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Macromolecules with Phosphorus Functionalities

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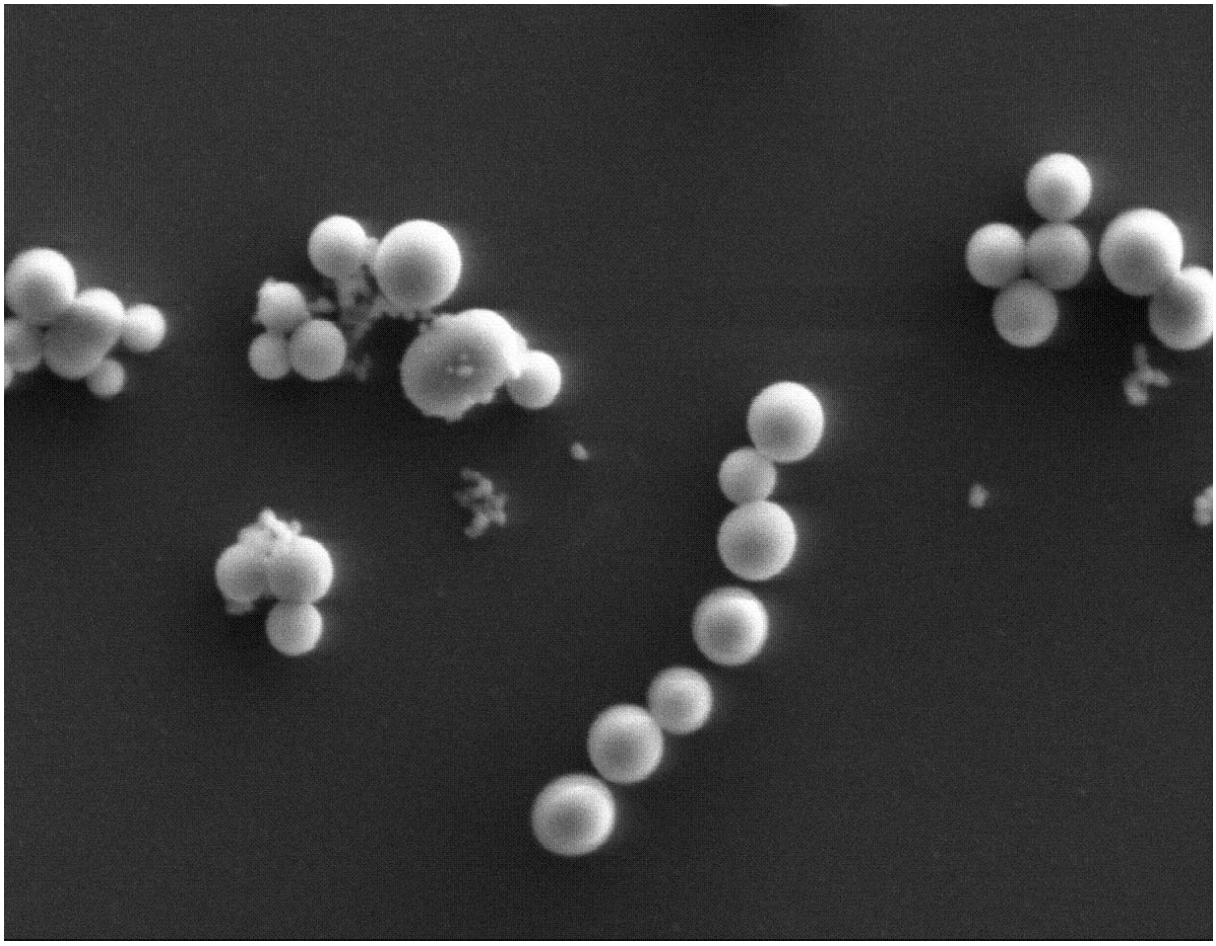
Macromolecules with Phosphorus Functionalities



Calcium carbonate ‘nano pearls’, grown under the influence of polyvinylphosphonic acid.

Amtierender Dekan: Prof. Dr. K.-D. Spindler

1. Gutachter: Prof. Dr. B. Rieger

2. Gutachter: Prof. Dr. Dirk Volkmer

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Contents

Abbreviations

AiBN	2,2-**A**zo-bis-**i**so**b**utyro**n**itrile
AcOAc	**Ac**etyl **ac**etate
ATRP	**A**tom **T**ransfer **R**adical **P**olymerization
b.p.	**B**oiling **p**oint
CMC	**C**ritical **M**icellular **C**oncentration (concentration at which a detergent spontaneously forms micelles)
DBO	**D**i**b**ezoylper**o**xide
DEG	**D**i**e**thylene **g**lycol
DEVP	**D**i**e**thyl**v**inyl **p**hosphonate
DIVP	**D**i**i**sopropyl**v**inyl **p**hosphonate
DMA	**D**i**m**ethyl **a**cetamide
DSC	**D**ifferential **S**canning **C**alorimetry
DSM	**D**igital **S**canning **M**icroscope
DVPO	**D**iphenyl**v**inyl **p**hosphine **o**xide
EA	**E**lemental **A**nalysis
EDX	**E**nergy **D**ispersive **X**-Ray Spectroscopy
EG	**E**thylene **g**lycol
FCS	**F**etal **c**alf **s**erum
FT	**F**ourier **T**ransformation
GM-CFS	**G**ranulocyte-**M**acrophage-**C**olony-**S**timulating **F**actor
GPC	**G**el **p**ermeation **c**hromatography
HS	**H**orse **s**erum
IMDM	**I**scove's **M**odified **D**ulbecco's **M**edium
IR	**I**nfra**r**ed spectroscopy
LDA	**L**ithium **d**iisopropyl**a**mide,
LTSA	**L**ithium-bis-(**t**rimethyl**s**ilyl)-**a**mide
MADIX	**Ma**cromolecular **D**esign via **I**nterchange of **X**anthates
MALDI	**M**atrix-**A**ssisted **L**aser **D**esorption/**I**onization
MEM	**M**inimal **E**ssential **M**edium
Mn	Mean **m**olecular weight of the polymer, **n**umber average
MTT	3-(4,5-Di**m**ethyl**t**hiazol-2-yl)-2,5-diphenyl**t**etrazoliumbromide
mU	**M**illi **u**nit. One milli unit represents the amount of enzyme which converts 1 nmol of acceptor substrates to product per minute.
Mw	Mean **m**olecular weight of the polymer, **w**eight average
n	Degree of polymerization
NMP	**N**itroxide **M**ediated **P**olymerization

NMR	**N**uclear **m**agnetic **r**esonance
Nu	**Nu**cleophile
PBS	**P**hosphate **B**uffer **S**aline
PE	**P**oly**e**thylene
PET	**P**oly**e**thylene **t**erephthalate
PIVP	**P**oly(di**i**sopropyl**v**inyl **p**hosphonate)
PP	**P**oly**p**ropylene
PS	**P**oly**s**tyrene
PVC	**P**oly**v**inyl**c**hloride
PVPA	**P**oly(**v**inyl **p**hosphonic **a**cid)
PVPO	**P**oly(diphenyl**v**inyl **p**hosphine **o**xide)
RAFT	**R**eversible **A**ddition-**F**ragmentation Chain **T**ransfer
rpm	**R**evolutions **p**er **m**inute
SDS	**S**odium **d**oceyl **s**ulfate
SFRP	**S**table **F**ree **R**adical **M**ediated **P**olymerization
TEMPO	2,2,6,6-**Te**tra**m**ethyl**p**iperidyl-1-**O**xyl
TGA	**T**hermo**g**ravimetric **A**nalysis
THF	**T**etra**h**ydro**f**urane
TIBA	**T**ri**i**so**b**utyl**a**luminium
TMEDA	**T**etra**m**ethyl**e**thylene**d**i**a**mine
UV-VIS	**U**ltra**V**iolet-**Vis**ible Spectroscopy
wt%	**w**eigh**t** percent
X	Ethyl -α-(O-ethyl**x**anthyl)propionate
ZIBMT	**Z**entral**i**nstitut für **B**io**m**edizinische **T**echnik

NMR signals

d	**d**oublet
dd	**d**oublet of **d**oublets
t	**t**riplet
m	**m**ultiplet
q	**q**uartet

Instruments

- ***NMR:*** Bruker AMX 500 spectrometer; Bruker AC 400 spectrometer
- ***GPC:*** *Water:* Waters 717 (autosampler), Waters 600E (pump), Waters 410 RI Refractometer, Eluent: LiChrosolv (Merck), colums: 2x Plgel 10μ Mixed-B LS (crosslinked PS, variable pore size, suitable for light scattering), PS Standard
  Chloroform, THF: Agilent 1100 (autosampler), SpectraSystem P2000 (pump), Shodex RI-71 (RI Refractometer), UV detector: Knauer, Eluent: THF p.a. (Merck), columns: Waters Styragel 5 μm: 1000 Å, 10 000 Å, PSS STV 5μm: 100 000 Å, Vorsäule PSS STV, PS Standard
- ***Spin-coating:*** Laurell WS–400A–6TFM/LITE;
  Conditions: 30 s / 4000 rpm, 7 μl/12 mm glass platelets
- ***EDX:*** Zeiss DSM 962, EDX-Detector (EDAX)
- ***EA:*** Elementar Analysensysteme Vario ELAnalysator
- ***MALDI:*** Bruker Daltonics REFLEX III, matrix: DHB (dihydroxy benzoic acid)
- ***IR:*** Bruker IFS 113-V
- ***TGA:*** Mettler Toledo TGA/SGTA 851
- ***CMC:*** dataphysics DCAT/SCAT 31, dynamic contact angle meter and tensiometer
- ***UV-VIS:*** analytikjena Specord 50
- ***dn/dc:*** Carl Zeiss Refraktometer 120709, 589 nm
- ***Light scattering:*** ALV/CGS-8F Laser Goniometer System (24.5°C, 632.8 nm), Software: ALV-500/E/EPP + ALV-60XO
- ***Light microscopy:*** Leica DMRX

1 General Introduction

Human history is often classified into periods named for their respective predominant tool-making materials. According to this nomenclature, we have now entered the age of plastics. Today's world is undeniably dominated by man-made polymers which are not only replacing traditional materials such as wood, glass, ceramics and metals but provide such an array of new functions that they effectively create completely new fields of application of their own. Adaptable within a broad range of physical and chemical properties, lightweight and resistant to corrosion, they are used to meet a limitless number of requirements both in daily-life and high-tech products.

Beside the high volume commodity plastics (polyethylene (PE), polypropylene (PP), polyvinylchloride (PVC), polystyrene (PS) and polyethylene terephthalate (PET)), with their millions of tons of annual production and consumption[1], functional synthetic polymers are increasingly prominent materials due to their unique properties and applications[2,3]. Usually based on simple linear backbones, the specific features of these polymers are determined by the presence of chemical functional groups dissimilar to those of the main chains. The functionality may be introduced as side groups, chain-end (telechelic), in-chain, block or graft structures. Materials with special topologies or architectures like stars, hyperbranched polymers or dendrimers (treelike structures) are also of great interest.

Functional polymers can be prepared either via chemical modification of already defined polymers, or via direct polymerization of functionalized monomers. The first method has the drawback of lacking control over molecular weight and functional group distribution, while the second requires careful adaptation of the polymerization technique to avoid side reactions of the desired functional groups.

1.1 Phosphorus-containing polymers

Phosphorus-containing polymers are found ubiquitarily in nature, from strictly inorganic elemental phosphorus to the core of life itself, DNA and RNA. Synthetic molecules bearing comparable functionalities can therefore easily interact with biological systems. On the other hand, phosphorus, be it in form of phosphanes or phosphates, readily binds to a great variety of metals leading to technical applications ranging from anti-corrosion coatings to finely tuned, highly selective catalysts whose efficacy and stability often depends on phosphorus-containing ligands. Macromolecules containing phosphorus may likewise find applications in these fields, with the added advantage of the polymeric backbone which may act as a scaffold protecting and stabilizing the functional group, an anchoring point for other polymers

(e.g. in coatings where the phosphorus attaches to the metal surface while the polymer chain interacts with the equally polymeric coating), or include other functionalities of its own.

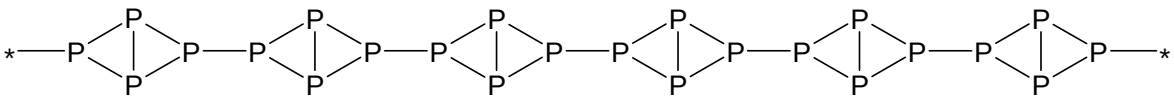


Figure 1: Red phosphorus

With the exception of red phosphorus, a modification of the element composed of linear chains of P_4 tetrahedrons (Figure 1), all other polymers contain other elements, too, so they may be divided into categories depending on whether the phosphorus is part of the main chain or a side group (Figure 2). In the latter cases it may be attached directly to the backbone or separated by a spacer. Special architectures, like dentritic structures, fall in between.

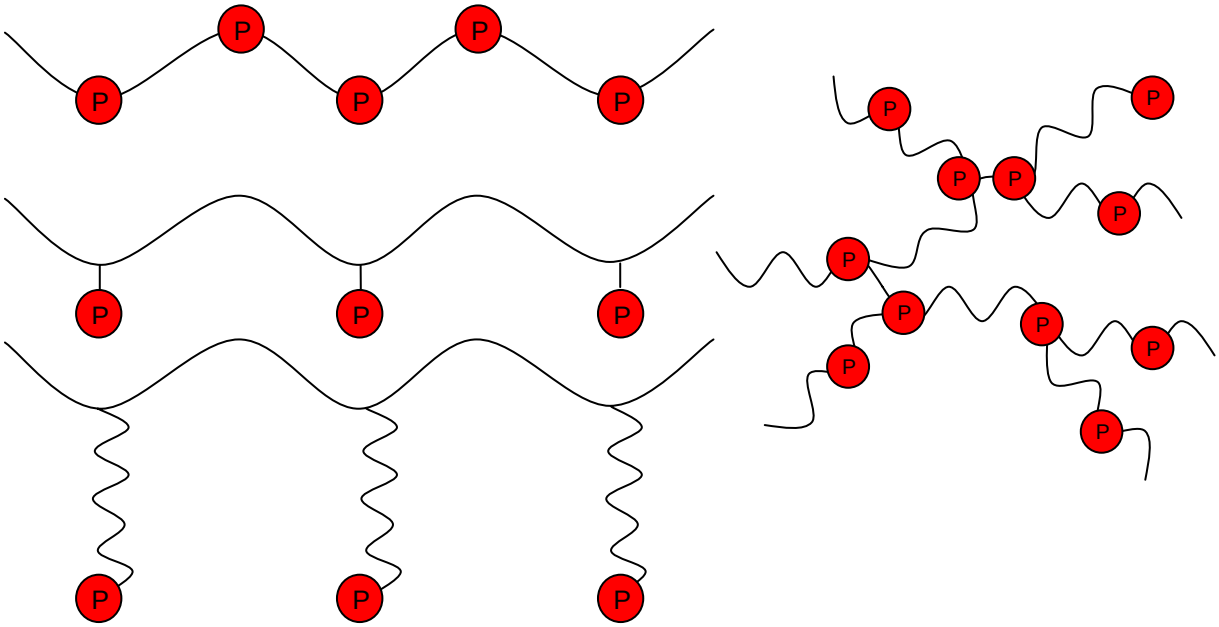


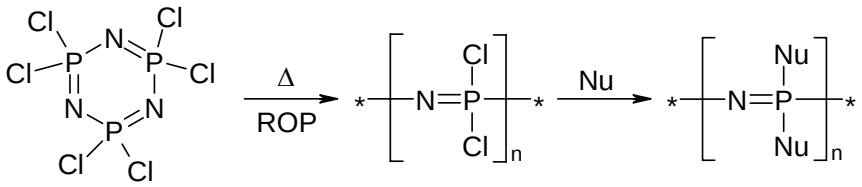
Figure 2: Phosphorus-containing polymers

Some examples of these polymers will now be shortly introduced.

1.1.1 Phosphorus in the main chain

1.1.1.1 Polyphosphazenes

Beside the various naturally occurring molecules, the most important phosphorus-containing polymers are polyphosphazenes. Most commonly synthesized by ring opening polymerization of hexachlorocyclotriphosphazene, they are based on an inorganic phosphorus-nitrogen backbone with variable side groups (Figure 3). Polyphosphazenes are used in many fields of application, from medicine to computer industry.



Nu = OR, NHMe, glucosyl, $(OCH_2CH_2)nOCH_3$, OCH_2CF_3 , OC_6H_4-PPh_2 , NHCH(R)COOEt, etc.

Figure 3: Polyphosphazenes

The widespread use is due to their remarkable features[4]: the polyphosphazene backbone is – despite the alternating double and single bonds – one of the most flexible known, comparable to silicone polymers, which is the main reason for the elasticity of many phosphazene polymers, earning them the denomination of “inorganic rubber”. It is also transparent to light from the near IR to the 220 nm region (UV), making these polymers both extraordinary stable to radiation in the visible and near UV range and interesting for applications as optical and photonic materials. Most polyphosphazenes are stable against hydrolysis, yet by careful choice of side groups such as amino acid esters, glucosyl, glyceryl, or imidazolyl units, they can be configurated to decompose in water to give biologically harmless products. These materials are important in the biomedical field[5]. Furthermore, many polyphosphazenes are fire resistant or fire retardant due to the presence of both phosphorus and nitrogen in the main chain, enabling application as advanced elastomers in aerospace engineering, for instance. Polyphosphazenes with alkyl ether side groups are soluble in and stable to water. They dissolve lithium salts and are promising candidates for the next generation of ion conductors for lithium batteries. Incorporation of acid functionalities in the organic side chains yields polymers that are good proton conductors. Unaffected by oxidation or reduction reactions, resistant to free radicals, fire retardant and with very low methanol diffusion coefficients, they have advantages over other advanced fuel cell membranes. Thus, they are candidates for use in direct methanol fuel cells and possibly in small scale hydrogen-oxygen fuel cells. The presence of transition metals in the side group structure introduces the prospect of macromolecular catalysis.

1.1.1.2 Polyphosphoesters

Polymers with phosphate groups in the main chain (Figure 4) are often proposed as biodegradable materials since the phosphate esters are readily cleaved by hydrolysis[6,7]. Equipped with predetermined breaking points in the polymer structure, such materials are not only environmentally benign but can also be used in drug delivery systems. Microspheres manufactured from these polymers and loaded with pharmaceuticals slowly disintegrate under physiological conditions, releasing a steady dosage of drugs over a prolonged time. Some experiments even indicate suitability as gene therapy vectors[8].

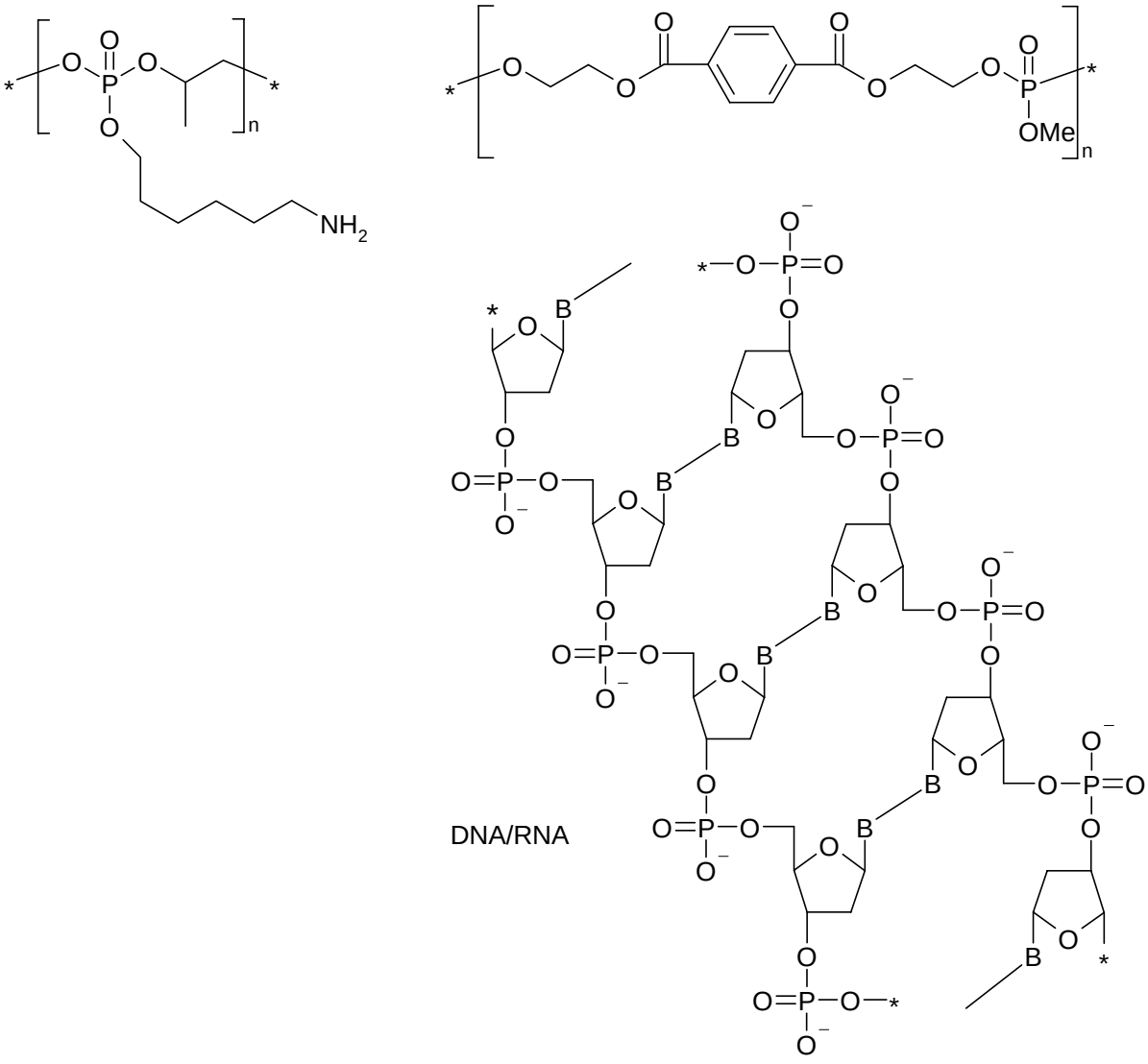


Figure 4: Polyphosphoesters

Last but not least, DNA and RNA are part of this group, as well. While an in-depth discussion of these molecules would go beyond the scope of this work, any application using artificially prepared strands of these polymers – be it for single molecule electronics[9], new vaccines[10] or sensors[11] – can also be considered an application of phosphorus-containing polymers, too.

1.1.2 Phosphorus side groups

Polymers with phosphorus-containing side chains (Figure 5) have been suggested and partly tested for various applications. From medicine[12,13,14] to paper processing[15], from deep oil drilling[16] to fuel cell development[17], a host of potential customers have shown their interest. Different materials have been investigated, but overall the polymers may be divided into two groups: Those with phosphorus bound covalently to carbon atoms (of the main chain), and those where the phosphorus moiety is attached via oxygen, as an ester of a phosphorus acid. Therefore the latter are susceptible to hydrolysis which may split off the pendant phosphorus.

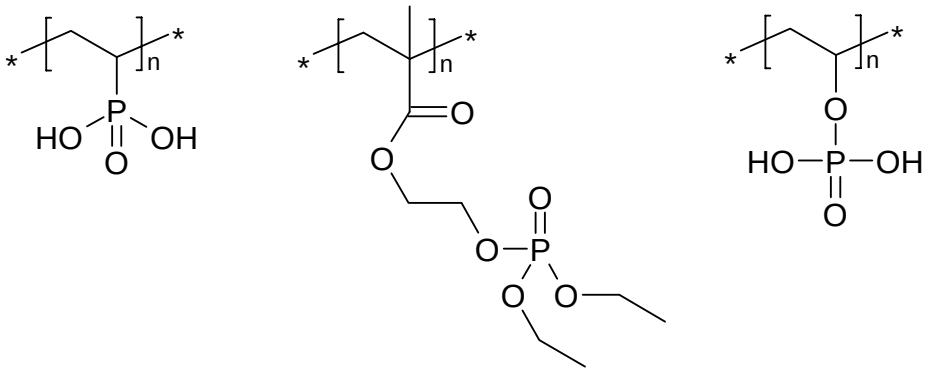


Figure 5: Polymers with phosphorus side chains

Phosphorus(V) moieties have been incorporated into a wide variation of synthetic polymers to improve flame retardancy[18,19,20,21,22]. Acrylates are easily modified by esterification; other methods are copolymerization with various phosphorus functionalized monomers.

Poly(vinyl alcohol) esters of phosphoric acid have been tried both as scale inhibitors, binding heavy metal ions (barium, calcium) before they form insoluble deposits clogging (oil) wells, and to reduce leaching of phosphoric acid from PEM fuel cells.

Poly(vinylphosphonic acid) has been investigated and partially commercialized as binder in bone or dental cements[12,13,14,23].

1.1.3 Phosphorus in dentritic polymers

These polymers, their synthesis and possible applications are described more in detail in chapter 3.

Two different sets of macromolecules are under investigation in this thesis: Linear polymers formed from various vinyl monomers with phosphonate, phosphine oxide and phosphonic acid side groups; and hyperbranched polymers linked via phosphorus atoms.

1.2 References

[1] PlasticsEurope*; An analysis of plastics production, demand and recovery for 2005 in Europe* Published Spring **2007**

[2] A. Akelah, A. Moet, "*Functionalized Polymers and Their Application*", 1st Ed., Chapman and Hall, **1990**.

[3] Fréchet J.M.J.; *Prog. Polym. Sci*.; **2005**; 30; 844-857

[4] Allcock H.R.; *J. Inorg. Organomet. Polym*.; **2006**; 16/4; 277-294

[5] Andrianov A.K.; Svirkin Y.Y.; LeGolvan M.P.; *Biomacromolecules;* **2004;** 5; 1999-2006

[6] Li Q.; Wang J.; Shahani S., Sun D.D.N., Sharma B., Elisseeff J.H., Leong K.W.; *Biomaterials;* **2006**; 27; 1027-1034

[7] Chen D.-P.; Wang J.; ; *Macromolecules;* **2006;** 39; 473-475

[8] Malyshev, A. V., *Phys. Rev. Lett.*; **2007**; 98/9; 096801

[9] Ezziane Z., *Nanotechnology*; **2006;** 17; R27-R39

[10] Glenting J.; Wessel S. *Microbial Cell Factories **;*** **2005**; 4:26

[11] Niemeyer, C.M.; *Nano Today*; **2007**; 2/2; 42-52

[12] Greish Y.E.; Brown P.W.; *Biomaterials*; **2001**; 22; 807-816

[13] Fennel B.; Hill R.G.; Akinmade A.; *Dent. Mater*.; **1998**; 14; 358-364

[14] Jin S.; Gonsalves K.E; *J. Mater. Sci.: Mater. Med.*; **1999**; 10; 363-368

[15] Chen X.; Huang R.; Pelton R.; *Ind. Eng. Chem. Res.*; **2005**; 44; 2078-2085

[16] Davis K.P.; Walker D.R.E.; Woodward G., Smith A.C.; *Patent: EP O 861 846 A2 19980902*; **1998**

[17] Kiefer J.; Uensal O.; Gordon C., Crivello J.; *Patent WO 03074597*; **2003**

[18] Price D. ; Pyrah K.; Hull T.R., Milnes G.J., Ebdon J.R., Hunt B.J., Joseph P.; *Polym. Degrad. Stab.;* **2002;** 77 / 2; 227-233

[19] Price D. ; Pyrah K.; Hull T.R., Milnes G.J., Ebdon J.R., Hunt B.J., Joseph P., Konkel C.S.; *Polym. Degrad. Stab;* **2001;** 74 / 3; 441-447

[20] Ebdon J.R.; Price D.; Hunt B.J., Joseph P., Gao F., Milnes G.J., Cunliffe L.K; *Polymer Polym. Degrad. Stab;* **2000;** 69 / 3; 267-277

[21] Ebdon J.R.; Hunt B.J.; Joseph P., Konkel C.S., Price D., Pyrah K., Hull T.R., Milnes G. J., Hill S. B., Lindsay C. I., McCluskey J., Robinson I.; *Polym. Degrad. Stab;* **2000;** 70 / 3; 425-436

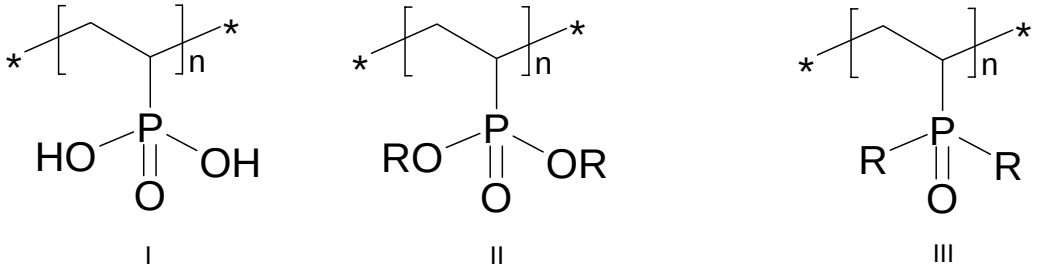
[22] Fried J.R.; *Polymer Science & Technology 2nd ed.;* **2003;** Prentice Hall

[23] Nicholson J.W.; Czarnecka B.; Limaowska-Shaw H.; *J. Oral Rehabil.;* **2003**; 30; 160-164

2 Polymers with Phosphorus Side Chains

2.1 Introduction

Linear poly(vinyl phosphonates), poly(vinylphosphine oxides) and poly(vinylphosphonic acids) are the topic of this chapter (Figure 6).



I II III

Figure 6: Poly(vinylphosphonic acid) (I), poly(vinyl phosphonates) (II), and poly(vinylphosphine oxides) (III)

2.1.1 Overview over existing research

Vinyl phosphonates[1,2] and vinyl phosphine oxides[3] have been known since at least the first half of the 20th century, and polymerization experiments started shortly after[4,5,6]. Yet most of them were unsuccessful. Even up to this date most published works have been restricted mainly to vinylphosphonic acid polymers, copolymers and polymer blends. Usually of poorly defined molecular weight and composition. The underlying reasons for these oversights may be found partly in the fact that the polymerization of the respective monomers is by no means trivial. Phosphorus compounds are used as stabilizers to protect other polymers[7,8] but the beneficial effect becomes detrimental when it comes to polymerizing the phosphorus compounds themselves. Radical polymerization of monomers bearing phosphorus in direct vicinity of a vinyl group produces only low yields of oligomeric materials containing many byproducts. Poly(vinylphosphonic acid) seems to be, to some extent, the exception to the rule. Produced either by radical polymerization and subsequent hydrolysis of vinyl phosphonous acid dichloride[9] or directly from vinyl phosphonic acid[10], it is the only representative of the group that is so far commercially available. Unsurprisingly, most of the literature exploring applications is confined to this polymer.

Another important point is that many investigators were not interested in the polymers per se. Polymers were used as received; or prepared, processed and tested for specific properties only, be it cell proliferation in a hydrogel[11] or the durability of a cement[13,12]. Generally speaking, a more profound study from a polymer chemist's point of view is, with the exception of some early, quite unsuccessful works, so far lacking.

Possible applications for such polymers are plenty. Whether in medicine or fuel cell development, the combination of a stable carbon backbone and phosphonic acid or ester groups could be of relevance for many cutting edge technologies.

Vinyl phosphonates and vinyl phosphine oxides have been treated with a wide variety of both radical and anionic initiators. Many of these experiments were done in the sixties to seventies when the materials were still new and the field of polymers in general burgeoning. Literature on them reached a first boom[3,4,5,6,13,14,15,16,17,18,19,20,21,22]. Copolymerization attempts were also done in abundance[4,14,15,16,19,21]. Yet polymer analysis was still in its early stages and what data is given about molecular weights and polymer composition indicates oligomers with less then ten repeating units and very ill-defined copolymers. Especially the portion of phosphorus compound in the copolymers is usually only a fraction of the portion in the feed.

After these first unsatisfying results, the uncooperative monomers were abandoned for a few decades. Vinylphosphonic acid next garnered interest as a polyelectrolyte with possible applications in the medical field[23,24,25,26,27,28,29], in anti-corrosion coatings[30] and for interpolymer complexation[31,32]. Polymer analysis still remains curiously vague. As a commercially available polymer, the polyacid is often used as received, with no further information given, neither of the educt nor the products.

Newer literature on poly(vinyl phosphonates) or –(phosphine oxides) are few and far between. Homopolymerizations were discarded in favor of copolymerizations with commodity polymers, be it to improve flame retardancy[33] or for more sophisticated applications like fuel cell membranes[34]. Still, the same problems are reported as for the pioneer works, namely a distinctively low incorporation rate of the phosphorus-containing monomer into the copolymer (e.g. 15 % incorporation for a 1:1 monomer feed).

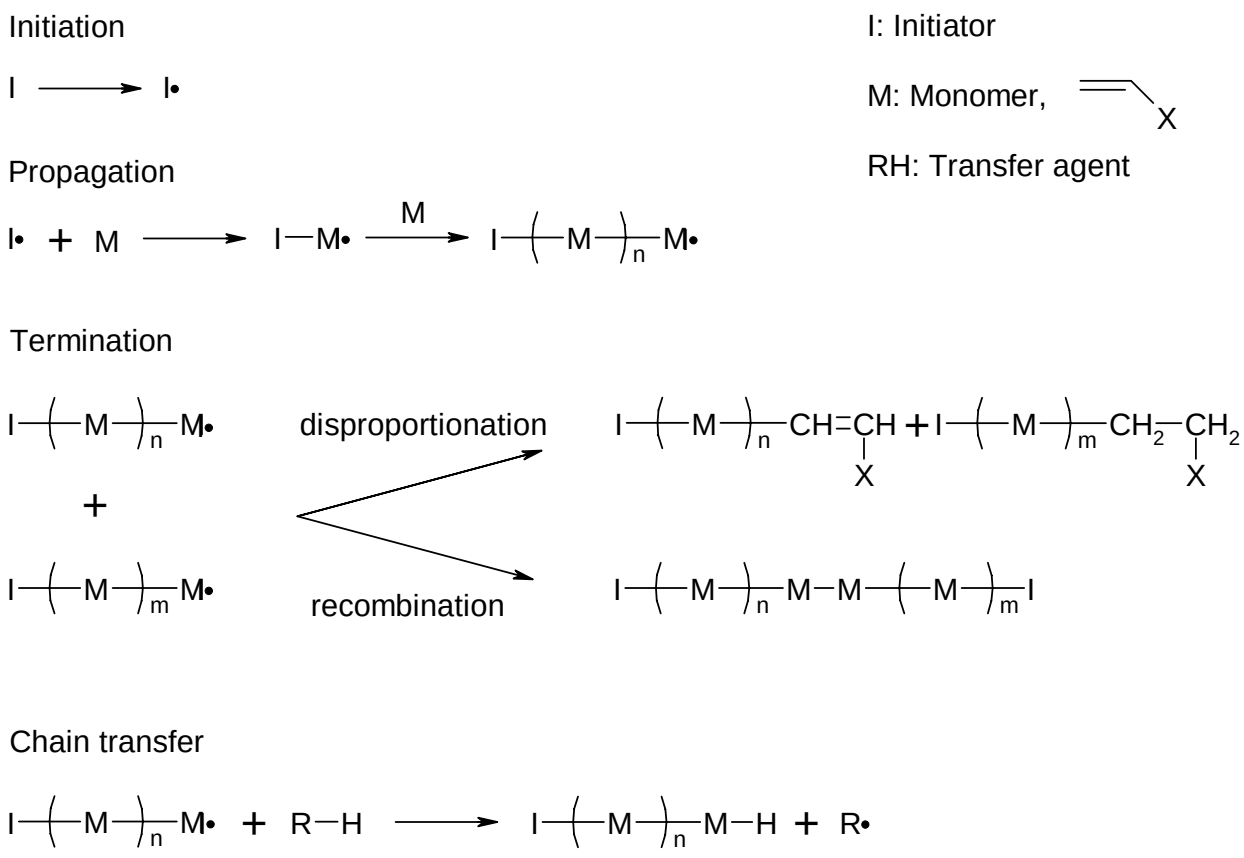
2.1.2 Polymerization techniques

Analogous to double bonds with an adjacent C=O group, the studied monomers are acceptor substituted vinyl compounds which may, for instance, undergo Michael additions[35, 36]. Due to this similarity with acrylates, in this work polymerization techniques were screened which are known to yield polyacrylates, namely radical, anionic and catalytic polymerization.

2.1.2.1 Radical polymerization[37]

The oldest and simplest polymerization technique is radical polymerization where both the initiating species and the propagating reactive center of the growing polymer chain are free radicals. Typical initiators are substances that are split homolytically into radicals with relative ease, either by the influence of elevated temperatures, electromagnetic radiation or a chemical reaction. Thermolysis is feasible for organic peroxides or azo compounds, for instance. Photolysis under UV light can occur with azo compounds, metal iodides or metal alkyls. Ionizing radiation can also be used to create free electrons, which then react with the monomer to produce radicals. Redox reactions, often involving metal ions such as the reaction of Fe^{2+} with hydrogen peroxide, are also possible radical sources.

Scheme 1



The radical produced in the initiating step is added to a monomer, thereby creating a new radical species, and by multiple repetitions of this propagation step a polymer chain is formed (Scheme 1). Propagation is fast compared to the initiation reactions, so new chains are started throughout the reaction time as long as there is initiator available. The chain is terminated either by the recombination of two radicals or by disproportionation. Chain transfer, the addition of hydrogen or any other atom to the radical at the end of the growing polymer, may also terminate the growth of an individual polymer chain. As the fragment left by this abstraction is again a radical that may initiate a new chain, the kinetic chain length – the rate of propagation to initiation – does not change, yet the mean molecular weight of the polymer decreases. This feature may be sought for or a nuisance, depending on the prospective application and desirable properties.

Radical polymerizations are the backbone of polymer industry. A wide variety of olefin monomers can be polymerized, initiation relies on easily available substances and the running system has a high tolerance for impurities. Practical problems like the increasing viscosity during the polymerization which leads to incomplete conversion, and removal of the substantial amount of heat evolving, are known for decades and led to the respective engineering solutions.

A major drawback of the radical polymerization is the broad molecular weight distribution due to uncontrolled termination and chain transfer reactions. Depending on the termination process, the theoretical minimum (without chain transfer) of Mw/Mn is 1.5 (for recombination) and 2 (for disproportionation), respectively[38]. For acrylates at elevated temperatures, disproportionation is the main termination process.

Another disadvantage is the lack of structural control. Atactic material is usually formed, except for low temperatures when syndiotactic sequences may prevail, due to their lower sterical hindrance. Branching may occur when a radical is transferred to another chain by abstraction of a mid-chain hydrogen.

Copolymers are limited to polymerizing a mixture of two (or more) monomers, resulting in statistical, alternating or somewhere in-between structures, depending on the respective monomer pair. Block copolymers can not be synthesized by this method, but graft polymers are possible if a finished polymer is irradiated to produce radicals along the chain and another monomer grown onto the chains.

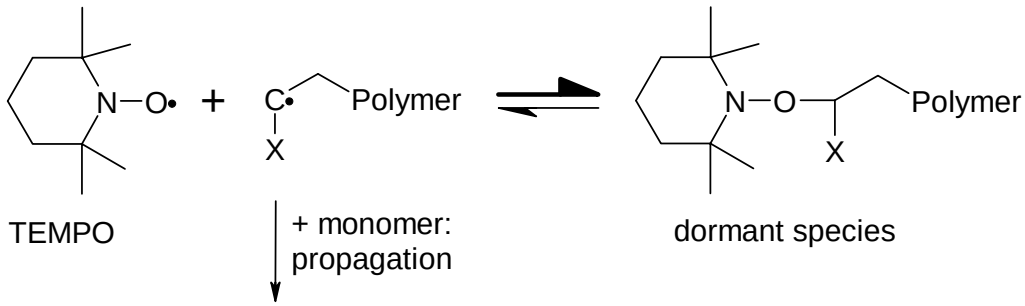
2.1.2.2 Controlled radical polymerization

At the end of the twentieth century, several new methods were discovered which allowed the development of living polymerizations using free radical chemistry[39]. Among the most versatile ones of these new techniques are the nitroxide mediated polymerization (NMP, also called stable free radical mediated polymerization (SFRP)), atom transfer radical polymerization (ATRP) and reversible addition-fragmentation chain transfer (RAFT) polymerization.

The common feature of these polymerization methods is the introduction of a dormant state, a reversibly capped radical at the end of the growing chains, thereby limiting the propagating radical concentration to levels that allow controlled polymerization. Dormant chains and active chains (those with a radical capable of adding more monomer) form an equilibrium that is designed to heavily favor the dormant state. Thus, termination is limited by the low concentration of active radicals.

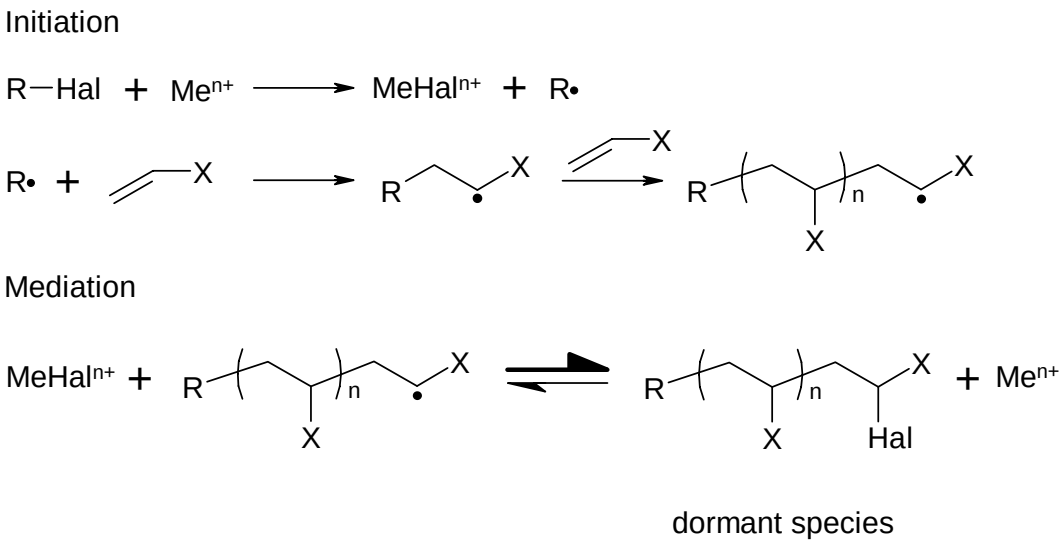
NMP[40,41,42,] uses a nitroxide-based radical scavenger, usually the stable free radical 2,2,6,6-tetramethylpiperidyl-1-oxyl (TEMPO) or derivatives thereof, to reversibly terminate the growing chains (Scheme 2). By limiting the concentration of the active species, the polymerization rate is curbed as well, leading to low yields even after prolonged reaction times. The addition of acetyl acetate accelerates the reaction distinctly.

Scheme 2



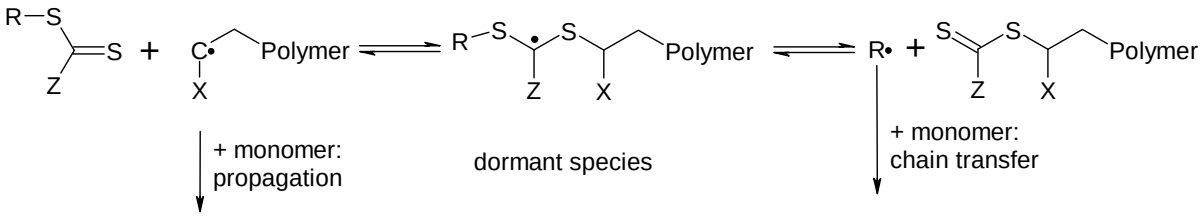
ATRP[43] involves the initiation of a free radical polymerization by a halogenated organic species in the presence of a metal halide (Scheme 3). In an oxidative addition the metal abstracts a halide from the organohalide, creating a radical that then starts free radical polymerization. After initiation and propagation, the radical on the active chain terminus is reversibly terminated (with the halide) by reacting with the catalyst (reductive elimination). Thus, the redox process gives rise to an equilibrium between dormant (polymer-halide) and active (polymer-radical) chains. The generally low solubility of the metal halides limits the availability of the catalyst. This may be rectified by the addition of a ligand, but the improved solubility of the catalyst also complicates subsequent catalyst removal from the polymer product.

Scheme 3



RAFT and a mechanistically identical process termed Macromolecular Design via Interchange of Xanthates (MADIX), invented by Rhodia[44,45], is a degenerative chain transfer process. Most RAFT agents contain thiocarbonyl thio groups, whereas MADIX refers specifically to the use of xanthates, both of which react with the radicals and form stabilized intermediates (Scheme 4).

Scheme 4



Z: OR' = xanthate
any = thiocarbonyl thio

2.1.2.3 Emulsion polymerization

A special type of radical polymerization is the emulsion polymerization in which the monomer is dispersed or emulgated with the help of surfactants in an aqueous solution of the water-soluble initiator. It should not be confused with suspension polymerization which is basically a bulk polymerization finely dispersed in water, and where the initiator is soluble in the monomer only, not in the aqueous medium. Persulfates are usually used as initiators for emulsion polymerizations.

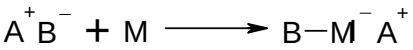
Advantages of emulsion polymerization include an excellent heat conductor as the continuous phase which prevents the formation of hotspots where excess heat would otherwise lead to gelation, side reactions, or even explosion. It also allows a higher overall temperature, so that high molecular weight polymers may be produced at fast polymerization rates. By contrast, in bulk and solution free radical polymerization, there is a tradeoff between molecular weight and polymerization rate. Viscosity stays the same during the reaction, allowing for complete conversion. The resulting latex is furthermore suitable for many applications without further processing. If a dry polymer is required, on the other hand, an energy-intensive process is necessary to remove the water. Surfactant residues and a high rate of chain transfer to polymer (due to the high conversion) may also cause problems.

2.1.2.4 Anionic Polymerization

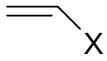
Anionic polymerizations (Scheme 5) are initiated either by a strong base and anion, such as an alkali amide, or an organometallic compound, such as lithiumalkyles or a Grignard reagent. To form a sufficiently stabilized anion, monomers with electronegative substituents are necessary. Formally, many anionic polymerizations have no termination step, yet the anions are very sensitive to traces of impurities. Oxygen, carbon dioxide or any kind of protic media are very efficient termination agents due to the high reactivity of the propagating ions. In an ideal system, nevertheless, the terminal anion persists even after complete consumption of the monomer for an indefinite period of time, as neither recombination nor disproportionation are feasible reactions for an anionic species. Therefore anionic polymerizations are also termed ‘living polymerizations’. The living character of the anion is especially useful to create block copolymers, either by addition of a second monomer to the living polymer or by coupling of living chain ends.

Scheme 5

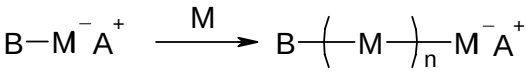
Initiation



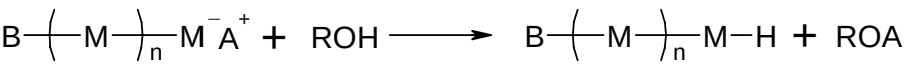
AB: Initiator

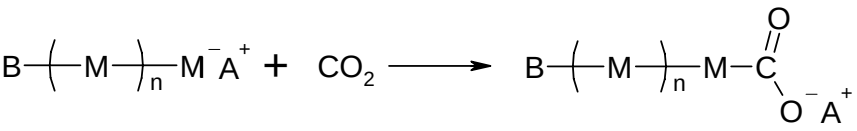
M: Monomer, 

Propagation

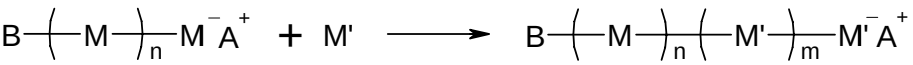


Termination





Block Copolymerization



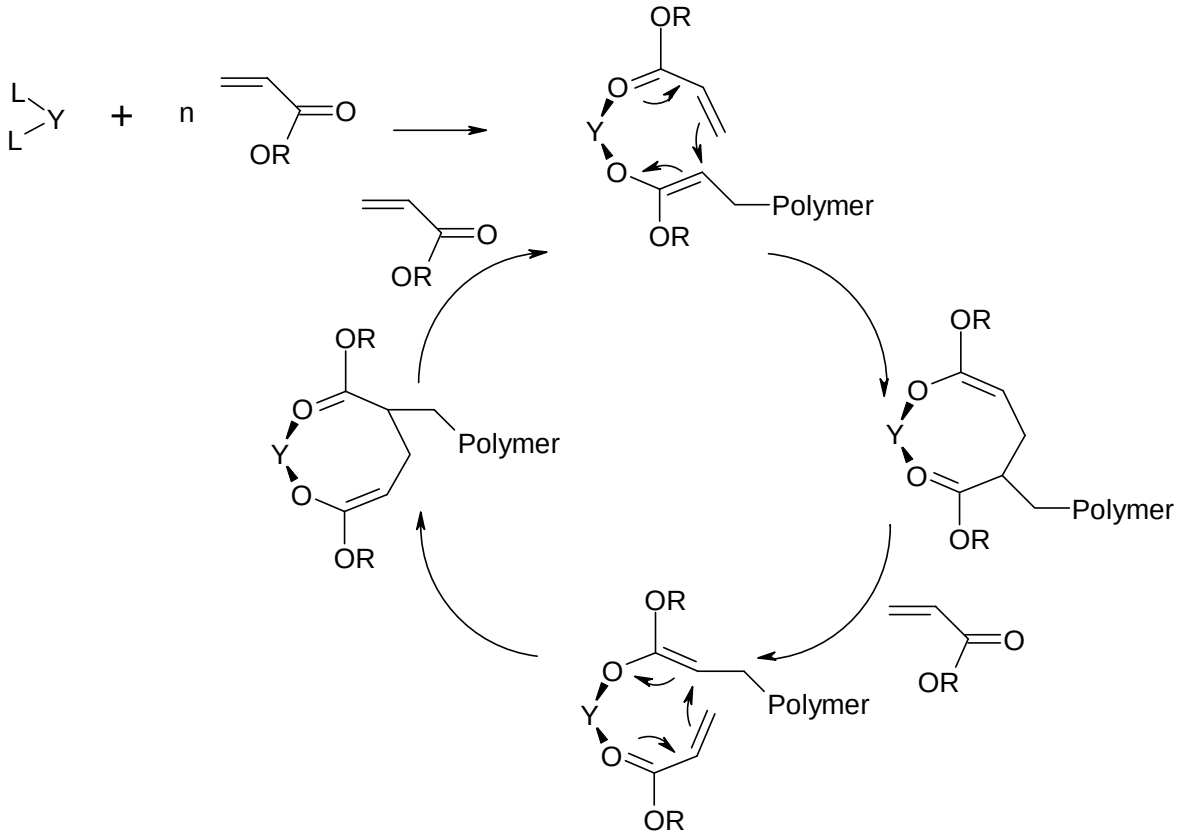
2.1.2.5 Catalytic polymerization[46,47]

A host of transition metal polymerization catalysts are known. Even for polar monomers like MMA, which present a certain challenge as they may bind or even react with the metal center, thereby disabling the catalyst, several possibilities do exist.

Of special interest for this work are the following systems: Lanthanide catalysts, cationic zirconocenes, and palladium catalysts, the latter especially for poly(ethylene)-acrylate copolymerizations.

Lanthanide catalysts, mainly lanthanocenes but also bulky alkyllanthanides, were developed by the group of Yasuda[48,49,50,51]. Both isotactic and syndiotactic polymers can be produced, depending on the catalyst used. Copolymers with ethylene have also been reported.

Scheme 6



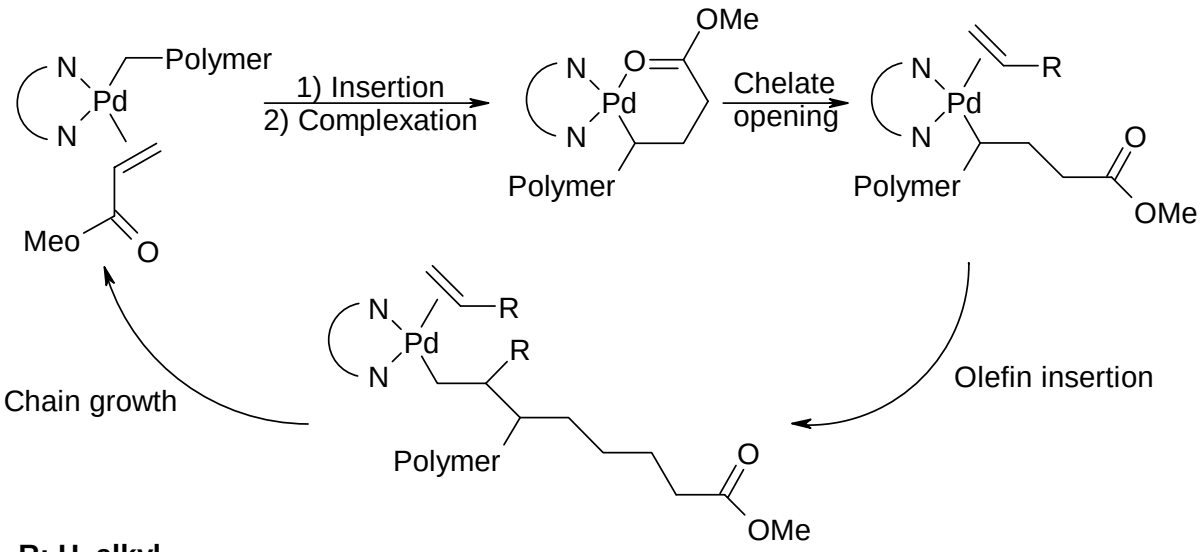
Mechanism (see Scheme 6): Depending on the active catalyst species the initiation step may vary; complexation of the monomer via the carbonyl functionality and subsequent formation of a metal-enolate adduct, are nevertheless the crucial points. After addition of the next monomer, an eight-membered ring intermediate is then formed, stabilizing the enol chain end and allowing monomer enchainment. During chain propagation, the chain end binds the lanthanide metal centre in enol form, while the penultimate MMA unit is complexed at its carbonyl group. New monomer units coordinate to the metal and open the ring, which is

recreated by an intramolecular Michael reaction between the enolate and the coordinated monomer.

For cationic zirconocenes[52,53] a similar mechanism was proposed. As the propagation step is analogous to that proposed for the group transfer polymerization of acrylates initiated by enol silanes[54], this polymerization reaction is sometimes termed the coordination group-transfer polymerization, yet this term is not used consequently in literature.

Palladium diimine catalysts, mainly introduced by Brookhard's group[55], are known for the copolymerization of polar monomers (e.g. MMA) with ethylene and α-olefins. Compared to the homopolymerization of the unpolar monomers, catalyst activity drops dramatically after the addition of the polar monomer. The resultant polymers are highly branched and amorphous for ethylene copolymers, with the acrylate incorporated predominately at the ends of branches. Long chain α-olefins as monomers result in more linear systems and a higher incorporation of MMA. This is caused by formation of a stable chelate complex after incorporation of one MMA unit (see Scheme 7). The effect is more pronounced for ethylene than for the higher α-olefins, as the difference in coordination energy is smaller between α-olefins and MMA than between ethylene and MMA, and the rates of olefin insertion is slower for the α-olefins. Thus, a less pronounced concurrence between propagation and chelation exists with α-olefins than with ethylene, producing the results mentioned above.

Scheme 7



R: H, alkyl

2.2 Results and Discussion

The synthesis of new functional polymers usually starts with the synthesis of the respective monomers, as they are not yet readily available. While vinylphosphonic acid is commercially available, vinyl phosphonates[1,1] and vinyl phosphine oxides have to be prepared prior to the polymerization. The reaction of dibromoethane with trialkyl phosphites in an Arbuzov reaction, followed by elimination of hydrogen bromide in the presence of a base, is a facile way to prepare vinyl phosphonates if R is at least an ethyl group. Dimethylvinyl phosphonate cannot be synthesized this way, due to interfering side reactions catalyzed by methyl bromide. Vinylphosphine oxides may be prepared analogously if a phosphinite is used in the Arbuzov reaction instead of the phosphite[56]. Preferable, at least for phenyl-substituted vinylphosphine oxides, is another synthetic route: the respective phosphine is prepared first and then oxidized with hydrogen peroxide.

2.2.1 General polymerization results

To gain a thorough overview of the polymerization behavior of the phosphorus-bearing monomers, all three major fields of initiation were tested: radical, ionic and catalytic. Radically induced polymerization, being the most variable technique, was further divided into thermally induced radical formation (‘radical polymerization’), controlled radical polymerization using the nitroxide- and xanthate-mediated radicals, UV radiation photolysis, and, as a special case of thermically induced radical polymerization, emulsion polymerization. Catalytic polymerization was attempted using three different metallocene catalysts, known for activity towards polar monomers. These experiments yielded no polymers at all and were abandoned after a few trials. The same was true when a palladium catalyst was used. Lanthanide catalysts, provided by Dr. Rabe (Munich), on the other hand, produced low molecular weight polymers.

Since the conversion of the monomers and the formation of byproducts are easily detectable, ^{31}P NMR was used as the method of choice to monitor the progress of the reaction.

Characterization of the resulting polymers was less straightforward. To identify the mean molecular weight, GPC and light scattering methods were used.

Gel permeation chromatography (GPC) using standard procedures greatly underestimated the molecular mass of the phosphorus polymers, routinely reporting masses lower than the molecular mass of the monomer, probably due to interactions with the column material. Even under the most optimized conditions (mobile phase: dimethyl acetamide (DMA), T: 80°C), the mean molecular weight Mw found by GPC was still only half of the mass reported by light scattering, which in turn was in close accordance to the values expected from the monomer to initiator ratio, for anionically prepared polymers.

Therefore polymer chain length was mainly analyzed *via* matrix assisted laser desorption ionization (MALDI) mass spectroscopy. Despite the fact that absolute values for mean molecular weight and polydispersity can not be obtained by this method, it nevertheless has the advantage of yielding chain length distributions for comparison of different polymerization techniques and data for endgroup analysis, simultaneously. As the actual weight of each chain is determinable by MALDI analysis, different endgroups are easily identified by their respective weight.

2.2.2 Radical polymerization

Examples for polymerization initiated via thermically induced radical formation ('radical polymerization') can be found in literature, but for the best of our knowledge, controlled radical polymerization using the nitroxide- and xanthate-mediated radicals, UV radiation photolysis, and, as a special case of thermically induced radical polymerization, emulsion polymerization have never been used for the homopolymerization of such monomers.

2.2.2.1 Radical polymerization

Radical polymerization was performed both in bulk and in solution. Both peroxide (DBO) and azo compounds (AiBN) were used as initiators. The yield was generally low, about 10-15 %, of a brown, resinous polymer of low molecular weight (degree of polymerization (n): 3-7) and showing many byproducts of partial decomposition. Results in solution were comparable to those of the bulk experiments. DVPO yielded slightly higher degrees of polymerization (3-12, compared to 3-7 for DIVP), but stayed in the oligomeric realm.

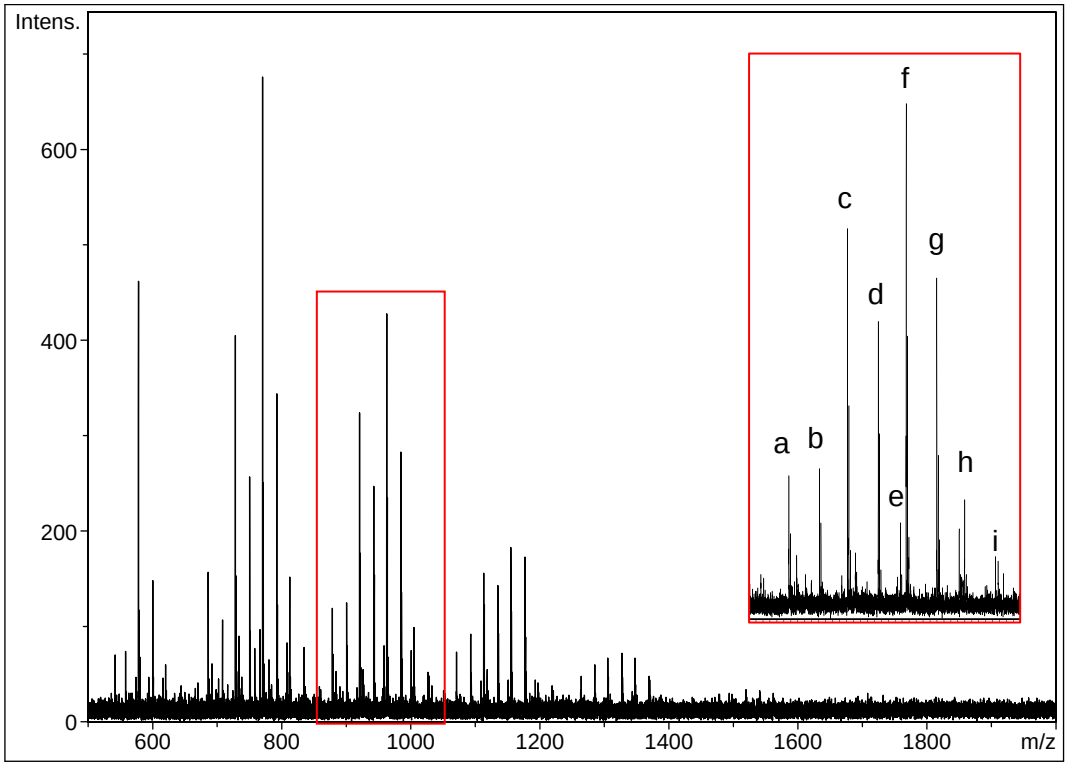
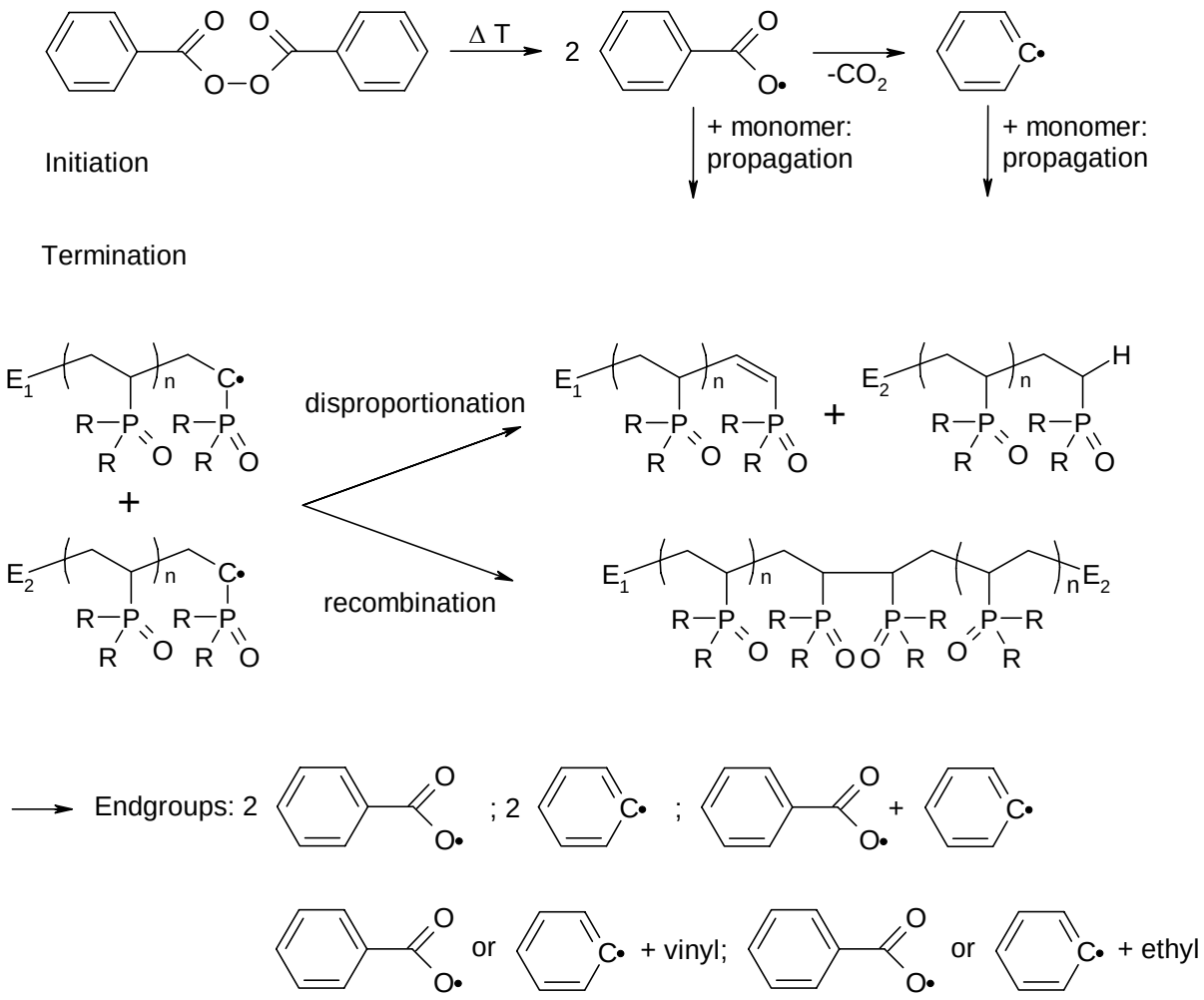


Figure 7: MALDI spectrum of PML 1, radical polymerization of DIVP, initiator: DBO.

As can be seen in the MALDI spectrum (Figure 7, Figure 9), for each distinct chain length a set of peaks occurred, corresponding to the different end groups resulting from the various initiation and termination reactions possible for radical polymerizations. Scheme 8 gives an overview over the expected end groups and their respective formation. Further species can be expected due to side reactions.

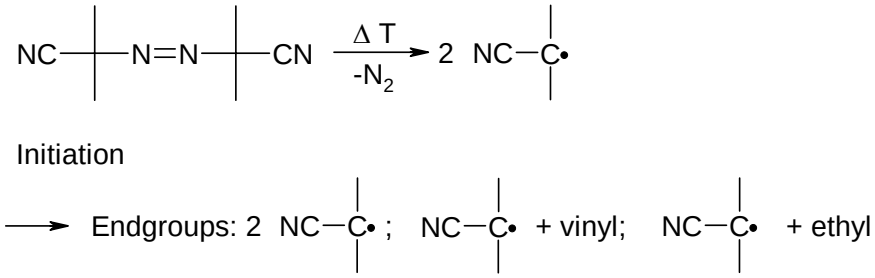
Scheme 8



On closer examination, most of these possible end groups can indeed be seen in the spectrum. The peaks highlighted in Figure 7 refer to the following oligomers: a: tetramer with one benzoyl and one vinyl/ethyl group (double peak with ∆m: 1); c: tetramer with two phenyl groups; e: tetramer with both a phenyl and a benzoyl group; g: tetramer with two benzoyl groups. Main peak f is a pentamer without initiator-related end groups – a product of side reactions, see 2.2.2.6; the other peaks also refer to side products.

For AiBN the initiation reaction is less complicated, resulting in a narrower variation of end groups (Scheme 9) and accordingly a less complicated MALDI spectrum (Figure 8). Sets of peaks occur nevertheless, due to variable termination reactions and/or side reactions. Again the main peaks are oligomers without end groups, the minor peaks a contain two isobutyronitrile groups, the rest are side products.

Scheme 9



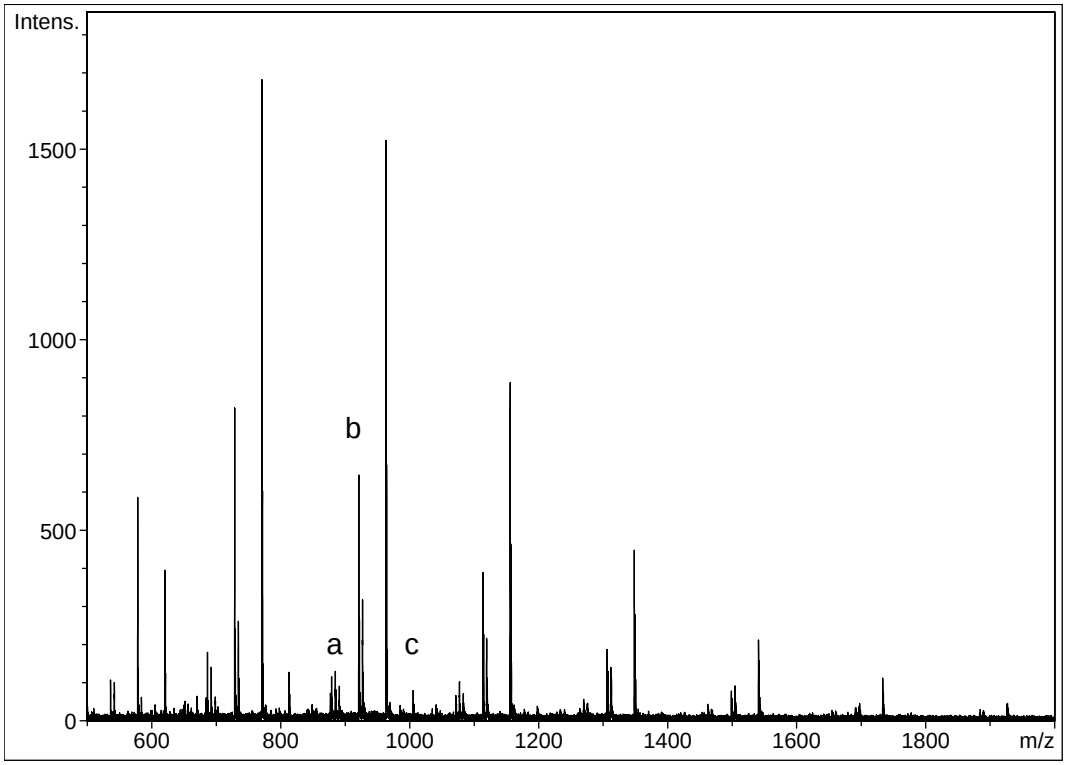


Figure 8: MALDI spectrum of PML 1R1, radical polymerization of DIVP, initiator: AiBN

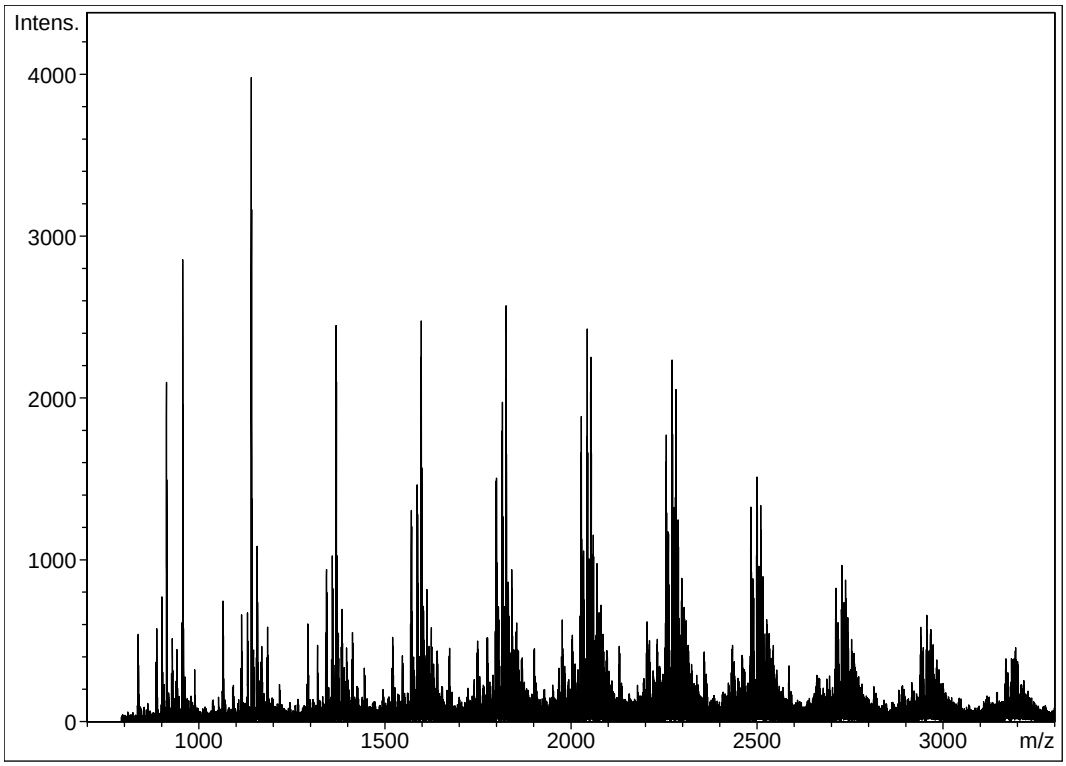


Figure 9: MALDI spectrum of PMLO 1, radical polymerization of DVPO, initiator: DBO

DVPO, most likely due to the phenyl groups stabilizing radicals on the adjacent phosphorus, shows a higher propensity for side reactions and consequently more complicated MALDI spectra (Figure 9).

Good results in radical polymerization were obtained with vinylphosphonic acid in ethylacetate, initiator: AiBN, as described by BASF.

2.2.2.2 Controlled radical polymerization

Controlled radical polymerization was performed solely in solution. Both NMP and MADIX were used.

The simplest system, composed of DBO and TEMPO, brought only negligible yields (1% after 72 h) of very low molecular weight polymers plus some decomposition byproducts.

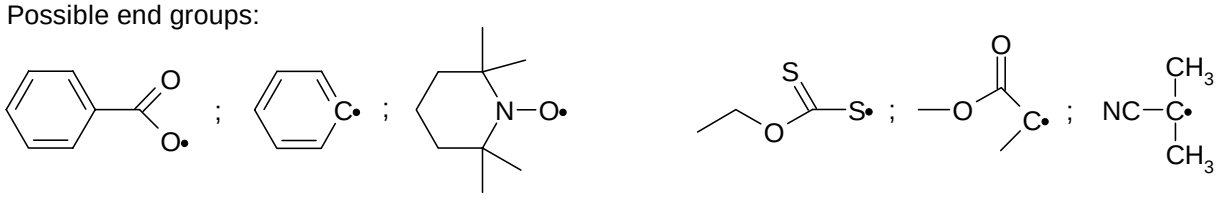
Adding a few drops of acetyl acetate sped up the reaction considerably, resulting in a 30 % yield after 24 h. Chain length increased, but remained in the area seen for other radical polymerizations.

Comparable results were obtained for the AiBN / xanthate system.

Due to the many species involved (Scheme 10), the MALDI spectra of polymers (see Figure 10 and Figure 11) produced by controlled radical polymerization, are more complicated than those for the free radical polymerization discussed in 2.2.2.1.

Scheme 10

Possible end groups:



NMP MADIX

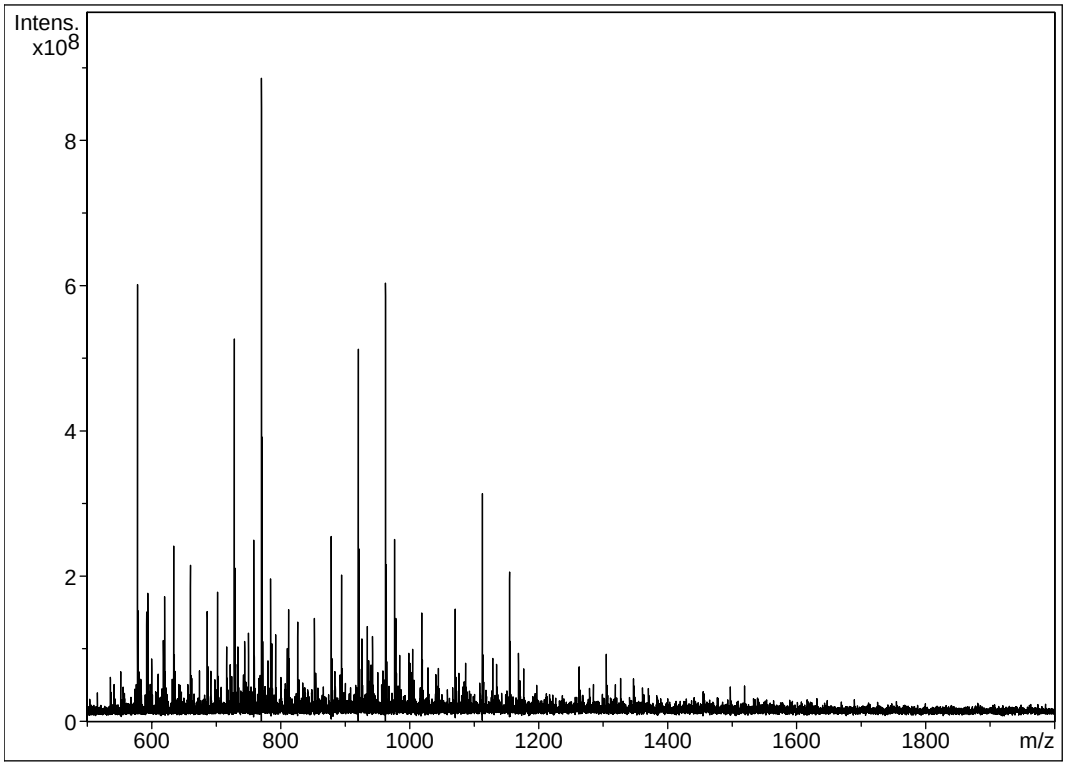


Figure 10: MALDI spectrum of PML 10, controlled radical polymerization of DIVP, initiator: DBO/TEMPO

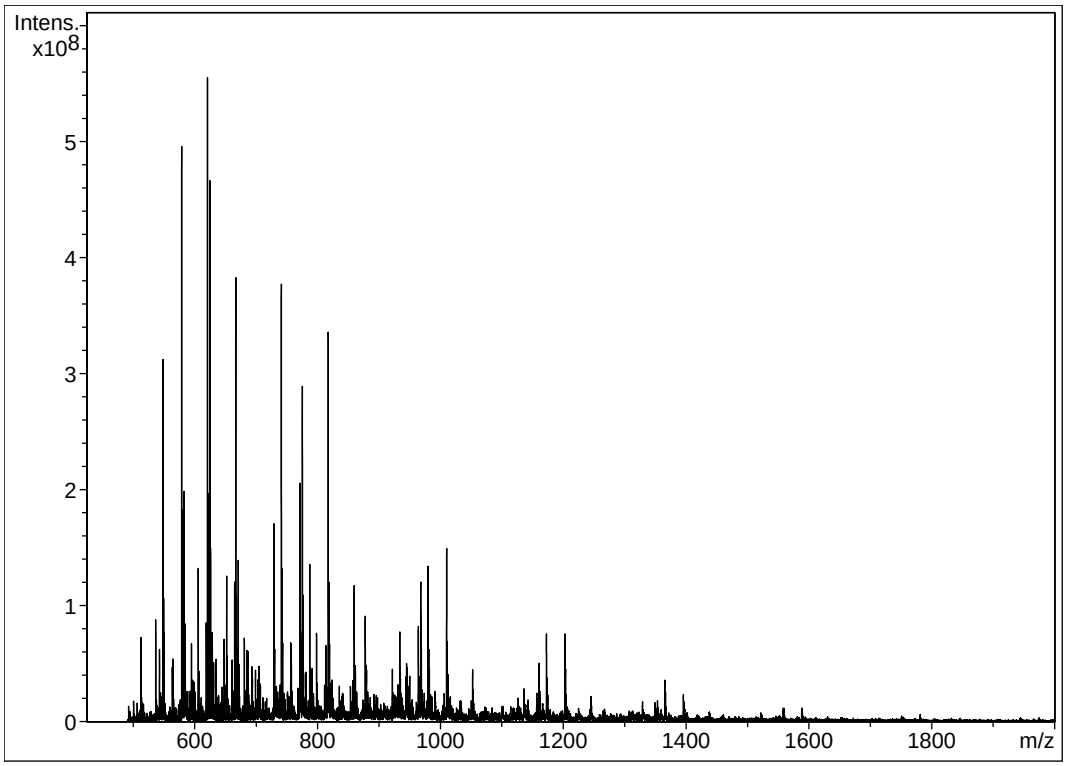


Figure 11: MALDI spectrum of PML 2R1, controlled radical polymerization of DIVP, initiator: AiBN/Xanthate

2.2.2.3 UV-Induced Polymerization

No autopolymerization could be seen under UV light in the presence of a sensibilisator (benzoephenone). Photolysis of AiBN brought no difference compared to the results of thermically induced radical polymerizations, except for an increase in side reactions yielding low molecular weight side products (Figure 12).

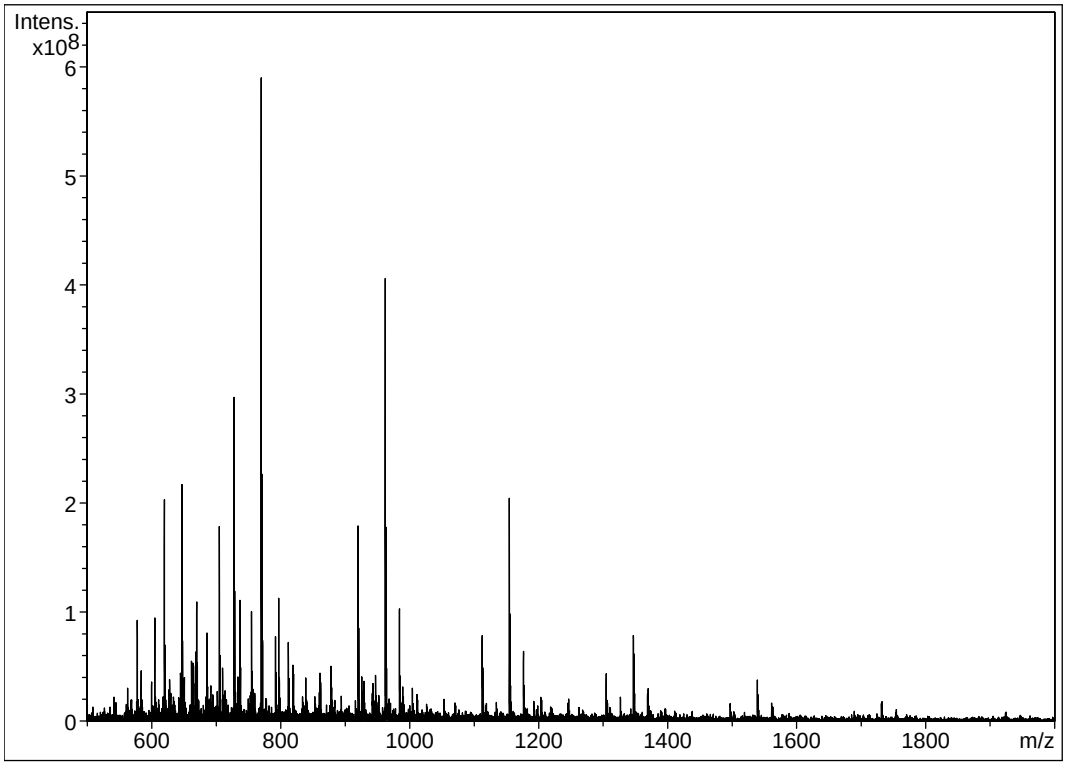


Figure 12: MALDI spectrum of PUML 8, radical polymerization of DIVP, initiator: AiBN + UV-irradiation

2.2.2.4 Emulsion Polymerization

Products typical for radical polymerizations were formed. Again DVPO (Figure 14) yielded higher degrees of polymerization than DIVP (Figure 13), but stayed in the oligomeric realm.

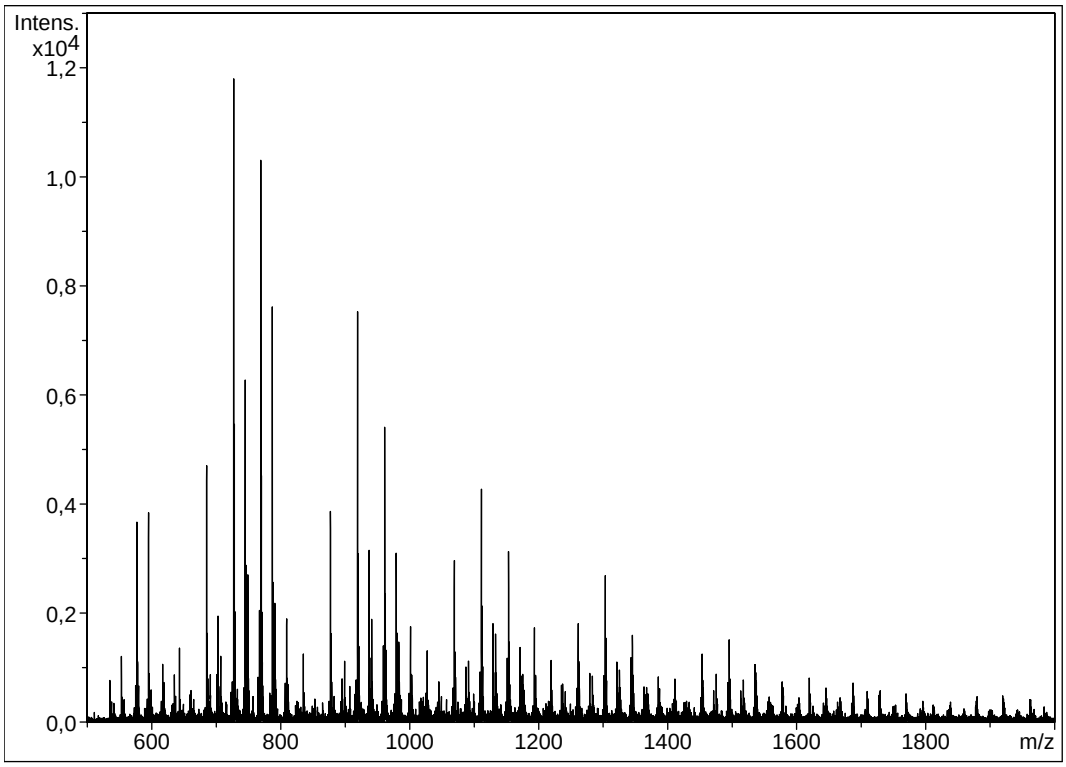


Figure 13: MALDI spectrum of PWML 1, emulsion polymerization of DIVP, initiator: $K_2S_2O_8$

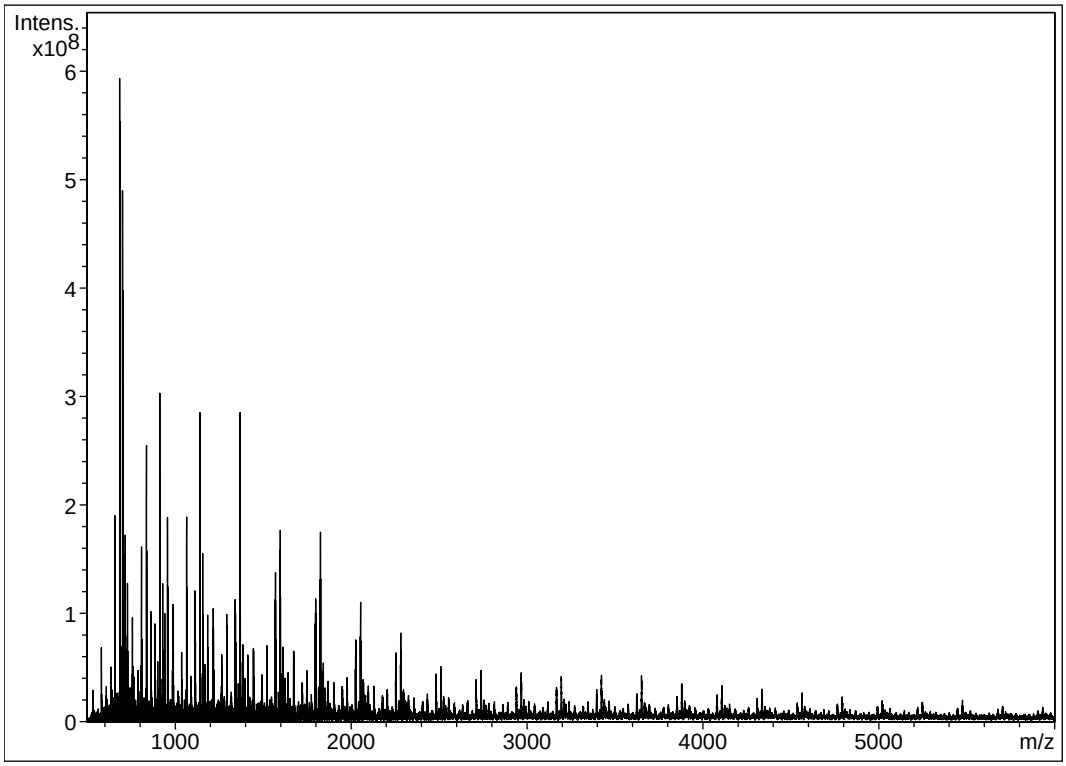


Figure 14: MALDI spectrum of PWML 9, emulsion polymerization of DVPO, initiator: $K_2S_2O_8$

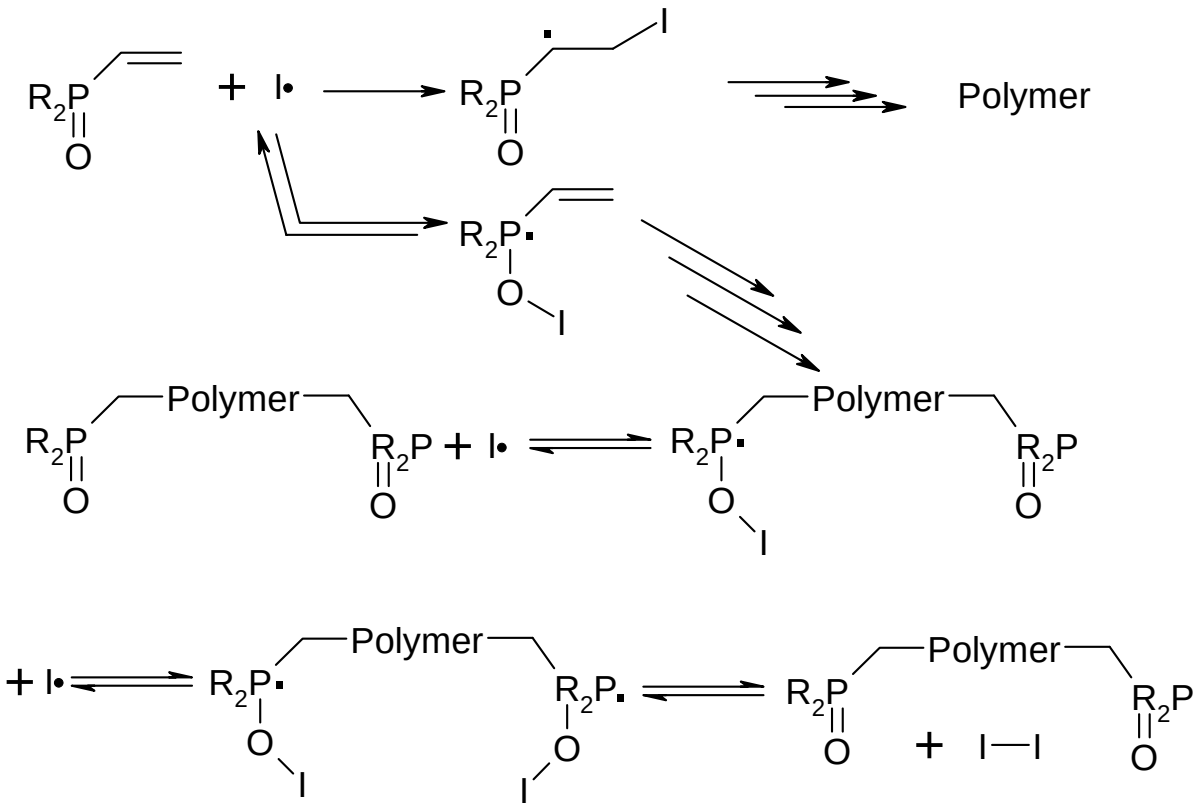
2.2.2.5 Radical copolymerization

Styrene, MMA, butylacrylate, and dimethyl maleate were used in experiments to produce co- and terpolymers containing phosphorus monomers by radical means. All copolymerizations were meant to generate random copolymers. While dimethyl maleate produced no polymers at all, the other comonomers formed mainly homopolymers – copolymers in case of the attempted terpolymer – with little or no conversion of the vinyl phosphonates and vinyl phosphine oxides. The technique used had no significant influence on the polymerization outcome. For a comprehensive summary of the copolymerization results see Table 3.

2.2.2.6 Discussion

A possible explanation for these results is the reaction of the initiating radicals with the P(V) side group instead of the vinyl moiety[57]. This reversible side reaction diminishes not only the amount of radicals available for polymerization but may lead to a locally increased concentration of radicals along the polymer chain that facilitates recombination (Scheme 11).

Scheme 11



For a summary of the polymerization results for radical polymerizations, see Table 1-Table 3.

Table 1: Radical polymerization - Homopolymerization of diisopropyl vinyl phosphonate.

Technique	Initiator	Reaction temperature	Solvent	Time	Yield	n[1]
Thermical	1 ‰ DBO	135 °C	-	24 h	10 %	3-7
	1 % AiBN	80 °C	Toluene	8 h	2 %	3-10
Contr. Radical	1 ‰ DBO/TEMPO	135°C	-	24 h	1 %	3-6
	1 ‰ DBO/TEMPO/AcOAc	135 °C	-	24 h	30 %	3-10
	1 % AiBN/X	80 °C	Toluene	24 h	30 %	3-8
UV-induced	1 % Benzoephenone	25 °C	Toluene	8 h	-	-
	1 % AiBN	25 °C	Toluene	8 h	90 %[2]	3-10
Emulsion	1 % $K_2S_2O_8$	100 °C	Water[3]	24 h	90 %	3-10

Table 2: Radical polymerization - Homopolymerization of diphenyl phosphine oxide.

Technique	Initiator	Reaction temperature	Solvent	Time	Yield	n
Thermical	-	135 °C	-	24 h	40 %	3-12
UV-induced	1 % Benzoephenone	25 °C	Toluene	8 h	-	-
	1 % AiBN	25 °C	Toluene	8 h	-	-
Emulsion	1 % $K_2S_2O_8$	100 °C	Water	24 h	25 %	3-25

Table 3: Radical polymerization **-** Copolymerization of vinylphosphorus monomers

Technique	Initiator	Monomer 1	Monomer 2	Solvent	Reaction conditions	Results
Thermical	1 %[4] DBO	DIVP (r)	Dimethylmaleate	Toluene	100 °C, 8 h	-
	1 % AiBN	DIVP (r)	Dimethylmaleate	Toluene	100 °C, 8 h	-
	1 % DBO	DIVP (r)	Styrene, butyl acrylate	Toluene	100 °C, 8 h	PS/PBuA, no conversion of DIVP
	1 % AiBN	DIVP (r)	Styrene, butyl acrylate	Toluene	100 °C, 8 h	PS/PBuA, no conversion of DIVP
	1 % AiBN	VPA (r)	Butyl acrylate	Water	100 °C, 24 h	PBuA, some conversion of VPA
Controlled radical	1 % AiBN/X	VPA (r)	MMA	Water, Ethanol	80°C, 24 h	-

[1] Degree of polymerization, as seen in the MALDI spectra
[2] High content of byproducts
[3] The monomer is not soluble in water.
[4] Based on total monomer content

Table 3 continued:

UV-induced	1 % AiBN	DIVP (r)	Styrene	Toluene	25 °C, 8 h	St oligomers, no conversion of DIVP
Emulsion	1 % $K_2S_2O_8$	DIVP (r)	Styrene	Water	100 °C, 8 h	PS, no conversion of DIVP
		DIVP (r)	Butyl acrylate	Water	100 °C, 8 h	PBuA, low conversion of DIVP
		DIVP (r)	Dimethylmaleate	Water	100 °C, 8 h	Short DIVP homopolymer, capping
		DPPO (r)	Styrene	Water	100 °C, 8 h	-

2.2.3 Anionic Polymerization

Anionic polymerization was performed solely in solution, never in bulk. As it proved to be exceedingly more successful than any polymerization involving radicals, a wide range of conditions were investigated to find the most suitable system. Colorful anions resulted from the initiation process (bright yellow for the phosphonates, deep red for the phosphine oxides), allowing a visual control of the presence of active species.

2.2.3.1 Anionic homopolymerizations

Taking conversion as a first order approximation for success to differentiate suitability of various systems (see Figure 15), toluene was found to be the solvent of choice and n- or sec-BuLi to be the best initiators.

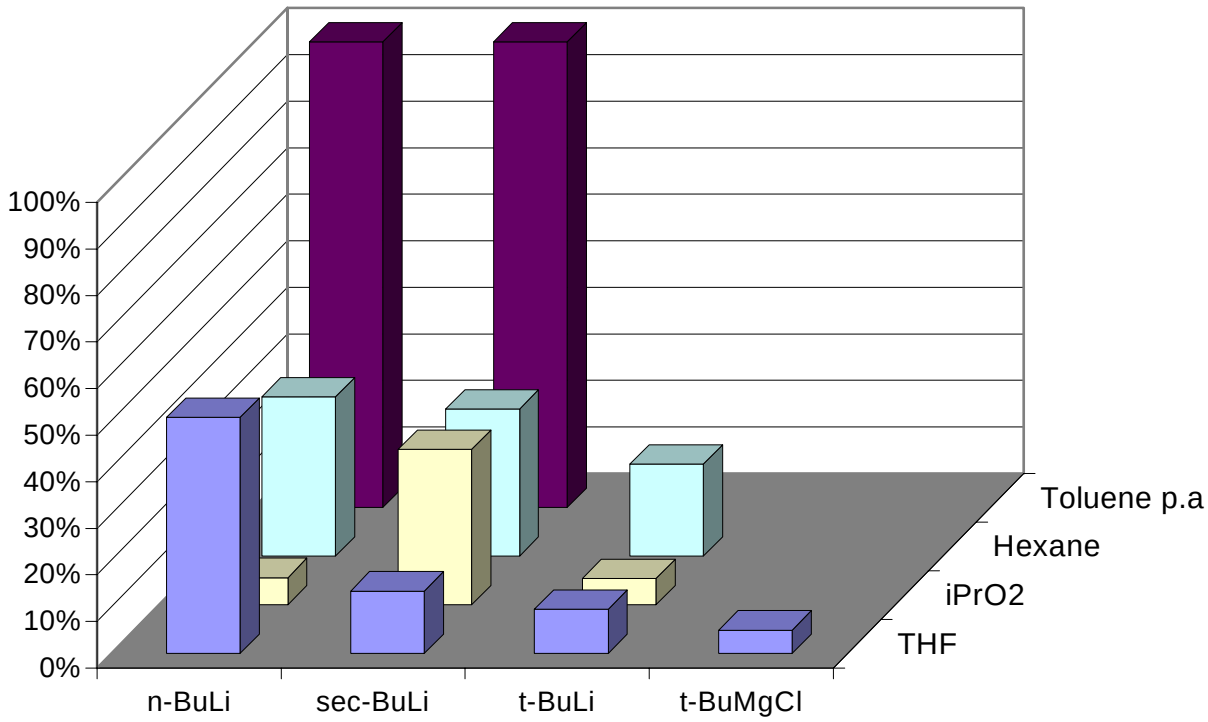


Figure 15: Conversion of DIVP monomer after 8h for different initiators and solvents

Similar results were obtained when comparing polymer chain length as determined from the MALDI spectra (see Figure 16, Figure 18 – Figure 22).

The double values for hexane (hexane (1) and hexane (2)) arise from the fact that higher molecular weights of the somewhat polar polymers were increasingly less soluble in the unpolar solvent. A fractionation by weight therefore occurred already during the polymerization reaction, with fraction (1) referring to the soluble, lower molecular weight fraction and (2) to the insoluble, higher molecular weight fraction.

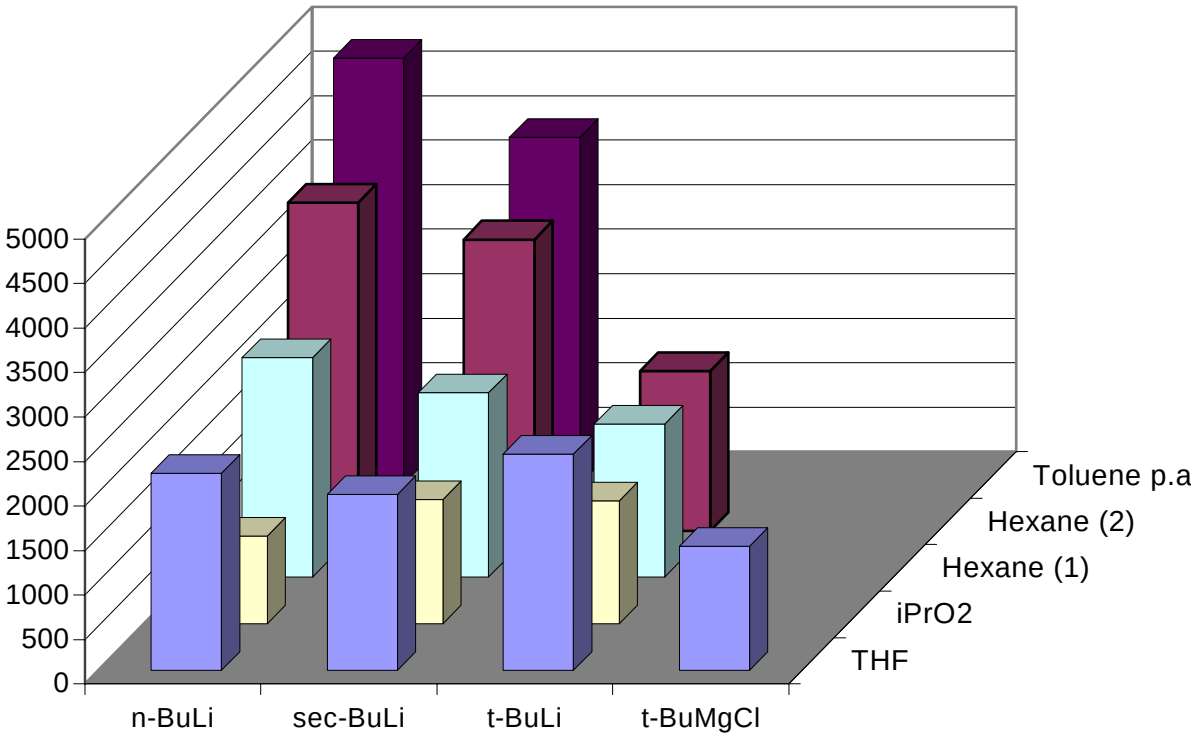


Figure 16: Mn of DIVP polymers after 8h for different initiators and solvents (values according to MALDI)

No influence of temperature was observed in the range between –50°C and room temperature (see Figure 17).

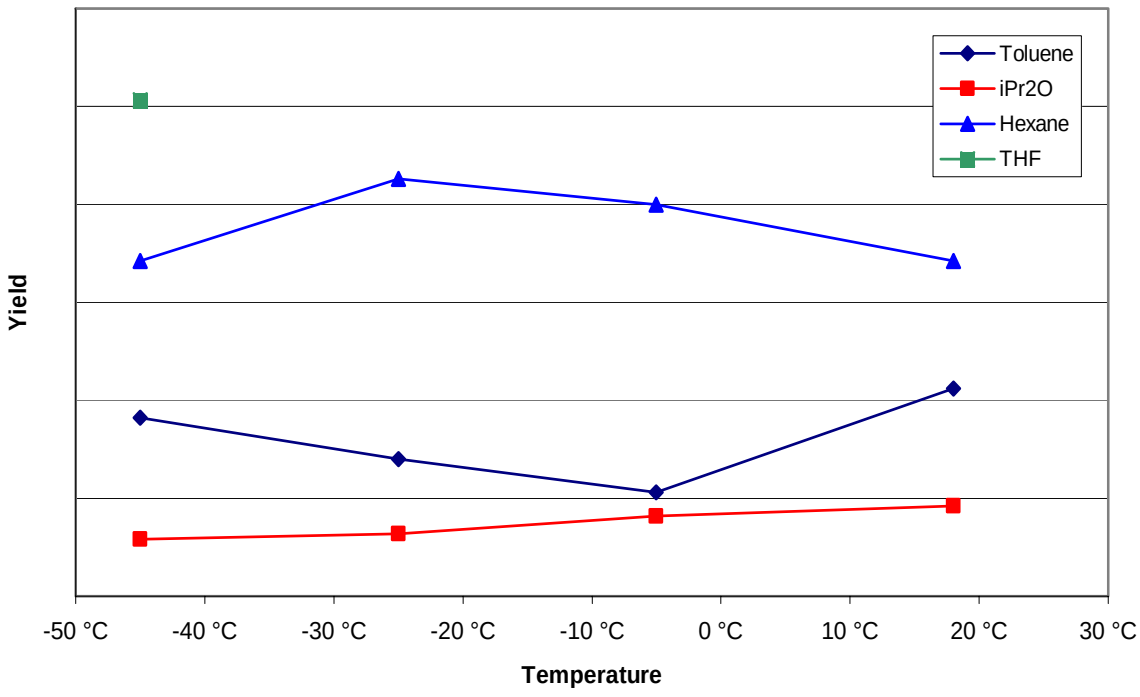


Figure 17: Conversion of DIVP monomer after 8h for different temperatures and solvents

To further extend the range of suitable initiators, n-BuLi was applied in combination with sparteine (to form a chiral initiator) and N,N,N',N'-tetramethylethylenediamine (TMEDA; to break up the BuLi clusters in the unpolar solvent toluene). The carbanion was even replaced with nitrogen, using the initiators lithium diisopropylamide (LDA) and lithium bis-(trimethylsilyl)-amide (LTSA). In all these cases a polymerization was found, though with slight variations in polymerization behavior and outcome. Especially the formation of an optically active polymer (due to a preferred helical arrangement induced by the chiral initiator BuLi/sparteine and stabilized by bulky sidegroups) could not be detected.
Yields for optimized anionic polymerizations were always quantitative, with chain lengths about one order of magnitude higher than for radically produced polymers. The resultant products were off-white solids, unmelting until 350°C when decomposition set in.

Compared with the results of the radical polymerizations, the well-defined initiation and termination reactions (the polymerization is quenched with methanol) led to much clearer MALDI spectra. Polar solvents (THF, diisopropyl ether) and bulky initiators (t-BuMgCl, t-BuLi; see Figure 18 and Figure 19) yielded not only much shorter polymer chains but also promote side reactions, as can be seen in the numerous peaks visible for each chain length.

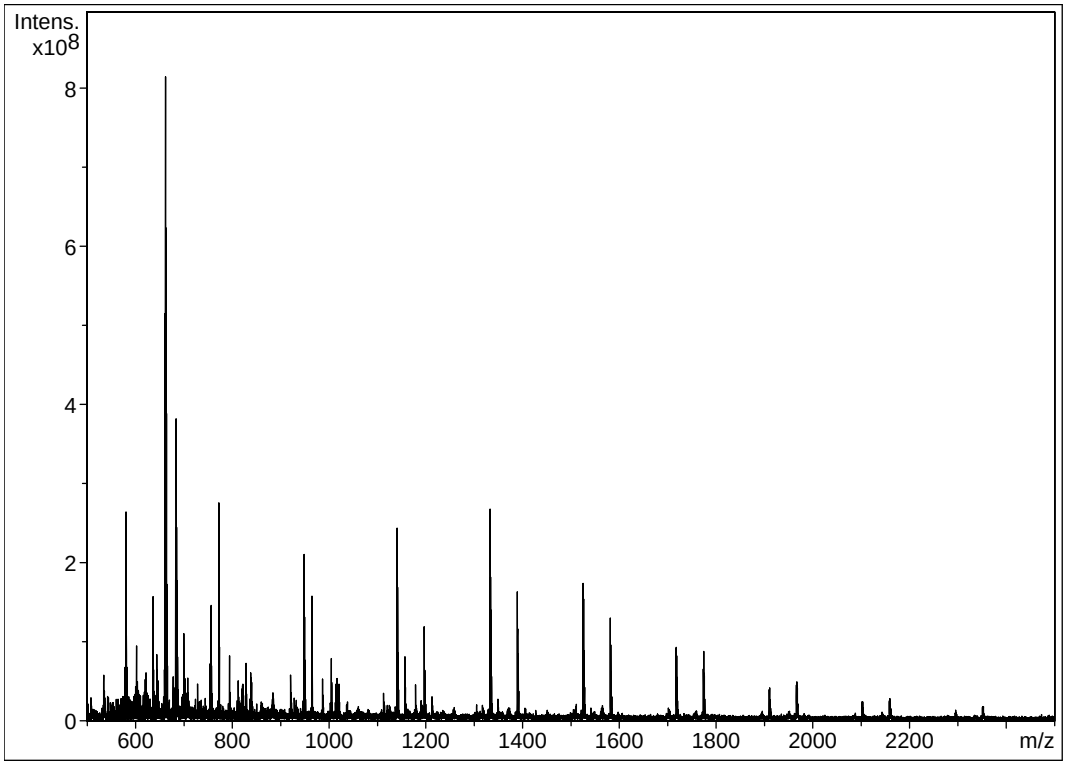


Figure 18: MALDI spectrum of PML 13, anionic polymerization of DIVP in THF, initiator: t-BuMgCl

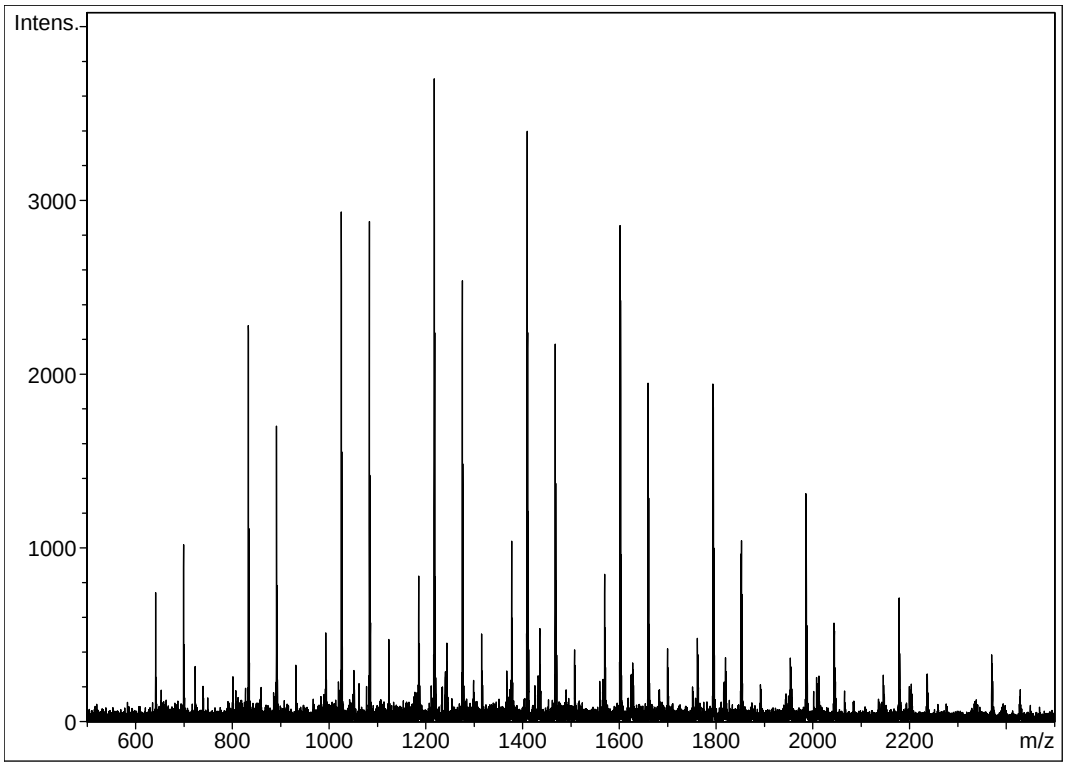


Figure 19: MALDI spectrum of PML 43, anionic polymerization of DIVP in diisopropyl ether, initiator: t-BuLi

Unpolar solvents (hexane, toluene; see Figure 20 to Figure 22) are much more preferable for the anionic polymerization of vinyl phosphonates and vinyl phosphine oxide monomers.

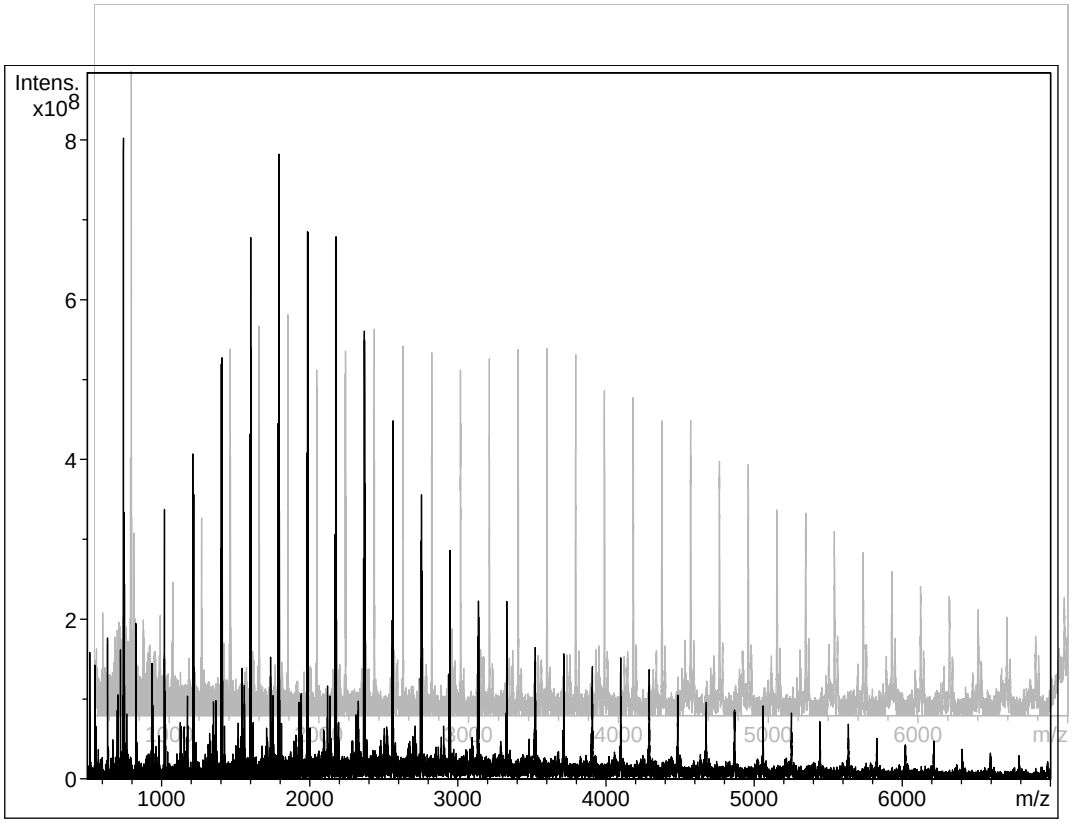


Figure 20: MALDI spectrum of PML 46, anionic polymerization of DIVP in hexane, initiator: s-BuLi. Soluble fraction black spectrum (front), insoluble fraction grey (behind).

The most obvious difference between the two is the fact, that for hexane the MALDI peaks correspond to a multiple of the respective monomer mass plus a butyl group from the initiator. A second series of very small peaks accompanies the main signals (left of the main peaks in Figure 20), they correspond to polymers lacking the butyl groups. For toluene these secondary peaks become the main peaks.

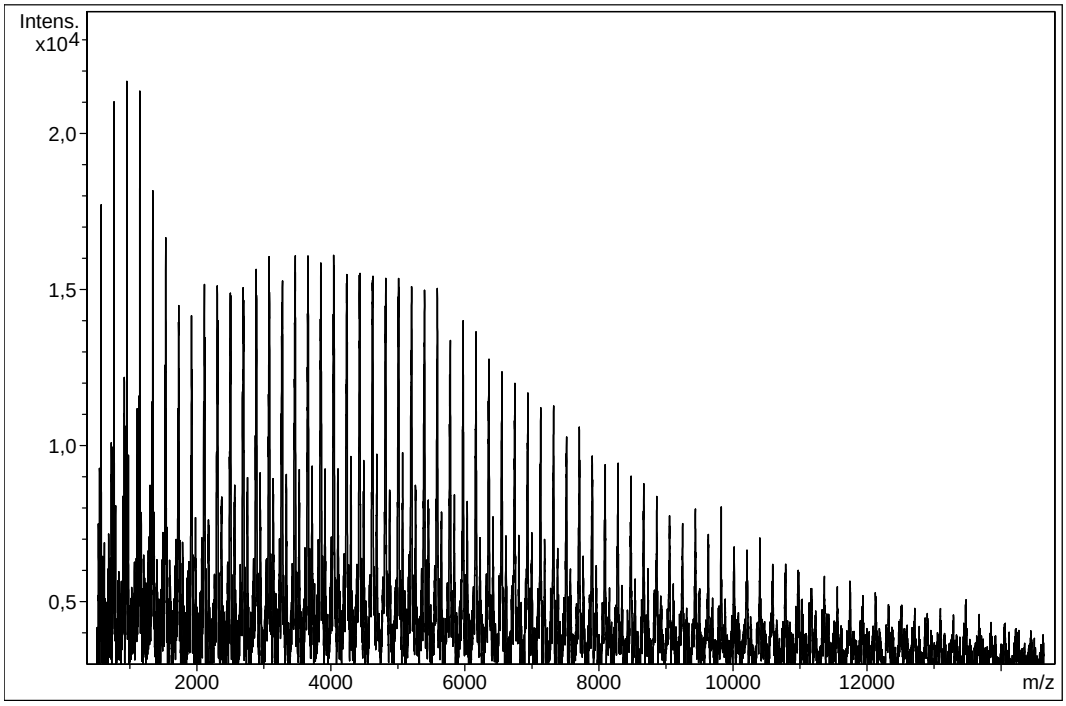


Figure 21: MALDI spectrum of PML 2A, anionic polymerization of DIVP in toluene, initiator: n-BuLi

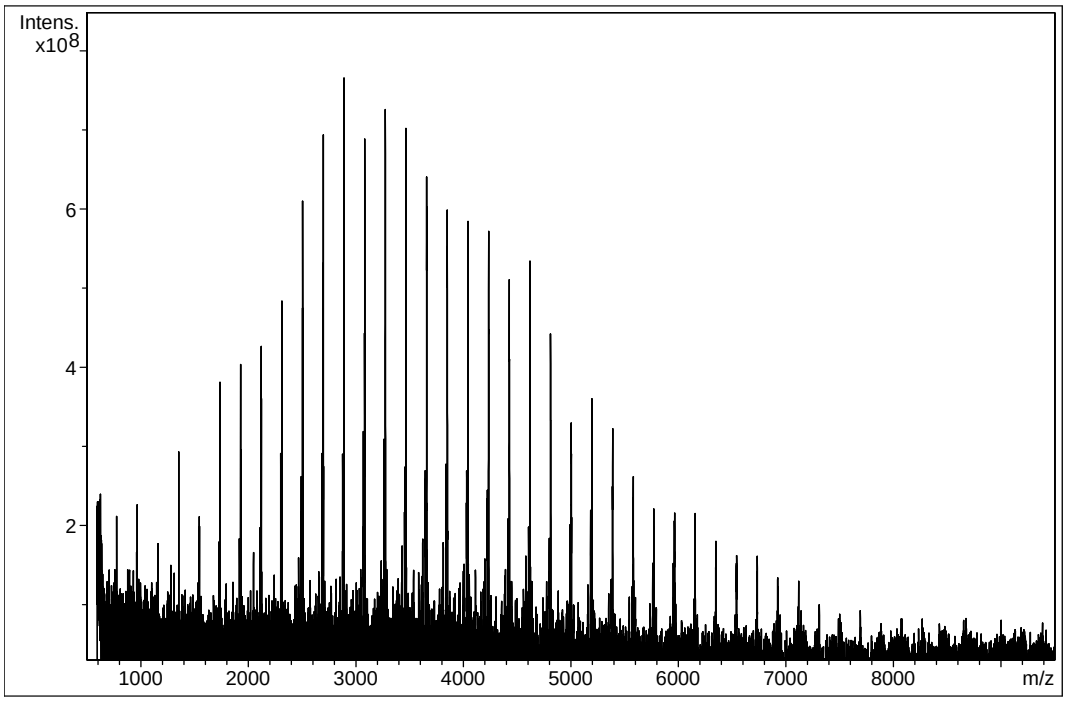


Figure 22: MALDI spectrum of PML 10A, anionic polymerization of DIVP in toluene, initiator: s-BuLi

The addition of sparteine to BuLi to form a complex which is then used as the initiator, results in a lower molecular weight and the attachment of an additional sparteine end group to those polymers with a butyl end group (Figure 23).

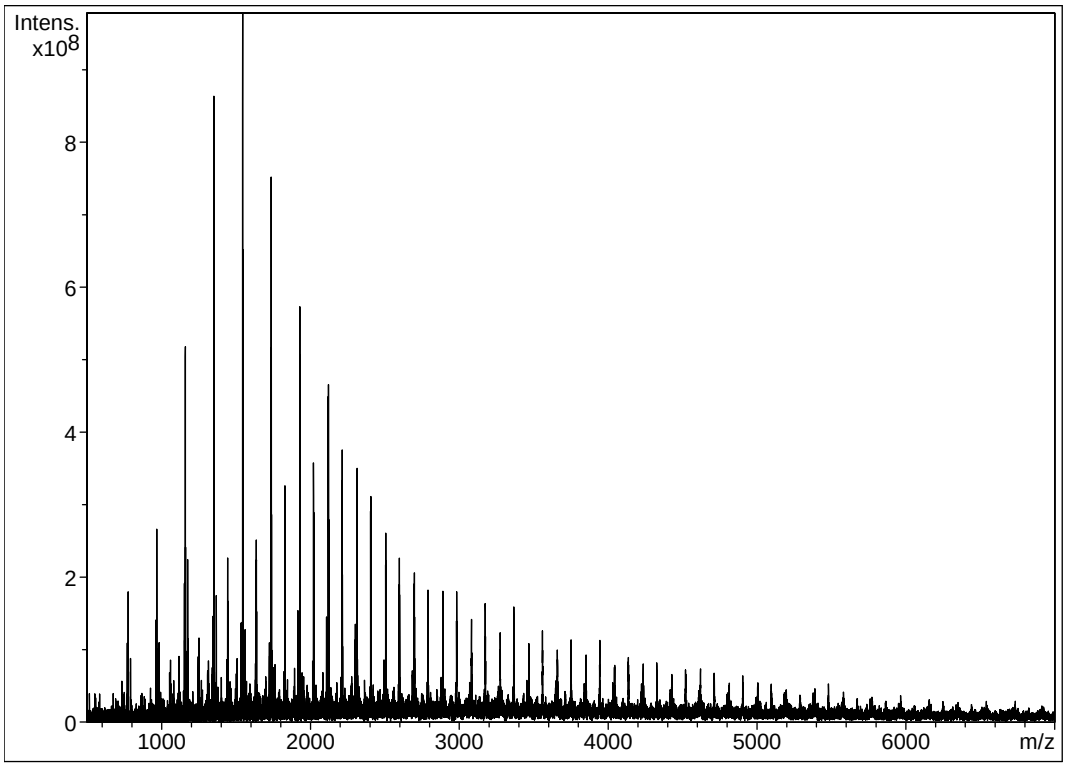


Figure 23: MALDI spectrum of PCML 5, anionic polymerization of DIVP in toluene, initiator: n-BuLi/sparteine

Replacing the carbanion with a nitrogen anion, does not change the polymerization behaviour significantly (Figure 24, Figure 25).

As for BuLi, the main series of MALDI peaks for a polymer prepared with LDA lacks the end group introduced by the initiator, here $N(iPr)_2$. The molecular weight remains in the range seen for n-/s-BuLi.

Lithium bis-(trimethylsilyl)-amide (LTSA), a sterically hindered, non-nucleophilic nitrogen base, is also able to polymerize the phosphorus monomers, though it is not a classical anionic initiator (no polymerization of styrene possible, for example). No initiator endgroups can be found at all in these experiments.

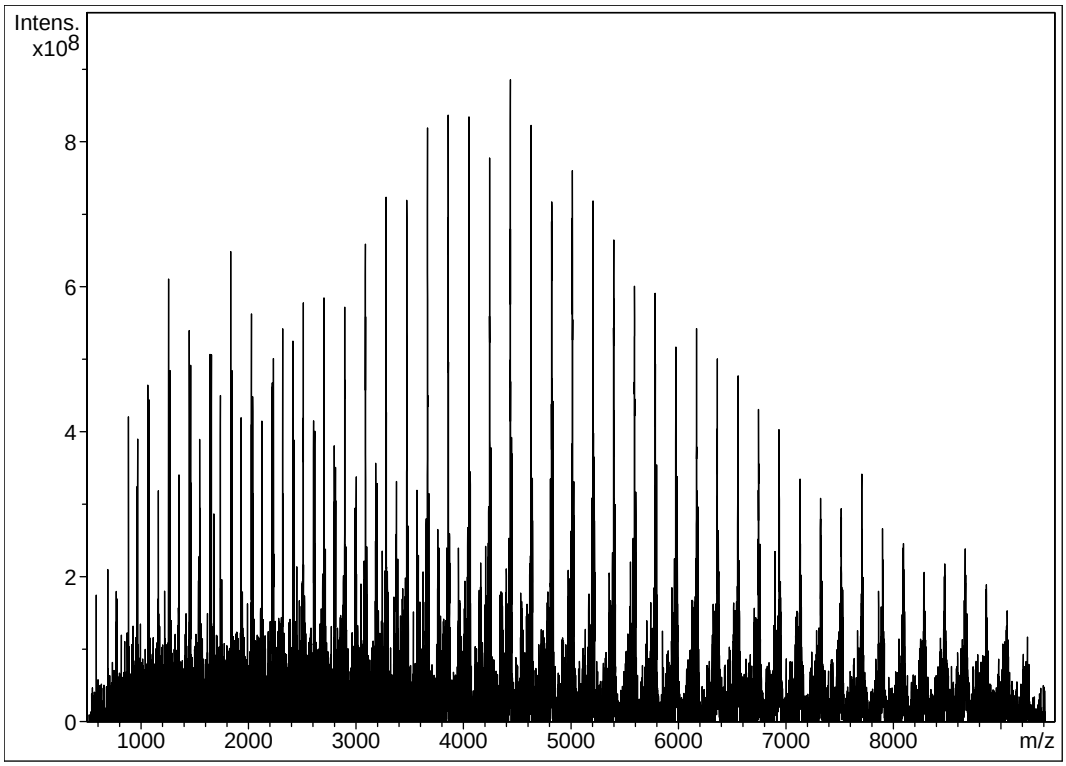


Figure 24: MALDI spectrum of PNML 2, anionic polymerization of DIVP in toluene, initiator: LDA

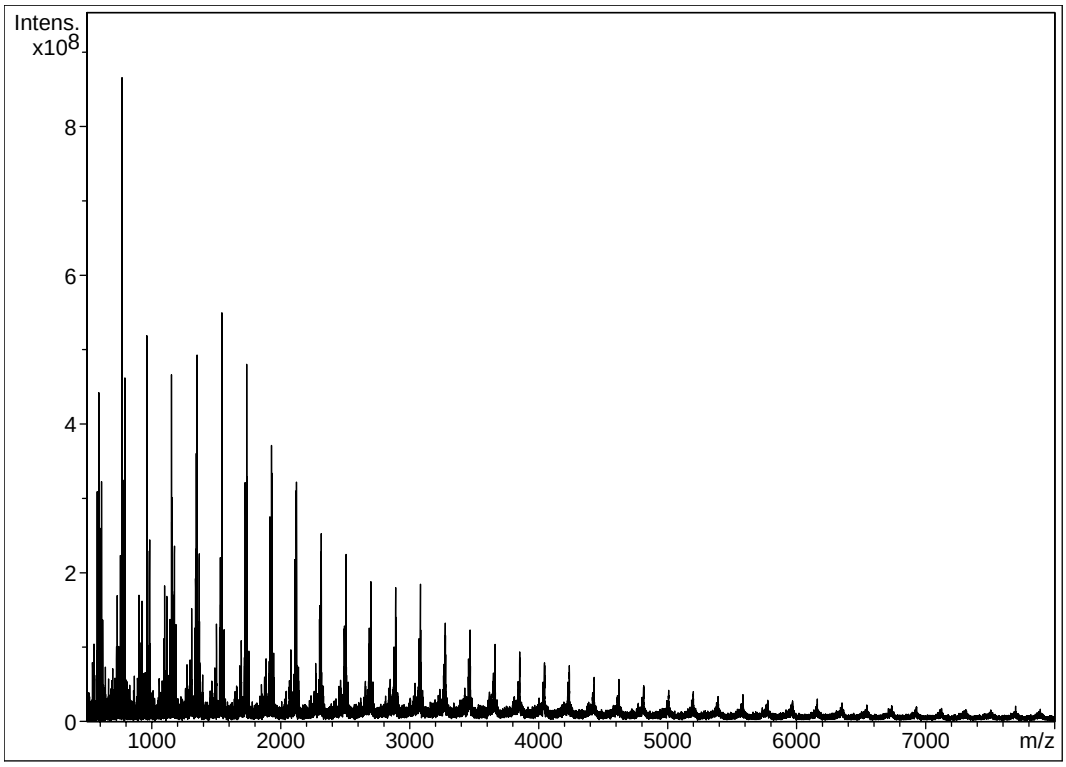


Figure 25: MALDI spectrum of PNML 6, anionic polymerization of DIVP in toluene, initiator: LTSA

Contrary to the radical polymerizations, DVPO formed somewhat shorter polymers than DIVP when initiated anionically (see Figure 26 and Figure 27). Otherwise the same polymerization behavior was observed.

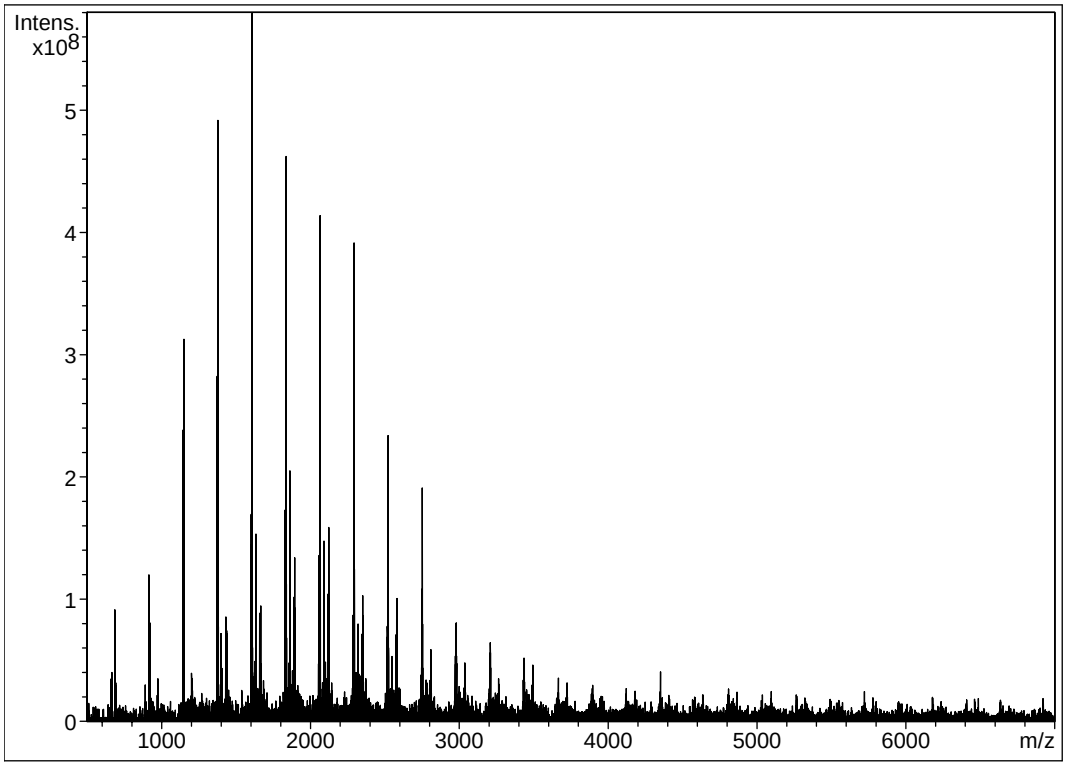


Figure 26: MALDI spectrum of PMLO 1A, anionic polymerization of DVPO in toluene, initiator: s-BuLi

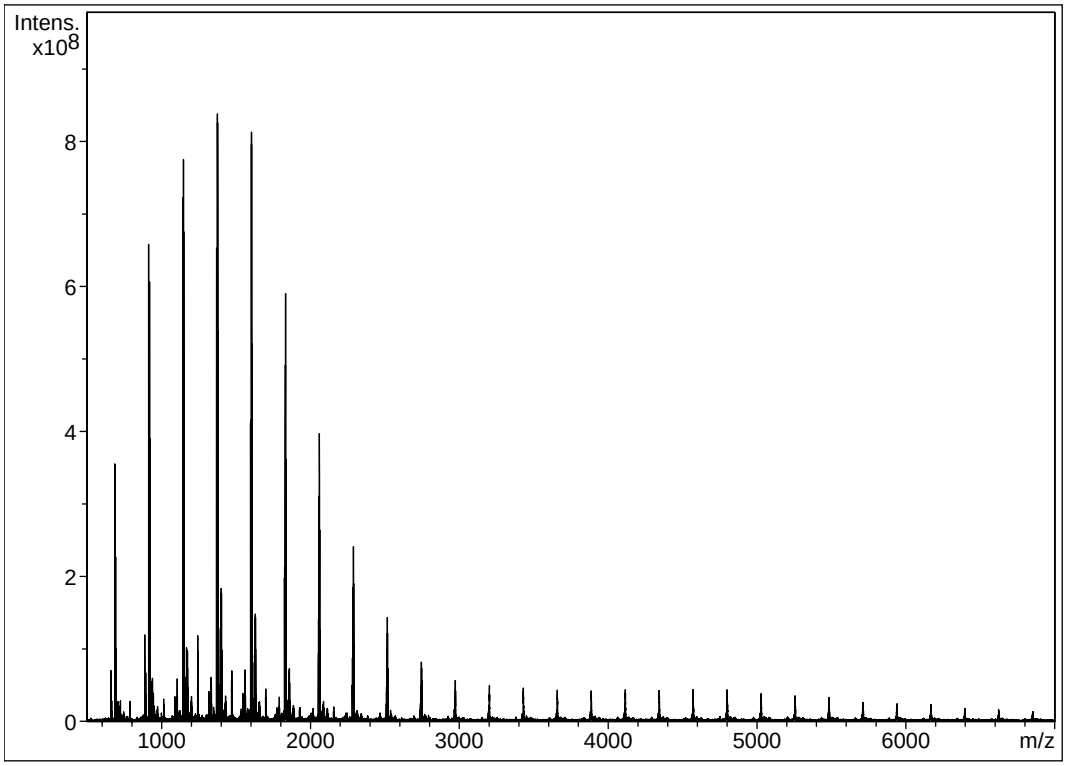


Figure 27: MALDI spectrum of PNML 5, anionic polymerization of DVPO in toluene, initiator: LDA

2.2.3.2 Anionic copolymerization

Copolymerization experiments were performed using styrene and MMA as comonomers, and both carbanions (n-BuLi) and nitrogen anions (LDA) as initiators. Homopolymerizations were used to assure that the respective comonomer would polymerize readily under the conditions involved.

Again a clear distinction has to be made between the results of polymerizations initiated by radicals and those started anionically. While no copolymers and very little to none phosphorus containing polymer was found in the former cases (for one remarkable exception, see below), the latter showed a strong preference for the phosphorus monomers.

A very interesting feature could be seen when anionic copolymerization of vinyl phosphonates / phosphine oxides and styrene or methacrylate was attempted. Contrary to previous expectations, no copolymers were formed, despite the living nature of the anions. If a random copolymerization was attempted by preparing a solution of both monomers and then adding the initiator, only a phosphonate homopolymer was formed. The same was true when DIVP was initiated first and the comonomer added later to the anionic system to create a block structure. In this case a capping effect, the addition of exactly one unit of the second monomer to the already formed phosphonate chain was also observed, as shown in Figure 28 for an attempted DIVP-*block*-St and in Figure 29 for a random copolymerization of DIVP and MMA.

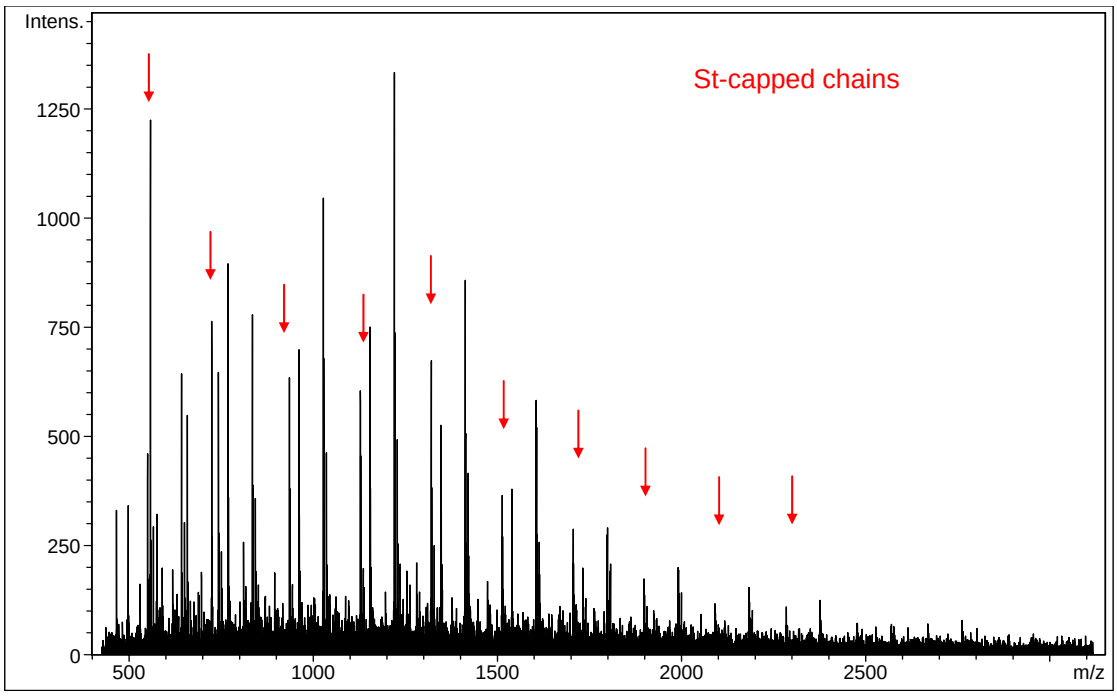


Figure 28: MALDI spectrum of the low weight fraction of a styrene capped DIVP-polymer. Major peaks left of indicated peaks refer to uncapped chains (double sets of peaks are due to addition of potassium from the matrix to the polymer chains).

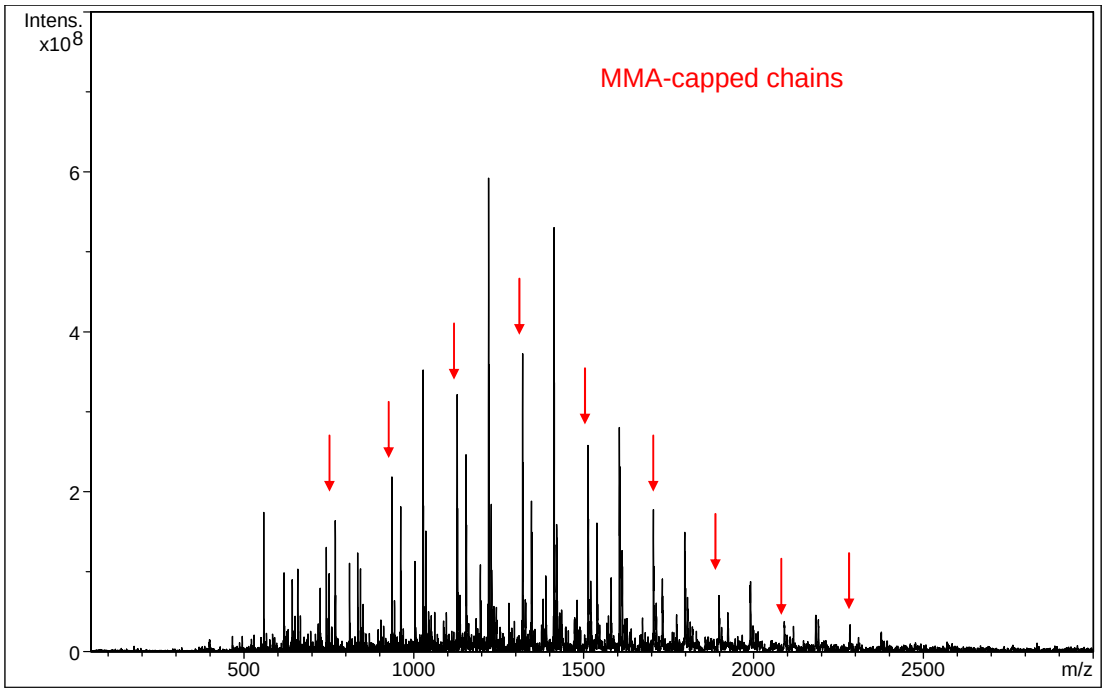


Figure 29: MALDI spectrum of the low weight fraction of a MMA capped DIVP-polymer. Major peaks left of indicated peaks refer to uncapped chains.

An effect which, surprisingly, may also be observed when doing a radical emulsion polymerization of DIVP and dimethylmaleate (see Figure 30).

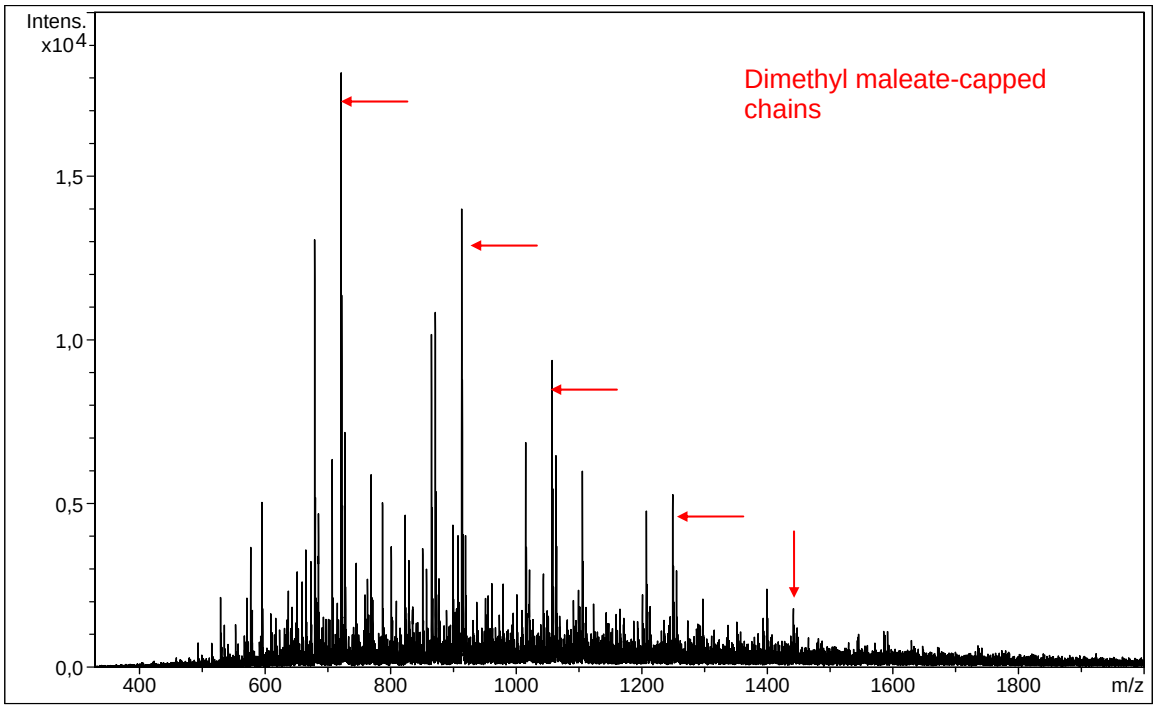


Figure 30: MALDI spectrum of dimethyl maleate capped DIVP-oligomer, major peaks left of indicated peaks refer to uncapped chains (multiple side peaks due to variable end groups and partial decomposition, see 2.2.2).

Performing the polymerization in reverse order (vinylic monomer-*block*-P-monomer) leads to the formation of two distinct polymers, one for each monomer, as can be seen in the GPC (see Figure 31). Extraction with methanol may be used to separate the two polymers.

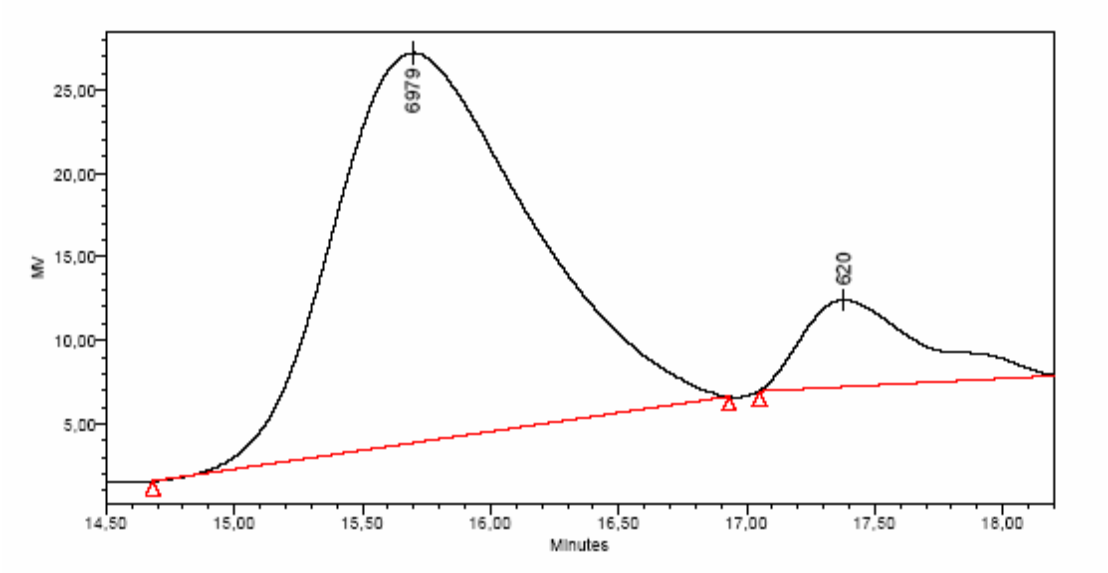


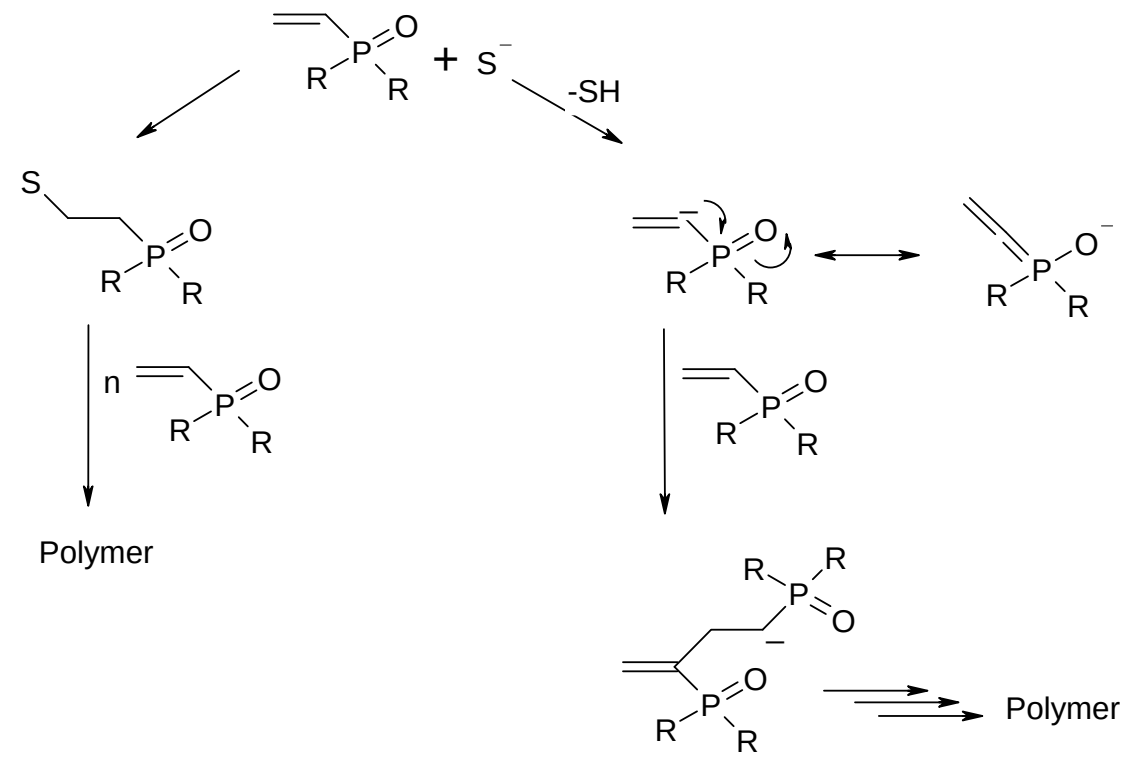
Figure 31: GPC of the mixture of PS and phosphonate polymer (the molecular weight for the latter underestimated by GPC)

2.2.3.3 Discussion[58]

MALDI brought up very interesting results: in all anionic experiments regardless of conditions or initiators, a certain fraction of polymers did not show end groups introduced by the initiators.

This could be explained if one assumes that the polymerization is not only initiated by nucleophilic attack of the initiator anion on the vinyl group, as would be expected for styrene, for example, but also by an acid-base reaction between initiator and the phosphorus substituted monomers (Scheme 12). The applied starting reagents are very strong bases (pKs n-BuLi > 50), so if the phosphorus group is suitably stabilizing, they may abstract a proton from the monomer, leaving again an anionic species which may then begin the polymerization reaction. Such anions are indeed well known in literature, as intermediates of the Horner-Emmons-Wadworth reaction[59,60]. Usually an electron acceptor substituted double bond is required for these reactions, but also unsubstituted vinyl groups were reported[61].

Scheme 12

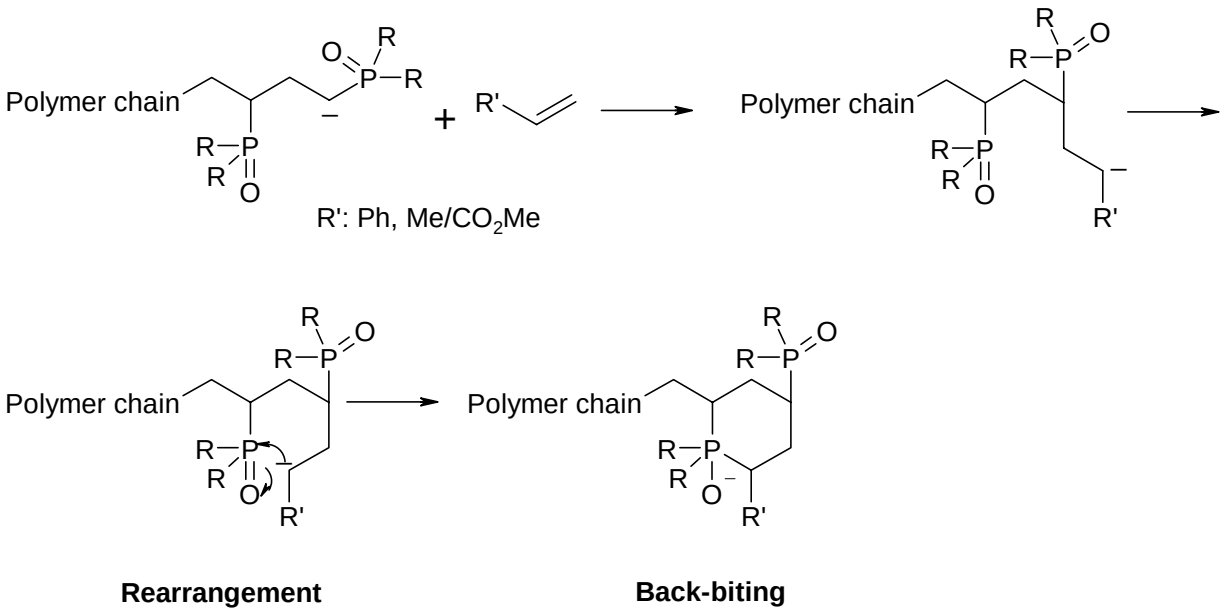


R: OiPr, Ph
S: Initiator

The same phenomenon would explain the unusual copolymerization behavior displayed by these monomers. In case of a styrene/MMA-*block*-P-monomer copolymer, the carbanion at the end of the growing polystyrene chain would again react as a base, initiating another, separate chain of vinyl phosphorus homopolymer. In random polymerizations the phosphorus

monomer is favored when hydrogen abstraction out-competes the more sterically hindered nucleophilic attack as a starting reaction. Finally, the reverse block copolymer P-monomer-*block*-styrene/MMA resulting only in capping, might be due to a back-biting process (see Scheme 13), stabilizing the anion to a degree unsuitable for further polymerization. As both the phenyl group and the carboxyl group are planar, they are less sterically crowded than the phosphorus monomers where the bulky tetrahedral substituents would render the six-membered ring unfavorable.

Scheme 13



To find further proof for this theory, lithium-bis-(trimethylsilyl)-amid (LTSA), a sterically hindered, non-nucleophilic base was used as initiator. LTSA is unable to polymerize styrene (100 % monomer recovery) but can be used to polymerize DIVP, producing a polymer with absolutely no initiator-related end groups.

Such a base-induced polymerization is known for ring-opening polymerizations, but most unusual for olefins.

A summary of the results of the anionic polymerization can be found in Table 4 to Table 6.

Table 4: Anionic polymerization **-** Homopolymerization of diisopropylvinyl phosphonate.

Initiator	Reaction temperature	Solvent	Time	Yield	Degree of polymerization[5]
1 % n-BuLi	25 °C	Toluene	8 h	100 %	3-75
	25 °C	THF	8 h	60 %	3-27
1 % sec-BuLi	25 °C	Toluene	8 h	100 %	3-75
	25 °C	THF	8 h	14 %	3-26
1 % t-BuLi	25 °C	Toluene	8 h	12 %	4-29
	25 °C	THF	8 h	9 %	4-26
1 % t-BuMgCl	25 °C	THF	8 h	12 %	3-10
1 % LDA	25 °C	Toluene	8 h	100 %	3-50
1 % n-BuLi/sparteine	25 °C	Toluene	8 h	95 %	3-35
1 % n-BuLi/TMEDA	25 °C	Toluene	8 h	100 %	3-50

Table 5: Anionic polymerization – Homopolymerization of diphenylvinylphosphine oxide.

Initiator	Reaction temperature	Solvent	Time	Yield	Degree of polymerization
1 % n-BuLi	25 °C	Toluene	8 h	90%	3-30
1 % LDA	25 °C	Toluene	8 h	100%	3-35
1 % n-BuLi/sparteine	25 °C	Toluene	8 h	95%	3-17
% n-BuLi/TMEDA	25 °C	Toluene	8 h	100%	3-25

Table 6: Anionic polymerization **-** Copolymerization of vinylphosphorus monomers

Initiator	Monomer 1	Monomer 2	Solvent	Conditions	Result
1 % n-BuLi	DIVP (b)	Styrene	Toluene	25 °C, 8 h	DIVP homopolymer, capping
	Styrene (b)	DIVP	Toluene	25 °C, 8 h	PS, DIVP homopolymer
	DIVP (r)	Styrene	Toluene	25 °C, 8 h	DIVP homopolymer
	DIVP (b)	MMA	Toluene	25 °C, 8 h	DIVP homopolymer
	MMA (b)	DIVP	Toluene	25 °C, 8 h	PMMA, no conversion of DIVP
	DIVP (r)	MMA	Toluene	25 °C, 8 h	DIVP homopolymer, capping
	DVPO (b)	Styrene	Toluene	25 °C, 8 h	DVPO homopolymer, capping
	Styrene (b)	DVPO	Toluene	25 °C, 8 h	PS, DVPO homopolymer
	DVPO (r)	Styrene	Toluene	25 °C, 8 h	DVPO homopolymer
1 % LDA	DIVP (r)	Styrene	Toluene	25 °C, 8 h	DIVP homopolymer

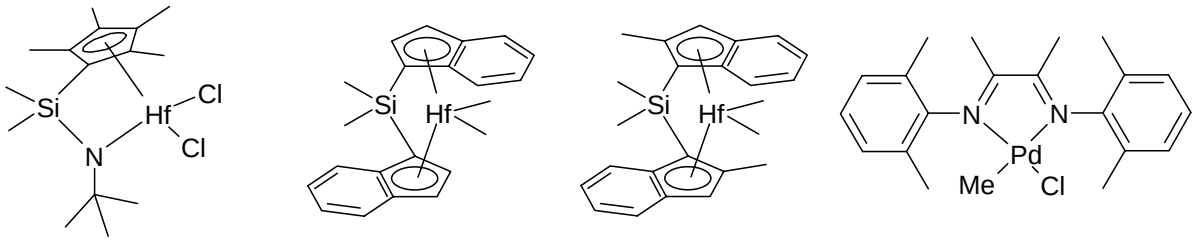
[5] As seen in the MALDI spectra.

2.2.4 Catalytic polymerization

Three different hafnocen catalysts (active for polar monomers) yielded no polymers.

Catalyst 1 (Figure 32) was used both for homopolymerization experiments with DIVP (at room temperature) and for copolymerization attempts with ethylene (30°C). TIBA was used to create the active species. Catalysts 2 and 3 were activated with equimolar amounts of tris-(pentafluorophenyl)-borane and the reaction performed at 0°C.

Catalyst 4 was activated with sodium-tetrakis-(bis(trifluormethyl)phenyl)-borate, and also used for both for DIVP (at room temperature) homopolymerization and copolymerization attempts with ethylene. No polymer was formed in either case.



1 **2** **3** **4**

Figure 32: Various catalysts used for polymerization of DIVP

Lanthanide catalysts, on the other hand, were able to produce polymers. The yttrium catalyst shown below (Figure 33) was used to homopolymerize DIVP.

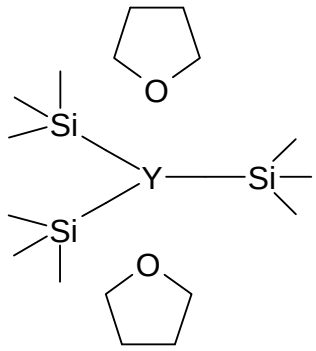


Figure 33: YR_3

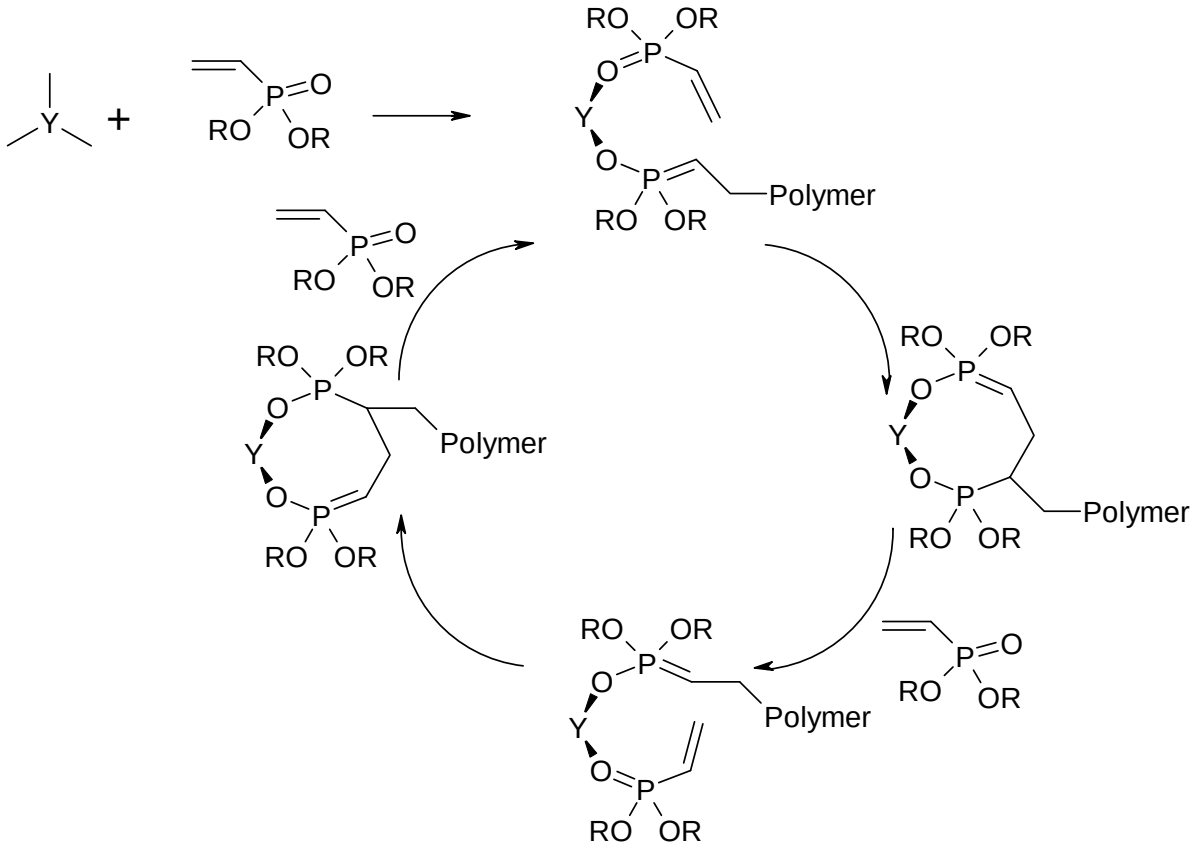
The reaction mechanism is as yet not entirely clear; experiments involving styrene, however, strongly indicate a group transfer polymerization. This is based on the following observations: YR_3 dissolved in toluene is colorless, yet it forms a pale yellowish solution after addition of DIVP, and a bright yellow to orange-brown solution when styrene is added. Addition of methanol immediately results in decoloration. This suggests the formation of either a complex or an anionic species. Nevertheless in attempts to homopolymerize styrene no polymer is formed even after 72 h at room temperature – higher temperatures were not attempted due to

the sensitivity of the catalyst. An anionic polymerization of DIVP by the yttrium alkyl in analogy to a lithium alkyl can therefore be ruled out.

A copolymerization experiment wherein styrene was added first to the catalyst solution and then, after several hours, DIVP was added as well, resulted in a PIVP homopolymer. After addition of the vinyl phosphonate monomer, the dark orange solution paled to light yellow when styrene was replaced by DIVP around the yttrium center. A group transfer polymerization, known for lanthanide catalysts polymerizing MMA, would explain these finds (Scheme 14).

MMA homopolymerizations as well as copolymers with vinyl phosphonate monomers would be needed to strengthen these arguments further. They were performed successfully in Dr. Rabe's group.

Scheme 14



2.2.5 Conclusions

As shown above, vinyl phosphonate and vinyl phosphine oxide monomers react under a broad variety of polymerization conditions. They do not, however, form more than oligomeric materials when initiated by radicals and also show strong reluctance to be incorporated into copolymers. This should be kept in mind when these or related monomers are used as additives to improve flame retardancy or other properties. Anionic polymerization, on the other hand, though following a rather unusual polymerization mechanism, allows not only a vast increase in molecular weight and yield, but also confines the formation of byproducts to a minimum. To illustrate this point a typical ^{31}P spectra of a polymer prepared by anionic polymerization is shown in Figure 34 in comparison with a commercial product[62] which was used in many recent investigations[28,63,64]. DIVP was polymerized as described in 2.3.2.5 and subsequently hydrolyzed in concentrated hydrochloric acid to yield the free polymeric acid, detectable in the spectra as a broad peak at 31 ppm. The polymer sample was analyzed without further purification, yet there are no byproducts (28.5-25 ppm) or monomer residues (16.4 ppm, about 30 mol%) visible as seen in the commercial product.

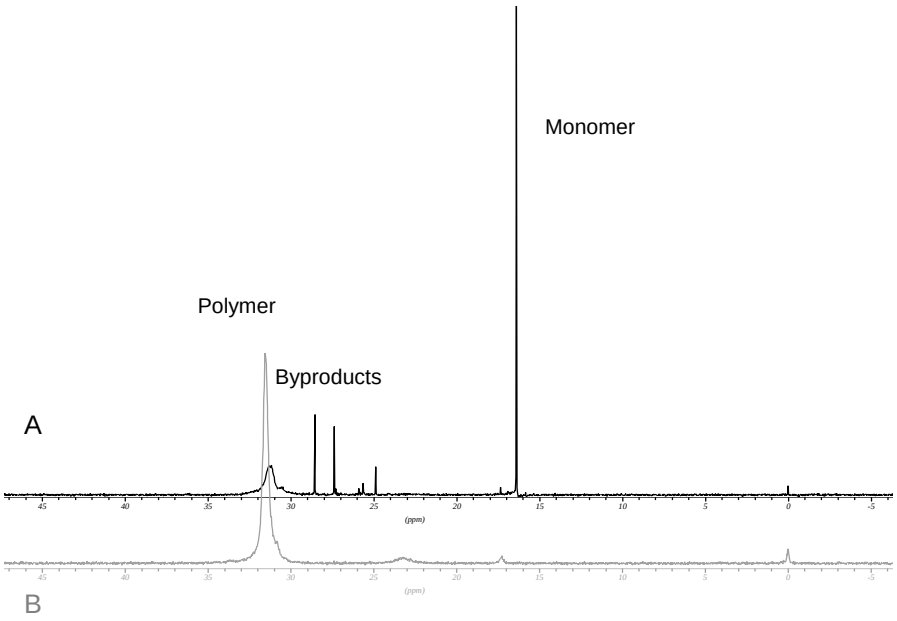


Figure 34. ^{31}P spectra (D_2O, H_3PO_4 standard) of commercially available poly(vinyl phosphonic acid) (A) and anionically prepared polymer (hydrolyzed PolyDIVP polymer) (B).

The main drawback of the anionic polymerization is its inability to produce copolymers.

2.2.6 Polymer properties

Functional polymers define themselves by their unusual properties, exceeding the range commonly associated with everyday plastics.

For the poly(vinyl phosphonates), -phosphine oxides and phosphonic acid, the phosphorus moiety is mainly responsible for these properties, as is the combination of carbon backbone and polar side group.

2.2.6.1 Thin films on glass surfaces

For a number of fields in which such polymers are showing potential for application, be it for biomedical devices or metal coatings, surface properties are of special interest. Therefore the morphology of thin polymer films was investigated by electron microscopy (see Figure 35 and Figure 36).

The studied films were prepared either by spin-coating or by evaporation of a volatile solvent (methanol) from small droplets. In accordance with the different polymer properties, different structures were observed. While the polyacid spreads uniformly over the glass due to interactions of the acid groups with the polar glass surface, the polyphosphonates and, even more pronounced, the unpolar polyphosphine oxides form globular structures with a few hundred nanometers in diameter.

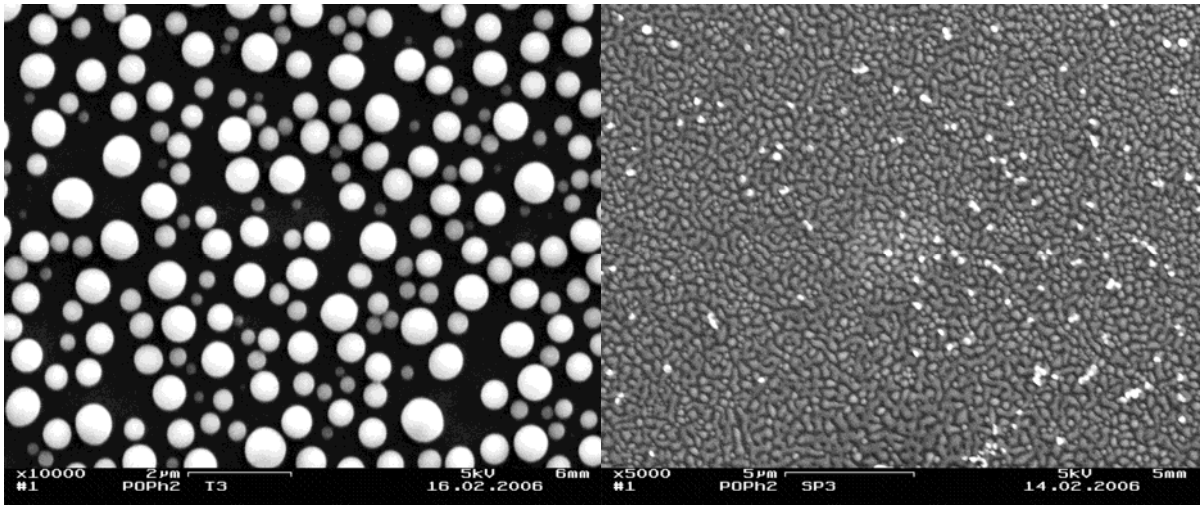


Figure 35: Electron microscopic picture of DVPO polymer as thin film on glass. Prepared by evaporation of a small droplet (left) or by spin-coating (right).

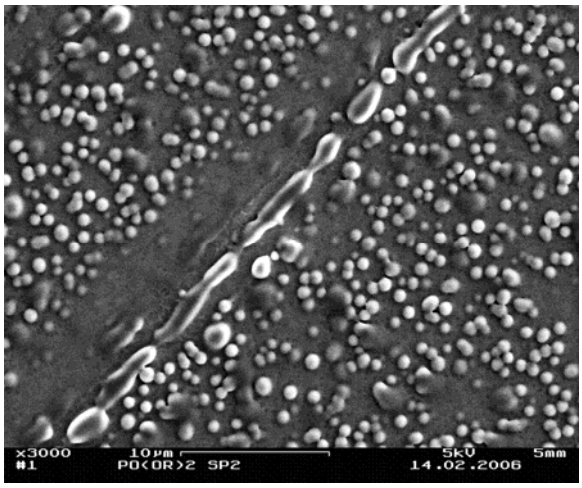


Figure 36: Electron microscopic picture of diisopropylvinyl phosphonate polymer as thin film on glass. Prepared by spin-coating.

2.2.6.2 Emulgating effect

While PVPO is overall too unpolar to form interactions with water, and PVPA, as a polyacid, is absolutely insoluble in aprotic organic solvents, for PIVP the combination of unpolar carbon backbone and polar side groups is well balanced. It exhibits a strong tendency to stabilize emulsions when in contact with both water and organic solvents. An exact CMC could not be measured, yet it was found to be about 0.3 mg/ml in water at 20°C.

Several experiments showed that for every 1 wt% of PIVP, 10 wt% of water may be incorporated into a stable emulsion with CH_2Cl_2, with no signs of breaking after 30 d.

2 wt% PIVP therefore allow an emulsion of 20 wt% water in dichloromethane, while a 10 wt% solution of polymer may incorporate equal amounts of water into the organic solvent.

2.2.6.3 Thermostability

As phosphorus compounds are common additives to improve flame retardancy, a high thermostability of the PIVP, PVPO and PVPA homopolymers is hardly surprising. All polymers were stable up to at least 250°C, when degradation sets in for the phosphonates (elimination of ester groups). For phosphonic acid and phosphine oxide TGA showed a first weight loss at temperatures above 400°C.

Less convenient for processing is the fact that no melting was observed up to 400 °C. DSC between -150°C and +150°C showed no glass transition either.

Compression molding was used to produce plates for elasticity measurements which showed flow under stress exceeding 0.35 MPa for a slow strain (5 mm/min) and 0.475 MPa (for a fast strain (50 mm/min), a behavior also indicative of a glassy state.

For future application a solution based application would probably be most convenient.

2.2.6.4 Complexation

The reaction of the polymers with various di- and trivalent ions (La^{3+}, Ca^{2+}, Fe^{2+}, Cu^{2+}; added as chlorides), yielded precipitates of complexes. For PVPA globular structures were prevalent, as shown in Figure 37.

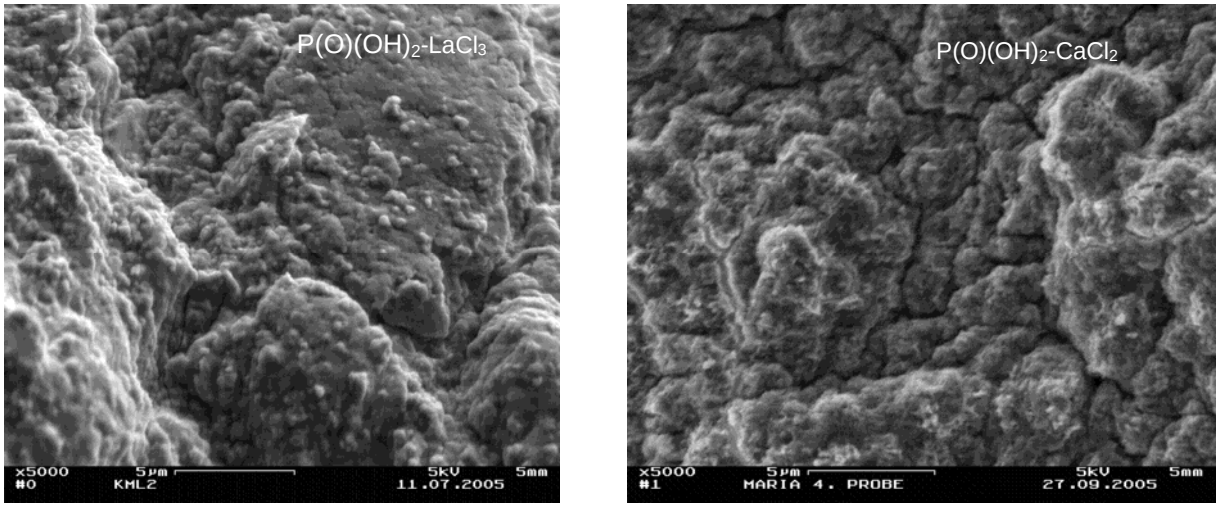


Figure 37: Electron microscopic images of PVPA-metal complexes

Structures of special interest were formed when the reaction of PVPA and $CaCl_2$ was performed not in bulk but in a very thin film and in the presence of carbon dioxide (Figure 38).

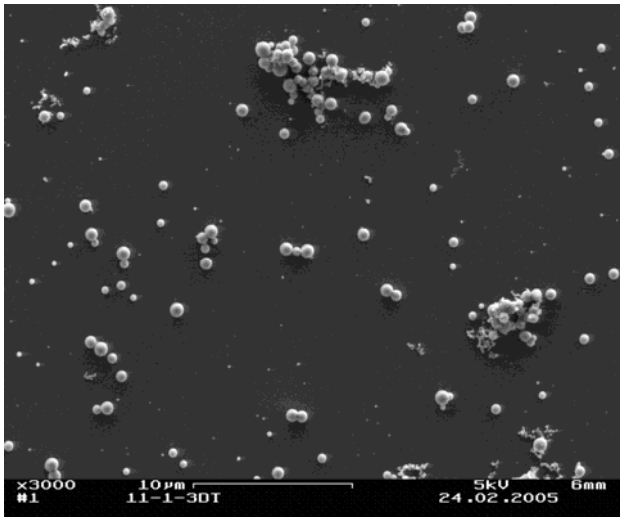


Figure 38: Electron microscopic images of $CaCO_3$ grown in the presence of PVPA

Small spheres of amorphous calcium carbonate were formed, with diameters in the range of 500 - 800 nm. With a size similar to the wavelength of visible light, possible applications would be in the field of photonics.

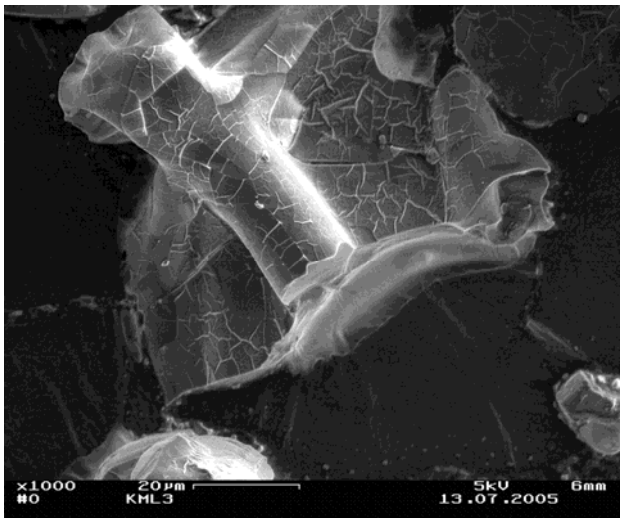


Figure 39: PVPO 'string' with $LaCl_3$

For the other polymers interesting features were found as well. PVPA forms a complex with Fe(II) that stabilizes it against oxidation by air, as seen by the yellow color that was persistent over weeks, unlike uncomplexed samples that turn brown within hours.
PVPO seems to form a network that is then filled with the respective metal salt, as seen in Figure 39.

2.2.6.5 Bioactivity

Polymers with phosphorus side chains are known to be biocompatible. Therefore the new polymers were also tested for interactions with biological systems. The results are described more in detail in chapter 4.

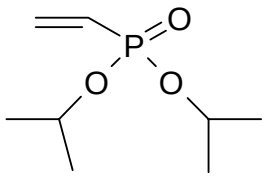
2.3 Experimental section

All chemicals used were of commercial grade and used as received, unless stated otherwise. Solvents were dried and purified by filtration over a short column of aluminum oxide as a standard procedure, and stored under argon. Solvents and monomers used for anionic polymerization were dried at least twice by stirring overnight with a suitable drying agent and subsequent distillation. Repeated freeze-evacuate-thaw circles were used to remove dissolved gases.

2.3.1 Monomer synthesis

Polyvinyl phosphonate monomers were prepared following literature known procedures.

2.3.1.1 Synthesis of diisopropyl vinyl phosphonate (DIVP)



2.3.1.1.1 Step 1: Synthesis of diisopropyl 2-bromoethyl phosphonate

In a flask equipped with a vigreux column with an attached distillation bridge, triisopropyl phosphite (1 equivalent) and 1,2-dibromo ethane (4 equ.) were heated to 165°C (bath temperature). Shortly after reaching this temperature isopropylbromide started to evolve and was distilled from the reaction mixture (b.p. 60 °C). After three hours the visible distillation was ended. The reaction mixture was stirred another four hours at 165°C, then it was allowed to cool to room temperature and stirred over night. Fractioned distillation was used to remove isopropylbromide residues (b.p. 60 °C), excess 1,2-dibromo ethane (b.p. 39 °C / 20 mbar) and finally clean product (b.p. 62°C / 0.1 mbar).
Yield: 80 %

NMR

^{1}H (400 MHz; $CDCl_3$; calibrated to $CHCl_3$: 7.26[65]; δ in ppm): 1.19 (d, 12H, CH_3), 2.16-2.25 (5x, 2 H, CH_2-P), 3.35-3.40 (q, 2 H, CH_2-Br), 4.55-4.60 (6x, 2H, CH)

^{31}P (162 MHz; $CDCl_3$; calibrated to H_3PO_4: 0; δ in ppm): 23.29

2.3.1.1.2 Step 2: Synthesis of diisopropyl vinyl phosphonate

In a flask equipped with a reflux condenser, diisopropyl 2-bromoethyl phosphonate and a 10% excess of triethyl amine were dissolved in toluene (1 mol/l over all reagents) and heated to reflux (120°C bath temperature). Within minutes a white precipitate began to form, namely triethyl amine hydrochloride. The reaction mixture was stirred for 7 h, then allowed to cool to room temperature and stirred over night. The salt was removed by filtration over a glass frit and washed with toluene. The extract was joined with the filtrate and the solvent removed in a rotary evaporator. The product was obtained by distillation as a clear, colorless liquid (b.p. 43°C/0.1 mbar): 91 %

NMR

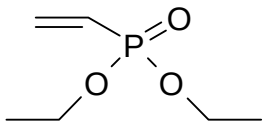
^{1}H (400 MHz; $CDCl_3$; calibrated to $CHCl_3$; δ in ppm): 1.30 (dd, 12H, CH_3), 4.62-4.70 (m, 2 H, CH_2-O), 5.97-6.12(m, 2 H, CH_2,Vinyl), 6.19-6.31 (m, 1H, CH-P)

^{13}C (100 MHz; $CDCl_3$; calibrated to $CHCl_3$; δ in ppm): 22.79 (CH_3), 68.91 (CH_2-O), 125.83+127.67 (CH-P), 132.88 (CH_2(Vinyl))

^{31}P (162 MHz; $CDCl_3$; calibrated to H_3PO_4; δ in ppm): 15.67

Elemental Analysis: C: 49.68%; H: 8.95% (calculated for $C_8H_{17}O_3P$, M: 192.20 g/mol: C: 50.00%; H: 8.92%; O: 24.97%; P: 16.12%)

2.3.1.2 Synthesis of diethyl vinyl phosphonate (DEVP)



Diethyl vinyl phosphonate (DEVP) was prepared analogously to DIVP.

2.3.1.2.1 Step 1: Synthesis of diethyl 2-bromoethyl phosphonate

In a flask equipped with a vigreux column with an attached distillation bridge, triethyl phosphite (1 equivalent) and 1,2-dibromo ethane (4 equ.) were heated to 165 °C (bath temperature). Shortly after reaching this temperature ethylbromide started to evolve and was distilled from the reaction mixture (b.p. 40 °C). After two hours the visible distillation was

ended. The reaction mixture was stirred another four hours at 165°C, then it was allowed to cool to room temperature and stirred over night. Fractioned distillation was used to remove ethylbromide residues (b.p. 40 °C), excess 1,2-dibromo ethane (b.p. 39 °C / 20 mbar) and finally clean product (b.p. 72 °C / 0.2 mbar): 78 %

NMR

^{1}H (400 MHz; $CDCl_3$; calibrated to $CHCl_3$; δ in ppm): 1.11 (t, 6H, CH_3), 2.11-2.21 (m, 2 H, CH_2-P), 3.27-3.35 (q, 2 H, CH_2-Br), 3.85-3.94 (m, 2H, CH_2-O)

^{31}P (162 MHz; $CDCl_3$; calibrated to H_3PO_4; δ in ppm): 25.36

2.3.1.2.2 Step 2: Synthesis of diethyl vinyl phosphonate

In a flask equipped with a reflux condenser, diethyl 2-bromoethyl phosphonate and a 10 % excess of triethyl amine were dissolved in toluene (1 mol/l over all reagents) and heated to reflux (120°C bath temperature). Within minutes a white precipitate began to form, namely triethyl amine hydrochloride. The reaction mixture was stirred for 7 h, then allowed to cool to room temperature and stirred over night. The salt was removed by filtration over a glass frit and extracted with toluene. The extract was joined with the filtrate and the solvent removed in a rotary evaporator. The product was obtained by distillation as a clear, colorless liquid (b.p. 39°C/0.1 mbar): 87 %

NMR

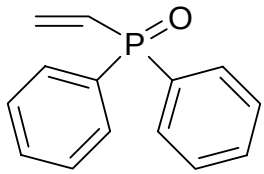
^{1}H (400 MHz; $CDCl_3$; calibrated to $CHCl_3$; δ in ppm): 1.09 (t, 6H, CH_3), 3.81-3.89 (m, 4 H, CH_2-O), 5.78-6.10 (m, 3 H, vinyl)

^{13}C (100 MHz; $CDCl_3$; calibrated to $CHCl_3$; δ in ppm):15.14 (CH_3), 60.44 (CH_2-O), 124.32+126.87 (CH-P), 133.89 (CH_2(Vinyl))

^{31}P (162 MHz; $CDCl_3$; calibrated to H_3PO_4; δ in ppm): 17.87

Elemental Analysis: C: 43.33 %; H: 8.03 % (calculated for $C_6H_{13}O_3P$, M: 164.14 g/mol: C: 43.91%; H: 7.98%; O: 29.24%; P: 18.87%)

2.3.1.3 Synthesis of diphenyl vinyl phosphine oxide (DVPO)



2.3.1.3.1 Step 1: Synthesis of diphenyl vinyl phosphine[66]

In a two-necked Schlenk flask equipped with reflux condenser and a dropping funnel, a solution of vinyl magnesium bromide (1 equivalent, 1 mol/l in THF) was cooled to 0°C. 0.5 equ. of chloro diphenyl phosphine in dry THF (2.6 mol/l) were slowly added (30 min), then the reaction mixture was allowed to warm to room temperature, stirred for 1 h and finally heated to reflux. After 20 h overall reaction time, the excess of Grignard reagent was hydrolyzed with 10 wt% NH_4Cl solution at 0°C. After phase separation the organic layer was washed with water, the aqueous phase extracted three times with toluene and the extract added to the organic phase. The latter was then dried over Na_2SO_4 and most of the solvent removed under reduced pressure. The raw product was distilled under vacuum to yield a clear, colorless liquid (b.p. 88°C/0.1 mbar): 78 %

NMR

^1H (400 MHz; $CDCl_3$; calibrated to $CHCl_3$; δ in ppm): 5.62-5.71 (ddd, 1H, CH_{cis}), 5.90-6.02 (ddd, 1H, CH_{trans}), 6.63-6.73 (dt, 1 H, CH-P), 7.34-7.49 (m, 6 H, $CH_{aromat.\ ortho,para}$), 7.41-7.46 (m, 4 H, $CH_{aromat.\ meta}$)

^{31}P (162 MHz; $CDCl_3$; calibrated to H_3PO_4; δ in ppm): -10.16

2.3.1.3.2 Step 2: Synthesis of diphenyl vinyl phosphine oxide

In a two-necked Schlenk flask equipped with reflux condenser and a dropping funnel, diphenhyl vinyl phosphine was dissolved in toluene. A 30 wt% aqueous solution of H_2O_2 was slowly added at room temperature and then the reagents heated to reflux. After 5 h the mixture was allowed to cool to room temperature and poured into 100 ml of water. A white precipitate formed at the interface of the aqueous and the organic layer. It was removed by filtration and proved to be pure product. The aqueous phase was washed three times with toluene, the combined organic solutions dried over Na_2SO_4 and most of the solvent removed. Another fraction of pure product precipitated from the concentrated solution. After filtration the rest of the solvent was removed from the mother liquor to yield another product fraction. Overall yield was therefore 94 %.

NMR

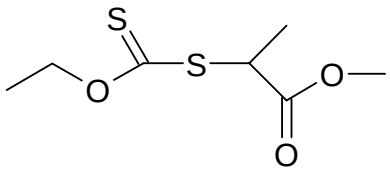
^{1}H (400 MHz; $CDCl_3$; calibrated to $CHCl_3$; δ in ppm): 6.21-6.38 (m, 2H, $CH_{2,vinyl}$), 6.60-6.75 (m, 1H, CH-P), 7.43-7.55 (m, 6 H, $CH_{aromat.\ ortho,para}$), 767.-7.74 (m, 4 H, $CH_{aromat.\ meta}$)

^{13}C (100 MHz; $CDCl_3$; calibrated to $CHCl_3$; δ in ppm): 128.15+128.27 ($CH_{aromat.\ meta}$), 130.34+131.51 ($CH_{,vinyl}$), 130.84+130.94 ($CH_{aromat.\ ortho}$), 131.31 ($CH_{aromat.\ ipso}$) 131.51 ($CH_{aromat.\ para}$), 134.29 ($CH_{2,vinyl}$ m)

^{31}P (162 MHz; $CDCl_3$; calibrated to H_3PO_4; δ in ppm): 24.33

Elemental Analysis: C: 73.69 %, H: 5.84 % (calculated for $C_{14}H_{13}OP$, M: 228.23 g/mol: C: 73.68%; H: 5.74%; O: 7.01%; P: 13.57%)

2.3.1.4 Synthesis of ethyl-α-(O-ethylxanthyl)propionate (X)



In a 1 l two-necked Schlenk flask equipped with reflux condenser, a solution of methyl α-bromopropionate (1 equivalent) in ethanol (0.6 mol/l) was cooled to 0°C. Potassium O-ethylxanthate (1.1 equ.) was slowly added and the reaction mixture stirred for 4 h at 0°C. Then water was added to dissolve the precipitated potassium salt. The aqueous solution was extracted three times with ether/pentane (1:2) and the extract concentrated in a rotary evaporator.

The product was recovered as a pale yellow liquid: 90 %

NMR

^{1}H (400 MHz; $CDCl_3$; calibrated to $CHCl_3$; δ in ppm): 1.41 (t, 3H, $\underline{CH_3}CH_2$), 1.54 (d, 3H, $\underline{CH_3}CH$), 3.75 (s, 3 H, CH_3O), 4.41 (q, 1 H, CH-S), 4.66 (dq, 1 H, CH_2-O)

^{13}C (100 MHz; $CDCl_3$; calibrated to $CHCl_3$; δ in ppm): 15.0 ($\underline{CH_3}CH_2$), 18.2 ($\underline{CH_3}CH$), 38.1 (CH-S), 53.3 (CH_3O), 69.3 (CH_2-O), 170.1 (C=O), 210.3 (C=S)

2.3.2 Polymerization

2.3.2.1 Radical Polymerization

Radical polymerization was performed both in bulk and in solution, using AiBN (only in solution) and DBO as starters.

To rule out autopolymerization, a sample of monomer was heated to reaction temperature without any initiator. No polymerization occurred, but discolored, slightly decomposed monomer was recovered.

To reduce the influence of oxygen, in all experiments the monomer was degassed prior to the polymerization and the reaction performed under an argon atmosphere.

For bulk polymerization standard conditions were as follows: A Schlenk flask was charged with 26 mmol (5 g in case of DIVP) of monomer mixed with 1 mol ‰ DBO, heated to 135 °C and stirred at this temperature for 24-72 h. Then the reaction mixture was allowed to cool to room temperature, stirred over night and unreacted monomer removed by distillation. The resultant polymer was dried under vacuum.

In solution: 26 mmol of monomer were dissolved in 60 ml of dry and degassed toluene, 1 mol% of AiBN added, and the solution heated to 70°C for 8 h. The reaction mixture was allowed to cool to room temperature, stirred over night and the solvent removed using a rotary evaporator. Monomer residues were removed by distillation and the resultant polymer was dried under vacuum.

The polymer obtained in these experiments was a golden to brown oil, due to low molecular weight and partial decomposition.

2.3.2.2 Controlled Radical Polymerization

Controlled radical polymerization was performed both in bulk and in solution, using AiBN/xanthate mixtures and DBO/TEMPO mixtures – with and without addition of acetyl acetate (AcOAc) – as initiators. Reaction procedures were the same as for the normal radical polymerizations, using the bulk condition for the DBO/TEMPO/AcOAc, and DBO/TEMPO systems and the solution technique for AiBN/xanthate.

2.3.2.3 UV-Induced Polymerization

UV-induced polymerization was performed similar to the thermically induced radical polymerization in solution, with the exception that instead of heating, the solution was irradiated with 150 W of UV-light (266 nm). An inbuilt cooling mantle assured that despite the vicinity of the powerful lamp, temperature inside the reaction vessel did not rise significantly above room temperature. In place of the initiator in the first experiments 1 mol%

benzophenone (sensibilizator) was added to induce autopolymerization. Later the photolysis of AiBN supplied the initiating radicals.

2.3.2.4 Emulsion Polymerization

16 mmol (3 g DIVP) monomer were dispersed in 60 ml of demineralized and degassed water, 1 mol % of $K_2S_2O_8$ added, and the solution heated to reflux for 24 h. The reaction mixture was allowed to cool to room temperature, stirred over night and the solvent removed using a rotary evaporator. The resultant polymer was then dried under vacuum.

2.3.2.5 Anionic Polymerization

Anionic polymerization was performed solely in solution. General procedures were as follows: 26 mmol of monomer were dissolved in 60 ml of thoroughly dried and degassed solvent, the solution brought to the desired temperature and 1 mol % of initiator added. Brightly colored anions formed, ranging from intense yellow for DIVP and DEVP to deep, dark red for DVPO. The solution was held at the appropriate temperature for 8 h, then 1 ml of methanol was added to quench the reaction, the color of the anion disappearing immediately. The reaction mixture was allowed to reach room temperature, stirred over night and the solvent removed using a rotary evaporator. The resultant polymer was then dried under vacuum.

In order to test the system, styrene was polymerized under the same conditions, the resultant polymer having an Mn as could be expected from the ratio monomer : initiator, and an Mw/Mn of 1.06. While the latter is not exactly what theory predicts for a truly living system, it was treated as sufficiently close to the ideal to serve as a standard for the reproducibility of the system.

All vessels used for anionic polymerization were dried at elevated temperatures (110°C) and under vacuum overnight, then purged with argon and kept under argon all the time. All solvents were dried at least twice by stirring over $LiAlH_4$ or sodium/benzoephenone at room temperature overnight in an argon atmosphere, followed by stirring under reflux for several hours and subsequent distillation. The distilled solvent was degassed thoroughly and stored under argon. Styrene was dried by stirring over $LiAlH_4$ at room temperature overnight under an argon atmosphere, then condensed into a storage vessel under reduced pressure. Monomers susceptible to reduction were dried several times over active aluminum oxide with subsequent distillation.

Whenever possible the whole polymerization reaction was performed inside a glovebox with an argon atmosphere, an oxygen content of less than 0.1 ppm and a humidity level of 0.3 ppm H_2O.

2.3.2.6 Copolymerizations

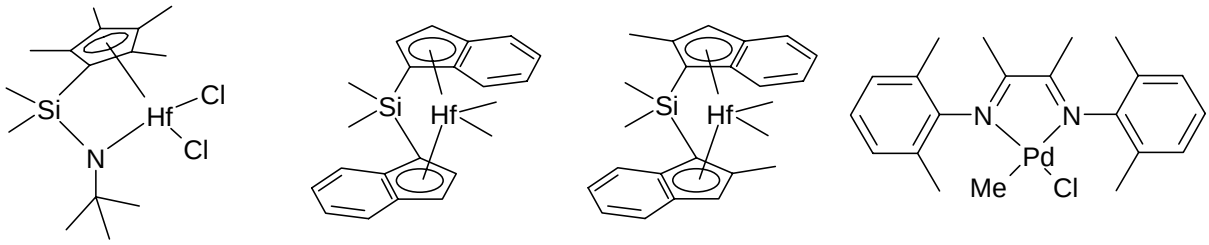
Copolymerizations were performed identically to homopolymerizations. For random copolymers equimolar mixtures of monomers were dissolved to produce the same molar concentration as used in the homopolymerizations and processed as described above. For block copolymers, one monomer was dissolved and initiated first and the second added after half of the reaction time. Again the total concentration was set in the same way as for the homopolymers and equally divided among both monomers.

2.3.2.7 Catalytic Polymerization

Catalyst 1 (Figure 40) was used both for homopolymerization experiments with DIVP and for copolymerization attempts with ethylene. For homopolymerizations general procedures were as follows: A 2 μM catalyst solution in toluene was pretreated with TIBA to create the active species. 15 mmol of monomer were dissolved in 5 ml of thoroughly dried and degassed toluene and 2.5 ml of catalyst solution added. A six-fold excess of activator (trityl-tetrakis-(pentafluorophenyl)-borate) was added to start the reaction and the reaction mixture stirred at room temperature for 3 days.

Catalysts 2 and 3 were activated with equimolar amounts of tris-(pentafluorophenyl)-borane and the reaction performed at 0°C. Initiator to monomer ratio was 1 to 100, no TIBA was added. Otherwise the procedure was mostly identical.

The palladium catalyst (4) was activated with sodium-tetrakis-(pentafluorophenyl)-borate and used for polymerization at room temperature. Otherwise see hafnocenes 2 and 3.



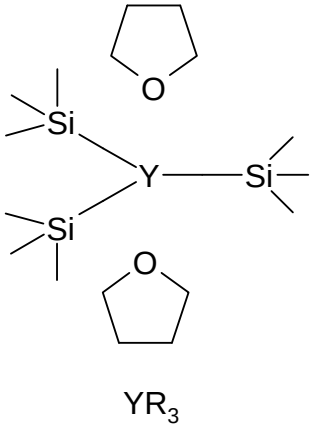
1 **2** **3** **4**

Figure 40: Various catalysts used for polymerization of DIVP

No polymers were obtained in all these experiments.

Lanthanide catalysts, on the other hand, were able to homopolymerize DIVP. Several different catalysts were successfully used in Dr. Rabe's lab[67], the catalyst YR_3 (see Figure 41, synthesized by Dr. Rabe's group and used as received) was used in the course of this thesis. General procedure as follows: the respective amount of catalyst (1 mol‰ to 1 mol%) was dissolved in 10 ml toluene and 5 mmol monomer added. The solution was then stirred at

room temperature for 8-72 h, quenched with methanol and the solvent removed under reduced pressure.



YR_3

Figure 41: YR_3

Copolymerization attempts with ethylene were nevertheless unsuccessful.

2.3.3 Hydrolysis of phosphonate polymers

While the phosphonate ester group is stable against H_2O and 1 molar solutions of HCl, acetic acid, Na_2CO_3, LiOH, NaOH and KOH for 24 h at 60°C, it is readily cleaved by refluxing concentrated hydrochloric acid.

General procedure used: A phosphonate polymer sample was suspended in concentrated hydrochloric acid under vigorous stirring. The reaction mixture was then brought to reflux and stirred at this temperature for 8 h. After cooling to room temperature, the excess acid was removed under reduced pressure, the polymer dissolved in pure water and again dried under reduced pressure to remove traces of HCl.

2.3.4 Complexation

For the complexation experiments in bulk, a solution of 5 wt% polymer in ethanol was prepared and the metal salts added. If a precipitate formed, it was removed by filtration, otherwise the solvent was removed and the residue studied by EDX and electron microscopy. The thin film experiment was performed in Prof. Volkmer's group. There glass slides were placed in the wells of a multi-well plate and 1 ml of an aqueous 10 mM $CaCl_2$ solution added. Then variable amounts of PVPA stock solution (30 wt%) between 110 - 200 μl were added, together with 200-x μl (x = amount of stock solution) water. The plate was placed in a CO_2 atmosphere for 12 h, and then the resultant $CaCO_3$ crystals washed with water and dried on air.

2.4 References

[1] Ford-Moore A.H.; Williams J.H.; *J. Chem. Soc.*; **1947**; 1465-1467

[2] Kosolapoff G.M.; ; *J. Am. Chem. Soc.;* **1948;** 70; 1971-1972

[3] Berlin K.D.; Butler G.B.; ; *J. Org. Chem*.; **1961**; 26/2; 2537-2538

[4] Arcus C.L.; Matthews R.J.S; *J. Chem. Soc.*; **1956**; 4607-4612

[5] Cooper R.S.; Patent: US 3,035,096; **1962**

[6] Allcock H.R.; Kugel R.L.; *J. Polym. Sci., Part A: Polym. Chem.;* **1963;** 1; 3627-3642

[7] Chanda M., Roy S.K., *In Plastics Technology Handbook, 3rd ed*; Marcel Dekker, Inc.; **1998**; p.98-103.

[8] Crosby R.C.; Flowers L.I.; Odle R.R., DeRudder J.L., Lin Y.G.; *Patent: EP 683200A1*; **1995**

[9] Braybrook J. H.; Nicholson J. W.; *J. Mater. Chem.* **1993**; 3/4; 361-365

[10] BASF product description, October 2006

[11] Tan J.; Gemeinhart R.A.; Ma M., Saltzman W.M.; *Biomaterials*; **2005**; 26; 3663-3671

[12] Nicholson J.W.; Czarnecka B.; Limaowska-Shaw H.; *J. Oral Rehabil.*; **2003**; 30; 160-164

[13] Gusev V.I.; Sophi V.F.; Minigulov R.M.; Khim. Vysokomol. Soedin. Neftekhim. (conference paper); **1973**

[14] Kraft P.; Yuen P.S.; ; *Patent: DE 2452369 19750522;* **1975**

[15] Levin Yu. A.; Gozman I.P.; Gaziaova L.Kh., Khristoforova Ya. I., Yagfarova T.A., Byl'ev V.A., Ivanuv B.E.; *Vysokomo.l Soedin., Ser. A;* **1974;** 16/1; 71-76
Levin Yu. A.; Fridman G.B.; Ivanov B. E.; *Vysokomol. Soedin., Ser. A;* **1975;** 17/4; 845-854.

[16] Marvel C.S.; Wright J.C.; *J. Polym. Sci.;* **1952;** 8 / 2; 255-256

[17] Miller R.C.; Patent: US 3,299,015; **1967**

[18] Pike R.M.; Cohen R.A.; *J. Polym. Sci*; **1960;** 44; 531-538

[19] Rabinowitz R. ; Pellon J.; J. Org. Chem.; **1961**; 26; 4623-4636
Rabinowitz R. ; Marcus R.; Pellon J.; *J. Polym. Sci. Part A;* **1964;** 2; 1233-1240

[20] Tsetlin B.L.; Medved T.Ya.; Chikishev Yu. G., Polikarpov Yu M., Rafikov S.R. Kabachnik M.I.; Vysokomol. Soedin.; **1961**; 3; 1117-1118

[21] Welch F.J.; Paxton H.J.; *J. Polym. Sci. Part A;* **1965;** 3; 3427-3437
Welch F.J.; *Patent: US 3,519,607;* **1970;**
Welch F.J.; Paxton H.J.; *Patent: US 3,422,079 ;* **1969;**
Welch F.J.; Paxton H.J.; *Patent: US 3,312,674;* **1967;**

[22] Patent: GB 909666 19621031; ; **1962**

[23] Ellis J.; Wilson A.D.; *J. Mat. Sci. Lett.;* **1990;** 9; 1058-1060

[24] Akinmade A.O.; Braybrook J.H.; Nicholson J.W.; *Polymer International;* **1994;** 34; 81-88

[25] Dadey E.J.; Patent: WO 97/37/680; **1997**

[26] Fennel B.; Hill R.G.; Akinmade A.; *Dent. Mater.;* **1998;** 14; 358-364

[27] Khouw-Liu V.H.W.; Anstice H.M.; Pearson G.J.; *J. Dent.;* **1999;** 27/5; 351-357
Khouw-Liu V.H.W.; Anstice H.M.; Pearson G.J.; *J. Dent.;* **1999;** 27/5; 359-365

[28] Greish Y.E., Brown P.W.; *J. Am. Ceram. Soc.;* **2002**, 85/7; 1738-1744
Greish Y.E., Brown P.W.; *Biomaterials;* **2001;** 22; 807-816

[29] Tan J.; Gemeinhart R.A.; Ma M., Saltzman W.M.; *Biomaterials;* **2005;** 26; 3663-3671

[30] Schultz P.B.; Guthrie J.D.; McCleary S.F., Marinelli J.M., Bovard F.S.; *Patent: US 2004/0043158 A1;* **2004**

[31] Nagarajan R.; Tripathy S.; Kumar J.; *Macromolecules;* **2000;** 33; 9542-47

[32] Zhou X.; Goh S.H.; Lee S.Y.; *Polymer;* **1997;** 38/21; 5333-5338
Lu Z.; Goh S.H.; Lee S.Y., ; *Macromol. Chem. Phys.;* **1999;** 200; 1515-1522
Luo X.; Goh S.H.; Lee S.Y., Tan K.L.; *Macromolecules;* **1998;** 31; 3251-3254
Liu Y.; Goh S.H.; Lee S.Y., Huan C.H.A.; *J. Polym. Sci.: Part B: Polym. Phys.;* **2000;** 38; 501-508

[33] Ebdon J.R.; Price D.; Hunt B.J., Joseph P., Gao F., Milnes G.J., Cunliffe L.K; *Polym. Degrad. Stab.;* **2000;** 69 / 3; 267-277

[34] Wu Q.; Weiss R.A.; *J. Polym. Sci.: Part B: Polym. Phys.*; **2004;** 42; 3628-3641

[35] Minami T.; Motoyoshiya J.; *Synthesis*; **1992**; 4; 333-349

[36] Gimbert C.; Lumbierres M.; Marchi C.; Moreno-Manas M.; Sebastian R. M.; Vallribera A.; *Tetrahedron*; **2005**; 61; 36;8598-8605.

[37] Cowie J.M.G.; Chemie und Physik der synthetischen Polymere; Friedr. Vieweg & Sohn Verlagsgesellschaft mbH, Braunschweig/Wiesbaden; **1997**

[38] Hiemenz P.C.; Polymer Chemistry; Marcel Dekker, Inc., New York; **1984**

[39] Fischer H.; *Chem. Rev*.; **2001**; 101; 3581-3610

[40] Georges M. K. ; Veregin R.P.N.; Kazmaier P.M., Hamer G.K.; *Macromolecules;* **1993;** 26; 2987-2988

[41] Malmström E.; Miller R.D.; Hawker C.J.; *Tetrahedron ;* **1997;** 53/45; 15225-1536

[42] Hawker C. J.; Bosman A.W.; Hart E.; *Chem. Rev.;* **2001;** 101; 3661-3688

[43] Kamigaito M.; Ando T.; Sawamoto M.; *Chem. Rev.;* **2001;** 101; 3689-3745

[44] Destarac M.; Taton D.; *40th International Symposium on Macromolecules (Paris, July 4 - 9, 2004);* **2004**

[45] Corpart P.; Charmot D.; Zard S.Z., Biadatti T., Michelet D.; *Patent: US 6,153,705;* **2000**

[46] Kuran W.; Principles of Coordination Polymerisation; John Wiley & Sons, Chichester; **2001**

[47] Gibson, V.C.; Spitzmesser S. K.; *Chem. Rev*.; **2003**; 103; 283-315

[48] Yasuda H.; Yamamoto H.; Yokota K.; Miyake S.; Nakamura A.; *J. Am. Chem. Soc.;* **1992,** 114, 4908-4910

[49] Yasuda H.; Yamamoto H.; Yamashita M.; Yokota K.; Nakamura A.; Mijake S.; Kai Y.; Kanehisa N.; *Macromolecules;* **1993;** 26; 7134-7143

[50] Desurmont G.; Tanaka M.; Li Y.; Yasuda H.; Tokimitsu T. ; Tone S. ; Yanagase A.; *J. Polym. Sci.: Part A: Polym. Chem.*; **2000**; 38; 4095-4109

[51] Yasuda H.; *J. Polym. Sci.: Part A: Polym. Chem.*; **2001;** 39; 1955-1969

[52] Collins, S.; Ward D.G.; *J. Am. Chem. Soc.;* **1992**; 114; 5460-5462

[53] Caporaso L.; Gracia-Budira J.; Cavallo L.; *J. Am. Chem. Soc.;* **2006**; 128; 16649-16654

[54] Webster O.W.; Hertler W.R.; Sogah D.Y., Farnham W.B., RajanBabu T.V.; *J. Am. Chem. Soc;* **1983**; 105; 5706-5708

[55] Mecking S.; Johnson L.K.; Wang L.; Brookhart M.; *J. Am. Chem. Soc.;* **1998**; 120; 888-899

[56] Rabinowitz R. ; Pellon J.; J. Org. Chem.; **1961**; 26; 4623-4636

[57] Emsley, Hall; *Chemistry of Phosphorus*; Harper&Row, London, **1976**; p.365

[58] Leute M., Rieger B., *Macromol. Rapid Comm*., submitted

[59] Minami T.; Motoyoshiya J.; *Synthesis*; ; **1992**; 4; 333-349

[60] Minami T.; Okauchi T.; Kouno R.; *Synthesis*; **2001**; 3; 349-357

[61] Inoue H.; Tsubouchi H.; Nagaoka Y., Tomioka K.; *Tetrahedron*; **2002**; 58; 83-90

[62] Poly(vinylphosphonic acid), 30% soln.; Polyscience Inc., Warrington, PA

[63] Liu Y.,Goh S.H.,Lee S.Y., Huan C.H.A., *J. Polym. Sci., Part B: Polym. Phys.,* **2000,** 38, 501-508

Luo X. Hu X. Y Zhaoa, S. H. Goh, X. D. Li ,*Polymer*, **2003**, 44/18, 5285-5291

[64] Nagarajan R.,Tripathy S.,Kumar J., *Macromolecules,* **2000,** 33, 9542-47

[65] Gottlieb H.E.; Kotlyar V.; Nudelman A.; *J. Org. Chem.*; **1997**, 62/21; 7512-7515

[66] Paetzhold E.; Michalik M.; Oehme G.; *J. Prakt. Chem. /Chem-Ztg;* **1997;** 339; 38-43

[67] PD Dr. Gerd Rabe, TU München, Department of Chemistry, Section of Inorganic Chemistry, *Personal Communication*, **2007**

3 Hyperbranched Polymers with Phosphorus at the Branching Points

3.1 Introduction

Literature concerning dendritic polymers, that is macromolecules with highly branched tree-like structures, can be found under key words such as arborols, cascade molecules or starburst dendrimers. Terminology had to be developed as the field evolved, so especially the early years (mid 1980s to late 1990s) use a confusing variety of denominations for the object of interest. To quote one of the grand old men of the field: “This was also the period that rich imagination not only flourished in the science but also in the nomenclature of these compounds.”[1] To clarify matters, here a short definition of the relevant terms.

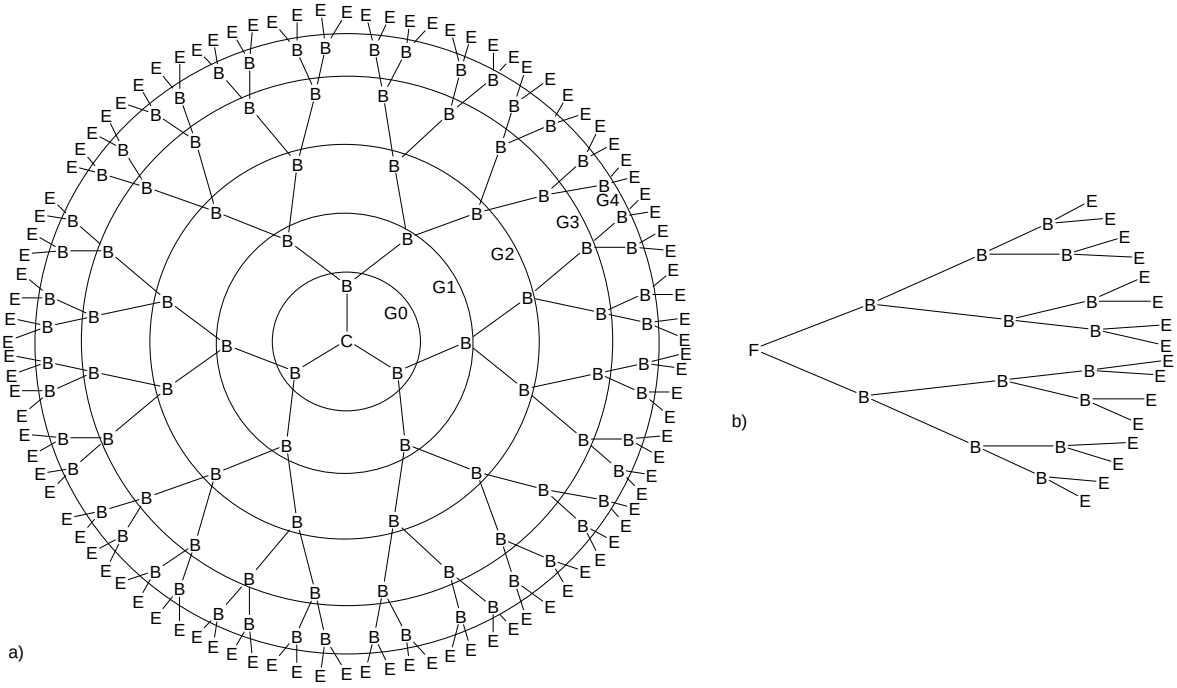


Figure 42: a) 4th generation (G4) Dendrimer; C: core unit, B: branching point, E: endgroup; b) Dendron; F: focal unit

Dendrimers (see Figure 42) are perfectly branched molecules, prepared by step-wise assembly of outer layers (generations) around a multifunctional core molecule. Since the conversion has to be 100 % in order to guarantee a defect-free structure, and the number of reactive centers in the outermost layer increases exponentially with each generation, the synthesis becomes more challenging with every step. In return, dendrimers may potentially approach structural and molar mass unity, a feature otherwise unique to biological macromolecules. Due to their unusual, globular, perfectly branched structure, combined with a high number of functional groups on the surface, excellent solubility, and very low solution

viscosity, dendrimers have attracted keen interest during the last years. They are intensively discussed for applications such as carrier molecules for pharmaceuticals[2,3] or even gene therapy vectors[4] and as model compounds for biopolymers, but also for sensor devices[5] and catalysis[6,7].

Dendrimers are mostly prepared by following a synthetic 'algorithm'. Two main synthetic routes are currently in use: The divergent growth method starts at a central, multifunctional core, building up additional layers (generations) step by step around it. In each generation, the number of functional groups (protected during the attachment step) increases exponentially with generation number. The second route, convergent growth, relies on the synthesis of dendrimer segments which in the final step are connected to a multifunctional core molecule. As the segments are assembled from the outside in, towards the focal unit, the number of functional groups which have to react is reduced. But again an elaborate, step-by-step synthesis is required. The inhibitively complicated synthesis of dendrimers is their major drawback, restricting their suitability for large scale application.

Dendrons differ from dendrimers in such that their focal point is not the center of a sphere but the tip of a cone. Dendrons may be regarded as dendrimers segments, in some cases even building blocks, see the convergent growth approach above.

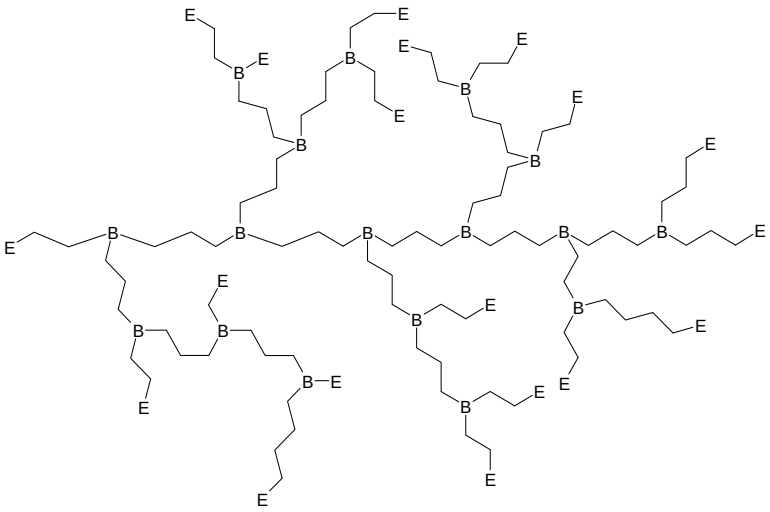


Figure 43: Hyperbranched polymer; B: branching point, E: endgroup

Hyperbranched polymers (Figure 43), on the other hand, are produced by a one-step, one-pot synthesis. Their structure is much less defined; they exhibit an extremely broad molar mass distribution and lower branching (controlled by statistics, 50% branching is the theoretical upper limit for an AB_2 monomer compared to the 100% of a dendrimer)[8]. By name, only a limited analogy to dendrimers and a close relation to classical polymers is implied, for historical reasons. Though known since at least the early 1950s, when Flory published a detailed theoretical description of the polycondensation of AB_2 or even AB_x

monomers, hyperbranched polymers found little interest until the 1980s, when – after the first synthesis of dendrimers[9] – highly branched systems were shown to exhibit remarkable material properties. While the dendrimers emerged from academic research, hyperbranched polymers were from the start related to industrial R&D, due to their less complicated, though by no means trivial, synthesis. Nevertheless, or maybe for that reason, they were seen as poor relatives of the perfect dendrimers, ill-defined and of little interest. Yet they share many characteristics with dendrimers, such as a higher solubility and low solution viscosity compared to linear analogues and a high number of functional end groups, and therefore today both groups are often discussed together, using the term dentritic polymers. The combination of the comparably easy synthesis and the property profile open applications for hyperbranched polymers in the fields of blends, coatings, and specialty polymers.

3.1.1 Dendritic polymers containing phosphorus

A large variety of dendrimers has been synthesized up to now. Architectures with structural units containing ether, amide, ester, quaternary phosphine, siloxane or transition metall functionalities were prepared[10,11].

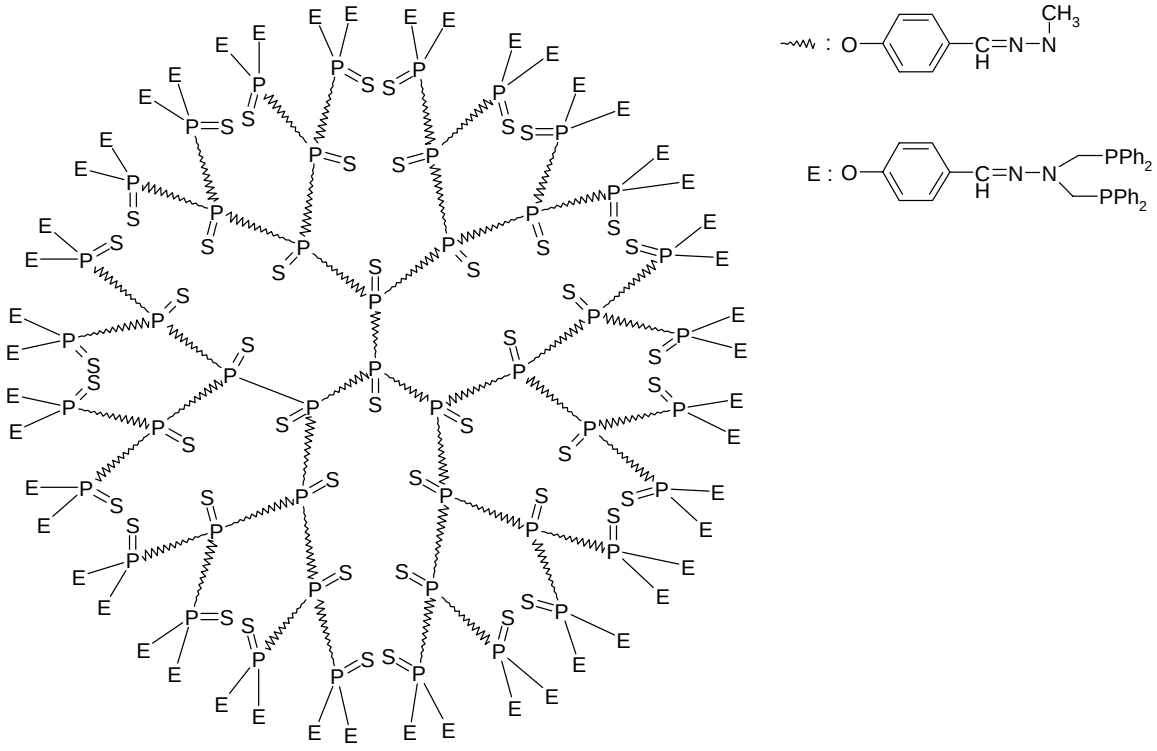


Figure 44: Typical phosphorus-containing dendrimer

Dendrimers[3,5,12,13] and dendrons[6,14] containing tertiary phosphorus moieties (Figure 44), either throughout the entire structure or as additional functional groups attached to the surface, are known in literature, with the most extensive work done by the group of

Caminade and Majoral[3,5,12,14,15,16,17,18,19], but examples of true hyperbranched polymers remain scarce.

One method for the synthesis of highly branched structures is the addition of a primary phosphine to a vinyl group bearing a phosphonate ester functionality. As both primary and secondary phosphines can undergo this reaction, the addition is performed twice with the same phosphine resulting in the first branching point. Reduction with lithium aluminium hydride converts the phosphonate esters to phosphines and, by multiple repetitions of the same reaction scheme, subsequent generations may be added.

The approach of this work was now to produce AB_2 monomers bearing functionalities that would allow an analogue reaction for the one-step synthesis of a phosphorus-containing hyperbranched polymer. In a slight variation of the above mentioned reaction, we chose A to be a P-H bond and B the carbon double bond (Figure 45), as secondary phosphines and phosphites are more stable than primary ones and therefore more liable to be synthesized and reacted in a controlled manner in the presence of another reactive functional group.

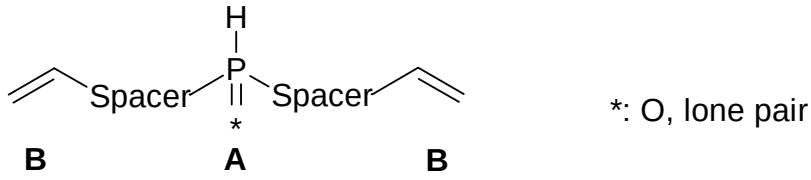
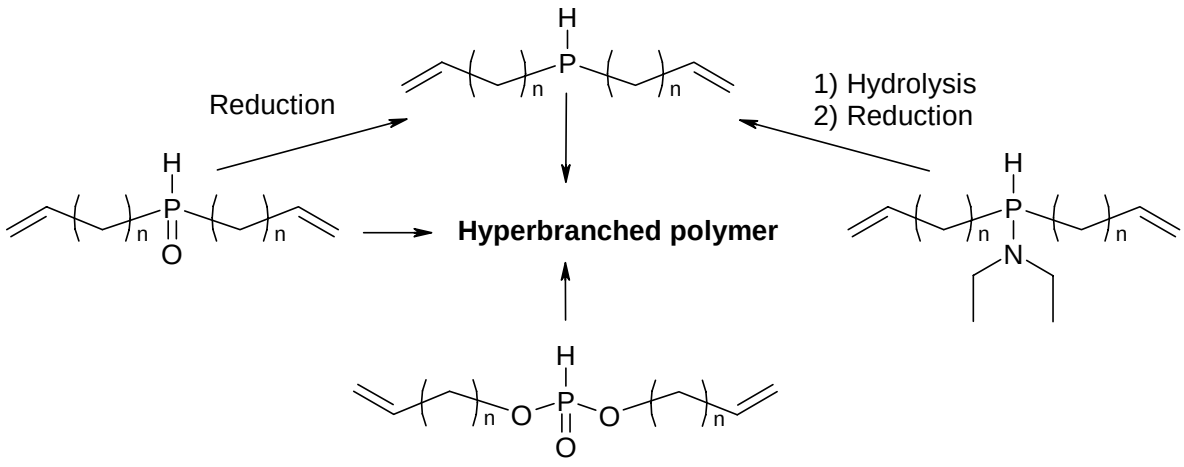


Figure 45: Phosphorus-based AB_2 monomers

Since not only phosphines may undergo this reaction, but also phosphine oxides and phosphites, a portfolio of different monomers was synthesized and investigated (see Scheme 15). The resultant hyperbranched polymer contains not only numerous phosphorus functionalities within its bulk, but also vinyl endgroups which may be further modified to suit future applications. The length of the alkyl spacer between the two functional groups was varied in length between short (n: 1) over medium (n: 3, 4) to long chains (n: 9).

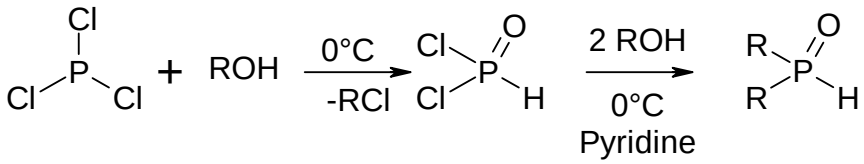
Scheme 15



Phosphites are susceptible to hydrolysis, which would disintegrate the polymer. This can be a vulnerability or a desired trait, depending on the application. Phosphines are sensitive to oxidation but the best complexing agents, and a phosphorus(III) at the bulk of the hyperbranched polymer might be shielded enough to be stabilized against air.

Synthesis of the phosphite AB_2 monomers is straight forward[20] (see Scheme 16).

Scheme 16

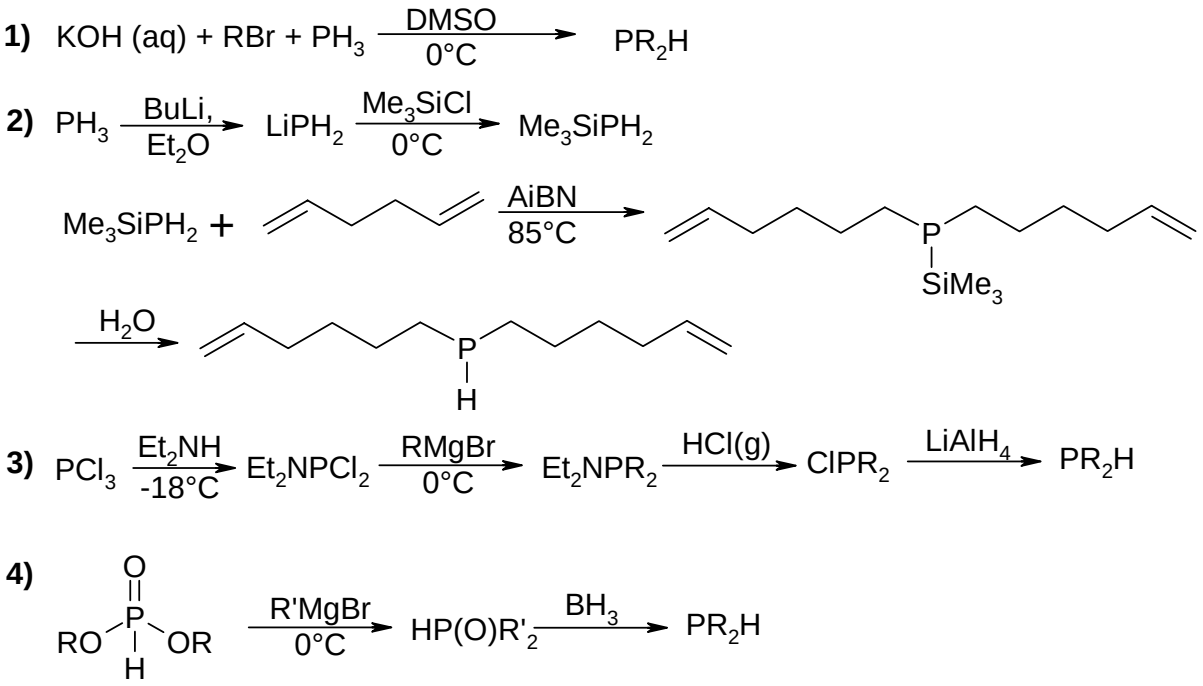


To use different alcohols in the first step and in the second, though seen in literature[21], was found to be not feasible here, as mixed products were always present and diminished the yield.

Phosphines and their derivatives can be produced by several different routes (Scheme 17):

1) By selective alkylation of PH_3 under phase transfer conditions[22]
2) By addition of dialkenes to a silylphosphide and subsequent hydrolysis[23,24]
3) Via diethylamino-dichloro-phosphine, nucleophile substitution and reduction[25,26]
4) Via an phosphine oxide with subsequent reduction[27,28]

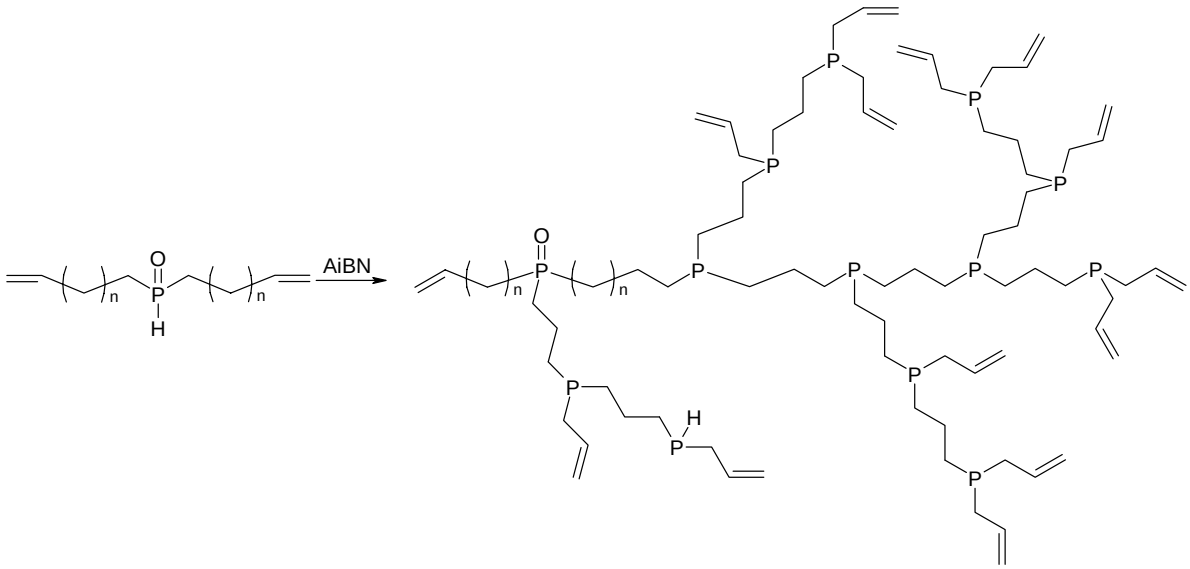
Scheme 17



Due to the dangers involved when working with the poisonous and spontaneously ignitable gas PH_3, the first two routes were not chosen for further pursuit, but the other two were both given a try.

Polymerization may be induced both by radicals or by acid / base catalysis[25,29,30], both methods were used in our experiments. An example of the reaction and the proposed product is shown below (Scheme 18), P-O double bonds and chain length variable were omitted on all but the first unit for clarity reasons.

Scheme 18



3.2 Results and Discussion

The investigations into this field of phosphorus-containing macromolecules ran into a two-fold obstacle. Either the monomer synthesis was unsuccessful, or the resulting monomers failed to form polymers. Neither the phosphine oxides nor the dichloro-diethylamino-phosphine derivatives could be synthesized with any degree of reproducibility, side reactions always resulted in a broad spectrum of secondary products (many missing either the carbon double bond, the P-H bond, or both) and minimal yields. The phosphites, on the other hand, were readily prepared, but would not form polymers, neither radically via AiBN, nor base-catalyzed. While the former reactions simply retained the monomer, in the latter cases hydrolysis took place, destroying part of the monomer.

3.2.1 Dialkenylphosphine oxides

While the synthesis of diallylphosphine oxide failed completely, dihexenylphosphine oxide could be prepared in moderate quantities, but was shown to undergo autopolymerization even at 4°C under an argon atmosphere. A controlled polymerization with AiBN was also performed, the resultant polymer was soluble, which indicates no or very little cross-linking. MALDI spectroscopy (Figure 46) showed species with a degree of polymerization between 3 and 15; the degree of branching could not be determined.

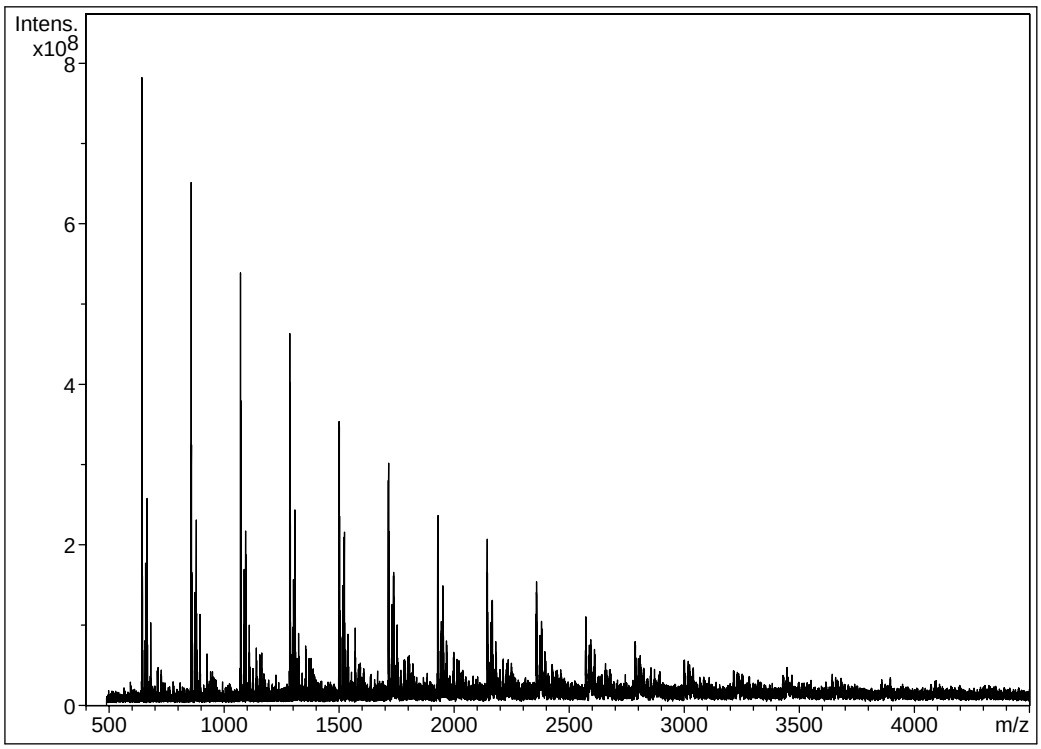


Figure 46: MALDI spectrum of the dihexenylphosphine oxide oligomer

Diundecenylphosphine oxide could also be prepared, but no polymer could be identified after reaction with AiBN.

Reduction of the phosphine oxide monomers or polymers was unsuccessful, too. $LiAlH_4$, $LiAlH_4/CeCl_3$[31] and $HSiCl_3$[32,33] all resulted in side products with missing alkene bonds but not in phosphines.

3.2.2 Dialkenyl phosphites

Diallyl, dipentenyl, dihexenyl and diundecenyl phosphites were all prepared in good to quantitative yields. Polymerization attempts both with AiBN and with sodium methanolate, on the other hand, failed. The diallyl phosphite monomer reacted readily but the resultant polymer was insoluble, most probably due to cross-linking. The longer alkyl chain spacers reduced the reactivity to a point where the monomer was recovered completely unchanged after reaction with AiBN and slightly hydrolyzed after reaction with NaOMe.

3.2.3 Dialkenyl-diethylamino-phosphines

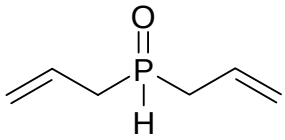
Dichloro-diethylamino-phosphine is easily prepared by the reaction of PCl_3 and diethyl amine. Its derivatization using Grignard reagents or lithium organyls, followed by hydrolysis and reduction, is a literature-known technique for the synthesis of secondary phosphines. The best yields are reported for aromates[25,34,35]; for alkyl substituted phosphines yields – if given at all – drop steadily with increasing chain length[36,37,38,39] and examples of alkenyl derivates are very scarce and limited to vinyl and allyl[40,41,42]. No longer chain alkenyl diethylamino-phosphines could be synthesized during this work, all products were mixtures of several phosphorus species as seen in the ^{31}P NMR and yields were generally low. Separation attempts, using either distillation or column chromatography over silica, resulted in even more undefined mixtures.

3.3 Experimental section

3.3.1 Monomer synthesis

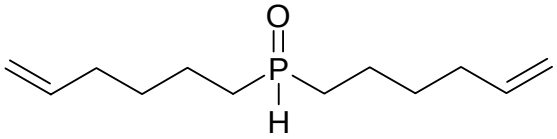
In order to prepare monomers procedures were employed, known from literature[20,,26,27,28].

3.3.1.1 Diallylphosphine oxide



To a stirred suspension of magnesium turnings (5 equivalents) in diethyl ether (0.1 g/ ml) ether a solution of allyl bromide (5 mol/l, 4 equ.) was added dropwise at 0°C (ice bath). The mixture was then stirred for several hours at room temperature, allowing the Grignard reagent to form. The solution was removed from the excess of magnesium, filtrated, and cooled again to 0°C. A solution of diethyl phosphite in diethyl ether (2 mol/l, 1.8 equ.) was added dropwise, and a lively reaction was observed. A white precipitate (magnesium salts) formed after a short time. Following the addition the reaction mixture was stirred at room temperature for four hours, and then the precipitate hydrolyzed with 25 mol% H_2SO_4. The phases were separated, the organic layer washed with saturated $NaHCO_3$-solution, then with NaBr-solution, and finally at least two times with water. The aqueous phase was extracted with diethyl ether, the combined organic extracts washed two times with water, then dried over Na_2SO_4, and the solvent removed under reduced pressure. The resultant liquid contained no carbon double bonds (NMR); the expected product was not formed.

3.3.1.2 Dihexenylphosphine oxide



To a stirred suspension of magnesium turnings (5 equivalents) in diethyl ether (0.1 g/ ml) a solution of hexenyl bromide (5 mol/l, 4 equ.) in diethyl ether was added dropwise at 0°C (ice bath). The mixture was then stirred for several hours at room temperature, allowing the Grignard reagent to form. The solution was removed from the excess of magnesium, filtrated, and cooled again to 0°C. A solution of diethyl phosphite in diethyl ether (2 mol/l, 1.8 equ.) was added dropwise, and a lively reaction was observed. A white precipitate (magnesium salts) formed after a short time. Following the addition, the reaction mixture was stirred at

room temperature for four hours, and then the precipitate hydrolyzed with 25 mol% H_2SO_4. The phases were separated, the organic layer washed with saturated $NaHCO_3$-solution, then with NaBr-solution and finally at least two times with water. The aqueous phase was extracted with diethyl ether. The combined organic phases were dried over Na_2SO_4, and the solvent removed under reduced pressure. A clear colorless liquid and some white solid were retained, containing unreacted educts as well as several phosphorus species, as seen in the ^{31}P NMR. Raw yield: 80%.

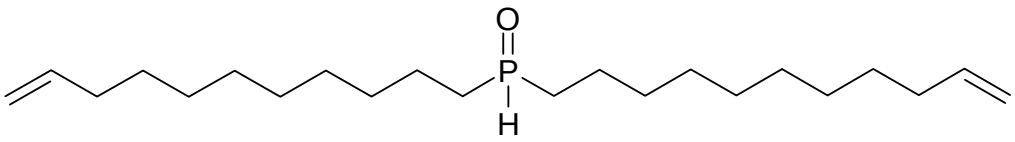
NMR

^{1}H (400 MHz; $CDCl_3$; calibrated to $CHCl_3$; δ in ppm): 1.48-1.82 (m, 12H, alkyl chain), 2.06-2.12 (q, 4H, CH_2-Vinyl), 5.02-5.04 (dd, 4 H, CH_2=), 5.72-5.80 (m, 2 H, CH=), 6.27+7.38 (2s, 1H, P-H)

^{13}C (100 MHz; $CDCl_3$; calibrated to $CHCl_3$; δ in ppm):21.01 (**CH_2**CH_2-Vinyl), 28.13+28.24 (CH_2-P), 29.68 (**CH_2**CH_2-P), 32.99, (CH_2-Vinyl), 114.90 (CH_2=), 137.73 (CH=)

^{31}P (162 MHz; $CDCl_3$; calibrated to H_3PO_4; δ in ppm): 35.17

3.3.1.3 Diundecenylphosphine oxide



To a stirred suspension of magnesium turnings (5 equivalents) in diethyl ether (0.1 g/ ml) a solution of undecenyl bromide in diethyl ether (3 mol/l, 4 equ.) was added dropwise at 0°C (ice bath). The mixture was then stirred for several hours at room temperature, allowing the Grignard reagent to form. The solution was removed from the excess of magnesium, filtrated, and cooled again to 0°C. A solution of diethyl phosphite in diethyl ether (2 mol/l, 1.8 equ.) was added dropwise, and a lively reaction was observed. A white precipitate (magnesium salts) formed after a short time. Following the addition, the reaction mixture was stirred at room temperature for four hours, and then the precipitate hydrolyzed with 25 mol% H_2SO_4. The phases were separated, the organic layer washed with saturated $NaHCO_3$-solution, then with NaBr-solution and finally at least two times with water. The aqueous phase was extracted with diethyl ether. A white solid formed during the extraction process, containing high amounts of the desired product. More product was recovered after removal of the solvents from the dried organic extracts. Overall yield: 70 %

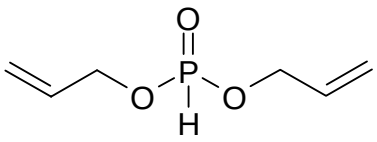
NMR

^{1}H (400 MHz; $CDCl_3$; calibrated to $CHCl_3$; δ in ppm): 1.20-1.38 (m, 12H, alkyl chain), 1.50-1.60 (m, 4H, **CH_2**CH_2-P)1.66-1.70 (m, 4H, CH_2-P), 1.95-2.00 (q, 4H, CH_2-Vinyl), 4.85-4.95 (dd, 4 H, CH_2=), 5.68-5.79 (m, 2 H, CH=), 6.22+7.34 (2s, 1H, P-H)

^{13}C (100 MHz; $CDCl_3$; calibrated to $CHCl_3$; δ in ppm): 27.82+28.47 (CH_2-P), 21.69, 28.77, 28.93, 29.00, 29.16, 29.26 (alkyl chain)**,** 30.49+30.63 (**CH_2**CH_2-P), 33.65 (CH_2-Vinyl), 114.05 (CH_2=), 138.93 (CH=)

^{31}P (162 MHz; $CDCl_3$; calibrated to H_3PO_4; δ in ppm): 36.25

3.3.1.4 Diallyl phosphite



To a solution of phosphorus trichloride in dichloromethane (1.65 mol/l) a solution of allyl alcohol (2.5 mol/l, 1 equivalent) was added dropwise at 0°C (ice bath). HCl gas evolved and was neutralized in a gas washing bottle with saturated $NaHCO_3$(aq). After 2 h, a solution of both allyl alcohol (2 equ.) and dry pyridine (2.1 equ.) in dichloromethane (10 mol/l over all reagents) was added dropwise at 0°C (ice bath). A white precipitate (pyridine hydrochloride) was formed immediately. The mixture was then stirred overnight at room temperature. A small amount of water were used to dissolve the precipitate, the phases were separated and the organic layer washed three times with water. The combined aqueous phases were extracted with dichloromethane. The organic extract was dried over Na_2SO_4, and the solvent removed under reduced pressure and the product recovered as a clear yellow liquid, 88 %.

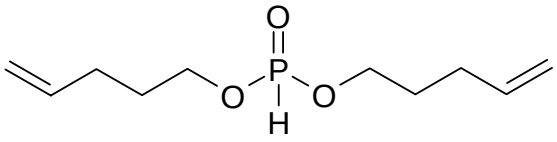
NMR

^{1}H (400 MHz; $CDCl_3$; calibrated to $CHCl_3$; δ in ppm): 4.42-4.49 (q, 4 H, CH_2-O), 5.12-5.27 (dd, 4 H, CH_2=), 5.576-5.85 (m, 2 H, CH=), 5.88+7.63 (2s, 1H, P-H)

^{13}C (100 MHz; $CDCl_3$; calibrated to $CHCl_3$; δ in ppm): 65.91 (CH_2-O), 118.29 (CH_2=), 132.16 (CH=)

^{31}P (162 MHz; $CDCl_3$; calibrated to H_3PO_4; δ in ppm): 8.49

3.3.1.5 Dipentenyl phosphite



To a solution of phosphorus trichloride in dichloromethane (1.66 mol/l) a solution of 4-pentenyl-1-ol (2.5 mol/l, 1 equivalent) was added dropwise at 0°C (ice bath). HCl gas evolved and was neutralized in a gas washing bottle with saturated $NaHCO_3$(aq). After 2 h, a solution of both 4-pentenyl-1-ol (2 equ.) and dry pyridine (2.1 equ.) in dichloromethane (10 mol/l over all reagents) was added dropwise at 0°C (ice bath). A white precipitate (pyridine hydrochloride) was formed immediately. The mixture was then stirred overnight at room temperature. A small amount of water were used to dissolve the precipitate, the phases were

separated and the organic layer washed three times with water. The combined aqueous phases were extracted with dichloromethane. The organic extract was dried over Na_2SO_4, then the solvent was removed under reduced pressure and the product recovered as a colorless clear liquid, 95 %.

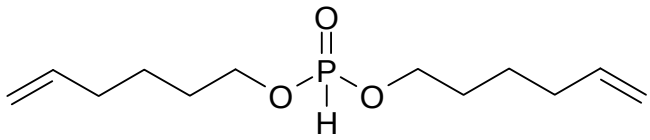
NMR

^{1}H (400 MHz; $CDCl_3$; calibrated to $CHCl_3$; δ in ppm): 1.60-1.67 (m, 4H, **CH_2**CH_2-O), 1.96-2.04 (q, 4H, CH_2-Vinyl), 3.90-3.95 (q, 4 H, CH_2-O), 4.83-4.92 (dd, 4 H, CH_2=), 5.58-5.68 (m, 2 H, CH=), 5.78+7.51 (2s, 1H, P-H)

^{13}C (100 MHz; $CDCl_3$; calibrated to $CHCl_3$; δ in ppm): 29.22 (**CH_2**CH_2-O), 29.28 (CH_2-Vinyl), 64.77 (CH_2-O), 115.37 (CH_2=), 136.74 (CH=)

^{31}P (162 MHz; $CDCl_3$; calibrated to H_3PO_4; δ in ppm): 8.45

3.3.1.6 Dihexenyl phosphite



To a solution of phosphorus trichloride in dichloromethane (1.66 mol/l) a solution of 5-hexenyl-1-ol (2.5 mol/l, 1 equivalent) was added dropwise at 0°C (ice bath). HCl gas evolved and was neutralized in a gas washing bottle with saturated $NaHCO_3$(aq). After 2 h, a solution of both 5-hexenol-1-ol (2 equ.) and dry pyridine (2.1 equ.) in dichloromethane (10 mol/l over all reagents) was added dropwise at 0°C (ice bath). A white precipitate (pyridine hydrochloride) was formed immediately. The mixture was then stirred overnight at room temperature. A small amount of water was used to dissolve the precipitate, the phases were separated and the organic layer washed three times with water. The combined aqueous phases were extracted with dichloromethane. The organic extract was dried over Na_2SO_4, then the solvent was removed under reduced pressure and the product recovered as a clear, pale yellow liquid, 90 %.

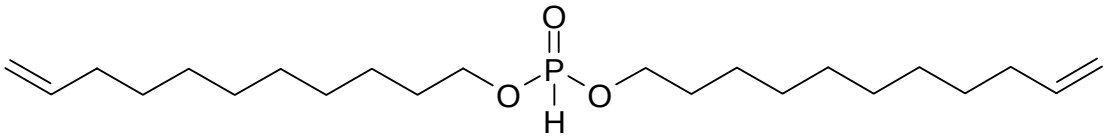
NMR

^{1}H (400 MHz; $CDCl_3$; calibrated to $CHCl_3$; δ in ppm): 1.44-1.47 (m, 4H, **CH_2**CH_2-Vinyl), 1.63-1.71 (m, 4H, **CH_2**CH_2-O), 2.02-2.06 (q, 4H, CH_2-Vinyl), 4.01-4.06 (m, 4 H, CH_2-O), 4.90-5.00 (dd, 4 H, CH_2=), 5.71-5.78 (m, 2 H, CH=), 5.89+7.62 (2s, 1H, P-H)

^{13}C (100 MHz; $CDCl_3$; calibrated to $CHCl_3$; δ in ppm): 24.51 (**CH_2**CH_2-Vinyl), 29.52 (**CH_2**CH_2-O), 32.85, (CH_2-Vinyl), 65.31 (CH_2-O), 114.74 (CH_2=), 137.81 (CH=)

^{31}P (162 MHz; $CDCl_3$; calibrated to H_3PO_4; δ in ppm): 8.35

3.3.1.7 Diundecenyl phosphite



To a solution of phosphorus trichloride in dichloromethane (1.66 mol/l) a solution of 10-undecenyl-1-ol (2.5 mol/l, 1 equivalent) was added dropwise at 0°C (ice bath). HCl gas evolved and was neutralized in a gas washing bottle with saturated $NaHCO_3$(aq). After 2 h, a solution of both 10-undecenyl-1-ol (2 equ.) and dry pyridine (2.1 equ.) in dichloromethane (10 mol/l over all reagents) was added dropwise at 0°C (ice bath). A white precipitate (pyridine hydrochloride) was formed immediately. The mixture was then stirred overnight at room temperature. A small amount of water was used to dissolve the precipitate, the phases were separated and the organic layer washed three times with water. The combined aqueous phases were extracted with dichloromethane. The organic extract was dried over Na_2SO_4, then the solvent was removed under reduced pressure and the product recovered as a clear, pale yellow liquid, 90%.

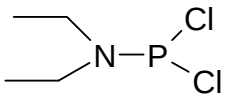
NMR

^{1}H (400 MHz; $CDCl_3$; calibrated to $CHCl_3$; δ in ppm): 1.10-1.24 (m, 12H, alkyl chain), 1.50-1.60 (m, 4H, **CH_2**CH_2-O), 1.75-2.00 (q, 4H, CH_2-Vinyl), 3.85-3.98 (m, 4 H, CH_2-O), 4.74-4.84 (dd, 4 H, CH_2=), 5.59-5.65 (m, 2 H, CH=), 5.75+7.48 (2s, 1H, P-H)

^{13}C (100 MHz; $CDCl_3$; calibrated to $CHCl_3$; δ in ppm): 25.34 (**CH_2**CH_2CH_2-O), 28.75 (**CH_2**CH_2-Vinyl), 28.95, 29.22, 29.29, 29.45 (alkyl chain)**,** 30.25 (**CH_2**CH_2-O), 33.64 (CH_2-Vinyl), 65.61 (CH_2-O), 113.94 (CH_2=), 138.77 (CH=)

^{31}P (162 MHz; $CDCl_3$; calibrated to H_3PO_4; δ in ppm): 8.32

3.3.1.8 Dichloro-diethylamino-phosphine



To a solution of phosphorus trichloride in dry diethyl ether (1.65 mol/l), cooled to a temperature never exceeding –20°C with dry ice / isopropanol, a solution of diethylamine (12.5 mol/l, 2 equivalents) was added dropwise. The mixture was then allowed reach room temperature and stirred for several hours. After removing most of the solvent by distillation (bp. 33°C), the product was recovered by distillation under reduced pressure, bp. 57°C at 0.1 mbar, as a clear colorless liquid. Yield: 88 %

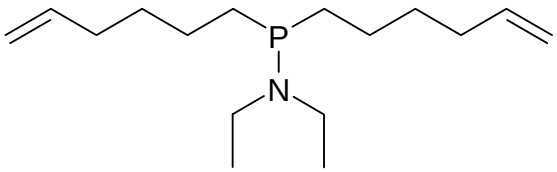
NMR

^{1}H (400 MHz; $CDCl_3$; calibrated to $CHCl_3$; δ in ppm): 1.15 (t, 6H, CH_3), 3.26-3.35 (m, 4H, CH_2)

^{13}C (100 MHz; $CDCl_3$; calibrated to $CHCl_3$; δ in ppm): 14.20 (d, CH_3), 41.81 (d, CH_2)

^{31}P (162 MHz; $CDCl_3$; calibrated to H_3PO_4; δ in ppm): 163.08

3.3.1.9 Dihexenyl-diethylamino-phosphine



To a stirred suspension of magnesium turnings (5 equivalents) in diethyl ether (0.1 g/ml) a solution of hexenyl bromide (3.3 mol/l, 4 equ.) in the same solvent was added dropwise at 0°C (ice bath). The mixture was then stirred for several hours at room temperature, allowing the Grignard reagent to form. The solution was removed from the excess of magnesium, filtrated, and cooled again to 0°C. A solution of dichloro-diethylamino-phosphine (1.5 mol/l, 1.8 equ.) in diethyl ether was added dropwise, and a lively reaction was observed. A white precipitate (magnesium salts) formed immediately. Following the addition the reaction mixture was brought to reflux for four hours, and then stirred at room temperature for another 20 h. The supernatant was removed by syringe, the precipitate extracted four times with 25 ml ether and the extracts combined with the supernatant. After removal of the solvent under reduced pressure, a clear colorless liquid was retained which contained several phosphorus species, as seen in the ^{31}P NMR.

Several trials with both smaller and bigger side groups (ethyl to phenyl groups) failed to produce any desirable products. Both Grignards reagents and lithium alkyls were used. This is partly in accordance with literature finds, that the reaction yields the less product the bigger the attached side groups become, unless the side group is an aromate.

3.3.2 Polymerization

To rule out autopolymerization, a sample of monomer was heated to reaction temperature without any initiator. No polymerization occurred, but discolored, slightly decomposed monomer was recovered.

3.3.2.1 Radical polymerization

5 mmol of monomer were dissolved in 10 ml of dry and degassed toluene, 10 mol% of AiBN added, and the solution heated to 70°C for 24 h. The reaction mixture was allowed to cool to room temperature, stirred over night and the solvent removed under reduced pressure. The resultant polymer was dried under vacuum.

3.3.2.2 Base-catalyzed polymerization

For a base-catalyzed addition of the P-H bond to a carbon double bond, metallic sodium (320 mg / 13.9 mmol) was dissolved in dry methanol (28 ml) to form a solution of sodium methanolate (0.5 M) which was then used as the initiator. The monomers (1-3 mmol) were dissolved in 5 ml of dry and degassed methanol, 10 mol% of MeONa added, and the solution stirred at room temperature for 24 h. The solvent was evaporated and the resultant product investigated by NMR.

3.3.3 Reduction of phosphine oxides

3.3.3.1 $LiAlH_4$

For a reduction with $LiAlH_4$, a slurry of 2.5 equivalents of hydride in dry diethyl ether (1 g / 20 ml) was prepared, and a solution of the respective phosphine oxide (1 equ.) in ether (1 mol/l) added dropwise at 0°C. The mixture was allowed to reach room temperature, stirred overnight and the excess reducing agent removed by filtration. The solvent was removed under reduced pressure. Though a distinct smell of phosphines was observed, no phosphine could be found by NMR (the product was kept under argon at all times), but a loss of vinyl groups was discernible.

3.3.3.2 $LiAlH_4/CeCl_3$

Cerium mediated reductions were performed analogously to those with pure $LiAlH_4$, with the exception that the reducing agent consisted of 2 equ. of $LiAlH_4$ and one equ. of $CeCl_3$ ($CeCl_3$* 7 H_2O dried under vacuum at 120°C to remove the water). No phosphines were observed but a decrease of vinyl protons in the NMR.

3.3.3.3 $HSiCl_3$

Reductions with silico-chloroform were performed in dry acetonitrile. The phosphine oxide and 6 equivalents of tributyl amine were dissolved (1 mol/l over all reagents) and heated to 70°C (bath temperature). $HSiCl_3$ (6 qu.) was added dropwise and the mixture stirred for another 2 h at 70°C. Then it was allowed to cool to romm temperature, the excess reducing agent hydrolyzed with 25 wt% NaOH(aq) and a sticky white precipitate formed. Extraction with dichloromethane and subsequent removal of the solvent under reduced pressure yielded a product similar to those observed for the other reducing agents.

3.4 References

[1] Kim Y.; J.Polym. Sci., Part A: Polym. Chem.; **1998**; 36; 1685-98

[2] Gillies E.R.; Fréchet J. M. J.; *Drug Discovery Today*; **2005**; 10/1; 35-43

[3] Solassol J.; Crozet C.; Perrier V., Leclaire J., Béranger F., Caminade A.-M., Meunier B., Dormont D., Majoral J.-P., Lehmann S.; *J.Gen. Virol.*; **2004**; 85; 1791-1799

[4] Manuta M.; Tan P.H.; Sagoo P., Kashefi K., George A.J.T.; *Nucleic Acids Res*., **2004**; 32; 9; 2730-2739; and references therein

[5] Caminade A.-M.; Majoral J.-P.; *Acc. Chem. Res.*; **2004**; 37/6; 341-348

[6] Miedaner A.; Curtis C.J.; Barkley R.M. ; DuBois D.L.; *Inorg. Chem.*; **1994**; 33; 5482-5490

[7] Dasgupta M.; Peori M.B.; Kakkar A.K.; *Coord. Chem. Rev.*; **2002**; 233-234; 223-235

[8] Flory P.; *J. Am. Chem. Soc.*; **1952**; 74; 2718-2723;

[9] Buhlmeier E.; Wehner W.; Vögtle F.; *Synthesis*; **1978**; 155

[10] Frey H.; Lach C.; Lorenz K.; *Adv. Mater.;* **1998;** 10; 279-291

[11] Jikei M.; Kakimoto M.; ; *Prog. Polym. Sci.;* **2001;** 26; 1233-1285

[12] Caminade A.-M.; Majoral J.-P.; *J. Mat. Chem*.; **2005**; 15; 3643-3649

[13] Engel R.; Rengan K.; Chan C.-S.; *Heteroat.Chem.*; **1993**; 4/2-3; 181-184

[14] Merino S.; Brauge L.; Caminade A.-M., Majoral J.-P., Taton D., Gnanou Y.; *Chem. – Eur. J.*; **2001**; 7/14; 3095-3105

[15] Baradji M.; Kustos M.; Caminade A.-M., Majoral J.-P., Chaudret B.; *Organometallics;* **1997;** 16; 403-410

[16] Blais J.-C.; Turrin C.-O.; Caminade A.-M., Majoral J.P.; *Analytical Chemistry;* **2000;** 72; 0597-5105

[17] Brauge L.; Magro G.; Caminade A.-M., Majoral J.-P.; *J. Am. Chem. Soc ;* **2001;** 123; 6698-6699

[18] Peleshanko S.; Majoral J.-P.; Caminade A.-M., Knoll W., Tsukruk V.; *Polym. Prep.;* **2002;** 43/2; 421

[19] Slany M.; Baradji M.; Casanove M.-J., Caminade A.-M., Majoral J.P., Chaudret B.; *J. Am. Chem. Soc. ;* **1995;** 117; 9764-9765

[20] Kamber M.; Just G.; *Can. J. Chem.;* **1985**; 63; 823-827

[21] Gibbs D.E.; Larsen C.; *Synthesis*; **1984**; 410-413

[22] Langhans K.P., Stelzer O., *Z. Naturforsch., B: Chem. Sci.,* **1990**, 45/2, 203-211

[23] Parshall G.W., Lindsey Jr R.V., *J. Am. Chem. Soc. ,* **1959,** 81, 6273-6275

[24] Schubert D.M., Hackney M. J., Brandt P.F., Norman A.D., *Phosphorus, Sulfur and Silicon,* **1997,** 123, 141-160

[25] U. Meier, *Dissertation University of Ulm*, **2003**

[26] Diemert K.; Kottwitz B.; Kuchen W.; *Phosphorus and Sulfur*; **1986**; 26; 307-320

[27] Arad-Yellin, R.; Zangen, M.; Gottlieb, H.; Warshawsky, A.; *J. Chem. Soc. Dalton Trans*.; **1990,** 7; 2081-2088

[28] Stankevic, M.; Pietrusiewicz, K. M.; *Syn. Lett*.; **2003**; 7; 1012 - 1016

[29] Bunlaksananusorn T.; Knochel P.; ; *Tetrahedron Lett.;* **2002;** 43; 5817-5819

[30] Stacey; Harris; *Org. React*.; **1963**; 13; 150; 218-224

[31] Imamoto T.; Takeyama T.; Kusumoto T.; *Chem. Lett.;* **1985;** ; 1491-1492

[32] Vineyard B.D.; Knowles W.S.; Sabacky M.J., Bachmann G.L., Weinkauff D.J.; *J. Am. Chem. Soc.;* **1977;** 99/18; 5946-5952

[33] Ramsden J.A.; Brown J.M.; ; *Tetrahedron Asymmetry;* **1994;** 5/10; 2033-2044

[34] Appel R.; Eichenhofer K.-W.; *Chem. Ber*.; **1971;** 104; 3859- 3874

[35] RajanBabu, T. V.; Ayers, Timothy A.; Hallidey, Gary A.; You, Kimberly K.; Calabrese, Joseph C.; *J. Org. Chem*.; **1997**; 62; 17; 6012-6028.

[36] Issleib K., Seidel W., *Chem. Ber.;* **1959**; 92, 2681-2694

[37] Petrov,K.A. et al.; *J.Gen.Chem.USSR (Engl.Transl.);* **1963**; 33; 882-884; *Zh. Obshch. Khim*.; **1963**; 33; 3; 896-899

[38] Genkina,G.K. et al.; *J.Gen.Chem.USSR (Engl.Transl.);* **1968**; 38; 2430-2433; *Zh. Obshch. Khim.;* **1968**; 38; 2513-2517.

[39] Voskuil,W.; Arens,J.F.; *Recl. Trav. Chim. Pays-Bas*; **1962**; 81; 993-1008.

[40] King,R.B.; Masler,W.F.; *J. Am. Chem. Soc*.; **1977**; 99; 12; 4001-4008.

[41] Haber, Steffen; Floch, Pascal Le; Mathey, Francois*; J. Chem. Soc. Chem. Commun*.; **1992**; 24; 1799-1800.

[42] Diemert, K.; Kottwitz, B.; Kuchen, W.; *Phosphorus Sulfur*; **1986**; 26; 307-320.

4 Biological tests

4.1 Introduction

A wide range of biocompatible materials – from metals over ceramics to natural and synthetic polymers – are currently in use for medical purposes.

Yet most of these substances were originally developed for applications outside medicine and had to be adapted to their new role in the vicinity of living tissue[1]. Only in recent years novel biomaterials were developed especially for medical use. In particular, artificial polymers are of great interest here, as in many cases special production methods, mainly tailor-made catalysts, allow a fine-tuning of material properties[2,3]. Still, the influence of the foreign body on the living organism has to be carefully evaluated. To be used as biomaterials, the polymers must be free from plasticizers, residue monomers, or catalysts, and should also withstand standard sterilization procedures to exclude the danger of viral or bacterial infections of the implant recipient. Furthermore, biocompatible materials can exhibit properties other than inertness, they may undergo interactions with the surrounding tissues, influencing cell growth, adhesion and differentiation.

A promising class of biocompatible materials are polymers with a phosphorus side group. Combining a stable carbon-carbon-backbone with a functionality mimicking the phosphate groups ubiquitous in living organisms, they might be used in a number of applications. One member of this group, the poly(vinyl phosphonic acid), has already been tested successfully for use in bone or dental cements[4,5,6]. Furthermore, their high thermal stability allows sterilization of these materials by using simply elevated temperatures without the necessity of adding harmful chemicals which then need to be removed again, prior to use.

A major drawback of these polymers is their synthesis. Commercially available poly(vinyl phosphonic acid), which has been used for the tests so far, is produced by a radical polymerization and subsequent hydrolysis. It contains about 15% of monomer residue and several sideproducts. New techniques providing better conversion and a purer polymer are therefore necessary.

Anionic polymerization can be used to produce these results, but is not feasible with the free acid, of course. Therefore vinylphosphonates were used as the starting materials, together with diphenylvinylphosphine oxide as a model compound not susceptible to hydrolysis. The attained poly(vinylphosphonates) were furthermore hydrolyzed to the respective polyacid.

4.2 Results and Discussion[7]

4.2.1 Toxicity

Since toxicity can manifest in various different ways due to the inherent complexity of living organisms, there exists no single test which certifies that the tested materials are nontoxic. Therefore three established assays were chosen to get relevant results about the toxicity of the phosphorus polymer materials:

- Agarose Overlay assay according to ASTM standard F 895 – 84
- A modified MTT (3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazoliumbromide) test
- A modified LDH (Lactate Dehydrogenase) test

These unspecific toxicity tests were combined with leaching tests to investigate the release of potentially harmful substances from the polymer samples into the surrounding medium.

4.2.1.1 Agarose Overlay Assay

Neutral red, a pH-indicator, is taken up by viable cells into the intact acidic lysosomes, resulting in a distinctive red coloring of vital cells. Nonvital cells remain colorless.

Poly(diisopropylvinyl phosphonate) (PIVP), poly(diphenylvinylphosphine oxide) (PVPO) and poly(vinylphosphonic acid) (PVPA) were examined. It was found that no lysosomes of the negative control (0.3%) were damaged and therefore colorless, and the same was true – within the variety of biological tests – of the three polymer compounds. All lysosomes of the positive control (99.4%) were damaged. The three materials were investigated in addition to a biocompatible (glass) and a nonbiocompatible control (copper). PVPO and PVPA did not differ from the glass control; PIVP, while producing colored cells like the other samples, showed morphological peculiarities (see Figure 47). The cells showed protrusions and swelling of the cell organelles, most likely mitochondria. This may indicate a high metabolic activity. The results of the MTT and LDH tests also suggest this.

4.2.1.2 MTT Reduction Assay (Modified)

This test assesses cell viability in terms of metabolic activity. Colorless MTT (2-(4,5-Dimethylthiazol-2-yl)-3,5-diphenyltetrazolium bromide) is taken up and converted by the active dehydrogenases of the undamaged mitochondria into a blue formazan product. High values in the MTT test relay to a high number of cells with intact mitochondrial dehydrogenases.

The results were compared with the result of a negative control (pure PBS), which was defined as 1.00 (100%). No cell damage could be assessed when cells were exposed to eluates from the test materials.

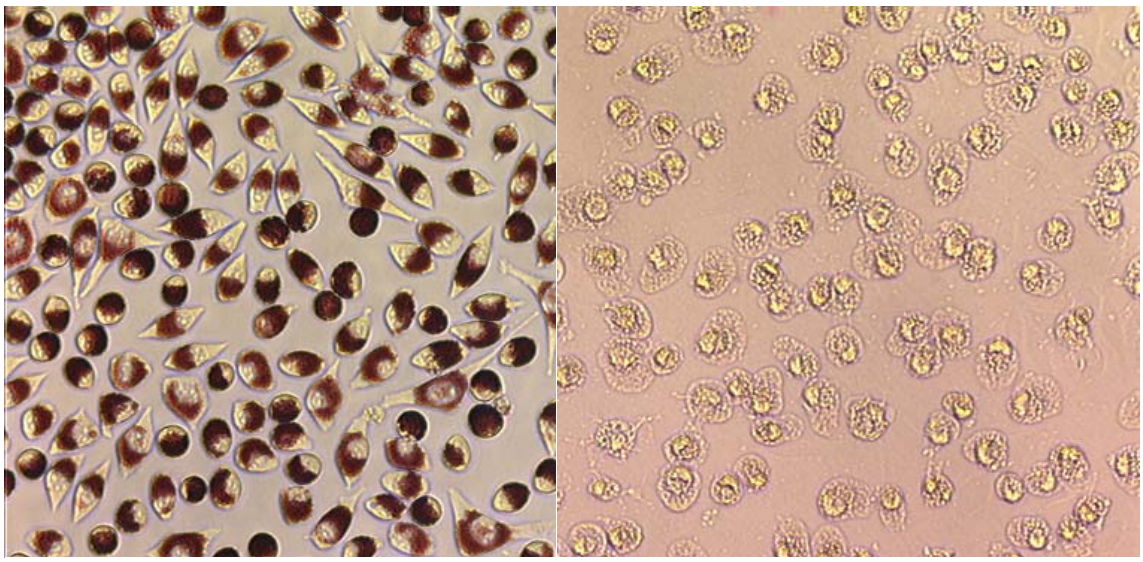
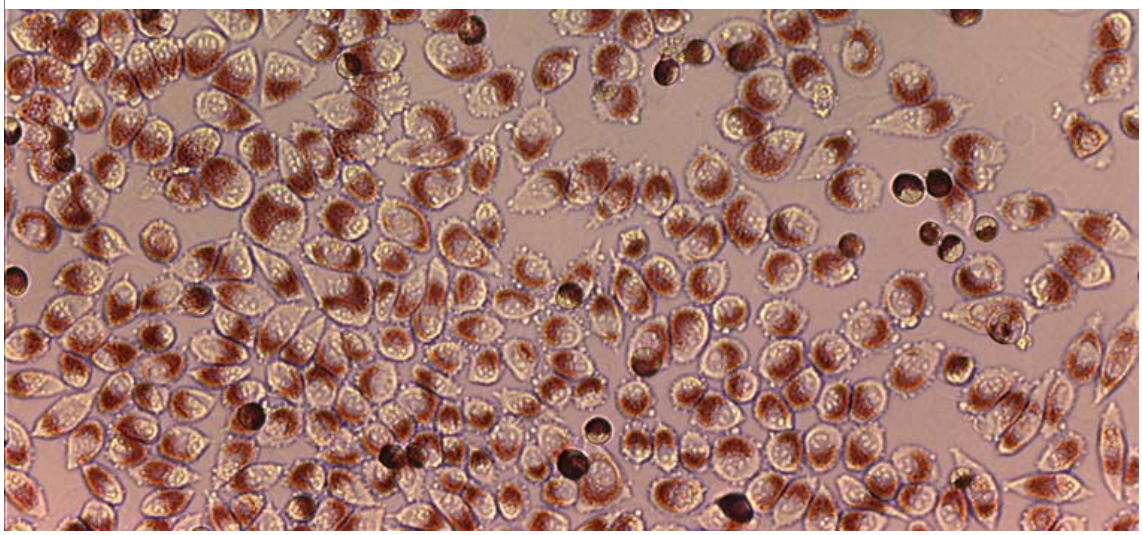


Figure 47: Agarose Overlay Assay. Controls (negative left, positive right) above; PIVP results below. Protrusions and swollen cell organelles are clearly visible



4.2.1.3 The Modified LDH Test

The lactate dehydrogenase test (LDH test) utilizes the quantitative release of the enzyme LDH from damaged/lysed cells into the cell culture medium. The enzyme then initiates a cascade of reactions finally resulting in a red formazan product. Like the MTT test, this allows to evaluate the influence of the soluble compounds of the polymers. High values in the MTT test relay to a high number of cells with damaged cell membranes.

In comparison to a negative control, no significant cell damage was caused by the phosphorus containing polymers.

All taken, the polymers can be said to be nontoxic and biocompatible, for detailed data see Table 7.

Table 7: Results of the toxicity tests

Test		PIVP	σ[6]	PVPO	σ	PVPA	σ
LDH [mU]	10 µl	1.212	0.069	1.12	0.297	1.17	0.17
	100 µl	1.123	0.066	1.025	0.036	1.147	0.005
MTT OD	10 µl	1.285	0.092	0.961	0.154	0.968	0.244
	100 µl	0.974	0.051	1.08	0.085	0.935	0.091
Agarose-Overlay	Untreated	1.08	0.060	1.01	0.045	1.02	0.286
	Extracted with PBS for 24 h	1.05	0.142	1.02	0.196	1.03	0.228

[6] Standard deviation

4.2.2 Bone Marrow Cell development

Human bone marrow cells were cultured for 90 days on polymer coated glass and their differentiation routes and matrix production studied.

General morphology

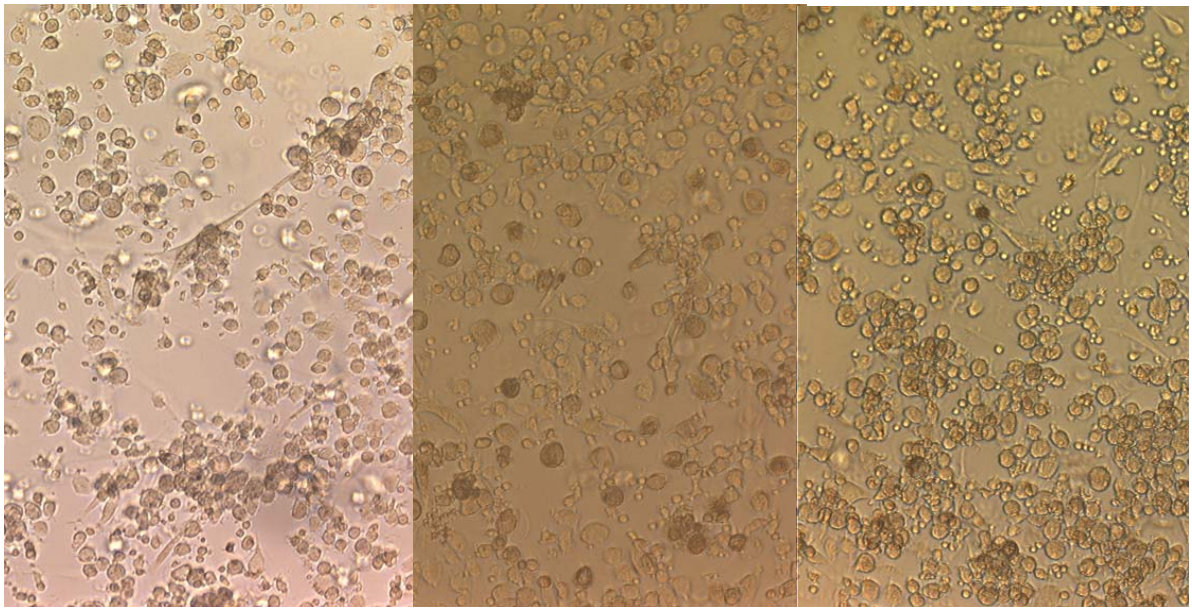


Figure 48: Light microscopic image of living human bone marrow cells on phosphorus polymers. PIVP (left), PVPO (middle), PVPA (right), magnification 100x

Using light microscopy for studing the morphology of native cell colonies on the polymer samples (Figure 48), the following was found:

- A high cell population density on both PVPO and PVPA, combined with a high number of clusters, feeder cells and small round cells (presumably stem cells or progenitor cells). Overall cell density was considerably lower on PIVP.
- Most cells on PIVP were middle-sized, presumably capable of ossification, and agglomerated into clusters. Feeder cells and small round cells were less prominent than on the other two materials.
- The PVPO material was uniformly covered with human bone marrow cells, clusters were formed only sporadically. Noticeable was the high number of club-shaped cells (fibroblasts), feeder cells appeared more rarely, small round and middle-sized cells in medium densities.
- Large numbers of small round cells (progenitor cells) were visible on PVPA. Few clusters were formed and fibroblastic cells were scarce. Feeder cells and middle-sized cells were present in medium numbers.

Histochemical studies

4.2.2.1 Silver staining as per von Kossa

This staining technique for bone tissue replaces the calcium ions in carbonates and phosphates with silver ions, followed by a reduction of the ions to metallic silver. Dark areas (dark brown – black) denote strong mineralization and therefore ossified tissue. Fibrous tissue is colored yellowish-brown.

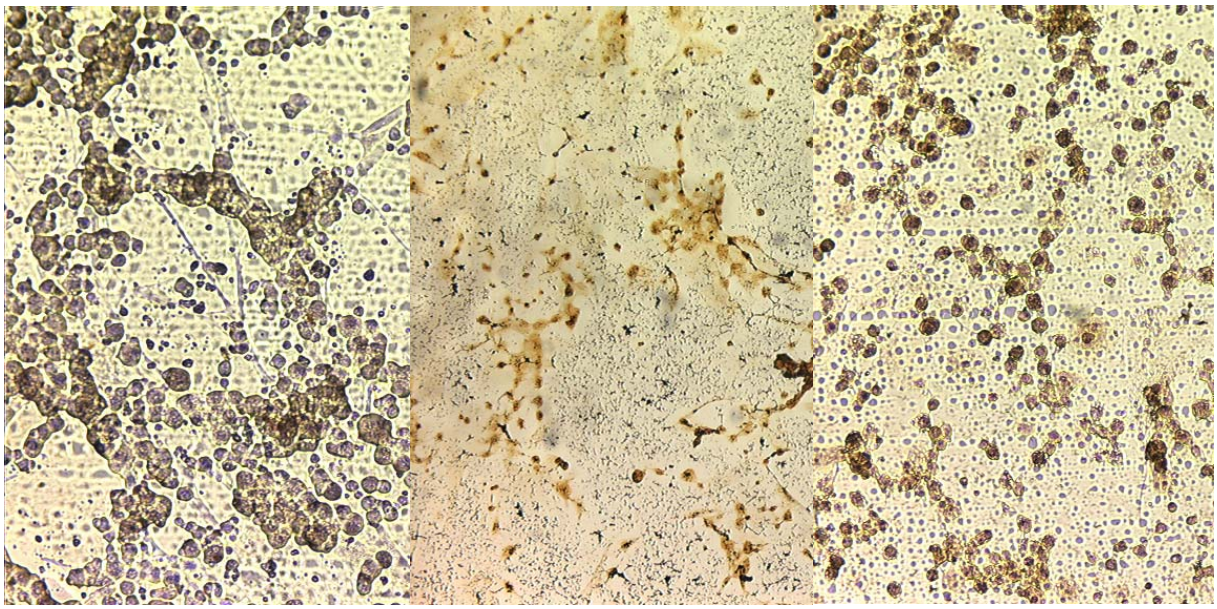


Figure 49: Von Kossa staining of human bone marrow cells grown on phosphorus polymers. PIVP (left), PVPO (middle), PVPA (right), magnification 100x

Due to the frequent intensive washing necessary in this staining procedure, a marked loss of (unattached) cells occurred, most evident for the PVPO samples.

PVPO

The few remaining cells on PVPO were mostly stained yellow-brown, club-shaped and agglomerated in closely packed, „fischzugartige“ assemblies, all typical for fibroblasts. Combined with the results from the native samples, this may lead to the assumption that the stem cells / progenitor cells in the bone marrow underwent a differentiation and/or selection toward fibroblasts on PVPO.

PVPA

The loss of cells due to washing was considerable less on PVPA than on PVPO. Some yellow-brown areas were visible but most cells were stained dark brown, denoting mineralization. Clusters were rare.

PIVP

Most cells on PIVP were stained dark brown to black. Notable was the high number of feeder cells, forming the substrate for numerous clusters. Medium amounts of small progenitor cells were present even after processing. Generally speaking, cells on this material seemed to be unusually large.

4.2.2.2 Lipid – marking with Sudan III

The high lipophily of Sudan III (1-(4-Phenylazo-phenylazo)-[2]naphthol) is used to distinguish fat cells, which might produce false positives in Von Kossa staining, from mineralized bone cells.

No fat cells were found on PIVP, only minimal amounts on PVPA and few on PVPO. Therefore the darkly stained cells are most likely cells beginning ossification and forming first mineralization products.

Immunhistology

4.2.2.3 Detection of stem cells / progenitor cells by anti-CD 34 antibody

Antibodies against the cell membrane cluster CD 34 were used to detect the presence of adhering stem or progenitor cells on the different materials.

CD 34 positive cells were found solely on PVPA. The lack of detectable cells on PIVP and PVPO may be attributed to the fact that no or very few progenitor cells adhered on these substances or that the cells had already differentiated beyond this stage. Another possible explanation would be the loss of only loosely attached cells during the staining procedure or a combination of these three possibilities.

4.2.2.4 Bone Sialo Protein (BSP) – detection by specific antibody

Bone Sialo Protein (BSP) is a marker for early osteoblastic cells. It is detectable in bone-forming cells even in early differentiation stages. So far it was not found in progenitor cells.

BSP staining was most pronounced on PIVP, less on PVPA and least on PVPO. This is another indication that PIVP induced a differentiation towards osteoblastic cells. Significantly less cells followed this route on PVPA and even less on PVPO.

4.2.2.5 Osteocalcin – detection by specific antibody

Cells on PVPO showed only low levels of osteocalcin. Somewhat more was detectable on PVPA. In the tissue samples grown on PIVP, on the other hand, a very strong osteocalcin

production was found (Figure 50). Since this material also gave rise to the highest concentration of BSP, the differentiation towards bone tissue and ossification was most pronounced on this polymer.

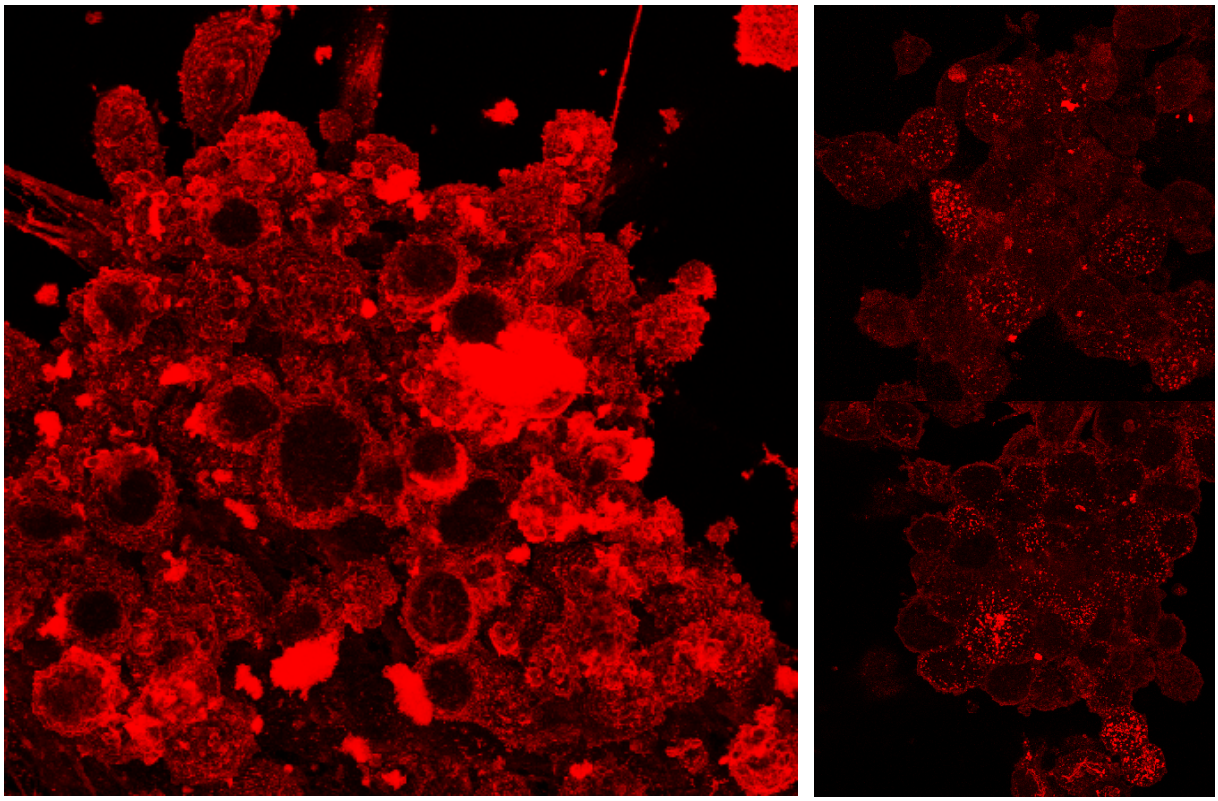


Figure 50: Osteocalcin antibody staining of human bone marrow cells grown on phosphorus polymers. PIVP (left), PVPO (right above), PVPA (right below), magnification 100x

Conclusions

Summarizing, the following can be said about the phosphorus containing polymers:
The three different materials had different properties in terms of cell adhesion, and probably caused the seeded human bone marrow cells to differentiate in different directions.

- PVPO could find application where a strong cell proliferation is desired without strong adhesion on the substrate.
- PVPA might be useful to retain a reservoir of undifferentiated progenitor cells.
- PIVP induces a rapid and extensive conversion of progenitor cells into osteoblastic tissue.

Cell adhesion on the substrate is an important factor in the description of these materials. Especially PVPO showed a high cell density loss due to washing when the situation in the native state and after the von Kossa staining were compared. Surprisingly this low adhesion is combined with a strong cell proliferation on this polymer. The mechanisms underlying these characteristic features are as yet unknown but should be further investigated in the future.

4.3 Experimental section

All biological tests were performed in the ZIBMT– Dept. Biomaterials, University of Ulm. Solutions of poly(diisopropylvinyl phosphonate) (PIVP), poly(diphenylvinylphosphine oxide) (PPVPO) and poly(vinylphosphonic acid) (PVPA) – the latter prepared by hydrolysis of poly(diisopropylvinyl phosphonate) – in methanol (10 mg/ml) were prepared and spin-coated on thin cover glass dics (Ø 12 mm). Electron microscopy was used to monitor the formation and regularity of the resultant films and EDX to verify the elemental composition.

4.3.1 Sterilization

The polymer samples were sterilized using high temperatures. The materials were put into a Heraeus Hot Air Sterilizer for two hours at 210 °C.

4.3.2 Cell Culturing

L929 cell-line:

The mouse fibroblast cells L929 were propagated under standard conditions (5% CO_2, 95% humidity, 36°C) in Eagle's Minimal Essential Medium (MEM), supplemented with 10% fetal calf serum (FCS) and 10 IU penicillin sulfate/ml medium, 100 mg Streptomycin sulfate /ml medium and 2mMol L-glutamine. When the L929 cells reached confluency, they were passaged with a split ratio of 1:20.

Human bone marrow cells:

Femoral bone marrow was harvested during implantation of the first total hip replacement prosthesis of otherwise healthy arthrotic patients. These cells were cultured for 90 days under standard conditions in Iscoves Modified Dulbeccos Medium (IMDM) supplemented with fetal calf serum (12.5 %), horse serum (HS, 12.5%), Hydrocortisone (2.4 ng/ml), Certomycin (50 mg/ L9 L-Glutamin (292.5 ng/ml) and NaHCO3 (0.3%). Interleukin 3 and Granulocyte-Macrophage-Colony-Stimulating-Factor (GM-CFS, 10 ng/ml) were added to promote growth. For the tests, cells were seeded in a density of 100000 cells/cm² polymer material.

4.3.3 Unspecific Toxicity Tests

The leaching tests were performed in phosphate buffered saline (PBS) with a physiological pH (7,2 – 7,4) and ion concentration (280 – 300 mOsmol). The polymer materials were extracted with PBS for 24 h at 37°C under steady rocking. Both extracted and untreated

samples were tested for toxicity in the Agarose Overlay Assay, the extracts were used in the MTT and LDH tests.

4.3.3.1 Agarose Overlay Assay

Procedure[8]: L929 mouse fibroblasts were seeded on polystyrene Petri dishes (Ø 2.7 cm) and cultivated for about 48 hours till they formed an incomplete monolayer. The cells were then covered with 2 ml of an agarose-medium. When the agarose layer was solidified the cells were incubated with 0.01% neutral red solution (1 ml) for 30 minutes at 37 °C. The solution was removed and the polymer samples were placed on top of the agarose layer. After another 24 hours of incubation the cultures were examined under an inverted microscope (Olympus, IMT-2) for cytolysis and cellular changes at a magnification of 200. Uncovered (polymer free) thin cover glass discs were used as negative controls and standard copper discs as positive, cell toxic controls.

4.3.3.2 MTT Reduction Assay (Modified[9])

For this test small aliquots (either 10 µl or 100 µl) of PBS extracts of the polymer materials (see leaching tests above) were added to the culture medium of L929 cells after 24 h of incubation. The cells were incubated for additional 24 hours, MTT solution added and incubated for another one hour. After solubilization of the formazan product in DMSO the absorbance of the supernatant was measured in a microplate photometer at a wavelength of 570 nm. Parallel the cell number was assessed by the use of a Coulter Counter and the absorbance set in relation with the cell number. For negative controls pure PBS was used.

4.3.3.3 The Modified LDH Test[10]

The LDH test was performed similar to the MTT test. The formazan product was quantified using a microplate photometer at a wavelength of 490 nm and *via* a standard curve the LDH concentration calculated (in mU, milliUnits). As for the MTT test, cell numbers were measured and the quantity of released LDH set in relation with the cell number. For negative controls pure PBS was used.

4.3.4 Bone Marrow Cell development

Histochemical Description

4.3.4.1 Von Kossa Staining

After a cultivation period of 90 days, human bone marrow cells growing on the polymer materials were washed with silver nitrate solution and incubated with a 5% silver nitrate solution for 15 minutes at room temperature in the dark. After this time the cells were fixed for 2 minutes at room temperature in a 5% sodium thiosulfate solution. The cells were then washed thoroughly with water, the nuclei stained with iron haematoxyline and the samples examined by light microscopy.

4.3.4.2 Lipid staining with Sudan III

After fixation in formaldehyde, cell preparations were stained with Sudan III solution (in water/ethanol/formaldehyde) for 3 minutes at room temperature. The cells were then washed thoroughly with water, cross-stained with haematoxyline and the samples examined by light microscopy.

Immunohistology

4.3.4.3 CD 34 antibody detection of stem cells / progenitor cells

After washing the cells with PBS buffer they were fixated for 30 minutes at room temperature in methanol / ethanol (v : v / 1 : 1) and washed again thrice with PBS. Then the primary antibody monoclonal (mouse) anti-human CD34 antibody, phycoerythrin-conjugated (Dako, Hamburg) was added and incubated for one hour at room temperature. Uncomplexed antibody was removed by rewashing with PBS.

All immunohistologically marked samples were stored at 4°C in the dark before they were examined using a Confocal Laser Scanning Microscope (Leica PF5).

4.3.4.4 Bone Sialo Protein Assay

Samples were prepared as for the CD 34 antibody test. Then the monoclonal antibody (mouse) against human Bone Sialo Protein (Chemicon, Hofheim) was added, diluted 1 : 30 in PBS, and incubated for one hour at room temperature. Uncomplexed antibody was removed by rewashing with PBS. Then the secondary antibody (TRITC conjugated Affinipure antibody rabbit anti-mouse (IgG, Dianova, Hamburg), dilution 1 : 100 in PBS, was added and again incubated for one hour at room temperature.

4.3.4.5 Osteocalcin

Samples were prepared as for the CD 34 antibody test. Then antibody (polyclonal antibody against human osteocalcin (rabbit), Chemicon, Hofheim was added, diluted 1 : 30 in PBS, and incubated for one hour at room temperature. Uncomplexed antibody was removed by rewashing with PBS. Then the secondary antibody (TRITC conjugated Affinipure antibody donkey anti-rabbit IgG, Dianova, Hamburg), dilution 1 : 100 in PBS, was added and again incubated for one hour at room temperature.

4.4 References

[1] Wise D.L. et al. (eds.); *Encyclopedic Handbook of Biomaterials and Bioengineering, Part A: Materials, vol. 1: ch. 2, 6; vol. 2: ch. 1*; Marcel Dekker; New York; **1995**

[2] Reuter P.; Fuhrmann R.; Mücke A.; Voegele J.; Rieger B.; Franke R.-P.; *Macromol. Biosci.* **2003**; 3; 123-130

Röhlke W.; Fuhrmann R.; Franke R.-P.; Mücke A.; Voegele J.; Rieger B.; *Macromol. Biosci.* **2003**, 3; 131-135

[3] Malinova V.; Rieger B.; Macromol. Rapid Comm.; **2005**; 26/12; 945-949

[4] Greish Y.E.; Brown P.W.; *Biomaterials*; **2001**; 22; 807-816

[5] Fennel B.; Hill R.G.; Akinmade A.; *Dent. Mater*.; **1998**; 14; 358-364

[6] Jin S.; Gonsalves K.E; *J. Mater. Sci.: Mater. Med.*; **1999**; 10; 363-368

[7] M. Leute, P. Reuter, R. Fuhrmann, B. Rieger, R.-P. Franke, *Macromol, Biosci.,* submitted

[8] Standard Test Method for Cytotoxicity (ASTMCO/Alkene Copolymers as a Promising Class of Biocompatible Materials, 1 125 Standard F: 895, Book 13.01

[9] Original procedure: Lindl T.; Bauer J., *Zell – und Gewebekultur*, 2nd Ed.; Gustav – Fischer Verlag Stuttgart, New York; **1989**

Modified procedure: Dept. Biomaterials, University of Ulm; Prof. Franke

[10] Original procedure: Decker T.; Lohmann-Matthes M.-L.; J*. Immunol. Methods*; **1988**; 115; 61-69

Modified procedure: Dept. Biomaterials, University of Ulm; Prof. Franke

Summary

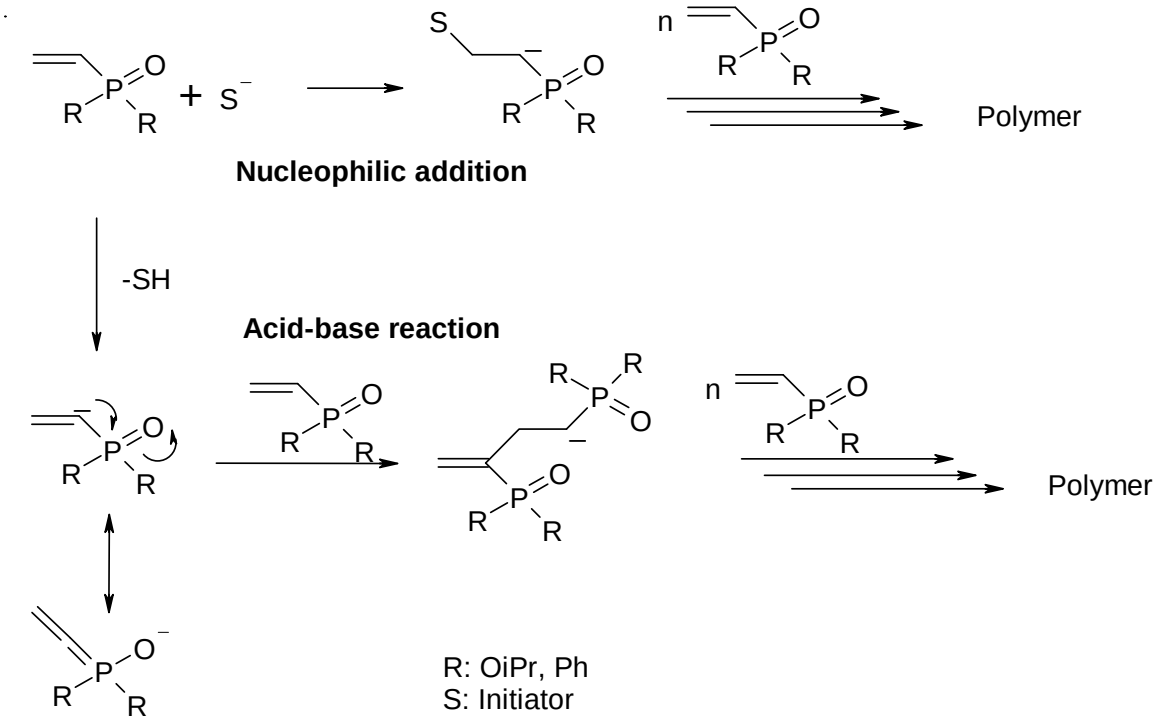
Macromolecules with phosphorus functionalities have been synthesized in the course of this thesis. Its main emphasis was on linear polymers prepared from diisopropylvinyl phosphonate and diphenylvinyl phosphine oxide, plus the polyacid yielded by hydrolysis of the polyphosphonates. A second, smaller part was dedicated to the exploration of hyperbranched polymers prepared from AB_2 monomers bearing one P-H group and two vinyl groups.

The polymerization of vinyl phosphonates and vinyl phosphine oxides by radical initiators yields only oligomeric materials. This is in accordance with literature-known results, yet the portfolio of polymerization techniques used on these monomers was extended to controlled radical polymerizations – both nitroxide- and xanthate-mediated – and UV-photolysis, as well as emulsion polymerization. While the latter two increase the conversion rates significantly, compared to standard radical polymerizations, the degree of polymerization of the resultant products remains the same. Controlled radical polymerization shows the same effect, yet to a lesser degree. Reactions of the phosphorus moieties that quenched the radicals necessary for propagation are a likely explanation for these results.

Anionic polymerization, on the other hand, produces polymers with a chain length increased by at least one order magnitude, quantitative yields and none of the byproducts formed by radical reactions. The molecular weights, determined by light scattering, were found in the range expected for the monomer-initiator ratio employed. Unusual finds concerning the occurrence of polymer chains lacking the end group introduced by the initiator, and the remarkable copolymerization behavior of the phosphorus monomers (see below) lead to the postulation of a new polymerization mechanism (see Scheme 19). An acid-base reaction competes with the nucleophilic attack in the initiation process for these monomers, an extraordinary find for the polymerization of vinyl groups.

It was found that the copolymerization of phosphorus-containing monomers is strongly hindered; in radical reactions a clear preference for the comonomers was prevalent, resulting in very low to non-existent incorporation rates. In anionic polymerizations the roles were reversed, here the polymerization of the vinyl phosphonates and vinyl phosphine oxides dominated, with no conversion of the comonomers.

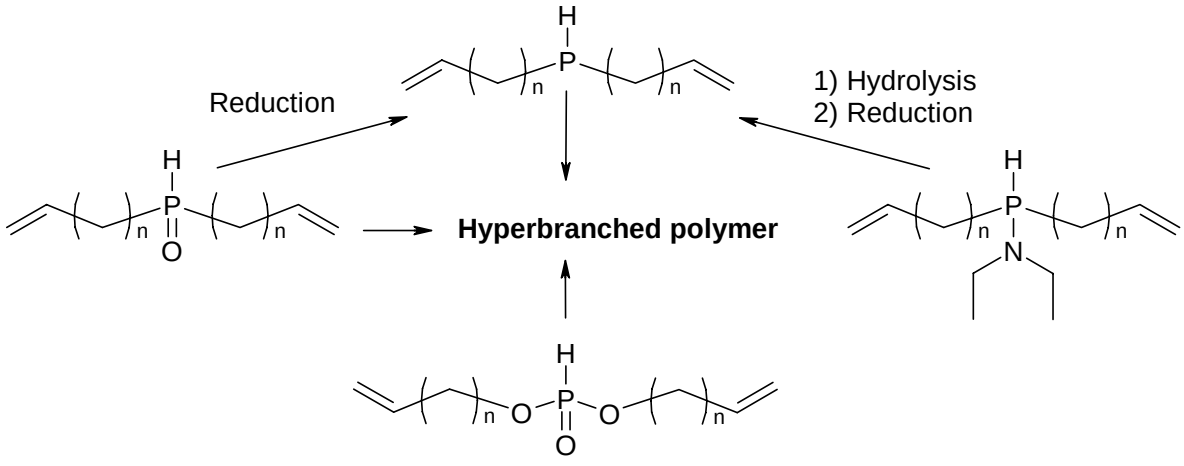
Scheme 19



Due to promising application possibilities in the medical field, the toxicological properties of these polymers were also investigated and their influence on the differentiation of bone marrow cells studied in detail.

A variety of monomers (see Scheme 20) were prepared for the synthesis of hyperbranched polymers with phosphorus at the branching points. First polymerization experiments were also performed, yet further investigations are needed for more substantial results.

Scheme 20



Zusammenfassung

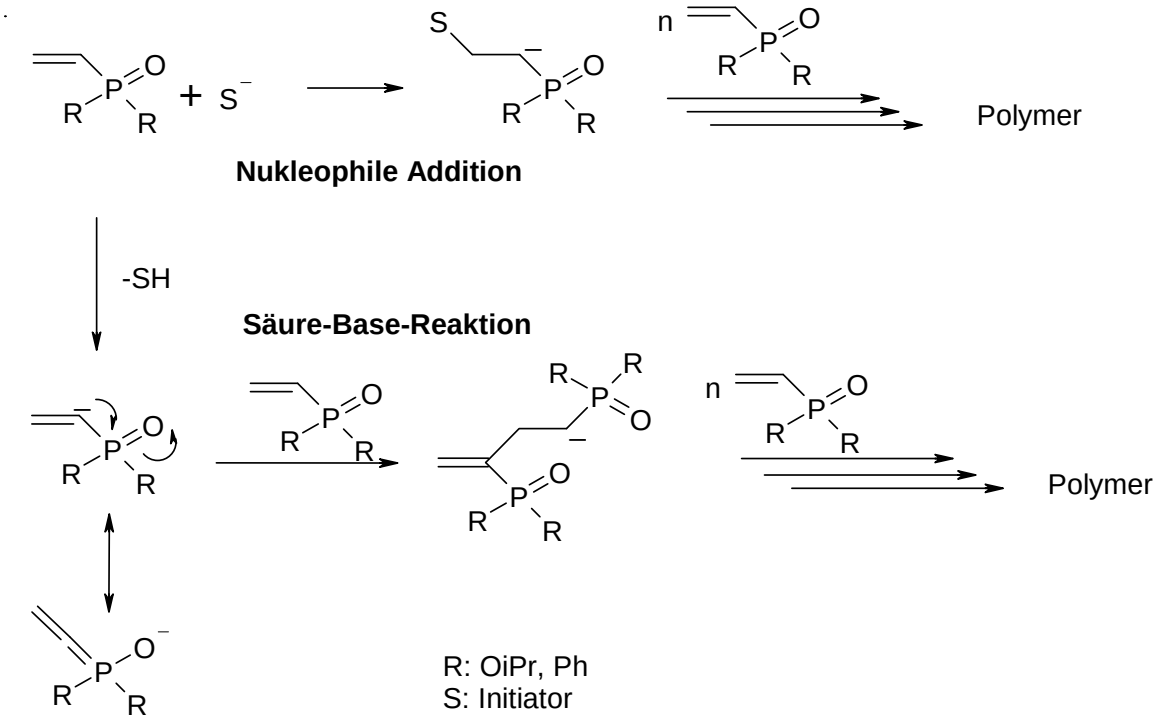
Im Rahmen dieser Arbeit wurden Makromoleküle mit Phosphorfunktionalitäten synthetisiert. Hauptsächlich wurden dabei lineare Polymere auf der Basis von Diisopropylvinylphosphonat und Diphenylvinylphosphinoxid sowie die durch Hydrolyse der Polyvinylphosphonate entstehende Polyphosphonsäure bearbeitet. Ein zweiter, kleinerer Teil war der Untersuchung hyperverzweigter Polymere gewidmet, welche aus AB_2-Monomeren mit einer P-H Gruppe und zwei Vinylgruppen, dargestellt werden können.

Die Polymerisation von Vinylphosphonaten und Vinylphosphinoxiden durch Radikale ergibt nur oligomere Materialien. Dies entspricht den literaturbekannten Ergebnissen, jedoch wurde das Spektrum der verwendeten Polymerisationstechniken um die kontrolliert-radikalische Polymerisation – sowohl Nitroxid- als auch Xanthat-mediiert – und UV-Photolyse, sowie die Emulsionspolymerisation erweitert. Während die beiden letzteren den Monomerumsatz im Vergleich zur standardmäßigen radikalischen Polymerisation bedeutend erhöhen, bleibt der Polymerisationsgrad der gebildeten Produkte gleich. Die kontrolliert-radikalische Polymerisation zeigt den gleichen Effekt, jedoch in geringerem Umfang. Diese Ergebnisse lassen sich wahrscheinlich durch ein Abfangen der zum Kettenwachstum notwendigen Radikale durch Reaktionen am Phosphor erklären

Die anionische Polymerisation, andererseits, ergibt Polymer mit um mindestens eine Größenordnung erhöhter Kettenlänge, quantitative Ausbeuten und vermeidet die bei Radikalreaktionen auftretenden Nebenprodukte. Die durch Lichtstreuung bestimmten Molekulargewichte liegen im Bereich, der sich aufgrund der verwendeten Monomer-Initiator-Verhältnisse erwarten lässt. Ungewöhnliche Ergebnisse bezüglich Polymeren, denen die durch den Initiator eingebrachte Endgruppe fehlt, sowie das bemerkenswerte Copolymerisationsverhalten dieser Monomere (siehe unten), führten zur Aufstellung eines neuen Polymerisationsmechanismus (siehe Schema 1). Bei den Phosphormonomeren konkurriert eine Säure-Base-Reaktion mit dem nukleophilen Angriff während der Startreaktion, ein äußerst ungewöhnliches Verhalten bei der Polymerisation von Vinylgruppen.

Die Copolymerisation der phosphorhaltigen Monomere stellte sich als stark gehindert heraus. In radikalischen Reaktionen zeigt sich eine deutliche Bevorzugung der Comonomere, so dass sich sehr geringe Einbauraten für die P-Monomere ergeben. Bei der anionischen Polymerisation kehren sich die Verhältnisse um, hier dominiert die Polymerisation der Vinylphosphonate und Vinylphosphinoxide, die Comonomere werden nicht umgesetzt.

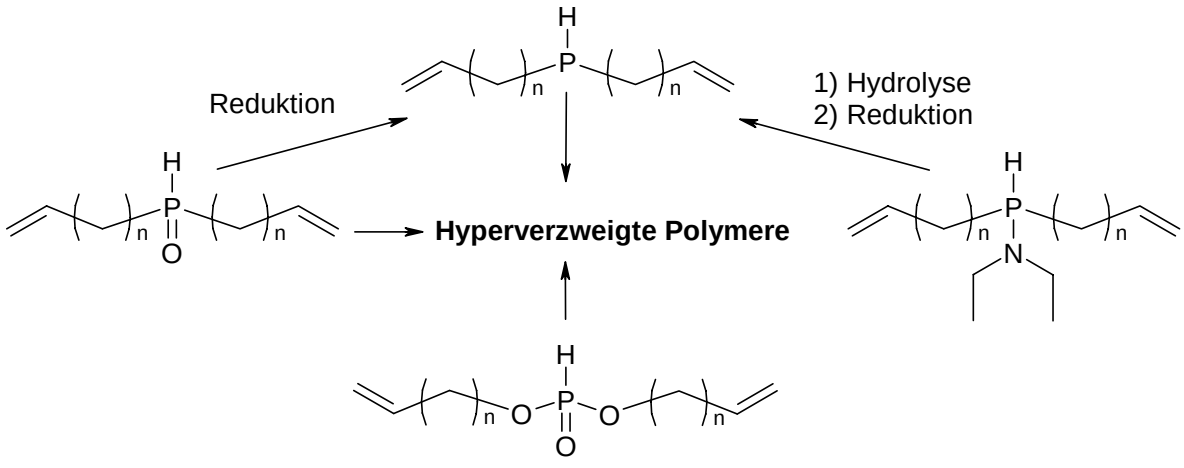
Schema 1



Da sich im medizinischen Bereich vielversprechende Anwendungsmöglichkeiten ergeben, wurden die toxikologischen Eigenschaften, sowie der Einfluss der phosphorhaltigen Polymere auf die Entwicklung von Knochenmarkszellen genauer untersucht.

Eine Variation von Monomeren (siehe Schema 2) zur Herstellung hyperverzweigter Polymere mit Phosphor an den Verzweigungsstellen wurden hergestellt und auch erste Polymerisationsexperimente unternommen. Weitere Versuche auf diesem Gebiet sind jedoch noch notwendig.

Schema 2



Declaration

The work on hand has been carried out between May 2003 and July 2007 in the department of Inorganic Chemistry II, Materials and Catalysis, University of Ulm, under the supervision of Prof. Dr. B. Rieger.

Herewith I declare that I have performed this work alone and only with the resources and references given.

Ulm,

Maria Leute

ERKLÄRUNG

Hiermit erkläre ich, dass ich die vorliegende Arbeit selbständig und nur unter Verwendung der angeführten Hilfsmittel angefertigt habe.

Ulm, Maria Leute

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