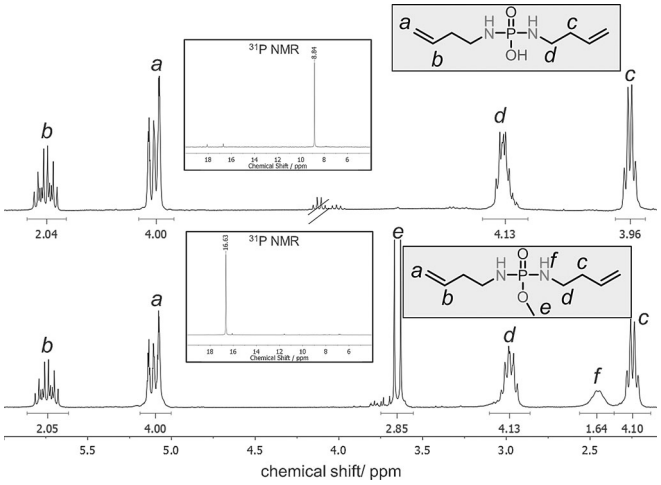
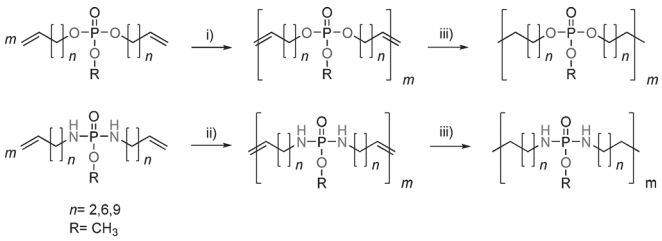


Figure 1. ^{1}H NMR (300 MHz, $CDCl_3$, 298 K) spectra of **11** (top) and **13** (bottom) (the inset shows the ^{31}P{H} NMR spectrum (202 MHz)).

Polymerization

The synthesis of PPEs and PPDAs was accomplished by acyclic diene metathesis (Scheme 3).[5c,6a,14] For PPEs, typically Grubbs' first generation catalyst leads to polymers with high molecular weights,[5b] but it produced only oligomers with phosphorodiamidates. Successful polymerization for PPDAs was observed either in bulk (if the monomer is liquid) or in solution (50 wt% in 1-chloronaphthalin) with 1 mol% of Hoveyda–Grubbs second generation catalyst at room temperature to 60 °C at reduced pressure. The phosphate monomers are liquids with low viscosity; during the polymerization, the viscosity increased and the temperature was raised (to 50 °C) to ensure efficient stirring for 8 to 16 h until the reaction mixture solidified. Owing to the higher viscosity of the phosphorodiamidates, their polymerization was conducted in solution and an additional 1 mol% catalyst was added to the mixture to promote the polymerization after 2 h until the solution was too viscous to allow efficient stirring (ca. 24 h). Catalyst deactivation oc-



Scheme 3. ADMET polycondensation of unsaturated phosphates and phosphorodiamidates (i) Grubbs first generation catalyst, 50 °C, bulk; (ii) Grubbs–Hoveyda second generation catalyst, RT, 1-chloronaphthalin; (iii) Pd/C, RT, CH_2Cl_2.

curred during the reaction, which was visible as the color changed during the polymerization in the case of Grubbs' first generation catalyst from purple to red and eventually to brown; in case of the Hoveyda–Grubbs second generation catalyst, the color changed from green to brown.

PPEs can be obtained with higher molecular weights compared with the PPDAs (Table 1). This is probably due to the polymerization of the PDAs at room temperature and in solution. To generate higher molecular weight PPDAs, the solution polymerization was conducted at 50 °C at a controlled reduced pressure of 100 mbar (Method E in Table 1). **Poly(8)** and **poly(13)**, which is water soluble, exhibit lower molecular weights probably owing to the negative neighboring effect described earlier.[6a] The successful polymerization can be detected easily from the ^{1}H NMR spectra as the terminal double bonds (at ca. $\delta = 5$ ppm and 6 ppm in the monomers) are transformed into internal double bonds during the polymerization, showing a broad resonance at approximately $\delta =$ 5.5 ppm (Figures 2 and 3). The overlay of the ^{1}H DOSY spectra of **14** and **poly(14)** proves the successful polymerization as the diffusion coefficient is shifted to lower values after the reaction (Figure 2 and the Supporting Information for other monomers).

In contrast to all monomers bearing a methoxy side chain, which undergo successful ADMET (acyclic diene metathesis), the monomers with OH side chains did not undergo efficient homopolymerization under these conditions and only oligomers were obtained. This is attributed to interactions of the P–OH groups with the catalyst. However, it was possible to generate copolymers of the "OH series" with monomers carrying methoxy side chains. PPEs and PPDAs in the range 1000–30 000 g mol^{-1} have been synthesized (Table 1 and the Supporting Information for further details).

In addition to the unsaturated polymers that were obtained directly after the metathesis, catalytic hydrogenation produces the saturated analogues. The hydrogenation was carried out at room temperature with palladium (10% Pd/C) at 25 bar (see the Experimental Section for details). Figure 3 shows the comparison of **poly(15)** and the hydrogenated **poly-H(15)**. After hydrogenation, the double bond resonances at approximately $\delta = 5$ ppm disappear, indicating the saturated materials.

Molecular weight determination of phosphorus-containing materials by gel permeation chromatography (GPC) is often difficult owing to possible column interactions.[5c,d] GPC measurements were only successful for the PPEs with our setup (see the Supporting Information); for PPDAs, GPC was not applicable. To estimate the molecular weights of the polymers, ^{1}H DOSY NMR spectroscopy calibrated with polystyrene (PS) standards of different molecular weights was used instead. The measurements revealed the diffusion coefficients of the polymers, which can be calibrated to polymer standards (the calibration curve is shown in the Supporting Information), allowing the determination of an apparent M_w of unknown polymers in solution without any column material (Table 1). This method has been previously used to study polymerization kinetics and to determine polymer molecular weights.[15]

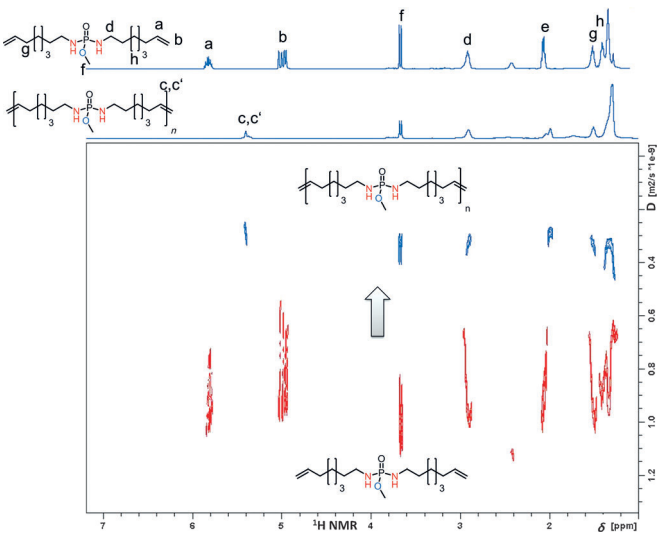


Figure 2. ^{1}H DOSY NMR spectrum of monomer **14** (red) and the respective polymer **poly(14)** (blue), proving the formation of internal double bonds at 5.4 ppm and the diffusion coefficient shift (500 MHz, 298 K, $CDCl_3$).

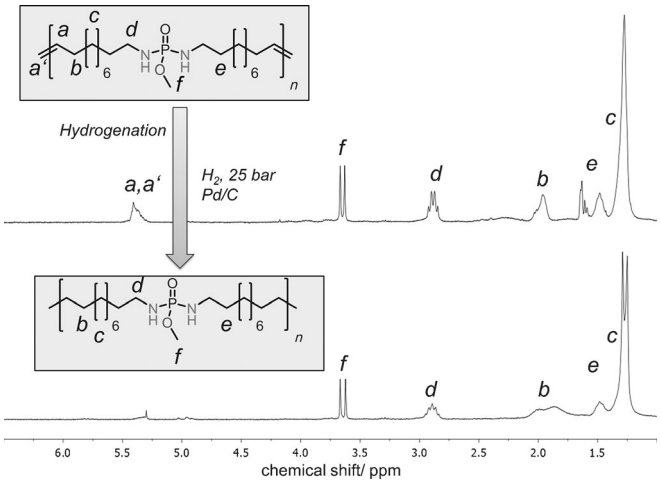


Figure 3. Comparison of the ^{1}H NMR spectra (300 MHz, $CDCl_3$, 298 K) of **poly(15)** (top) and **poly-H(15)** (bottom).

Table 1. Molecular weight of polymers from the ADMET polycondensation of phosphates and phosphorodiamidates.

Polymer	Conditions[a]	M_{wGPC}[b] [g mol^{-1}]	M_{wNMR}[c] [g mol^{-1}]	$Đ$
Poly(8)	A	1400	–	1.23
Poly-H(8)	D	1200	–	1.20
Poly(13)	A	–	1100	–
Poly-H(13)	C	–	1000	–
Poly(9)	A	19700	–	4.32
Poly-H(9)	D	21300	–	5.46
Poly(14)	B	–	2800	–
Poly-H(14)	C	–	2400	–
Poly(10)	A	19900		2.41
Poly-H(10)	D	16400	–	3.19
Poly(15)	B	–	6500	–
Poly(15)	E	–	12000	–
Poly-H(15)	C	–	5800	–
Poly(5–10)	A	9500	–	1.75
Poly(6–10)	A	13900	–	1.92
Poly(7–10)	A	12000	–	2.49
Poly(11–13)	B	–	1000	–
Poly(12–15)	B	–	8000	—

[a] Conditions: A = bulk, 50 °C, 16 h; B = 50 wt% solution of 1-chloronaphthalin, RT; C = CH_2Cl_2, RT, 16 h; D = toluene, RT, 16 h; *E* = 50 wt% solution of 1-chloronaphthaline, 50 °C. [b] Determined by GPC in THF measured by refractive index detector. [c] Determined by ^{1}H DOSY NMR spectroscopy.

Table 2. Thermal properties of polymers measured by DSC and TGA.

Polymer	T_g [°C]	ΔC_p [J g^{-1} K^{-1}]	T_m [°C]	ΔH_m [J g^{-1}]	T_{on}[a] [°C]	$T_{50\%}$ [°C]
Poly(8)	−65.4	0.438	–	–	212	364
Poly-H(8)	−67.9	0.369	–	–	211	272
Poly(9)	−49.6	0.439	–	–	287	314
Poly-H(9)	–	–	13.8	−37.22	259	314
Poly(10)	−52.4	0.317	17.2	−26.42	282	300
Poly-H(10)	−45.0	0.389	57.7	−61.79	288	314
Poly(13)	−22.3	0.521	–	–	142	368
Poly-H(13)	−27.1	0.498	–	–	185	343
Poly(14)	37.2	0.0746	–	–	194	393
Poly-H(14)	–	–	22.4	−2.73	231	373
Poly(15)	–	–	50.4	−23.94	267	441
Poly-H(15)	–	–	77.3	−52.20	217	395
Poly(5–10)	−50.4	0.474	10.0	−25.40	247	279
Poly(6–10)	−46.9	0.316	9.9	−29.67	278	292
Poly(7–10)	−43.9	0.400	21.1	−39.00	287	296
Poly(11–13)	−33.4	0.531	–	–	107	482
Poly(12–15)	−9.1	0.296	–	–	220	449

[a] T_{on} was monitored at a degradation degree of 5%.

Thermal properties

PPEs are used as flame retardant additives. In addition to the phosphorus, PP(D)As have shown a synergistic effect of P and N to give high thermal stabilities.[16] Furthermore, the charring is relatively high compared with PPEs, which leads to the decrease of pyrolysis gases.[17] The thermal properties of the polymers were examined by thermogravimetric analysis (TGA) and differential scanning calorimetry (DSC) under a nitrogen atmosphere. The PPEs exhibited glass transition temperatures of −30 to −70 °C. For unsaturated PPEs with six and fourteen methylene groups in the backbone, no melting was observed, whereas **poly(10)** with 20 methylene groups exhibited a melting point of approximately 17 °C.

In comparison with PPEs, the thermal properties of PPDAs differ strongly: all PPDAs exhibit higher glass transitions and/or melting temperatures (Figure 4 and Table 2).

In Figure 4a and b, the DSC traces of PPDAs **poly(13)** and **poly(15)** were compared with their phosphate analogues **poly(8)** and **poly(13)**. The main chain and the side chain of the polymers are kept the same except that the two "ester oxygen atoms" were exchanged by amidate linkages (NH instead of O). For the amorphous materials **poly(8)** and **poly(13)**, the glass transition temperatures of the PPDA **poly(13)** are more than 40 °C higher than for the PPE analogue **poly(8)** (Figure 4a). Furthermore, the PPDA **poly(15)** (T_m = ca. 50.4 °C) shows an increase in the melting point of more than 30 °C compared with its PPE equivalent **poly(10)** (T_m = 17.2 °C). The melting enthalpy is rather similar for both materials (ΔH_m(PPE) = 26.42 J g^{-1}; ΔH_m(PPDA) = 23.94 J g^{-1}). For PPDA **poly(15)**, the glass transition cannot be detected from the DSC curve.

After hydrogenation, higher melting points and higher melting enthalpy values for both polymers are observed. The saturated PPDA **poly-H(15)** exhibits the highest melting point of the P-containing polymers prepared by ADMET to date: 77.3 °C (ΔH_m = −52.20 J g^{-1}) compared with 50.4 °C (ΔH_m = 23.94 J g^{-1}) for the unsaturated **poly(15)** owing to the disappearance of the double bonds, which act as a defect during the crystallization of the polymer (Table 2). The PPE equivalent **poly-H(10)** shows a melting endotherm at approximately 57.7 °C (ΔH_m = 61.79 J g^{-1}).

The PPDAs exhibit strongly different thermal stabilities compared with the PPEs as detected by TGA measurements (Figure 4, Table 2). The starting degradation temperature of PPDAs is lower than that of the PPEs; however, the temperature range in which the degradation occurs is much broader with several degradation steps (Figure 4c, and Table 2 lists the onset of the mass loss (T_{on}) and the 50% weight loss temperature ($T_{50\%}$)). The phosphorodiamidate unit degrades first at approximately 375 °C and afterwards the carbon backbone degrades at approximately 450 °C. Furthermore, the residue obtained after TGA (under N_2) up to 600 °C remains approximately 30 wt%, rendering the PPDAs interesting for future flame-retardant materials.

Hydrolytic stability

In contrast to poly(phosphazene)s, only a few studies on the hydrolytic stabilities of low-molecular-weight phosphorodiamidates,[18] PPAs,[9] or PPDAs[10] have been conducted. Compared with polyamides based on carboxylic acids and amines, the phosphoramidate bond is relatively labile and can be hydrolyzed under mild acidic conditions,[8] although they are rather stable under basic conditions.

The hydrolytic stabilities of PPDAs have been investigated at different pH values. The kinetics of hydrolysis of the water-soluble monomers **11** and **13** and their respective polymers

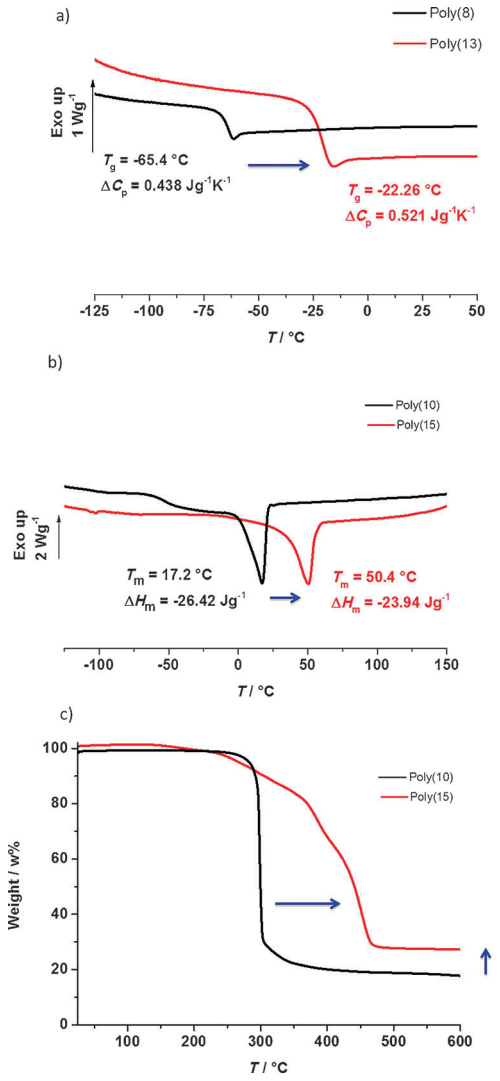


Figure 4. DSC thermograms of a) **poly(8)** versus **poly(13)**, b) **poly(10)** versus **poly(15)**, and c) TGA of **poly(10)** versus **poly(15)**.

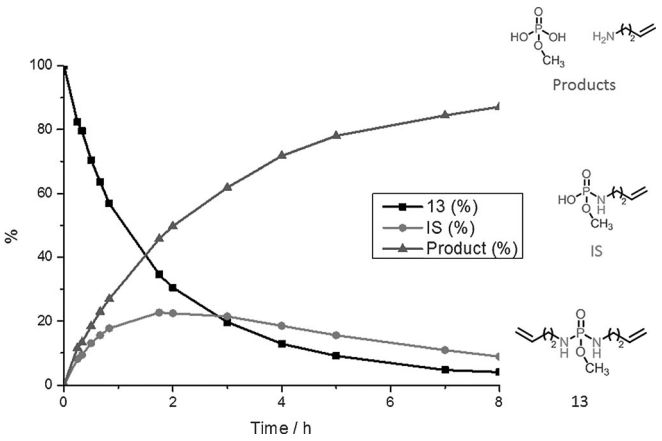


Figure 5. Monitoring the degradation of the P–N bonds in **13** at pH 1.0 by ^{1}H NMR spectroscopy.

were measured by ^{1}H NMR spectroscopy. The hydrolysis of **11** and **13** was studied in aqueous buffer solutions at different pH values (based on deuterium oxide, the conversion of pD = pH+0.4 was assumed[19]) and monitored by ^{1}H NMR spectroscopy. Two separate resonances can be used to analyze the degradation. The signal of the methylene group next to the amidate linkage ($\delta \approx 3.0$ ppm) is detected as a multiplet and the pendant methoxy group shows up as a doublet owing to coupling with phosphorus ($\delta = 3.65$ ppm, $J = 11.2$ Hz; the Supporting Information shows the degradation in aqueous buffer solutions at pH 1.0, 3.0, 5.0, 7.0, 8.0, and 13.0). Monomer **13** was degraded at a pH of 1.0 (Figure 5). The degradation was monitored from the ^{1}H NMR spectra by following the integral values of the methoxy resonance.

In general, the cleavage of the P–N bonds is strongly pH-dependent and shows the highest degradation rate at pH 1.0, reaching full completion after 10 h. The cleavage at pH 3.0 and 5.0 is significantly slower than at pH 1.0. At pH 7.0, 8.0, and 13.0, the PPDA main chain remained stable for at least 70 days. However, under basic conditions, the P–OCH_3 ester hydrolyzes selectively and no further backbone degradation is observed (Figure 6 and Figure S16 in the Supporting Information). The degradation for **poly(13)** was also compared with the degradation of the monomer **13**: as expected, the degradation kinetics are very similar (Figure 5 and the Supporting Information).

All other polymers were water insoluble. To study the degradation of the hydrophobic polymers, **poly(15)** was converted into polymer nanoparticles by a miniemulsion solvent evaporation process.[20] A chloroform solution of **poly(15)** was dispersed by ultrasonication in an aqueous Lutensol solution with subsequent evaporation of the organic solvent. A stable PPDA-nanoparticle dispersion (diameter ca. 240 nm determined from dynamic light scattering) was obtained. After the addition of HCl (to pH 1.0), the degradation of the nanoparticles was studied. Owing to the hydrophobicity of the polymer, complete backbone degradation was achieved after 7 days at room temperature. The ^{31}P NMR spectra prove the polymer partly degraded after 3 days and completely degraded after 7 days (see the Supporting Information).

These properties mean that the material is capable of specific cleavage of the side chain at basic conditions or the total degradation of the polymer backbone at acidic conditions. PPDAs would consequently present a new class of (bio)degradable polymers for various applications, especially because of the specific degradation of side or main chains. These results indicate selective cleavage or control of the degradation profile of PPDAs by adjusting of the pH value is possible.

Conclusions

A library of novel poly(phosphorodiamidate)s (PPDAs) and structural analogues poly(phosphoester)s (PPEs) was prepared by ADMET polycondensation. Polymers of variable hydrophilicity were generated, carrying either a pendant methyl ester or a free P–OH group. Both unsaturated and saturated (after hydrogenation) polymers were realized. The monomers with the methoxy side chains can be polymerized in all cases, whereas the monomers carrying pendant P–OH groups only undergo

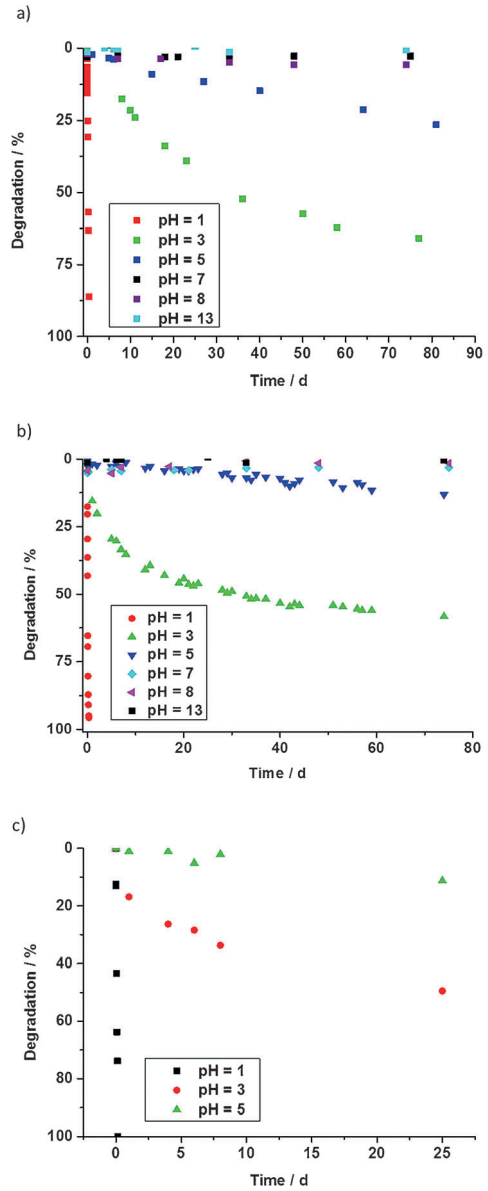


Figure 6. Degradation of phosphoramidate bonds in monomers **11** (a), **13** (b), and **poly(13)** (c) at different pH values monitored by ^{1}H NMR spectroscopy.

copolymerization under certain conditions. Their molecular weights were determined either by GPC or by ^{1}H DOSY NMR spectroscopy. The polymers of both series were compared with respect to their thermal behavior (stability, T_g, T_m) and hydrolytic degradation. Glass transitions and melting points are typically higher in the case of PPDAs compared with their structurally analogous PPEs. The P–N bonds in PPDAs can be degraded by acidic hydrolysis, but are rather stable under basic conditions. In contrast, the pendant P–O bond in PPDAs hydrolyses selectively under basic conditions without degradation of the backbone. Hydrophobic polymers were transformed into aqueous nanoparticle dispersions by a miniemulsion protocol: they show slow hydrolysis under acidic conditions over a period of several days. The specific degradation might be an interesting feature for future applications. Combined with the high thermal stabilities and melting points, PPDAs might find applications as novel biodegradable materials for tissue engineering or drug delivery or also as flame-retardant materials.

Experimental Section

Monomer syntheses

8-Azide-1-octene (1): 8-Azide-1-octene **1** was synthesized similarly to the literature procedure by Li et al.[21] NaN_3 (3.4 g, 52.3 mmol, 2.0 equiv) was added in one portion to a stirred solution of 8-bromo-1-octene (5.00 g, 26.2 mmol, 1.0 equiv) in dry DMF (50 mL) at 80 °C. After 16 h of stirring at 80 °C, the solution was poured into H_2O (200 mL). The reaction mixture was extracted with ethyl acetate (3×50 mL) and the combined organic phases were washed with brine. The organic phase was dried over anhydrous $MgSO_4$ and concentrated in vacuo. The crude 8-azide-1-octene **1** (3.8 g, 95 %) was used in the next step without further purification.

11-Azide-1-decene (2): 11-Azide-1-decene **2** was prepared from 11-bromo-1-decene as reported by Tsai et al. with modifications.[22] 11-Bromo-1-decene (5.00 g, 21.4 mmol, 1.0 equiv) was added in a solution of dry DMF (50 mL) and NaN_3 (2.8 g, 42.9 mmol, 2.0 equiv) was added in one portion at 80 °C. The reaction mixture was stirred for 16 h at 80 °C and filtered. The organic phase was extracted with *n*-hexane (3×25 mL) separated and combined, dried over anhydrous MgSO4, and concentrated in vacuo. The crude 11-azide-1-decene **2** (3.9 g, 93 %) was used in the next step without further purification.

7-Octen-1-amine (3) and 10-decen-1-amine (4): 7-Octen-1-amine and 10-decen-1-amine, **3** and **4**, were synthesized by following the reported procedure with modifications.[23] A mixture of the azide **1** or **2** (26.2 mmol, 1.0 equiv) and Ph_3P (78.5 mmol, 3.0 equiv) in a 10:1 solution of H_2O (8 mL) in THF (80 mL) was stirred at 60 °C for 16 h. Subsequently, THF was removed under reduced pressure. The aqueous residue was dissolved in acetonitrile (100 mL) with HCl (10 mL, 10 wt %). After 1 h of stirring, the acetonitrile was removed. H_2O (150 mL) was added to the mixture and the aqueous phase was extracted once with CH_2Cl_2 (1×25 mL). The aqueous phase was freeze dried. Amine **3** (90 %) or **4** (87 %) was obtained and used in the next step without further purification.

Representative procedure for synthesis of the "hydroxy- and methylphosphate monomers"

Bis-(but-3-en-1-yl)-methylphosphate (8): A mixture of 3-buten-1-ol (11.1 g, 13.3 mL, 0.154 mol, 1.8 equiv) and Et_3N (15.6 g, 21.4 mL, 0.154 mol, 1.8 equiv) in toluene (20 mL) was added to a stirred solution of $POCl_3$ (13.1 g, 8.0 mL, 0.0856 mol, 1.0 equiv) in toluene (50 mL) at room temperature. The resulting dispersion was stirred overnight at room temperature. Subsequently, Et_3N·HCl was removed by filtration. The filtrate was dried under reduced pressure to remove solvents and excess $POCl_3$. Diethyl ether (40 mL) was added to dissolve the dialkenyl chlorophosphate intermediate. The solution was stirred vigorously with water (ca. 25 mL) for 48 h with, exchanging the water phase several times.

The following purification was carried out with the water-soluble monomer **5**: The combined water phases were extracted with ethyl acetate (3×50 mL), combined, and concentrated at reduced pressure to yield pure di-(but-3-en-1-yl) phosphate **5** (Yield: 15.5 g, 0.075 mol; 88 %).

The following purification was carried out with water-insoluble monomers **6** and **7**: The diethyl ether phase was dried and the solvent was removed at reduced pressure. The residue containing the

dialkylene phosphates (**6** or **7**) was used without further purification.

Compound **5** (7.0 g, 0.0340 mol, 1.0 equiv) was mixed and stirred with trimethyl orthoacetate (8.2 g, 8.4 mL, 0.0679 mol, 2.0 equiv) at 80 °C. After stirring overnight, water was added to deactivate the excess trimethyl orthoacetate. The water phase was extracted with CH_2Cl_2 (3×50 mL) and the extract was dried. After distillation at 90 °C (5×10^{-2} mbar) pure **8** was obtained as a colorless oil (Yield: 5.5 g, 0.0250 mmol; 74%). ^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ = 5.88–5.67 (ddt, J = 17.0, 10.3, 6.7 Hz, 2H), 5.19–5.01 (m, 4H), 4.17–3.97 (q, J = 6.9 Hz, 4H), 3.85–3.61 (d, J = 11.1 Hz, 3H), 2.53–2.32 ppm (q, J = 6.7 Hz, 4H); ^{13}C{H} NMR (126 MHz, 298 K, $CDCl_3$): δ = 133.4, 117.8, 66.91, 66.86, 54.34, 54.27, 34.74, 34.69 ppm; ^{31}P{H} NMR (202 MHz, 298 K, $CDCl_3$): δ = 0.03 ppm; ESI-MS: *m/z* 243.04 $[M+Na]^+$; elemental analysis calcd (%) for $C_9H_{17}O_4P$ (220.09): C 49.09, H 7.78; found: C 49.23, H 7.61.

Bis-(but-3-en-1-yl)-phosphate (5): Following the representative procedure described above, **5** was obtained as a yellowish oil (Yield: 15.5 g, 0.0750 mol; 88%). ^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ = 11.84–11.30 (s, 1H), 5.96–5.67 (ddt, J = 17.0, 10.3, 6.7 Hz, 2H), 5.33–4.91 (m, 4H), 4.27–3.89 (q, J = 7.0 Hz, 4H), 2.59–2.40 ppm (q, J = 6.7 Hz, 4H); ^{13}C{H} NMR (126 MHz, 298 K, $CDCl_3$): δ = 133.43, 133.39, 117.84, 117.78, 67.02, 66.97, 66.9, 66.8, 34.73, 34.68, 34.73, 34.68 ppm; ^{31}P{H} NMR (202 MHz, 298 K, $CDCl_3$): δ = 0.20 ppm; ESI-MS: *m/z* 657.08 $[3M+K]^+$, 863.11 $[4M+K]^+$, 1069.17 $[5M+K]^+$; elemental analysis calcd (%) for $C_8H_{15}O_4P$ (206.07): C 46.60, H 7.33; found: C 46.45, H 7.27.

Bis-(oct-7-en-1-yl)-phosphate (6): Following the representative procedure described above until the synthesis steps of **5** using 7-octen-1-ol, **6** was obtained as a yellowish oil (Yield: 54%). ^{1}H NMR (300 MHz, 298 K, $CDCl_3$): δ = 5.97–5.57 (m, 2H), 5.08–4.82 (m, 4H), 4.52–4.15 (s, 5H), 4.13–3.89 (d, J = 6.8 Hz, 4H), 2.22–1.89 (d, J = 6.8 Hz, 4H), 1.82–1.49 (m, 4H), 1.52–0.97 ppm (m, 15H); ^{13}C{H} NMR (126 MHz, 298 K, $CDCl_3$): δ = 137.1, 137.0, 112.4, 112.3, 75.4, 75.1, 74.9, 65.61, 65.56, 44.1, 31.8, 31.7, 28.3, 28.2, 26.9, 26.84, 26.81, 26.7, 23.4, 6.7 ppm; ^{31}P{H} NMR (202 MHz, 298 K, $CDCl_3$): δ = −1.15 ppm; ESI-MS: *m/z* 319.17 $[M+H]^+$, 637.31 $[2M+H]^+$, 955.47 $[3M+H]^+$; elemental analysis calcd (%) for $C_{16}H_{31}O_4P$ (318.20): C 60.36, H 9.81; found: C 60.13, H 9.93.

Bis-(undec-10-en-1-yl)-phosphate (7): Following the representative procedure described above until the synthesis steps of **5** using 10-decen-1-ol, **7** was obtained as a yellowish oil (Yield: 60%). ^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ = 8.89–8.70 (s, 2H), 5.93–5.68 (ddt, J = 16.9, 10.2, 6.7 Hz, 2H), 5.09–4.82 (m, 4H), 4.17–3.78 (q, J = 6.7 Hz, 4H), 2.12–1.94 (q, J = 6.9 Hz, 4H), 1.79–1.60 (p, J = 6.7 Hz, 4H), 1.49–1.14 ppm (d, J = 44.5 Hz, 26H); ^{13}C{H} NMR (126 MHz, 298 K, $CDCl_3$): δ = 139.3, 114.3, 76.9, 67.91, 67.86, 34.0, 30.4, 30.3, 29.62, 29.58, 29.57, 29.30, 29.27, 29.1, 25.6 ppm; ^{31}P{H} NMR (202 MHz, 298 K, $CDCl_3$): δ = 1.18 ppm; ESI-MS: *m/z* 403.26 $[M+H]^+$, 805.48 $[2M+H]^+$, 1207.73 $[3M+H]^+$; elemental analysis calcd (%) for $C_{22}H_{43}O_4P$ (402.29): C 65.64, H 10.77; found: C 65.65, H 10.88.

Bis-(oct-7-en-1-yl)-methylphosphate (9): Following the representative procedure described above (without purification by distillation) using 7-octen-1-ol, **9** was obtained as a yellowish oil (Yield: 92%). ^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ = 5.91–5.67 (ddt, J = 16.9, 10.2, 6.7 Hz, 2H), 5.12–4.83 (m, 4H), 4.11–3.96 (q, J = 6.7 Hz, 4H), 3.83–3.70 (dd, J = 11.1, 6.4 Hz, 3H), 2.14–1.97 (q, J = 7.8 Hz, 4H), 1.80–1.60 (p, J = 6.7 Hz, 4H), 1.52–1.28 ppm (dd, J = 19.2, 7.2 Hz, 13H); ^{13}C{H} NMR (126 MHz, 298 K, $CDCl_3$): δ = 139.0, 114.44, 114.40, 67.93, 67.88, 67.8, 67.7, 54.2, 54.2, 33.7, 30.38, 30.36, 30.3, 28.84, 28.79, 28.74, 28.70, 28.68, 28.67, 28.65, 25.42, 25.39, 25.36 ppm; ^{31}P{H} NMR (202 MHz, 298 K, $CDCl_3$): δ = 0.33 ppm; ESI-MS: *m/z* 333.18 $[M+H]^+$, 355.15 $[M+Na]^+$, 687.32 $[2M+Na]^+$; elemental analysis calcd (%) for $C_{17}H_{33}O_4P$ (332.21): C 61.42, H 10.01; found: C 61.68, H 10.17.

Bis-(undec-10-en-1-yl)-methylphosphate (10): Following the representative procedure described above (without purification by distillation) using 10-undecen-1-ol, **10** was obtained as a yellowish oil (Yield: 86%). ^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ = 5.94–5.66 (ddt, J = 13.5, 10.1, 6.7 Hz, 2H), 5.11–4.80 (dd, J = 30.3, 13.4 Hz, 4H), 4.14–3.93 (q, J = 6.6 Hz, 4H), 3.86–3.64 (d, J = 11.0 Hz, 3H), 2.17–1.91 (q, J = 6.8 Hz, 4H), 1.76–1.50 (m, 6H), 1.46–1.15 ppm (d, J = 43.3 Hz, 27H); ^{13}C{H} NMR (126 MHz, 298 K, $CDCl_3$): δ = 139.2, 114.2, 67.94, 67.89, 54.2, 54.1, 33.9, 30.40, 30.35, 29.54, 29.48, 29.21, 29.18, 29.0, 25.5 ppm; ^{31}P{H} NMR (202 MHz, 298 K, $CDCl_3$): δ = −1.51 ppm; ESI-MS: *m/z* 417.25 $[M+H]^+$, 439.23 $[M+Na]^+$, 833.51 $[2M+H]^+$, 855.46 $[2M+Na]^+$; elemental analysis calcd (%) for $C_{23}H_{45}O_4P$ (416.31): C 66.31, H 10.89; found: C 66.37, H 10.81.

Representative procedure for synthesis of the phosphorodiamidate monomers

***N,N′*-Bis-(but-3-en-1-yl)-phosphorodiamidate (11)**: A mixture of 3-buten-1-amine (1.5 g, 1.9 mL, 0.0211 mol, 2.0 equiv) and Et_3N (2.2 g, 3.1 mL, 0.0222 mol, 2.1 equiv) in toluene (20 mL) was added to a stirred solution of $POCl_3$ (1.6 g, 1.0 mL, 0.0106 mol, 1.0 equiv) in toluene (50 mL) at room temperature. The resulting dispersion was stirred overnight at room temperature and then filtered to remove Et_3N·HCl. The solvent of the filtrate was removed under reduced pressure. Ethyl acetate (50 mL) was added to dissolve the dialkenyl chlorophosphorodiamidate intermediate and 4-dimethylaminopyridine (DMAP; 100 mg, 0.819 mmol) was added. The resulting mixture was stirred vigorously with water for 48 h, exchanging the water several times. The ethyl acetate phases were combined and washed with 10% HCl solution and brine. After removing the solvent under reduced pressure, pure di-(but-3-en-1-yl) phosphorodiamidate **11** was obtained as a yellowish oil (Yield: 0.86 g, 0.00424 mmol; 73%). ^{1}H NMR (300 MHz, 298 K, $CDCl_3$): δ = 5.94–5.44 (td, J = 17.1, 6.9 Hz, 2H), 5.28–4.90 (m, 4H), 3.19–2.81 (m, 4H), 2.42–2.11 ppm (q, J = 6.7 Hz, 4H); ^{13}C{H} NMR (176 MHz, 298 K, $CDCl_3$): δ = 135.1, 117.4, 77.2, 77.1, 76.9, 40.3, 35.8 ppm; ^{31}P{H} NMR (202 MHz, 298 K, $CDCl_3$): δ = 8.84 ppm; ESI-MS: *m/z* 391.21 $[2M-H_2O+H]^+$, 803.36 $[3M-2H_2O+Na]^+$; elemental analysis calcd (%) for $C_8H_{17}N_2O_2P$ (204.10): C 47.05, H 8.39, N 13.72; found: C 47.14, H 8.39, N 13.58.

***N,N′*-Bis-(oct-7-en-1-yl)-phosphorodiamidate (12)**: Following the representative procedure described above using 7-octen-1-amine **3**, **12** was obtained as a yellowish oil (Yield: 62%). ^{1}H NMR (300 MHz, 298 K, D_2O): δ = 6.08–5.70 (ddt, J = 17.0, 10.2, 6.7 Hz, 2H), 5.14–4.90 (m, 4H), 3.10–2.84 (t, J = 7.5 Hz, 4H), 2.21–1.89 (q, J = 7.0 Hz, 3H), 1.78–1.51 (p, J = 7.1 Hz, 4H), 1.51–1.19 ppm (m, 12H); ^{13}C{H} NMR (126 MHz, 298 K, $CDCl_3$): δ = 142.6, 116.6, 42.0, 41.9, 35.4, 30.31, 30.18, 30.1, 29.2, 29.14, 29.09, 28.1, 27.9, 27.91, 27.90, 27.88 ppm; ^{31}P{H} NMR (202 MHz, 298 K, $CDCl_3$): δ = 8.26 ppm; ESI-MS: *m/z* 637.44 $[2M-H_2O+Na]^+$, 915.55 $[3M-2H_2O+H]^+$, 1251.89 $[4M-3H_2O+K]^+$; elemental analysis calcd (%) for $C_{16}H_{33}N_2O_2P$ (316.23): C 60.73, H 10.51, N 8.85; found: C 60.59, H 10.56, N 8.81.

Representative procedure for synthesis of the methylphosphorodiamidate monomers

***N,N′*-Bis-(but-3-en-1-yl)-methylphosphorodiamidate (13)**: A mixture of 3-buten-1-amine (1.787 g, 2.300 mL, 25.12 mmol, 2.0 equiv), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU; 4.015 g, 3.944 mL, 26.38 mmol, 2.1 equiv), and DMAP (384 mg, 3.14 mmol, 0.25 equiv) in CH_2Cl_2 (10 mL) was added to a stirred solution of methyl dichlo-

rophosphate (1.871 g, 1.260 mL, 12.56 mmol, 1.0 equiv) in CH_2Cl_2 (20 mL) at room temperature. The resulting solution was stirred overnight at room temperature. The solvent of the filtrate was removed under reduced pressure. The resulting residue was dissolved in diethyl ether. The diethyl ether phase was washed with 10% HCl solution, $NaHCO_3$ solution, and brine. After removing the solvent under reduced pressure, pure **13** was obtained as a yellowish oil (Yield: 1.92 g, 8.79 mmol; 70%). ^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ = 5.81–5.67 (ddt, J = 17.1, 10.2, 6.9 Hz, 2H), 5.13–5.07 (m, 4H), 3.67–3.63 (d, J = 11.2 Hz, 3H), 3.02–2.94 (ddq, J = 13.0, 6.5, 3.1 Hz, 4H), 2.66 (s, 2H), 2.28–2.21 ppm (q, J = 6.7 Hz, 4H); ^{13}C{H} NMR (126 MHz, 298 K, $CDCl_3$): δ = 135.4, 117.3, 51.8, 40.3, 36.2, 36.1 ppm; ^{31}P{H} NMR (202 MHz, 298 K, $CDCl_3$): δ = 16.67 ppm; ESI-MS: *m/z* 219.11 $[M+H]^+$, 241.08 $[M+Na]^+$; elemental analysis calcd (%) for $C_9H_{19}N_2O_2P$ (218.12): C 49.33, H 8.78, N 12.84; found: C 49.11, H 8.70, N 12.96.

***N,N′*-Bis-(oct-7-en-1-yl)-methylphosphorodiamidate (14)**: Following the representative procedure described above using 7-octen-1-amine **3**, **14** was obtained as a yellowish oil (Yield: 84%). ^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ = 5.75–5.71 (td, J = 16.9, 6.7 Hz, 2H), 4.93–4.86 (m, 4H), 3.58–3.57 (d, J = 11.2 Hz, 3H), 2.82 (m, 4H), 2.34–2.33 (d, J = 6.8 Hz, 2H), 1.98–1.97 (q, J = 6.8 Hz, 4H), 1.42–1.18 ppm (m, 23H); ^{13}C{H} NMR (176 MHz, 298 K, $CDCl_3$): δ = 138.9, 132.12, 132.06, 131.9, 128.53, 128.46, 114.3, 70.6, 51.7, 41.2, 41.1, 33.7, 32.0, 31.9, 29.7, 28.81, 28.75, 28.7, 26.6 ppm; ^{31}P{H} NMR (202 MHz, 298 K, $CDCl_3$): δ = 16.87 ppm; ESI-MS: *m/z* 331.28 $[M+H]^+$, 683.47 $[2M+Na]^+$, 1013.76 $[3M+Na]^+$; elemental analysis calcd (%) for $C_{17}H_{35}N_2O_2P$ (330.24): C 61.79, H 10.68, N 8.48; found: C 61.67, H 10.57, N 8.32.

***N,N′*-Bis-(undec-10-en-1-yl)-methylphosphorodiamidate (15)**: Following the representative procedure described above using 10-undecen-1-amine **4**, **15** was obtained as a yellowish oil (Yield: 73%). ^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ = 5.88–5.65 (td, J = 16.9, 6.7 Hz, 2H), 5.05–4.83 (m, 4H), 3.79–3.43 (d, J = 11.2 Hz, 3H), 2.97–2.74 (t, J = 7.9 Hz, 4H), 2.57–2.30 (d, J = 8.0 Hz, 2H), 2.13–1.89 (m, 4H), 1.53–1.38 (m, 4H), 1.38–1.09 ppm (d, J = 46.7 Hz, 27H); ^{13}C{H} NMR (176 MHz, 298 K, $CDCl_3$): δ = 139.2, 132.11, 132.06, 131.9, 128.52, 128.45, 114.1, 53.6, 51.69, 51.67, 41.6, 41.2, 39.8, 33.8, 32.02, 31.99, 29.52, 29.42, 29.36, 29.3, 29.2, 29.1, 28.9, 27.7, 26.7 ppm; ^{31}P{H} NMR (202 MHz, 298 K, $CDCl_3$): δ = 17.03 ppm; ESI-MS: *m/z* 415.37 $[M+H]^+$, 437.35 $[M+Na]^+$, 829.72 $[2M+H]^+$, 851.69 $[3M+Na]^+$, 1266.03 $[3M+H]^+$; elemental analysis calcd (%) for $C_{23}H_{47}N_2O_2P$ (414.34): C 47.05, H 8.39, N 13.72; found: C 47.14, H 8.39, N 13.58.

Representative procedure for the ADMET polymerization of the methylphosphate and methylphosphorodiamide monomers

Poly(8): Bis-(but-3-en-1-yl)-methylphosphate **8** (1.0 g, 4.54 mmol) and Grubbs catalyst (first generation: 37.4 mg, 0.0454 mmol, 1 mol%; or Hoveyda–Grubbs second generation catalyst: 2 mol% and 2 mol% after 2 h for PPDAs) were placed in a glass Schlenk tube equipped with a magnetic stir bar under an argon atmosphere. The reaction was carried out under reduced pressure (to remove the ethylene gas evolving during the metathesis reaction) in bulk or solution at temperatures between RT and 50 °C for 16 h. **Poly(8)** was obtained in bulk as a brownish viscous oil in quantitative yield. Purification: tris-(hydroxymethyl) phosphine (ca. 50 equiv with respect to the catalyst) was added to a solution of CH_2Cl_2 and the polymer. After the addition of water, the emulsion was stirred for several hours until the CH_2Cl_2 phase was almost colorless. The CH_2Cl_2 phase was washed with aqueous 10% HCl and finally with brine to remove the catalyst residue. The CH_2Cl_2 phase was separated, dried over magnesium sulfate ($MgSO_4$), filtered, and concentrated at reduced pressure (Yield: 920 mg, 4.18 mmol; 92%). ^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ = 5.64–5.41 (m), 4.18–3.92 (m), 3.84–3.63 (m), 2.53–2.25 ppm (m); ^{13}C{H} NMR (126 MHz, 298 K, $CDCl_3$): δ = 128.2, 127.3, 67.2, 67.14, 67.11, 67.09, 66.92, 66.88, 54.4, 54.33, 54.31, 54.29, 33.70, 33.65, 28.70, 28.65 ppm; ^{31}P{H} NMR (202 MHz, 298 K, $CDCl_3$): δ = 0.08 ppm.

Representative procedure for catalytic hydrogenation[6a]

Polymer **poly(8)** (100 mg), CH_2Cl_2 (5 mL), and 10% Pd/C catalyst (5 mg) were charged into a reactor and flushed with argon. Hydrogenation was then performed with vigorous stirring under a hydrogen pressure of 25 bar at room temperature for 16 h. The solution was filtered over Celite® and polymer **poly-H(8)** was isolated after solvent evaporation in a yield of 80%.

Poly-H(8): Hydrogenation of **poly(8)**: yield: 82%. ^{1}H NMR (300 MHz, 298 K, $CDCl_3$): δ = 4.12–3.84 (m), 3.84–3.48 (m), 1.76–1.50 (m), 1.50–1.10 ppm (m); ^{13}C{H} NMR (126 MHz, $CDCl_3$): δ = 67.9, 67.6, 67.0, 54.2, 33.6, 33.5, 31.3, 30.2, 30.1, 25.0, 22.5, 14.0 ppm; ^{31}P{H} NMR (202 MHz, 298 K, $CDCl_3$): δ = 0.38 ppm.

Poly(9): The reaction was carried out following the general procedure above with bis-(oct-7-en-1-yl)-methylphosphate **9** (150.0 mg, 0.451 mmol) as the monomer for 16 h (yield: 85%). ^{1}H NMR (250 MHz, 298 K, $CDCl_3$): δ = 5.42–5.14 (m), 4.11–3.82 (m), 3.78–3.59 (m), 2.07–1.78 (m), 1.74–1.45 (m), 1.45–1.07 ppm (m); ^{13}C{H} NMR (126 MHz, 298 K, $CDCl_3$): δ = 138.87, 130.90, 130.25, 130.0, 129.8, 114.3, 67.83, 67.78, 67.4, 67.3, 54.08, 54.08, 54.06, 33.6, 32.5, 32.4, 31.7, 30.3, 30.2, 29.6, 29.5, 28.7, 27.6, 27.1, 26.1, 25.3, 25.0, 24.8 ppm; ^{31}P{H} NMR (202 MHz, 298 K, $CDCl_3$): δ = 0.39 ppm.

Poly-H(9): Hydrogenation of **poly(9)**. Yield: 78%. ^{1}H NMR (300 MHz, 298 K, $CDCl_3$): δ = 4.06–3.85 (m), 3.76–3.61 (m), 1.72–1.44 (m), 1.44–1.06 ppm (m); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 67.9, 67.8, 54.1, 54.0, 31.9, 30.32, 30.26, 29.63, 29.58, 29.5, 29.2, 27.6, 27.3, 26.6, 26.5, 26.4, 25.4, 24.7, 22.7, 22.6, 14.1 ppm; ^{31}P NMR (202 MHz, 298 K, $CDCl_3$): δ = 0.37 ppm.

Poly(10): The reaction was carried out following the general procedure above with bis-(undec-10-en-1-yl)-methylphosphate **10** (250.0 mg, 0.600 mmol) as the monomer for 8 h (yield: 78%). ^{1}H NMR (700 MHz, 298 K, $CDCl_3$): δ = 5.91–5.66 (m), 5.44–5.23 (m), 5.04–4.85 (m), 4.07–3.94 (m), 3.79–3.67 (m), 2.08–1.87 (m), 1.76–1.55 (m), 1.47–1.08 ppm (m); ^{13}C{H} NMR (176 MHz, $CDCl_3$): δ = 130.4, 130.0, 69.0, 68.0, 54.20, 54.16, 32.7, 30.5, 30.4, 29.8, 29.62, 29.56, 29.3, 27.4, 25.6 ppm; ^{31}P{H} NMR (284 MHz, 298 K, $CDCl_3$): δ = 0.83 ppm.

Poly-H(10): Hydrogenation of **poly(10)**. Yield: 84%. ^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ = 4.17–3.97 (m), 3.86–3.68 (m), 1.77–1.52 (m), 1.47–1.08 ppm (m); ^{13}C{H} NMR (126 MHz, $CDCl_3$): δ = 67.9, 67.8, 54.1, 54.0, 31.9, 30.33, 30.27, 29.72, 29.70, 29.67, 29.6, 29.53, 29.51, 29.3, 29.2, 25.4, 25.4, 22.7, 14.1 ppm; ^{31}P{H} NMR (202 MHz, 298 K, $CDCl_3$): δ = 0.38 ppm.

Poly(13): The reaction was carried out following the general procedure above with Hoveyda–Grubbs second generation catalyst (11.4 mg, 0.00908 mmol, 2×2 mol%) and *N,N′*-bis-(but-3-en-1-yl)-methylphosphorodiamidate **13** (100.0 mg, 0.458 mmol) as the monomer in bulk for 16 h and in a 50 wt% 1-chloronaphthalin solution for 20 h (yield: 75%). ^{1}H NMR (300 MHz, 298 K, $CDCl_3$): δ = 5.62–5.53 (m), 5.15–5.07 (m), 3.62–3.59 (m), 3.53–3.32 (m), 2.91–2.89 (m), 2.25–2.10 ppm (m); ^{13}C{H} NMR (126 MHz, 298 K, $CDCl_3$): δ = 135.4, 131.2, 129.8, 128.7, 127.0, 117.32, 117.29, 117.25, 115.6, 51.9, 43.1, 43.0, 40.6, 40.2, 36.1, 34.9, 34.5, 17.6 ppm; ^{31}P{H} NMR (202 MHz, 298 K, $CDCl_3$): δ = 16.98 ppm.

Poly(*N*,*N*′-hexan-1-yl methylphosphorodiamidate) (Poly-H(13)): Hydrogenation of **poly(13)**. Yield: 70%. ^{1}H NMR (300 MHz, 298 K, $CDCl_3$): $\delta = 3.69–3.59$ (m), 2.94–2.87 (m), 1.60–1.40 (m), 1.39–1.30 ppm (m); ^{13}C{H} NMR (126 MHz, $CDCl_3$): $\delta = 51.7$, 45.5, 41.2, 40.9, 34.10, 34.05, 29.7, 19.9, 13.7 ppm; ^{31}P{H} NMR (202 MHz, 298 K, $CDCl_3$): $\delta = 17.20–16.91$ (m).

Poly(14): The reaction was carried out following the general procedure above with the Hoveyda–Grubbs second generation catalyst (6.0 mg, 0.00964 mmol, 2×2 mol%) and *N*,*N*′-bis-(oct-7-en-1-yl)-methylphosphorodiamidate **14** (100.0 mg, 0.241 mmol) as the monomer in a 50 wt% 1-chloronaphthalin solution for 16 h (yield: 73%). ^{1}H NMR (500 MHz, 298 K, $CDCl_3$): $\delta = 5.55–5.24$ (m), 5.11–4.85 (m), 3.78–3.53 (m), 3.05–2.68 (m), 2.14–1.80 (m), 1.72–1.01 ppm (m); ^{13}C{H} NMR (176 MHz, 298 K, $CDCl_3$): $\delta = 130.5$, 130.3, 130.1, 53.4, 53.1, 51.7, 41.2, 32.5, 32.0, 29.5, 29.3, 28.8, 27.1, 26.7, 26.3 ppm; ^{31}P{H} NMR (121.5 MHz, 298 K, $CDCl_3$): $\delta = 17.05$ ppm (m).

Poly-H(14): Hydrogenation of **poly(14)**. Yield: 67%. ^{1}H NMR (300 MHz, 298 K, $CDCl_3$): $\delta = 3.70–3.59$ (m), 2.97–2.83 (m), 1.50–1.35 (m), 1.36–1.23 ppm (m); ^{13}C{H} NMR (75 MHz, CD_2Cl_2): $\delta = 41.5$, 32.5, 32.4, 32.2, 30.08, 30.0, 29.7, 27.2, 23.1, 14.3 ppm; ^{31}P{H} NMR (202 MHz, 298 K, $CDCl_3$): $\delta = 16.63$ ppm (m).

Poly(15): The reaction was carried out following the general procedure above with the Hoveyda–Grubbs second generation catalyst (6.0 mg, 0.00964 mmol, 2×2 mol%) and *N*,*N*′-bis-(undec-10-en-1-yl)-methylphosphorodiamidate **15** (100.0 mg, 0.241 mmol) as the monomer in a 50 wt% 1-chloronaphthalin solution for 16 h (yield: 71%). ^{1}H NMR (500 MHz, 298 K, $CDCl_3$): $\delta = 5.38–5.34$ (m), 3.66–3.60 (m), 2.89–2.85 (m), 2.50–2.26 (m), 1.97–1.93 (m), 1.47–1.43 (m), 1.28–1.24 ppm (m); ^{13}C{H} NMR (176 MHz, $CDCl_3$): $\delta = 130.3$, 129.9, 51.68, 51.66, 41.2, 32.59, 32.55, 32.04, 32.00, 29.8, 29.51, 29.46, 29.51, 29.46, 29.3, 29.2, 29.1, 27.2, 26.8 ppm; ^{31}P{H} NMR (202 MHz, 298 K, $CDCl_3$): $\delta = 17.00$ ppm (m).

Poly-H(15): Hydrogenation of **poly(15)**. Yield: 81%. ^{1}H NMR (500 MHz, 298 K, $CDCl_3$): $\delta = 3.67–3.56$ (m), 2.97–2.78 (m), 2.53–2.41 (m), 1.53–1.37 (m), 1.37–1.10 ppm (m); ^{13}C{H} NMR (75 MHz, CD_2Cl_2): $\delta = 41.5$, 32.3, 30.1, 29.8, 27.2, 23.1, 14.3 ppm; ^{31}P{H} NMR (202 MHz, 298 K, $CDCl_3$): $\delta = 17.19$ ppm.

Representative procedure for the ADMET copolymerization of methylphosphate monomers and methylphosphorodiamidate monomers

Copolymer of monomer 5 and 10 (Poly(5–10)): Bis-(undec-10-en-1-yl)-methylphosphate **10** (200 mg, 0.480 mmol, 3 equiv), bis-(but-3-en-1-yl)-phosphate **5** (33 mg, 0.160 mmol, 1 equiv), Grubbs first generation catalyst (5.3 mg, 0.0064 mmol, 1 mol%; or Hoveyda–Grubbs second generation catalyst: 2 mol% and 2 mol% after 2 h for PPDAs) were placed in a glass Schlenk tube equipped with a magnetic stirrer bar under an argon atmosphere. The reaction was carried out at reduced pressure at a temperature of 50 °C for 16 h for phosphate-based polymers and **poly(11–13)**. For polymer **poly(12–15)**, the reaction was carried out in a 50 wt% 1-chloronaphthalin solution at reduced pressure at room temperature. **Poly(5–10)** was obtained as an off-white viscous oil in quantitative yield after 16 h. Purification: see above. Yield: 91%. ^{1}H NMR (300 MHz, 298 K, $CDCl_3$): $\delta = 5.64–5.21$ (m), 4.15–3.89 (m), 3.82–3.61 (m), 2.55–2.24 (m), 2.10–1.84 (m), 1.78–1.54 (m), 1.51–1.11 ppm (m); ^{13}C{H} NMR (75 MHz, 298 K, $CDCl_3$): $\delta = 130.3$, 129.8, 67.9, 54.1, 32.6, 30.3, 30.2, 29.7, 29.5, 29.4, 29.2, 27.2, 25.4 ppm; ^{31}P{H} NMR (121.5 MHz, 298 K, $CDCl_3$): $\delta = 1.38–0.50$, 0.50–0.25 ppm.

Copolymer of monomers 6 and 10 (Poly(6–10)): The reaction was carried out following the general procedure above with bis-(oct-7-en-1-yl)-phosphate **6** (51 mg, 0.160 mmol, 1 equiv) as hydroxyl monomer for 16 h. Yield: 86%. ^{1}H NMR (300 MHz, 298 K, $CDCl_3$): $\delta = 5.49–5.23$ (m), 4.15–3.90 (m), 3.84–3.68 (m), 2.15–1.86 (m), 1.82–1.52 (m), 1.53–1.14 ppm (m); ^{13}C{H} NMR (75 MHz, 298 K, $CDCl_3$): $\delta = 130.5$, 130.3, 130.1, 129.8, 67.9, 67.8, 54.1, 54.0, 32.6, 32.5, 30.3, 30.2, 29.7, 29.5, 29.4, 29.2, 27.2, 25.4 ppm; ^{31}P{H} NMR (121.5 MHz, 298 K, $CDCl_3$): $\delta = 1.45–0.58$, 0.57–0.20 ppm.

Copolymer of monomers 7 and 10 (Poly(7–10)): The reaction was carried out following the general procedure above with bis-(undec-10-en-1-yl)-phosphate **7** (51 mg, 0.160 mmol, 1 equiv) as hydroxyl monomer for 16 h. Yield: 93%. ^{1}H NMR (300 MHz, 298 K, $CDCl_3$): $\delta = 5.49–5.25$ (m), 4.21–3.90 (m), 3.86–3.66 (m), 2.13–1.83 (m), 1.81–1.49 (m), 1.49–1.14 ppm (m); ^{13}C{H} NMR (75 MHz, 298 K, $CDCl_3$): $\delta = 130.3$, 129.8, 67.9, 67.8, 54.1, 54.0, 53.4, 32.6, 30.33, 30.24, 29.7, 29.5, 29.2, 27.2, 25.4 ppm; ^{31}P{H} NMR (121.5 MHz, 298 K, $CDCl_3$): $\delta = 1.40–0.75$, 0.39–0.19 ppm.

Copolymer of monomers 11 and 13 (Poly(11–13)): The reaction was carried out following the general procedure above with the Hoveyda–Grubbs second generation catalyst (14.4 mg, 0.0229 mmol, 2×2 mol%), *N*,*N*′-bis-(but-3-en-1-yl)-phosphorodiamidate **11** (23.4 mg, 0.115 mmol, 1 equiv) as hydroxyl monomer and *N*,*N*′-bis-(but-3-en-1-yl)-methylphosphorodiamidate **13** as methyl monomer (100 mg, 0.458 mmol, 8 equiv) for 16 h. Yield: 88%. ^{1}H NMR (300 MHz, 298 K, $CDCl_3$): $\delta = 5.62–5.14$ (m), 3.71–3.50 (m), 3.50–3.33 (m), 3.14–2.65 (m), 2.36–2.01 ppm (m); ^{13}C{H} NMR (75 MHz, 298 K, CD_2Cl_2): $\delta = 136.2$, 134.3, 131.5, 130.3, 129.2, 117.9, 117.0, 43.3, 40.9, 40.7, 39.6, 36.5, 35.2, 34.8, 32.1, 23.0, 21.2, 18.3, 17.8, 14.3 ppm; ^{31}P{H} NMR (121.5 MHz, 298 K, CD_2Cl_2): $\delta = 17.28$, 8.68 ppm.

Copolymer of monomers 12 and 15 (Poly(12–15)): The reaction was carried out following the general procedure above with the Hoveyda–Grubbs second generation catalyst (8.0 mg, 0.0128 mmol, 2×2 mol%), *N*,*N*′-bis-(but-3-en-1-yl)-phosphorodiamidate **11** (23.4 mg, 0.080 mmol, 1 equiv) as hydroxyl monomer and *N*,*N*′-bis-(but-3-en-1-yl)-methylphosphorodiamidate **13** as methyl monomer (100 mg, 0.241 mmol, 3 equiv) for 16 h. Yield: 82%. ^{1}H NMR (300 MHz, 298 K, $CDCl_3$): $\delta = 5.58–5.22$ (m), 3.82–3.54 (m), 3.05–2.76 (m), 2.14–1.84 (m), 1.71–1.43 (m), 1.43–1.03 ppm (m); ^{13}C{H} NMR (75 MHz, 298 K, CD_2Cl_2): $\delta = 130.7$, 41.5, 33.0, 32.4, 30.00, 29.99, 29.7, 29.5, 27.2, 18.1 ppm; ^{31}P{H} NMR (121.5 MHz, 298 K, CD_2Cl_2): $\delta = 17.88$, 12.76, 9.44 ppm.

Procedure for hydrolytic degradation

11, **13**, or **poly(13)** (6.0 mg) were dissolved into deuterated buffer solution (0.6 mL; pH 1.0: 0.136 mM hydrogen chloride/potassium chloride solution, pH 3.0: 0.088 mM hydrogen chloride/potassium hydrogen phthalate solution, pH 5.0: 0.100 mM sodium acetate/acetic acid solution, pH 7.0: 0.01 mM phosphate buffered saline (PBS) buffer solution, pH 8.0: 0.015 mM borax/hydrogen chloride solution, pH 13: 0.145 mM sodium hydroxide/potassium chloride solution). The mixtures were poured into NMR tubes and measured during the degradation.

Preparation of PPDA nanoparticles

Poly(15) (30 mg) was dissolved in chloroform (1 g, 846 μg) and added to an aqueous solution of Lutensol AT50 (30 mg) in water (5 g). The two-layer system was sonicated with a Brandon W450-D sonifier with a 1/4 tip at 70% amplitude in a pulsed regime (30 s sonication, 10 s pause) under ice cooling. The obtained miniemul-

sion was stirred in the open at 40 °C for 16 h to evaporate the organic solvent. The obtained nanoparticles (ca. 240 nm from DLS) were divided into volumes of 500 μL and concentrated HCl (40 μL) was added to each vial. Every other day one of those suspensions was freeze dried, dissolved in deuterated chloroform, and measured by $^{31}P\{H\}$ NMR spectroscopy.

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Keywords: acyclic diene metathesis · degradation · phosphorus · poly(phosphoester) · poly(phosphorodiamidate)

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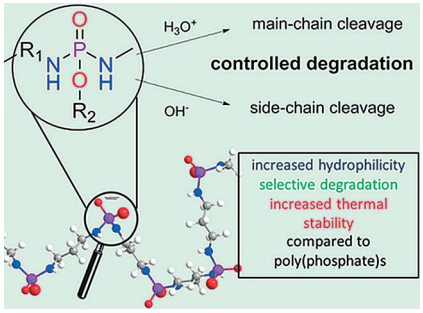
FULL PAPER

Poly(phosphorodiamidate)s have been prepared by ADMET (acyclic diene metathesis) polycondensation. These novel materials with adjustable hydrophilicity represent an alternative to poly(phosphazene)s or poly(phosphoester)s and exhibit a precise degradation profile.



Phosphorus-Containing Polymers

*M. Steinmann, M. Wagner, F. R. Wurm**

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Poly(phosphorodiamidate)s by Olefin Metathesis Polymerization with Precise Degradation