UNIVERSITEIT GENT

FACULTY OF SCIENCES

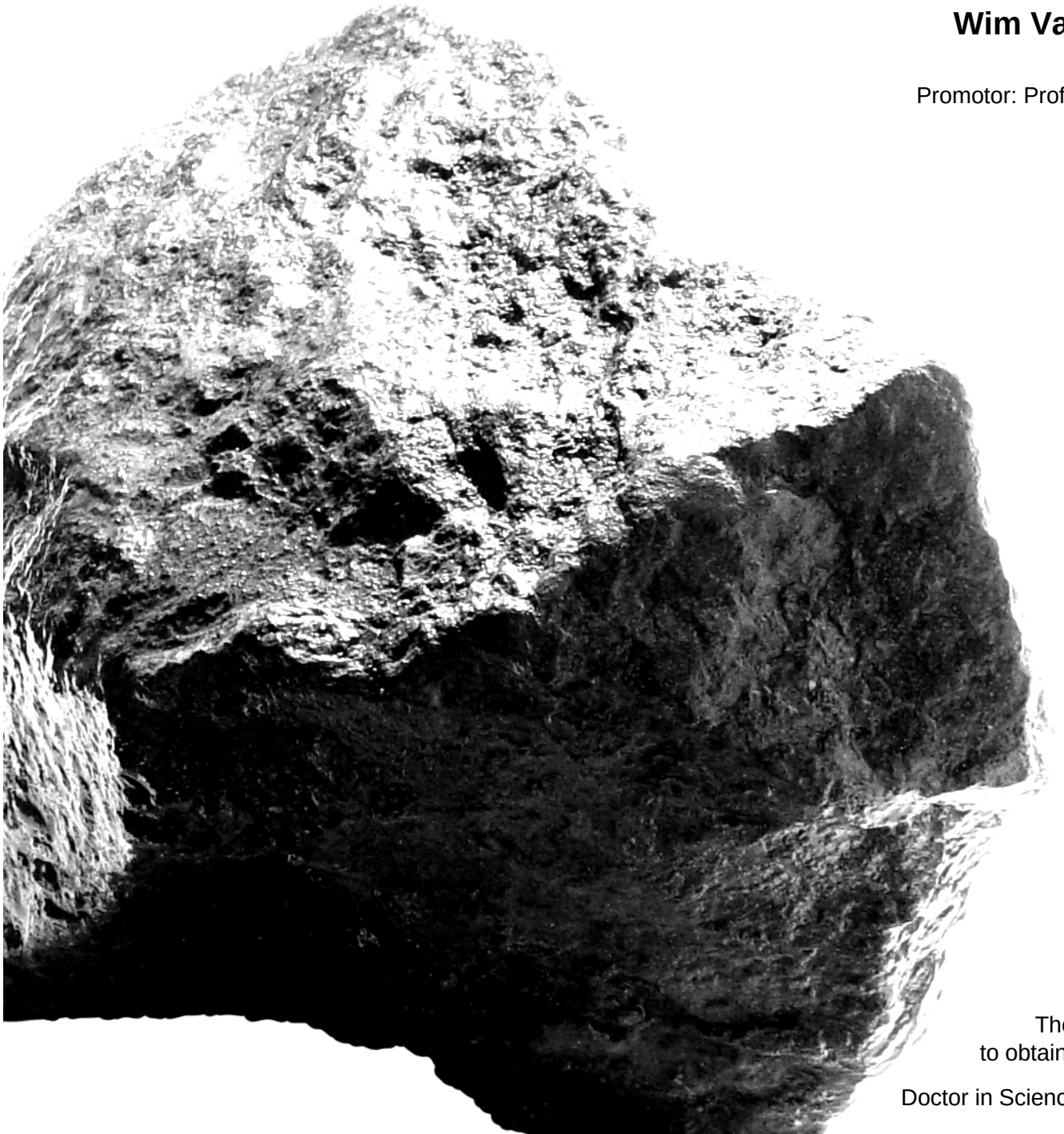
**Department of Organic Chemistry**
**Polymer Chemistry Research Group**

# Novel Routes for the Design of Poly((meth)acrylic acid) Containing Polymer Structures by Controlled Radical Polymerization

**Wim Van Camp**

Promotor: Prof. F. Du Prez

**2007**



Thesis submitted
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Absorptie van water
laat sporen
op onbeschreven blad
ent dankbaarheid
en later
kiemt vriendschap op
onontgonnen pad

Voor mijn Pépé Gustaaf Goossens
(7/12/1919 – 17/02/2007)

en de hele familie.

Research financed by a PhD grant of the Institute for the Promotion of Innovation through Science and Technology in Flanders (IWT-Vlaanderen), Belgium.

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# *Chapter I*
# *Introduction, aim and outline*

# I Introduction, aim and outline

In this thesis, we focus on the preparation of amphiphilic poly((meth)acrylic acid) (P(M)AA) containing polymer architectures. P(M)AA polymers are of vast interest for a wide range of applications, because of their pH-responsive nature and hydrophilic characteristics, and for their interaction with metal ions.[1-4] The market for PMAA and PAA is huge (5-10.000.000 ton/year; 10-20 million euro market), and key players are Arkema, BASF, Du Pont, Noveon and Rohm & Haas, to mention just a few.

Stimuli-sensitive amphiphilic block copolymers are a well-known class of intelligent polymers with a variety of promising potential applications, e.g. entrapment of environmental pollutants[5], catalysis[6], stabilizers in emulsion polymerization[7], drug carriers[8], nanoreactors[9] and polymeric surfactants[10, 11]. P(M)AA containing amphiphilic copolymers are used for example as emulsifiers, stabilizers[7], surfactants, dispersants[12-14], wetting agents, etc. Their application fields include cosmetics, paints, coatings, textiles, paper industry[12-14], pharmaceuticals, bio-applications[15], drug delivery systems, and many others. Poly((meth)acrylic acid) polymers are also used as superabsorbants (e.g. in diapers) and flocculants[4], as stain retardants in carpets, for entrapment of environmental pollutants in water treatment[3], etc…

In order to be able to further improve and adjust the properties of the current materials, the ability to synthesize these polymers with good control over the molar mass, chain architecture and polydispersity is of great importance. It is clear that controlled/living polymerization techniques are a prerequisite for their successful synthesis. Traditional polymerization routes towards well-defined P(M)AA containing polymers include living anionic[16] and group-transfer[17] polymerization techniques, both operating using protected analogues of the (meth)acrylic acid monomers. However, ionic polymerization techniques show some practical disadvantages (e.g. requirement for extremely pure reagents, low

functional group tolerance, limited combination with other monomers or polymer segments,…).

As radical polymerization has many advantages compared to other polymerization processes as for instance ionic polymerizations, several methods for controlling radical polymerization have been developed and extensively studied since the last 10-15 years.[18-21] **Chapter II** aims to give an introduction on controlled radical polymerization (CRP), focuses on the fundamental characteristics of CRP and describes the main types of CRP techniques (atom transfer radical polymerization (ATRP), reversible addition fragmentation chain transfer (RAFT) polymerization, and nitroxide mediated polymerization (NMP), respectively). Further on, the applicability of the different CRP methods is discussed with regard to their relative advantages and limitations. Finally, an overview of some of the current industrial implementations of CRP is given, showing its industrial importance.

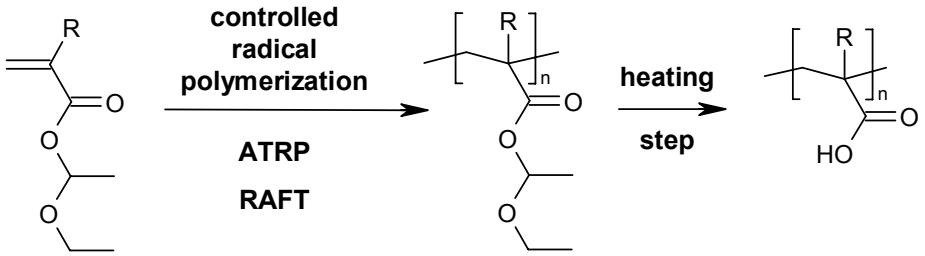
As the synthesis of well-defined P(M)AA containing polymers by CRP techniques is not straightforward and is still an ongoing challenge, **Chapter III** describes the current state-of-the-art in the field. The ATRP, RAFT and NMP methods are discussed and an overview is given with regard to the synthesis of well-defined P(M)AA containing polymers.

**Chapter IV** overviews the possibilities of "click" chemistry in the world of polymers, which has become a hot topic in polymer synthesis during the last 3 years. As ATRP is one of the most powerful and most employed polymerization methods in modern material science[18-25], the combination of "click" chemistry and ATRP is discussed in detail.

**Chapter V** reports on the ATRP of 1-ethoxyethyl (meth)acrylate (EE(M)A), which is evaluated as a novel route towards the synthesis of P(M)AA containing polymers.[26, 27] The ATRP of EE(M)A offers a solution to the challenges that remain for the synthesis of well-defined P(M)AA containing polymers by CRP techniques (see Chapter III). Although it is possible to directly polymerize acrylic acid by RAFT[28, 29] or NMP[30], their practicability for the synthesis of (block) copolymers with a variety of apolar monomers is strongly limited because polar polymerization conditions are needed. Moreover, these two polymerization techniques are, from a synthetic point-of-view, not the most practical ones when it comes to the design of more complex polymer architectures, such as star, graft and brush copolymers. From a synthetic viewpoint, ATRP is the preferred technique but, unfortunately, ATRP is not able to polymerize acidic monomers due to a side reaction of

the monomer with the metal complex that is used in this polymerization process.[31] Strategies to overcome these complications include the use of the sodium salt of methacrylic acid[32], or the use of protected derivatives of the acidic monomers, most commonly tert-butyl (meth)acrylate[33-35] or benzyl (meth)acrylate[36]. In all these cases, a post-polymerization deprotection and purification step are required to generate the desired polyacid. Unfortunately, this procedure is not always straightforward.

To avoid this additional purification step, **Chapter V** describes the use of 1-ethoxyethyl as the protecting group for (meth)acrylic acid. Poly(1-ethoxyethyl methacrylate) (PEEMA) and poly(1-ethoxyethyl acrylate) (PEEA) are novel precursors for poly(methacrylic acid) (PMAA) and poly(acrylic acid) (PAA), respectively. They have the unique property that deprotection is carried out by a heating step, with the loss of ethyl vinyl ether (boiling point: 33 °C) as a gas, preventing the need of an additional purification step after deprotection.




**Controlled radical polymerization (ATRP, RAFT) of EE(M)A to yield PEE(M)A, and subsequent deprotection to P(M)AA by a heating step. (R=H or $CH_3$ for EEA and EEMA, respectively).**

First, the homopolymerization of EE(M)A by ATRP was studied in detail, as well as the deprotection of the PEE(M)A polymers to the corresponding P(M)AA polymers. This part of the research was done in collaboration with the research group of S. Bon (Warwick University, UK). Further on, using a "tailor-made" disulfide containing initiator, PAA brushes were prepared which were used to create gold surfaces with pH-switchable properties. Characterization of the pH-responsive gold surfaces was done in collaboration with the research group of S. Demoustier-Champagne (Université Catholique de Louvain, UCL, Belgium).

Moreover, to illustrate the general applicability of EEA, various PEE(M)A containing polymers were prepared, including block copolymers, "block-like" copolymers, and random copolymers.

In **Chapter VI** the ATRP of EEA was applied to synthesize a variety of poly(isobornyl acrylate)-poly(acrylic acid) (PiBA-PAA) block copolymers. Although PiBA is a polyacrylate with some interesting properties such as a high glass transition temperature, the conrolled synthesis of PiBA has not been described before. Therefore, we include here a detailed study of the homopolymerization of iBA, which is a prerequisite to synthesize well-defined PiBA-PAA polymers. Preliminary results about these PiBA-PAA polymers acting as pigment stabilizing polymers are reported as well. This study is done in collaboration with the research group of Prof. Eisenbach (University of Stuttgart, Germany) and Prof. Zubov (Lomonosov Moscow State Academy of Fine Chemical Technology, Russia).

In **Chapter VII**, the polymerization of EEA using the RAFT polymerization technique is investigated to further illustrate the versatility of the use of the 1-ethoxyethyl acrylate strategy.[37] This part of the research has been done in collaboration with Dr. R. Hoogenboom and Prof. U. Schubert (Eindhoven University of Technology, the Netherlands). Although it is possible to directly polymerize acrylic acid by RAFT, polar reaction conditions have to be applied, which means that (block) (co)polymers with a variety of apolar monomers cannot be synthesized in a straightforward manner. RAFT of EEA circumvents this problem. The investigations were performed using a high-throughput workflow equipped with synthesis robots and fast analysis equipment demonstrating the added value in polymer research.

**Chapter VIII** evaluates the combination of ATRP of EEA and the copper(I) catalyzed "click" 1,3-dipolar cycloaddition reaction of azides and terminal alkynes as a method to synthesize amphiphilic polymer structures. Using our EEA strategy, we aim to broaden the application field with the synthesis of polymer structures containing PAA segments. A modular approach has been applied: the synthesis of polymers with alkyne functionalities as well as azide functionalities has been evaluated. Then, the "click" coupling reaction of these polymers was investigated to obtain block copolymers and, for the first time, comb/brush copolymers by a combination of ATRP and "click" chemistry.

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# *Chapter II*
# *Controlled radical polymerization*

## Abstract

The development of various controlled radical polymerization (CRP) methods during the last 10-15 years has lead to an unprecedented opportunity in materials design. This chapter aims to give an introduction, focuses on the fundamental characteristics of CRP and describes the main types of CRP techniques. Further on, the applicability of the different CRP methods is discussed with regard to their relative advantages and limitations. Finally, we give an overview of some of the current industrial implementations of CRP, showing its industrial importance.

# II
# Controlled radical polymerization

## II.1. Importance of radical polymerization

Free radical polymerization (FRP) has many advantages compared to other polymerization processes such as ionic polymerizations and polycondensation reactions. Advantages are the simple experimental setup, the use of inexpensive or easy to prepare and purify reagents, in addition to tolerance toward functional groups, solvents and impurities. By comparison with for instance ionic polymerizations, FRP does not require stringent process conditions and can be used for the (co)polymerization of a vast variety of vinyl monomers. Nearly 50% of all commercial synthetic polymers are prepared using radical chemistry, providing a spectrum of materials for an extensive range of markets.[2] However, the major limitation of FRP is poor control over some of the key elements of the process due to unavoidable radical termination reactions, which limits the design of specific materials for all kinds of applications. However, because of extensive research during the last 10-15 years, several procedures for controlling radical polymerization have been developed.[1, 3-5]

## II.2. Importance of controlled radical polymerization

Controlled radical polymerization (CRP) now allows the preparation of well-defined polymers with controlled molecular weight, polydispersity, composition, chain architecture, and site-specific functionalities (Figure II-1).[6] These properties lead to an unprecedented opportunity in materials design, including the ability to prepare bioconjugates, organic/inorganic composites, and surface-tethered copolymers.

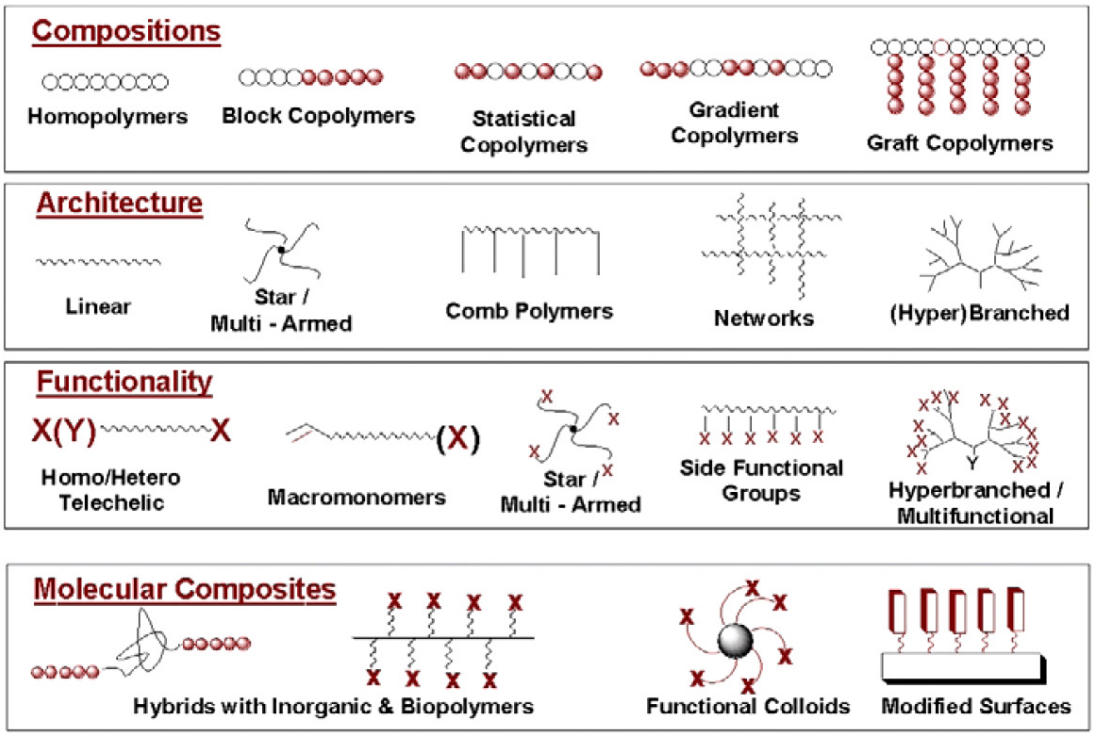


**Figure II-1 Examples of molecular structures attained through the use of controlled radical polymerization methods.[6]**

In the following part will be described how this control over the radical polymerization process has been achieved. However, we will first shortly focus on the fundamentals of controlled polymerization.

## *II.3. Fundamentals of controlled polymerization*

A controlled/"living" polymerization was defined by Swarc[7] as a polymerization reaction that proceeds without the occurrence of any irreversible termination or transfer reactions. In combination with some side conditions such as 1) fast initiation in comparison to propagation, and 2) fast exchange between species of various reactivities in comparison to propagation, polymers with the following characteristics are obtained:[8-11]

- Controlled molecular weights, with the degree of polymerization ($DP_n$) predetermined by the ratio of the concentrations of consumed monomer to the introduced initiator. $DP_n = \Delta$ [Monomer] / $[Initiator]_0$.
- Polydispersities close to Poisson distribution. $DP_w / DP_n \approx 1 + 1/DP_n$.
- All chains end-functionalized.

Experimentally, the best way to evaluate a polymerization technique for its livingness is to follow the kinetics of the polymerization and the evolution of the molecular weight ($M_n$), polydispersity (PDI) and functionalities with conversion. Well-controlled systems should provide:

- Linear kinetic plots in semilogarithmic coordinates ($\ln([M]_0/[M])$ vs time), if the reaction is first order in monomer concentration. Acceleration on such plots may indicate slow initiation whereas deceleration may indicate termination or deactivation of the catalyst. (Figure II-2 a)
- Linear evolution of molecular weights ($DP_n$) with conversion. Molecular weights lower than predicted (see above) indicate transfer, higher molecular weights indicate inefficient initiation or chain coupling. (Figure II-2 b)
- Polydispersities should decrease with conversion for systems with slow initiation and slow exchange.

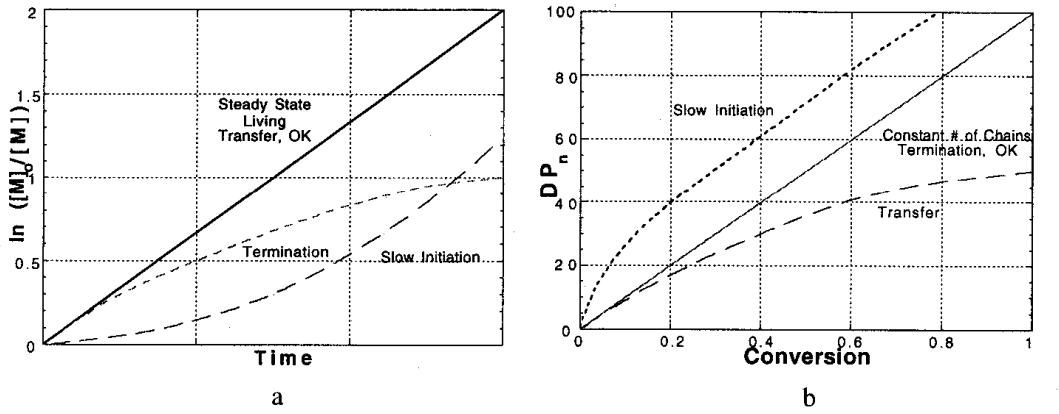


**Figure II-2** **Effects of slow initiation, transfer, termination and exchange on (a) first order kinetic plot: $\ln([M]_0/[M])$ as a function of time and (b) degree of polymerization as a function of conversion.**[1]

## *II.4. From free radical polymerization to controlled radical polymerization…*

As the absence of termination and transfer reactions is the main requirement to obtain a controlled polymerization system, this is the main challenge for the development of controlled **radical** polymerization systems. In all radical polymerizations, biradical termination occurs at a rate, $R_t$, which is dependent on the concentration of radicals, $[P^\bullet]$,

where $R_t = k_t [P^\bullet]^2$. The rate of propagation, $R_p$, is given by $R_p = k_p [M] [P^\bullet]$ (M = monomer).

The key of success to controlled radical polymerization is the development of a polymerization system where the lifetime of the propagating chains is extended.

## *II.5. Main types of controlled radical polymerization*

In the past 10 – 15 years, a number of controlled radical polymerization (CRP) methods have been developed and the three most promising are: transition-metal-catalyzed atom transfer radical polymerization (ATRP), reversible addition-fragmentation chain transfer (RAFT) polymerization, and stable free radical polymerization (SFRP), most commonly nitroxide mediated polymerization (NMP).[1, 3-5] A schematic overview of the mechanism of the three main methods for controlled radical polymerization is given in Figure II-3.

**SFRP or NMP**
**Thermal dissociation of dormant species ($k_a$) provides a low concentration of radicals**

**ATRP**
**Transition metal (Y) activation ($k_a$) of a dormant species with a radically transferable atom**

**Degenerative Transfer or RAFT**
**Majority of chains are dormant species that participate in transfer reactions ($k_{exch}$) with a low concentration of active radicals**

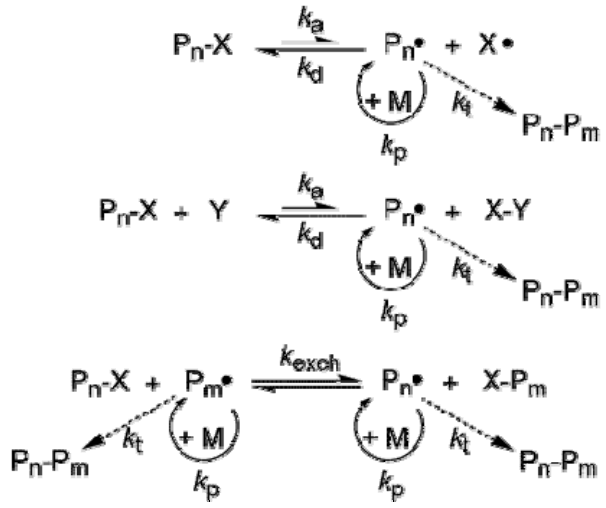


**Figure II-3 Three main methods for controlled radical polymerization.[6]**

In order to extend the lifetime of the propagating chains, each of these controlled radical polymerization methods relies on establishing a dynamic equilibrium between a low concentration of active propagating chains ($P_n^\bullet$) and a predominant amount of dormant chains ($P_n$-X) that are unable to propagate (addition of monomer M - $k_p$) or terminate ($k_t$). The total small number of dead chains ($k_t$) produced in a CRP can be neglected in comparison with the total amount of chains which are "living".

In the case of NMP, the concentration of active propagating chains is kept low by spontaneous reversible homolytic cleavage of a dormant chain end (activation/deactivation - $k_a/k_d$). ATRP involves a catalytic reversible homolytic cleavage of a covalent bond via a redox process. RAFT is based on a bimolecular exchange between growing radicals and a dormant species.

Each of these techniques will be discussed more in detail in the following paragraphs.

## II.5.1. Atom transfer radical polymerization (ATRP)

### II.5.1.1. Mechanism

Atom transfer radical polymerization (ATRP) was developed in 1995 and further refined by several research groups including the ones of Sawamoto[12-15], Matyjaszewski[16-21], Haddleton[22-26], Armes[27-30], and others[31-35].

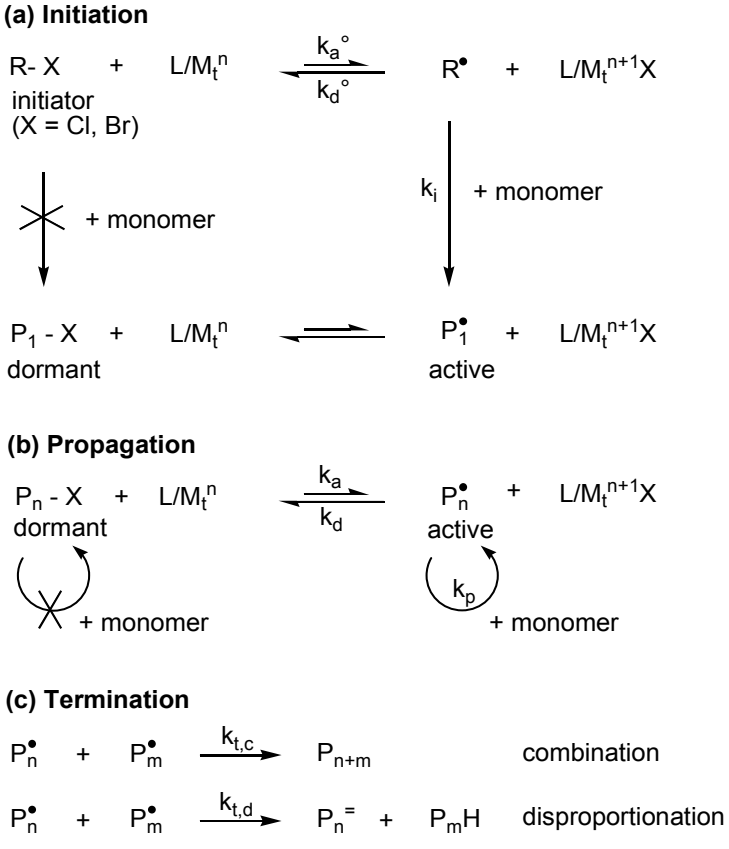


**Figure II-4 Detailed reaction mechanism of atom transfer radical polymerization.**

The polymerization mechanism of ATRP (see Figure II-4) is based on the cleavage of a halogen atom of the initiator R-X ($k_a$°) or a dormant polymer chain $P_n$-X ($k_a$) by a transition metal complexed with a ligand (L) in its lower oxidation state ($M_t^n$/L). An alkyl radical $R^\bullet$ or an active polymer chain $P_n^\bullet$ is generated and the transition metal complex is transformed to its higher oxidation state (X-$M_t^{n+1}$/L). In the propagation step, monomer is added to grow a polymer chain ($k_p$, $k_i$ when monomer is added to $R^\bullet$) until the dormant species $P_n$-X is formed again by abstraction of a halogen atom of X-$M_t^{n+1}$/L with formation of $M_t^n$/L ($k_d$). Control over chain length (molecular weight), molecular weight distribution and functionality is thus obtained by a dynamic equilibrium ($k_a/k_d$) between a dormant chain $P_n$-X and an active chain $P_n^\bullet$ by an exchange of electrons (redox process) between the transition metal complex and the radical chain ends of the active species. However, termination can result in a small amount of coupled polymer chains $P_n$-$P_m$ in case of combination ($k_{t,c}$), or can result in disproportionated chains $P_n^=$ or $P_mH$ in case of disproportionation ($k_{t,d}$).

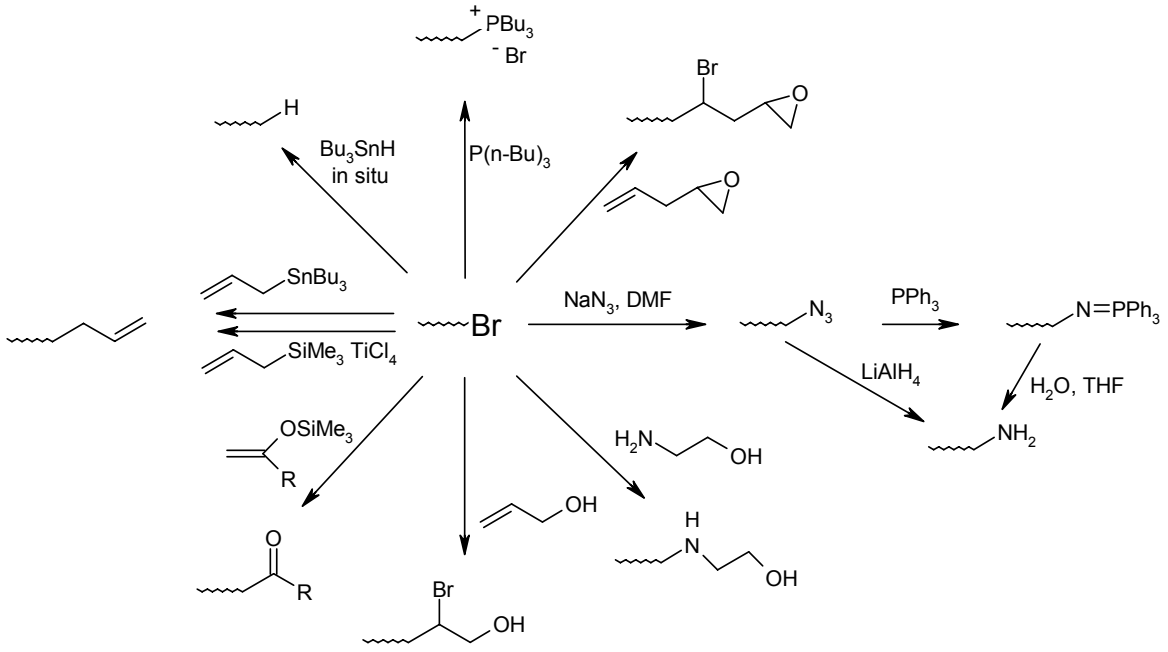


**Figure II-5** **Some examples of the displacement of the terminal halogen in ATRP polymers using electrophilic, nucleophilic, and radical reactions.[19]**

With the ATRP method, a wide range of polymer architectures can be prepared, for instance block copolymers, star copolymers, star block copolymers, random copolymers, gradient copolymers, "blocky" gradient copolymers, graft copolymers, hyperbranched (co)polymers,…

The ATRP technique has also the advantage that the terminal halogen in the polymers can easily be displaced to other end groups using various electrophilic, nucleophilic and radical reactions (see Figure II-5).[18, 19, 36, 37]

### II.5.1.2. Various components of the ATRP mechanism

#### *II.5.1.2.1. Initiator*

The role of the initiator is to provide a radical via the first activation/deactivation cycle of the polymerization. Most of the initiators thus far successfully employed are organic halides with a carbon-halogen bond, which can easily generate a radical species through electronic and steric effects of their substituents.[15] Also sulfonyl halides have been used as initiators for ATRP by Percec *et al.*[32-35, 38] The initiator has to be selected carefully, in accordance with the structure and reactivity of the monomer and the used metal complex.[39] Initiation has to be quantitative and the initiation step has to be fast in comparison to propagation in order to obtain a controlled polymerization.

Thanks to the tolerance of controlled radical polymerization to functional groups, the initiator can be applied to introduce various functionalities into the polymer.[15, 40, 41] Examples are the use of a disulfide-containing initiator to introduce disulfide bonds into a polymer[42, 43], hydroxyl-containing initiators[44-46], alkyne-containing initiators[47, 48], nucleoside-containing initiators[49-51],… Some examples are shown in Figure II-6.

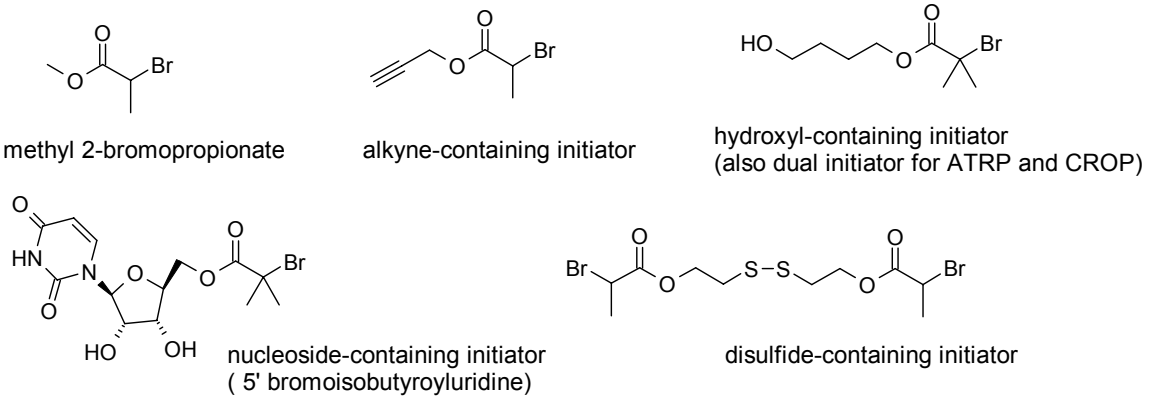


**Figure II-6 Some examples of initiators used for ATRP.**

Moreover, initiators containing additional initiating groups for other (distinct) controlled polymerization techniques than ATRP (e.g. for cationic ring opening polymerization (CROP) of THF) can be used.[52-55]

#### *II.5.1.2.2. Transition metal*

Different transition metals such as Cu[17], Ru[14], Ni[31], Fe[56, 57], and less frequently Re[58], Pd[59], Mo[60, 61] have been used for ATRP. Cu is definitely the most studied and most used transition metal. Copper-based catalyst complexes show a good reactivity, many ligands are commercially available or easy to synthesize, and copper complexes show a high selectivity for atom transfer (they posses a low affinity for e.g. alkyl radicals).[1] Because of the toxicity of the catalyst and the intense colour of the resulting polymers, various post-polymerization purification methods have been developed for removal of the catalyst.[62] As removal of the catalyst is a rather expensive and time-consuming process, research concerning the development of solid-phase catalyst systems has been reported by several groups. [63-69]

#### *II.5.1.2.3. Ligand*

For Cu-catalyzed ATRP, most commonly amine ligands are used, which can be classified according to their number of nitrogen atoms. Some examples are shown in Figure II-7.

- Bidentate ligands (2 N atoms): e.g. 2,2'-bypiridines[16, 17] or *N*-alkyl-2-pyridine methane imines[22, 24] (Schiff base).
- Tridentate ligands (3 N atoms): e.g. *N, N, N', N'', N''*-pentamethyldiethylene-triamine (PMDETA)[70].
- Quadridentate ligands (4 N atoms): e.g. 1,1,4,7,10,10-hexamethyldiethylene-tetramine (HMTETA)[70] or *N,N,N',N',N'',N''*-hexamethyl(tris(2-aminoethyl)-amine ($Me_6$TREN)[71, 72].

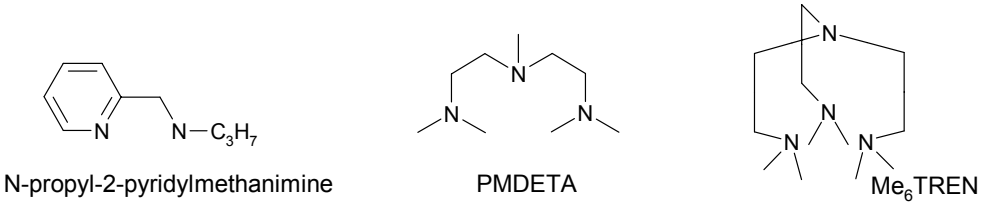


**Figure II-7 Some examples of ligands used for ATRP.**

These ligands have the following purposes: they solubilise the transition metal (homogeneous reaction medium) and they have an influence on the ATRP equilibrium by means of their electronic and steric effects. The choice of ligand influences the activity of the transition metal complex, and thus the radical concentration in the polymerization system. A more reducing catalyst complex (with lower redox potential) usually shows a higher catalytic activity (higher $k_a/k_d$ value). [73, 74]

#### *II.5.1.2.4. Monomer*

ATRP can be applied for the polymerization of a wide range of monomers such as styrenes, acrylates, methacrylates, acrylonitriles, (meth)acrylamides,… , as well in bulk as in solvent.[18, 20, 75]. However, ATRP shows some restrictions for the polymerization of acid-containing monomers such as for instance (meth)acrylic acid, because of competitive complexation of the monomer with the metal catalyst, disrupting the ATRP equilibrium[20].

### II.5.1.3. Kinetics of ATRP

The kinetic equation for ATRP can be derived from the reaction scheme shown in Figure II-4.[76]

If assumed that initiation is quantitative and fast in comparison to propagation, and that termination can be ignored, the rate for activation ($R_a$) and deactivation ($R_d$) is:

$$R_a = k_a [P_n - X][M_t^n]$$

$$R_d = k_d [P_n^\bullet][X - M_t^{n+1}]$$

If the steady-state concentration of the propagating radicals can be assumed, $R_a = R_d$ applies. This means that an equation for the concentration of growing polymer chains can be derived:

$$[P_n^\bullet] = \frac{k_a}{k_d}[P_n - X]\frac{[M_t^n]}{[X - M_t^{n+1}]}$$

The rate of polymerization ($R_p$) (or the decrease of monomer concentration [M]) is given by:

$$R_p = -\frac{d[M]}{dt} = k_p[P_n^\bullet][M] = k_p^{app}[M]$$

This makes, with $[RX]_0 = [P_n\text{-}X]$ for a quantitative and fast initiation:

$$R_p = k_p \frac{k_a}{k_d}[P_n - X]\frac{[M_t^n]}{[X - M_t^{n+1}]}[M] = k_p \frac{k_a}{k_d}[RX]_0 \frac{[M_t^n]}{[X - M_t^{n+1}]}[M]$$

This means that the polymerization rate $R_p$ is first order in monomer M, initiator R-X and transition metal complex $M_t^n$. Integration with the condition that $[M] = [M]_0$ if $t = 0$ leads to the following formula:

$$\ln \frac{[M]_0}{[M]} = k_p \frac{k_a}{k_d}[P_n - X]\frac{[M_t^n]}{[X - M_t^{n+1}]}t = k_p^{app} t$$

Plotting of $\ln \frac{[M]_0}{[M]}$ as a function of time leads to a straight line with $k_p^{app}$ as the slope for a controlled polymerization (see also §II.3. Fundamentals of controlled polymerization, and Figure II-2). The linear behavior means that the radical concentration remains constant throughout the polymerization. However, it should be noted that a slight deviation from linearity is often observed as a result of termination reactions in the early stages of the polymerization reaction, because the equilibrium between the active and dormant polymer chains is not yet fully established.[77, 78]

### II.5.2. Reversible addition-fragmentation chain transfer polymerization (RAFT)

Reversible addition-fragmentation chain transfer polymerization (RAFT) was first reported in 1998 by Rizzardo *et al.*[79-83] and Charmot *et al.*[84].

The mechanism of the RAFT process is believed to involve a series of reversible addition-fragmentation steps as shown in Figure II-8. Addition of a propagating radical $P_n^\bullet$ to the thiocarbonylthio compound gives an adduct radical that fragments to a polymeric thiocarbonylthio compound and a new radical $R^\bullet$. The radical $R^\bullet$ then re-initiates polymerization to give a new propagating radical $P_m^\bullet$. Subsequent addition-fragmentation steps set up an equilibrium between the propagating radicals $P_n^\bullet$ and $P_m^\bullet$ and the dormant polymeric chains by the way of an intermediate radical. This equilibration of the growing chains gives rise to a narrow molecular weight distribution. Throughout the polymerization (and at the end) the vast majority of the polymer chains are end capped by a thiocarbonylthio group (dormant chains), so the concentration of active (free) radicals remains low and termination reactions are minimized. The RAFT method allows the

synthesis of well-defined random, block copolymers, gradient copolymers as well as star copolymers.[82, 85-90]

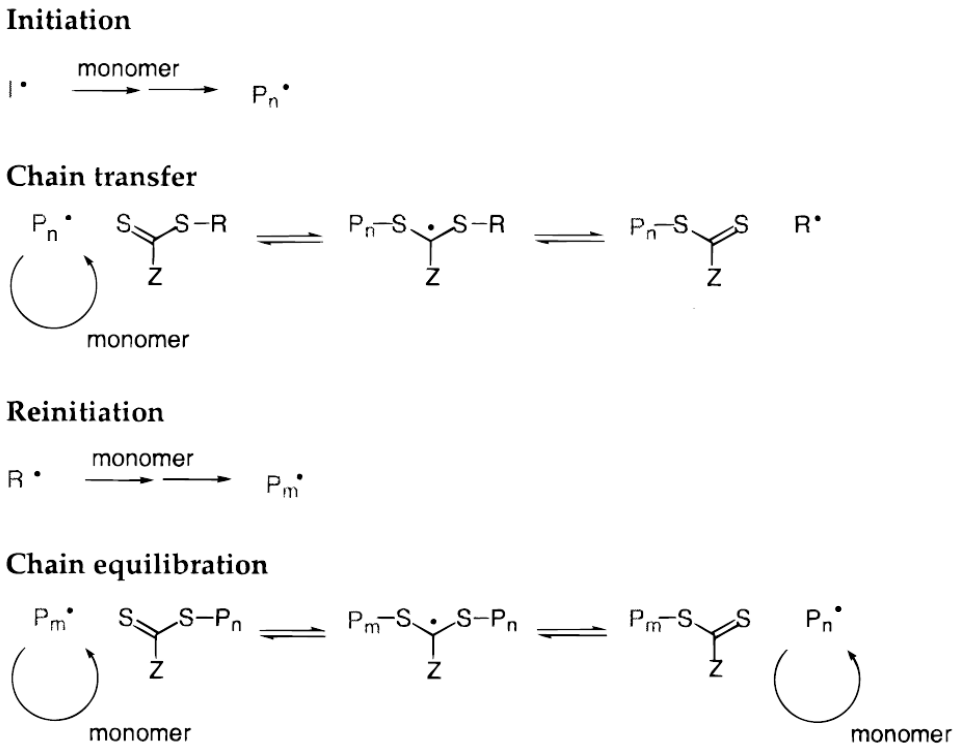


**Figure II-8** **Mechanism of reversible addition-fragmentation chain transfer polymerization.**

The group of Rizzardo *et al.* developed this CRP method making use of dithioester transfer agents[79-83], while Charmot *et al.* developed a similar method based on xanthate agents, named MADIX (macromolecular design via interchange of xanthate)[84].

For the initiation, thus for the generation of radicals, conventional free radical polymerization initiators are used (e.g. AIBN). However, there is often an optimal ratio for the amount of initiator to RAFT agent.[91]

The general structure of the RAFT agent is Z-C(=S)S-R (see Figure II-8). Z is an activating group[92] (e.g. aryl, alkyl, NR', SR',…), while R is a radical leaving group[93] (e.g. $CH_2Ph$, $C(CH_3)_2Ph$, $CH(CH_3)Ph$, $C(CH_3)(CN)CH_2CH_2C(O)OH$, $C(CH_3)_2CN$,…). For the MADIX process, Z = Z'-O (Z' is e.g. $C_2H_5$, $C_{12}H_{25}$, $CH_2CF_3$, $CH(CF_3)[P(O)(OEt)_2]$)[94, 95]. For an optimal control over the polymerization, the RAFT agent has to be fine-tuned by the design of the Z and R substituents for the polymerization of different monomers.

### II.5.3. Nitroxide mediated polymerization (NMP)

Nitroxide mediated polymerization (NMP) belongs to the class of stable free radical polymerizations. It was first reported by Rizzardo *et al.* in 1985[96] and also Georges *et al.* made a lot of efforts in the field[97-99]. The stable free radicals, which originate from spontaneous homolytic cleavage (thermal dissociation) of a nitroxide compound at elevated temperature, combine with the radical at the end of the growing polymer chains with the formation of a covalent bond in the dormant species (see Figure II-3). In this way, the concentration of active radicals in the system is kept low and control over the polymerization is established.

For NMP, a number of nitroxides have been used. In the first reports, the use of cyclic nitroxides such as TEMPO (2,2,6,6-tetramethyl-1-piperidinoxyl) is described.[97-99] However, only styrene and some derivatives of styrene could be polymerized, and due to the high polymerization temperature that is required, side reactions such as self-initiation in the case of styrene limit the control. Later reports describe the use of other non-cyclic similar compounds such as SG1[100, 101] (N-tert-butyl-N-(1-diethyl phosphono-2, 2-dimethyl propyl)). With the use non-cyclic nitroxide compounds, the monomer range was extended to acrylates[100], acrylic acid[102-105] and dienes[106]. Polymerization of methacrylates remains uncontrolled due to disproportionation of the nitroxide and the growing radical when TEMPO is used[107, 108], while the use of non-cyclic nitroxides such as SG1 leads to a high concentration of radicals because of a high $k_a/k_d$ constant, which results in irreversible termination[109]. However, Charleux *et al.* proved that a better control can be obtained by copolymerizing a limited amount of styrene, which lowers the $k_a/k_d$ equilibrium constant.[110]

## *II.6. Applicability of the different CRP methods*

ATRP, RAFT and NMP are currently the three most commonly used methods for controlled radical polymerization, but it is obvious that each of these three major systems exhibits some relative advantages and limitations, depending on the monomers used, the particular synthetic targets, and additional requirements concerning functionality, purity, reaction medium such as bulk, solution or biphasic, environmental issues, and the cost of the final product.[4]

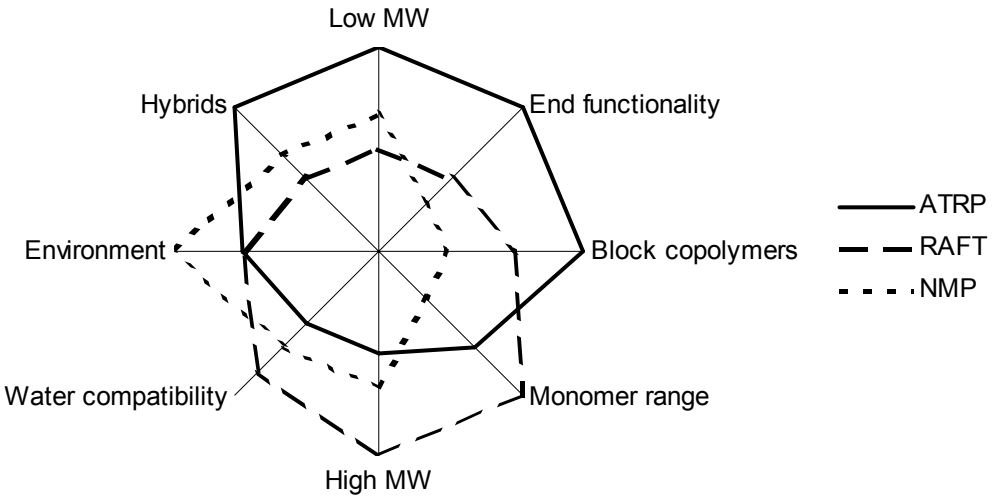


**Figure II-9** **Relative advantages and limitations of ATRP, RAFT and NMP as applied to the synthesis of low and high molecular weight (MW) polymers, block copolymers, end-functional polymers, hybrids, the range of polymerizable monomers, compatibility with aqueous systems, and environmental issues.[4]**

Figure II-9 attempts to illustrate some areas in which ATRP, RAFT and NMP may be easier, simpler, more precise, less expensive or more versatile. Of course this qualitative picture will change with the developments of new control agents, with improvement in polymerization catalysts, conditions, etc..., or perhaps the development of entirely new systems.

## *II.7. Industrial importance of CRP: an overview*

While the initial drive for the development of controlled radical polymerization (CRP) was rather academic and involved the preparation of polymers with novel architectures and functionality, the current focus of research also involves preparing and fabricating materials for specific applications. Now that well-defined polymers with controlled molecular weight, polydispersity, composition, chain architecture, and site-specific functionalities have become accessible (see Figure II-1), also commercial corporations are going to drive focused application research, attracted by the high added value of such materials. All these mentioned synthetic properties strongly influence the range of applicability, the efficiency and the final properties of the produced materials.

Target applications include the components of coatings, adhesives, nonionic surfactants, dispersants, polar thermoplastic elastomers, bulk performance materials, membranes, personal care products, detergents, double hydrophilic block copolymers for crystal engineering and drug delivery systems, gels and hydrogels, lubricants and additives, surface modifiers, hybrids with natural and inorganic polymers, various bio- and electronic materials, etc… An overview is given below.[6]

One of the earliest adopters of CRP was DuPont Performance Coatings[111], which now prepares several commercial components of paints, coatings, and inks using CRP. Cumulative commercial production of materials made with various CRP techniques now totals several million Euros and is slowly but steadily growing, year by year. The most commercially important polymer architectures for DuPont and other corporations are block copolymers; di- and tri-block structures have been commercialized in multiple applications. DuPont maintains a very active research and development effort in the general area of CRP and expects to see new products based on these synthetic techniques in the next few years.

The self-organizing ability of block copolymers has been exploited by IBM[112] to create Si memory chips using new nanoscale manufacturing techniques, and this method will be extended to provide a general approach to surface modification and nanoscopic templates.[113]

Ciba[114] has focused on the preparation of amphiphilic graft copolymers by copolymerization of macromonomers with other monomers using both ATRP and NMP to give well-defined comb-copolymers[115]. Its first CRP-based products are acrylic block copolymers, commercialized in 2004 as EFKA, which offer superior rheological performance and improved stabilization of pigment dispersions in coating applications.

RohMax Oil Additives[116], a subsidiary of Degussa[117], discussed commercially feasible and economically acceptable conditions for ATRP preparation of additives based on long chain poly(alkyl methacrylates) that are suitable for use as components of lubricating oils. Degussa[117] has also developed the commercial capability to prepare block copolymers and remove traces of catalysts from the products.

PPG[118] indicated that materials prepared by ATRP offer many benefits over those prepared by other polymerization processes, including the ability to control the polymer molecular weight and achieve a narrow molecular weight distribution. PPG also noted that

another substantial benefit of ATRP is the ability to manipulate the composition, functionality, and architecture of (co)polymers. This permits the formation of complicated structures, such as block, gradient, comb, and star copolymers, which are being evaluated as components of various coating materials.

**Figure II-10 Kaneka ATRP pilot plant in Kashimi, Japan.[119]**

Kaneka[119] announced that it currently has a large pilot unit producing commercial samples (Figure II-10) and is constructing a full-scale plant to produce reactive telechelic materials using ATRP.

Products include a range of moisture-curable and addition-curable polyacrylates directed at sealant and adhesive markets. The main advantages over current products are high heat, oil, and ultraviolet resistance. One of the advantages that arise from the use of environmentally stable materials is their nonstaining characteristics. The benefits are seen in the lack of surface contamination on artificial marble attached to the exterior of buildings by sealants prepared using ATRP (compare Figure II-11 a with Figure II-11 b).

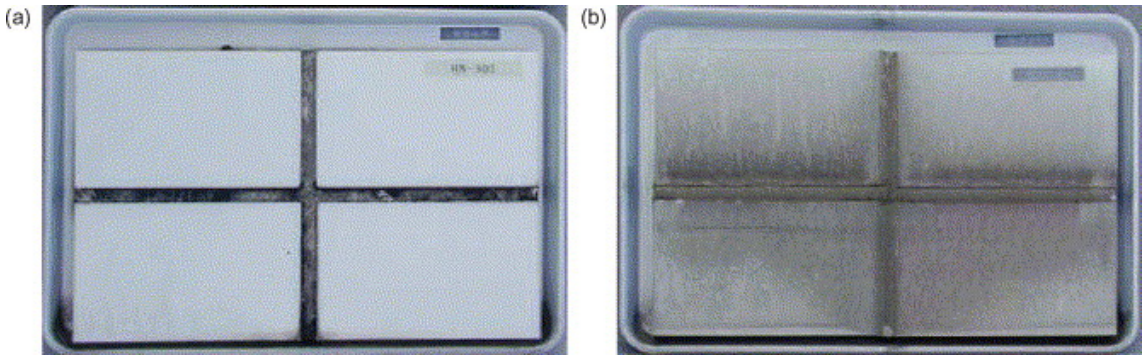


**Figure II-11 Tiles attached with (a) acrylate-based sealant prepared by ATRP; and (b) conventional silicone-based sealant, showing the effect of contamination. Incorporation of acrylate segment by ATRP strongly improves the properties of the sealant (Courtesy of Y. Nakagawa, Kaneka).[6, 119]**

The noncontamination properties of similar products also allow retention of the self-cleaning properties of $TiO_2$-treated glass currently being introduced by PPG[118] for use in offices and residential buildings. The heat and oil resistance of the materials prepared by ATRP also provide ideal materials for the formation of liquid-based gaskets for use in various engines.

Arkema[120], formerly AtoFina, and Dionex are currently considering commercialization of products based on CRP. Arkema has developed a novel class of stable free radical mediator (SG-1)[100, 101] for CRP of acrylate monomers and claims they are suitable for preparing high solids coating resins with controlled rheology. The company is planning on introducing block copolymers based on acrylate and methacrylate monomers as toughening agents.

Dionex[121] uses ATRP to nanoengineer the stationary phase of chromatographic columns. An example is the preparation using a 'grafting from' technique of columns for separation of bioactive materials. Dionex has produced a high-resolution, immobilized metal affinity chromatography (IMAC) column capable not only of peptide and protein enrichment, but also of the separation of components within the classes in the same run. This is accomplished by grafting a hydrophilic layer from the particle surface, reacting the polymer grafts with chelating groups, and then inducing chain collapse by introducing Cu ions for intramolecular coordination crosslinking to form tethered metal-polymer composite nanoparticles. The tethered nanocomposite particles interact with the eluants, causing separation of proteins that differ by only one methyl substituent.

## *II.8. Conclusion*

It is clear that the development of controlled radical polymerization methods and all advances made in the field have provided synthetic chemists with the ability to prepare materials that were impossible to synthesize a decade ago. Controlled synthesis and processing now allows the properties of materials to be characterized and readily manipulated on the nanoscale. As a result, numerous corporations in a broad range of markets are preparing a spectrum of new materials. They now have the capability to tailor the properties of their products to their customers' needs.

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# *Chapter III*
# *Poly((meth)acrylic acid) polymers by CRP: current status*

## Abstract

Poly((meth)acrylic acid) (P(M)AA) is a very important polymer for a variety of applications because of its pH-responsive nature, its hydrophilic characteristics, and its interaction with metal ions. As controlled polymerization techniques have to be applied to synthesize well-defined P(M)AA containing polymers, this chapter is meant to give an overview of the current status in the field. Hereby is focussed on radical polymerization techniques, because of its attractiveness for both the academic as the industrial world.

# III
# Poly((meth)acrylic acid) polymers by CRP: current status

## III.1. "Traditional" synthesis of P(M)AA-containing polymers

As clearly illustrated in the introduction of this thesis (see Chapter I), poly((methacrylic acid) (P(M)AA) is an important polymer in a lot of application fields. Traditional polymerization routes towards well-defined P(M)AA-containing polymers include ionic polymerization techniques.[1, 11, 12] Because the application of these techniques is not compatible with functional monomers (functionalities in the system would cause termination of the growing chains), typically protected analogues[13] of the (meth)acrylic acid monomers have been employed, followed by a deprotection step, e.g. hydrolysis of the protecting ester groups. The propagation reaction of the anionic polymerization of e.g. *tert*-butyl methacrylate (tBMA) happens through a nucleophilic attack of the carbanion to the polarized olefinic bond of the monomer (see Figure III-1). Because of the ionic nature of the species, termination reactions with $H_2O$ or other impurities in the reaction mixture can only be avoided when all reagents are strictly purified and dried. Typically, tBMA is polymerized at -78 °C.[14] Monomers polymerizable by anionic techniques are rather limited and include styrenes, (protected) (meth)acrylates, acrylonitrile, butadiene and isoprene.

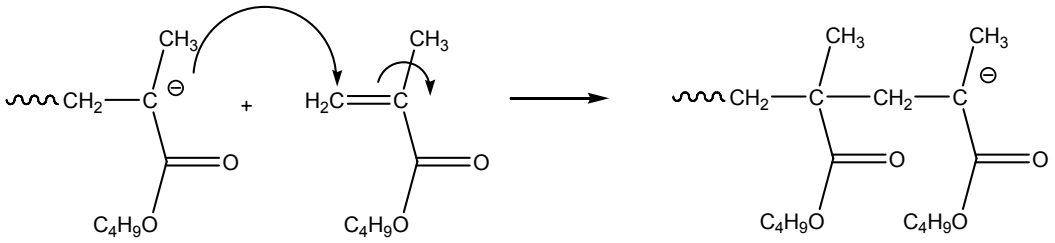


**Figure III-1** **Propagation reaction of the anionic polymerization of *tert*-butyl methacrylate: nucleophilic attack of the carbanion to the polarized olefinic bond of the monomer.**

Because of the rather stringent reaction conditions and the mentioned limitation towards the synthesis of functional materials by ionic techniques, and because of the attractiveness of radical polymerization for industrial applications (as discussed in Chapter II), more recently controlled radical polymerization techniques have been investigated for the synthesis of P(M)AA-containing polymers. However, it should be noted that acrylic acid exhibits a very high rate constant of propagation in free radical polymerization[15], together with a propensity for self-initiation[16], both being able to ruin control over the polymerization reaction.

In the following, the ATRP, RAFT and NMP method will be discussed and an overview will be given with regard to the synthesis of P(M)AA containing polymers.

## III.1.1. P(M)AA and ATRP

### III.1.1.1. Direct polymerization of (M)AA

ATRP is commonly not able to polymerize acidic monomers due to a complexation of the monomer with the metal complex. Patten and Matyjaszewski state that "acrylic and methacrylic acid cannot be polymerized with currently available ATRP catalysts, because these monomers react rapidly with the metal complexes to form metal carboxylates that are inefficient deactivators and cannot be reduced to active ATRP catalysts".[17] In addition, nitrogen-containing ligands can be protonated, which interferes with the metal complexation ability.

### III.1.1.2. Use of sodium salt analogue of (M)AA

One strategy to overcome the above mentioned complications, as reported by Armes *et al.* in 1999, is the ATRP synthesis of methacrylic acid (MAA) (co)polymers in aqueous media, using the sodium salt analogue of MAA.[18] However, no details were given on the control of the polymerization. Moreover, with this method, only water soluble copolymers can be synthesized, which strongly limits the variety of copolymers that can be prepared. Armes admitted in a later publication, where he describes the polymerization of sodium 4-vinylbenzoate, another acidic monomer, that although the polymerization of sodium methacrylate was an important "proof of concept" experiment, the conversion of sodium methacrylate to polymer was both slow and substantially incomplete, with yields of only 70-80 % being obtained after 21 h at 90 °C.[19] In contrast to the polymerization of sodium methacrylate, for sodium 4-vinylbenzoate excellent yields were obtained in short reaction

times even at 20 °C. However, sodium 4-vinylbenzoate is too expensive to be of commercial interest. Still researching the synthesis of polyacids by ATRP without protecting group chemistry, the polymerization of hydroxyethyl methacrylate and subsequent esterification with excess acid anhydride was reported recently (see also § III.1.1.4).[20, 21] Anyway, this can not be considered as a straight-forward approach for the synthesis of polyacids.

### III.1.1.3. Use of protected derivatives of (M)AA

Another strategy to prepare P(M)AA containing polymers by ATRP is the polymerization of protected derivatives of the acidic monomers. Frequently used derivatives include tert-butyl (meth)acrylate[22-24] (tB(M)A) and benzyl (meth)acrylate[25] (Bn(M)A), while tetrahydropyranyl methacrylate[26] (THPMA) and *p*-nitrophenyl methacrylate[27] (NPMA) were also employed in ATRP systems (see Figure III-2).

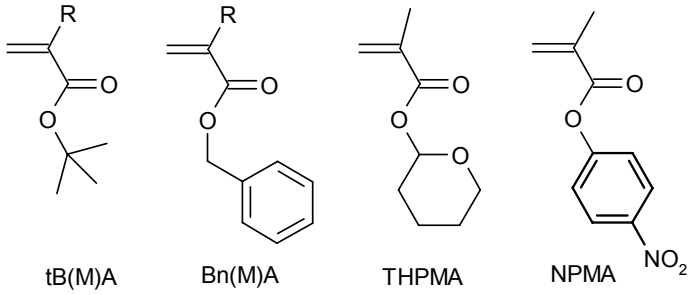


**Figure III-2** **Frequently used protected analogues of acrylic acid (R = H) and methacrylic acid (R = $CH_3$).**

Most interest has been related with the synthesis of block copolymers and more complex polymer systems that contain (meth)acrylic acid segments, following the general trend in modern material science. Tert-butyl acrylate has been employed most frequently, probably because of the feasibility to control the polymerization and relatively easy hydrolysis.

Using the ATRP process, block copolymers can be generated from a macroinitiator synthesized by either ATRP or even from a different mechanism (cationic, anionic, etc.).[28-31] More than any other CRP technique, ATRP shows its versatility in this matter. Furthermore, the growth of subsequent blocks can be achieved from an isolated macroinitiator or by in situ addition of a second monomer to a reaction near completion.

After synthesis of the precursor polymers, quantitative deprotection of the protecting groups is the key step to prepare well-defined polymers containing (meth)acrylic acid segments. In all cases, a post-polymerization deprotection and purification step is required to

generate the desired polyacid. However, this procedure is not always straightforward. Quite a few problems were encountered when removing the protecting groups.

Figure III-3 tries to give an overview of the deprotection of some frequently used precursor polymers of poly((meth)acrylic acid), with some typical deprotection conditions.

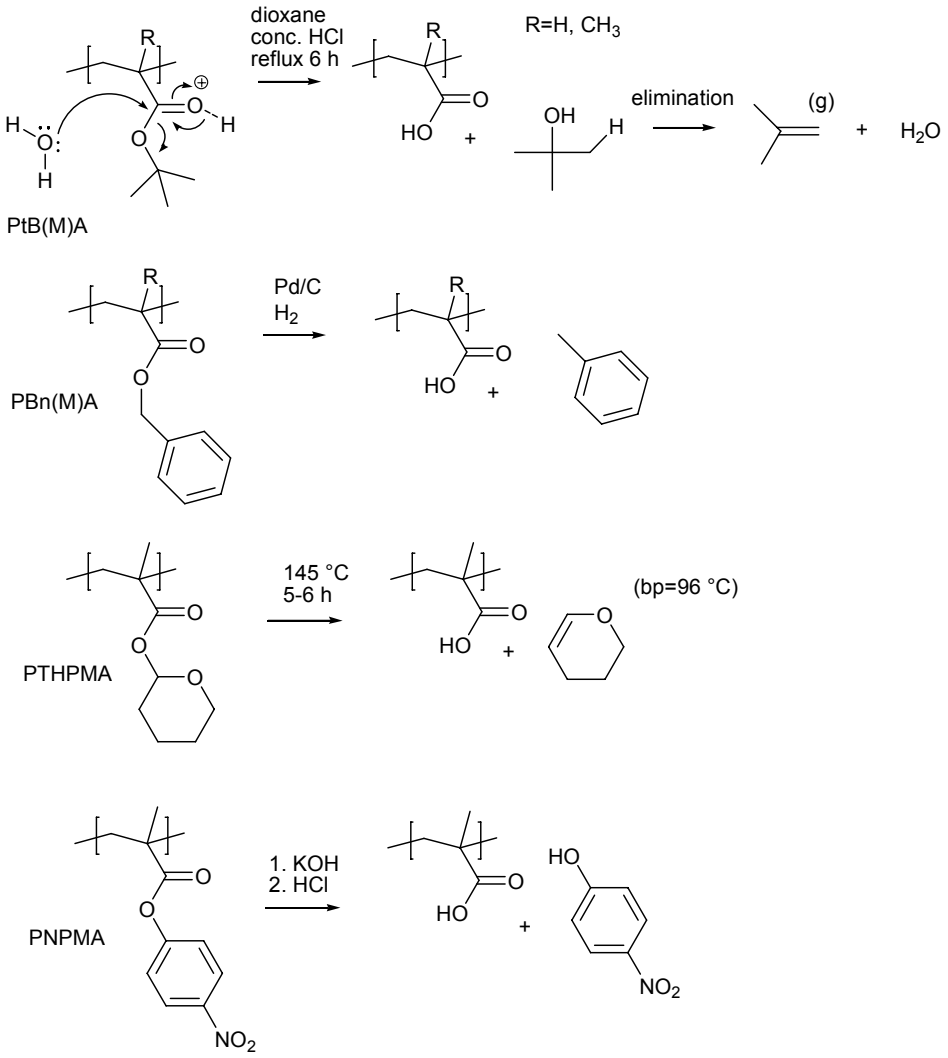


**Figure III-3** **Deprotection of precursor polymers PtB(M)A, PBn(M)A, PTHPMA, and PNPMA to P(M)AA, and some typical reaction conditions.**

The following paragraphs aim to give an overview of the use of the various protected monomers.

#### *III.1.1.3.1. tert-butyl (meth)acrylate*

Tert-butyl(meth)acrylate (tB(M)A) is definitely the most commonly used protected monomer for (meth)acrylic acid. For example, the controlled synthesis of a poly(tert-butyl

acrylate) (PtBA) precursor could be attained using the CuBr/N,N,N′,N″,N″-pentamethyldiethylenetriamine (PMDETA) catalyst system.[22, 24] The use of PtBA as a macroinitiator allows for the preparation of amphiphilic block copolymers, after the hydrolysis of the ester groups.[22] In addition, the preparation of an ABC triblock copolymer, PtBA-b-polystyrene-b-poly(methyl acrylate) (PtBA-b-PS-b-PMA), was reported.[24] Characterization of aqueous micellar solutions of amphiphilic PS-PAA block copolymers (via PS-PtBA) was investigated towards the control of the number of particles in emulsion polymerization.[32] ATRP has been also employed for the synthesis of amphiphilic block copolymers containing methacrylic acid segments, such as PS-b-PMAA[33] and poly(methyl methacrylate)-b-PMAA[34], through hydrolysis of the tert-butyl groups of the PtBMA block.

Wooley *et al.* employed ATRP for the polymerization of tBA, methyl acrylate (MA), and styrene to generate well-defined diblock and triblock copolymers, which were converted to PAA-b-PMA and PAA-b-PMA-b-PS via a hydrolysis reaction.[35] The self-assembly of the ABC-type amphiphilic triblock copolymer in aqueous solution, followed by conversion into stable complex nanostructures via cross-linking reactions between the hydrophilic PAA chains comprising the peripheral layers, produced mixtures of spherical and cylindrical topologies. The same research group also combined anionic ring-opening polymerization and ATRP for the synthesis of block copolymers containing (meth)acrylic acid segments. For example, an amphiphilic block copolymer, poly(ε-caprolactone)-b-PAA (PCL-b-PAA), was prepared by selective hydrolysis of a PCL-b-PtBA precursor, which was synthesized by anionic ring-opening polymerization of ε-caprolactone followed by ATRP of tBA.[36]

The combination of cationic polymerization and ATRP was also reported. For example, Kennedy *et al.* reported the synthesis of a series of novel block copolymers consisting of polyisobutylene (PIB) and PMAA segments. The synthesis of diblocks (PIB-b-PMAA), triblocks (PMAA-b-PIB-b-PMAA), and three-arm star-blocks $(PIB\text{-}b\text{-}PMAA)_3$ consisting of rubbery, long PIB blocks connected to short blocks of PMAA is described.[37]

The use of dual/heterofunctional initiators is another strategy to combine mechanistically distinct polymerization reactions.[38] For example, it has been applied by Du Prez *et al.* for the synthesis of novel well-defined polytetrahydrofuran-b-PAA (PTHF-b-PAA) and poly(methyl vinyl ether)-b-PAA (PMVE-b-PAA) block copolymers.[39-41] Making use of a sequential process, THF and MVE were first polymerized by cationic polymerization, and after isolation a hydrolizable PtBA segment was synthesized by ATRP.

Besides the synthesis of all these linear structures, also a lot of P(M)AA containing branched (co)polymers have been synthesized, including dendritic, comb-shaped, and star polymers, as well as segmented copolymers, which include amphiphilic graft copolymers, comb copolymers, starblock copolymers, etc… For synthetic details we refer to a recent review written by Müller.[1]

Hydrolysis of tB(M)A containing polymers is usually performed by stirring (eventually combined with refluxing) the polymer solution with a strong acid, such as HCl, *para*-toluenesulfonic acid or trifluoroacetic acid. Althought this is considered as a relatively easy method, it remains quite labour intensive, and for applications/synthesis in an industrial environment, the use of strong acids is not very attractive.

#### *III.1.1.3.2. benzyl (meth)acrylate*

Munirasu *et al.* reported on the rapid ATRP of benzyl methacrylate (BnMA) at ambient temperature for the synthesis of various block copolymers such as AB diblock, BAB symmetric and asymmetric triblocks, and ABABA pentablock copolymers, with styrene as the second monomer.[25] Debenzylation is carried out by hydrogenolysis with Pd-C and $H_2$, as usual. They observed no problems with the hydrogenolysis and found that deprotection of the benzyl group was quantitative. However, other groups reported some problems to reach 100% deprotection, although they used GTP instead of ATRP for the synthesis of BnMA-containing polymers. For instance, (benzyl methacrylate)-rich copolymers could not be debenzylated completely and catalyst residues limit the utility.[42-44] Vamvakaki *et al.* reported in one paper that for oligo(ethylene glycol) monomethyl ether monomethacrylate (OEGMA) and BzMA containing block copolymers quantitative debenzylation only could be achieved for polymers containing less than 54 mol% BzMA.[42] At higher BzMA contents (e.g. 79 mol%) deprotection was substantially incomplete. Moreover, in all cases the deprotected copolymers suffered from catalyst contamination. Ultrafiltration using 0.20 μm filters failed to remove these catalyst residues.

#### *III.1.1.3.3. 2-tetrahydropyranyl methacrylate*

2-tetrahydropyranyl methacrylate (THPMA) has been used quite frequently as a protected monomer in group transfer polymerization[42, 44-49], but only one report of the use of THPMA in ATRP reactions has been found. Lu *et al.* described the synthesis of well-defined amphiphilic PTHPMA-*b*-polyfluorene-*b*-PTHPMA triblock copolymers containing conjugated

polyfluorene segmentes and PMAA segments that were obtained by decomposition of the PTHPMA segments at about 145 °C.[26] The precursor block copolymers were prepared by using ATRP with a 2-bromoisobutyrate end-capped polyfluorene as the macroinitiator. The block copolymers were found to form aggregates in water, as revealed by UV–vis and fluorescent spectroscopy and 1H NMR studies.

Anhydride formation was reported to occur as a side reaction, but the anhydride that was eventually formed during the thermolysis could be successfully transformed to the corresponding acid by hydrolysis in warm water. However, Armes *et al.*, who used THPMA as precursor of MAA for the synthesis of poly(2-(dimethylamino)ethyl methacrylate-block-methacrylic acid) (PDMAEMA-*b*-PMAA) polymers by GTP, observed significant broadening of the molecular weight distribution of the PDMAEMA homopolymer under the same conditions.[45] Alternatively, THPMA units can be deprotected by mild acid hydrolysis.

Hawker *et al.* polymerized the acrylate version of this monomer, 2-tetrahydropyranyl acrylate (THPA) by RAFT for the synthesis of block copolymers with styrene.[50] Cleavage of the tetrahydropyranyl ester upon reaction with acetic acid in a mixture of tetrahydrofuran and water afforded the amphiphilic block copolymers. In the same paper, it was also noted that the polymerization of THPA under NMP conditions was not successful, due to uncontrolled cleavage of the THP group at the elevated temperatures of the polymerization system, which resulted in poorly defined polymers.

#### *III.1.1.3.4. p-nitrophenyl methacrylate*

The preparation of PS-b-PMAA block copolymer was achieved by hydrolysis of PS-b-poly(NPMA) obtained via ATRP.[27] The copolymer was dissolved in THF and a solution of potassium hydroxide in ethanol (1 M, KOH/NMPA = 4:1 in molar ratio) was added and refluxed for 24 h. Then excess aqueous solution of hydrogen chloride was added. The precipitate was collected by filtration and dried under vacuum for 24 h at 50 °C.

### III.1.1.4. Other routes to carboxylic acid containing polymers by ATRP

In 2004, Armes *et al.* reported on a postpolymerization modification of polymers prepared by ATRP to introduce carboxylic acid groups.[20, 21, 51] The reported modification consists of the reaction of hydroxy group-containing polymers with succinic anhydride. In particular, 2-hydroxyethyl methacrylate was polymerized by ATRP, and subsequently reacted with succinic anhydride (SA) or 1,2-cyclohexanedicarboxylic acid anhydride (CDA) in pyridine at

room temperature during 48 hours to yield poly(2-(succinyloxy)ethyl methacrylate) (PSEMA) or poly(2-(2-(carboxylic acid)cyclohexylcarboxy)ethyl methacrylate) (PCEMA), respectively (see Figure III-4).

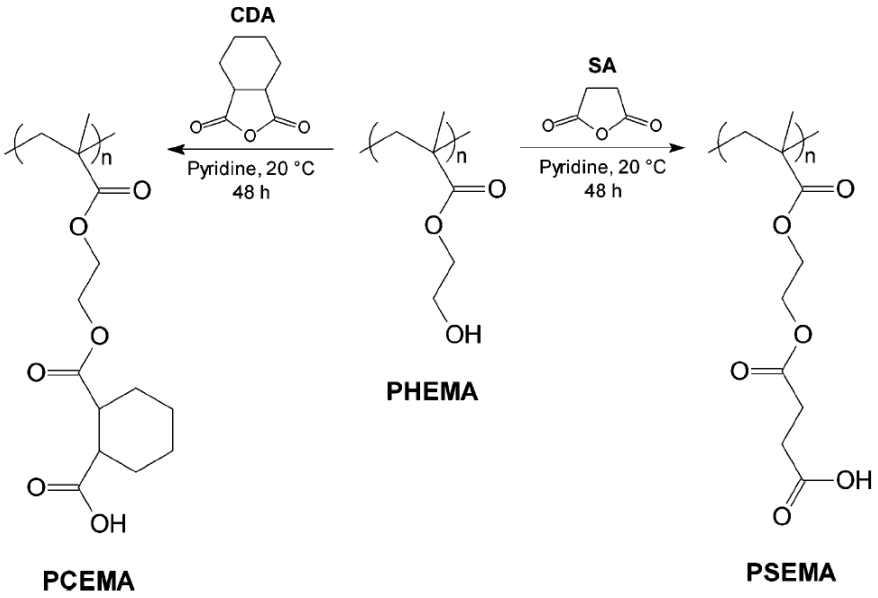


**Figure III-4** **Esterification of poly(2-hydroxyethyl methacrylate) (PHEMA) with succinic anhydride (SA) or 1,2-cyclohexanedicarboxylic acid anhydride, under mild conditions, to give the corresponding carboxylic acid containing polymers (PSEMA and PCEMA, respectively).**

A similar modification was done starting from poly(glycerol monomethacrylate) functionalized multiwalled carbon nanotubes by ATRP to give the corresponding polyacid functionalized multiwalled carbon nanotubes.[52]

An alternative approach for the preparation of well-defined polyacids, reported in 2005, was proposed by the research group of Matyjaszewski.[53] They described the polymerization of a novel monomer, 3-azidopropyl methacrylate (AzMA), via ATRP with good control over the molecular weight distribution and with retention of chain functionality. Poly(AzMA), with pendant azide functionalities, was then coupled with 4-pentynoic acid via the highly efficient Cu(I) catalyzed 1,3 dipolar "click" cycloaddition reaction of azides and alkynes (for more details, see Chapter IV) to yield well-defined polymers with the desired carboxylic acid functionalities (see Figure III-5).

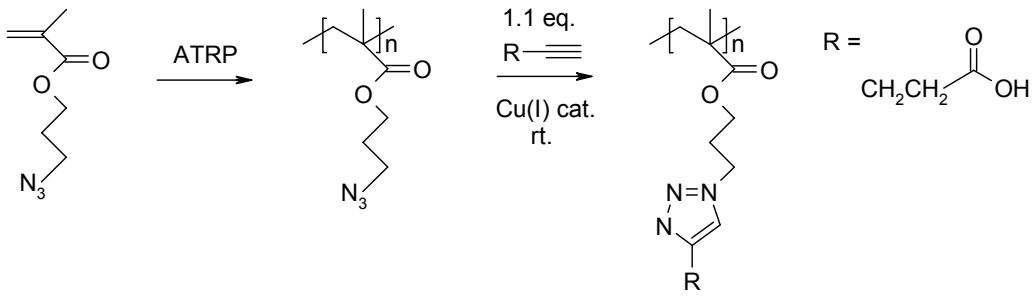


**Figure III-5** **Synthesis of poly(3-azidopropyl methacrylate) via ATRP and subsequent Cu(I) catalyzed 1,3 cycloaddition "click" coupling with 4-pentynoic acid to yield polyacid.**

## III.1.2. P(M)AA and RAFT

With RAFT, the first example of acrylic acid controlled homopolymerization was reported by Rizzardo *et al.* in 1998[54, 55], but no detailed information was provided. The polymerization was carried out in dimethylformamide solution at 60°C, low polydispersities were obtained but the polymerization proceeded extremely slow. Later on, block copolymers of AA and N-isopropylacrylamide (NIPAAm) were synthesized and investigated for their response to combined external stimuli (pH and temperature, respectively).[56, 57]

Ladavière *et al.* examined a series of RAFT agents to control the free-radical polymerization of acrylic acid in alcohol or water solution, and they came to the conclusion that phenoxyxanthates and trithiocarbonates were particularly well-suited.[5] The mechanism of the RAFT of acrylic acid using a trithiocarbonate as a chain transfer agent is shown in Figure III-6. Recently, the same group completed this work with a thorough examination of the controlled character of the polymerization and its limitations.[7] In a further study it was shown that for instance transfer to solvent is an important limiting factor.[6] They are very interested in these materials as they act as very efficient dispersants of $CaCO_3$, $TiO_2$ and kaolin.[5-7, 9] They also described the application of RAFT to the synthesis of controlled poly(n-butyl acrylate)-*b*-poly(acrylic acid) block copolymers and their use as stabilizers in emulsion polymerization.[58]

The controlled homopolymerization of acrylic acid was also performed by another group in the presence of dibenzyl trithiocarbonate, under $^{60}Co$ irradiation at room temperature.[59]

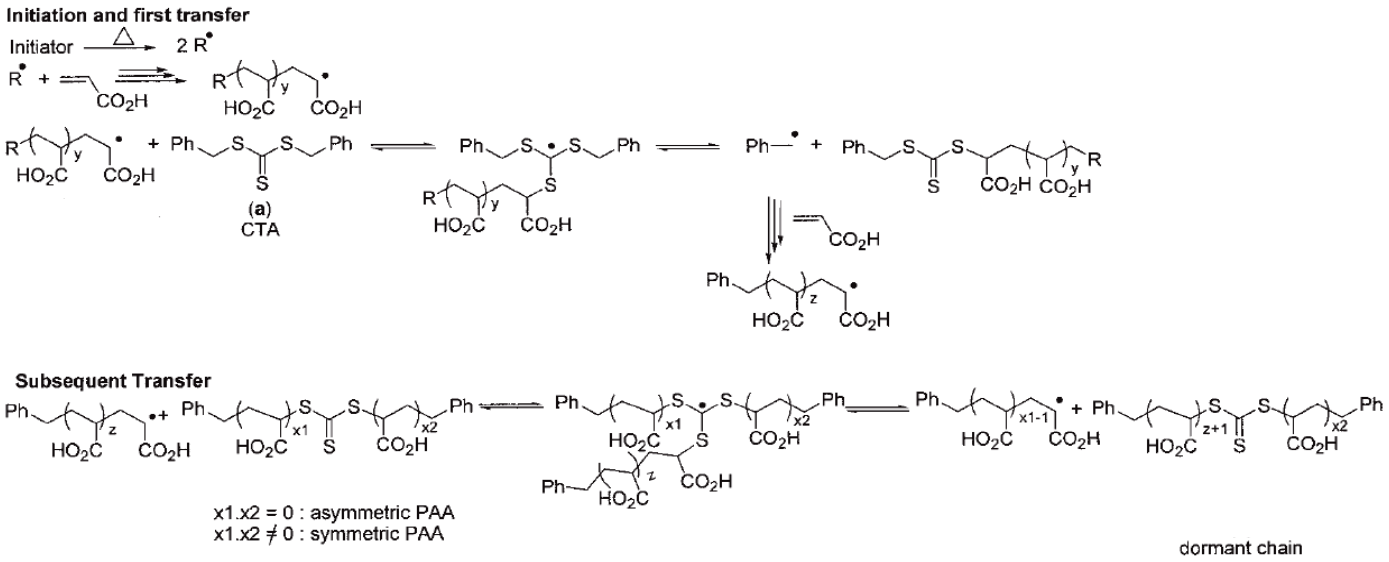


**Figure III-6 Mechanism of the RAFT of acrylic acid using a trithiocarbonate as a chain transfer agent.**[1, 2, 5-7]

Similarly, the MADIX process was successfully used in aqueous solution to prepare well-defined poly(acrylic acid) homopolymer and hydrophilic copolymers based on acrylamide and acrylic acid.[60, 61]

Jérôme *et al.* synthesized a double-hydrophilic copolymer by copolymerizing acrylic acid and a poly(ethylene oxide) end-capped by a methacrylate, with dibenzyltrithiocarbonate as a chain transfer agent.[62]

Very recently (in 2006), RAFT of AA has also been applied to:

- tune the hydrophilicity of gold nanoparticles templated in star block copolymers by direct chemisorption of trithiocarbonate-containing PAA chains[63]
- synthesize PAA, under gamma-irradiation in aqueous media[64]
- directly grow ionic polymers on multi-walled carbon nanotubes via surface RAFT polymerization[65]
- synthesize polystyrene-b-PAA as building block for polypyrrole-containing block copolymers of which the porous films act as a scaffold for cell growth[66]
- prepare in one pot micelles with a cross-linked PAA core[67]

Methacrylic acid has also been copolymerized by the RAFT technique, but only a few reports were found.[68, 69]

### III.1.3. P(M)AA and NMP

The first report of the controlled homopolymerization of acrylic acid (AA) by the NMP method (with SG1 as the nitroxide) was only published in 2003 by Charleux *et al.*[70] As the rate constant of propagation of acrylic acid is very large, the key to success was to moderate its reactivity by a low activation-deactivation equilibrium constant between active macroradicals and SG1-capped dormant chains (Figure III-7). However, because of lack of control in concentrated reaction mixtures, solvent polymerization was required. 1,4-dioxane was chosen as the solvent as it met the requirement to be a good solvent for the monomer, polymer, alkoxyamine initiator and nitroxide SG1, but chain transfer to 1,4-dioxane was the most restrictive event in the process and led to a drastic molar mass limitation (± 10.000 Da). Moreover, also chain transfer to polymer was reported.

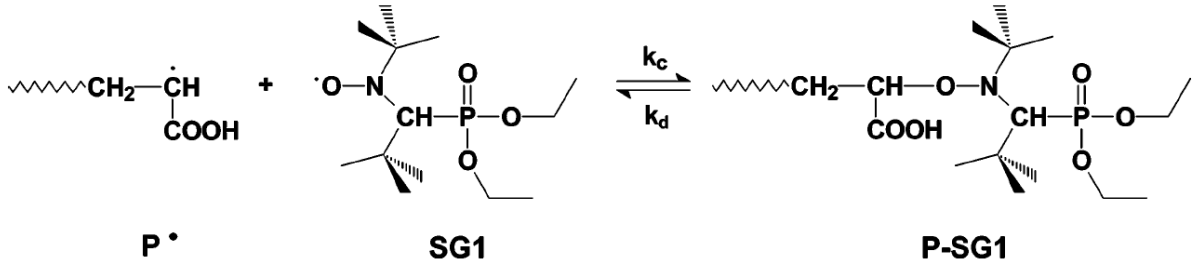


**Figure III-7** **Activation-deactivation equilibrium of the nitroxide mediated homopolymerization (with SG1) of acrylic acid.[70]**

In earlier reports (with TEMPO as the nitroxide), difficulties were encountered to get well-defined homopolymers or copolymers from the direct (co)polymerization of acrylic acid. The acidic group was supposed to be involved in side reactions that lead to decomposition of the nitroxide, which was actually seen for strong organic acids.[71-73] Nevertheless, NMP of AA was reported in two papers before the report of Charleux *et al.* in 2003. Using 2,2,5-trimethyl-4-phenyl-3-azahexane-3-nitroxide, Benoit *et al.* were able to copolymerize acrylic acid with n-butyl acrylate in bulk, up to 50 mol % of the acidic comonomer, in a controlled fashion, but no attempt of homopolymerization, either in bulk or in solution has been reported.[72] Another paper reports on the polymerization of sodium acrylate by NMP in water-solution, using poly(sodium 4-styrenesulfonate) macroinitiators end-capped with water-soluble nitroxides, but the controlled behavior was not demonstrated.[74]

Shortly after the publication in 2003, the group of Charleux has continued its research on the preparation of PAA-containing polymers using NMP[75-78]. The direct synthesis of controlled poly(styrene-co-acrylic acid)s of various compositions by nitroxide-mediated

random copolymerization was reported[75], as well as the synthesis of amphiphilic gradient poly(styrene-co-acrylic acid) copolymers[77]. However, copolymers with a high hydrophobic character (> 70 % of styrene) are not accessible due to the limited solubility of styrene in dioxane. Indeed, acrylic acid requires a rather polar polymerization medium, limiting the amount or choice of other monomers and/or polymer segments. In addition, these gradient copolymers were evaluated as stabilizers in emulsion polymerization. Also poly(sodium acrylate)-b-polystyrene and poly(sodium acrylate)-b-poly(n-butyl acrylate) amphiphilic diblock copolymers, which are able to self-assemble in water, were prepared starting from a water-soluble poly(sodium acrylate) alkoxyamine macroinitiator.[78]

Recently, also other groups have applied the NMP strategy to synthesize polystyrene-b-poly(acrylic acid)[72, 79, 80], and PAA initiated from a silica substrate[81].

## *III.2. Conclusion*

As a conclusion, it can be stated that the synthesis of well-defined poly((meth)acrylic acid) containing polymers by controlled radical polymerization (CRP) techniques is not straightforward and is still an ongoing challenge. However, a lot of efforts in the field have been done, and the recent development of CRP techniques such as RAFT and NMP have shown to be methods for the direct polymerization of acrylic acid.

Direct polymerization of acrylic acid is however not a complete solution, because this approach requires a rather polar reaction medium, which limits the choice of other monomers and/or segments. Another challenge that remains is the synthesis of more complex architectures such as graft, star or brush copolymers. For these architectures, ATRP has proven to be the most versatile CRP method. Unfortunately, this method is not compatible with (meth)acrylic acid, due to side reactions. Therefore, protected derivatives of (meth)acrylic acid have been used. This requires however a postpolymerization deprotection and purification step, which is quite labour intensive.

The aim of this Ph.D. thesis was to look for an alternative strategy that can offer a solution to the mentioned problems. A general applicable precursor strategy seems to be the most useful approach. This approach not only prevents direct polymerization of (meth)acrylic acid which is undesired because of the requirement of a polar reaction medium, but also allows the use of the ATRP technique which is of great importance for the synthesis of functional and/or

complex polymer structures. It is clear that deprotection of the precursor polymer (segment) to poly((meth)acrylic acid) should proceed *via* a general applicable and simple procedure, preferably without the need for any additional purification step.

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# *Chapter IV*
# *“Click” chemistry in polymer world*

## Abstract

In recent years, chemical transformations that were described by Noble prize winner Sharpless as “click” reactions have become a hot topic. In particular, the Cu(I) catalyzed Huisgen 1,3 dipolar cycloaddition of azides and terminal alkynes turned out to be very popular. Only about three years ago, this type of “click” reaction was introduced into polymer synthesis. Shortly after, the combination of “click” chemistry and atom transfer radical polymerization (ATRP) was reported. This chapter aims to summarize the possibilities of “click” reactions in the world of polymers. In addition, since ATRP is one of the most employed polymerization methods in modern material science, a detailed overview is given of the possibilities and opportunities that arise from the combination of ATRP and “click” reactions.

# IV
# “Click” chemistry in polymer world

## IV.1. What is “click” chemistry?

Recent years have witnessed rapid development in the field of chemical transformations that were described by Noble prize winner **Sharpless** and co-workers as “click” reactions.[1] These reactions consist of the formation of molecules through heteroatom C-X-C links, and are inspired by nature. Indeed, all nucleic acids, proteins and polysaccharides are built up with small subunits stitched together by carbon-heteroatom bonds. The great interest in these reactions arises from their specific characteristics such as almost quantitative yields, applicability under mild reaction conditions, high selectivity for one single product, and tolerance to a broad variety of functional groups. “Click” reactions achieve their required characteristics by having a high thermodynamic driving force, usually greater than 80 kJ/mol. Some interesting background information on “click” chemistry can be found in the side section on the next page.

In particular, Sharpless and co-workers popularized in organic synthesis the Huisgen 1,3 dipolar cycloaddition of azides and terminal alkynes.[1-3] The coupling of an azide and a terminal alkyne by a 1,3 dipolar cycloaddition reaction leads to the formation of a 1,2,3-triazole ring, a chemically very stable compound (see Figure IV-1).

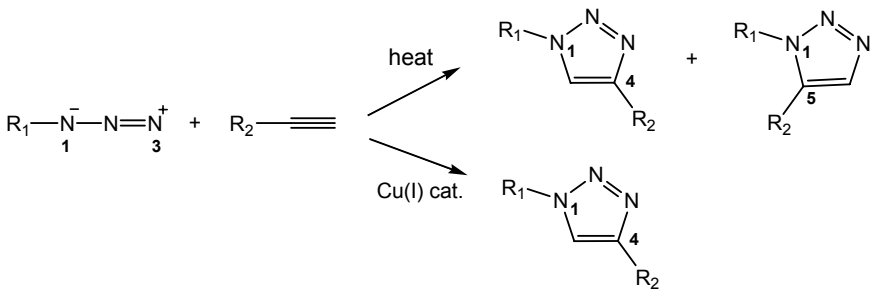


**Figure IV-1** **Schematic depiction of the 1,3 dipolar cycloaddition of azides and terminal alkynes (thermal and copper(I) catalyzed).**

## *“Click” chemistry: some background info…*[1]

Examination of nature's favorite molecules reveals a striking preference for making carbon-heteroatom bonds over carbon-carbon bonds; surely no surprise given that carbon dioxide is nature's starting material and that most reactions are performed in water. Nucleic acids, proteins, and polysaccharides are condensation polymers of small subunits stitched together by carbon-heteroatom bonds. Even the 35 or so building blocks from which these crucial molecules are made each contain, at most, six consicutive C-C bonds, except for the three aromatic amino acids. Starting from nature's approach, the development of a set of powerful, highly reliable, and selective reactions for the rapid synthesis of useful new compounds and combinatorial libraries through heteroatom links (C-X-C), is called “click” chemistry.[1]

A set of criteria that a process must meet to be useful in this context has been defined. The reaction must be modular, wide in scope, give very high yields, generate only inoffensive byproducts that can be removed by nonchromatographic methods, and be stereospecific (but not necessarily enantioselective). The required process characteristics include simple reaction conditions (ideally, the process should be insensitive to oxygen and water), readily available starting materials and reagents, the use of no solvent or a solvent that is benign (such as water) or easily removed, and simple product isolation. Purification - if required - must be by nonchromatographic methods, e.g. crystallization or distillation, and the product must be stable under physiological conditions.

“Click” reactions achieve their characteristics by having a high thermodynamic driving force, usually > 80 kJ/mol. Therefore, they proceed rapidly to completion and are highly selective for a single product. A focus on making carbon-heteroatom bonds must be accompanied by the use of preformed carbon-carbon bonds. The best, and most energetic, of these building blocks are olefins and acetylenes. Chemists have access to a wide variety of such materials, ranging from naturally occurring terpenes to olefins available from petrochemical industry (see Figure IV-2).[4] Carbon-heteroatom bond forming reactions include the following classes:

- cycloadditions of unsaturated species, especially 1,3-dipolar cycloaddition reactions, but also the Diels-Alder family of transformations
- nucleophilic substitution chemistry, like ring-opening reactions of strained heterocyclic electrophiles such as epoxides, …
- carbonyl chemistry of the non-aldol type, such as formation of ureas, thioureas, aromatic heterocycles, amides, …
- additions to C-C multiple bonds, especially oxidative cases such as epoxidation, but also Michael additions of Nu-H reactants.

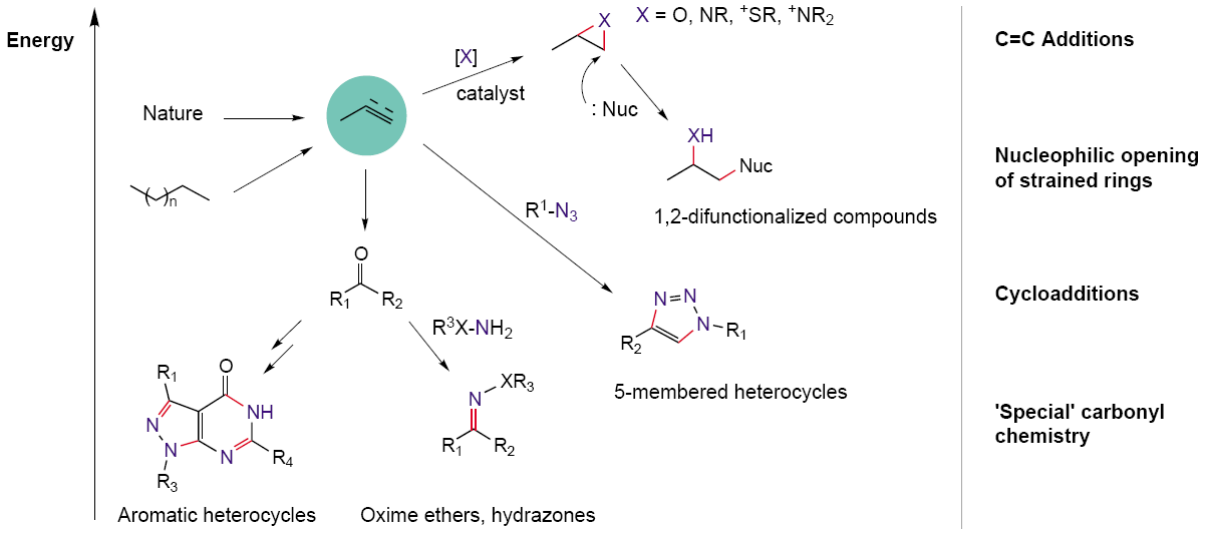


**Figure IV-2** **“Click” chemistry: energetically highly favorable linking reactions. Unsaturated compounds provide the carbon framework. New groups are attached via carbon-heteroatom bonds.**[1]

The non-catalyzed reaction tends to give a mixture of the 1,4 and 1,5 isomer, while the Cu(I) catalyzed reaction leads to selective formation of the 1,4 isomer (see Figure IV-1). The use of a Cu(I) catalyst was only reported in 2002.[5, 6] In addition to their high selectivity for the 1,4 regioisomer, Cu(I) catalyzed reactions proceed much faster (till $10^7$ times faster) which makes that mild reaction temperatures (such as room temperature) are accessible. In the following paragraph, the reaction mechanism of the Cu(I) catalyzed azide-alkyne cycloaddition reaction will be explained more in detail.

## *IV.2. Mechanism of the Cu(I) catalyzed azide-alkyne cycloaddition*

Although the reaction mechanism of the Cu(I) catalyzed azide-alkyne cycloaddition has not been revealed completely yet, it is considered to proceed via a stepwise mechanism and it is believed that copper-acetylide complexes are responsible for the catalytic effect.[5, 7-9] It appears that the Cu(I) catalyst makes the acetylene moiety more activated toward the 1,3 dipolar azide. A mechanistic proposal for the Cu(I) catalyzed azide-alkyne cycloaddition reaction is shown in Figure IV-3.[5] The catalytic cycle starts with the formation of a Cu(I) acetylide that takes part in a stepwise sequence, which proceeds via a six-membered copper-containing intermediate (see Figure IV-3).

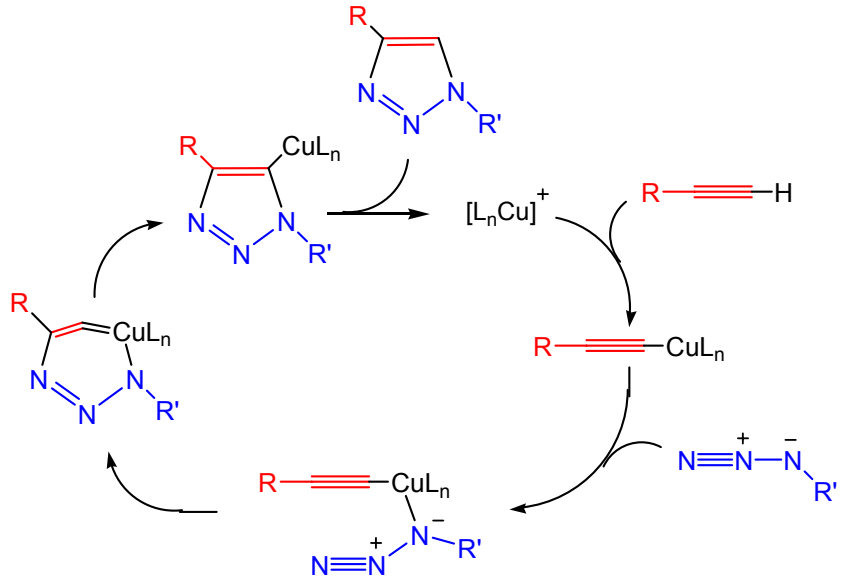


**Figure IV-3 Mechanistic proposal for the Cu(I) catalyzed 1,3 cycloaddition of azides and terminal alkynes.[5, 8]**

The Cu(I) catalyst can either be added to the reaction medium from the start or it can be generated *in situ* by reduction of a Cu(II) salt. One example is the use of a Cu(I)Br ATRP-based catalyst solubilised by a nitrogen ligand[10]. Another catalyst that is frequently used is based on Cu(II) sulphate that is being reduced to Cu(I) by adding sodium ascorbate in the reaction medium.

## *IV.3. "Click" reactions in polymer world: possibilities*

Since their "description" as a new class of reactions by Sharpless *et al.*, "click" reactions have gained an increasing success, according to the exponential rise of the annual number of publications about this particular research topic (see Figure IV-4). During the last 2 years, "click" cycloadditions have also become very popular in polymer chemistry (also see Figure IV-4), as a useful tool for functionalizing synthetic macromolecules and synthesizing a wide range of polymer architectures.[11-38]

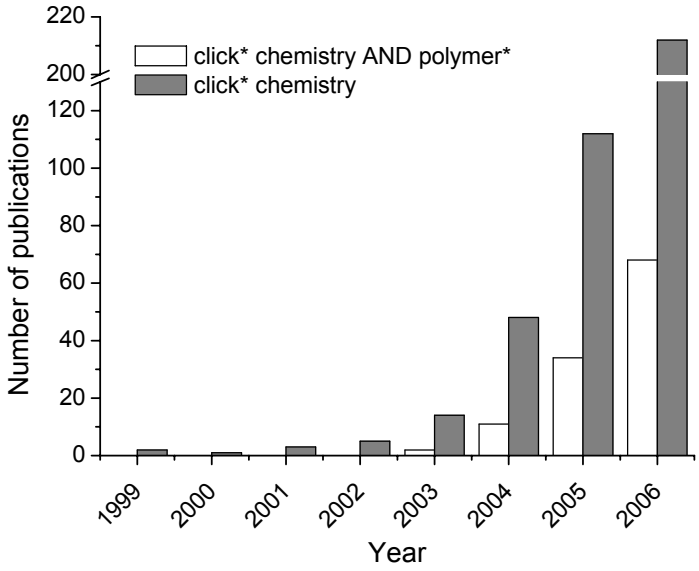


**Figure IV-4** **Number of publications per year about "click" chemistry according to a search on *Web of Science* (05/01/2007).**

The transfer of "click" chemistry from organic synthesis into polymer synthesis first started with the very influential works of Fréchet and Hawker. Their early publications in the field illustrated that the 1,3-dipolar cycloaddition of azides and alkynes is a promising reaction for preparing either dendrimers[21, 30, 32, 35] or functional linear polymers[15, 22]. An

example of the synthesis of well-defined dendrimers using the 1,3-dipolar “click” cycloaddition reaction is shown in Figure IV-5.[35] The monomeric unit 1-propargylbenzene-3,5-dimethanol contained the alkyne functionality, while the core (1,2-bis(2-azidoethoxy)ethane) and the growing dendrimers contain the azide groups necessary for this “click” reaction. The first generation dendrimer was further reacted to the third generation dendrimer. These dendrimers were also used as cross-linking agents to produce shell “click” cross-linked nanoparticles starting from micelles with incorporated alkyne functions.[17]

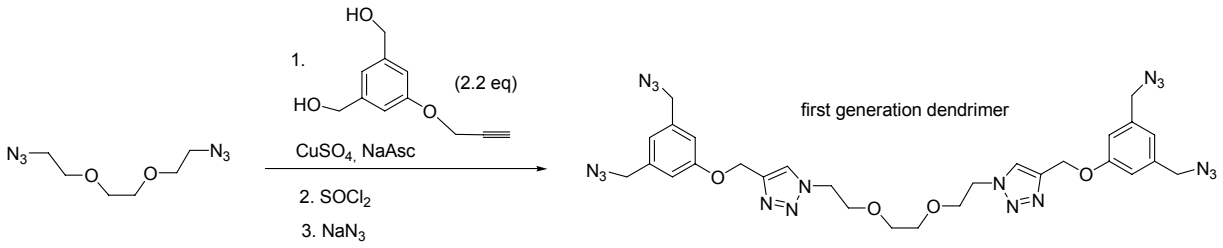


**Figure IV-5** **Synthesis of a first generation dendrimer using the 1,3-dipolar “click” cycloaddition reaction.[35]**

Shortly after, several research groups reported on the combination of “click” chemistry and controlled radical polymerization, more precisely atom transfer radical polymerization (ATRP). Such a step was important since ATRP is probably one of the most powerful and most employed polymerization methods in modern material science.[39-46] Although many efforts have been done already, one great challenge remains the post-modification of the materials. Since in most of the cases post-modification of polymers should be quantitative to be useful, “click” chemistry presents itself as a convenient and powerful tool to further broaden the range of possibilities of ATRP in this field, as quantitative yields are attainable.

The bromine chain ends of polymers prepared by ATRP can easily be transformed into azides by nucleophilic substitution[39, 43, 46, 47] (see also chapter II) and subsequently reacted with functional alkynes. This strategy was used for preparing either well-defined telechelic polymers or block copolymers.[14, 24, 29, 33, 36] Additionally, functional initiators or monomers (i.e., azide or alkyne functional molecules) can be used in ATRP for preparing well-defined “clickable” polymers.[18, 23, 24, 27, 29] A detailed overview of the combination of “click” chemistry and ATRP is given in § IV.4.

Recently, also more and more reports on the combination of “click” chemistry with other controlled polymerization techniques are being published. Jordan *et al.* reported on the

synthesis of a new 2-oxazoline with a pendant alkyne function and copolymerized it via living cationic polymerization, resulting in well-defined polymers without protecting step.[31] The further reaction with azide compounds provides 1,2,3-triazole rings in the polymer side chains in a quantitative yield. Jérôme *et al.* reported on the combination of ring-opening polymerization of ε-caprolactone and “click” chemistry towards functionalization of aliphatic polyesters.[26] Parrish *et al.* prepared poly(ethylene glycol) and peptide-grafted aliphatic polyesters by synthesizing novel aliphatic polyesters with pendant acetylene groups by controlled ring-opening polymerization that were subsequently used for grafting poly(ethylene glycol) and oligopeptide moieties by Cu(I) catalyzed addition of azides and alkynes.[25] Hoogenboom *et al.* described the synthesis of star-shaped poly(ε-caprolactone) *via* “click” chemistry.[48] Also the combination of ring-opening metathesis polymerization (ROMP) with “click” chemistry has been reported.[12] 7-Oxynorbornene derivatives were polymerized by the ROMP technique after which alkyne or azide functionalities were incorporated. A final “click” reaction with the appropriate complementary azide or alkyne compound provided polymers with alkyl or thymine functionalized side chains. Undoubtedly, the exploration of the possibilities created by combination of “click” chemistry and controlled polymerization techniques has only just started.

The “click” chemistry approach even showed the possibility of the design of a completely new versatile monomer family (see Figure IV-6). Functionalized 4-vinyl-1,2,3-triazoles were prepared, combining many of the outstanding features of traditional monomers such as styrenics, vinyl pyridines, and acrylates.[49]

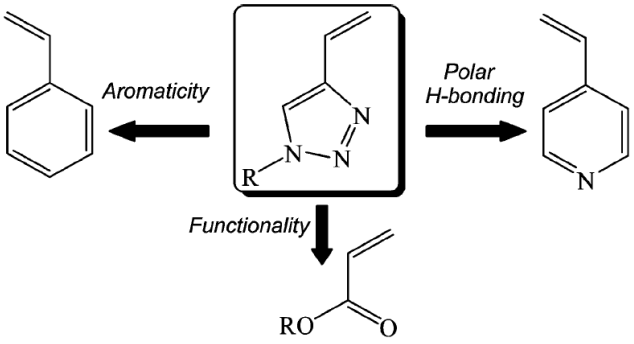


**Figure IV-6** **Functionalized 4-vinyl-1,2,3-triazoles monomer family and its similarities with traditional vinyl systems.**

Hilborn *et al.* reported on the formation of hydrogels via “click” chemistry by introducing azide and alkyne pendant groups onto both poly(vinyl alcohol) and poly(ethylene glycol)

(PEG), and mixing the polymers in the presence of a copper catalyst.[50] Hawker *et al.* also prepared well-defined hydrogel networks using diacetylene-functionalized PEG and tetraazide-functionalized PEG.[51] The efficiency of this reaction was proved by adding an alkyne-functionalized chromophore to the gel; UV and fluorescence measurements showed only 0.2 % of unreacted azide moieties.

The biocompatibility of the 1,3 cycloaddition of azides and terminal alkynes was also demonstrated, as it has been applied with success in a number of biological systems, showing again its wide applicability. For instance, it has been employed for bacterial cell surface labelling[52], conjugation of biological polymers to viruses[53-55], conjugation of synthetic polymers to peptides[33], attachment of proteins to solid surfaces[56-58], and the preparation of cyclodextrin[59] and cyclopeptide[60, 61] analogues. The triazole products are more than just passive linkers; they readily associate with biological targets, through hydrogen bonding and dipole interactions, and therefore, "click" chemistry is also having a growing impact on drug discovery.[4]

Additionally, the 1,3-dipolar cycloaddition reaction has been used to tune the surface functionality of different polymeric or non-polymeric materials such as electrode surfaces[62], gold[63] or silica particles[64], and porous beads[61, 65]. It has also been employed in the field of microcontact printing where it was used to modify azide- or alkyne-functionalized self-assembled monolayers.[66, 67]

Until now, 2 patents have been published concerning the combination of "click" chemistry in the field of polymers. One of them, titled "preparation of functional polymers" belongs to the research group of Matyjaszewski.[68] The development of a polymer consisting of 5-vinyl tetrazole monomer units for coating applications is described. It contains general claims about the use of "click" reactions to attach functional groups to well-defined polymers.

Another patent is titled "polymeric materials via click chemistry" and belongs to Fokin, Finn and Sharpless.[69] It describes the polycondensation of low molecular weight azides and alkynes by using the "click" cycloaddition reaction. Application as adhesive material in coatings is described.

## *IV.4. ATRP in combination with "click" chemistry: current status*

This paragraph aims to give an overview of the possibilities and opportunities that arise from the combination of ATRP and "click" reactions. Generally, "click" reactions have been used in this field for 2 main purposes:

- for the synthesis of various polymers, where alkyne or azide functionalized polymers and alkyne- or azide containing compounds are used as building blocks.
- for the preparation of functional polymers, for either creating end-functionalized polymers or introducing functionalities along the polymer side chain.

### IV.4.1. "Click" chemistry for the synthesis of polymers

#### IV.4.1.1. block copolymers

One of the earliest reports on the combination of ATRP and "click" chemistry was published in 2004 by Van Hest *et al.*[24] He reported on the preparation of polymeric building blocks containing terminal azide and alkyne functionalities via ATRP. These building blocks

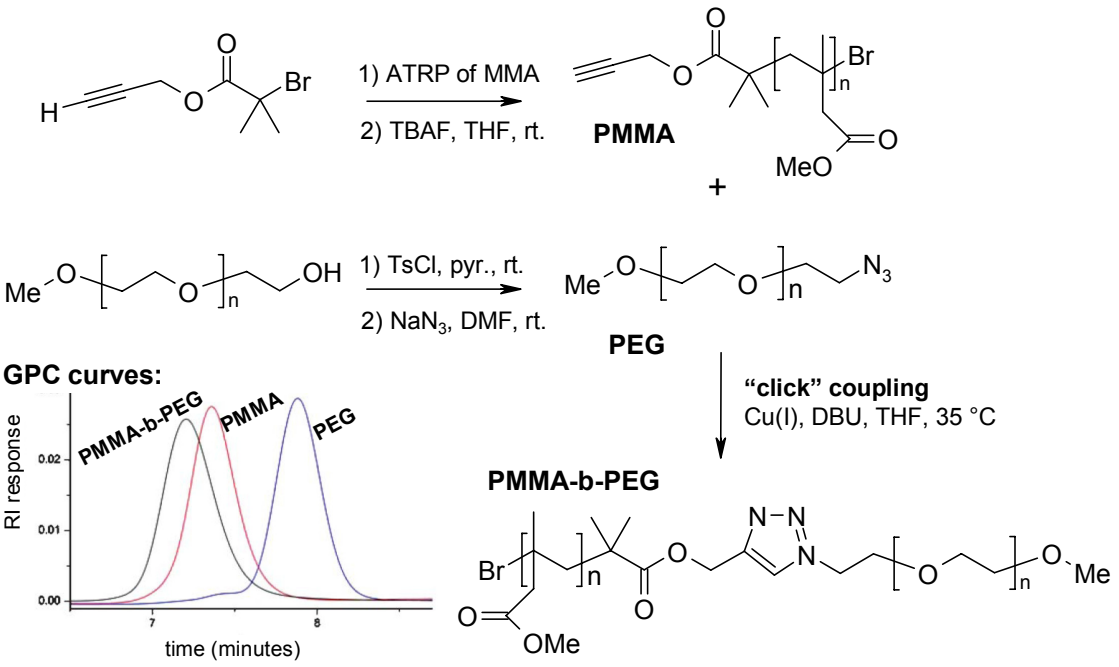


**Figure IV-7** **Synthesis of alkyne functionalized PMMA and azide functionalized PEG, and subsequent "click" coupling to PMMA-b-PEG block copolymer (with GPC curves).**

were then used to modularly synthesize block copolymers via 1,3 dipolar cycloaddition reactions (see Figure IV-7). The main advantage of this approach is that the separate blocks can be fully analyzed (e.g. determination of molecular weight and molecular weight distribution) prior to coupling.

The applied strategy is as follows. The alkyne functionality was introduced in a series of poly(methyl methacrylate) (PMMA) and polystyrene (PS) polymers utilizing an alkyne functionalized initiator. The alkyne functionality of this initator was protected with a trimethylsilyl group in order to prevent complexation with the copper catalyst during polymerization, after which this protective group was removed quantitatively using tetrabutylammonium fluoride (TBAF). On the other hand, azide mono- and bifunctionalized PS was obtained by replacement of the Br endgroup by azides using azidotrimethylsilane and TBAF. Moreover, the hydroxyl group of commercially available poly(ethylene glycol) methyl ether (PEG) was converted into an azide or alkyne functionality. The thus obtained polymer building blocks were coupled via 1,3 dipolar cycloaddition between the azide and alkyne end groups using Cu(I) and 1,8-diaza[5.4.0]bicycloundec-7-ene (DBU). Gel permeation chromatography was used to proof that these coupling reactions lead to the formation of block copolymers. Interestingly, a slight excess of PEG or PMMA was used (1.2 equivalents) in order to drive the “click” reactions to completion. The excess of PEG could be removed by a washing step, while in case of PMMA-b-PS, the excess alkyne-functionalized PMMA was scavenged by a “click” reaction onto azide functionalized PMMA.

#### IV.4.1.2. star polymers

The first synthesis of star polymers by a coupling procedure using a combination of ATRP and “click” chemistry was also reported by Matyjaszewski *et al*.[37] Polystyrene (PS) linear chains with high azido chain-end functionality (prepared by ATRP) were coupled with multifunctional alkyne-containing coupling agents (see Figure IV-8) under mild conditions to produce linear and star polymers with different arm numbers. The influence of several parameters on the efficiency of the “click” coupling reaction was studied, including the molecular weight of the PS-$N_3$ polymer, the presence of an added reducing agent, Cu(0), and the stoichiometry between the azide and alkyne groups. The results indicated that the yield of the coupled product was higher when a lower molecular weight PS-$N_3$ was employed in conjunction with a small amount of reducing agent, and the molar ratio of azide and alkyne groups was close to 1.

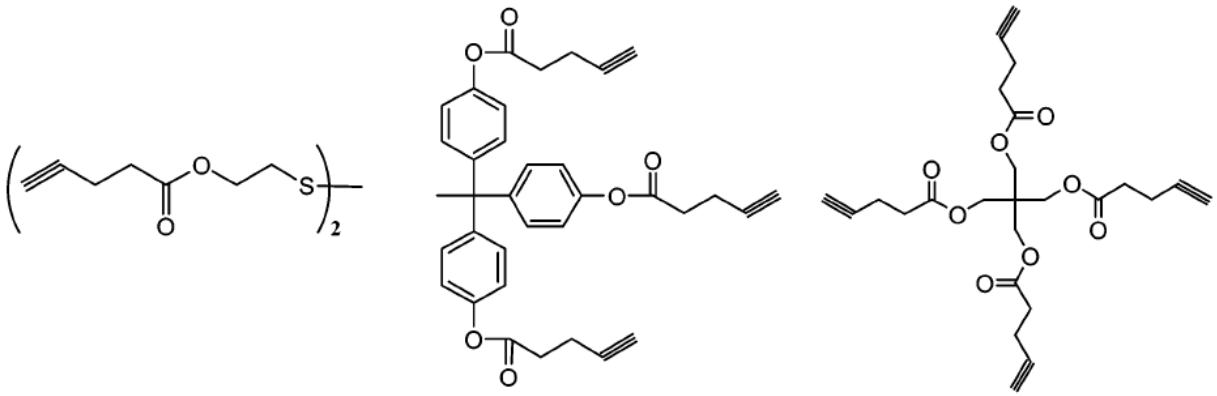

**Figure IV-8** **Multifunctional alkyne-containing coupling agents used to prepare star polymers through coupling with azido-functionalized polystyrene linear chains.**

### IV.4.1.3. “bio” polymers

The group of Haddleton utilized “click” chemistry in combination with living radical polymerization for the synthesis of neoglycopolymers.[18] First, novel well-defined alkyne side chain functional polymers were synthesized by (co)polymerizing a trimethylsilyl protected alkyne-containing methacrylate monomer by ATRP. After deprotection of the alkyne functions, grafting of protected and unprotected carbohydrates is achieved via either “clicking” a C-6 or an anomeric azide (α or β) onto these polymers by Cu(I) catalyzed “click” chemistry, providing a simple and efficient route to synthetic glycopolymers (see Figure IV-9). This strategy provides a powerful tool for the synthesis of libraries of materials that differ only in the nature of the sugar moiety presented on a well-defined polymer scaffold.

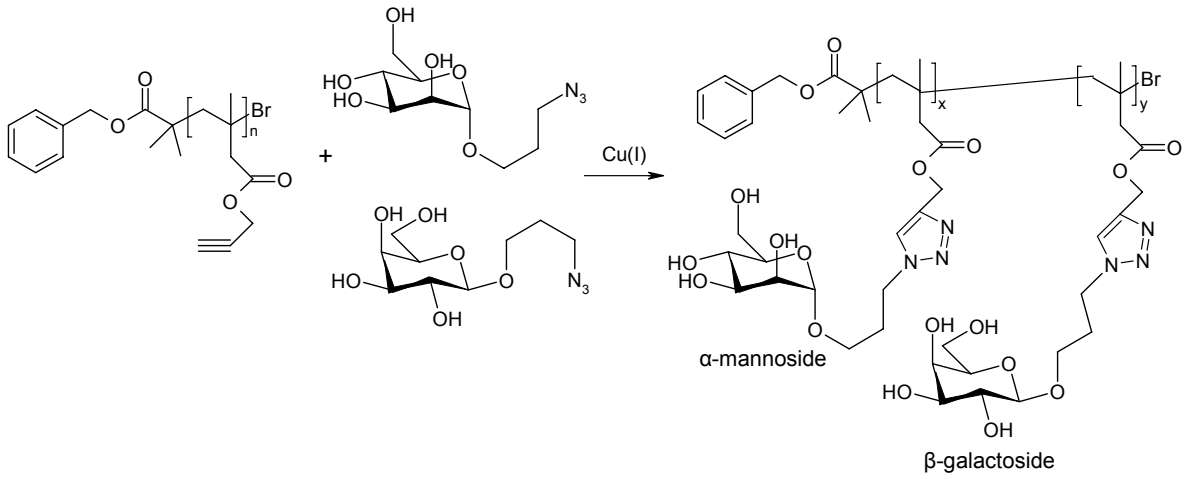


**Figure IV-9** **Synthesis of neoglycopolymers by grafting azido-functionalized carbohydrates onto alkyne-containing polymers by Cu(I) catalyzed cycloaddition reaction.**

### IV.4.1.4. high molecular weight polymers

Matyjaszewski *et al.* made use of ATRP to produce homo- and hetero telechelic polymers that were subsequently used in step-growth "click" coupling reactions to yield high molecular weight polymers.[29] This route was demonstrated to be a convenient alternative to other coupling reactions applied to polymers prepared by ATRP, such as atom transfer radical coupling[70] or reversible thiol oxidative coupling[71]. α-Alkyne-ω-azido-terminated polystyrene (PS) was click coupled at room temperature in DMF with a CuBr catalyst (see Figure IV-10, a). Remarkably, as a result of the click reaction being conducted in DMF, no additional ligand was necessary to solubilize the CuBr catalyst. Additionally, because both ATRP and azide-alkyne click reactions are catalyzed by Cu(I) compounds, a one-pot ATRP-nucleophilic substitution-click coupling process was attempted. This particular approach has led to only moderate success. Another, more successful method involved α,ω-diazido-terminated PS being polymerized with propargyl ether at room temperature to yield higher molecular weight PS (see Figure IV-10, b). In all cases, the resulting click coupled PS was polydisperse. The latter reaction was also used to study the effects of several parameters (ligand, solvent, reducing agent, metal) of the Cu(I) catalyzed azide-alkyne cycloaddition reaction.[72]

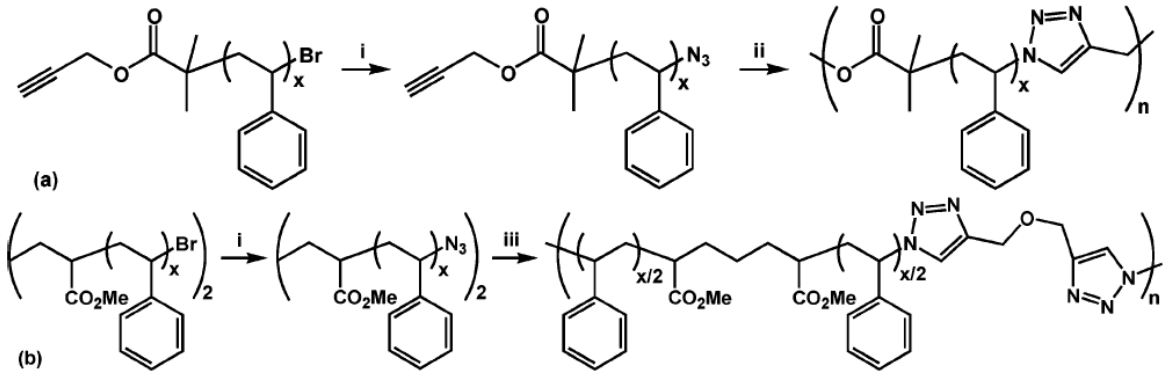


**Figure IV-10** **"Click" coupling reactions using telechelic polymers prepared by ATRP: (a) coupling of α-alkyne-ω-azido-terminated polystyrene, (b) coupling of diazo-terminated polystyrene with propargyl ether. Reaction conditions: *i.* $NaN_3$, DMF, rt., *ii.* CuBr, DMF, rt., *iii.* propargyl ether, DMF, rt.**

### IV.4.1.5. macrocyclic polymers

Grayson *et al.* used α-alkyne-ω-azido-terminated polystyrene prepared via ATRP to create well-defined macrocyclic polymers via "click" cyclization (see Figure IV-11).[19] Synthetic routes for the preparation of macrocyclic polymers have long been a goal for polymer chemists because of their unique topology and specific physical properties.[73] The key of

success for the creation of macrocyclic polymers was the concentration of the polymer in the reaction mixture, because this parameter determines whether the α,ω-functionalized polymer will prefer cyclization or condensation. The condensation of α,ω-functionalized polystyrene was earlier reported by Matyjaszewski *et al.*[29] They reported an unreacted low molecular weight impurity, likely the result of cyclization. Grayson *et al.* found that dilution of the concentration below 0.1 mM favored intramolecular cyclization, while dilution above that concentration favored condensation. Also continuous addition of the polymer to the reaction medium helped avoiding intermolecular reactions.

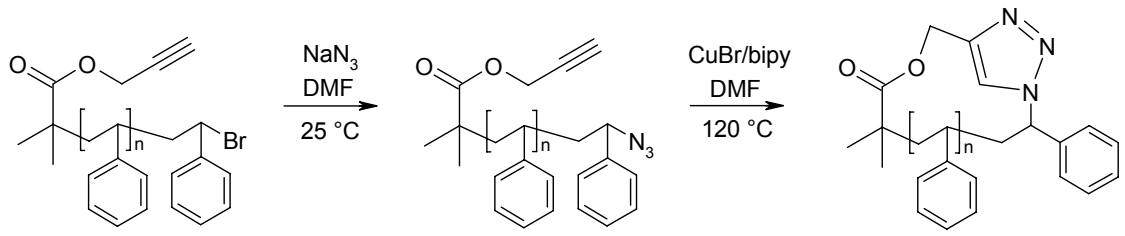


**Figure IV-11 Terminal azidation and “click” cyclization of polystyrene prepared via ATRP.**

### IV.4.1.6. networks

Finn *et al.* used ATRP and “click” chemistry for the synthesis of model networks.[16] They have applied ATRP of *tert*-butyl acrylate with a bifunctional initiator to obtain telechelic polymers that were modified by treatment with sodium azide. The polymer network was then produced by introducing tri- and tetraacetylene cross-linkers. The bifunctional initiator contained a cleavable function at its center, providing the ability to study the network structure, such as the number of unreacted functionalities.

## IV.4.2. “Click” chemistry for preparation of functional polymers

Control over polymer functionalities is a truely essential issue in polymer synthesis, since functional groups can be used for performing further modifications such as the reinitiation of polymerizations, creation of supramolecular linkages, conjugation of macromolecules or adsorption of polymers on surfaces.

### IV.4.2.1. End-functional polymers

Lutz *et al.* combined ATRP with "click" chemistry to introduce various functionalities into a polymer and demonstrated it to be a versatile method for the preparation of various end-functional polymers.[36] Br chain ends of polymers prepared using ATRP were transformed into azides and reacted with alkynes containing various essential functionalities (see Figure IV-12).

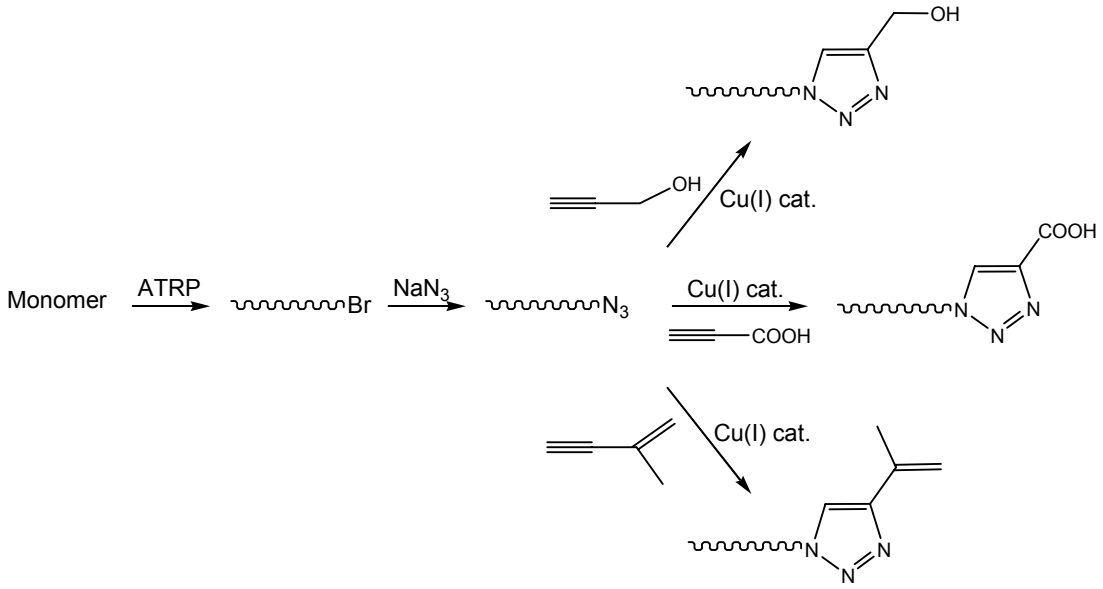


**Figure IV-12 Transformation of bromine end-functional polymer into various functional polymers.**

Also in order to introduce various functionalities, Haddleton *et al.* described a one-pot tandem living radical polymerization-Huisgens ("click") cycloaddition process.[23] In fact, ATRP and "click" cycloaddition reactions could share the same catalyst, and research was focused on catalysis by *N*-alkyl-2-pyridylmethanimine/Cu(I)Br complexes. The synthetic strategy involved the synthesis of appropriate azido-initiators, polymerization of methacrylic monomers in the presence of the mentioned Cu(I)-based catalyst, followed by a subsequent *in situ* "clicking" to functional terminal alkynes (see Figure IV-13).

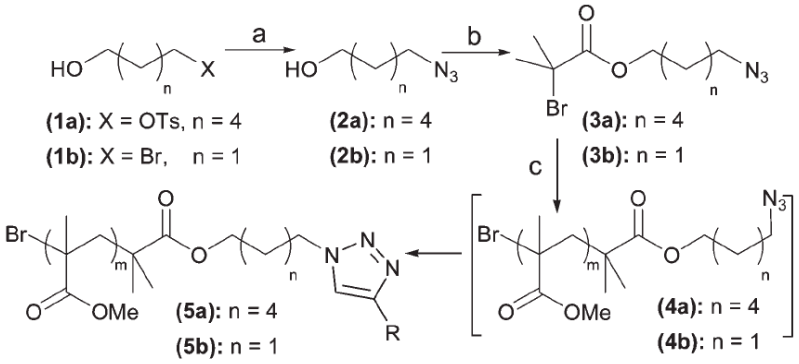


**Figure IV-13** **One-pot tandem living radical polymerization and "click" cycloaddition process. Reagants and conditions: a) $NaN_3$, acetone-water, reflux, b) 2-bromoisobutyryl bromide, $Et_3N$, $Et_2O$, 0°C to ambient temp., c) *i.* methyl methacrylate *N*-alkyl-2-pyridylmethanimine-Cu(I)Br, *ii.* RC≡CH.**

Sumerlin *et al.* employed the combination of ATRP and "click" chemistry to prepare well-defined ω-(meth)acryloyl macromonomers in an efficient manner.[38] Poly(n-butyl acrylate) (PBA), polystyrene (PS), and PS-b-PBA were prepared by ATRP and subsequently derivatized to contain azido end groups. The reaction of the azido-terminated polymers with alkyne-containing acrylate and methacrylate monomers resulted in near-quantitative chain end functionalization.

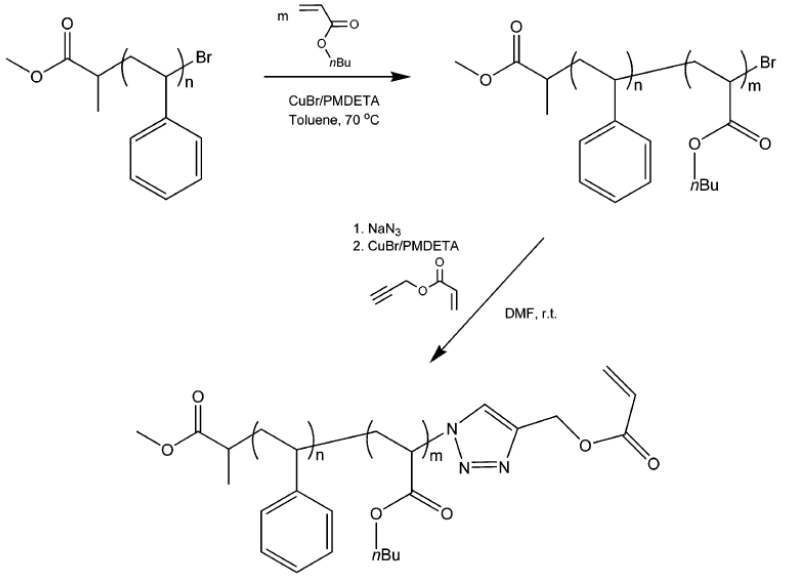


**Figure IV-14** **Polymerization of *n*-butyl acrylate from a polystyrene macroinitiator and subsequent derivatization by *in situ* azidation/coupling.**

Macromonomers of various molecular and architectures were prepared by this method. The end group transformations that were necessary to incorporate the polymerizable functionality were accomplished either as a stepwise series of discrete reactions or as an in situ process, wherein azidation was immediately followed by azide-alkyne coupling in situ. In both cases, the degree of end group functionalization generally exceeded 90%. To demonstrate polymerizability, examples of methacryloyloxy-PBA and acryloyloxy-PS macromonomers were homopolymerized by conventional radical polymerization in toluene. The macromonomers and polymacromonomers were characterized by a combination of size exclusion chromatography using refractive index, light scattering, and viscosity detection, as well as $^{1}$H NMR spectroscopy and $^{1}$H-$^{1}$H NMR correlation spectroscopy.

### IV.4.2.2. Side chain-functionalized polymers

In a collaboration with our research group, Matyjaszewski and Du Prez *et al.* reported on the synthesis of well-defined copolymers with 5-vinyltretrazole units via combination of ATRP (co)polymerization of acrylonitrile and “click” chemistry-type postpolymerization modification.[28] Well-defined homo- and copolymers of acrylonitrile were prepared by ATRP, which were further modified using a “click” chemistry reaction with sodium azide and zinc chloride to yield polymeric materials with 5-vinyltetrazole units (see Figure IV-15). The produced tetrazole-containing polymers had markedly better solubility or swellability in protic solvents (methanol or aqueous base solutions) compared to the precursors. Tetrazoles with no substituent at any of the nitrogen atoms ($RCN_4H$) are acidic, with p$K_a$ values similar to carboxylic acids. They are important compounds for the design of drugs such as antibiotics, antiviral, antiallergic, antihypertensive, and radioprotective agents.

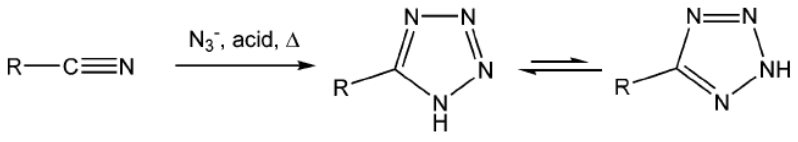


**Figure IV-15 Reaction of nitriles with azides to yield tetrazoles.**

Matyjaszewski *et al.* polymerized via ATRP propargyl methacrylate (PgMA) and 3-azidopropyl methacrylate (AzMA).[27] These monomers have an acetylene or azido pendant group, respectively. These pendant functionalities are capable of participating in a Cu(I) catalyzed 1,3 dipolar cycloaddition reaction of azides and alkynes, and in this way, various functional polymers were prepared. ATRP of PgMA resulted in polymers with high

polydispersities, multimodal molecular weight distributions, and cross-linked networks at moderate to high conversion. The poor results obtained with this particular monomer were attributed to addition of the propagating radicals to the acetylene group, transfer reactions, and/or interference with the catalyst. In contrast to the polymerization of PgMA, the polymerization of AzMA by ATRP was performed with good control over the polymerization reaction. The poly(AzMA) was “click” coupled with various alkyne-containing compounds such as propargyl alcohol, propargyl triphenylphosphonium bromide, propargyl 2-bromoisobutyrate, and 4-pentynoic acid to introduce respectively alcohol, triphenyl phosphonium, carboxylic acid or 2-bromoisobutyrate functionalities (see Figure IV-16). Interestingly, the coupling of 4-pentynoic acid, or other acid-containing alkynes, is in fact an alternative strategy for introducing carboxylic acids groups that are typically incompatible with ATRP conditions (see also Chapter III). All coupling reactions could be conducted at room temperature without significant excess of any reagents, and yields were nearly quantitative.

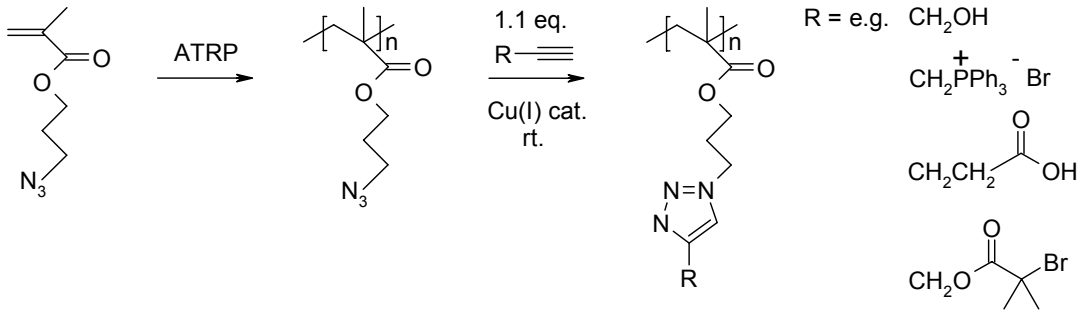


**Figure IV-16** **Synthesis of poly(3-azidopropyl methacrylate) via ATRP and postpolymerization modification with various functional alkynes via Cu(I) catalyzed 1,3 dipolar cycloaddition “click” reaction.**

## *IV.5. Conclusion*

It has been shown that the copper(I) Huisgen 1,3 dipolar cycloaddition of azides and terminal alkynes, a type of a “click” chemistry reaction, is of great importance in the field of polymer chemistry. Indeed, these “click” type synthetic procedures are highly attractive because of their near quantitative yields and absence of side reactions, while they are performed under mild reaction conditions.

It is clear that “click” chemistry has provided synthetic polymer chemists with a powerful tool for further broadening the possibilities of controlled polymerization techniques,

especially in the field of functionalization of macromolecules, and preparing a range of polymer architectures and materials.

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# *Chapter V*
# *ATRP of EE(M)A: novel route towards P(M)AA containing polymers*

## Abstract

This chapter starts with a detailed study of the polymerization of 1-ethoxyethyl (meth)acrylate (EE(M)A) by ATRP. For the first time, this precursor monomer of (meth)acrylic acid is polymerized by ATRP. It is shown that the corresponding poly((meth)acrylic acid) (P(M)AA) polymers can be obtained by a simple heating step. Using a disulfide containing initiator, poly(acrylic acid) brushes were prepared, which were used to create gold substrates with pH-switchable properties. Moreover, to illustrate the general applicability of EE(M)A, various PEE(M)A containing polymers were prepared, including block copolymers, "block-like" copolymers, and random copolymers. In addition, the ATRP of EEA was also combined with the cationic ring opening polymerization of tetrahydrofuran.

# V
# ATRP of EE(M)A: novel route towards P(M)AA containing polymers

## V.1. Introduction

As was concluded from the discussion in Chapter III, the synthesis of poly((meth)acrylic acid) (P(M)AA) containing polymers by controlled radical polymerization is not straightforward and is still an ongoing challenge.

This chapter investigates the use of 1-ethoxyethyl as the protecting group for (meth)acrylic acid. Homopolymers of EEA and EEMA as well as a wide variety of PEE(M)A containing copolymers have been synthesized by the ATRP technique. Poly(1-ethoxyethyl methacrylate) (PEEMA) and poly(1-ethoxyethyl acrylate) (PEEA) are novel precursors for poly(methacrylic acid) (PMAA) and poly(acrylic acid) (PAA), respectively. In this case, deprotection is carried out by a heating step, with the loss of ethyl vinyl ether (boiling point: 33 °C) as a gas, preventing the need of an additional purification step after deprotection.

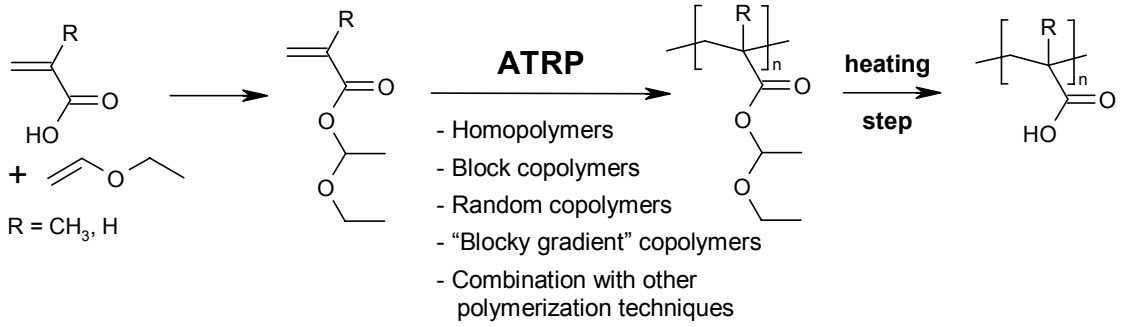


**Figure V-1** **Synthesis of 1-ethoxyethyl (meth)acrylate (EE(M)A), ATRP to PEE(M)A, and subsequent deprotection to P(M)AA by a heating step.**

The EE(M)A strategy was applied to the synthesis of a variety of block, "block-like" and random copolymers with PEE(M)A segments by ATRP to demonstrate the versatility of our approach in the synthesis of more complex polymer architectures. These (block) copolymer structures are of main scientific interest due to their phase separation and solution aggregation behavior. In addition, the ATRP of EEA has been combined with another controlled polymerization technique (cationic ring opening polymerization of tetrahydrofuran). These precursor polymers lead to well-defined P(M)AA (co)polymers after deprotection by a heating step (see Figure V-1).

## *V.2. Homopolymerization of EE(M)A*

### V.2.1. Synthesis of the monomer: 1-ethoxyethyl (meth)acrylate

The monomers, 1-ethoxyethyl methacrylate (EEMA) and 1-ethoxyethyl acrylate (EEA), were synthesized by the acid catalyzed addition reaction of (meth)acrylic acid to ethyl vinyl ether (see Figure V-1), as previously described.[1, 2]

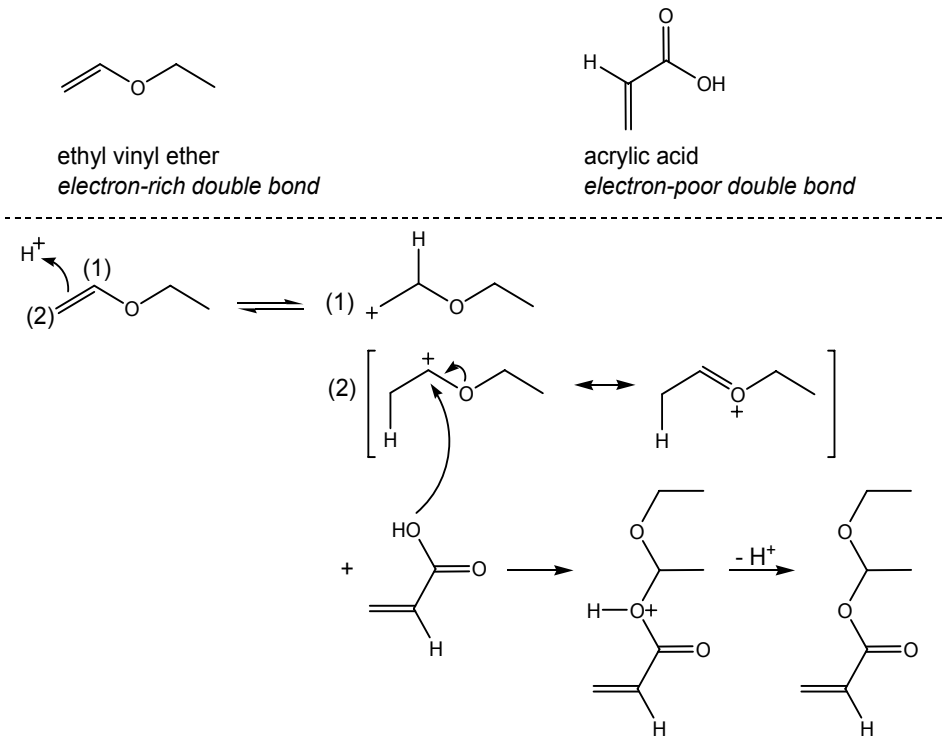


**Figure V-2 Reaction mechanism for the synthesis of 1-ethoxyethyl acrylate (EEA).**

The mechanism for the synthesis of EEA is shown in Figure V-2. Actually, there are 2 possibilities for the addition of the acidic proton to the electron-rich double bond of ethyl vinyl ether. Addition to position (2) is more favourable, because the intermediate product is stabilized through the existence of 2 resonance structures. Electrophilic addition to (meth)acrylic acid does not occur because of the electron-poor character of the double bond. Nucleophilic attack of (meth) acrylic acid to the electron-deficient carbon atom, followed by proton transfer, provides the monomer 1-ethoxyethyl (meth)acrylate.

The synthesis of the monomers can easily be performed on a large scale (typically 400 mL), and with a yield of about 90 %. The monomer is purified by a high vacuum distillation in order to reduce the boiling temperature of EEA to prevent deprotection to (meth)acrylic acid. For example, the $^{1}$H NMR spectrum of 1-ethoxyethyl acrylate is shown in Figure V-3.

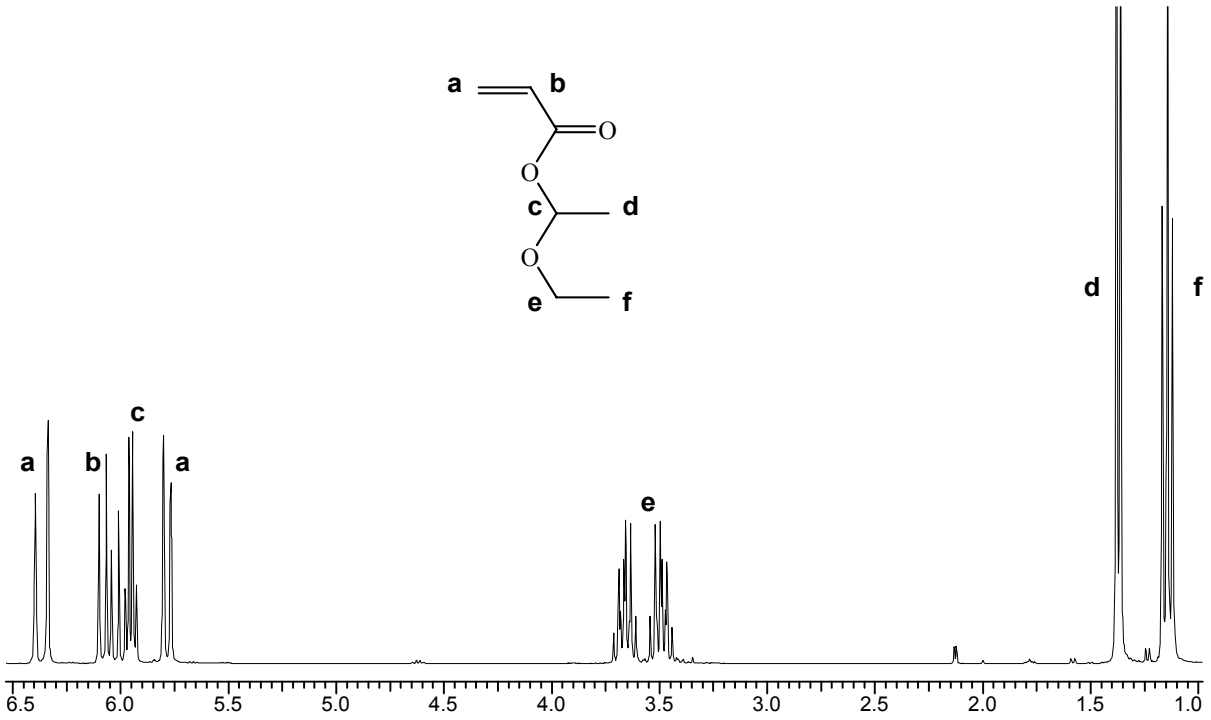


**Figure V-3** **$^{1}$H NMR spectrum of 1-ethoxyethyl acrylate ($CDCl_3$, 300 MHz).**

Note that also other vinyl ether compounds can be used to synthesize similar acetal-containing 1-alkoxyalkyl (meth)acrylate monomers (see Figure V-4). To illustrate this variety of monomers that can be prepared, also 1-isobutoxyethyl acrylate (R2 = isobutyl) was synthesized, starting from isobutoxy vinyl ether. Different R2 and R3 groups influence the deprotection step, as different side products are formed.[2] Figure V-5 shows the $^{1}$H NMR spectrum of 1-*iso*butoxyethyl acrylate.

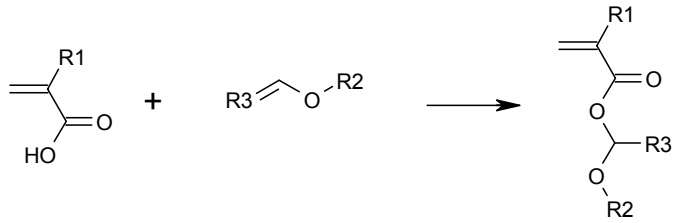


**Figure V-4** **Synthesis of a variety of acetal-containing protected (meth)acrylic acid monomers.**

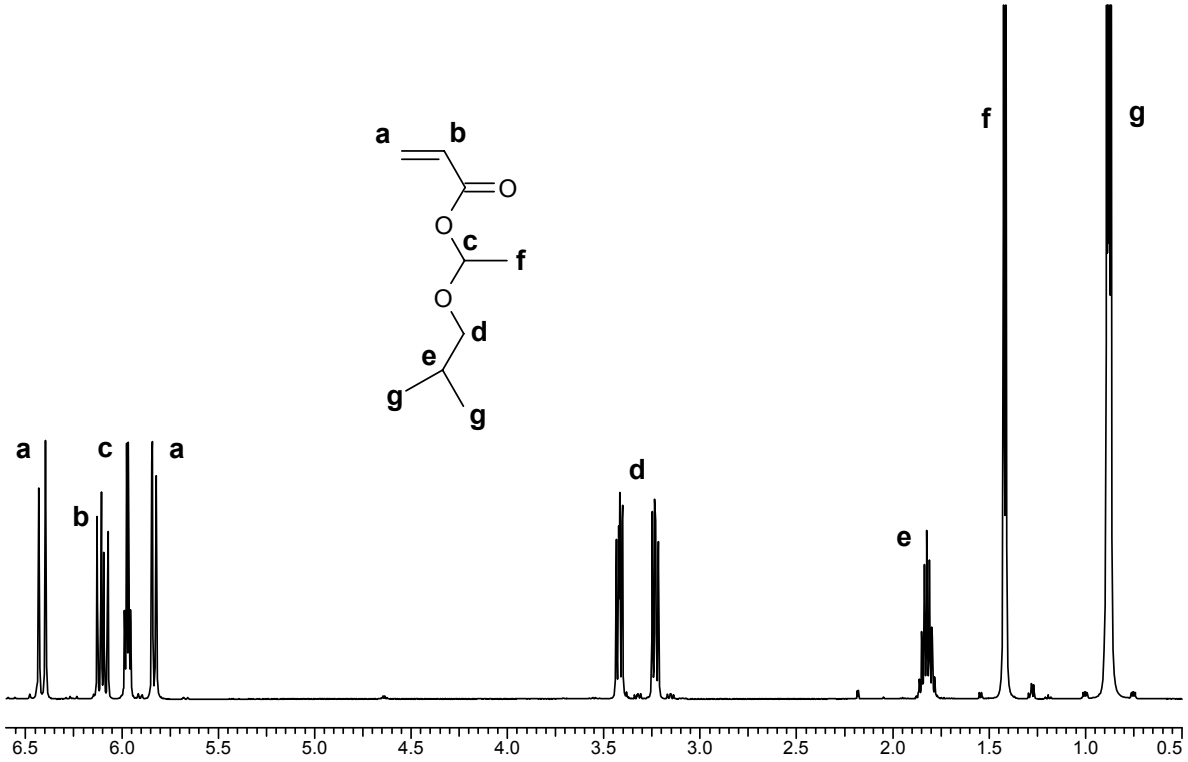


**Figure V-5** **$^1$H NMR spectrum of 1-isobutoxyethyl acrylate ($CDCl_3$, 300 MHz).**

## V.2.2. Polymerization of EE(M)A

Our ATRP formulations are based on the ones originally described by both Haddleton and Matyjaszewski.[3-7] Initiators, catalysts, ligands and solvents were varied to optimize polymerization conditions (see Table V-1).

**Table V-1** **Summary of the reaction conditions and results of the polymerizations of 1-alkoxyethyl (meth)acrylates using ATRP.**

| Entry | Initiator[a] | Ligand[a] | Mon.[b] | $[M]_0/[In]_0/[Cu]_0/[ligand]^c$ | Temp. (°C) | Time (min) | Conv. (%)[d] | $M_{n,th}$ (g.mol$^{-1}$) | $M_{n,exp}$ (g.mol$^{-1}$) | $M_w/M_n$ |
|---|---|---|---|---|---|---|---|---|---|---|
| 1[e] | **4** | **1** | EEMA | 50/1/5/10 | 50 | 135 | 78 | 6400 | 11700[f] | 1.40[f] |
| 2[g] | **4** | **2** | EEMA | 50/1/0.5/0.75 | 50 | 60 | 50 | 4200 | 4600[h] | 1.23[h] |
| 3[i] | **3** | **2** | EEMA | 80/1/0.5/0.75 | 90 | 180 | 55 | 7100 | 7100[h] | 1.26[h] |
| 4[j] | **3** | **2** | EEMA | 80/1/0.5/0.75 | 90 | 180 | 53 | 7000 | 6300[h] | 1.16[h] |
| 5[j] | **3** | **5** | EEMA | 50/1/0.5/0.75 | 90 | 180 | 17 | 1500 | 2100[h] | 1.25[h] |
| 6[k] | **6** | **2** | EEA | 50/1/1/1 | 50 | 270 | 68 | 5100 | 5000[h] | 1.10[h] |
| 7[l] | **6** | **2** | EEA | 50/1/1/1.1 | 60 | 180 | 88 | 6500 | 7300[h] | 1.18[h] |
| 8[m] | **6** | **7** | EEA | 200/1/1/1 | 30 | 120 | 47 | 13700 | 11500[h] | 1.35[h] |
| 9[k] | **6** | **2** | iBEA | 50/1/1/1 | 50 | 330 | 62 | 5500 | 4000[h] | 1.14[h] |

[a.] The following legend is used: **1** *N*-octyl-2-pyridylmethanimine, **2** *N,N,N',N'',N''*-pentamethyldiethylenetriamine (PMDETA), **3** 2,2,2-trichloroethanol, **4** ethyl-2-bromoisobutyrate, **5** 1,1,4,7,10,10-hexamethyldiethylene-tetramine (HMTETA), **6** methyl-2-bromopropionate, **7** tris[2-(dimethylamino)ethyl]amine ($Me_6$TREN). [b.] EEMA: 1-ethoxyethyl methacrylate, EEA: 1-ethoxyethyl acrylate, iBEA: isobutoxyethyl acrylate. [c.] $[M]_0$, $[In]_0$, $[Cu]_0$ and [ligand] = initial concentration of monomer, initiator, copper catalyst and ligand respectively. [d.] Calculated from $^1$H NMR. [e.] 50 v% toluene; CuBr catalyst. [f.] GPC system 2 (with THF as eluent and PMMA standards). [g.] 50 v% anisole, CuCl catalyst, 20 mol% $CuCl_2$ added. [h.] GPC system 1 (with $CHCl_3$ as eluent and polystyrene PS standards). [i.] 55 v% anisole, CuBr catalyst, 20 mol% $CuBr_2$ added. [j.] 55 v% anisole, CuCl catalyst, 20 mol% $CuCl_2$ added. [k.] 25 v% acetone, CuBr catalyst. [l.] bulk polymerization, CuBr catalyst. [m.] 25 v% anisole, CuBr catalyst.

In the ATRP of **1-ethoxyethyl methacrylate** (EEMA) the choice of initiator and ligand is quite important to obtain good control over the polymerization reaction (entry 1-5, Table V-1). With Haddleton's *N*-octyl-2-pyridylmethanimine ligand[8] (**1**), the rate of polymerization is slow and a fivefold excess of CuBr was used to obtain a reasonable polymerization rate. Due to the high CuBr concentration and the absence of Cu(II)Br in the beginning of the reaction, the system tries to attain equilibrium on its own by radical termination. Because of this, the observed molecular weight is higher than expected as the initiator efficiency is reduced. The presence of termination reactions can also be concluded from the gel permeation chromatography (GPC) analysis: a low-molecular weigh tailing can be observed, resulting from dead chains formed by termination during the early stages of the polymerization, leading to a polymer with a broad polydispersity (1.40).

In addition, a large excess of Cu needs to be avoided because of its difficult removal and the risk for Cu-catalyzed hydrolysis of the EEMA. One way to reduce the amount of copper in the reaction medium is to make use of a more active ligand. When a more active ligand is used, the ATRP equilibrium is shifted more to the side of the active, radical-bearing species (see Chapter II, Figure II.4).[9, 10] A more active ligand makes that less copper is needed to obtain the same or higher concentration of radicals (and thus polymerization speed). As a result of a higher concentration of radicals in the system, the polymerization reactions proceed faster. However, one should take care that the concentration of radicals does not reach a level at which termination and/or transfer reactions become competitive side reactions.

Indeed, polymerizations carried out using N,N,N',N",N"- pentamethyldiethylenetriamine (**2**, PMDETA) as ligand resulted in faster overall rates of polymerization (with respect to the copper concentration). Using PMDETA, 10 times less copper can be used, which makes the removal of the copper much more easy. Good control of chain growth throughout the polymerization was obtained upon addition of 20 mol% Cu(II)$Cl_2$ (with respect to overall Cu concentration) prior to reaction. This control was further optimized with the use of 2,2,2-trichloroethanol[11, 12] (**3**) as initiator instead of ethyl-2-bromoisobutyrate (**4**) (Table V-1, entry 3-4). The use of Cu(I)Br or Cu(I)Cl in combination with 20 mol% Cu(II)$Br_2$ or Cu(II)$Cl_2$ revealed better results for the Cu(I)Cl/Cu(II)$Cl_2$ catalyst system. Using this Cu(I)Cl/Cu(II)$Cl_2$ catalyst system, a lower polydispersity could be obtained in comparison to reactions without added Cu(II)$Cl_2$, as evidenced by GPC analysis (see Figure V-6). Adding Cu(II )species shifts the ATRP equilibrium to the left (see Chapter II, Figure II.4), with a decrease of the radical concentration as a result, and thus termination reactions are more suppressed. Apparently, 2,2,2-trichloroethanol gives less rise to termination reactions in the beginning of polymerization reaction. Although 2,2,2-trichloroethanol contains 3 Cl atoms, Destarac *et al.* showed that only one Cl atom is capable of initiation.[12]

The plot of the average molar mass ($M_n$) as a function of conversion shows a linear behavior (see Figure V-7, left). On the other hand, the first order kinetic plot of the polymerization of EEMA shows a deviation from linearity (see Figure V-7, right), which is probably due to partial deprotection of EEMA to methacrylic acid. Methacrylic acid poisons the catalyst[13], thus lowering the active amount of catalyst in the polymerization mixture, and as a result, the concentration of radicals in the system decreases. If the concentration of radicals in the system would decrease as a result of radical termination (e.g. chain coupling

reactions), the plot of the $M_n$ vs. conversion would also show a deviation, which is not observed in this case.

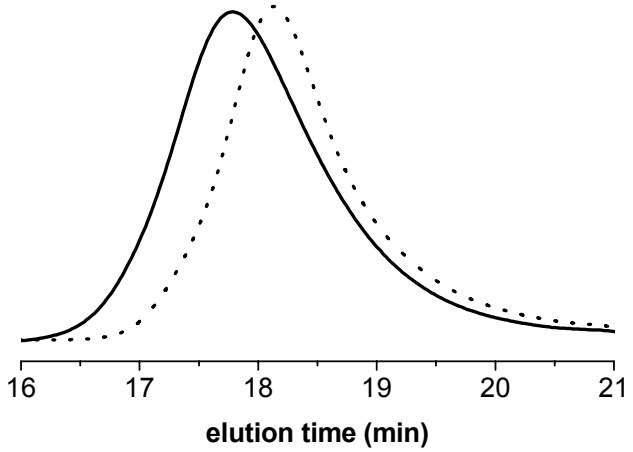


**Figure V-6** **GPC traces of the polymerization of EEMA using 2,2,2-trichloroethanol as initiator, with Cu(I)Br/Cu(II)$Br_2$ (solid line) and Cu(I)Cl/Cu(II)$Cl_2$ (dotted line) as the catalyst. (Table V-1, entry 3 and 4, respectively).**

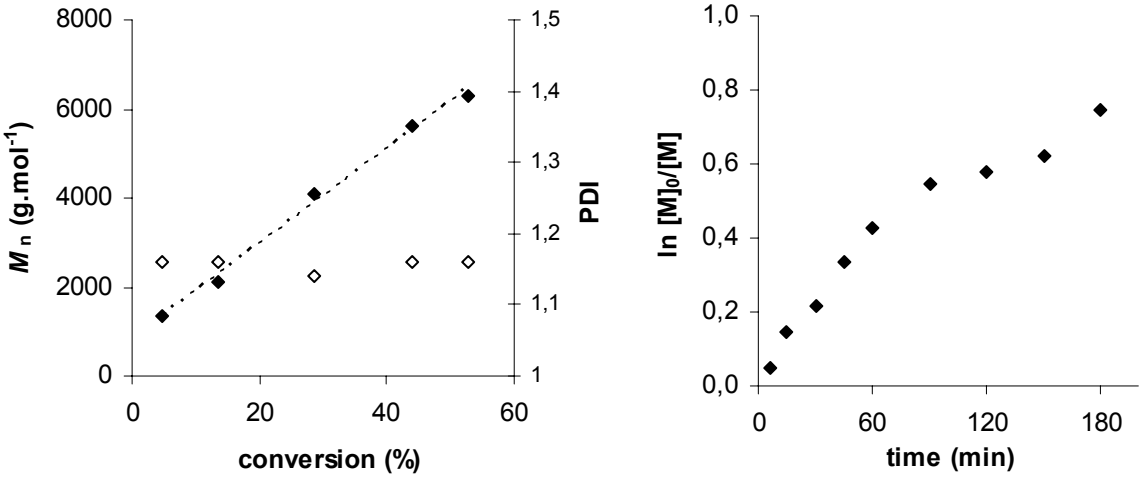


**Figure V-7** **Left: average molar mass ($M_n$, ♦) and polydispersity (PDI, ◊) as function of conversion of the polymerization of EEMA. Right: first order kinetic plot of the polymerization of EEMA (♦). (Table V-1, entry 4).**

The corresponding acrylate version of the monomer, **1-ethoxyethyl acrylate** (EEA) was also polymerized [entry 6-8, Table V-1]. In this case, a common initiator for acrylates, methyl-2-bromopropionate (**5**) was used. Using PMDETA as the ligand and CuBr as the catalyst resulted in a near-monodisperse polymer (PDI = 1.10). The first order kinetic plot of the polymerization and the average molar mass as a function of conversion both show the

expected linear behavior (see Figure V-8), and polymerizations showed a good reproducibility of the average molecular weight ($M_n$) at different temperatures. When the more reactive ligand tris[2-(dimethylamino)ethyl]amine (**6**) ($Me_6$TREN) was used, a polymer with higher molecular weight but broader molecular weight distribution was obtained. Isobutoxyethyl acrylate (see §V.2.1) was also polymerized successfully (Table V-1, entry 9).

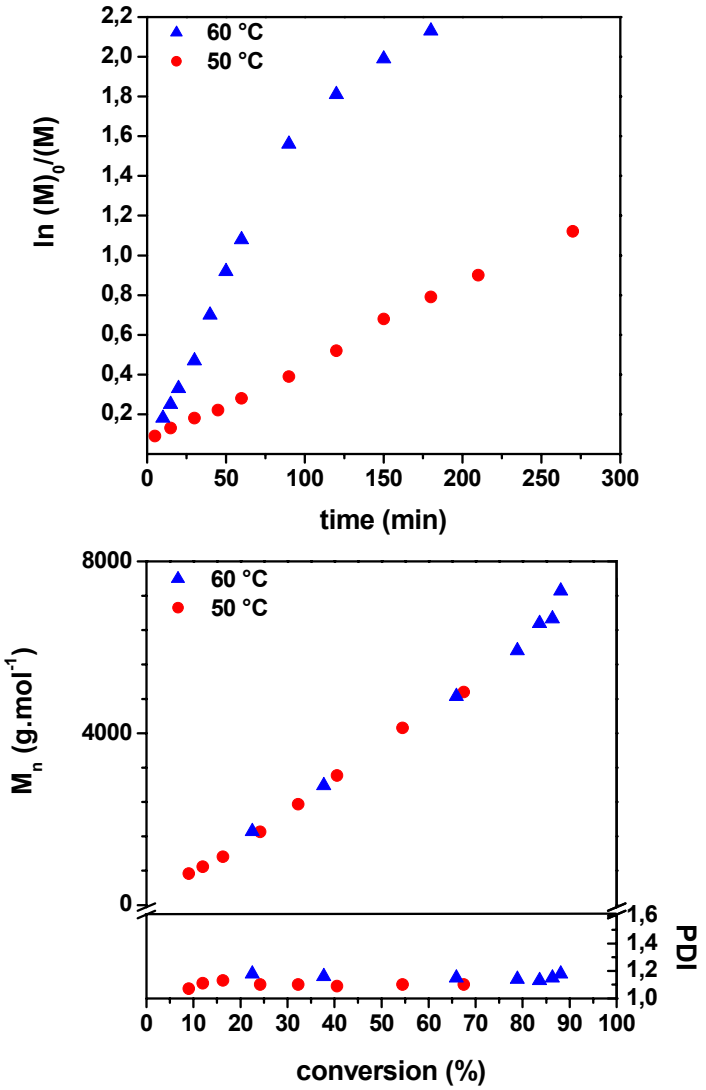


**Figure V-8** **First order kinetic plot (top) and increase of $M_n$ and evolution of PDI as a function of conversion (bottom) of the polymerization of EEA with MBP as the initiator at 50 and 60 °C (Table V-1, entry 6 and 7, respectively).**

In this paragraph, we have demonstrated that ATRP is a suitable technique for the polymerization of 1-ethoxyethyl(meth)acrylate. To illustrate the general applicability of the polymerization of an acetal-containing monomer, also *iso*butoxyethyl acrylate was polymerized successfully. Well-defined homopolymers with a controlled molecular weight

and a narrow molecular weight distribution were obtained. These polymers are precursor polymers for poly((meth)acrylic acid. In the next paragraph, the deprotection of PEE(M)A to P(M)AA by a heating step is investigated.

## V.2.3. Deprotection of PEE(M)A to P(M)AA

When PEE(M)A is exposed to heat, the polymer will transform into P(M)AA with loss of ethyl vinyl ether, which is released as a gas (boiling point: 33 °C). This is definitely the main advantage of the use of 1-ethoxyethyl as the protecting group rather than using the tert-butyl or benzyl protecting group, as the corresponding polymer can be easily deprotected to P(M)AA without any side products that remain in the product. The EE(M)A strategy prevents the need of an additional purification step after deprotection. The deprotection of PEE(M)A is schematically depicted in Figure V-9. In addition to the easy deprotection method, a property switch from a hydrophobic to a more hydrophilic material is obtained, which makes this approach useful for the use of these polymers in, for instance, thermoresponsive systems or in photoresist technology.

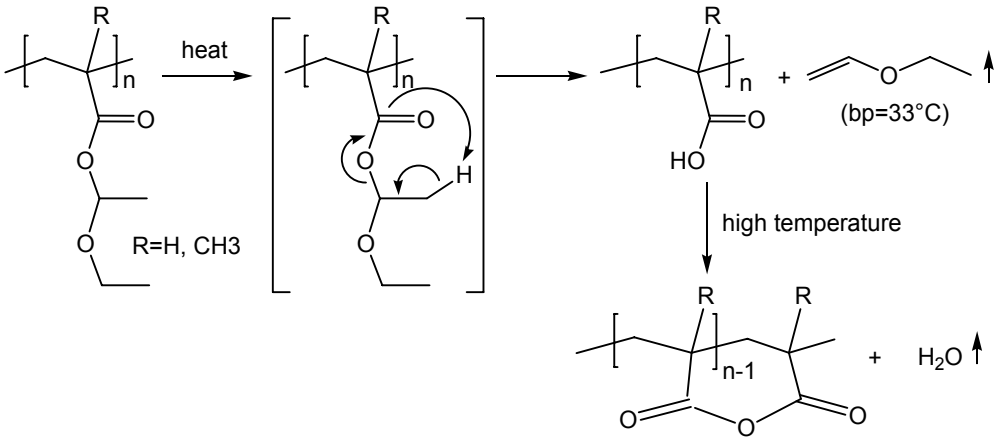


**Figure V-9 Schematic depiction of the thermolysis of PEE(M)A to P(M)AA, and anhydride formation.**

Figure V-10 illustrates the deprotection of a purified sample of PEEMA by thermogravimetric analysis (TGA) at different temperatures (90, 120, 140, 160 °C).

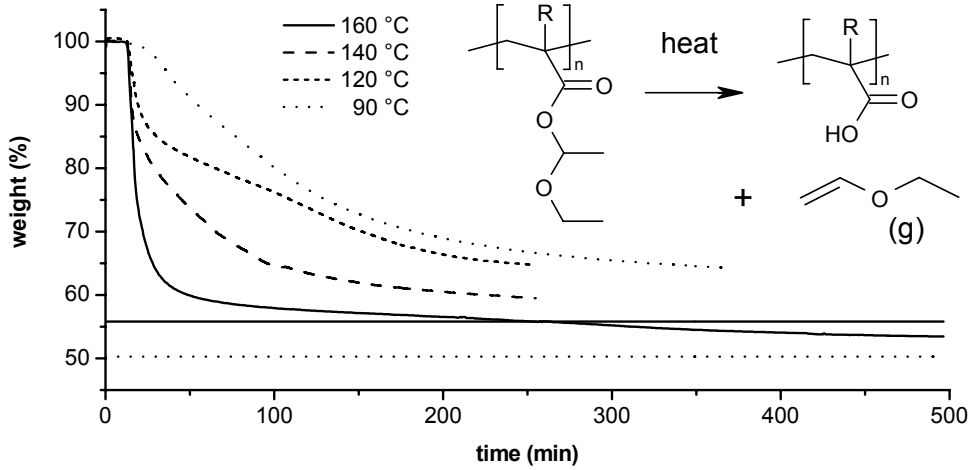


**Figure V-10** **Isothermal TGA at 90, 120, 140 and 160 °C under N2 atmosphere (heating rate 10 °C/min) of PEEMA [entry 1, Table 1]. The horizontal solid line corresponds with 100 % deprotection to PMAA, the dotted one to 100 % anhydride formation.**

At high temperature, deprotection proceeds fast, but anhydride formation (see Figure V-9) occurs as a side reaction, resulting in partial cross-linking of the formed PMAA. After about 30 minutes at 160 °C, about 90 % of the deprotection is complete. For entry 1, with a theoretical $DP_n$=50 and a conversion of 78 %, the experimental $DP_n$ is 39 for complete initiation; the theoretical weight loss for 100 % deprotection is thus 39 times the molecular weight (MW) of ethyl vinyl ether, which corresponds to a weight loss of 44.2 % (taking into account the MW of the initiator). Further decrease in weight is explained by anhydride formation with loss of water (total weight loss: 49.7 %).

Deprotection can be performed in bulk, by spreading out the polymer over a surface, or larger quantities can also be deprotected in solution at lower temperatures (e. g. reflux in solvent).

TGA analysis was also performed using an apparatus that is coupled with a mass spectrometer. In this way, the degradation products can be chemically analyzed. TGA analysis was performed from 35-800 °C and the release products in the temperature range of 120-200 °C were analyzed in the coupled mass spectrometer (see Figure V-11). The m/z range with the highest intensity for pure ethyl vinyl ether was scanned. By comparison of the mass spectrum of pure ethyl vinyl ether and the experimental spectrum that was obtained during the deprotection step, it was confirmed that ethyl vinyl ether is released.

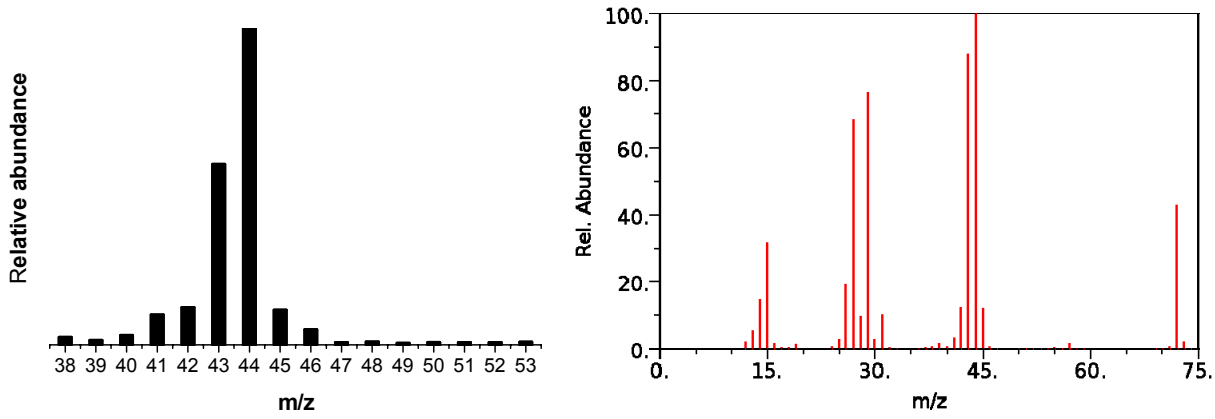


**Figure V-11** **Left: Experimental mass spectrum of release product during deprotection of PEEMA in TGA apparatus. (temperature range: 120-200 °C) [entry 1, Table V-1]. Right: mass spectrum of ethyl vinyl ether (http://webbook.nist.gov/chemistry).**

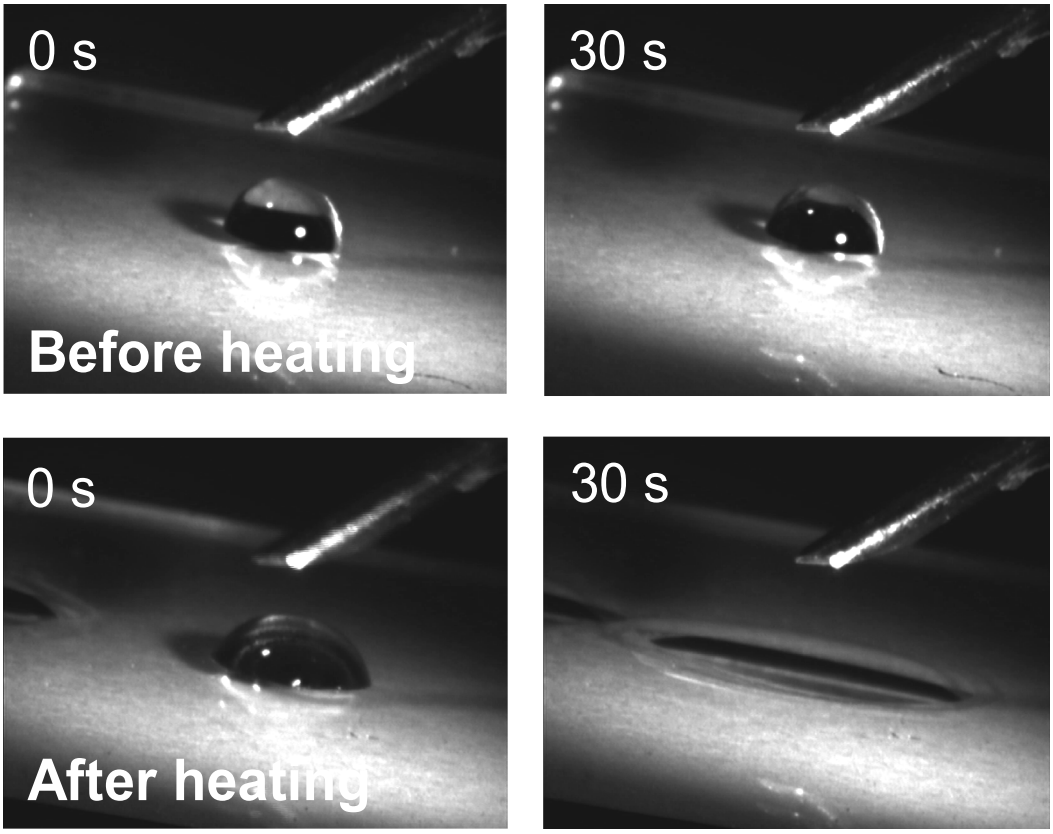


**Figure V-12** **Water droplets on a film of PEEMA [entry 1, Table 1] before heating (top) and after heating the film at 160 °C for 30 minutes (bottom).**

Contact angle measurements show a significant change in hydrophilicity before and after thermolysis, confirming that deprotection has occurred (see Figure V-12). A thin polymer

film was made by spin coating on a glass plate (from a 15 w% solution in toluene) and a drop of $H_2O$ was added before and after heating the film at 160 °C for 30 min. On the glass plate with the unheated polymer film, the water drop does not spread. When the same experiment is repeated with a previously heated polymer film, the water drop starts spreading out quickly over the surface.

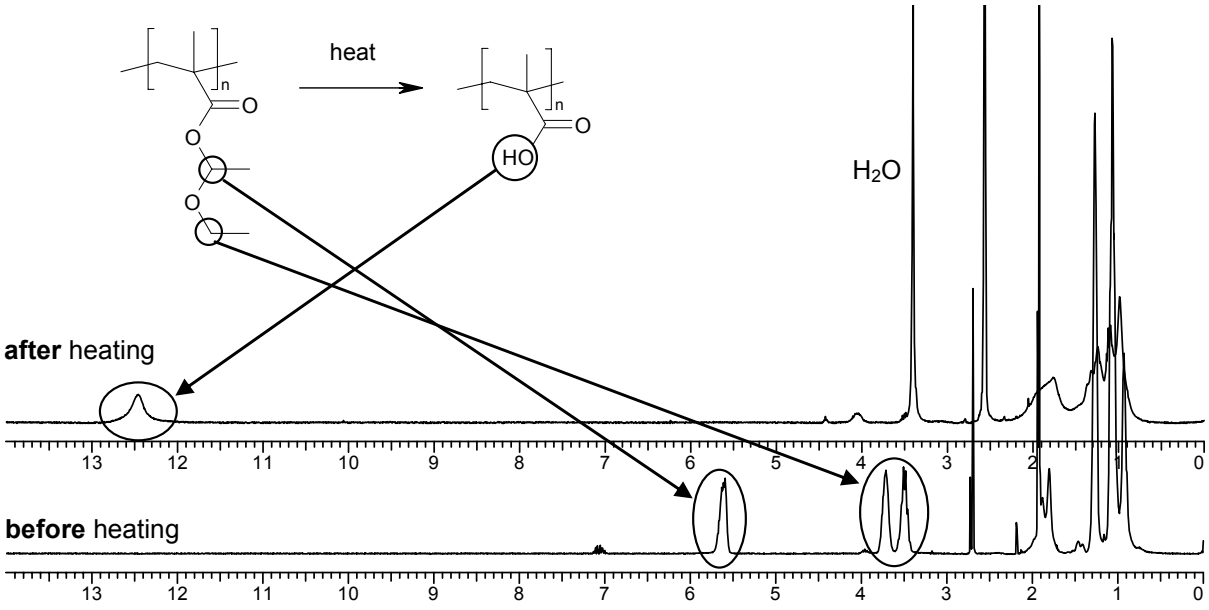


**Figure V-13** **$^1$H NMR spectra of a sample of PEEMA before heating (in acetone-$d_6$) and after heating (in DMSO-$d_6$).**

$^1$H NMR experiments (see Figure V-13) confirm that deprotection is quantitative by disappearance of the characteristic PEEMA peaks (3.4-3.9 and 5.6-5.8 ppm in acetone-$d_6$) and the appearance of a peak at 12.4 ppm (NMR solvent: DMSO-$d_6$) after the heating process (bulk sample heated for 30 min. at 160°C), which arises from the carboxylic acid functionalities.

IR spectroscopy was also used to confirm the deprotection. After deprotection, a broad absorption band at 3500-2500 became visible.

In summary, we have demonstrated that ATRP is a suitable technique for the polymerization of 1-ethoxyethyl(meth)acrylate. Well-defined homopolymers can be prepared, which can be deprotected to give the corresponding polyacids by heating, without the need for an additional purification step.

## V.2.4. Microwave-assisted ATRP of EEA at higher temperature

In addition to the above described experiments, the polymerization of EEA was further investigated with regard to the applied polymerization temperature. A temperature screening for the ATRP of EEA was performed using an automated synthesizer equipped with a microwave heating system.[14] It was reported earlier that microwave heating does not affect the kinetic behavior of the ATRP reaction[15]. Also in our case, no microwave effects were observed (see further).

For these experiments, all reactions were performed in bulk with a ratio of $[M]_0/[In]_0/[Cu]_0/[ligand]$ equal to 50/1/1/1.1.

**Table V-2** **Results of the polymerization of EEA by ATRP at different temperatures. Reactions were performed in bulk with $[M]_0/[In]_0/[Cu]_0/[ligand]$[a] = 50/1/1/1.1.**

| Entry | Temp. (°C) | Time | Conv.[b] (%)[c] | $M_{n,th}$ (g.mol$^{-1}$) | $M_{n,exp}$[c] (g.mol$^{-1}$) | $M_w/M_n$[c] |
|---|---|---|---|---|---|---|
| 1 | 60 | 1 h | 71 | 5300 | 5300 | 1.21 |
| 2 | 60 | 2 h | 79 | 5900 | 6400 | 1.23 |
| 3 | 70 | 1 h | 79 | 5900 | 6900 | 1.19 |
| 4 | 70 | 2 h | 91 | 6700 | 8600 | 1.34 |
| 5 | 80 | 1 h | 90 | 6700 | 8300 | 1.40 |
| 6 | 80 | 2 h | 92 | 6800 | 8600 | 1.36 |
| 7 | 90 | 2 h | 91 | 6700 | 8900 | 1.54 |
| 8 | 100 | 2 h | 89 | 6600 | 8500 | 1.55 |
| 9 | 120 | 1 h | 88 | 6500 | 6600 | 1.55 |

[a.] $[M]_0$, $[In]_0$, $[Cu]_0$ and [ligand] = initial concentration of monomer, initiator, copper catalyst and ligand respectively. [b.] Determined from $^1$H NMR. [c.] GPC system 3.

From the results in Table V-2, it can be concluded that the monomer conversion increases with increasing temperature for the reactions performed at 60, 70 and 80 °C (from 71 % at 60°C to 79 % at 70 °C to 90 % at 80 °C for a polymerization time of 1 hour). For polymerization temperatures higher than 80 °C, the conversion does not increase anymore, even at longer reaction time. The lower conversions and lower average molecular weights ($M_{n,exp}$) that are observed at higher temperature (≥ 90 °C) are attributed to partial

deprotection of monomer or polymer due to the high polymerization temperature at longer reaction times and temperature. Also termination reactions were observed, as evidenced by GPC analysis which reveals a shoulder at higher molecular weight (see Figure V-14; polyacrylates terminate *via* coupling reactions predominantly). For temperatures higher than 90 °C, the $M_{n,exp}$ decreases again, probably due to deprotection of the ethoxy ethyl group (see Table V-2, entry 8-9). For temperatures ≥ 90 °C, deprotection was indeed observed in the $^1$H NMR analysis of samples taken at the end of the reaction, which shows signals arising from deprotection of EEA to acrylic acid (at 6.46 and 6.51 ppm, see Figure V-15).

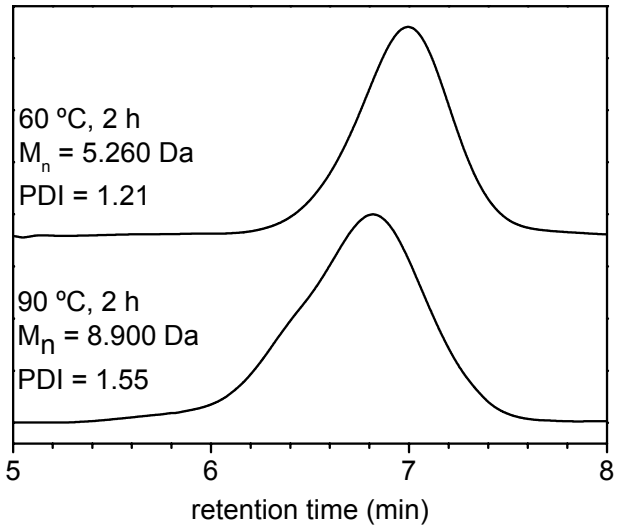


**Figure V-14** **GPC traces of the polymerization of EEA by ATRP after 2 hours, at 60 and at 90 °C (GPC system 3).**

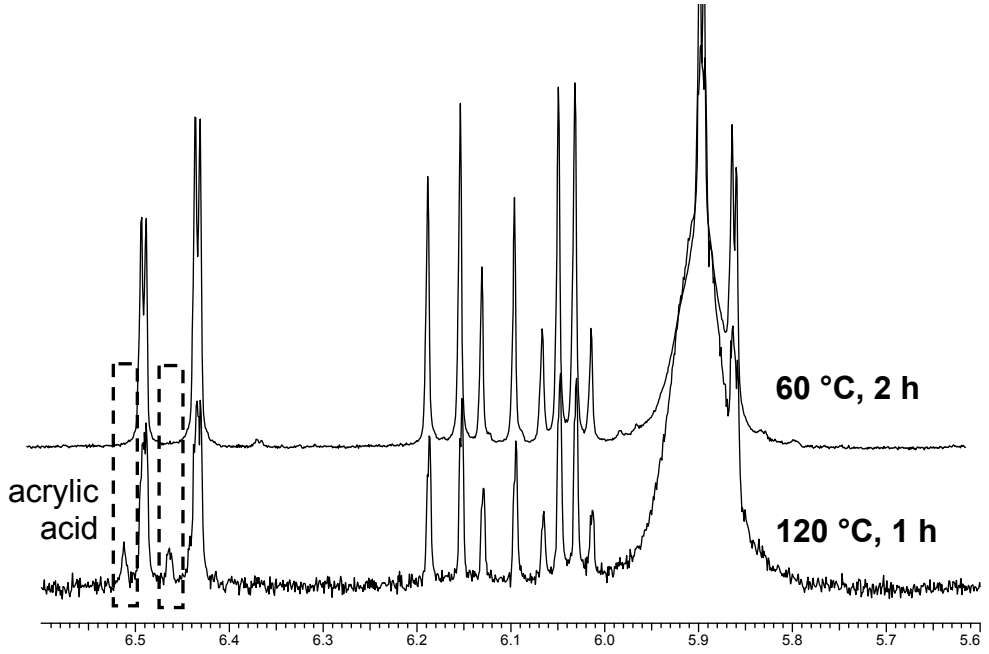


**Figure V-15** **$^1$H NMR spectrum of the polymerization of EEA by ATRP at 60 °C (2 h, top) and at 120 °C (1 h, bottom). (Table V-2, entry 2 and 9).**

For the reaction at 90 °C, a kinetic run was performed to investigate the influence of the higher polymerization temperature on the kinetics of the ATRP reaction of EEA (see Figure V-16). In addition, the reaction was performed using a microwave heating system as well as conventional heating in an oil bath to see if the microwave heating influences the polymerization.

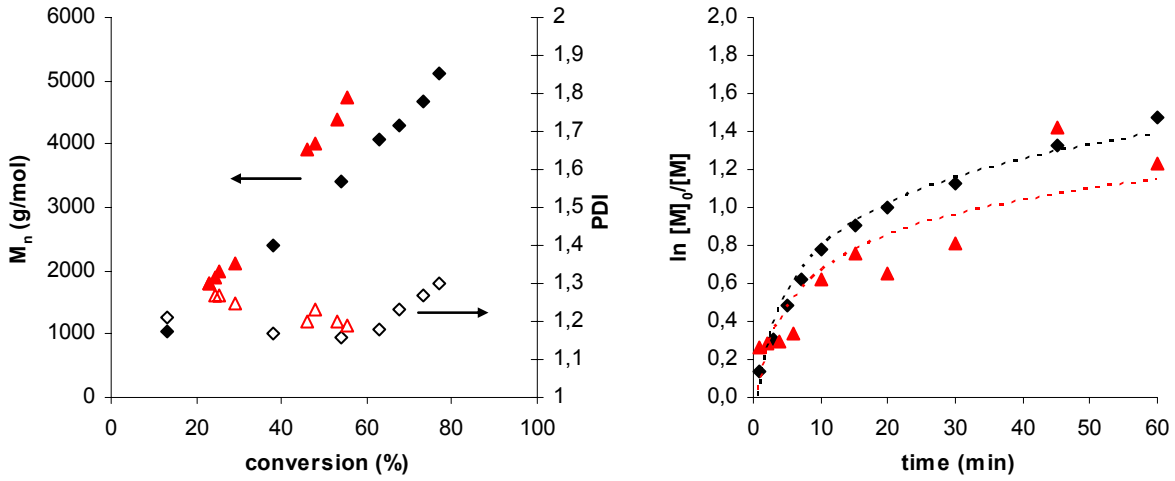


**Figure V-16** **Polymerizations of EEA at 90 °C with a MW heating system (▲) or in an oil bath (♦). Left: average molar mass ($M_n$) and polydispersity (PDI) as function of conversion of the polymerization of EEA (♦: GPC system 1; ▲: GPC system 3). Right: first order kinetic plot of the polymerization of EEA.**

The kinetic analysis shows that no significantly different behavior arising from the different heating systems could be observed. Both polymerizations show a deviation from linearity in the first order kinetic plot (Figure V-16, right), which is due to partial deprotection of EEA units to AA, lowering the active catalyst concentration (see also §V.2.2). The linear increase of the $M_n$ vs. conversion (Figure V-16, left) shows that polymers with a controlled molecular weight can be prepared, while the polydispersity remains low throughout the polymerization reaction (the slight difference of the $M_n$ arises from the different GPC systems). Only at high conversions a slight increase of the polydispersity is observed, due to chain coupling.

In summary, the polymerization of EE(M)A by ATRP and subsequent deprotection was demonstrated to be a facile way to obtain poly((meth)acrylic acid) polymers. In the next part of this chapter, this strategy has been used to prepare PAA polymers with a disulfide bond. By tethering the PAA polymers to a gold substrate, the preparation of pH-responsive gold substrates is aimed.

## *V.3. Stimulus-responsive PAA brushes on gold substrates: synthesis of PAA with a disulfide functionality*

### V.3.1. Introduction

The fabrication of stimulus-responsive surfaces has attracted considerable attention in recent years because of potential applications in many fields ranging from biotechnology and biomaterials to advanced microelectronics. Smart responsive polymer coatings can adapt or change surface properties (wetting, reactivity, adhesion, roughness, …) via external stimuli. Among the various methods reported to prepare polymer brushes on gold substrates, the grafting-to method, in which preformed polymer chains in solution are tethered to the surface, is particularly useful to obtain polymer brushes with narrow molecular weight distribution.[16]

Using the newly developed EEA strategy, we report on a new route to prepare gold surfaces with switchable properties by tethering poly(acrylic acid) (PAA) containing a disulfide (S-S) bond onto a gold surface. As poly(acrylic acid) is a pH-responsive polymer, pH-switchable gold surfaces are obtained in this way. Characterization of the pH-responsive gold surfaces was done in collaboration with the research group of Dr. S. Demoustier-Champagne (Université Catholique de Louvain, UCL, Belgium).

### V.3.2. Synthetic strategy

Figure V-17 gives an overview of the reaction steps that have to be carried out for the preparation of poly(acrylic acid) polymers with a disulfide functionality (PAA-S-S-PAA).

As explained already in the introduction, acrylic acid can not be polymerized directly via ATRP because of a side reaction of the acid group with the transition metal complex.[13] Therefore, the preparation of PAA-S-S-PAA starts with the above developed strategy using ATRP of 1-ethoxyethyl acrylate (EEA), and in this case a disulfide-containing initiator was used: bis(2-hydroxyethyl) disulfide bis(2-bromopropionate).[17, 18] After polymerization of EEA, the PEEA-S-S-PEEA was deprotected to PAA-S-S-PAA by a heating step. In the following paragraphs, these reaction steps for the synthesis of PAA-S-S-PAA will be discussed more in detail.

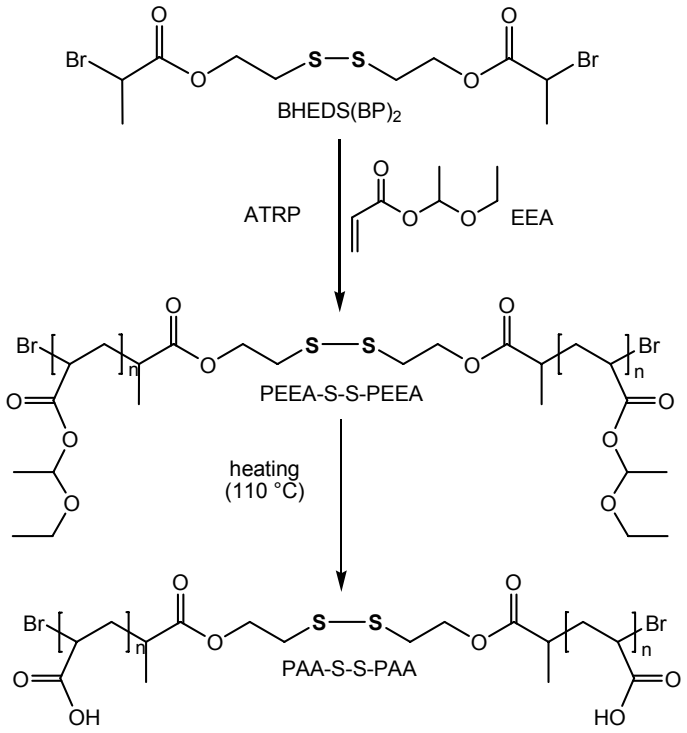


**Figure V-17** **Synthetic strategy for the preparation of poly(acrylic acid) (PAA) with a disulfide functionality.**

## V.3.3. Synthesis of S-S containing initiator

As illustrated in Figure V-18, the preparation of PAA-S-S-PAA makes use of a difunctional initiator that contains a disulfide bond. The initiator bis(2-hydroxyethyl) disulfide bis(2-bromopropionate) (BHEDS(BP)$_2$) was synthesized by esterification of bis(2-hydroxyethyl)disulfide (BHEDS) and 2-bromopropionic acid.

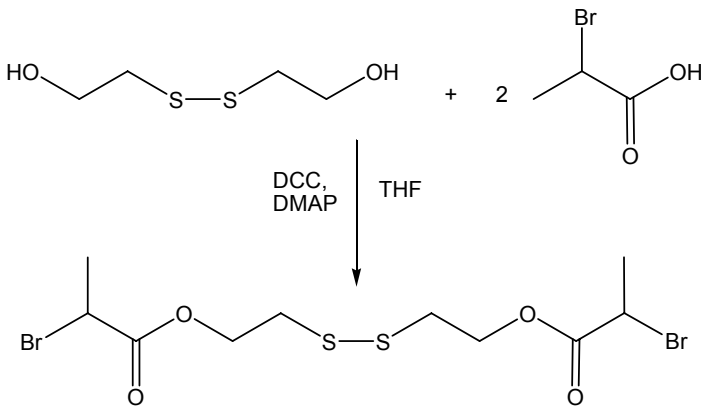


**Figure V-18** **Synthesis of disulfide-containing initiator: bis(2-hydroxyethyl) disulfide bis(2-bromopropionate).**

Dicyclohexyl carbodiimide (DCC) was used as the esterification agent and 4-(*N,N*-dimethylamino)pyridine (4-DMAP) acted as a catalyst. The general mechanism for esterification using DCC and 4-DMAP is shown in Figure V-19.

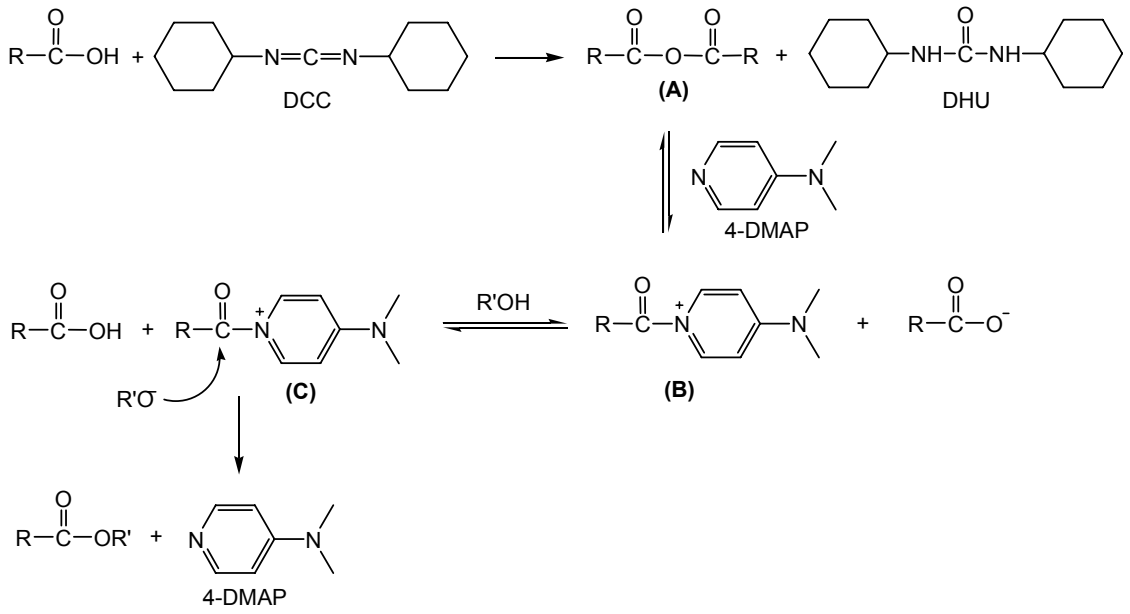


**Figure V-19 General mechanism for the esterification reaction using DCC and 4-DMAP.**

The carboxylic acid is converted in an anhydride compound (A), which forms with 4-DMAP an acyl pyridinium species (B). Equilibration of (B) with an alcohol leads to the formation of an ionic compound (C). A nucleophilic attack of R'O$^-$ to the acyl group of (C) generates the ester compound and releases the catalyst 4-DMAP again. During the reaction, dicyclohexyl ureum (DHU) is formed, which is filtered off afterwards.

The $^1$H NMR spectrum of BHEDS(BP)$_2$ is shown in Figure V-20. The spectrum proves that the desired compound has been formed. The signals at 2.88 and 3.89 ppm can be attributed to a small amount of unreacted diol or a small fraction of monofunctional product (only reaction of 1 OH of the diol has occurred). However, this is no problem as later on, the polymers that will be prepared with this initiator will be tethered to a gold surface, which implies breaking of the disulfide bond.

The IR spectrum of BHEDS(BP)$_2$ shows the following characteristic absorption bands: C-H stretch at 2860-3000 cm$^{-1}$ (strong), C=O (ester) at 1735 cm$^{-1}$ (strong), $CH_3$ bending at 1450 and 1375 cm$^{-1}$ (strong), C-O at 950-1300 cm$^{-1}$ (strong), C-S at 800 cm$^{-1}$ (weak) and C-Br stretch at 675 cm$^{-1}$ (strong).

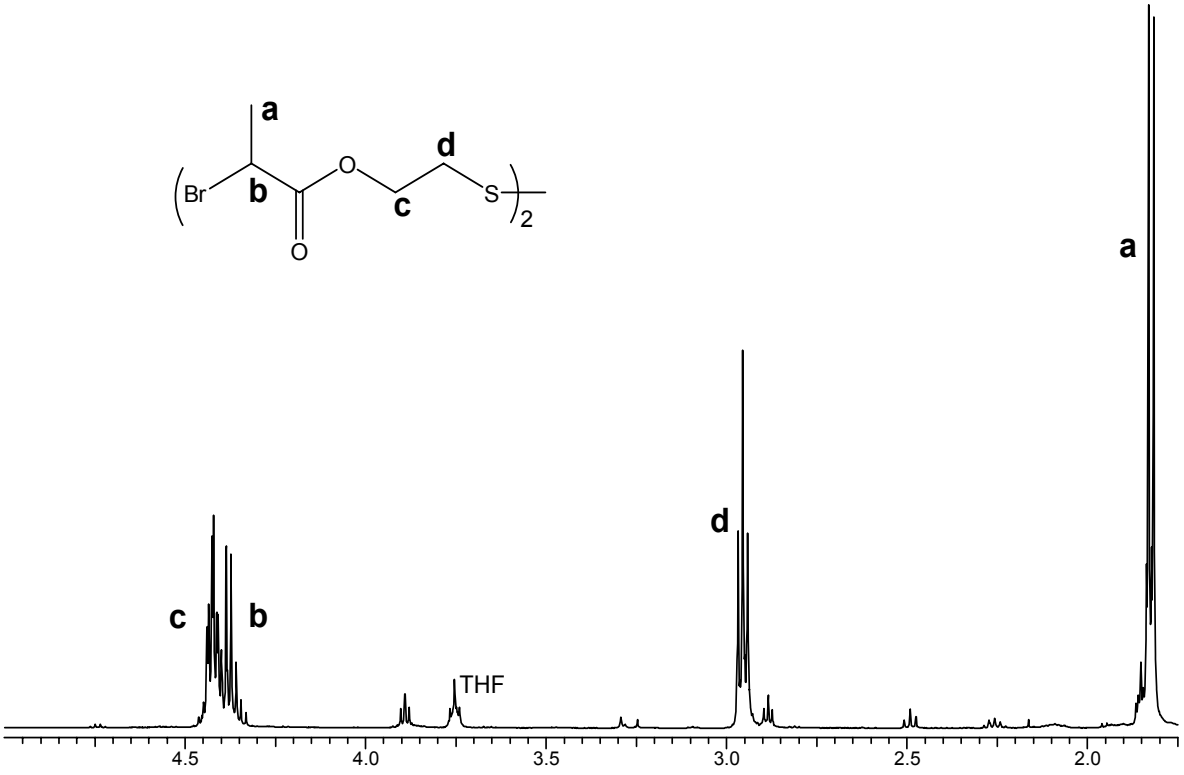


**Figure V-20** **$^1$H NMR spectrum of disulfide containing initiator BHEDS(BP)$_2$ ($CDCl_3$, 500 MHz).**

## V.3.4. ATRP of EEA with S-S containing initiator

The second step consists in polymerizing EEA using the S-S containing initiator. Table V-3 (see next page) gives an overview of the reaction conditions and the results of the different ATRP polymerizations that were performed.

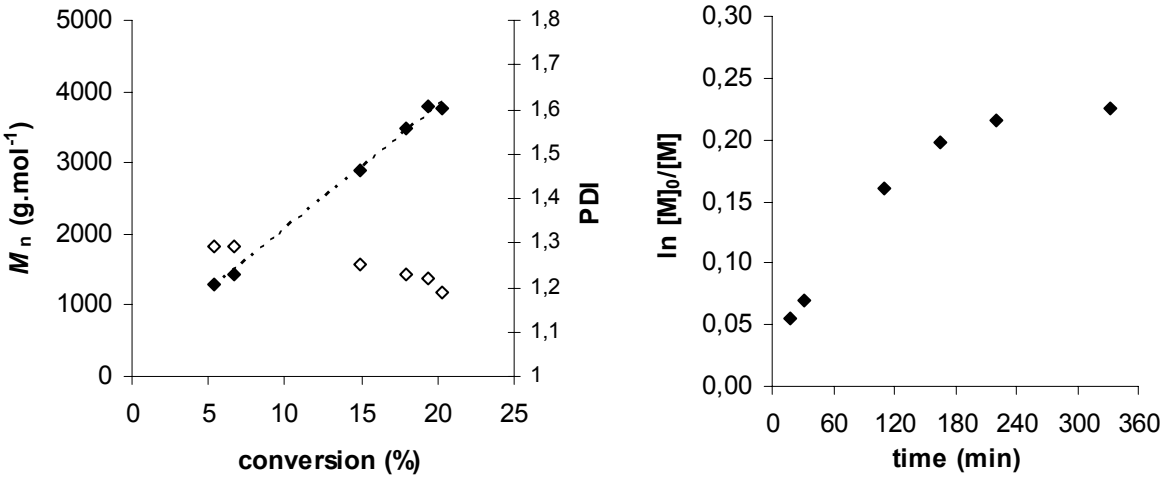


**Figure V-21** **Left: average molar mass ($M_n$, ♦) and polydispersity (PDI, ◊) vs. conversion (with trend line) for the polymerization of EEA using BHEDS(BP)$_2$ as initiator (Table V-3, entry 1). Right: first order kinetic plot.**

**Table V-3 Summary of the reactions conditions and results of the polymerization of EEA by ATRP using $BHEDS(BP)_2$ as disulfide-containing initiator.**

| Entry | $[M]_0/[In]_0/[Cu]_0/[ligand]$[a] | Temp. (°C) | Time (min) | Conv.[b] (%) | $M_{n,th}$ ($g.mol^{-1}$) | $M_{n,exp}$[c] ($g.mol^{-1}$) | $M_w/M_n$[c] |
|---|---|---|---|---|---|---|---|
| 1 | 100/1/0.5/0.5 | 50 | 332 | 20 | 3300 | 3800 | 1.19 |
| 2 | 100/1/2/2 | 50 | 238 | 68 | 10200 | 12300 | 1.22 |
| 3 | 200/1/2/2 | 50 | 148 | 34 | 10200 | 12800 | 1.17 |
| 4 | 200/1/4/4 | 50 | 960 | 75 | 22000 | 23600 | 1.67 |
| 5 | 400/1/4/4 | 50 | 143 | 21 | 12500 | 12800 | 1.12 |
| 6 | 200/1/2/2 | 60 | 146 | 61 | 18000 | 19600 | 1.19 |
| 7 | 200/1/2/2 | 70 | 90 | 84 | 24600 | 21900 | 1.18 |

[a] $[M]_0$, $[In]_0$, $[Cu]_0$ and [ligand] = initial concentration of monomer, initiator, copper catalyst and ligand respectively. [b] Determined from $^1H$ NMR. [c] GPC system 1.

For the first experiment (entry 1, Table V-3), a ratio of monomer/initiator/catalyst/ligand $[M]_0/[In]_0/[Cu]_0/[ligand]$ = 100/1/0.5/0.5 was used. To check if the polymerization of EEA under these reaction conditions exhibits a controlled character, a kinetic study was performed (Figure V-21). The first order kinetic plot shows a deviation from linearity at about 120 minutes reaction time. Deviation from linearity in the first order kinetic plot is observed when the concentration of radicals in the system decreases. Often, the decrease of the concentration of radicals during the polymerization is due to combination of 2 radical species, which occurs when the concentration of radicals in the polymerization is too high. However, in this case, the decrease of the concentration of radicals is more likely to arise from a side reaction between the monomer and the copper catalyst. During the polymerization of EEA, it can not be avoided (especially at longer reaction times) that a small amount of the monomer (or the corresponding polymer) shows some deprotection, resulting in a small concentration of carboxylic acid groups in the polymerization mixture. The carboxylic acid groups form a complex with the Cu(II) species, which is insoluble.[13] As a result, the actual copper concentration and thus the concentration of radicals is lowered.

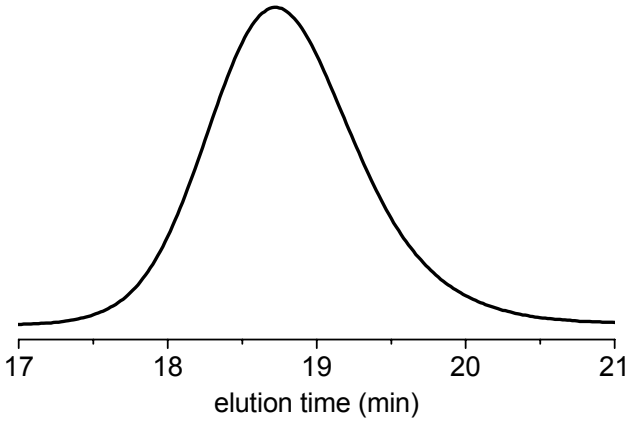


**Figure V-22** **GPC trace of the polymerization of EEA using a disulfide containing initiator BHEDS(BP)$_2$ (entry 1, Table V-3). (GPC system 1)**

In addition, if the decrease of the radical concentration arises from radical termination, the GPC analysis will reveal a broadened molecular weight distribution with traces of high molecular weight species (coupling reactions) and/or traces of low molecular weight polymers (dead chains). In our case, a symmetrical GPC curve is obtained, which confirms the hypothesis of partial deprotection (see Figure V-22). For entry 1 (Table V-3), the polymerization stops at about 20% monomer conversion, and a number average molecular weight ($M_n$) of 3800 g.mol$^{-1}$ was reached.

The next set of ATRP reactions was performed in order to find the right reaction conditions to obtain polymers with a higher molecular weight. As the copper concentration can be considered as an important polymerization parameter, the influence of the copper concentration was further examined. For entry 2 (Table V-3), the copper concentration was 4 times higher (2 equivalents instead of 0.5). As a result, a conversion of 68 % was reached in a shorter time. However, the broad molecular weight distribution which shows a multimodal character reveals that control over the polymerization reaction is lost under these conditions (see Figure V-23). It can be concluded that the copper concentration was in this case too high.

If the same reaction conditions are applied, but with an increase of the theoretical degree of polymerization ($DP_{th}$, or $[M]_0/[I]_0$) to 200, the copper concentration is lowered (entry 3, Table V-3). The reaction exhibited a controlled behavior (see Figure V-24, ■). Although the

conversion was again lower, a higher $M_n$ was reached (12800 g.mol$^{-1}$) because of the increased $DP_{th}$. An increase of the copper concentration (entry 4, Table V-3) gave rise to a higher conversion (75 %), but just as in the case of entry 2 (Table V-3), control over the polymerization was lost, as evidenced by the high polydispersity of the obtained polymer (1.67). Further increase of $DP_{th}$ resulted in a controlled behavior of the polymerization reaction but again the conversion was rather low (21 %).

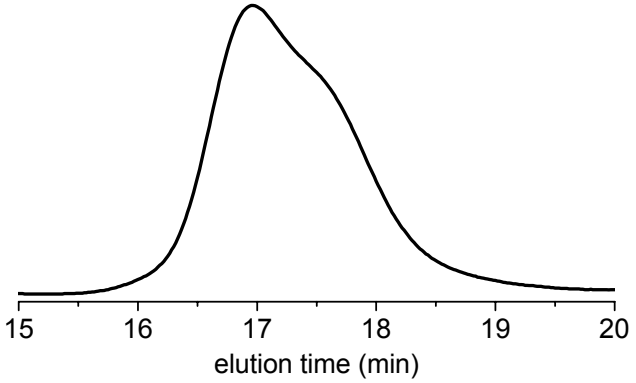


**Figure V-23** **GPC trace of the polymerization of EEA using a disulfide containing initiator BHEDS(BP)$_2$ (entry 2, Table V-3). (GPC system 1).**

In a next set of polymerizations, the influence of the polymerization temperature was investigated. Starting from the conditions that were applied for reaction HP7D2 with a ratio of $[M]_0/[In]_0/[Cu]_0/[ligand]$ = 200/1/2/2 at 50 °C, the polymerization temperature was increased to 60 °C (entry 6, Table V-3). This resulted in a higher monomer conversion (61 %) and thus in a polymer with a higher $M_n$ (19600 g.mol$^{-1}$), while the polymerization was still performed with good control. Further increase of the temperature to 70 °C (entry 7, Table V-3) resulted in an even higher monomer conversion (84 %) leading to a polymer with $M_n$ = 21900, in a shorter reaction time. In each case, a good control over the polymerization reaction was obtained, as evidenced by the linear behavior of the first order kinetic plot and the linear increase of the $M_n$ as a function of conversion, while the polydispersity (PDI) remains narrow (see Figure V-24). After deprotection by heating at 110 °C in toluene, PAA-S-S-PAA with the desired S-S bond is obtained after precipitation in hexane.

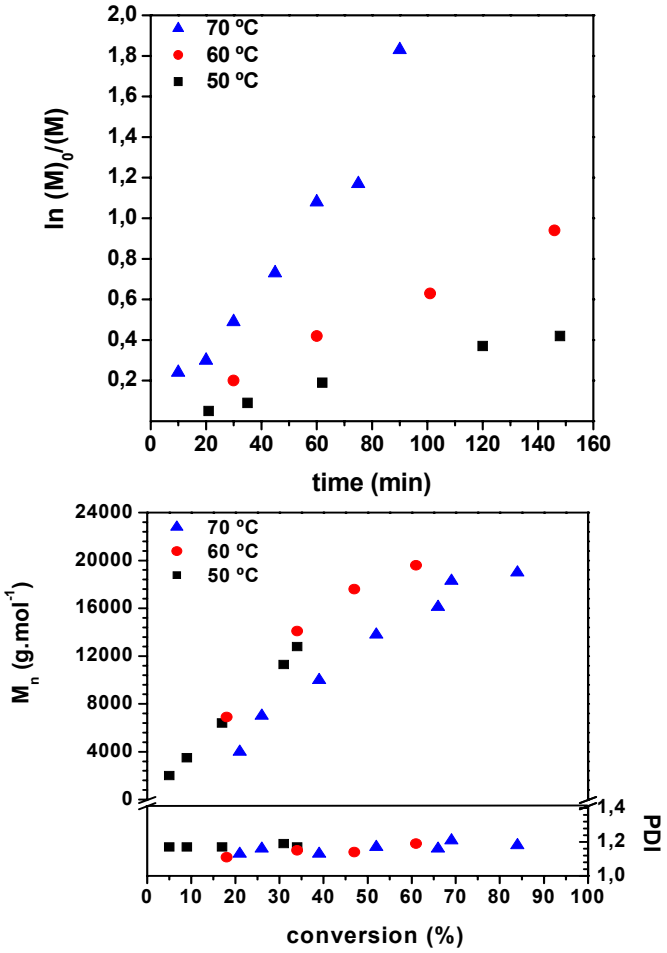


**Figure V-24** **First order kinetic plot (top) and increase of $M_n$ and evolution of PDI as a function of conversion (bottom) of the polymerization of EEA with disulfide containing initiator BHEDS(BP)$_2$ and ratio $[M]_0/[In]_0$/ $[Cu]_0/[ligand]$ = 200/1/2/2 at 50, 60 and 70 °C (entry 3, 6 and 7 (Table V-3), respectively).**

## V.3.5. Characterization of PAA-S-S-PAA

In this paragraph, the pH-responsiveness of the prepared PAA-S-S-PAA polymers is investigated. In the present study, we report on the preparation of gold surfaces with switchable properties.

Among the various methods reported to prepare polymer brushes on gold substrates, the grafting-to method, in which preformed polymer chains in solution are tethered to the surface, is particularly useful to obtain polymer brushes with a narrow molecular weight distribution.[16]

The brushes were prepared by dipping gold substrates into a solution of PAA-S-S-PAA in ethanol for 72 h, followed by a careful rinsing. The presence of the PAA polymer onto the substrates was confirmed by X-ray photoelectron spectroscopy (XPS). A schematic depiction of the gold substrate with PAA brushes and the C1s XPS spectrum of a PAA-functionalized gold substrate are shown in Figure V-25. The C1s spectrum exhibits two main components. The peak centered at 284.9 eV is attributed to aliphatic carbon atoms. The other component appearing around 289 eV is characteristic for the double C=O bond of the carboxylic acid groups.

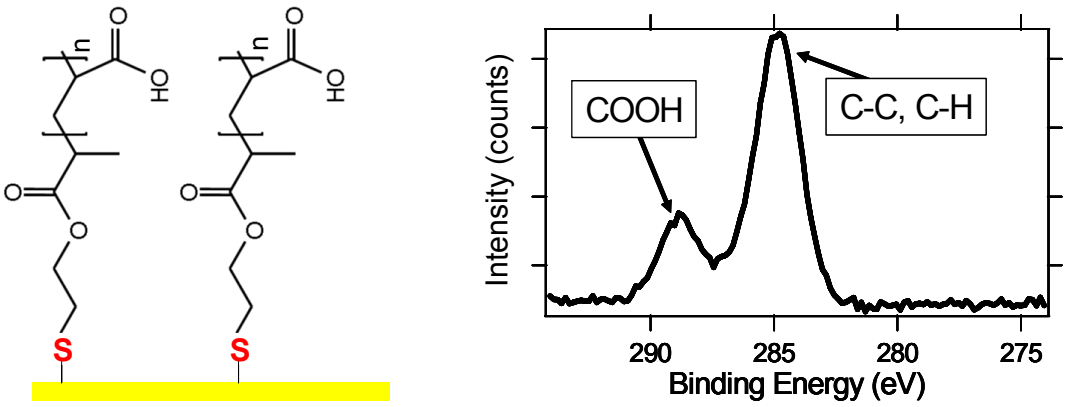


**Figure V-25** **Gold substrate functionalized with PAA-S-S-PAA: schematic depiction (left) and XPS spectrum (right).**

The PAA-functionalized gold surfaces were characterized by atomic force microscopy (AFM) in water. The influence of the pH of the aqueous environment on the surface properties was investigated. The characterization was done in water at a relatively low pH (pH = 5) on one hand, and at a relatively high pH (pH = 9) on the other hand.

The topographic images and the corresponding height profiles that were obtained by AFM in water at different pH values show the typical features of a brush regime in its collapsed and swollen state, respectively (see Figure V-26). At pH = 5, PAA is protonated and thus less soluble. At this pH, the polymer chains shrink or collapse, so they exhibit a small hydrodynamic volume. At pH = 9, the PAA chains are deprotonated and thus negatively charged. At this pH, they show a higher hydrodynamic volume, which is called the "swollen" state. The topographic images and the height profiles show these typical features of the polymer chains in their "collapsed" (pH = 5) and their "swollen" state (pH = 9).

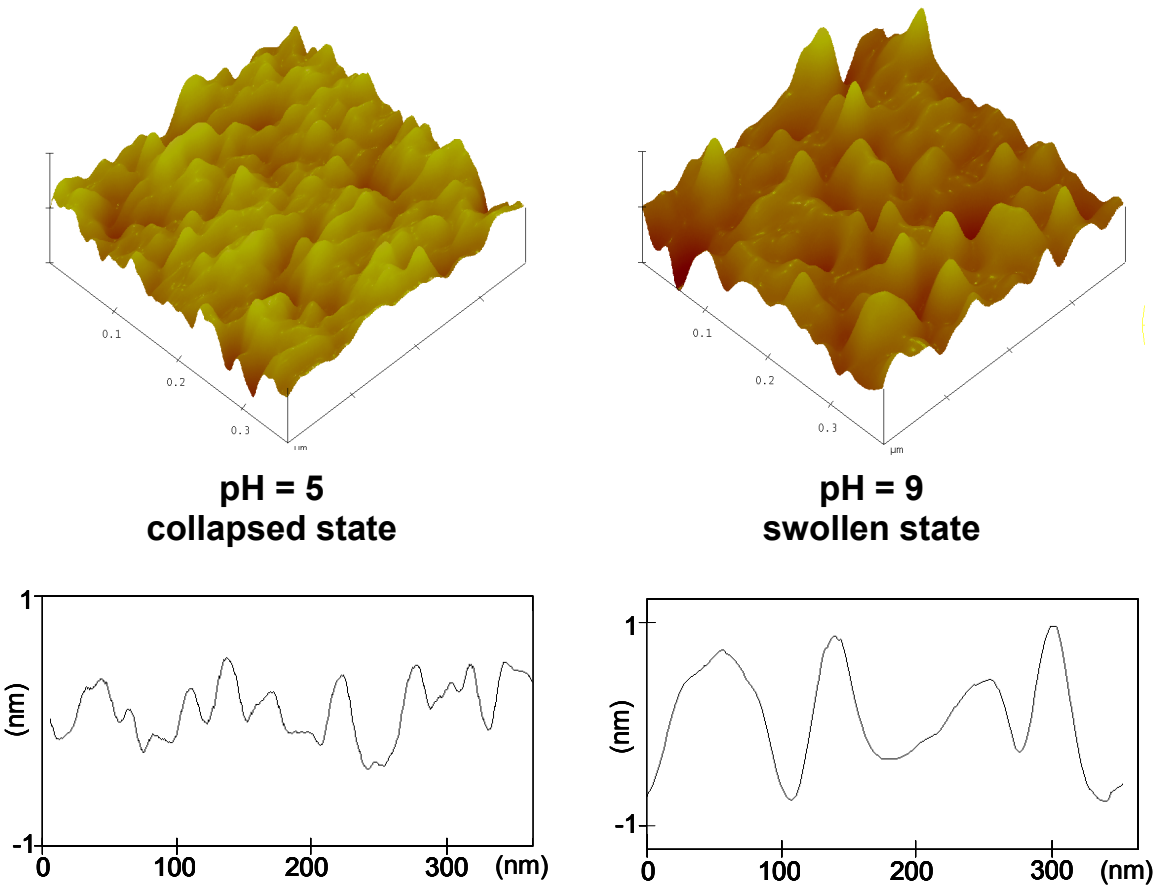


**Figure V-26** **Topographic images (top) and the corresponding height profiles (bottom) of a gold surface functionalized with PAA-S-S-PAA: collapsed state (at pH = 5) and swollen state (at pH = 9).**

One efficient technique to evaluate the thickness of the PAA layer is AFM in the force spectroscopy mode. Figure V-27 shows typical approach profiles, obtained in water at two different pH's, between a bar silicon nitride tip and a PAA layer grafted on a gold substrate.

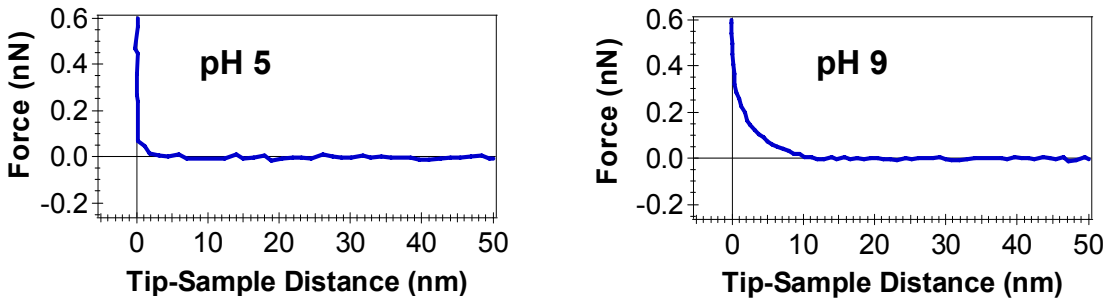


**Figure V-27** **Force as a function of tip-surface distance for the collapsed state (pH = 5, left) and for the swollen state (pH = 9, right).**

The observed profile curves (increasing repulsive forces during the approach) are typical signatures of a polymer brush under compression in a good solvent (at pH = 9) and a bad solvent (at pH = 5). The average thickness of the swollen (± 10 nm) and collapsed film (± 2 nm) was estimated by the onset of the repulsive forces detected in the approach profiles. The relatively high collapsing capacity of the brushes is an indication that the grafting density regime is only moderately dense. For a high grafting density regime, the difference betweeen collapsed and swollen brush thickness would be smaller. Classical scaling concepts for polymer brushes like the widely used Alexander - de Gennes model[19, 20] could not be used for this system, because of the swollen chains are charged.

In conclusion, we have demonstrated that the functionalization of a gold surface with a pre-synthetized poly(acrylic acid) containing a disulfide (S-S) bond is an efficient and facile route to obtain pH-responsive switchable gold surfaces. The influence of the pH is clearly demonstrated by atomic force microscopy. The topographic images, the corresponding height profiles and the force profiles all evidence a high swelling capacity: the thickness of the polymer chains in their swollen state (at pH 9) was estimated to be at least 5 times the thickness of the polymer chains in their collapsed state (at pH 5), which is an important feature for potential applications.

## *V.4. Block copolymers with PEE(M)A segments: macroinitiator strategy*

Block copolymers have been prepared via a macroinitiator strategy on one hand (discussed in this paragraph) and via sequential monomer addition on the other hand (see §V.6, synthesis of "block-like" copolymers). In addition, block copolymers were also synthesized by a combination of the ATRP of EEA and another controlled polymerization technique (see §V.5). Block copolymers with PEE(M)A segments have been prepared by ATRP, starting from different macroinitiators. A summary of the reaction conditions and the data of the polymers that were used as a macroinitiator are given in Table V-4. Figure V-28 displays the monomers that were used for the synthesis of the various macroinitiators. Poly(methyl methacrylate) (PMMA), polystyrene (PS), poly(isobornyl acrylate) (PiBA), poly(n-butyl acrylate) (PnBA) and PEEA macroinitiators were prepared with various molecular weights (ranging from ± 1.000 - ± 10.000 g.mol$^{-1}$) and narrow molecular weight distribution (typically 1.10 - 1.15, except for PiBA).

Table V-5 gives an overview of the performed block copolymerizations. As the polymerization of EE(M)A requires relatively low reaction temperatures (preferably below 70 °C) to avoid deprotection, EE(M)A is usually polymerized as the second block.

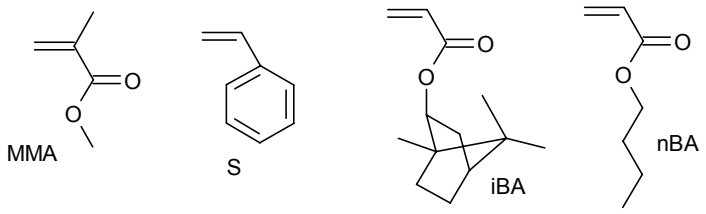


**Figure V-28** **Monomers used for the synthesis of various macroinitiators. MMA: methyl methacrylate, S: styrene, iBA: isobornyl acrylate, nBA: n-butyl acrylate.**

**Table V-4** **Summary of the reaction conditions and the data of the polymers that were used as a macroinitiator for block copolymerizations with EE(M)A (see Table V-5).**

| Entry* | Initiator[a] | Ligand[a] | $[M]_0/[In.]_0/[Cu]_0/[ligand]$[b] | Temp. (°C) | Time (min) | Conv. (%)[c] | $M_{n,exp}$ ($g.mol^{-1}$) | $M_w/M_n$ |
|---|---|---|---|---|---|---|---|---|
| $PMMA_{80}$[d] | **1** | **2** | 100/1/5/10 | 50 | 120 | - | 8000[e] | 1.11[e] |
| $PMMA_{71}$[d] | **1** | **3** | 100/1/1/1 | 90 | 130 | 65 | 8900[f] | 1.10[f] |
| $PS_{21}$[g] | **4** | **5** | 100/1/0.5/0.5 | 90 | 60 | 20 | 2100[f] | 1.11[f] |
| $PiBA_{17}$[h] | **4** | **5** | 100/1/0.5/0.5 | 75 | 45 | 19 | 2600[f] | 1.33[f] |
| $PiBA_{51}$[h] | **4** | **5** | 200/1/0.5/0.5 | 75 | 120 | 26 | 7600[f] | 1.30[f] |
| $PnBA_{15}$[g] | **4** | **5** | 20/1/0.5/0.5 | 20 | 330 | 77 | 1900[f] | 1.14[f] |
| $PEEA_7$[i] | **4** | **5** | 10/1/0.5/0.5 | 50 | 30 | 30 | 900[f] | 1.13[f] |

* PMMA: poly(methyl methacrylate), PS: polystyrene, PiBA: poly(isobornyl acrylate), PnBA: poly(n-butyl acrylate), PEEA: poly(1-ethoxyethyl acrylate). [a.] The following legend is used: **1** ethyl-2-bromoisobutyrate, **2** *N*-octyl-2-pyridylmethanimine **3** *N*-propyl-2-pyridylmethanimine, **4** methyl-2-bromopropionate,, **5** *N,N,N',N'',N''*-pentamethyldiethylenetriamine (PMDETA). [b.] $[M]_0$, $[In.]_0$, $[Cu]_0$ and [ligand] = initial concentration of monomer, initiator, copper catalyst and ligand respectively. [c.] Calculated from $^1H$ NMR. [d.] Cu(I)Br catalyst, 50 v% toluene. [e.] GPC system 2. [f.] GPC system 1. [g.]. Cu(I)Br catalyst, bulk polymerization. [h.] Cu(I)Br catalyst, 25 v% ethyl acetate. [i.] Cu(I)Br catalyst, 50 v% ethyl acetate.

On one hand, poly(methyl methacrylate) (PMMA) and polystyrene (PS) macroinitiators were used for the synthesis of block copolymers (see Table V-5, entry 1-3). Although these copolymerizations proceeded in a controlled way, the presence of unreacted macroinitiator in

the system could not be avoided (see Figure V-29). PMMA and PS are often used because of their high glass transition temperature ($T_g$), but are difficult to prepare with high Br end functionality, even at low monomer conversions, due to termination and transfer reactions and also thermal initiation in case of styrene.

**Table V-5** **Summary of the reaction conditions and results of the block copolymerizations of EE(M)A by ATRP.**

| Entry[a] | Initiator[b] | Mon.[c] | Ligand[d] | $[M]_0/[In.]_0/[Cu]_0/[ligand]$[e] | Temp. (°C) | Time (min) | Conv.[f] (%) | $M_{n,exp}$ ($g.mol^{-1}$) | $M_w/M_n$ |
|---|---|---|---|---|---|---|---|---|---|
| 1[g] | $PMMA_{80}$ | EEMA | **1** | 65/1/5/10 | 50 | 80 | 14 | 10600[h] | 1.08[h] |
| 2[i] | $PMMA_{17}$ | EEMA | **2** | 150/1/0.5/1 | 50 | 120 | 34 | 18600[j] | 1.19[j] |
| 3[k] | $PS_{21}$ | EEA | **2** | 50/1/1/1 | 50 | 240 | 71 | 6400[j] | 1.28[j] |
| 4[k] | $PiBA_{17}$ | EEA | **2** | 150/1/3/4.5 | 70 | 245 | 32 | 14100[j] | 1.22[j] |
| 5[k] | $PiBA_{51}$ | EEA | **2** | 200/1/3/4.5 | 70 | 80 | 14 | 11300[j] | 1.32[j] |
| 6[k] | $PnBA_{15}$ | EEA | **2** | 50/1/1/1 | 50 | 240 | 76 | 6600[j] | 1.18[j] |
| 7[k] | $PnBA_{15}$ | EEA | **2** | 50/1/1/1 | 60 | 180 | 77 | 6700[j] | 1.26[j] |
| 8[k] | $PEEA_7$ | tBA | **2** | 50/1/1/1 | 50 | 300 | 42 | 2900[j] | 1.14[j] |

[a] All reactions were performed using Cu(I)Br as catalyst. [b.] For synthetic details, see Table V-4. [c.] EEMA: 1-ethoxyethyl methacrylate, EEA: 1-ethoxyethyl acrylate, tBA: *tert*-butyl acrylate. [d.] **1** *N*-octyl-2-pyridylmethanimine, **2** *N,N,N',N'',N''*- pentamethyldiethylenetriamine (PMDETA) [e] $[M]_0$, $[In.]_0$, $[Cu]_0$ and [ligand] = initial concentration of monomer, initiator, copper catalyst and ligand respectively. [f.] Calculated from $^1$H NMR. [g] 50 v% toluene. [h] GPC system 2. [i.] 50 v% anisole. [j.] GPC system 1. [k.] bulk polymerization.

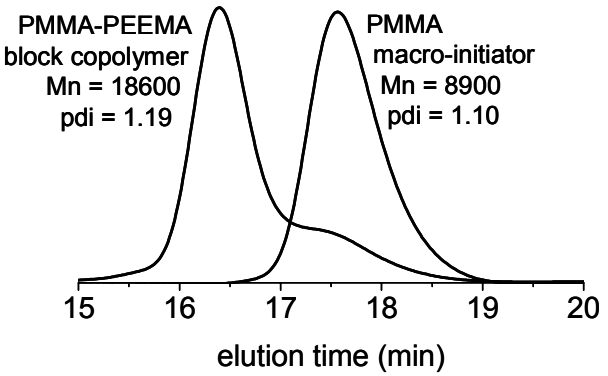


**Figure V-29** **GPC analysis of the block copolymerization of EEMA starting from a PMMA macroinitiator (Table V-5, entry 2). (GPC system 1)**

For the polymerization of MMA, the overall concentration of radicals in the ATRP system is quite high due to the rather high ATRP equilibrium constant, and as a result, termination reactions are often observed[11]. This leads to dead polymer chains that contain no bromine end group, and these chains will not act as a macroinitiator when a block copolymerization is performed. Another related problem which is particularly observed in the polymerization of methacrylates is a slow initiation rate compared to propagation rate. This results in a low initiator efficiency and thus rather uncontrolled molecular weights (see also Chapter II, §II.3).[21] Acrylates on the other hand show a higher $k_p$ value but a lower $k_a$, leading to a lower ATRP equilibrium constant, thus less radicals in the system and thus to lower amounts of dead chains due to termination reactions, while the ratio of initiation rate to propagation rate is much higher.

In the case of styrene, thermal self-initiation[22] of the polymerization reaction is often observed, leading to a side product without the desired end group. In addition, for the ATRP synthesis of PS, detailed studies using nuclear magnetic resonance[23] and two-dimensional liquid chromatography[24], have proven that PS with an end group functionality of more than 90% is difficult to reach, even at low monomer conversion. Indeed, block copolymerizations performed with a PS macroinitiator showed also the presence of unreacted macroinitiator.

When PiBA was used as the macroinitiator, unreacted macroinitiator in the polymerization mixture could be avoided, as can be observed from the GPC curves, which do not show any shoulder (Figure V-30). For more details on the controlled ATRP synthesis of PiBA and PiBA containing copolymers, we refer to Chapter VI.

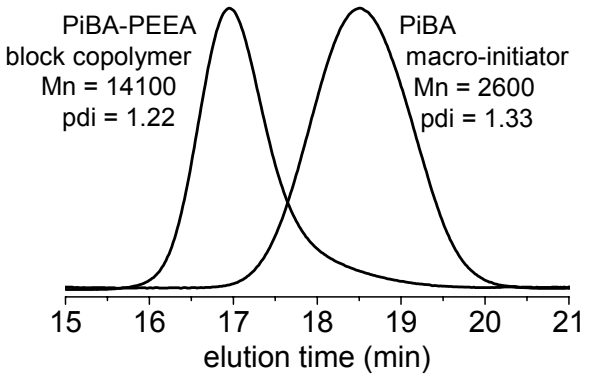


**Figure V-30** **GPC analysis of the block copolymerization of EEMA starting from a PiBA macroinitiator (Table V-5, entry 4). (GPC system 1).**

To yield the corresponding PiBA-*b*-PAA polymer, the PiBA-*b*-PEEA polymer was then heated at 80 °C for 24 h. TGA experiments confirmed total conversion of PiBA-*b*-PEEA to PiBA-*b*-PAA. A TGA analysis of $PiBA_{51}$-*b*-$PEEA_{30}$ (Table V-5, entry) before and after the heating step is shown in Figure V-31. For the unprotected $PiBA_{51}$-*b*-$PEEA_{30}$, TGA analysis reveals a weight decrease at 150 °C, which corresponds to the deprotection step to yield $PiBA_{51}$-*b*-$PAA_{30}$ with loss of vinyl ether (volatile compound, bp = 33 °C). Taking into account the molecular composition of $PiBA_{51}$-*b*-$PEEA_{30}$, and the molecular weight of iBA (= 208.3 $g.mol^{-1}$), EEA (= 144.17 $g.mol^{-1}$) and EVE (= 72.11 $g.mol^{-1}$), the theoretical weight after the deprotection can be calculated. For $PiBA_{51}$-*b*-$PEEA_{30}$, the theoretical weight after deprotection to $PiBA_{51}$-*b*-$PAA_{30}$ is 85.5 %. TGA analysis reveals a weight loss of 14 %. It can thus be concluded that the theoretical weight after deprotection of $PiBA_{51}$-*b*-$PEEA_{30}$ to $PiBA_{51}$-*b*-$PAA_{30}$ by a heating step is in good agreement with the experimental value. The TGA analysis of a deprotected polymer (Figure V-31, dotted line) does not show any weight loss at 150 °C, showing that deprotection was complete. The weight loss from about 200 °C originates from the loss of the isobornyl group, while above 300 °C, also the polymer backbone decomposes. These conclusions are confirmed by the absolute values of the weight losses.

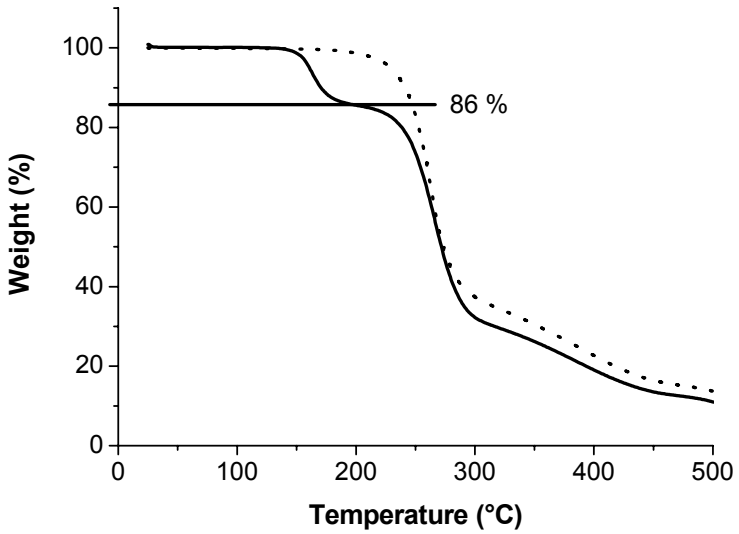


**Figure V-31** **TGA analysis of $PiBA_{51}$-*b*-PEEA56 (before deprotection, solid line) and $PiBA_{51}$-*b*-PAA56 (after deprotection by heating at 80 °C for 24 h, dotted line).**

If a combination of a PEEA/PAA segment and a low $T_g$ segment is desired, a poly(n-butyl acrylate) macroinitiator could be used ($T_g$ = -54 °C[25]) (see Table V-5, entry 6-7).

Polymerizations were carried out with CuBr and PMDETA as the ligand, in bulk. These block copolymerizations were performed with good control over the polymerization reaction, as confirmed by the linear behavior of both the first order kinetic plot and the plot of the $M_n$ as a function of conversion (see Figure V-32). From GPC analysis, it can be concluded that functionalization of the macroinitiator is close to 100 % (Figure V-33, left). Only a small fraction (< 5 %) of unreacted macroinitiator was observed in the system, causing a slight increase of the PDI of the polymer with increasing conversion. This small fraction of unreacted macroinitiator is attributed to radical termination during the start of the synthesis of the macro-initiator, when the ATRP equilibrium is not fully established yet.

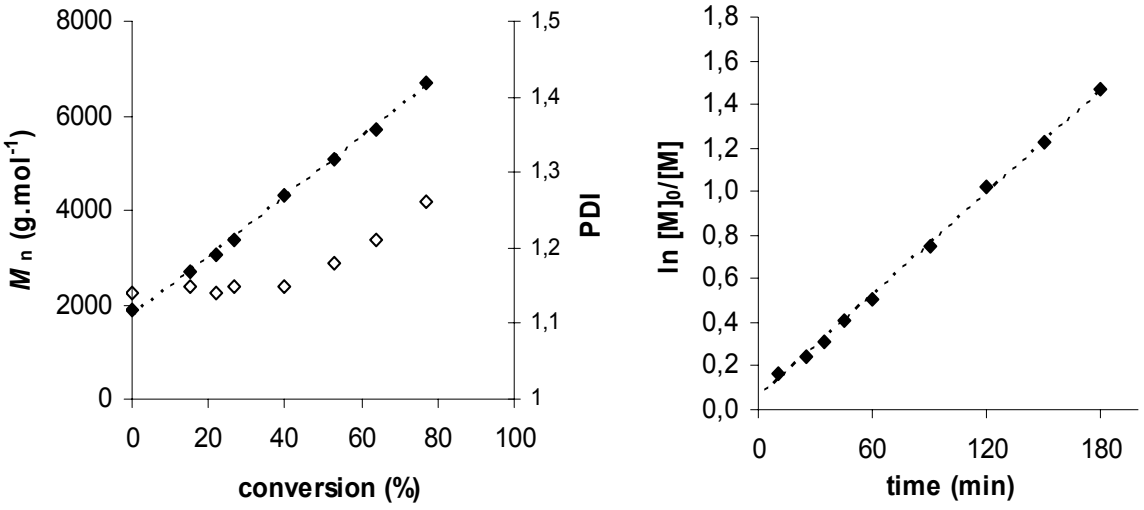


**Figure V-32** **Average molar mass ($M_n$, ♦) and polydispersity (PDI, ◊) vs. conversion (left) and the first order kinetic plot (right) of a block copolymerization of EEA starting from a PnBA macro-initiator (Table V-5, entry 7). Dotted lines are trend lines.**

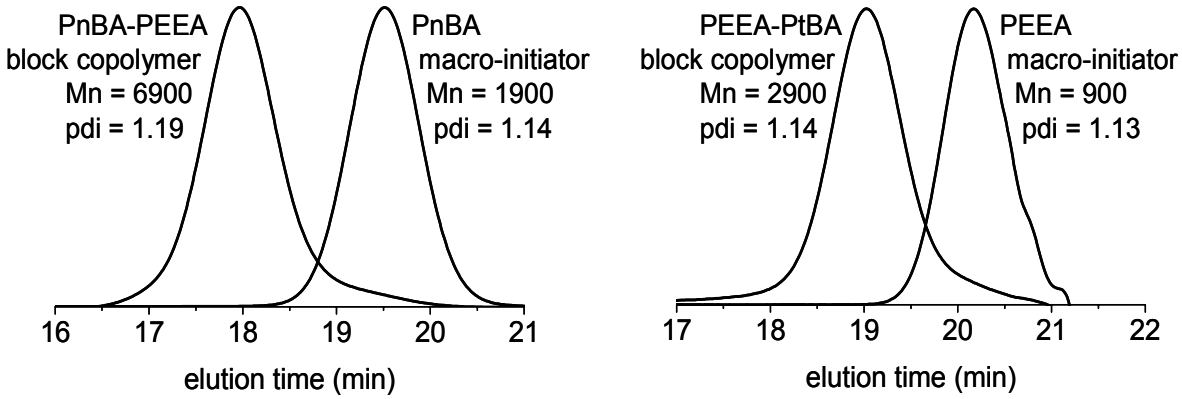


**Figure V-33** **GPC analysis of block copolymerizations of EEA and nBA (left; Table V-5, entry 7) or tBA (right; Table V-5, entry 8). (GPC system 1).**

In addition, block copolymers have also been prepared starting from a PEEA macroinitiator, in the case that low reaction temperatures could be used for the ATRP of the second block. As an example of a block copolymer with PEEA as the first block, a block copolymer with poly(tert-butylacrylate) (PtBA) as second segment was synthesized. The SEC traces reveal that this was done in a controlled way (Table V-5, entry 8; Figure V-33, right). Although we demonstrated that block copolymers with PEE(M)A as the first block can be synthesized, the reverse way is often more convenient because of the rather high temperatures that are needed for the polymerization of some monomers. Even minor deprotection of the PEE(M)A segments could destroy the catalyst system during the synthesis of the second block.

## *V.5. Block copolymers with PEE(M)A segments: combination with CROP of THF*

Further on, the ATRP of EE(M)A was also combined with other controlled polymerization techniques. This is illustrated with the synthesis of a polytetrahydrofuran-*b*-PEEA (PTHF-*b*-PEEA) block copolymer, for which the PTHF macroinitiator was synthesized by cationic ring opening polymerization (CROP) using a dual initiator 4-hydroxybutyl-2-bromoisobutyrate (HBBIB)[26-28]. The use of a dual initiator allows the combination of mechanistically distinct polymerization reactions (e.g. ATRP and CROP). In this way, a variety of different monomers and their specific properties are combined. A review regarding the synthesis of block copolymers with dual initiators was recently published by Bernaerts *et al.*[29]

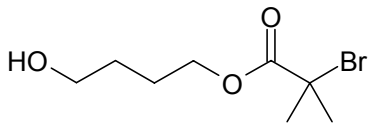


**Figure V-34 Dual initiator HBBIB.**

Dual initiator HBBIB not only contains the hydroxyl group that is necessary for the CROP of THF, but also a bromine end group that is necessary for ATRP to polymerize EEA as the second block (see Figure V-34). We will not go into detail about the CROP of THF using this dual initiator, as this was subject of another Ph.D. thesis in our research group.[30] Table V-6 summarizes the reaction conditions and results of the polymerization of EEA as

the second block starting from a PTHF macroinitiator that was prepared using HBBIB. All reactions were performed in bulk, and the initial monomer to macro-initiator ratio ($[M]_0/[In.]_0$) was varied.

A kinetic study of the polymerization of EEA using a $PTHF_{42}$ macroinitiator is shown in Figure V-35 (Table V-6, entry 2).

**Table V-6** **Summary of the reaction conditions and results of the block copolymerizations of EEA by ATRP, starting from a PTHF macroinitiator.**

| Entry | Initiator | $M_n$ In.[a, b] | $M_w/M_n$[a] In. | $[M]_0/[In.]_0/[Cu]_0/[ligand]$[c] | Temp. (°C) | Time (min) | Conv. (%)[d] | $M_{n,exp}$[a] (g.mol$^{-1}$) | $M_w/M_n$[a] |
|---|---|---|---|---|---|---|---|---|---|
| 1 | $PTHF_{68}$ | 5200 | 1.21 | 150/1/1/1 | 50 | 150 | 25 | 17400 | 1.12 |
| 2 | $PTHF_{42}$ | 3300 | 1.17 | 50/1/1/1 | 50 | 120 | 74 | 11500 | 1.15 |

[a.] GPC system 1 [b.] A conversion factor of 0.5 relative to polystyrene standards was applied. [c.] $[M]_0$, $[In]_0$, $[Cu]_0$ and [ligand] = initial concentration of monomer, initiator, copper catalyst and ligand respectively. [d.] Determined from $^1$H NMR.

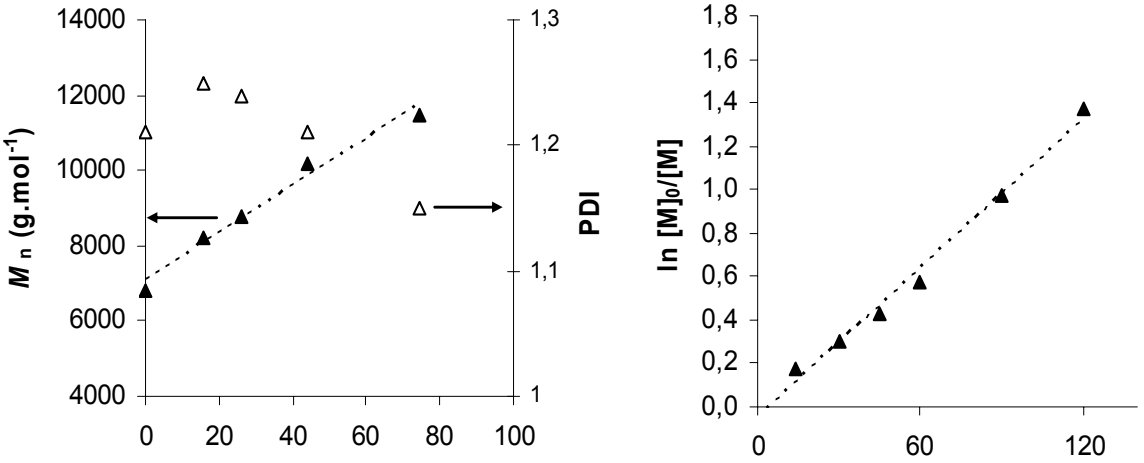


**Figure V-35** **Left: average molar mass ($M_n$, ♦) and polydispersity (PDI, ◊) vs. conversion (GPC system 1) of a block copolymerization of EEA starting from a PTHF macro-initiator (Table V-6, entry 2).Right: first order kinetic plot. Dotted lines are trend lines.**

The linear increase of the average molar mass as a function of conversion and the linear behavior of the first order kinetic plot demonstrate the controlled behavior of the polymerization reaction. GPC analysis shows that well-defined polymers with a narrow molecular weight distribution are obtained, and no residual macro-initiator was observed (see Figure V-36).

Thermogravimetric analysis of the $PTHF_{68}$ macro-initiator and the $PTHF_{68}$-*b*-$PEEA_{37}$ block copolymer (see Figure V-37) demonstrates that $PTHF_{68}$-$PEEA_{37}$ can be deprotected to $PTHF_{68}$-*b*-$PAA_{37}$ without degradation of the PTHF segment. Taking the molecular composition of $PTHF_{68}$-*b*-$PEEA_{37}$ (Table V-6, entry 1) into account, the theoretical weight loss that corresponds to the release of volatile ethyl vinyl ether is 24.1 %. From TGA, an experimental weight loss of 23.0 % (at 180 °C) is obtained, showing a good agreement between the theoretical and experimental value.

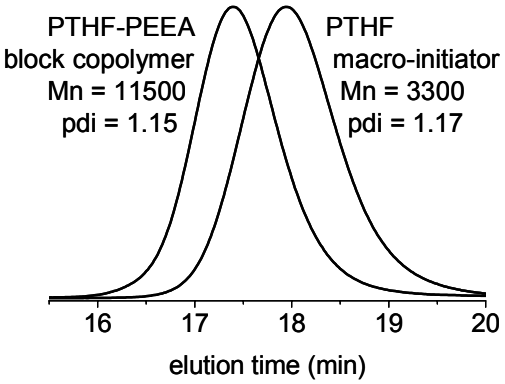


**Figure V-36** **GPC analysis of the block copolymerization of EEA starting from a PTHF macro-initiator (Table V-6, entry 2). (GPC system 1)**

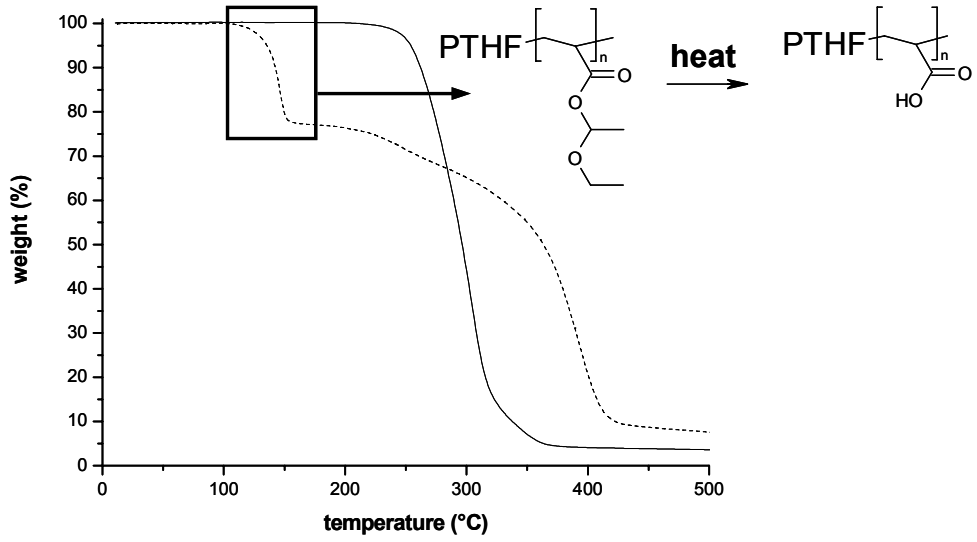


**Figure V-37** **Thermogravimetric analysis (heating rate: 10 °C/min; $N_2$ atmosphere) of $PTHF_{68}$ macro-initiator (___) and $PTHF_{68}$-$PEEA_{37}$ block copolymer (---) (Table V-6, entry 2)**

## V.6. "Block-like" and random copolymers with PEE(M)A segments

Copolymer structures have also been synthesized by sequential monomer addition of 2 monomers during the polymerization reaction. In comparison to the above described macroinitiator strategy, the advantage of this procedure is the more simple experimental procedure. The sequential monomer addition strategy is a one-pot synthesis, without any purification step after the synthesis of the first block. As one of the two monomers is only added after the first monomer reached a fixed conversion, these copolymer structures are therefore called "block-like" copolymers. For high conversion of the first monomer before adding the second monomer, a copolymer with a structure close to that of a block copolymer will be obtained. Currently, a Ph.D. research work in our research group is investigating these polymer architectures more in detail with regard to their synthesis and their different properties compared with pure block copolymers.[31] According to the relative reactivity of both monomers, we can split up "block-like" copolymers into two classes (see Figure V-38). If the two monomers show a distinct reactivity, a gradual change in repeat unit composition (= a gradient) along the second segment will be obtained, and therefore these copolymers are named "blocky gradient" copolymers.[32] On the other hand, when both monomers show an equal reactivity, no gradient composition is obtained, and the corresponding structures are therefore named "blocky random" copolymers.

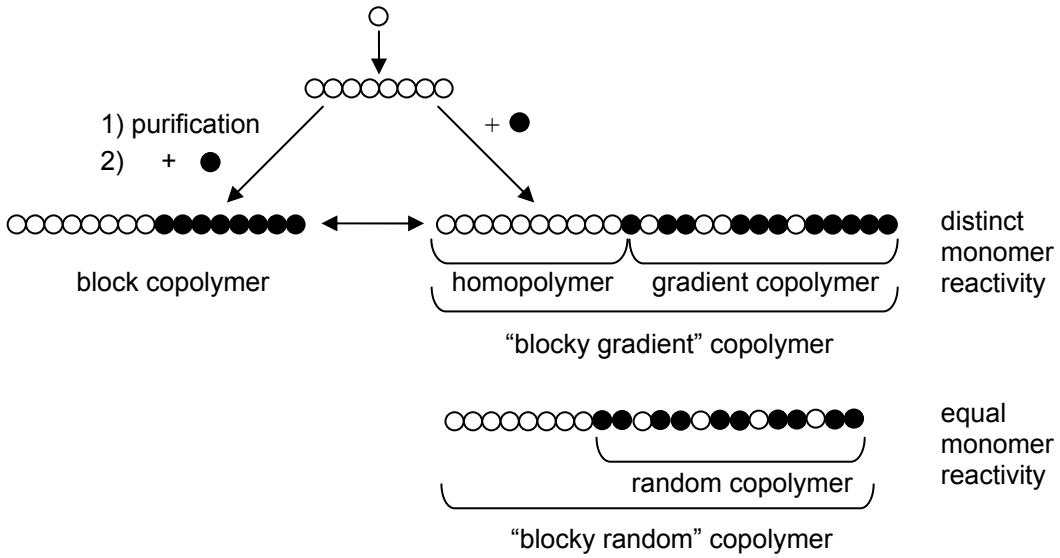


**Figure V-38** **Left: schematic depiction of the macroinitiator strategy yielding block copolymers. Right: schematic depiction of sequential monomer addition, yielding "blocky gradient" or "blocky random" copolymers.**

In our case, tert-butyl acrylate (tBA) and EEA were chosen as the monomers to perform a copolymerization reaction using sequential monomer addition (Table I, entry 8-9).

Analysis of the first order kinetic plot of a 1:1 random copolymerization of EEA and tBA (Table V-7, entry 3) revealed that both monomers show a nearly equal reactivity (see Figure V-39), resulting in a random copolymer composed of almost equal amounts of EEA and tBA.

**Table V-7** **Summary of the reaction conditions and results for the synthesis of PEEA containing "block-like" and random copolymers by ATRP.**

| **"Block-like" copolymers by sequential monomer addition** | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Entry[a]** | **$[M_1]_0$:$[MBP]_0$:$[PMDETA]_0$:$[CuBr]_0$[b]** | **Temp. (°C)** | **Time (min)** | **$DP_{th}$ 2nd block** | **Total time (min)** | **$M_{n,exp}$[c] (g.mol$^{-1}$)** | **$M_w/M_n$[c]** | **Final composition[d]** |
| 1[e] | 20:1:1:1 | 50 | 30 | 20 | 150 | 4600 | 1.12 | $PtBA_{10}$//$PtBA_8$/$PEEA_{17}$ |
| 2 | 20:1:1:1 | 50 | 40 | 50 | 300 | 4800 | 1.18 | $PEEA_{12}$//$PEEA_2$/$PtBA_{19}$ |
| **Random copolymers** | | | | | | | | |
| **Entry** | **$[M_1]_0$:$[M_2]_0$:[f] $[MBP]_0$:$[PMDETA]_0$:$[CuBr]_0$** | **Temp. (°C)** | **Time (min)** | **Conv. $M_1$, $M_2$[g] (%)** | | **$M_{n,exp}$[c] (g.mol$^{-1}$)** | **$M_w/M_n$[c]** | **Final composition[d]** |
| 3 | 20:20:1:1:1 | 50 | 180 | 88, 87 | | 6300 | 1.18 | $PEEA_{18}$/$PtBA_{17}$ |

[a] All polymerizations were carried out with methyl-2-bromopropionate (MBP) as initiator, Cu(I)Br as catalyst and *N,N,N',N'',N''*- pentamethyldiethylenetriamine (PMDETA) as ligand, in bulk. [b.] $[M_1]_0$, $[MBP]_0$, $[CuBr]_0$ and [PMDETA] = initial concentration of first monomer, methyl-2-bromopropionate, Cu(I)Br and PMDETA respectively. [c.] GPC system 1. [d.] Determined from conversion; notation $A_x$//$A_y$/$B_z$: the first block contsists of x units of monomer A and the second segment is a copolymer of y units of monomer A and z units of monomer B. [e.] 33 v% of ethyl acetate added for the synthesis of the first block. [f.] $[M_1]_0$, $[M_2]_0$ = initial concentration of first and second monomer. [g.] Determined by $^1$H NMR.

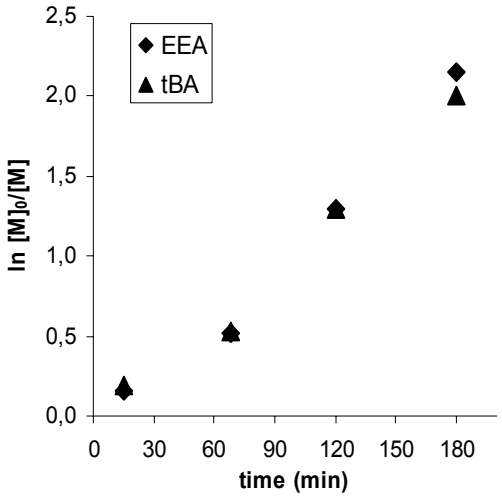


**Figure V-39** **First order kinetic plot for the random copolymerization of EEA and tBA (monomer feed 1:1), showing a nearly equal reactivity for EEA and tBA. (Table V-7, entry 3).**

In this way, the molecular architecture obtained by sequential monomer addition is intermediate to those of block and random copolymers. Thus, the resulting copolymer consists of a first block of tBA or EEA and a random second block of tBA and EEA. Because of this specific composition distribution, the repulsive inter-chain interactions are less strongly changing along the chain in comparison to conventional block copolymers. Therefore these polymers may be of special interest for specific applications such as stabilization of dispersions, micellization applications, etc.[32, 33].

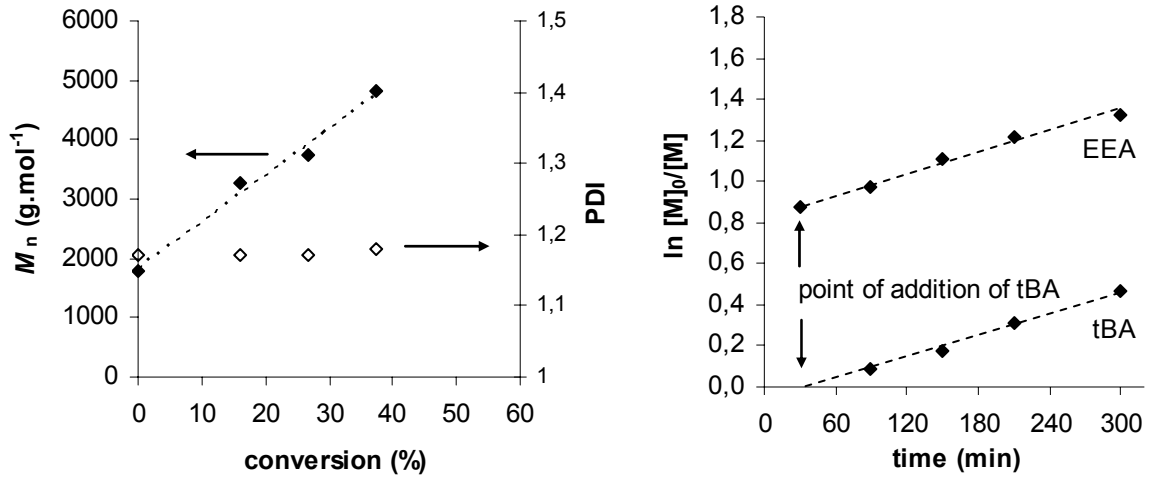


**Figure V-40** **Left: average molar mass ($M_n$, ♦) and polydispersity (PDI, ◊) vs. conversion of tBA (GPC system 1) for the synthesis of a "block-like" copolymer with a first "block" of EEA (Table V-7, entry 2) .Right: first order kinetic plot of EEA and tBA. Dotted lines are trend lines.**

Well-defined copolymers composed of EEA and tBA have been synthesized by ATRP with PEEA as the first part (Table V-7, entry 2), as well as by adding EEA as the second monomer (Table V-7, entry 1). In each case, well-defined polymers were obtained. The kinetic data for the synthesis of a "block-like" copolymer with a first block of PEEA (Table V-7, entry 2) are shown in Figure V-40. The linear increase of the $M_n$ vs. conversion of tBA (starting point: addition of tBA) and the linear behavior of the first order kinetic plot of both EEA and tBA show the controlled character of the polymerization. Moreover, the similar slope of the first order kinetic plot reveals equal reactivity for EEA and tBA.

Deprotection to the PAA containing polymer was performed by heating the polymer sample at 80 °C for 24 hours. To verify that deprotection did not result in broadening of the molecular weight distribution, methylation[34] (see exp. part, §V.9.2) of a deprotected sample

was carried out. GPC analysis revealed no broadening of the molecular weigth distribution (Figure V-41).

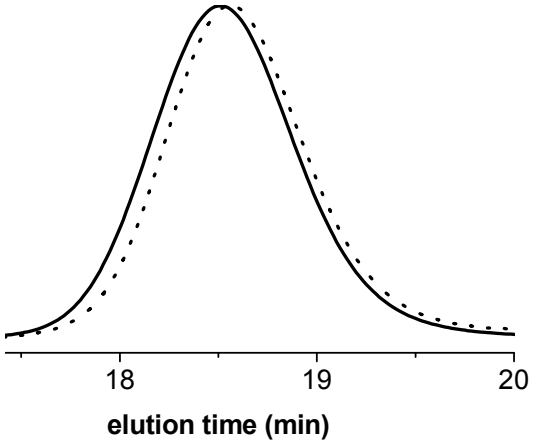


**Figure V-41** **GPC analysis of $PtBA_{10}$//$PtBA_8$/$PEEA_{17}$ (solid line; Table V-7, entry 1) and the corresponding deprotected $PtBA_{10}$//$PtBA_8$/$PAA_{17}$ after methylation (dotted line). (GPC system 1).**

## *V.7. Conclusion*

In this chapter it has been demonstrated that atom transfer radical polymerization (ATRP) is a suitable technique to polymerize 1-ethoxyethyl methacrylate (EEMA) and 1-ethoxyethyl acrylate (EEA), resulting in polymers with a good control of average molar mass ($M_n$) and narrow molecular weight distribution. Common initiators as well as tailor-made initiators have been used, as demonstrated with the use of a disulfide containing initiator. These PEE(M)A polymers are novel precursors for poly(methacrylic acid) and poly(acrylic acid), respectively. Using tailor-made initiators, the polymer properties can be adjusted to specific applications. In our case, the use of a disulfide containing initiator leads to the preparation of PAA with a disulfide bond, which allowed us to create pH-responsive gold surfaces. The PAA-functionalized gold surfaces were characterized by atomic force microscopy in water to investigate their pH-responsive behavior.

Moreover, various PEE(M)A containing polymers were successfully prepared, including block copolymers, “block-like” copolymers, and random copolymers. In addition, the ATRP of EEA was also combined with the cationic ring opening polymerization of tetrahydrofuran. The poly((meth)acrylic acid) (P(M)AA) containing copolymers can be obtained by a heating

step, without further purification. As a conclusion, it has been shown that the EE(M)A strategy is an easy and general applicable strategy for the synthesis of a wide variety of P(M)AA containing polymer structures.

## V.8. Acknowledgement

Special thanks to Dr. Stefan Bon (Warwick University, United Kingdom) for the excellent collaboration and his advice on the ATRP of EE(M)A. Thanks to Dr. R. Hoogenboom and Prof. U. Schubert (Eindhoven University of Technology, the Netherlands) for using their microwave automated synthesizer for the ATRP of EEA at higher temperatures. Also thanks to Dr. S. Demoustier-Champagne, H. Alem and Dr. A. Duwez (Université Catholique de Louvain, UCL, Belgium) for their work on the characterization of the pH-responsive gold substrates. Dr. Els Bruneel (Ghent University) is acknowledged for the TGA-MS measurements.

## V.9. Experimental part

### V.9.1. Materials

Methacrylic acid (Acros Organics, 99.5 %) and acrylic acid (Acros Organics, 99.5 %) were purified by distillation with phenothiazine as inhibitor. Ethyl vinyl ether (Aldrich, 99 %) and isobutyl vinyl ether (Fluka, 99%) was distilled before use. $Mg_6Al_2(OH)_{16}CO_3.4H_2O$ was obtained from Kisuma Chemicals. Cu(I)Br and Cu(I)Cl were purified first by stirring with acetic acid, then by washing with methanol, and finally by drying in a vacuum oven at 70 °C.[35] *N,N,N',N'',N''*-pentamethyldiethylenetriamine (PMDETA, Aldrich, 99 %) was distilled (85-86 °C/12 mmHg). *N*-propyl-2-pyridylmethanimine[8], *N*-octyl-2-pyridylmethanimine[8], tris[2-(dimethylamino)ethyl]amine[36, 37] ($Me_6$TREN) and 4-hydroxybutyl-2-bromoisobutyrate[26-28] (HBBIB) were synthesized according to literature procedures. Isobornyl acrylate (iBA, Aldrich, tech.) was purified by vacuum distillation (121 °C/18 mmHg). Methyl methacrylate (MMA), *tert*-butyl acrylate (tBA), styrene and *n*-butyl acrylate (nBA) were also distilled prior to use. Methyl-2-bromopropionate (MBP, Acros, 99 %), ethyl 2-bromoisobutyrate (Aldrich, 98 %), 2,2,2 trichloroethanol (Acros, 99%), 2-bromopropionic

acid (Acros, 99 %), bis(2-hydroxyethyl) disulfide (Aldrich), *N, N'*-dicyclohexylcarbodiimide (DCC, Acros, 99 %), 4-dimethylaminopyridine (4-DMAP, Acros, 99 %), tetrabutyl ammoniumfluoride (1.0 M solution in THF, 99 %), tetrabutyl ammonium hydrogen sulphate (Acros, 98 %), and (trimethylsilyl)diazomethane (2.0 M solution in diethyl ether, Aldrich) were used as received. Solvents were purchased from Aldrich (HPLC grade) and used without purification. All other chemicals were used as received.

### V.9.2. Characterization

**$^{1}$H NMR** and **$^{13}$C NMR** spectra were recorded on a Bruker AM500 spectrometer (500 MHz) or a Bruker Avance 300 spectrometer (300 MHz) at room temperature.

**EI-MS** spectra were recorded with a HP Engine 5958A Mass spectrometer (70 eV).

Contact angle measurements were performed using a Motic M700 microscope equiped with a Jenalux20 illuminator and a JVC-601 Colour Video Camera. Data were analysed using Image Pro Plus software.

**Gel permeation chromatography** (GPC) analyses were carried out on 3 systems. GPC system 1 is a Waters instrument, with refractive index (RI) detector (2410 Waters), equipped with $10^3$ - $10^4$ and $10^5$ Å serial columns. Polystyrene (PS) standards were used for calibration, and $CHCl_3$ was used as an eluent at a flow rate of 1.5 mL min$^{-1}$. In order to be able to measure the PAA containing (co)polymers on GPC system 1 without problems of absorption of the hydrolyzed polymer on the column, the PAA segment was methylated with a (trimethylsilyl)diazomethane solution[34]. Methylation converts the PAA segment into a poly(methyl acrylate) segment, which does not interact with the GPC-column and gives reliable GPC results when $CHCl_3$ is used as a solvent with polystyrene standards. Typically, 50 mg of a sample was dissolved in a mixture of THF and water (overall volume: 10 mL). The yellow solution of (trimethylsilyl)diazomethane was added dropwise at room temperature. Upon addition, bubbles appeared and the solution became instantaneously colorless. Addition of the methylation agent was continued until the solution became yellow and stopped bubbling. Then, an excess of methylation agent was added and the solution was stirred for 3 hours more at room temperature. GPC system 2 is a system equipped with a guard column and two mixed bed E colums (Polymer Labs) operating using tetrahydrofuran as eluent at a flow rate of 1 mL min$^{-1}$ at room temperature. The molar mass distributions (MMD) were detected using differential refractive index and were calibrated specifically

using narrow MMD PMMA standards. GPC System 3 is a Shimadzu system equipped with a SCK-10A system controller, a LC-10AD pump, a RID-10A refractive index detector and a PL gel 5 μm Mixed-D column at 50 ºC utilizing a chloroform/triethylamine/ isopropanol (94/4/2) mixture as eluent at a flow rate of 1 $mL.min^{-1}$. The molecular weights were calculated on the basis of poly(methyl methacrylate) standards.

The **microwave-assisted ATRP** reactions were performed in a monomode microwave automated synthesizer (Emrys$^{TM}$ Liberator, Biotage) with a uniform microwave field.

**Infrared** spectra were obtained with a Perkin Elmer 1600 Series FTIR.

**Thermogravimetric analysis** was done with a Thermal Sciences PL-TGA 1000 system or with a Mettler Toledo TGA/SDTA851e instrument under air or nitrogen atmosphere at a heating rate of 10 °C/min from 25 °C-800 °C.

**TGA-MS** experiments were performed with a TA Instruments SDT2960 simultaneous TGA-DTA instrument coupled with a quadrupole Thermolab mass spectrometer. The sample was heated at a heating rate of 10 °C/min under air atmosphere (100 mL/min).

**XPS** was performed on a SSIX probe (SSX 100/206) spectrometer from Fisons equipped with a monochromatic Al Kα X-ray source (hν = 1486.7 eV). Spectra were recorded at a take-off angle of 35° (angle between the plane of the sample surface and the entrance lens of the analyzer) with a pass energy of 150 eV.

**AFM**-based force spectroscopy experiments and imaging were carried out in water (at pH 5 or 9) with a PicoSPM equipped with a fluid cell (Molecular Imaging) and controlled by Nanoscope III electronics (Digital Instruments). Silicon nitride cantilevers with a spring constant of 0.05 $N.m^{-1}$ were used. The data were processed using a program developed in Igor Pro (WaveMetrics, Inc.) to extract from every curve the onset of repulsive tip-sample interaction.

### V.9.3. Synthesis of the monomer: 1-ethoxyethyl (meth)acrylate

Procedure for the synthesis of 1-ethoxyethyl (meth)acrylate (EE(M)A): Under a nitrogen atmosphere, 1.0 mol (68.6 mL) of acrylic acid or 1.0 mol (85.2 mL) of methacrylic acid was added slowly at 0 °C to a mixture of 1.2 mol (114.9 mL) of ethyl vinyl ether and 0.002 mol (0.2 g) of phosphoric acid as a catalyst. The mixture was stirred at room temperature for 48 h. The catalyst was then absorbed on $Mg_6Al_2(OH)_{16}CO_3.4H_2O$. After filtration the excess vinyl

ether was evaporated. The product was distilled at reduced pressure with phenothiazine as inhibitor. The boiling point was 32 °C (6 mbar) for 1-ethoxyethyl methacrylate (EEMA) and 47 °C (18 mbar) for 1-ethoxyethyl acrylate (EEA). Yields are about 90 %. Spectral data:

**EEMA:**

$^{1}$H NMR ($CDCl_3$, δ, ppm): 1.21 [3H, t, -$OCH_2CH_3$], 1.43 [3H, d, -$COOCH(CH_3)$], 1.95 [3H, s, $CH_2=C(CH_3)$], 3.52-3.75 (2H, m, -$OCH_2$-], 5.59 [1H, s, $CH_2=C(CH_3)$-], 5.99 [1H, q, -$COOCH(CH_3)$], 6.15 [1H, s, $CH_2=C(CH_3)$-]

$^{13}$C NMR ($CDCl_3$, δ, ppm): 14.9 [-$OCH_2CH_3$], 18.1 [$CH_2=C(CH_3)$-], 20.8 [-$COOCH(CH_3)$-], 64.5 [-$OCH_2$-], 96.6 [-$COOCH(CH_3)$], 125.6 [$CH_2=C(CH_3)$-], 136.2 [$CH_2=C(CH_3)$-], 166.9 [-COO-]

EI-MS: (MM of EEMA = 144) 143, 129, 115, 99, 89, 73, 61, 55, 45

IR ($cm^{-1}$, neat KBr pellets): 2980.1 ($CH_3$); 2931.7 ($CH_2$); 1715.5 (C=C-COOR); 1637.4; 1453.3; 1383.6 ($CH_3$); 1356.7; 1317.6; 1296.4; 1170.5, 1131.9, 1072.8, 1036.9 (acetal); 1007.3; 948.0; 853.0; 652.8

**EEA:**

$^{1}$H NMR ($CDCl_3$, δ, ppm): 1.07 [3H, t, -$OCH_2CH_3$], 1.30 [3H, d, -$COOCH(CH_3)$], 3.40-3.63 (2H, m, -$OCH_2$-], 5.73 [1H, d, $CH_2$=CH-], 5.90 [1H, q, -$COOCH(CH_3)$], 6.00 [1H, dd, $CH_2$=CH-], 6.30 [1H, d, $CH_2$=CH-]

$^{13}$C NMR ($CDCl_3$, δ, ppm): 14.9 [-$OCH_2CH_3$], 20.8 [-$COOCH(CH_3)$], 64.6 [-$OCH_2$-], 96.3 [-$COOCH(CH_3)$], 128.5 [$CH_2$=CH-], 130.9 [$CH_2$=CH-], 165.6 [-COO-]

EI-MS: (MM of EEA = 158) 157, 143, 129, 117, 113, 99, 89, 73, 69, 45, 41

### V.9.4. Polymerization of EE(M)A

A typical polymerization procedure is as follows (e.g. Table V-1, entry 1): First, the monomer was passed through a small column of basic $Al_2O_3$ to remove traces of residual acid. A mixture of 0.120 mol (20 mL) of 1-ethoxyethyl methacrylate, 20 mL of toluene as a solvent (50 v%) and 0.024 mol (5.60 mL) of *N*-octyl-2-pyridylmethanimine as a ligand was degassed by several freeze-pump-thaw cycles. Cu(I)Br (0.012 mol, 1.72 g) was added and the reaction flask was placed in an oil bath at 50 °C. When the reaction mixture reached the

desired reaction temperature, the polymerization was started by adding 0.0024 mol (0.352 mL) of ethyl-2-bromoisobutyrate as initiator. The reaction was ended by cooling the reaction mixture in liquid nitrogen. The resulting polymer was purified by passing the diluted reaction mixture over a column of neutral $Al_2O_3$ to remove the copper catalyst. After evaporating the excess solvent, the polymer was precipitated in cold methanol. For polymerizations of EEA, the monomer was removed by high vacuum.

## V.9.5. Microwave-assisted ATRP of EEA at higher temperature

A stock solution of EEA (20 mL, 0.139 mol), PMDETA ($3.05 .10^{-3}$ mol, 0.529 g, 0.637 mL) as ligand and methyl 2-bromopropionate ($2.77 .10^{-3}$ mol, 0.540 g, 0.407 mL) as initiator was bubbled with $N_2$ for 1 h, and Cu(I)Br ($2.77 .10^{-3}$ mol, 0.398 g) was added. Process vials were filled with 2 mL of stock solution, a magnetic bar was added and the vials were sealed with a Teflon septum. The reaction mixtures were one by one automatically inserted into the microwave cavity and magnetically stirred at the desired reaction temperature (60-120 °C) during different periods of time. The reactions were stopped by quickly cooling to room temperature.

For polymerizations carried out with conventional heating (using an oil bath), the procedure is identical to the one described in §V.9.4.

## V.9.6. PAA with a disulfide functionality

### V.9.6.1. Synthesis of bis(2-hydroxyethyl)disulfide bis(2-bromopropionate): disulfide-containing initiator

Bis(2-hydroxyethyl)disulfide (7.83 mL , 9.88 g, $6.40 .10^{-2}$ mol) is dissolved in 200 mL THF. The mixture is cooled to 0 °C by placing it in an ice water bath and 11.9 mL (0.128 mol) 2-bromopropionic acid is added under stirring. Then, 26.44 g (0.128 mol) DCC is dissolved in 100 mL of THF, and also added to the reaction mixture. The mixture is stirred for 10 minutes at 0 °C. After that, a solution of 0.35 g 4-DMAP in 5 mL of THF is added dropwise over a period of 5-10 minutes. The heterogeneous reaction mixture is then stirred at room temperature for 24 hours. The precipitated dicyclohexyl ureum is filtered off and the precipitate was washed with 100 mL THF. After evaporating the solvent, bis(2-hydroxyethyl)disulfide bis(2-bromopropionate) is obtained as a yellow viscous product. Crystalline impurities are removed by filtration.

#### V.9.6.2. ATRP of EEA with disulfide-containing initiator

A typical polymerization procedure is as follows (e.g. entry 1, Table V-3). A mixture of 0.0347 mol (5.0 mL) of the monomer EEA and 0.347 $.10^{-3}$ mol (0.072 mL) of PMDETA as the ligand was added to a reaction flask and was bubbled with $N_2$ for 1h to remove oxygen from the reaction mixture. After that, Cu(I)Br (0.347 $.10^{-3}$ mol, 0.050 g) was added and the reaction flask was placed in an oil bath at 50 °C. When the reaction mixture reached the desired reaction temperature, the polymerization was started by adding 0.694 $.10^{-3}$ mol (0.098 mL) of bis(2-hydroxyethyl)disulfide bis(2-bromopropionate) as the initiator. Samples were withdrawn periodically to monitor the monomer conversion (by $^1$H NMR) and the average molecular weight (by GPC). The reaction was ended by cooling the reaction mixture in liquid nitrogen. The resulting polymer was dissolved in THF and the diluted reaction mixture was passed over a column of neutral $Al_2O_3$ to remove the copper catalyst. After evaporating the excess solvent, the residual monomer was removed by vacuum.

### V.9.7. Block copolymers with PEE(M)A segments: macroinitiator strategy

#### V.9.7.1. Synthesis of the macroinitiator

A typical procedure for the synthesis of a macroinitiator is as follows (e.g. Table V-4, $PnBA_{15}$). A mixture of 0.0694 mol (10.0 mL) of the monomer nBA and 1.74 $.10^{-3}$ mol (0.362 mL) of PMDETA as the ligand was added to a reaction flask and was bubbled with $N_2$ for 1h to remove oxygen from the reaction mixture. After that, Cu(I)Br (1.74 $.10^{-3}$ mol, 0.249 g) was added and the reaction flask was placed in an oil bath at 20 °C. When the reaction mixture reached the desired reaction temperature, the polymerization was started by adding 3.47 $.10^{-3}$ mol (0.387 mL) of methyl 2-bromopropionate as the initiator. Samples were withdrawn periodically to monitor the monomer conversion (by $^1$H NMR) and the average molecular weight (by GPC). The reaction was ended by cooling the reaction mixture in liquid nitrogen. The resulting polymer was dissolved in THF and the diluted reaction mixture was passed over a column of neutral $Al_2O_3$ to remove the copper catalyst. After evaporating the excess solvent, the residual monomer was removed by vacuum

#### V.9.7.2. Synthesis of block copolymer with PEE(M)A segment

A typical block copolymerization procedure (e.g.Table V-5, entry 5) is as follows. The monomer EEA was passed through a small column of basic alumina to remove traces of residual acid. The $PnBA_{15}$ macroinitiator (1.0 g; 0.526 mmol) was dissolved in the monomer EEA (3.79 mL; 0.0263 mol). The mixture was degassed by bubbling with $N_2$ for 1 h. Cu(I)Br (0.0755 g; 0.526 mmol) was added and the flask was immersed in a water bath at 50 °C. The polymerization was started by adding ligand PMDETA (0.110 mL; 0.526 mmol). After termination in liquid nitrogen, the block copolymer was dissolved in THF, and passed through a column with neutral alumina to remove the copper catalyst. The solvent was evaporated and the monomer was removed under high vacuum.

### V.9.8. Block copolymers with PEE(M)A segments: combination with CROP of THF

A typical polymerization procedure for the synthesis of a PTHF-*b*-PEEA block copolymer is as follows (Table V-6, entry 1). The monomer EEA was passed through a small column of basic alumina to remove traces of residual acid. The PTHF macroinitiator[28] (1.0 g; 0.19 mmol) was dissolved in the monomer EEA (4.1 mL; 0.028 mol), and the mixture was degassed by bubbling with N2 for 1h. Cu(I)Br (0.0271 g; 0.189 mmol) was added under nitrogen atmosphere, and the reaction flask was immersed in a water bath thermostated at 50 °C. Polymerization was started by adding PMDETA (0.039 mL; 0.19 mmol). Samples were withdrawn periodically to monitor monomer conversion (by $^1$H-NMR) and molecular weight (by GPC). After termination in liquid nitrogen (150 min, 25 % conversion), block copolymers were dissolved in THF, and purified by elution through neutral alumina. Solvent was evaporated, and the residual monomer was removed under high vacuum. For thermolysis of the PTHF-*b*-PEEA block copolymer, the sample (typically 0.5 g) was spread out on a glass surface, and heated in an oven at 80 °C for 48 h.

### V.9.9. "Block-like" and random copolymers with PEE(M)A segments

In the case of sequential monomer addition, a homopolymerization was started (see §V.9.4), and a second monomer was added at the chosen time (for reaction conditions: see Table V-7). For random copolymers, the same procedure was followed as for the

homopolymers, except that the reaction mixture contained two monomers (reaction conditions: see Table V-7).

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# *Chapter VI*
# *Synthesis of PiBA-b-PAA block copolymers*

## Abstract

In this chapter, we report on the synthesis of well-defined amphiphilic poly(isobornyl acrylate-*b*-acrylic acid) (PiBA-*b*-PAA) block copolymers. Because PiBA polymers exhibit interesting physical characteristics, we report first a detailed study of the homopolymerization of iBA. Also PiBA containing block copolymers are synthesized, and we focus on the preparation of amphiphilic PAA-containing block copolymers. The precursor monomers 1-ethoxyethyl acrylate as well as tert-butyl acrylate have been used to synthesize the precursor polymers for the PiBA-*b*-PAA block copolymers. In addition, these PiBA-PAA block copolymers are investigated as pigment stabilizers for aqueous pigment dispersions. Preliminary results of this research are reported.

# VI
# Synthesis of PiBA-b-PAA block copolymers

## VI.1. Introduction

Poly(isobornyl acrylate) (PiBA) has some interesting physical properties, such as their high glass transition temperature ($T_g$) of about 100 °C (94 °C[1]), HB hardness (19.6 kg/mm at 20 °C) and refractive index (1.5061 at 20 °C).[2] In general, polyacrylates have a low $T_g$ but the bulky side group of isobornyl acrylate (Figure VI-1) is responsible for the high $T_g$, which is comparable to the one of poly(methyl methacrylate) ($T_g$ = 105 °C[1]) or polystyrene ($T_g$ = 100 °C[1]). Although PiBA polymers exhibit these specific characteristics, only a limited number of publications have been published concerning their synthesis. Earlier reports include brief descriptions of the controlled radical polymerization of PiBA containing (co)polymers by atom transfer radical polymerization (ATRP)[2-6]and nitroxide mediated polymerization (NMP)[7].

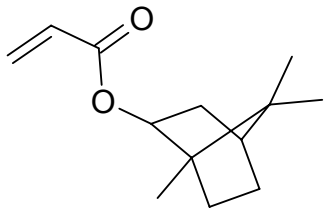


**Figure VI-1 Isobornyl acrylate.**

For the NMP of isobornyl acrylate (iBA)[7], it was found that the copolymerization of iBA with styrene shows a continuous decrease of the polymerization rate with increasing content of iBA. At iBA contents above 50 mol% hardly any polymerization was observed. Moreover, a controlled homopolymerization of iBA using a macroinitiator was not possible.

For the ATRP of iBA, one report is found concerning the synthesis of low molecular weight (theoretical degree of polymerization < 25) homopolymer of iBA.[2] It was reported that the kinetics are first order with respect to monomer concentration, and molecular weights can be controlled by the ratio of monomer to initiator. However, these conclusions were based on a single experiment. Also multiblock copolymers including PiBA containing segments were prepared by ATRP and evaluated as drug delivery matrices for the controlled release of paclitaxel from coronary stents.[8]

Another paper reports on the synthesis of a thermoplastic elastomer with polyisobutene (PIB) mid block and either polystyrene, poly(methyl acrylate), poly(methyl methacrylate) or PiBA hard blocks by using "living" carbocationic polymerization in combination with mechanism transformation to controlled radical polymerization.[3] More precisely, starting from $\alpha,\omega$-difunctional polyisobutene Cl-PIB-Cl capped with several units of styrene (St) synthesized by "living" carbocationic polymerization (thus Cl-St-PIB-St-Cl), a PiBA-*b*-PIB-*b*-PiBA triblock copolymer was prepared by ATRP of iBA. However, no details about kinetics or control over the polymerization of iBA were reported.

Further on, ATRP of iBA was also briefly described as a part of the synthesis of poly(methyl acrylate)-*b*-poly(isobornyl acrylate) (PMA-*b*-PiBA) star-block copolymers.[4-6] In this case, a hexafunctional PMA star polymer initiated by a hexa-functional cyclotriphosphazene was used as a macroinitiator for the ATRP of iBA. Again, apart from some gel permeation chromatography (GPC) curves, no details about control over the polymerization are given. In all these cases, iBA was chosen for the high $T_g$ of the corresponding polymer.

Generally, because of this high $T_g$, PiBA is particularly interesting as an alternative to polystyrene (PS) or poly(methyl methacrylate) (PMMA). However, the synthesis of PS or PMMA with a high end group functionality (> 90 %) is not straightforward (see Chapter V, §V.4)

Therefore, we report here a detailed study of the homopolymerization of iBA. Also block copolymerizations with a PiBA macroinitiator and other monomers are studied. Hereby we focus on the preparation of amphiphilic PAA-containing block copolymers, as they are of great for a wide range of applications. The precursor monomers 1-ethoxyethyl acrylate as well as tert-butyl acrylate have been used to synthesize the precursor polymers for the PiBA-*b*-PAA block copolymers.

A general overview of the performed reactions for the synthesis of a PiBA-*b*-PAA block copolymer using the EEA strategy is depicted in Figure VI-2.

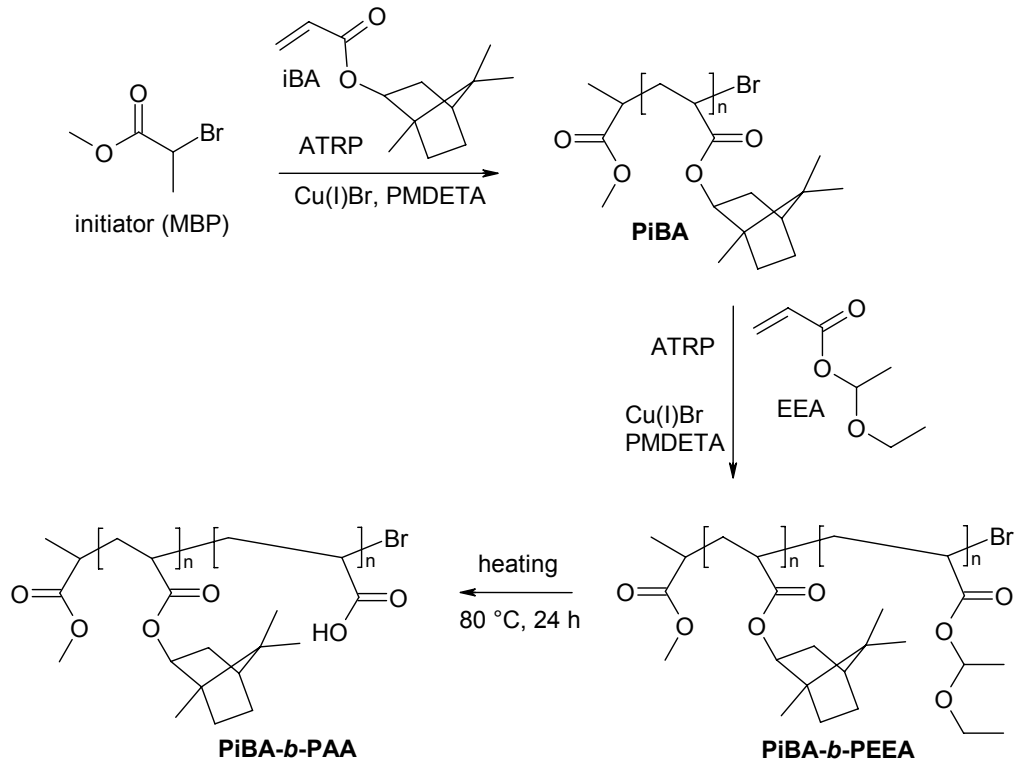


**Figure VI-2** **Schematic depiction for the synthesis of PiBA-*b*-PAA block copolymers using EEA as the protected acrylic acid monomer.**

## *VI.2. Homopolymerization of PiBA*

The first step of the preparation of a well-defined PiBA-*b*-PAA block copolymer consists in the synthesis of a well-defined PiBA macroinitiator. As none of the above mentioned publications report on a detailed kinetic study of the polymerization of iBA by ATRP, we have first studied the polymerization of iBA in detail. The reaction conditions and results are summarized in Table VI-1.

In a first set of experiments, the influence of the use of different solvents on the homopolymerization of iBA was investigated (Table VI-1, entry 1-9). For all homopolymerizations, methyl 2-bromopropionate (MBP) was used as the initiator, in combination with Cu(I)Br/PMDETA (*N,N,N′,N″,N″*-pentamethyldiethylenetriamine) as the catalyst system. When bulk polymerization was performed, a polymer with a rather high polydispersity ($M_w/M_n$ = 1.41) was obtained (Table VI-1, entry 1). With acetone as

solvent, a polymer with a lower polydispersity index (1.19) was obtained (Table VI-1, entry 2). However, the polymerization rate was quite slow, as a result of the applied polymerization temperature that is rather low because of the boiling point of acetone (56 °C). However, reasonable polymerization rates could be obtained by using an excess of Cu(I)Br (4 equivalents relative to initiator) (Table VI-1, entry 3). Anyhow, this approach is likely to be prevented as a high copper concentration is rather disadvantageous. Due to the high CuBr concentration and the absence of Cu(II)Br in the beginning of the reaction, the system tries to attain equilibrium on its own by radical termination, resulting in dead polymer chains and thus loss of end group functionality. In addition, a large excess of copper is to avoid because of its difficult removal.

**Table VI-1 Summary of the data and results of the synthesis of various PiBA homopolymers by ATRP.**

| Entry[a] | $[M]_0/[In]_0/[Cu]_0/[ligand]$[b] | solvent | Temp. (°C) | Time (min) | Conv.[c] (%) | $M_{n,exp}$[d] ($g.mol^{-1}$) | $M_w/M_n$ |
|---|---|---|---|---|---|---|---|
| 1 | 100/1/1/1 | none | 90 | 50 | 77.2 | 9900 | 1.41 |
| 2 | 75/1/1/1 | acetone (25 v%) | 50 | 1530 | 7.1 | 2100 | 1.19 |
| 3 | 75/1/4/4 | acetone (25 v%) | 50 | 250 | 65 | 8200 | 1.27 |
| 4 | 100/1/0.5/0.5 | toluene (50 v%) | 90 | 255 | - | 5800 | 1.38 |
| 5 | 100/1/0.5/0.75 | dioxane (25 v%) | 90 | 225 | - | 9200 | 1.37 |
| 6 | 100/1/0.5/0.75 | dioxane (25 v%) | 90 | 60 | 21 | 2500 | 1.41 |
| 7 | 100/1/0.5/0.75 | EtOAc (25 v%) | 77 | 60 | 27 | 3300 | 1.26 |
| 8 | 100/1/0.5/0.75 | EtOAc (25 v%) | 77 | 60 | 27 | 3700 | 1.31 |
| 9 | 100/1/0.5/0.75 | EtOAc (25 v%) | 77 | 45 | 19 | 2600 | 1.33 |
| 10 | 200/1/0.5/0.5 | EtOAc (25 v%) | 77 | 390 | 28 | 8300 | 1.25 |
| 11 | 200/1/0.5/0.5 | EtOAc (25 v%) | 77 | 215 | 24 | 7600 | 1.24 |
| 12 | 100/1/1.5/1.5 | EtOAc (33 v%) | 77 | 250 | 93 | 14500 | 1.16 |
| 13 | 100/1/1.5/1.5 | EtOAc (33 v%) | 77 | 150 | 78 | 10600 | 1.14 |
| 14[e] | 200/1/0.5/0.75 | EtOAc (33 v%) | 77 | 60 | 36 | 10600 | 1.17 |

[a.] All reactions were carried out using methyl 2-bromopropionate (MBP) as initiator, Cu(I)Br as catalyst and *N,N,N',N'',N''*- pentamethyldiethylenetriamine (PMDETA) as ligand. [b.] $[M]_0$, $[In]_0$, $[Cu]_0$ and [ligand] = initial concentration of monomer, initiator, copper catalyst and ligand respectively. [c.] Calculated from $^1$H NMR. [d.] Relative to polystyrene standards. [e.] reaction was carried out using dimethyl 2,6-dibromoheptanedioate as initiator.

Higher polymerization rates could also be obtained with a lower copper concentration (0.5 equivalent relative to initiator) in combination with a higher polymerization temperature, when a high-boiling solvent such as toluene is used (Table VI-1, entry 4). However, a polymer with a rather high polydispersity was obtained (1.38). The use of 1,4 dioxane did not significantly influence the polydispersity (Table VI-1, entries 5-6). Finally, ethyl acetate (EtOAc) was found to be a better solvent than toluene or 1,4-dioxane, as polydispersities were found to be as low as 1.14 for conversions up to about 90 % (Table VI-1, entries 7-13). The molecular weight of the polymers could be varied with conservation of good control by increasing the monomer to initiator ($[M]_0/[In]_0$) ratio (Table VI-1, entry 11) or increasing the copper concentration from 0.5 to 1.5 equivalents, which enables a higher monomer conversion (Table VI-1, entry 12-13). Also a macroinitiator with two initiator groups was synthesized using dimethyl 2,6-dibromoheptanedioate as a difunctional initiator (Table VI-1, entry 14).

The controlled character of the polymerization reaction is proved by the linear increase of the number average molecular weight ($M_n$) as a function of conversion, while the polydispersity (PDI) remains narrow throughout the polymerization reaction (see Figure VI-3, left). Also the first order kinetic plot shows a linear behaviour, indicating a controlled reaction (Figure VI-3, right). However, for entry 10 of Table VI-1, the first order kinetic plot shows a small deviation at longer reaction time.

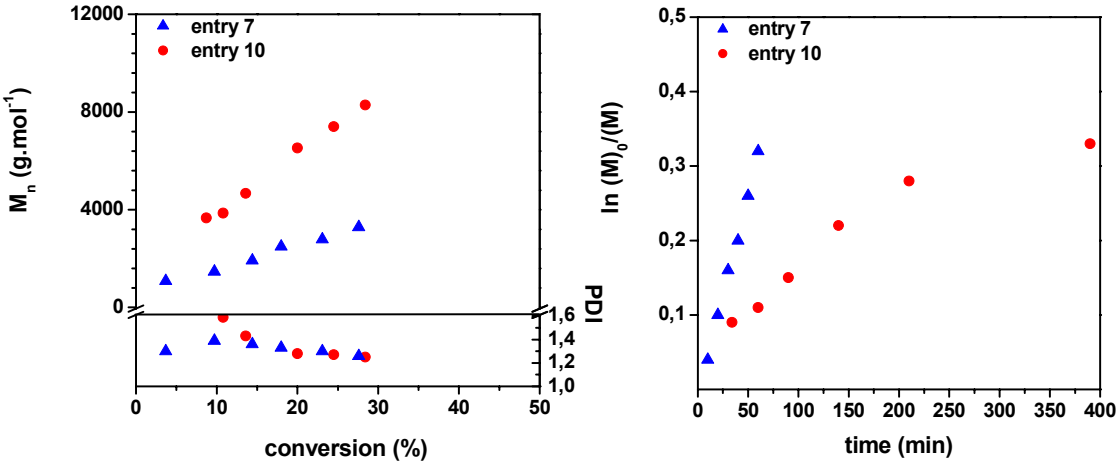


**Figure VI-3** **ATRP of iBA. (Left) increase of $M_n$ and evolution of PDI as a function of conversion, (Right) first order kinetic plot.**

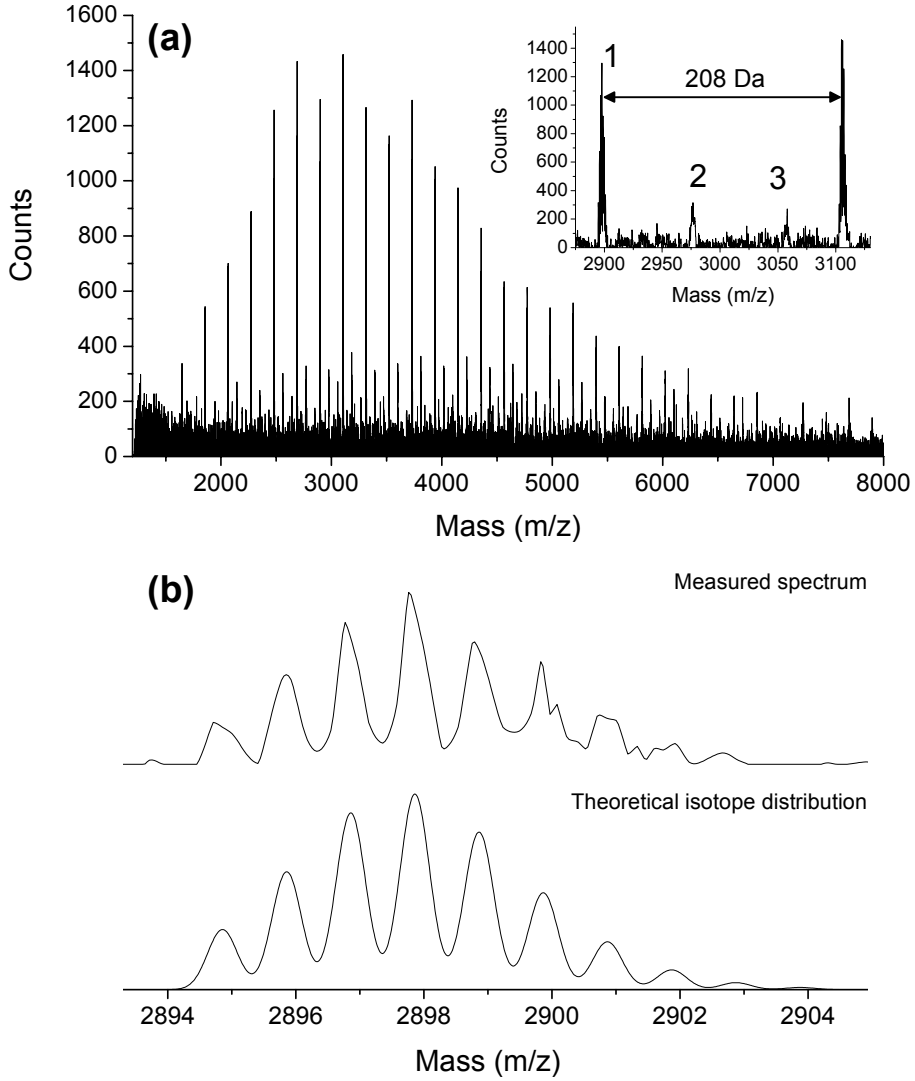


**Figure VI-4** **MALDI-TOF MS spectrum of PiBA (Table VI-1, entry 8). (a) Complete spectrum and inset of 2830-3150 Da. (b) Comparison of measured isotope distribution (top) and theoretical isotope distribution of $C_4H_7O_2(C_{13}H_{20}O_2)_{13}BrNa$ (bottom).**

Matrix assisted laser desorption/ionization time of flight mass spectroscopy (MALDI-TOF MS) was carried out onto one of the purified polymers (Table VI-1, entry 8) (see Figure VI-4). The mass difference between two successive, analogous signals is 208 Da, which is equal to the molar mass of the repeating unit in PiBA. Upon comparison between the experimental and theoretical distributions (Figure VI-4, b), the main series (1) can be attributed to the sodium adduct of PiBA initiated by MBP with a bromine end group. Besides this main series, two unknown minor series (2 and 3) are also observed. The recombined polymer with an initiator fragment at each end (calculated m/z = 2902.98 Da) nor a series attributed to disproportionation (calculated m/z = 3023.08 Da) could be

detected. Nevertheless, MALDI-TOF analysis confirms the controlled character of the ATRP reaction.

## *VI.3. Synthesis of PiBA-b-PAA block copolymers*

### VI.3.1. Synthesis of PiBA-*b*-PtBA and PiBA-*b*-PAA

Some of the above synthesized PiBA polymers were used as a macroinitiator to synthesize amphiphilic PiBA-*b*-PAA block copolymers. *Tert*-butyl acrylate (tBA) and 1-ethoxyethyl acrylate (EEA) were polymerized as the second monomer and both have been evaluated as precursor monomers for the preparation of the PAA segment. Transformation of the PEEA segment to PAA was done by a heating step, while the conversion of the PtBA segment to PAA was done by hydrolysis[9, 10].

**Table VI-2 Summary of the reaction conditions and results for the synthesis of PiBA containing block copolymers by ATRP.**

| Entry[a] | In.[b] | $[M]_0/[In.]_0/[Cu]_0/[ligand]$[c] | Solvent | Temp. (°C) | Time (min) | Conv.[d] (%) | $M_{n,exp}$[e] ($g.mol^{-1}$) | $M_w/M_n$ | Composition[f] |
|---|---|---|---|---|---|---|---|---|---|
| 15 | 13 | 260/1/3/4.5 | 50 v% EtOAc | 75 | 540 | 18 | 12300 | 1.18 | $PiBA_{73}$-*b*-$PtBA_{38}$ |
| 16 | 13 | 300/1/3/4.5 | 50 v% BuOAc | 90 | 430 | 64 | 16600 | 1.23 | $PiBA_{73}$-*b*-$PtBA_{98}$ |
| 17 | 8 | 200/1/3/4.5 | 25v% EtOAc | 50 | 270 | 36 | 13800 | 1.15 | $PiBA_{25}$-*b*-$PEEA_{70}$ |
| 18 | 10 | 200/1/3/4.5 | - | 50 | 250 | 19 | 13700 | 1.21 | $PiBA_{55}$-*b*-$PEEA_{38}$ |
| 19 | 10 | 200/1/3/4.5 | - | 60 | 240 | 37 | 17700 | 1.26 | $PiBA_{55}$-*b*-$PEEA_{75}$ |
| 20 | 11 | 200/1/3/4.5 | - | 60 | 160 | 25 | 16100 | 1.35 | $PiBA_{51}$-*b*-$PEEA_{56}$ |
| 21 | 11 | 200/1/3/4.5 | - | 60 | 80 | 14 | 11300 | 1.32 | $PiBA_{51}$-*b*-$PEEA_{30}$ |
| 22 | 9 | 150/1/3/4.5 | - | 70 | 245 | 45 | 14100 | 1.22 | $PiBA_{17}$-*b*-$PEEA_{72}$ |
| 23 | 14 | 300/1/3/4.5 | - | 70 | 395 | 19 | 15100 | 1.18 | $PEEA_{25}$-*b*-$PiBA_{72}$--*b*-$PEEA_{25}$ |

[a.] All reactions were carried out using Cu(I)Br as catalyst and *N,N,N',N'',N''*- pentamethyldiethylenetriamine (PMDETA) as ligand. [b.] See Table VI-1. [c.] $[M]_0$, $[In.]_0$, $[Cu]_0$ and [ligand] = initial concentration of monomer, macroinitiator, copper catalyst and ligand respectively. [d.] Calculated from $^1$H NMR. [e.] Relative to polystyrene standards.[f.] Determined from $^1$H NMR.

A general overview of the performed reactions for the synthesis of a PiBA-*b*-PAA block copolymer using the EEA strategy is depicted in Figure VI-2. Table VI-2 gives an overview of the performed block copolymerizations.

First, a PiBA macroinitiator (Table VI-1, entry 13) was used to initiate the polymerization of tBuA (Table VI-2, entry 15-16). Cu(I)Br was used as catalyst with PMDETA as ligand. For all reactions, three equivalents of Cu catalyst relative to the macroinitiator concentration were used in order to reach a sufficiently fast reaction speed. As the conversion of entry 15 (Table VI-2) reached only 18%, the polymerization temperature was raised to 90 °C for entry 16 (Table VI-2). In order to make this possible the solvent was changed from EtOAc to BuOAc, which has a higher boiling point. This resulted in a conversion of 64%. All block copolymerizations with tBA resulted in the formation of block copolymers with narrow polydispersities (≤ 1.23).

Besides tBuA, also EEA was polymerized as the second block (Table VI-2, entry 17-23). Also in this case, Cu(I)Br in combination with PMDETA was used as the catalyst system. Using macroinitiators with different molecular weights and different reaction conditions for the polymerization of the second block (e.g. variation of polymerization temperature and time, and the use of solvent), a variety of PiBA-*b*-PEEA block copolymers was prepared with different ratio of PiBA/PEEA content and different lengths of the PiBA and PEEA segment. In all cases, well-defined PiBA-*b*-PEEA block copolymers with a controlled molecular weight and a narrow molecular weight distribution were obtained. Using a difunctional macroinitiator (with two initiator groups), also a triblock copolymer PEEA-*b*-PiBA-*b*-PEEA was prepared (Table VI-2, entry 23).

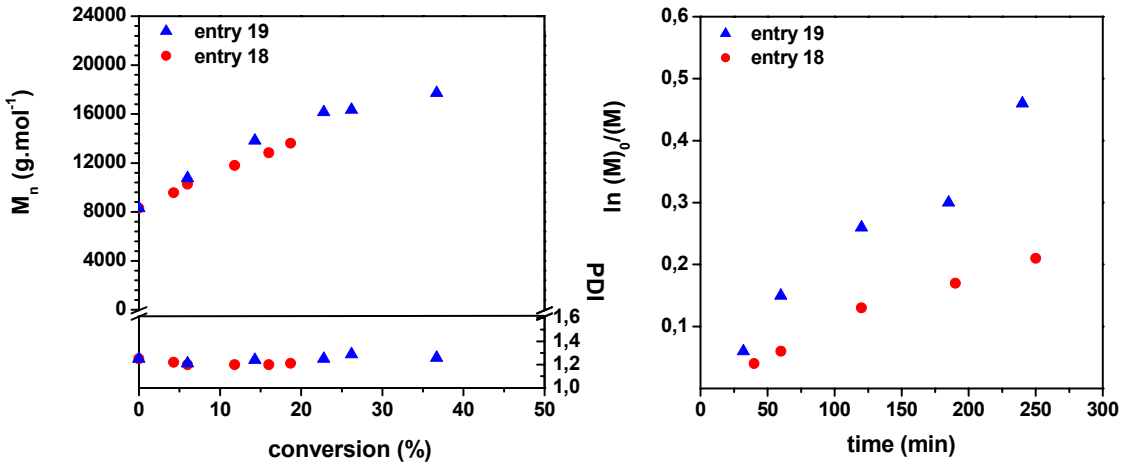


**Figure VI-5** **ATRP of EEA starting from a PiBA macroinitiator. (Left) increase of $M_n$ and evolution of PDI as a function of conversion. (Right) first order kinetic plot.**

A kinetic analysis of the block copolymerization shows the controlled behaviour of the polymerization reaction. The increase of the molecular weight as a function of conversion shows a linear behaviour, while polydispersity decreases during the polymerization reaction (see Figure VI-5, left). Also the first order kinetic plot shows a linear behaviour. (see Figure VI-5, right). In GPC analysis, almost no unreacted macroinitiator could be observed (Figure VI-6, see solid and dotted line). This means that a pure block copolymer is obtained. Moreover, it proves that the polymerization of iBA (synthesis of the PiBA macroinitiator) under the used polymerization conditions occurs with only minimal loss of bromine end group.

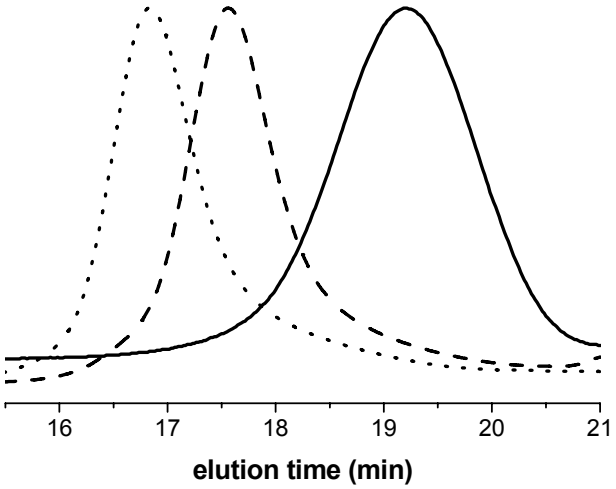


**Figure VI-6** **GPC analysis of $PiBA_{17}$ macroinitiator (solid line) [entry 9, Table VI-1] and the corresponding $PiBA_{17}$-*b*-$PEEA_{72}$ block copolymer (dotted line) [entry 22, Table VI-2]. The dashed line represents GPC analysis of the deprotected block copolymer, after methylation[11].**

## VI.3.2. Deprotection of precursor polymers to PiBA-*b*-PAA

### VI.3.2.1. Hydrolysis of PiBA-*b*-PtBA to PiBA-*b*-PAA

In order to create amphiphilic block copolymers starting from the above synthesized PiBA-*b*-PtBA, the tert-butyl ester groups have to be hydrolysed. Trifluoroacetic acid (TFA) in dichloromethane has been used for this purpose, following a well-established procedure.[9, 10] The hydrolysis of tert-butyl ester groups of a PtBA homopolymer by TFA is proved by FT-IR analysis (see Figure VI-7, a). After the hydrolysis reaction (dotted line),

the acid functionality is clearly visible as a broad absorption from 2300 to 3800 $cm^{-1}$. Moreover, an absorption at 1710 $cm^{-1}$ appears, due to the carbonyl vibration of the carboxylic acid side chains. TFA is considered to be a selective reagent for the hydrolysis of tert-butyl ester groups in the presence of other ester groups. Nevertheless, the stability of the isobornyl ester group under these reaction conditions was checked. Figure VI-7, b shows the FT-IR spectrum of PiBA homopolymer before and after hydrolysis with TFA (solid and dotted line, respectively). The spectrum before reaction is characterized by the strong carbonyl ester vibration at 1725 $cm^{-1}$. However, after reaction with TFA, a broad absorption from 2300 to 3800 $cm^{-1}$ appears together with an absorption at 1710 $cm^{-1}$. These absorptions arise from the formation of carboxylic acid moieties.

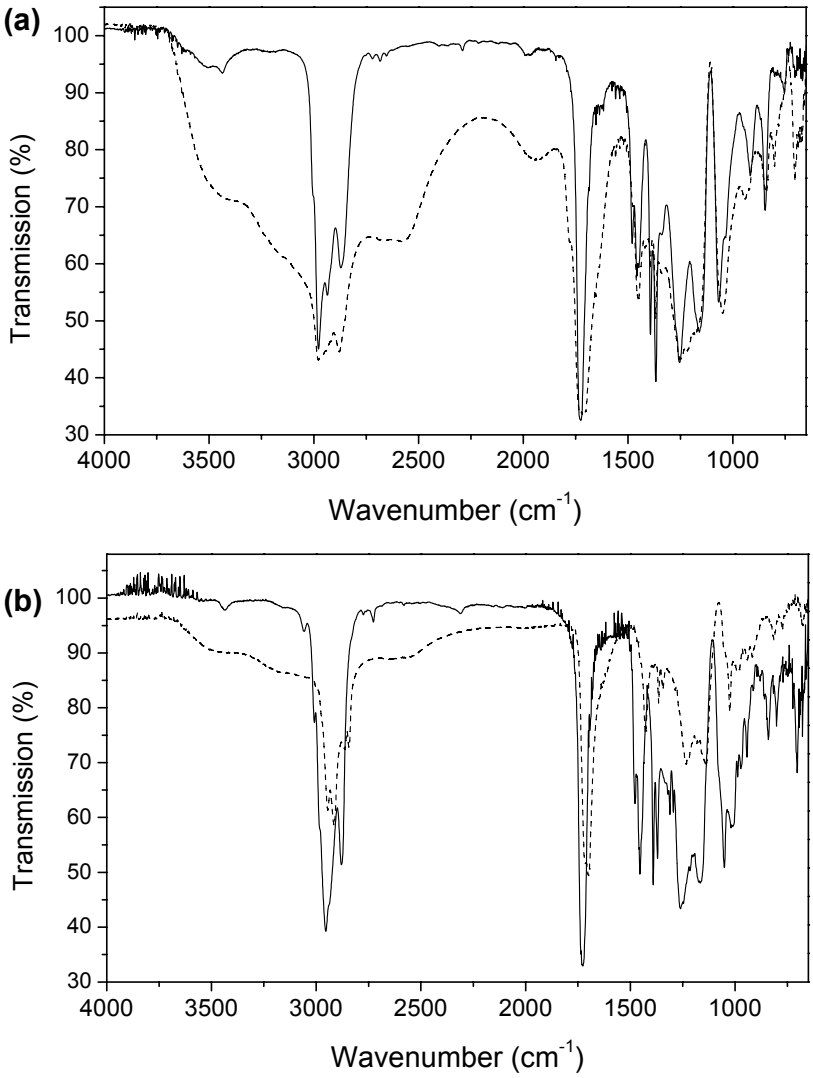


**Figure VI-7** **FT-IR spectra of (a) PtBA (—) and PtBA after hydrolysis using trifluoroacetic acid (---); (b) PiBA (—) and PiBA after hydrolysis using trifluoroacetic acid (---).**

The hydrolysis of PiBA was also confirmed by $^{1}$H-NMR analysis (see Figure VI-8). The ratio of the integrations of a signal of the polymer backbone (signal **a**) and the signal of the side chain (signal **b**) should be 1/1. The increased ratio of integrations of the signals of polymer backbone and side chains after reaction with TFA indicates that part of the side chains disappeared due to hydrolysis. Furthermore, the signal of proton **b** is shifted to a higher ppm value and a broad signal at 3.4 ppm is observed.

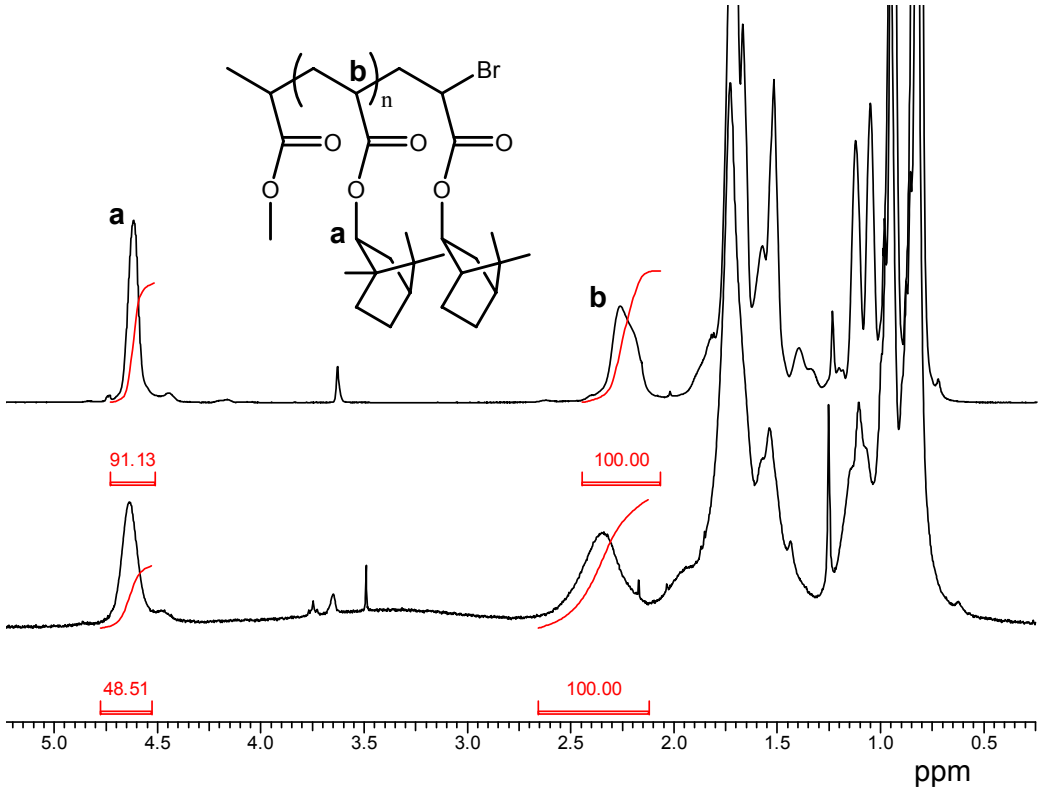


**Figure VI-8** **$^{1}$H NMR spectra of PiBA (top) and PiBA after hydrolysis using trifluoroacetic acid (bottom). (entry 13, Table VI-1) ($CDCl_3$)**

The above described observations show that the use of the tert-butyl protecting group is not a straightforward approach to synthesize amphiphilic PiBA-*b*-PAA block copolymers, because of hydrolysis of the PiBA segment. Although we expect that the hydrolysis of PiBA might be prevented by a further optimization of the experimental conditions for the hydrolysis procedure, EEA was used as precursor monomer to synthesize the PAA segment.[12-14] In this case, deprotection is done by heating instead of hydrolysis (see §VI.3.2.2).

### VI.3.2.2. Deprotection of PiBA-*b*-PEEA to PiBA-*b*-PAA by a heating step

After synthesis of the PiBA-*b*-PEEA block copolymers, they are converted to the corresponding PiBA-*b*-PAA block copolymers by a heating step (see also Chapter V, §V.4). All polymers were heated in an oven at 80 °C for 24 hours in order to avoid anhydride formation. A TGA analysis of sample $PiBA_{51}$-*b*-$PEEA_{56}$ before and after the heating step is shown in Figure VI-9, and reveals a weight decrease of 21 % at 150 °C (theoretical weight loss: 21.6 %). The TGA analysis of the deprotected polymer does not show any weight loss at 150 °C, confirming that deprotection was complete. Moreover, TGA analysis of the PiBA macroinitiator (Figure VI-9, dashed line) clearly shows that deprotection to the amphiphilic PiBA-*b*-PAA polymer can be done without danger for degradation of the PiBA segment. The absence of weight loss has also been demonstrated during an isothermal TGA experiment at 95 °C for 24 hours. No weight loss was observed (0.2 %). These experiments confirm that the PEEA segment can be selectively converted to PAA.

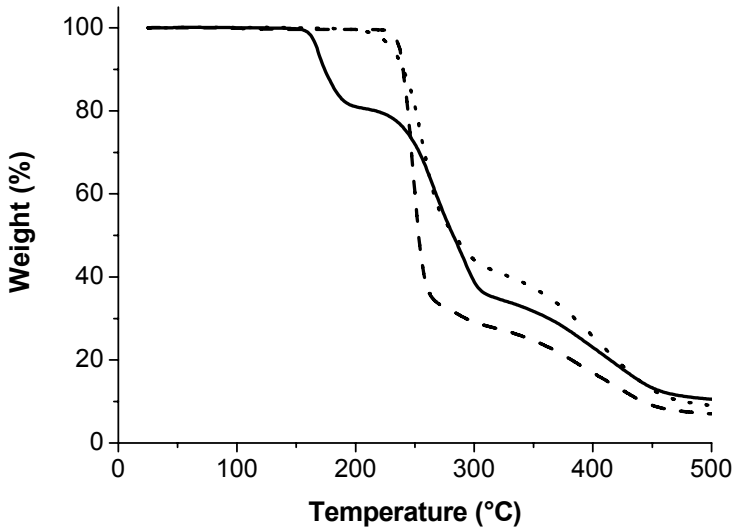


**Figure VI-9** **TGA analysis of $PiBA_{51}$-*b*-$PEEA_{56}$ (before deprotection, solid line), PiBA macroinitiator (dashed line) and $PiBA_{51}$-*b*-$PAA_{56}$ (after deprotection by heating at 80 °C for 24 h, dotted line) [entry 20, Table VI-2].**

$^1$H NMR also confirmed total conversion of PiBA-*b*-PEEA to PiBA-*b*-PAA, as the characteristic polymer peaks of PEEA have disappeared and a signal arising from carboxylic acid functionalities (at 12.4 ppm, in DMSO-$d_6$) is observed.

Water drops on a polymer surface show the influence of the polymer composition (see Figure VI-10). Two PiBA-*b*-PAA block copolymers were compared with a PiBA and PAA homopolymer. The contact angle of the water drops on the polymer surface clearly shows a decrease with increasing PAA content of the polymer surface.

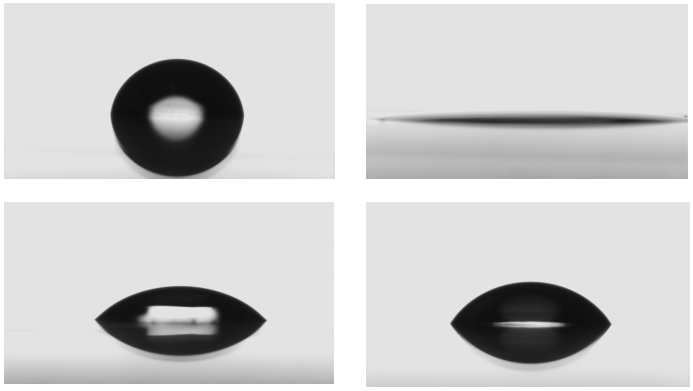

**Figure VI-10** **Water drops on a surface of $PiBA_{51}$ (top left, entry 11, Table VI-1), $PAA_{28}$ (top right, commercial sample), $PiBA_{51}$-*b*-$PAA_{56}$ (bottom left, entry 20, Table VI-2) and $PiBA_{51}$-*b*-$PAA_{30}$ (bottom right, entry 21, Table VI-2). Drop age = 120 seconds.**

To verify if deprotection of the PEEA segment to the PAA segment by a heating step does not lead to broadening of the molecular weight distribution, the carboxylic acid groups of a PiBA-*b*-PAA sample were methylated with trimethylsilyldiazomethane[11] and a GPC analysis was performed. GPC analysis revealed a monomodal and narrow molecular weight distribution, which shows no distortion in comparison with the corresponding PiBA-*b*-PEEA sample (see Figure VI-6, compare dotted and dashed line).

In addition, the transition of PiBA-*b*-PEEA to PiBA-*b*-PAA was also identified using atomic force microscopy (AFM). PiBA-*b*-PEEA block copolymers show a phase separated morphology because of the different properties of the polymer segments. According to the relative composition of the block copolymers, different morphologies can be observed. For the simplest and most extensively studied coil-coil diblock copolymers, the molecular weight, volume fraction of the component, and the degree of segment incompatibility as

expressed by the Flory-Huggins parameter $\chi$ are the three independent parameters used to determine thermostable morphologies[15, 16]. As shown in Figure VI-11, uniform-sized spheres, cylinders, and lamellae, as well as complex bicontinuous nanostructures, are theoretically predicted and experimentally observed by varying these parameters.[15-19]

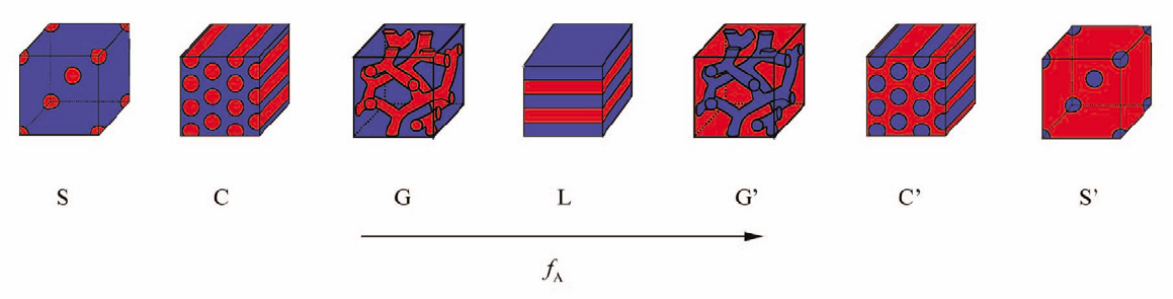


**Figure VI-11** **Prediction of the thermodynamic equilibrium phase structures for conformationally symmetric diblock copolymers. Phases are labelled as: L (lamellar), C (hexagonal cylinders), G (bicontinuous cubic), S (body-centered cubic spheres). $f_A$ is the volume fraction.[19]**

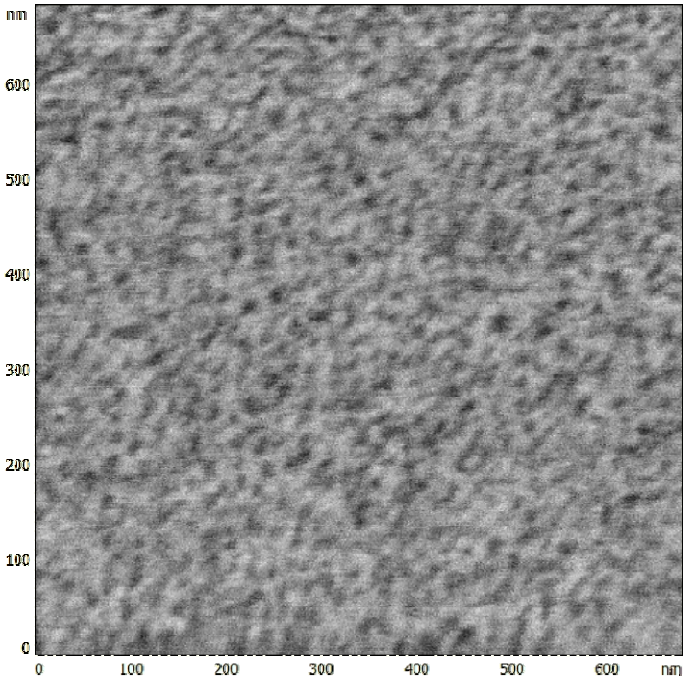


**Figure VI-12** **AFM phase image (tapping mode) of $PiBA_{55}$-*b*-$PEEA_{75}$ block copolymer at room temperature. (entry 19, Table VI-2)**

When the PiBA-*b*-PEEA polymer is subjected to heating and thus deprotection occurs to PiBA-*b*-PAA, it is expected that the phase contrast will change as PAA is highly polar. Figure VI-12 shows the AFM phase image of a $PiBA_{55}$-*b*-$PEEA_{75}$ block copolymer at room temperature. The phase image shows phase separation, and a cylindrical pattern can be observed.

To investigate the change in phase morphology that is expected to occur when the PiBA-*b*-PEEA is heated (so that deprotection to PiBA-*b*-PAA occurs), the PiBA-*b*-PEEA was analyzed by an AFM apparatus equipped with a heatable sample stage. First, the sample stage of the AFM was heated to 120 °C. Then, the Si wafer with the PiBA-*b*-PEEA sample was fitted on the sample stage and the AFM experiment was started (time = 0 min, see Figure VI-13). Figure VI-13 shows two AFM phase images that were obtained by scanning the same area successively, the first image is displayed at the bottom of the figure and the second one on top (note that the area is scanned from the bottom to the top; it takes 5 minutes to complete the AFM image). At the bottom of the AFM image, a similar cylindrical pattern is observed as the one that was observed in the image that was obtained at room temperature (see Figure VI-12). As the image is being further recorded, the phase contrast becomes more clear (see middle area of Figure VI-13). This is the result of 2 factors: first, the PEEA segment becomes more and more deprotected; secondly, the ability of the chains to phase separate is increased as they have become more mobile because the temperature is now above the glass transition temperatures ($T_g$) of both polymer segments. The area in the middle of Figure VI-13 shows the cylindrical pattern, with the cylinders parallel to the air interface as a result of the increased mobility. The bottom of the second image (= scan of the same area) shows about the same pattern as the top of the first one, and the pattern is further changing as the image is further being recorded. The observations are clearly time related. The top of the second image shows again changes, and the phase contrast is gradually decreasing.

These changes are attributed to the fact that the chains are now highly flexible ($T > T_g$) and the apolar segments are orienting themselves towards the air interface (which is apolar). As a result, the PAA is located more in the inner area of the polymer film. When the sample is allowed to cool down to 30 °C and the applied conditions are changed from ‘soft’ tapping to ‘hard’ tapping, the cylindrical pattern becomes again visible: the AFM tip is now able to get through the PiBA-rich upper layer (Figure VI-15).

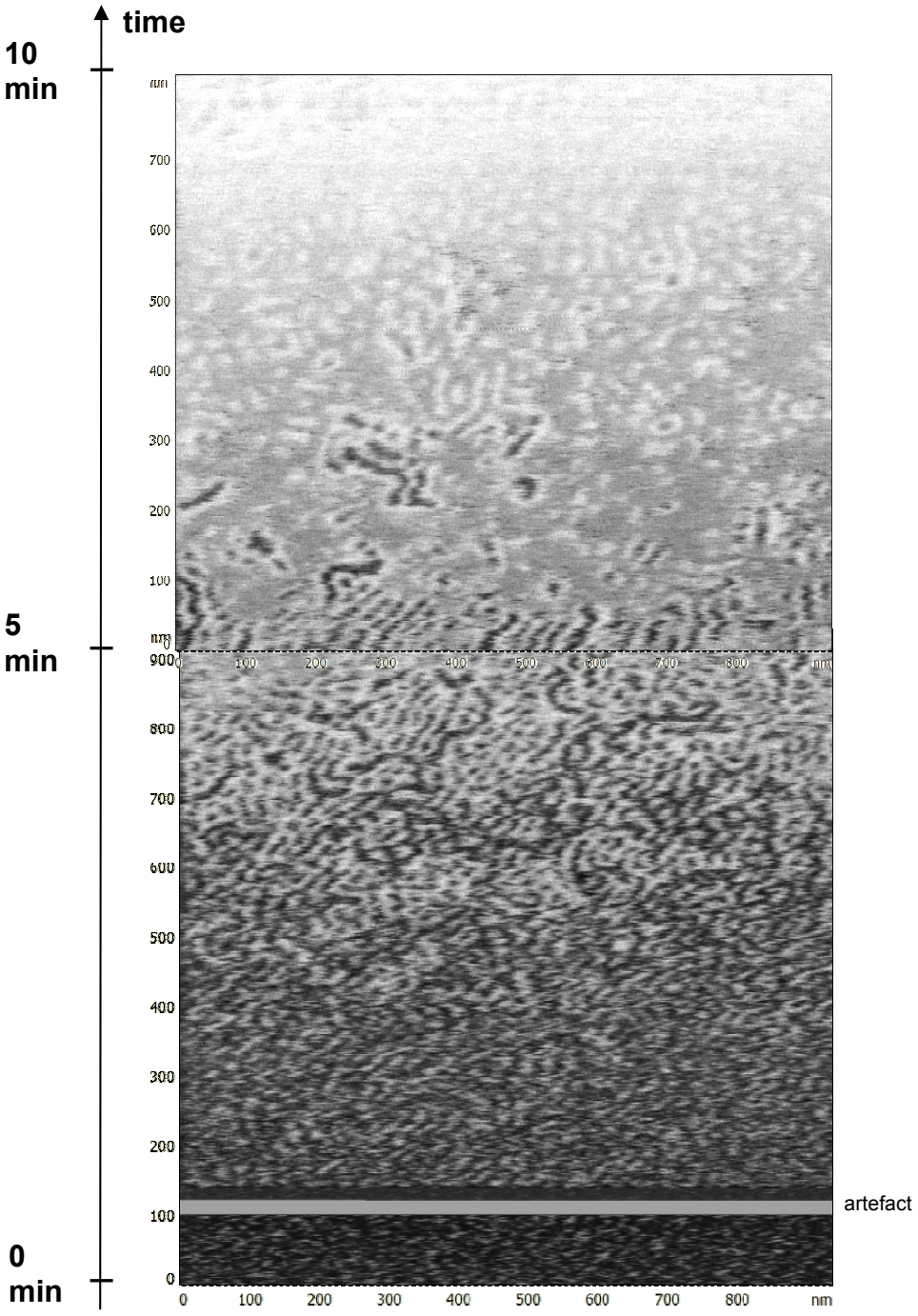


**Figure VI-13** **2 consecutive AFM phase images (tapping mode) of $PiBA_{55}$-*b*-$PEEA_{75}$ block copolymer (same scan area) at 120 °C. (entry 19, Table VI-2)**

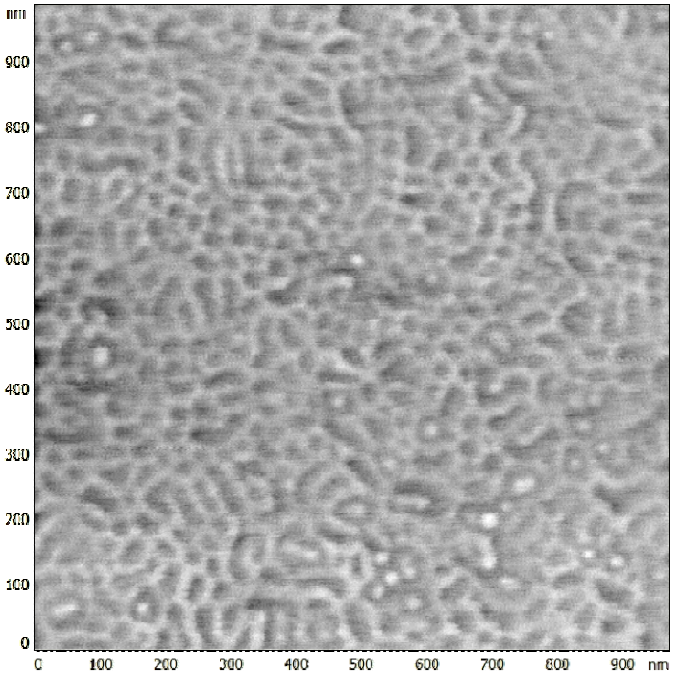


**Figure VI-15** **AFM phase image (tapping mode) of $PiBA_{55}$-*b*-$PAA_{75}$ block copolymer (same scan area) after cooling to 30 °C. (entry 19, Table VI-2)**

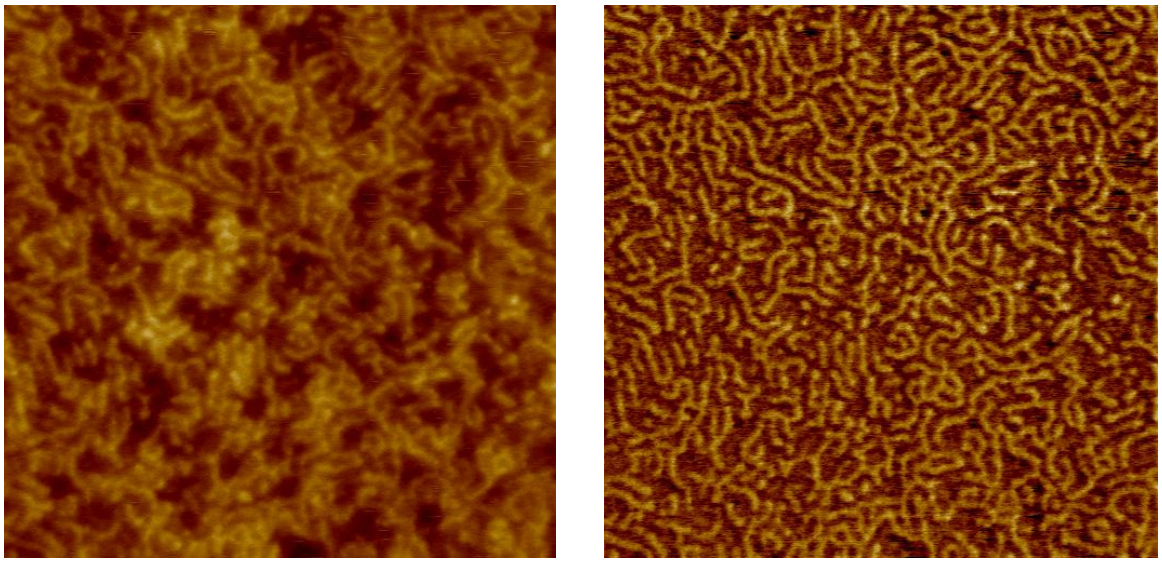


**Figure VI-14** **AFM images (1x1 µm; tapping mode) of $PiBA_{55}$-*b*-$PAA_{75}$ block copolymer obtained through deprotection of $PiBA_{55}$-*b*-$PEEA_{75}$ and annealing at 80 °C for 48 hours. (entry 19, Table VI-2)**

In addition to the above described experiments where the in situ deprotection of the PiBA-*b*-PEEA block copolymer was investigated, a PiBA-*b*-PEEA sample was put in an

oven at 80 °C for 48 hours for deprotection and annealing, after which it was analyzed by AFM. After the annealing process, the AFM image shows a cylindrical pattern, of which the cylinders are oriented parallel to the surface (see Figure VI-14, height and phase image).

## *VI.4. PiBA-PAA block copolymers as pigment stabilizing polymer structures*

In the previous parts of this chapter, the synthesis of various PiBA-*b*-PAA block copolymers was described. In this part, the use of PiBA-*b*-PAA block copolymers as pigment stabilizers is described. Preliminary results of this research are reported below.

### VI.4.1. Introduction

Pigments are powders consisting of agglomerates of individual pigment particles with a typical diameter of 20-300 nm.[20] In order to obtain a better storage and color stability, they have to be dispersed and stabilized as separate particles. Generally, the dispersion process for aqeous dispersion consists of three steps. First, the dispersant (in our case a block copolymer) is dissolved in an organic solvent together with the pigment (if the pigment is hydrophobic), and the solution is added to water. In a second step, agglomerates are broken down to separate particles by mechanical (high speed) stirring. After evaporation of the solvent, the pigment particles are stabilized by the dispersant which adsorbs at the pigment surface. For a lot of applications (e. g. paints), it is important that the pigment particles remain in the dispersed state during the production process, storage, use and drying of the paints.

In recent years, aqueous colloidal dispersions of pigments have been of increasing interest from both scientific and practical points of view. In order to achieve a good stabilization in aqueous pigment dispersions, many formulations were proposed.[21-24] In most cases, these are multicomponent formulations and contain water soluble polymers.[25] The stabilization mechanism is still not completely clear, but the best stabilization effects are achieved with amphiphilic copolymers. For stabilization of hydrophobic pigments, the hydrophobic polymer segments are adsorbed at the particle surface, while hydrophilic segments float free in the aqueous dispersion medium. In the case of hydrophilic pigments, the hydrophilic polymer segments adsorb at the pigment particles.

According to the chemical nature of the block copolymer, two stabilization mechanisms can be distinguished. The first one makes use of steric stabilization. The polymer chains surrounding the pigment particles prevent the particles to agglomerate. The second stabilization method makes use of ionic stabilization. One polymer segment adsorbs at the pigment particle, while the other polymer segment, which contains ionic groups, is floating in the water. In this way, the pigment particles are surrounded by a charged coating, and thus two pigment particles are prevented to approach because of electrostatic repulsion.

Eisenbach *et al.* have studied block and graft copolymers composed of acrylic acid, styrene and isobutene as stabilizers of $TiO_2$[26] and 'carbon black' dispersions[27]. Mühlebach applied controlled radical polymerization for the preparation of acryl based dispersants. The temperature dependant colloidal stabilization of copper phtalocyanine (CuPc) and carbon black by different poly(methyl vinyl ether) and poly(isobutyl vinyl ether) containing polymer structures was recently reported by Zubov and Du Prez *et al.*[23]

### VI.4.2. Influence of the polymer composition for pigment stabilization

In a collaboration with the research group of Prof. Zubov (Lomonosov Moscow State Academy of Fine Chemical Technology, Russia) and Prof. Eisenbach (University of Stuttgart, Germany), the pigment stabilizing properties of various PiBA and PAA containing copolymer structures (homopolymers, block copolymers, "blocky gradient" copolymers as well as random copolymers) are currently being investigated. The final aim of this research is the comparison of the pigment stabilizing properties of block copolymers on one hand and "blocky gradient" copolymers on the other hand. This research is part of the Ph.D. thesis of Bart Dervaux.[28] In this chapter, preliminary results about pigment stabilization experiments of CuPc and $TiO_2$ by PiBA-*b*-PAA block copolymers are reported in order to show the applicability of the novel structures. Details on the physical background of the observed phenomena will not be discussed. Block copolymers with different ratios of PiBA and PAA, and different composition (diblock and triblock copolymers, respectively) were evaluated as stabilizers of aqueous dispersions of hydrophilic $TiO_2$ and hydrophobic CuPc, two well-known pigments.

For example, the pigment particles in aqueous dispersions of hydrophobic CuPc are, without treatment with polymers, not wetted and as a result the pigment particles they float on the water surface because of their hydrophobic character. Mechanical stirring and ultrasonic treatment do not change this situation. A uniform dispersion is only obtained in the presence of a dispersant, in this case PiBA and/or PAA containing copolymers. After a while, sedimentation of the pigments is observed.

This sedimentation behaviour was used to evaluate the pigment stabilizing properties of a series of polymers: PiBA and PAA homopolymers, and various PiBA-*b*-PAA block copolymers. As data reported in literature[23, 25] showed that ultrasonic treatment of aqueous dispersions of pigments in the presence of polymeric stabilizers leads to a significant enhancement of the stability of these dispersions, the stability of the aqueous dispersions was examined with and without ultrasonic treatment.

**Table VI-3 Dispersion stability of $TiO_2$ and CuPc aqueous dispersions stabilized by various PiBA and/or PAA containing (block) (co)polymers.**

| Polymer | Dispersion stability (half-time of the sedimentation, days) | | | |
|---|---|---|---|---|
| | $TiO_2$ dispersion | | CuPc dispersion | |
| | Without ultrasonic treatment | After ultrasonic treatment | Without ultrasonic treatment | After ultrasonic treatment |
| $PiBA_{72}$[a] | 0,2 | 4 | 3 | 10 |
| $PAA_{28}$[b] | 2 | 10 | 0,3 | 2 |
| $PiBA_{51}$-*b*-$PAA_{56}$[c] | 2 | 14 | 4 | 20 |
| $PiBA_{51}$-*b*-$PAA_{30}$[c] | 0,1 | 1 | 5 | 45 |
| $PiBA_{17}$-*b*- $PAA_{72}$[c] | 3 | 30 | 0,2 | 5 |
| $PAA_{25}$-*b*-$PiBA_{72}$-*b*-$PAA_{25}$[c] | 0,3 | 7 | 3 | 14 |

[a.] see entry 15, Table VI-1. [b.] commercial sample, obtained from Aldrich. [c.] see Table VI-2 for reaction conditions.

The colloidal stability of the aqueous dispersions was monitored by sedimentation measurements of 1 % dispersions of CuPc and $TiO_2$. The relative volume of the dispersion

is measured as a function of time. An important value is the 'half-time of sedimentation', which is the time needed for sedimentation of 50 volume%. The results of the colloidal stability of $TiO_2$ and CuPc aqueous dispersions in the presence of the above mentioned PiBA and/or PAA containing polymer structures are summarized in Table VI-3. All employed block copolymers allow to obtain pigment dispersions in the absence as well as in the presence of ultrasonic treatment.

The comparison of the sedimentation half times of the non-ultrasonic-treated and treated systems (see Table VI-3) clearly shows that, irrespective of the constitution of the block copolymer, the ultrasonification substantially improves the dispersion stability as reflected from the comparison of the sedimentation half times of the non-treated and treated systems. The data also reveal that there is an optimal copolymer structure with regard to the block length ratio, which is in accordance with previously discussed constitutional effects.[23] There is a distinct effect of the pigment surface nature on the polymer structure acting as the best stabilizer. For dispersions of hydrophobic CuPc pigment, $PiBA_{51}$-*b*-$PAA_{30}$ with a ratio PiBA/PAA of ± 2 revealed the best result. The PiBA adsorbs to the CuPc particles, while the ionic PAA segment floats in the aqueous medium, where it provides ionic stabilization (see Figure VI-16). For dispersions of hydrophilic $TiO_2$ pigment, $PiBA_{17}$-*b*-$PAA_{72}$ with a long hydrophilic PAA block showed good stabilization. In this case, PAA absorbs to the surface of the pigment particles, while the PiBA segment provides steric stabilization (Figure VI-16).

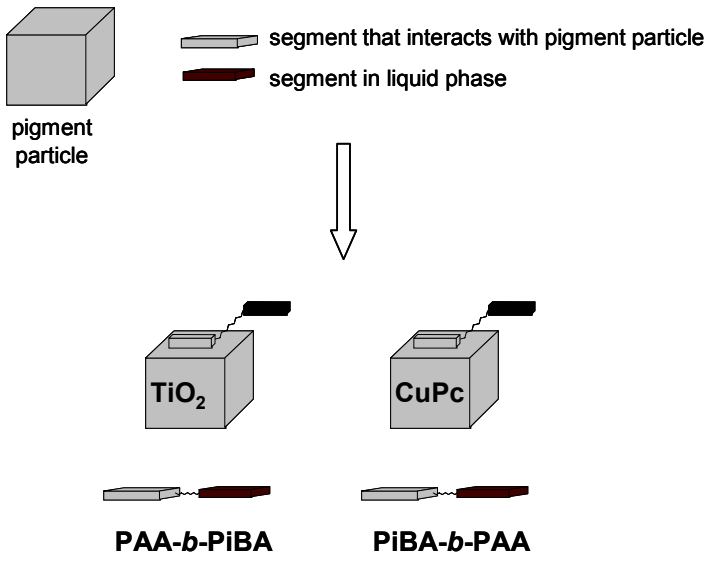


**Figure VI-16** **Schematic depiction of the adsorption of amphiphilic PiBA-*b*-PAA block copolymers at hydrophilic $TiO_2$ and hydrophilic CuPC pigment particles.**

Currently, experiments are carried out to further investigate the effect of the ultrasonic treatment as the effect on the pigment-polymer interaction and the exact nature of the adsorption layers are still obscure.

## VI.5. Conclusion

In this chapter, we have reported on the synthesis of amphiphilic PiBA containing polymers by controlled radical polymerization. First, a detailed study of the homopolymerization of iBA by atom transfer radical polymerization was carried out. Starting from well-defined PiBA macroinitiators, the 1-ethoxyethyl acrylate strategy as well as the use of tert-butyl acrylate was applied to synthesize precursor polymers for PiBA-*b*-PAA block copolymers with various compositions. Both strategies were evaluated for the synthesis of well-defined PiBA-*b*-PAA block copolymers. It was found that the use of tert-butyl acrylate as the precursor monomer for the PAA segment was not appropriate as selective deprotection was not possible. Degradation of the PiBA segment during the deprotection of the tert-butyl groups could not be avoided. In contrast, deprotection of the 1-ethoxyethyl protecting group of the PEEA segment by a heating step lead to the desired amphiphilic PiBA-*b*-PAA polymers. In addition, the PiBA-*b*-PAA block copolymers of various compositions were investigated as pigment stabilizers for aqueous pigment dispersions of $TiO_2$ and CuPc. For dispersions of the hydrophilic $TiO_2$ pigment, PiBA-*b*-PAA block copolymers with a long PAA block showed good stabilization while for dispersions of the hydrophobic CuPc pigment, block copolymers with a longer hydrophobic segment resulted in the best stabilization effect.

## VI.6. Acknowledgement

Thanks to Dr. Daan Wouters and ing. Hanneke Thijs (Eindhoven University of Technology, research group of Prof. U. Schubert, the Netherlands) for the AFM experiments and the contact angle measurements, respectively. Also thanks to Prof. Zubov (Lomonosov Moscow State Academy of Fine Chemical Technology, Russia) and Dr. Nikolay Bulychev and Prof. Eisenbach (University of Stuttgart, Germany) for the

collaboration and experimental work on the pigment stabilization effects of PiBA-*b*-PAA block polymers.

## *VI.7. Experimental part*

### VI.7.1. Materials

Isobornyl acrylate (iBA, Aldrich, tech.) was purified by vacuum distillation (121 °C/18 mmHg). *Tert*-butyl acrylate (tBA, Fluka, 98 +%) was purified by vacuum distillation (60 °C/60 mmHg). 1-Ethoxyethyl acrylate (EEA) was synthesized by the acid catalyzed addition reaction of acrylic acid to ethyl vinyl ether as described previously[14], and purified by vacuum distillation (30 °C/7 mbar). Cu(I)Br (Aldrich, 98 %) was purified by stirring with acetic acid, then by filtering and washing with methanol, and finally by drying in a vacuum oven at 70 °C. *N,N,N′,N″,N″*-pentamethyldiethylenetriamine (PMDETA, Acros, 99 +%) was distilled (85-86 °C/12 mmHg). Methyl-2-bromopropionate (MBP, Acros, 99 %) and dimethyl 2,6-dibromoheptanedioate (BHD, Aldrich, 97 %) were used as received. (Trimethylsilyl)diazomethane (2.0 M solution in diethyl ether, Aldrich) was used as received. Poly(acrylic acid) with an average molecular weight was obtained from Aldrich. As pigments, the titanium dioxide rutil pigment Kronos 2310 with particle size 0.3 μ, and β-copper phthalocyanine (β-CuPc) with primary particle size 0.1 μm were chosen. Solvents were purchased from Aldrich (HPLC grade) and used without purification. All other chemicals were used as received.

### VI.7.2. Characterization

**$^1$H NMR** spectra were recorded in $CDCl_3$ at room temperature, with a Bruker AM500 or a Bruker Avance 300 spectrometer.

**GPC analysis** was performed on a Waters instrument, using a refractive index detector (2410 Waters), equipped with Waters Styragel $10^3$-$10^4$-$10^5$ Å serial columns (5 μm particle size) at 35 °C. Polystyrene standards were used for calibration and $CHCl_3$ as eluent at a flow rate of 1.5 mL/min. For GPC analysis of the PAA containing block copolymers, the block copolymers were first modified by methylation of the carboxylic acid groups using trimethylsilyldiazomethane (see Chapter V, §V.9.2).[11]

**Gas Chromatography** was performed on a GC8000 from CE instruments with a DB-5MS column (60 m * 0.249 mm * 0.25 μm) from J&W scientific. Detection was done with an FID-detector. Injector and detector temperatures were kept constant at 250 °C. The column was initially set at 50 °C for 3 min, followed by a heating rate of 20 °C/min until 230 °C and kept for 8 min at this temperature. Conversion was determined by using ethyl acetate or decane as internal standard.

**Thermogravimetric analysis** (TGA) was performed with a Mettler Toledo TGA/SDTA851e instrument under air atmosphere at a heating rate of 10 °C/min from 25 °C-800 °C.

**Contact angle measurements** were performed on polymer films that were prepared by spin coating of THF solutions (20 mg/mL) of the PiBA or PiBA-*b*-PAA polymers on pre-cleaned microscopy slides at 1000 rpm during 90 seconds using a WS-400/500 series spin coater from Laurell Technologies Corporation. The commercial PAA sample was spin coated from a methanol solution. An automated OCA30 optical contact angle measuring instrument from Dataphysics was used to determine the contact angles of water.

**Matrix assisted laser desorption/ionization time of flight** (MALDI-TOF) mass spectra were recorded on an Applied Biosystems Voyager DE STR MALDI-TOF spectrometer equipped with 2 m linear and 3 m reflector flight tubes and a 337 nm nitrogen laser (3 ns pulse). All mass spectra were obtained with an accelerating potential of 20 kV in positive ion mode and in linear and/or reflector mode. *trans*-2-[3-(4-*tert*-butylphenyl)-2-methyl-2-propenylidene]malononitrile (BMPM) (20 mg/mL in THF) was used as a matrix, $NaF_3Ac$ (1 mg/mL) was used as a cationating agent, and polymer samples were dissolved in THF (2 mg/mL). Analyte solutions were prepared by mixing 10 $\mu$L of the matrix, 5 $\mu$L of the salt, and 5 $\mu$L of the polymer solution. Subsequently, 0.5 $\mu$L of this mixture was spotted on the sample plate, and the spots were dried in air at room temperature. A poly(ethylene oxide) standard ($M_n$ = 2000 g/mol or 5000 g/mol) was used for calibration. All data were processed using the Data Explorer (Applied Biosystems) and the Polymerix (Sierra Analytics) software package.

**Infrared** spectra were obtained with React-IR 4000 instrument from Mettler Toledo.

**Atomic Force Microscopy** (AFM) imaging was performed with two systems. The first system is a SMENA-P47H scanning probe microscope with a heatable sample holder (up to 300 °C) (NTMDT, Moscow, Russia). The second one is a Multimode scanning probe

microscope from Digital Instruments (Santa Barbara, CA, USA). The samples were probed under varying tapping conditions using NSG11S tips from NTMDT. Samples were prepared by spin coating a solution (4.5 mg/mL) onto Si substrates.

### VI.7.3. Synthesis of PiBA homopolymer

A typical polymerization procedure is as follows (e.g. entry 11, Table VI-1). A mixture of 0.11361 mol (24.0 mL) of the monomer iBA and 2.8402 x $10^{-4}$ mol (0.059 mL) of PMDETA as the ligand was bubbled with $N_2$ for 1h to remove oxygen. Ethyl acetate as the solvent was also bubbled with $N_2$ for 1h to remove oxygen and 8 mL (25 vol%) ethyl acetate was added to the reaction flask. Cu(I)Br (2.8402 x $10^{-4}$ mol, 0.04074 g) was added under $N_2$ atmosphere, and the reaction flask was placed in an oil bath at 75 °C When the reaction mixture reached the desired reaction temperature, the polymerization was started by adding 5.6803 x $10^{-4}$ mol (0.063 mL) of methyl-2-bromopropionate as the initiator. Samples were withdrawn periodically to monitor the monomer conversion (by $^1$H-NMR) and the average molecular weight (by GPC). The reaction was ended by cooling the reaction mixture in liquid nitrogen. The resulting polymer was dissolved in THF and the copper catalyst was removed by passing the diluted reaction mixture over a column of neutral $Al_2O_3$. After evaporating the excess solvent, the polymer was precipitated in methanol (10-fold excess).

### VI.7.4. Synthesis of PiBA-PAA block copolymer

A typical block copolymerization procedure is as follows (entry 21, Table VI-2). The monomer EEA was passed through a small column of basic alumina to remove traces of residual acid. The PiBA macroinitiator (HP14I3; 4.075 g; 38.15 x $10^{-5}$ mol) was dissolved in the monomer EEA (11 mL; 76.30 x $10^{-3}$ mol), and oxygen was removed from the mixture by bubbling with $N_2$ for 1h. Cu(I)Br (0.165 g; 1.150 x $10^{-3}$ mol, 3eq. relative to initiator) was added under nitrogen atmosphere, and the reaction flask was immersed in an oil bath thermostated at 50 °C. Polymerization was started by adding PMDETA (0.360 mL; 1.725 .$10^{-3}$ mol) as the ligand. Samples were withdrawn periodically to monitor the monomer conversion (by $^1$H-NMR) and the average molecular weight (by GPC). The reaction was ended by cooling the reaction mixture in liquid nitrogen. The block copolymer was dissolved in THF, and the copper was removed passing the diluted reaction

mixture over a column of neutral $Al_2O_3$. Solvent was evaporated, and the polymer was precipitated in cold methanol (10-fold excess).

For the synthesis of a PAA-*b*-PiBA-*b*-PAA triblock copolymer (entry 21, Table VI-2), a PiBA macroinitiator was prepared using a difunctional initiator dimethyl 2,6-dibromoheptanedioate (BHD), and further steps are identical.

### VI.7.5. Hydrolysis of PtBA segment to PAA

A typical procedure is as follows. The PtBA containing polymer was dissolved in $CH_2Cl_2$ and a three-fold molar excess of trifluoroacetic acid (TFA) with respect to the tert-butyl ester groups was added. The mixture was stirred at room temperature for 2 h. In the next step, solvent and TFA were evaporated, and the polymer was precipitated in cold hexane. The final polymer was dried under vacuum.

### VI.7.6. Deprotection of PEEA segment to PAA by heating

For thermolysis of the PiBA-*b*-PEEA block copolymers, a sample (typically 0.5 g) was spread out on a glass surface and heated in an oven at 80 °C for 24 hours. TGA analysis confirmed total conversion of PiBA-*b*-PEEA to PiBA-*b*-PAA.

### VI.7.7. Pigment stabilization techniques

For the preparation of aqueous pigment dispersions, the pigment was added to water alone or together with the polymer dissolved in tetrahydrofuran and dispersing of the pigment was first achieved by means of a laboratory stirrer (700 rpm for 10 min). When ultrasonification was applied, the system was subsequently treated with ultrasound for 2 min with an ultrasonic generator Branson Sonifier B-12 with actual power of 1.5 W/sm$^2$. Colloidal stabilization of the aqueous dispersions was monitored by sedimentation measurements of 1 % dispersions of CuPc and $TiO_2$.

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# *Chapter VII*
# *RAFT of EEA*

## Abstract

In Chapter V and VI we have shown that ATRP is a suitable technique to synthesize well-defined poly(1-ethoxyethyl (meth)acrylate) (PEE(M)A) containing copolymers. In this chapter, the polymerization of EEA using reversible addition fragmentation chain transfer (RAFT) polymerization is investigated to further illustrate the versatility and the general applicability of the use of the 1-ethoxyethyl acrylate strategy. The investigations were performed using a high-throughput workflow equipped with synthesis robots and fast analysis equipment demonstrating the added value in polymer research.

# VII
# RAFT of EEA

## VII.1. Introduction

To show the versatility and the general applicability of the use of the 1-ethoxyethyl acrylate (EEA) strategy, EEA has also been polymerized utilizing reversible addition fragmentation chain transfer (RAFT) polymerization[1, 2]. First, the homopolymerization of EEA with the RAFT technique was investigated in detail. In a second part, RAFT of EEA was combined with a variety of other monomers to yield PEEA containing block copolymers and derived polymer structures. Deprotection to the corresponding amphiphilic poly(acrylic acid) (PAA) containing polymers was carried out by a simple heating step.

Block copolymers are of main scientific interest due to their phase separation[3-5] and solution aggregation behavior[6-9]. To obtain significant phase separation, the combined polymer segments need to have different properties. Therefore, amphiphilic block copolymers are often used since the difference between the hydrophobic and hydrophilic blocks leads to demixing of the polymer chains and thus to a nanoscopic phase separation. Moreover, amphiphilic block copolymers are known to self-assemble in water to form a variety of micellar structures.[6-10] Poly(acrylic acid) (PAA) is a frequently used hydrophilic polymer in these amphiphilic block copolymers. To incorporate PAA in well-defined (block) copolymers, it has to be synthesized via a controlled polymerization technique.[11] So far, unprotected acrylic acid (AA) has been polymerized successfully utilizing reversible addition fragmentation chain transfer (RAFT) polymerization[1, 2], and nitroxide mediated polymerization (NMP)[12, 13]. In addition, the sodium salt of acrylic acid has been polymerized with atom transfer radical polymerization (ATRP).[14] Even though it is possible to directly polymerize acrylic acid, the applied polymerization solvents need to be polar implying that block copolymers with a variety of apolar monomers cannot be synthesized in a straightforward manner. To overcome this solvent incompatibility, the protected analogues

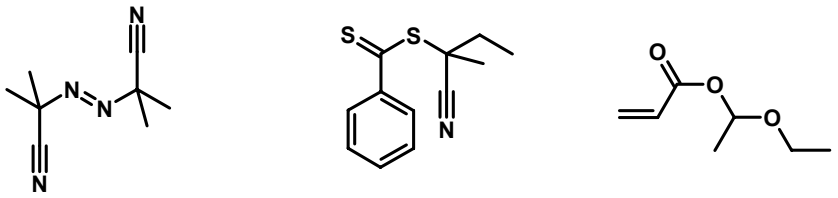
tert-butyl acrylate[15, 16], and benzyl acrylate[17] are often used followed by a deprotection step.[11] However, these strategies include postpolymerization deprotection and subsequent purification of the poly(acrylic acid). To avoid these steps, ATRP of 1-ethoxyethyl acrylate (EEA) was described in Chapter V and VI.[18-20] The applied 1-ethoxyethyl protecting group could be easily removed by thermolysis preventing the need of an additional purification step after deprotection. However, the applied copper(I) mediated ATRP is quite sensitive to residual acrylic acid that is able to coordinate the copper(I) ions and protonate the nitrogen ligands, leading to an uncontrolled polymerization.[21] Therefore, the EEA has to be stringently purified and the polymerization process has to be performed at moderate temperatures to prevent deprotection of the monomer during the polymerization reaction.

In this chapter, RAFT polymerization of 1-ethoxyethyl acrylate is described for the first time. This part of the research has been done in collaboration with Dr. R. Hoogenboom and Prof. U. Schubert (Eindhoven University of Technology, the Netherlands). RAFT polymerizations are insensitive to acid groups making the monomer purification less critical. Moreover, partial deprotection of the monomer does not influence the RAFT polymerization allowing higher polymerization temperatures when compared to ATRP. The current investigations were performed utilizing a high-throughput workflow that was previously applied for the temperature optimization of RAFT polymerization processes[22]. The use of combinatorial and high-throughput experimentation in polymer science is steadily increasing.[23-25] In addition, different deprotection methods of the resulting PEEA will be discussed leading to well-defined poly(acrylid acid)s (PAA) or to cross-linked poly(acrylic acid)s. To end with, the possibility of synthesizing block and "block-like" copolymers containing a PEEA segment via RAFT polymerizations in an apolar solvent will be demonstrated for a variety of structures.

## *VII.2. Homopolymerization of EEA*

The reversible addition fragmentation chain transfer (RAFT) polymerization of 1-ethoxyethyl acrylate (EEA) with azoisobutyronitrile (AIBN) as initiator and 2-cyano-2-butyl dithiobenzoate (CBDB) as RAFT agent (see Figure VII-1, top) was investigated in toluene. For more information about the role of the different species, we refer to Chapter II, §II.5.2. The control over the radical polymerization is achieved by establishing an equilibrium

between a dormant polymeric RAFT agent and the free polymeric radicals as depicted in Figure VII-1 (bottom). This equilibrium controls the amount of free radicals present and thus determines the polymerization speed and, even more importantly, it determines the probability of chain termination and chain transfer reactions. When appropriate reaction conditions are applied, chain termination is reduced to a minimum resulting in a controlled radical polymerization in which all polymer chains have a (dormant) radical chain end. As a result, all polymer chains will grow with similar rates resulting in a narrow molecular weight distribution. Moreover, the controlled polymerization method allows the synthesis of well-defined random, gradient and block copolymers.[26-28]




**RAFT mechanism:**

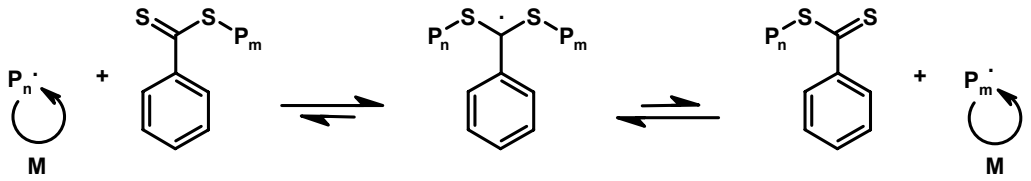



**Figure VII-1** **Reagents (top) and mechanism (bottom) for the investigated RAFT polymerization of 1-ethoxyethyl acrylate (EEA) with azobisisobutyronitrile (AIBN) as initiator and 2-cyano-2-butyl dithiobenzoate (CBDB) as RAFT agent.**

Recent investigations revealed an optimal RAFT to initiator ratio of 1:0.25 for the polymerization of methyl methacrylate (MMA) utilizing CBDB as RAFT agent and AIBN as initiator in toluene.[22] This ratio was found to be the optimum regarding both control and speed of the polymerization. Therefore, the current investigations on the RAFT polymerization of EEA with CBDB and AIBN in toluene were all conducted at this optimal RAFT to initiator ratio of 1:0.25 aiming for a degree of polymerization of 100 units. The polymerizations were performed in parallel utilizing a Chemspeed Accelerator SLT100 synthesis robot equipped with an array of individually heatable reactors (see Figure VII-2).

**Figure VII-2** **Chemspeed Accelerator SLT100 synthesis robot (left) equipped with an array of individually heatable reactors (right).**

During the polymerization run, six polymerization temperatures (50, 60, 70, 80, 90 and 100 ºC) were investigated. In addition, for each temperature, two experiments were performed to verify the reproducibility of the polymerization reactions. During the polymerization processes, samples were taken at 2, 4, 6, 8, 10 and 15 hours to investigate the development of the molecular weight as a function of time by gel permeation chromatography (GPC). The conversion as a function of time was not investigated during this screening since the objective was to investigate the feasibility of the RAFT polymerization to obtain well-defined poly(EEA). Moreover, measuring the conversion by gas chromatography (GC) or by gravimetrical analysis would lead to misleading results due to the thermal degradation of both monomer and polymer while conversion determination by $^{1}$H-NMR spectroscopy would result in a serious bottleneck in the present high-throughput workflow. The plots of the number average molecular weight ($M_n$) as a function of time demonstrate the good reproducibility of the RAFT polymerizations of EEA (see Figure VII-3). The polymerizations at 50, 60 and 70 ºC showed a clear increase of $M_n$ against time, whereby the polydispersity indices (PDI's) remained at values below 1.3. Figure VII-4 left depicts the GPC traces obtained for one of the polymerizations at 70 ºC demonstrating the increase of molecular weight as a function of time. Note that a small shoulder at the higher molecular weight side appears with higher conversion suggesting the occurrence of chain termination by radical coupling. In contrast to the polymerizations at 50, 60 and 70 ºC, the polymerizations at 80, 90 and 100 ºC did not reveal an increase of molecular weight as a function of polymerization time, because relatively high conversions were already reached within the first 2 hours.

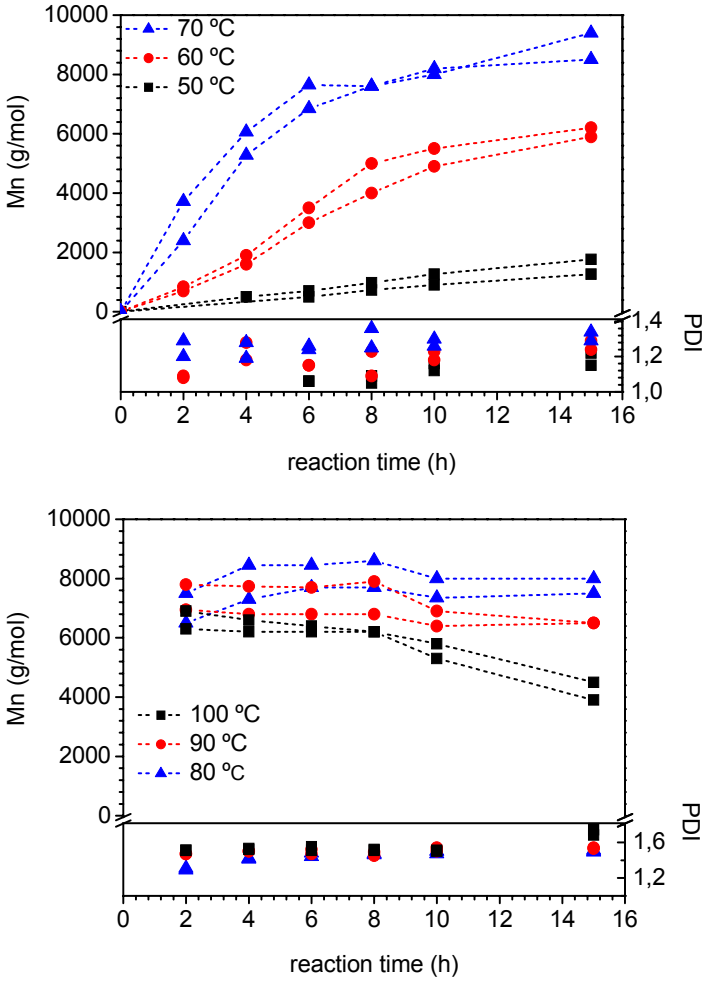



**Figure VII-3** **Development of the number average molecular weight ($M_n$) and molecular weight distribution (PDI) as a function of time for the RAFT polymerizations of EEA at 50, 60, 70 °C (top), 80, 90 and 100 °C (bottom). The results of two experiments are shown for each polymerization temperature. GPC eluent: $CHCl_3$:$NEt_3$:*i*-PrOH 94:4:2.**

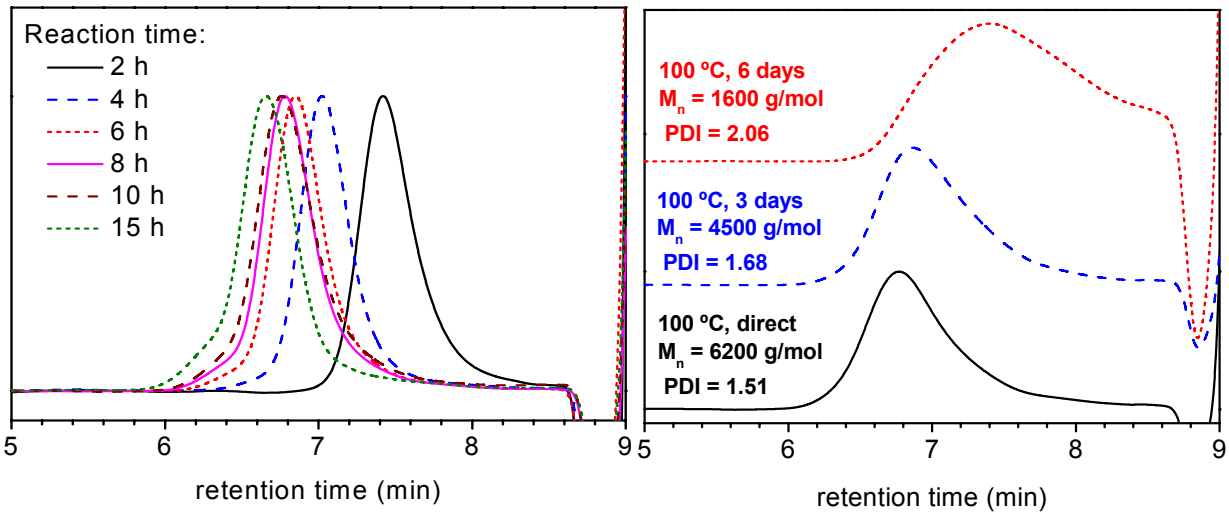



**Figure VII-4** **Left: GPC traces of the RAFT polymerization of EEA at 70 °C. Right: GPC traces of the samples obtained from the polymerization of EEA at 100 °C demonstrating the deprotection during the polymerization reaction. GPC eluent: $CHCl_3$:$NEt_3$:*i*-PrOH 94:4:2.**

All obtained final $M_n$'s are lower than the theoretical values ($M_{n,th}$ = 14.700 for 100% monomer conversion), which is partially due to the PMMA standards used for calibrating the GPC system but also due to incomplete conversion, as determined by $^1$H-NMR spectroscopy for the final samples (reaction time = 15 h): T = 50 ºC: 19%; T = 60 ºC: 55%; T = 70 ºC: 82%; T = 80 ºC: 94 %; T = 90 ºC: 94% and T = 100 ºC: 83 %. Moreover, both molecular weight and PDI values are influenced by (partial) deprotection of the PEEA. This deprotection can not only occur during the synthesis but also in the GPC eluent. Interactions of the acid with the column material can not be avoided (utilizing chloroform as eluent) resulting in longer retention times and tailing of the signals. This effect is clearly demonstrated in Figure VII-4 (right), showing the GPC traces of the final polymer obtained at 100 ºC (stored in the GPC eluent), first directly after synthesis, then after 3 days and then after 6 days: the more (partial) deprotection occurs, the more tailing is observed, resulting in lower retention times. The interactions of the polymer with the column material upon deprotection also explain the decrease of $M_n$ in time for the polymerizations performed at 80, 90 and 100 ºC (see Figure VII-3, bottom). From this temperature screening, it can be concluded that 70 ºC is the optimal temperature for the RAFT polymerization of EEA, providing a good balance between reaction speed and control over the polymerization without significant deprotection during the polymerization reaction.

Deprotection of PEEA can be performed to obtain near-monodisperse poly(acrylic acid) (PAA). Different ways of deprotection resulting in linear or, if so desired, cross-linked PAA were investigated. The first method of deprotection was already shortly mentioned in the previous section by the change in GPC traces over time (Figure VII-4, right). All GPC samples (in the $CHCl_3$/$NEt_3$/i-PrOH (94/4/2) eluent) from the temperature screening were kept at ambient temperature for two weeks during which the polymers precipitate, indicating that PAA was formed. The samples were more than 90% deprotected as determined by $^1$H-NMR spectroscopy for a few randomly chosen samples. GPC analysis of these PAA samples was performed utilizing DMF as eluent to suppress the interactions between the acid groups and the column material. The resulting plots of $M_n$ as a function of time are depicted in Figure VII-5.

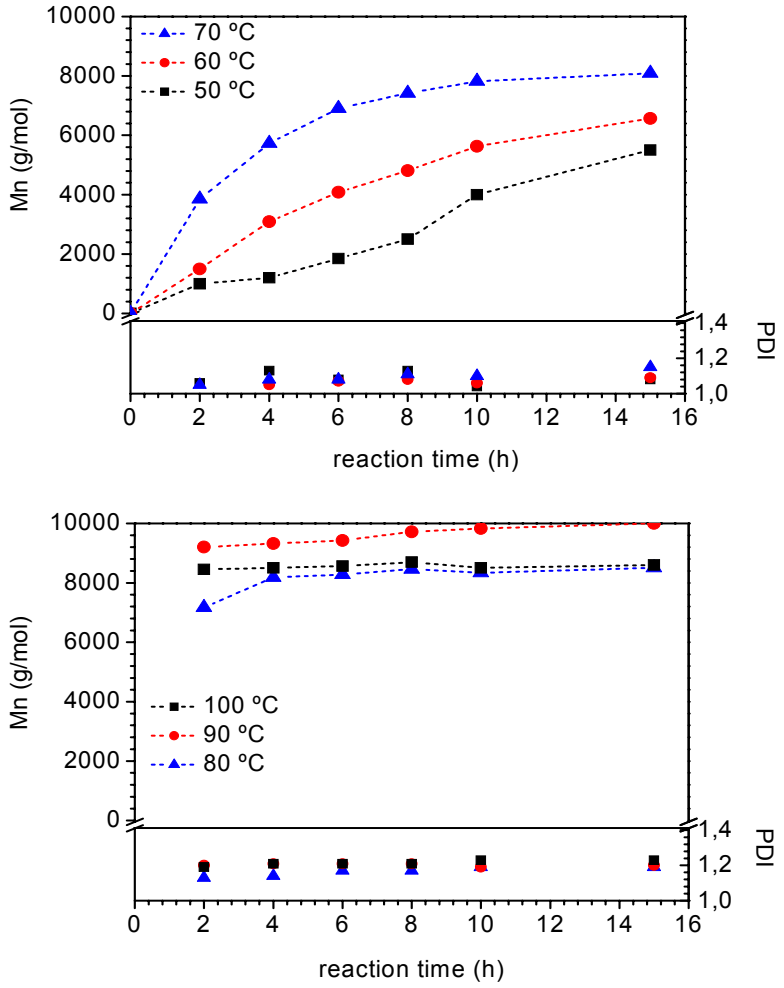



**Figure VII-5** **Number average molecular weights ($M_n$) and molecular weight distributions (PDI) of PAA obtained after deprotection of the samples taken during the RAFT polymerizations of EEA at 50, 60, 70 °C (left), 80, 90 and 100 °C (right). GPC eluent: DMF.**

For all investigated temperatures an increase of $M_n$ as a function of conversion is observed for the PAA samples with DMF as eluent, in contrast to the $M_n$'s obtained with $CHCl_3$ as eluent (Figure VII-3). Moreover, narrow molecular weight distributions (PDI < 1.20) were obtained for all investigated samples proving the possibility of creating near-monodisperse PAA via RAFT polymerization of the protected EEA monomer. In addition, these results prove that the RAFT polymerizations at 80, 90 and 100 °C were also controlled, despite the fact that partial deprotection already took place during the polymerizations. The second method of deprotection, by a heating process or thermolysis, was previously demonstrated for PEE(M)A synthesized by ATRP in Chapter V.[18-20] Note that the results of the thermolysis strongly depend on the thermolysis conditions. At lower temperature, under conditions where anhydride formation of the PAA is prevented during the thermolysis, near-monodisperse PAA

is formed, just as described in Chapter V. At higher temperature and/or during longer periods of heating, anhydride formation occurs, resulting in cross-linked PAA.

In the previous sections, we have demonstrated the possibility to polymerize EEA in a controlled way utilizing the RAFT mechanism. The subsequent deprotection to well-defined PAA or cross-linked PAA was discussed as well.

## *VII.3. Derived block and "block-like" copolymer structures with PEEA segments*

In a next step, the controlled synthesis of block and "block-like" copolymers (see also Chapter V) containing a PEEA segment was investigated in an apolar solvent (toluene). In this way, block copolymers containing a PAA segment can be obtained via synthesis in an apolar solvent, which would be unattainable by the direct polymerization of AA.

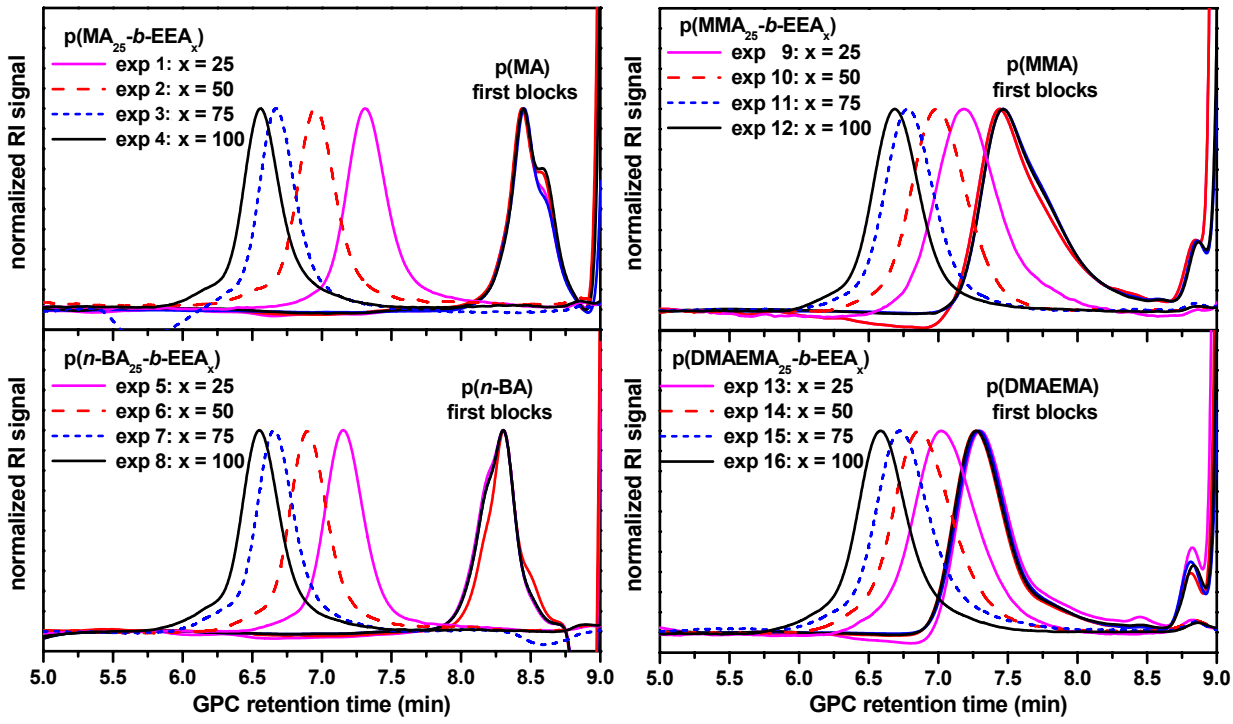



**Figure VII-6** **GPC traces of the first blocks and the final block/"block-like" copolymers consisting of a MA (left top), *n*-BA (bottom left), MMA (top right) or DMAEMA (bottom right) first block (25 units) and an EEA (25, 50, 75 and 100 units for 100% conversion) second block. GPC eluent: $CHCl_3$:$NEt_3$:iPrOH 94:4:2.**

The copolymerizations were performed at the optimal temperature of 70 ºC. The block and "block-like" copolymers were prepared by sequential monomer addition. The synthesis

robot was applied for the synthesis of 16 block copolymers with a theoretical degree of polymerization ($DP_{th}$) of 25 units for the first block that is composed of methyl acrylate (MA) (experiments 1-4), *n*-butyl acrylate (*n*-BA) (exp 5-8), methyl methacrylate (MMA) (exp 9-12) or N,N-(dimethylamino)ethyl methacrylate (DMAEMA) (exp 13-16). The second block is a PEEA block with a $DP_{th}$ of 25, 50, 75 or 100 units. The first blocks were polymerized for 3 hours after which a sample was taken for GPC analysis to determine the experimental molecular weight. Subsequently, EEA was immediately added without purification of the first block and the polymerizations were continued for 12 hours. The obtained GPC traces of both the first blocks and the final block/"block-like" copolymers are depicted in Figure VII-6.

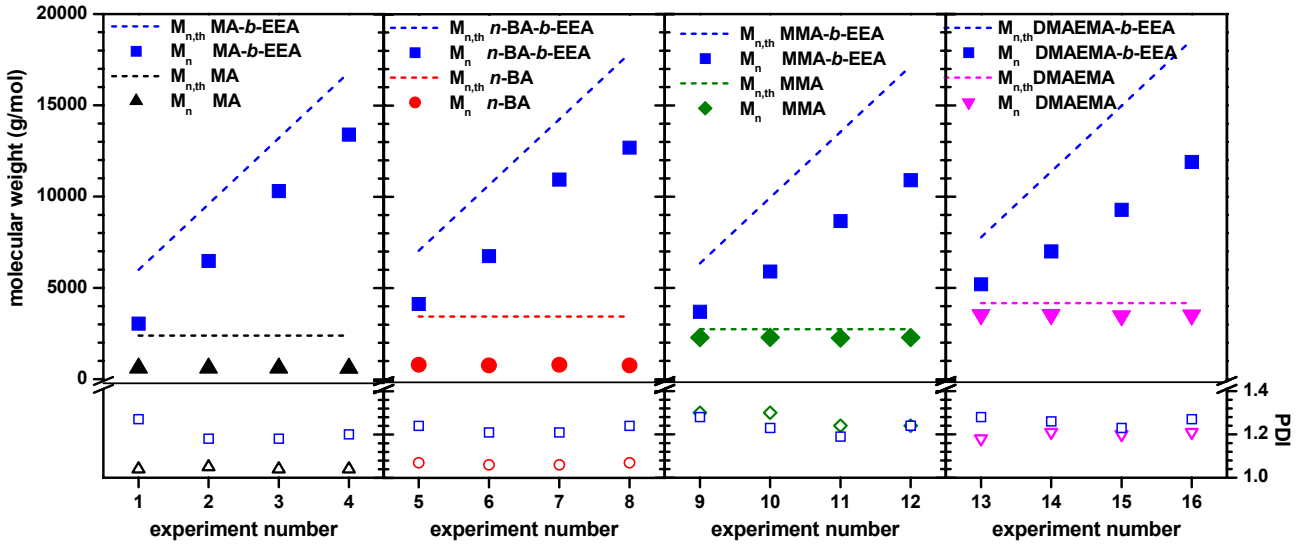



**Figure VII-7** **Number average molecular weights ($M_n$) and molecular weight distributions (PDI) obtained for the first blocks and for the final block copolymers of MA, *n*-BA, MMA or DMAEMA (25 units) with EEA (25, 50, 75 and 100 units for 100% conversion). All $M_n$ values are calculated against pMMA standards. GPC eluent: $CHCl_3$:$NEt_3$:iPrOH.**

The GPC curve overlap of the first blocks demonstrates the good reproducibility of the RAFT polymerizations in the synthesis robots (Figure VII-6). Moreover, the final block/"block-like" copolymers show the expected shift towards higher molecular weights (lower retention times) with increasing EEA units. The shoulders in the GPC traces of the first blocks are due to the low conversions resulting in incomplete equilibration between polymeric RAFT-agent and the free polymeric radicals (Figure VII-1). Figure VII-7 plots the $M_n$'s and PDI values that were calculated (PMMA calibration) from the GPC traces of the first blocks

and the resulting block copolymers, clearly demonstrating the ability to synthesize EEA containing block copolymers.

The polymerizations with an acrylate monomer (MA or *n*-BA) as first block showed $M_n$'s lower than the $M_{n,th}$ for the first block indicating insufficient reaction times. This is in agreement with recent investigations that showed incomplete (50%) conversion for the polymerization of MA utilizing similar conditions with a monomer to RAFT ratio of 100.[30] After addition of the EEA to the active centers of the first block, the polymerization was continued resulting in copolymers with a short first block of MA or *n*-BA and a random/gradient second block of MA and EEA or *n*-BA and EEA. The molecular weights of the resulting copolymers largely exceeded the $M_{n,th}$ of the first block demonstrating that indeed both the first monomer (MA or *n*-BA) and EEA were copolymerized. Thus in this case, "block-like" polymers are obtained (see also discussion in Chapter V). The molecular weights obtained for the methacrylate (MMA or DMAEMA) first blocks revealed a monomer conversion close to 100 % as can be seen by the close resemblance with the theoretical molecular weights (it was assumed that the PMMA standards provide reliable molecular weight data for PDMAEMA). After addition of the second monomer EEA, the block copolymers were successfully synthesized as can be concluded from the GPC analysis. Also for these copolymerizations, the reaction times for the second blocks were insufficient resulting in lower molecular weights than theoretical, whereby it is noteworthy to mention that also the applied PMMA calibration could lead to lower observed molecular weights for the PEEA block. For all synthesized EEA containing copolymers, the molecular weight distributions were relatively narrow (PDI < 1.30) indicating good control over the copolymerizations.

The composition of the resulting block copolymers was further determined by $^1$H NMR spectroscopy (Table VII-1). The integral ratios of the $CH_2$ and/or $CH_3$ resonances next to the ester groups (MA, *n*-BA, MMA, DMAEMA: 3.65, 4.05, 3.60 or 4.10 ppm, respectively) or the ether bond (EEA: 3.50 and 3.72 ppm) in the polymers were used to determine the ratio of the two present monomers. For the MA and MMA containing copolymers, the integral of the CH resonance of EEA (5.90 ppm) was also used to calculate the monomer ratios, because the $CH_3$ resonances of MA and MMA overlapped with the $CH_2$ signals of EEA. Moreover, the integrals of the aromatic resonances of the RAFT agent were applied to calculate the number average degree of polymerization ($DP_n$) for the monomers present in the block copolymers.

**Table VII-1 Compositions of the synthesized block copolymers as determined by $^1$H-NMR spectroscopy.**

| Exp Nr | Monomer A | $DP_{A,th}$[a] | $DP_{EEA,th}$[b] | $f_{EEA,th}$[c] | $DP_{A,NMR}$[d] | $DP_{EEA,NMR}$[e] | $f_{EEA,NMR}$[f] |
|---|---|---|---|---|---|---|---|
| 1 | MA | 25 | 25 | 0.5 | 19 | 9 | 0.32 |
| 2 | MA | 25 | 50 | 0.67 | 17 | 22 | 0.56 |
| 3 | MA | 25 | 75 | 0.75 | 18 | 35 | 0.66 |
| 4 | MA | 25 | 100 | 0.8 | 20 | 52 | 0.72 |
| 5 | *n*-BA | 25 | 25 | 0.5 | 18 | 20 | 0.53 |
| 6 | *n*-BA | 25 | 50 | 0.67 | 18 | 44 | 0.71 |
| 7 | *n*-BA | 25 | 75 | 0.75 | 19 | 73 | 0.79 |
| 8 | *n*-BA | 25 | 100 | 0.8 | 22 | 87 | 0.80 |
| 9 | MMA | 25 | 25 | 0.5 | 23 | 6 | 0.21 |
| 10 | MMA | 25 | 50 | 0.67 | 23 | 12 | 0.34 |
| 11 | MMA | 25 | 75 | 0.75 | 23 | 20 | 0.47 |
| 12 | MMA | 25 | 100 | 0.8 | 23 | 32 | 0.58 |
| 13 | DMAEMA | 25 | 25 | 0.5 | 22 | 8 | 0.27 |
| 14 | DMAEMA | 25 | 50 | 0.67 | 22 | 20 | 0.48 |
| 15 | DMAEMA | 25 | 75 | 0.75 | 22 | 35 | 0.61 |
| 16 | DMAEMA | 25 | 100 | 0.8 | 22 | 51 | 0.70 |

[a.] $DP_{th}$ of monomer A. [b.] $DP_{th}$ of EEA. [c.] theoretical (mol) fraction of EEA. [d.] DP of monomer A determined from $^1$H NMR analysis. [e.] DP of EEA determined from $^1$H NMR analysis. [f.] (mol) fraction of EEA determined from $^1$H NMR analysis.

$^1$H NMR spectroscopy proved the successful incorporation of the EEA monomer in the block/"block-like" copolymers. Moreover, the NMR data confirmed the incomplete polymerization of the EEA second blocks as was already indicated by GPC characterization. The block copolymerizations with an acrylate monomer as first block seem to have a higher reactivity to the EEA, which is also an acrylate, than the polymerizations with a methacrylate first block. In addition, the *n*-BA and DMAEMA first blocks resulted in a higher degree of polymerization of EEA compared to the MA and MMA copolymerizations.

Deprotection of the EEA containing block copolymers was performed by heating the $CDCl_3$ $^1$H NMR solutions under pressure for 3 hours to 80 ºC in closed 2 mL vials. After three hours, the block copolymer solutions with a high EEA content became cloudy indicating deprotection of the acrylic acid. $^1$H NMR spectroscopy in DMSO-$d_6$ revealed 85-100% deprotection for a few randomly selected block copolymers, showing that deprotection was nearly complete after this time interval. The GPC traces for the p(MA-b-AA), p(*n*-BA-b-AA), p(MMA-b-AA) and p(DMAEMA-b-AA) are depicted in Figure VII-8. The GPC analysis revealed monomodal distributions and low polydispersity indices (PDI < 1.20) for all block

copolymers demonstrating that deprotection resulted in well-defined PAA containing block/"block-like" copolymers. However, some of the GPC traces show slight shoulders at lower retention times (higher molecular weight) indicative of minor cross-linking reactions.

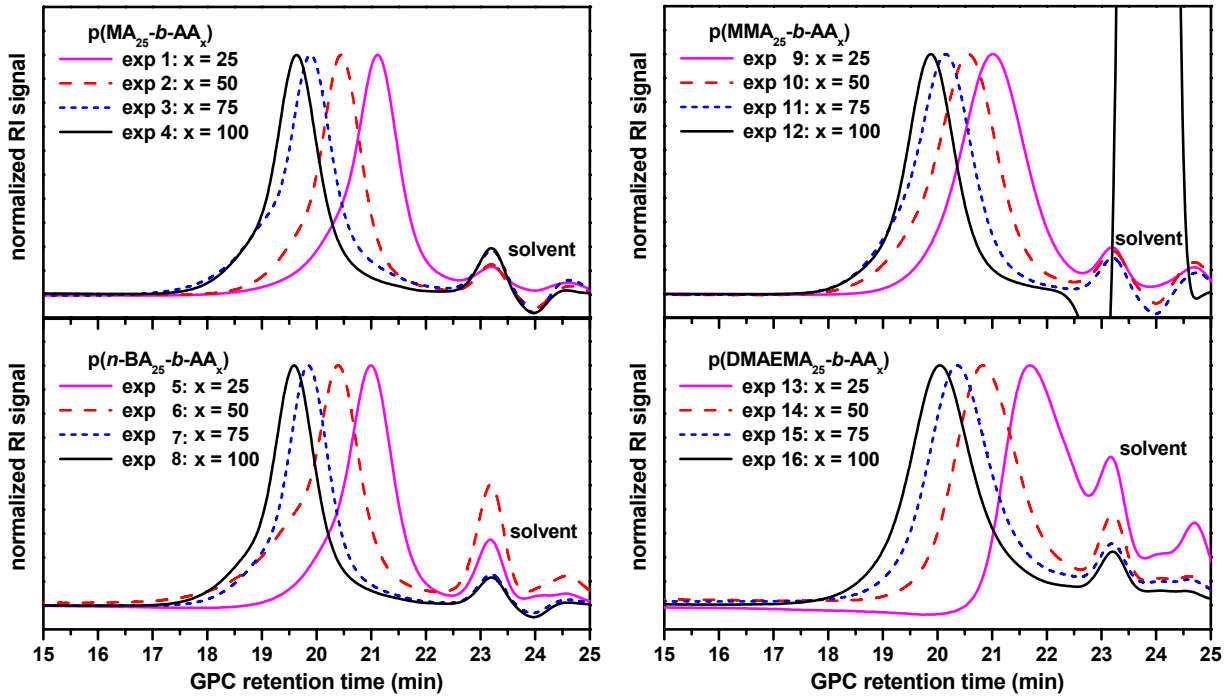



**Figure VII-8** **GPC traces of the p(MA-b-AA) (top left), p(*n*-BAA-b-AA) (bottom left), p(MMA-b-AA) (top right) and p(DMAEMA-b-AA) (bottom right) obtained by deprotection of the corresponding EEA containing block copolymers. GPC eluent: DMF.**

## *VII.4. Conclusion*

The successful polymerization of 1-ethoxyethyl acrylate (EEA) via a RAFT polymerization process was demonstrated. Temperature optimization revealed an optimum polymerization temperature of 70 ºC providing an optimal balance between control over the polymerization and reaction speed without significant deprotection. At lower temperatures, the polymerization proceeded very slowly, whereas deprotection was observed at higher temperatures. In addition, the direct synthesis in toluene of block and "block-like" copolymer structures with an EEA containing second block, without purification of the first block, was demonstrated. Copolymerizations with acrylate (MA or *n*-BA) first blocks revealed short first blocks (insufficient reaction times) and thus "block-like" structures are obtained, with a random/gradient type second block. When methacrylates (MMA or DMAEMA) were applied

as monomers for the synthesis of the first blocks, the block copolymers were successfully synthesized without significant incorporation of the first monomer in the EEA block. Thermal deprotection of these block/"block-like" copolymers was performed at 80 ºC resulting in the corresponding well-defined PAA containing block/"block-like" copolymers. The successful (co)polymerizations of EEA utilizing RAFT offer many possibilities for the straightforward synthesis of PAA containing copolymers without the need for polar solvents or labor-intensive deprotection steps.

The discussed investigations were all performed utilizing a high-throughput workflow equipped with synthesis robots and fast analysis equipment demonstrating the added value of such approaches in polymer research.

## *VII.5. Acknowledgement*

Special thanks to Dr. R. Hoogenboom and Prof. U. Schubert (Eindhoven University of Technology, the Netherlands) for the excellent collaboration.

## *VII.6. Experimental part*

### VII.6.1. Materials

Methyl acrylate (MA), *n*-butyl acrylate (*n*-BA), methyl methacrylate (MMA) and N,N (dimethylamino)ethyl methacylate (DMAEMA, all obtained from Aldrich) were purified by passing over a basic aluminum oxide filtration column. 1 Ethoxyethyl acrylate was prepared as described in literature.[18] Azobisisobutyronitrile (AIBN, Aldrich) was recrystallized from methanol. 2 Cyano-2-butyl dithiobenzoate (CBDB) was prepared according to a literature procedure for a related compound.[31] Analytical grade solvents were purchased from Biosolve Ltd. All solutions were deoxygenated by purging with argon gas prior to use.

### VII.6.2. Instrumentation

Polymerizations were performed on a Chemspeed AcceleratorTM SLT100 automated synthesizer. This synthesis robot was equipped with a four needle head, a solid dosing unit, and an array of 16 parallel 13 mL glass reactors. The reactors could be heated by a Huber

Unistat Tango (heating range: -40 ºC to 145 ºC) via their double jackets. The temperature optimization was performed with an array of individually heatable reactors. In this array, each reactor has a separate ceramic heating mantle and an internal temperature sensor providing the possibility to perform 16 parallel reactions at 16 different temperatures (ambient temperature to 230 ºC). Moreover, the reactors were equipped with a cold-finger reflux condenser that could be cooled or heated from –5 ºC till 50 ºC. An inert atmosphere was maintained by applying a 1.1 bar flow over the reactors and a 1.5 bar argon flow through the hood of the Accelerator.[32]

Gel permeation chromatography (GPC) of poly(EEA) and the copolymers was measured on a Shimadzu system equipped with a SCK-10A system controller, a LC-10AD pump, a RID-10A refractive index detector and a PL gel 5 μm Mixed-D column at 50 ºC utilizing a chloroform/triethylamine/ isopropanol (94/4/2) mixture as eluent at a flow rate of 1 $mL.min^{-1}$. GPC characterization of the poly(acrylic acid) samples was performed on a Waters system with a 1515 pump, a 2414 refractive index detector and a Waters Styragel HT4 column utilizing N,N-dimethylformamide with $5.10^{-3}$ M $NH_4PF_6$ as eluent at a flow rate of 0.5 $mL.min^{-1}$ at 50 °C. The molecular weights were calculated on the basis of poly(methyl methacrylate) standards. $^1$H-NMR spectra were recorded on a Varian Mercury 400 spectrometer or a Varian Gemini 300 spectrometer. Chemical shifts are given in ppm relative to TMS or solvent signals. Thermogravimetric analyses were performed utilizing a Netsch TG 209 F1 Iris apparatus.

### VII.6.3. Homopolymerization of EEA – parallel temperature optimization

To obtain an inert atmosphere, the hood of the AcceleratorTM was flushed for at least 90 minutes with argon before starting the polymerization procedure. An inert atmosphere was created inside the individually heatable reaction vessels by performing three cycles of heating (120 ºC) under vacuum (15 min at ~ 25 mbar) followed by argon flushing (1 min). During the polymerizations, the temperature of the cold-finger reflux condensers was set to – 5 ºC. 1-Ethoxyethyl acrylate (1.360 g; 9.34 mmol) and stock solutions of AIBN (1.450 mL; 0.016 M) and CBDB in toluene (1.450 mL; 0.065 M) were dispensed into the reaction vessels resulting in 4.2 mL reaction mixtures with EEA/RAFT/initiator = 100/1/0.25 and 2.2 M monomer concentration. The mixtures were heated (50, 60, 70, 80, 90, 100 ºC; each temperature twice) and vortexed at 600 rpm for 15 hours, whereby samples (100 μL aliquots) were taken from

each reactor to 2.0 mL vials prefilled with GPC eluent (1.0 mL; chloroform /triethylamine/isopropanol) at 2, 4, 6, 8, 10 and 15 hours polymerization time. These samples were used for GPC analysis.

### VII.6.4. Synthesis of block/"block-like" copolymerizations with EEA

The copolymerizations were performed in a similar manner utilizing an array of 16 parallel 13 mL reactors with a double jacket for heating. After creating an inert atmosphere in the hood and the reaction vessels, the monomers (MA, *n*-BA, MMA and DMAEMA), stock solutions of AIBN and CBDB in toluene and toluene were dispensed into the reactors resulting in 1.5 mL polymerization mixtures with a monomer/RAFT/initiator ratio of 25/1/0.25 and a monomer concentration of 2.2 M. Four separate polymerizations were performed for each monomer. After three hours polymerization time, samples (100 μL aliquots) were taken from each reactor to 2.0 mL vials prefilled with GPC eluent (1.0 mL; chloroform/triethylamine/isopropanol). Subsequently, the second monomer (EEA) was added to the reaction vessels. For each first monomer, four different amounts of EEA (470, 940, 1410 or 1880 μL) were added to the four separate reactions resulting in a theoretical amount for full conversion of 25, 50, 75 or 100 units EEA and the polymerizations were continued for 12 hours.

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# *Chapter VIII*
# *“Click” chemistry for the synthesis of amphiphilic polymer structures*

## Abstract

In this chapter, the combination of ATRP of EEA and the copper(I) catalyzed “click” 1,3-dipolar cycloaddition reaction of azides and terminal alkynes was evaluated as a method to synthesize amphiphilic polymer structures. Using our EEA strategy, the application field was broadened with the synthesis of polymer structures containing PAA segments. A modular approach has been used: polymers with alkyne functionalities as well as azide functionalities have been synthesized. These polymers were subsequently “click” coupled to obtain block copolymers and, for the first time, comb/brush copolymers were synthesized by a combination of ATRP and “click” chemistry.

# VIII
# "Click" chemistry for the synthesis of PAA containing polymer structures

## VIII.1. Introduction

Since their description as a new class of reactions by Sharpless *et al.*, "click" reactions have gained an increasing success.[1] During the last 2 years, particularly the Cu(I) catalyzed "click" cycloaddition reaction of azides and terminal alkynes has become very popular in polymer chemistry, as a useful tool for functionalizing synthetic macromolecules and synthesizing a wide range of polymer architectures.[2-26] For a detailed description of "click" chemistry and an overview about the possibilities of "click" chemistry in the field of polymer synthesis, please see Chapter IV.

One of the most desirable qualities for reactions used in polymer chemistry is that they proceed quantitatively, as otherwise a mixture of reaction products is obtained, leading to badly defined properties of the end products. The Cu(I) catalyzed "click" cycloaddition reaction of azides and terminal alkynes meets this requirement entirely. Moreover, these reactions proceed under mild reaction conditions and are tolerant to a broad variety of functional groups. The coupling of an azide and a terminal alkyne by a 1,3 dipolar cycloaddition reaction leads to the formation of a 1,2,3-triazole ring, a chemically very stable compound.

As within the field of polymer synthesis, atom transfer radical polymerization (ATRP) is probably one of the most powerful and most employed polymerization methods in modern material science[27-34] (see also Chapter II), recently several research groups reported on the combination of "click" chemistry and ATRP. The bromine chain ends of polymers prepared by ATRP can easily be transformed into azides by nucleophilic substitution[31, 34, 35] (see also chapter II) and subsequently reacted with functional alkynes.[36]

This strategy was used for preparing either well-defined telechelic polymers or block copolymers.[5, 15, 20, 24, 25] Additionally, functional initiators or monomers (i.e., azide or alkyne functional molecules) can be used in ATRP for preparing well-defined "clickable" polymers.[9, 14, 15, 18, 20] A detailed overview of the combination of "click" chemistry and ATRP is given in Chapter IV, § IV.4. Moreover, because both ATRP and azide-alkyne "click" reactions are catalyzed by Cu(I) compounds, the combination of these two techniques shows to be an industrially attractive approach.

In this chapter, the synthesis of poly(acrylic acid)-containing block copolymers and comb/brush copolymers using a combination of ATRP and "click" chemistry has been studied. For the synthesis of the poly(acrylic acid) (PAA) segments, our strategy with the use of 1-ethoxyethyl acrylate (EEA) as the protected monomer will be employed. A modular approach has been used: polymers with alkyne functionalities as well as azide functionalities have been synthesized. These polymers were subsequently "click" coupled to obtain the desired block- and comb/brush copolymers (see Figure VIII-1).

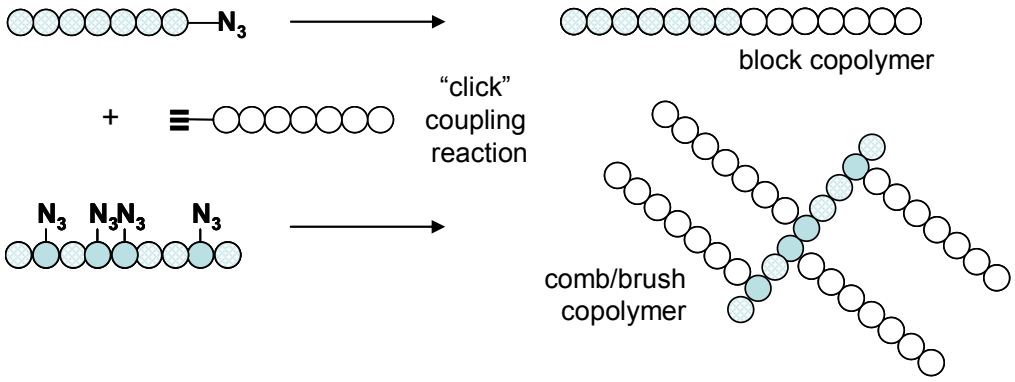


**Figure VIII-1 Schematic depiction of the synthesis of block and comb/brush copolymers using "click" chemistry.**

The following 2 paragraphs describe the preparation of polymer building blocks with alkyne and azide functionalities, respectively.

## *VIII.2. Synthesis of polymers with alkyne functionality*

A functional initiator has been used for the synthesis of PAA segments with an alkyne functionality. The initiator that has been used in this case is propargyl 2-bromopropionate.

## VIII.2.1. synthesis of alkyne-containing initiator: propargyl 2-bromopropionate

Propargyl 2-bromopropionate is an alkyne-containing initiator, which is prepared by esterification of propargyl alcohol and 2-bromopropionic acid, with the help of DCC (*N, N'*-dicyclohexylcarbodiimide) and 4-DMAP (4-dimethylaminopyridine) as the catalyst (see Figure VIII-2). The mechanism for the synthesis is similar to the synthesis of the earlier used disulfide containing initiator (see Chapter VI).

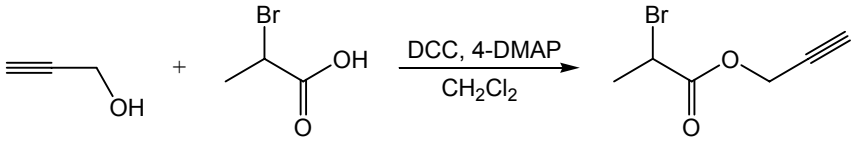


**Figure VIII-2** **Synthesis of alkyne-containing initiator: propargyl 2-bromopropionate.**

The $^1$H NMR spectrum and IR spectrum of propargyl 2-bromopropionate are displayed in Figure VIII-3.

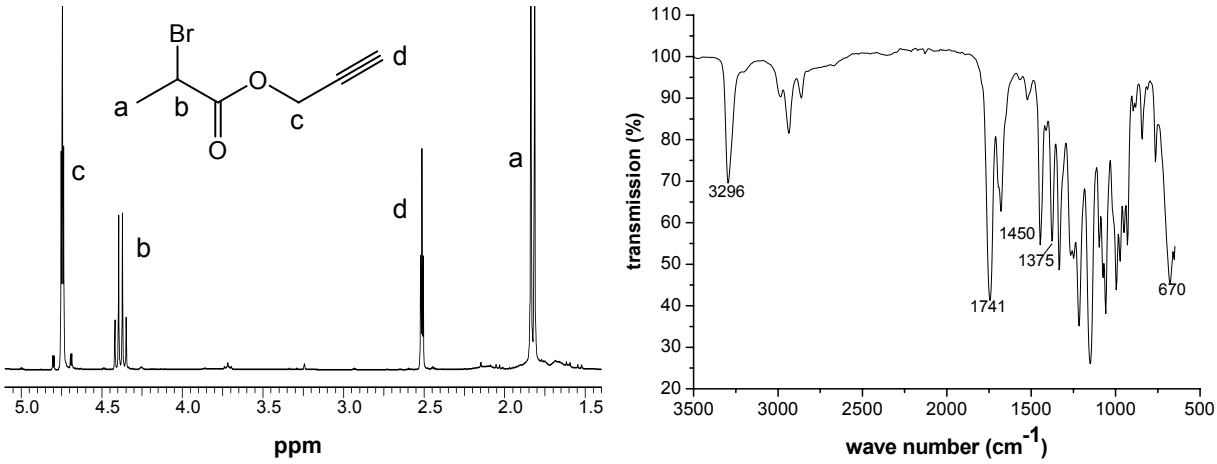


**Figure VIII-3** **left: $^1$H NMR spectrum ($CDCl_3$, 300 MHz); right: IR spectrum (right) of propargyl 2-bromopropionate.**

Both the $^1$H NMR and IR spectrum confirm the synthesis of the desired compound. The IR spectrum clearly shows the characteristic alkyne C-H stretch at 3296 cm$^{-1}$. Other characteristic absorptions: C-H stretch at 2860-3000 cm$^{-1}$, C=O (ester) at 1741 cm$^{-1}$, $CH_3$

bending at 1450 and 1375 $cm^{-1}$, C-O (ester) at 950-1300 $cm^{-1}$, and C-Br stretch at 670 $cm^{-1}$.

### VIII.2.2. ATRP of EEA with alkyne-containing initiator

The PAA segments for the synthesis of the block- and comb copolymers are prepared with EEA as the protected monomer (see also Chapter V). Polymerizations were carried out using Cu(I)Br as the catalyst in combination with PMDETA as the ligand. Propargyl 2-bromopropionate was used to introduce the desired alkyne functionalities. The amount of catalyst relative to the initiator concentration, the theoretical degree of polymerization ($DP_{th}$, $[M]_0/[In]_0$) and the polymerization temperature were varied to optimize the polymerization conditions (see Table VIII-1).

**Table VIII-1** **Summary of the reaction conditions and results of the polymerizations of EEA using propargyl 2-bromopropionate as the alkyne-containing initiator by ATRP.**

| Entry[a] | $[M]_0/[In]_0/[Cu]_0/[ligand]$[b] | Temp. (°C) | Time (min) | Conv.[c] (%) | $M_{n,th}$ ($g.mol^{-1}$) | $M_{n,exp}$[d] ($g.mol^{-1}$) | $M_w/M_n$[d] |
|---|---|---|---|---|---|---|---|
| HP7B1 | 50/1/2/2 | 50 | 306 | 23 | 2000 | 3000 | 1.33 |
| HP7R1 | 50/1/1/1 | 60 | 391 | 49 | 3700 | 5300 | 1.29 |
| HP7P1 | 50/1/1/1 | 70 | 300 | 81 | 6000 | 8200 | 1.34 |
| HP7Q1 | 100/1/1/1 | 70 | 378 | 42 | 6200 | 6100 | 1.17 |
| HP7Q2 | 100/1/1/1 | 70 | 300 | 38 | 5600 | 6700 | 1.12 |
| HP7Q3 | 100/1/1/1 | 70 | 326 | 33 | 4900 | 4700 | 1.22 |
| HP7Q4 | 100/1/1/1 | 70 | 307 | 40 | 5900 | 4600 | 1.21 |

[a.] All polymerizations were performed in bulk, with propargyl 2-bromopropionate as initiator, Cu(I)Br as catalyst and PMDETA as ligand. [b.] $[M]_0$, $[In]_0$, $[Cu]_0$ and [ligand] = initial concentration of monomer, initiator, copper catalyst and ligand respectively. [c.] Calculated from $^1H$ NMR. [d.] relative to polystyrene standards.

For polymers with $DP_{th}$ = 50, higher conversions were obtained (up to about 80 %) with increasing polymerization temperature. Nevertheless, termination reactions during the early stages of the polymerization could not be avoided, as evidenced by the experimental average molecular weight ($M_{n,exp}$) being higher than the theoretical one ($M_{n,th}$) and the rather high polydispersity. By increasing the $DP_{th}$, the overall concentration of radicals in

the reaction medium is lowered and thus termination reactions are suppressed, resulting in a better accordance with the $M_{n,th}$. Best results for the polymerization were obtained at a temperature of 70 °C, with a ratio of initial concentration of monomer/ initiator/catalyst/ligand $[M]_0/[In]_0/[Cu]_0/[ligand]$ equal to 100/1/1/1. With these conditions, polymers with a low polydispersity ($M_w/M_n$) and a controlled molecular weight were obtained.

A kinetic study was carried out to further investigate the controlled behaviour of the polymerization reaction using this alkyne-containing initiator. Although the first order kinetic plot shows some deviation from linearity, the linear increase of the average molecular weight ($M_n$) as a function of conversion, narrow molecular weight distribution, and the symmetrical GPC curves reveal the controlled character of the polymerization (see Figure VIII-4). The deviation of the first order kinetic plot could be ascribed to poisoning of the Cu catalyst because of complexation of a small fraction of deprotected monomer or polymer with the copper species (as observed before, see Chapter V).

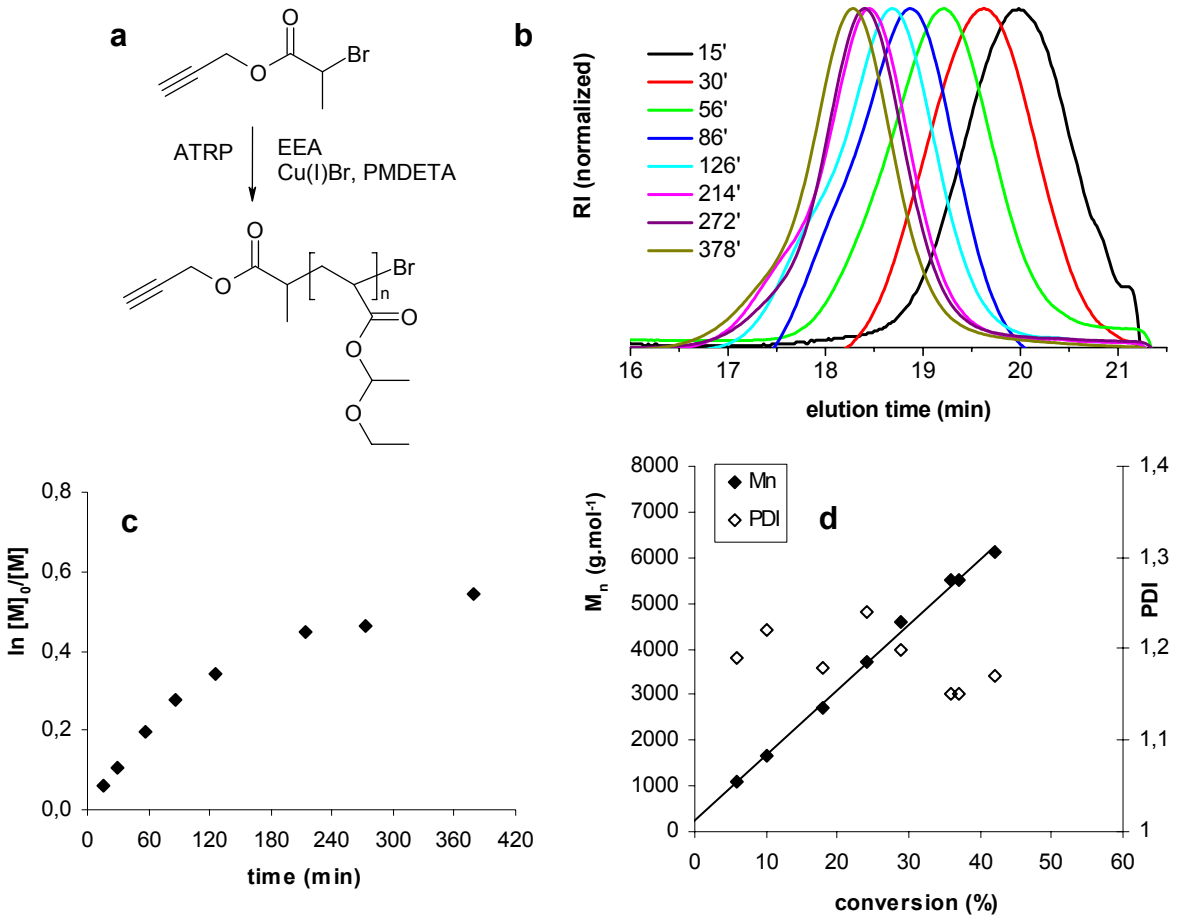


**Figure VIII-4** **ATRP of EEA using an alkyne-containing initiator (HP7Q1). (a) schematic depiction, (b) GPC analysis, (c) first order kinetic plot, (d) increase of $M_n$ and evolution of PDI as a function of conversion. (With trend line in graph (d)).**

As a conclusion, the polymerization of EEA with propargyl 2-bromopropionate shows to be an appropriate strategy for the preparation of polymers with a terminal alkyne functionality.

## *VIII.3. Synthesis of polymers with azide functionality*

Besides alkyne-functionalized polymers, also azide-containing polymers have to be prepared in order to be able to perform a "click" coupling reaction.

In case of the synthesis of block copolymers, the polymer segments should only bear one azide group. By "click" coupling with a polymer with a terminal alkyne function, a block copolymer is formed. The terminal azide group can be introduced in the polymer either by nucleophilic substitution or by making use of an azide-containing initiator (same strategy as in § VIII.2.2).

If the synthesis of comb copolymers is desired, a number of azide functionalities have to be incorporated into the polymer chain. This can be executed by creating a polymer chain with a number of azide functionalities into the polymer backbone, e.g. by copolymerizing an azide-containing monomer with any other monomer. In our case, isobornyl acrylate (iBA) is used as the second monomer. By coupling with an alkyne-containing polymer, the comb copolymers are created.

### VIII.3.1. Terminal azide functionality

Two methods are proposed for the synthesis of polymers with one azide functionality: the bromine chain ends of the polymers prepared *via* ATRP can be converted into an azide group by nucleophilic substitution, or an azide-containing initiator can be used for the synthesis of these polymers.

#### VIII.3.1.1. Nucleophilic substitution of bromine end group

One important issue for the synthesis of azide-terminated polymer chains *via* nucleophilic substitution of the bromine end group is that the polymers need to have a high degree of end group functionality. Every polymer chain that does not contain a bromine atom at the end, will not dispose of an azide functionality.

As it is known from earlier studies that a high degree of end group functionality can be obtained with the synthesis of polyacrylates (> 90 %; see also Chapter VI), hydrophobic isobornyl acrylate (iBA) was chosen as the monomer. This particular acrylate was chosen because of the corresponding glass transition temperature ($T_g$) of the polymer is quite high, which makes purification of the polymers easy, as they can be obtained by simple precipitation (in methanol). Although polystyrene (PS) and poly(methyl methacrylate) (PMMA) also exhibit a high $T_g$, a high degree of end group functionality is difficult to obtain.[25, 37, 38] For more details on PiBA polymers, we refer to Chapter VI.

Table VIII-2 summarizes the reaction conditions and the results for the PiBA polymers that were subsequently used for the further substitution of the bromine end group to an azide end group.

**Table VIII-2 Summary of the reaction conditions and results of the polymerizations of iBA to yield PiBA-Br that was subsequently transformed to PiBA-$N_3$.**

| Entry[a] | $[M]_0/[In]_0/[Cu]_0/[ligand]$[b] | Temp. (°C) | Time (min) | Conv.[c] (%) | $M_{n,th}$ (g.mol$^{-1}$) | $M_{n,exp}$[d] (g.mol$^{-1}$) | $M_w/M_n$ |
|---|---|---|---|---|---|---|---|
| AzHP14F3 | 200/1/0.5/0.5 | 90 | 60 | 33 | 7000 | 7700 | 1.32 |
| AzHP14I1 | 100/1/0.5/0.5 | 90 | 120 | 33 | 3700 | 10400 | 1.31 |

[a.] All polymerizations were performed in 25 v% of ethyl acetate as solvent, with methyl 2-bromopropionate as initiator, Cu(I)Br as catalyst and PMDETA as ligand. [b.] $[M]_0$, $[In]_0$, $[Cu]_0$ and [ligand] = initial concentration of monomer, initiator, copper catalyst and ligand respectively. [c.] Calculated from $^1$H NMR. [d.] A conversion factor of 1.4 relative to polystyrene standards was applied.

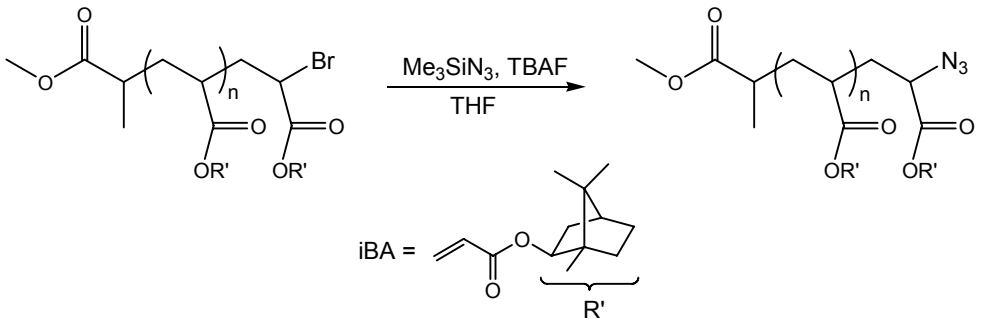


**Figure VIII-5 Transformation of the bromine end group of PiBA to an azide by nucleophilic substitution.**

Nucleophilic substitution of the bromine end groups of PiBA was performed by reaction with azidotrimethylsilane ($Me_3SiN_3$) and tetrabutylammonium fluoride (TBAF) in tetrahydrofuran (THF) as the solvent (see Figure VIII-5).[35] The role of TBAF is to bring the nucleophilic azide anion in the organic phase, so that substitution of the bromine can occur. This increases the reaction speed and makes the reaction proceed at room temperature.

$^1$H NMR spectroscopy was used to check the transformation of bromine into an azide functionality. The $^1$H NMR spectra of PiBA-Br and PiBA-$N_3$ are shown in Figure VIII-6.

The multiplet that arises from the proton next to the bromine group of PiBA-Br completely disappears after the azidation reaction. On the other hand, the $^1$H NMR spectrum of the PiBA-$N_3$ end product shows a signal that arises from the proton next to the azide functionality.

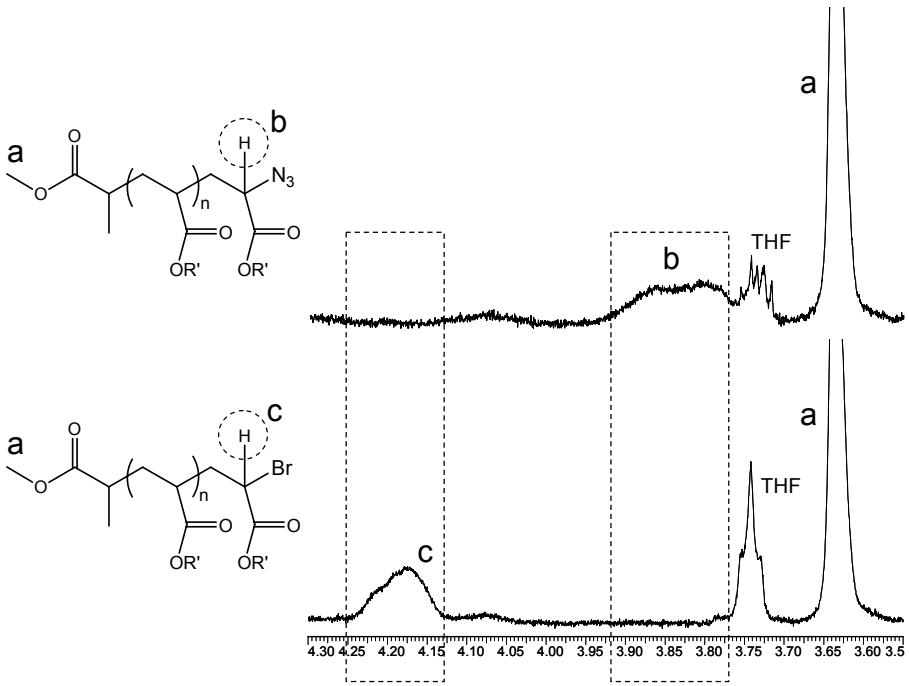


**Figure VIII-6 Transformation of PiBA-Br into PiBA-$N_3$ (AzHP14F3), as evidenced by $^1$H NMR ($CDCl_3$, 500 MHz).**

### VIII.3.1.2. Use of azide containing initiator: 2-(2-azidoethoxy) ethyl bromoisobutyrate

Another strategy that has been employed to obtain a polymer with a terminal azide is the use of an azide-containing initiator. The advantage of the use of a functional initiator is that all polymer chains contain the desired functionality, whether the bromine end group is

preserved during the polymerization or not. In addition, this strategy implies that the azide functional polymers can be prepared in one single step: this strategy does not require an end group modification after the polymerization step.

The initiator 2-(2-azidoethoxy)ethyl bromoisobutyrate was kindly supplied by the research group of professor P. Dubois (University of Mons-Hainaut, Belgium).[39] iBA as well as EEA were polymerized using this initiator. The polymerization conditions and results are summarized in Table VIII-3.

**Table VIII-3** **Summary of the reaction conditions and results of ATRP of acrylates with 2-(2-azidoethoxy)ethyl bromoisobutyrate as azide-containing initiator.**

| Entry[a] | Monomer | $[M]_0/[In]_0/[Cu]_0/[ligand]$[b] | Temp. (°C) | Time (min) | Conv.[c] (%)[c] | $M_{n,exp}$[d] ($g.mol^{-1}$) | $M_w/M_n$ |
|---|---|---|---|---|---|---|---|
| HP14N3A1[e] | iBA | 50/1/2/2 | 50 | 120 | - | 3400 | 1.54 |
| HP7N3A1[f] | EEA | 50/1/1/1 | 60 | 160 | 54 | 6400 | 1.28 |

[a.] All polymerizations were performed with methyl 2-bromopropionate as initiator, Cu(I)Br as catalyst and PMDETA as ligand. [b.] $[M]_0$, $[In]_0$, $[Cu]_0$ and [ligand] = initial concentration of monomer, initiator, copper catalyst and ligand respectively. [c.] Calculated from $^1H$ NMR. [d.] Relative to polystyrene standards. [e.] Polymerization of isobornyl acrylate. [f.] Polymerization of 1-ethoxyethyl acrylate.

The polymerization of iBA with this initiator yielded a polymer with a relatively high polydispersity (1.54) (Table VIII-3, HP14N3A1). Apparently the reaction conditions were not optimal, and have to be further optimized.

Better results were obtained when EEA was polymerized (Table VIII-3, HP7N3A1). In this case, reaction conditions were selected according to the results that were obtained with the alkyne functionalized initiator. Figure VIII-7 shows the first order kinetic plot, and the increase of the average molecular weight ($M_n$) as a function of conversion while the polydispersity remains narrow. However, a small amount of chain coupling could be observed in the GPC analysis (see Figure VIII-7, b).

It can be concluded that the use of an azide-containing initiator is a suitable strategy to prepare polymers with a terminal azide functionality.

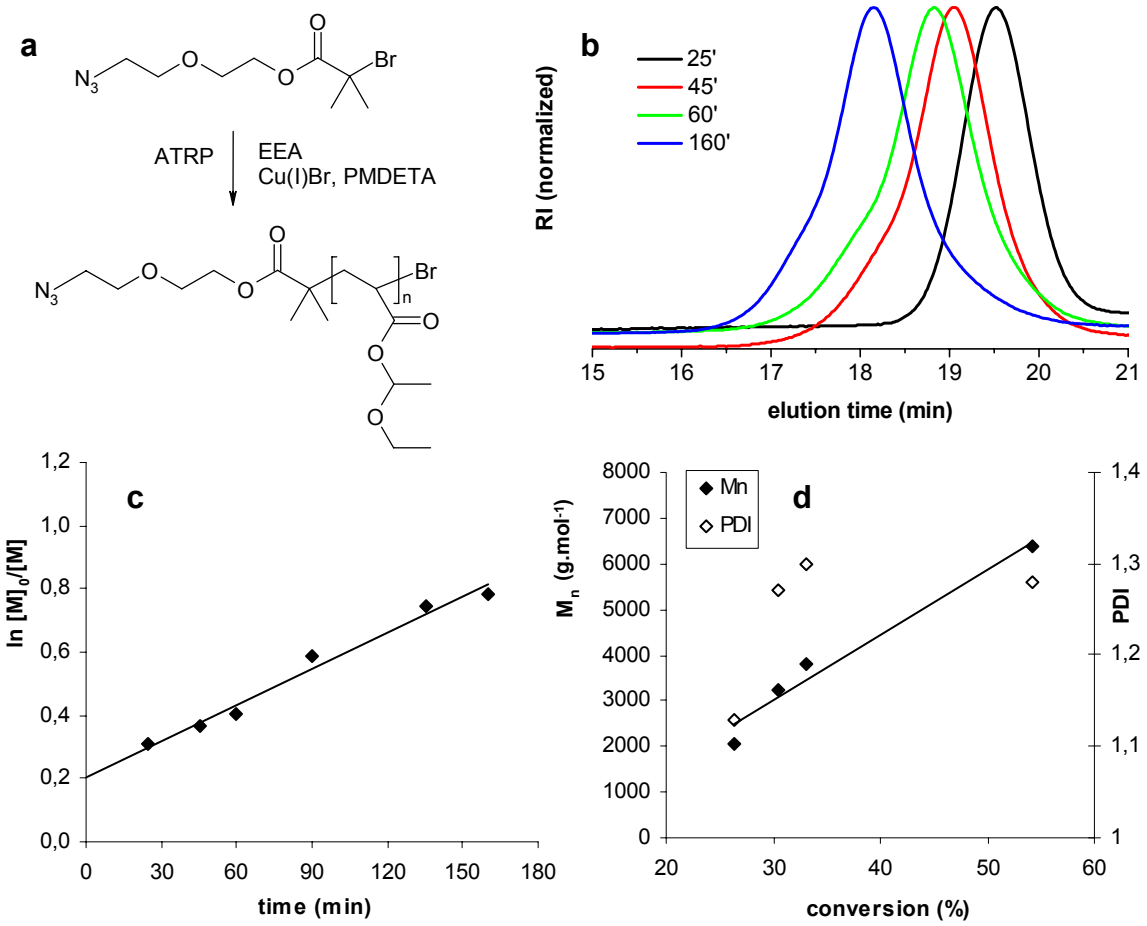


**Figure VIII-7** **ATRP of EEA using an azide-containing initiator (Table VIII-3, HP7N3A1). (a) schematic depiction, (b) GPC analysis, (c) first order kinetic plot, (d) increase of $M_n$ and evolution of PDI vs. conversion. (With trend line in graph (c) and (d)).**

## VIII.3.2. Multiple azide functionalities

In order to synthesize comb copolymers, a polymer backbone with multiple (pendant) azide groups will be "click" coupled with alkyne-terminated polymer chains. The polymer backbone is prepared by copolymerization of 3-azidopropylmethacrylate (AzMA), as the azide-containing monomer, and isobornyl acrylate as the second monomer.

### VIII.3.2.1. Synthesis of 3-azidopropyl methacrylate (AzMA)

The synthesis of AzMA is a two step reaction (see Figure VIII-8).[18] The first step consist of the preparation of 3-azidopropanol by nucleophilic substitution of the chlorine atom of 3-chloropropanol *via* reaction with sodium azide. The azide anion is driven into

the organic phase by adding tetrabutylammonium hydrogen sulphate, which also increases the reaction speed. 3-azidopropanol is purified by distillation. In the second step 3-azidopropyl methacrylate is formed by addition of 3-azidopropanol to the carbonyl group of methacryloyl chloride (1.2 equivalents). Triethylamine is added to neutralize the acid (HCl) that is released.

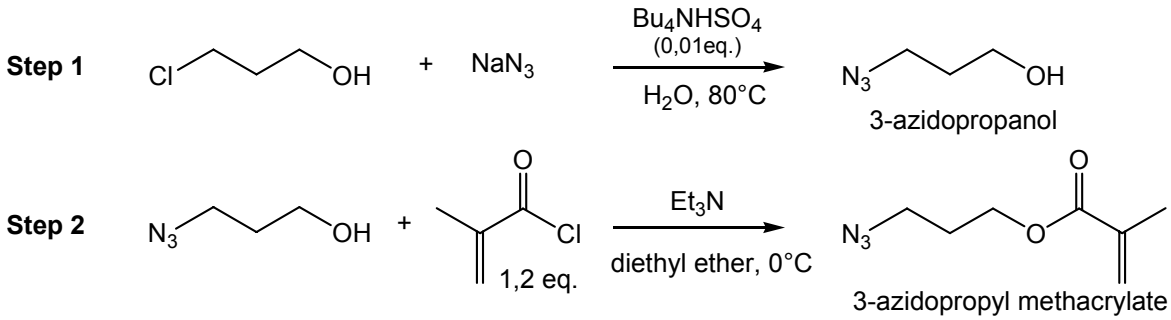


**Figure VIII-8 Synthesis of 3-azidopropyl methacrylate, a two step reaction.**

The $^{1}$H NMR spectrum shows that the desired compound is formed (see Figure VIII-9). Destillation was not performed because of safety reasons. Sumerlin *et al.* reported that special care should be taken not to heat the azide compound above 75-80 °C because it becomes shock-sensitive at elevated temperatures.[18]

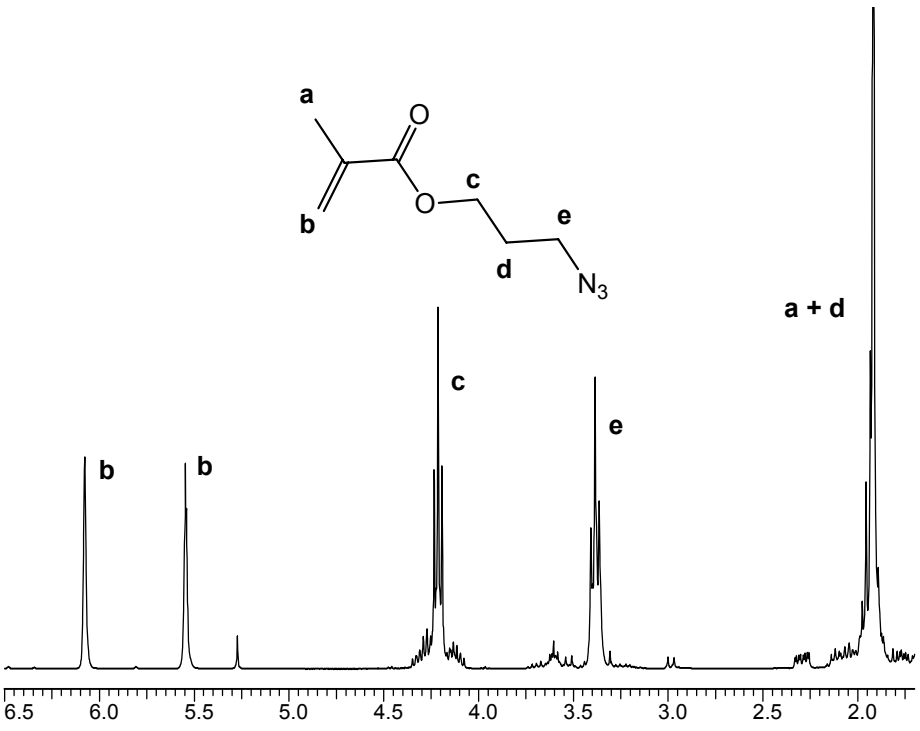


**Figure VIII-9 $^{1}$H NMR spectrum of 3-azidopropyl methacrylate ($CDCl_3$, 300 MHz)**

### VIII.3.2.2. Copolymerization of AzMA

For the preparation of the polymer backbone of the comb copolymer, iBA and AzMA are copolymerized to yield a random copolymer (see discussion further) containing multiple azide functionalities (see Figure VIII-10).

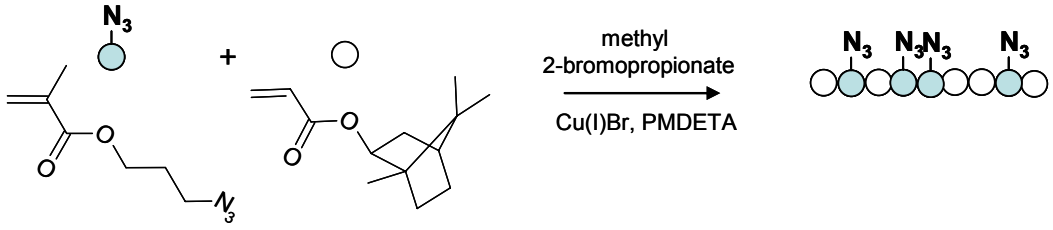


**Figure VIII-10 Schematic depiction of the copolymerization of iBA and AzMA to yield a random copolymer containing multiple azide functionalities.**

Different ratios of iBA and AzMA were used in the starting mixture (ratio of iBA:AzMA 4:1 and 1:1 for reaction CPA1/CPA2 and CPB1, respectively). The reaction conditions and results of these experiments are shown in Table VIII-4. The reactions were performed in acetone as the solvent (25 v%) and Cu(I)Br/PMDETA was used as the catalyst complex.

**Table VIII-4 Summary of the reaction conditions and results of the copolymerizations of iBA and AzMA by ATRP.**

| Entry[a] | $[iBA]_0/[AzMA]_0/[In]_0/[Cu]_0/[ligand]$[b] | Temp. (°C) | Time (min) | Conv.[c] iBA (%) | Conv.[c] AzMA (%) | Composition[d] | $M_{n,exp}$[e] ($g.mol^{-1}$) | $M_w/M_n$ |
|---|---|---|---|---|---|---|---|---|
| CPA1 | 60/15/1/2/2 | 50 | 273 | 39 | 75 | $iBA_{24}$/ $AzMA_9$ | 3700 | 1.23 |
| CPA2 | 60/15/1/2/2 | 50 | 240 | 40 | 87 | $iBA_{24}$/ $AzMA_{12}$ | 5000 | 1.32 |
| CPB1 | 38/38/1/2/2 | 50 | 180 | 30 | 61 | $iBA_{12}$/ $AzMA_{23}$ | 9600 | 1.57 |

[a.] All polymerizations were performed in 25 v% of acetone as solvent, with methyl 2-bromopropionate as initiator, Cu(I)Br as catalyst and PMDETA as ligand. [b.] $[iBA]_0$, $[AzMA]_0$, $[In]_0$, $[Cu]_0$ and [ligand] = initial concentration of isobornyl acrylate, 3-azidopropyl methacrylate, initiator, Cu(I)Br catalyst and ligand respectively. [c.] Calculated from $^1H$ NMR. [d.] Calculated from conversion of both monomers. [e.] relative to polystyrene standards.

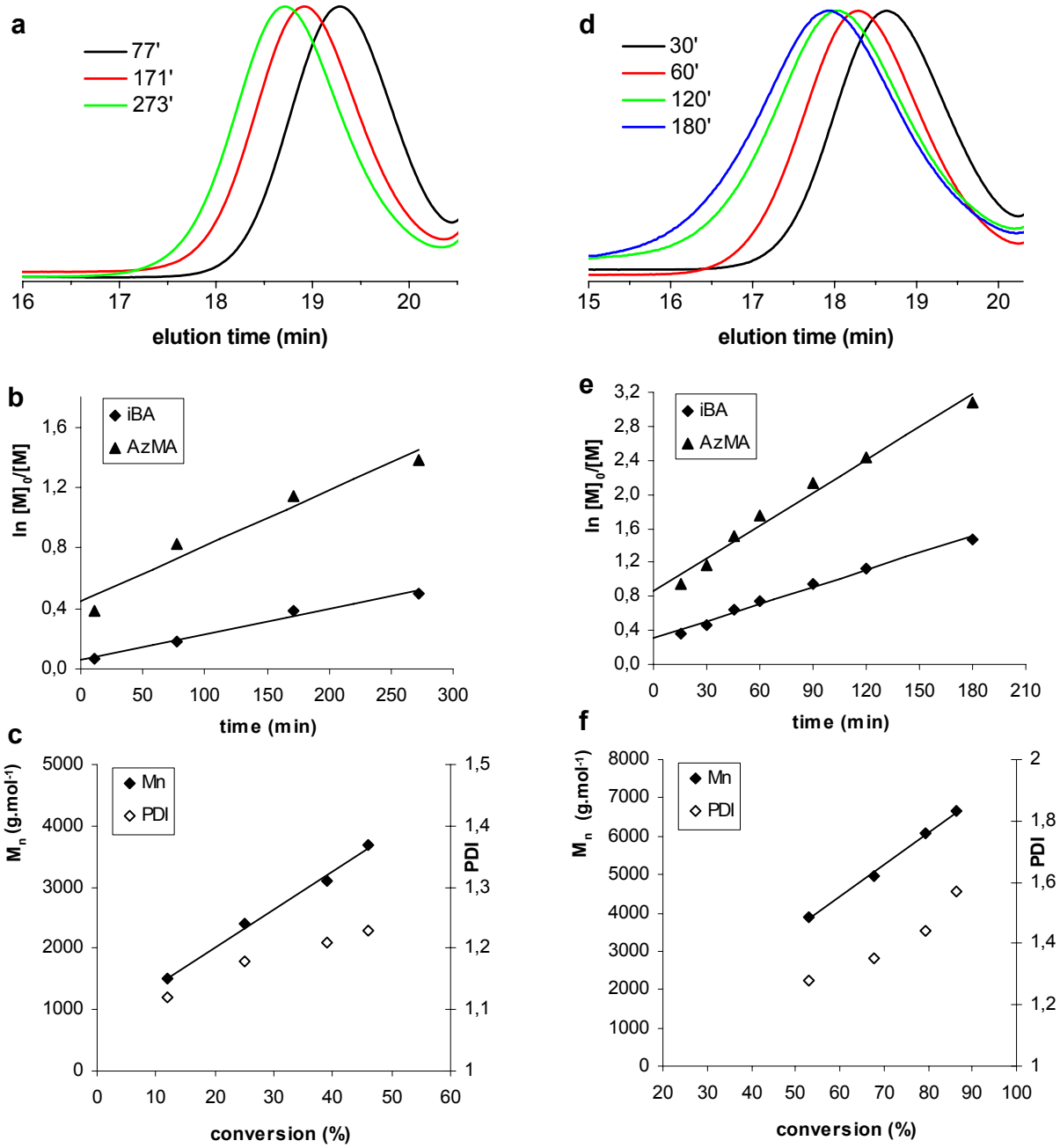


**Figure VIII-11** **GPC traces (a, d), first order kinetic plot (b, e), and increase of $M_n$ vs. conversion (c, f) of the copolymerization of iBA and AzMA (reaction CPA1 (left) and CPB1 (right), respectively).**

A kinetic run was performed for both reactions to check if the polymerizations proceeded in a controlled way. Both reaction CPA1/CPA2 and CPB1 turned out to be well-controlled (see Figure VIII-11 left and right, respectively), as evidenced by the linearity of the first order kinetic plot (for both monomers) and the linear increase of the $M_n$ versus total conversion (taking into account the relative amount of each monomer in the reaction mixture). The GPC traces reveal a unimodal molecular weight distribution, with a symmetrical shape.

However, the polydispersity is slightly higher than typically observed for ATRP reactions, and is increasing during the copolymerization reaction. The reason for this is probably the rather high conversion of AzMA, which polymerizes faster than the iBA monomer. Rather high polydispersities for PAzMA were also reported by Sumerlin *et al.*, and this was attributed to a slight amount of low molecular weight tailing or small degree of potential side reactions that are known to occur with azide moieties *via* either thermal or photochemical pathways.[18]

Because of the higher reactivity of AzMA compared to iBA, the result of the copolymerization reaction is in fact a gradient copolymer. Similar observations were made by other groups when copolymerizing methacrylates and acrylates.[40, 41] Thus, in the beginning of the reaction, AzMA is consumed a lot faster than the iBA; after a while less and less AzMA is available in the reaction mixture and as a result iBA will be incorporated more into the copolymer during the final stages of the polymerization.

## VIII.4. "Click" reactions with azide- and alkyne-containing polymers

After the synthesis of azide terminated and alkyne containing polymers, the synthesis of block and comb copolymers using the Cu(I) catalyzed "click" cycloaddition reaction was investigated. By combining hydrophilic PAA segments with hydrophobic polymer segments, we further extend the application of "click" chemistry toward the synthesis of amphiphilic polymer structures. As, just like for ATRP, the "click" 1,3 dipolar cycloaddition reaction is catalyzed by Cu(I) species, complexation with poly(acrylic acid) poisons the catalyst, thus preventing the reaction to take place. Again, the developed EEA-strategy circumvents these problems.

In addition, the main advantage of the "click" chemistry method is the intrinsic modular approach. This approach enables full analysis (e.g. molecular weight distribution) of the separate segments prior to coupling. This is in contrast to the synthesis of these polymers using the so-called macroinitiator approach or the sequential monomer addition method, where complete formation of block copolymers is hard to assess and characterization of the individual blocks is difficult.

In addition to the above mentioned advantages of the "click" chemistry approach, the synthesis of comb or brush copolymers may be simplified as well. For example, one way to obtain comb/brush copolymers is the (co)polymerization of macromonomers by ATRP, which is often complicated due to viscosity reasons and problems with quantitative end group transformations. Using the "click" chemistry strategy, the synthesis of comb/brush copolymers could be simplified to the synthesis of a (co)polymer containing "clickable" groups (the "backbone") on one hand, and the synthesis of a linear polymer containing a complimentary "clickable" end group (the actual brushes attached to the "backbone") on the other hand. Because of the power of the Cu(I) catalyzed "click" reaction, coupling of the segments can be performed in more attractive conditions (including lower viscosity of the reaction mixture and lower reaction temperatures) compared to conditions needed for the polymerization and end-group modifications necessary for the macromonomer strategy.

### VIII.4.1. Formation of block copolymers

For the synthesis of block copolymers *via* "click" chemistry is desired, an azide terminated poly(isobornyl acrylate) chain (PiBA-$N_3$) should be "click" coupled with a polymer chain that contains one single alkyne functionality, in this case poly(1-ethoxyethyl acrylate) (PEEA-≡ ). In this way, block copolymer structures are prepared making use of the modular "click" chemistry approach (see Figure VIII-12). After deprotection of the PEEA segment to PAA, the desired amphiphilic block copolymer is obtained.

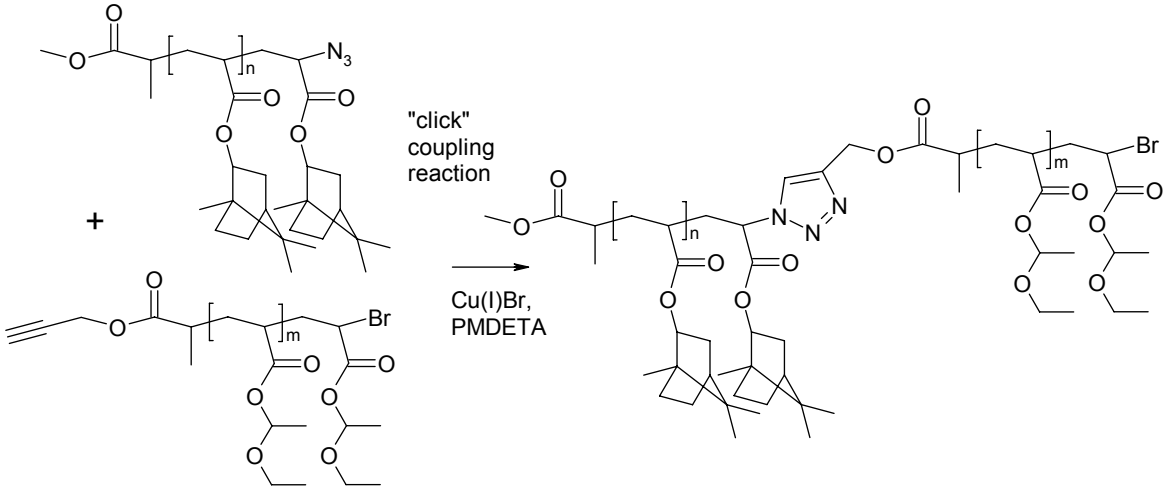


**Figure VIII-12 Formation of a poly(iBA-*b*-EEA) block copolymer by Cu(I) catalyzed "click" coupling reaction of PiBA-$N_3$ and PEEA-≡ .**

The results and data of the performed "click" reaction are given in Table VIII-5. A model experiment was performed at room temperature in THF as the solvent, with [PiBA-$N_3$]/[PEEA-≡] = 1 / 2. Cu(I)Br in combination with PMDETA acted as the catalyst complex.[24] In a recent study, it was found that the use of PMDETA as the ligand showed the highest catalytic activity relative to those of other metal complexes.[36] A three-fold excess of Cu(I)Br and ligand relative to alkyne end groups was used, according to literature conditions.[25]

**Table VIII-5 Summary of the data and results of the "click" coupling reaction between PiBA-N3 and PEEA-≡ , yielding a block copolymer.**

| Entry | $M_n/M_p/PDI^a$ PiBA-$N_3$[b] | $M_n/M_p/PDI^a$ PEEA-≡ [c] | $M_n/M_p/PDI^a$ coupled product[d] | Composition[e] coupled product |
|---|---|---|---|---|
| CLC1 | 7400/9000/1.30 | 6700/7500/1.12 | 11500/14100/1.25 | $PiBA_{50}$-*b*-$PEEA_{43}$ |

[a.] relative to polystyrene standards. [b.] AzHP14I4. [c.] HP7Q2. [d.] after purification (removal of excess PEEA) [e.] Determined *via* $^1$H NMR analysis of the purified product by comparing the integration of PiBA and PEEA signals. $DP_n$ of PiBA was found by GPC analysis (applying a conversion factor of 1.4 (calibration of GPC was done with polystyrene standards)).

Coupling of the two polymer segments was proved by GPC analysis, as the coupled product reveals a shift towards higher molecular weight in comparison to the starting products. Figure VIII-13 (a) shows the GPC traces of the "click" coupling reaction CLC1 of PiBA containing an azide function and PEEA with a terminal alkyne function before the coupling reaction (0', mixture of start products), after 5 minutes (5'), and overnight. The GPC trace of the coupled product has a bimodal character, which is due to the excess of PEEA-≡ in the reaction mixture. Note that the coupling reaction is complete after 5 minutes, as no difference between the GPC analysis of a sample taken after 5 minutes or overnight can be observed.

After removal of the copper by filtration over an $Al_2O_3$ column, the excess of PEEA-≡ was removed by selective precipitation of the reaction mixture in cold methanol (methanol is a non-solvent for PiBA, and a good solvent for PEEA). Figure VIII-13 (b) shows the GPC analysis of the purified coupled product by selective precipitation in methanol. The unimodal character proves that the excess of PEEA was removed successfully.

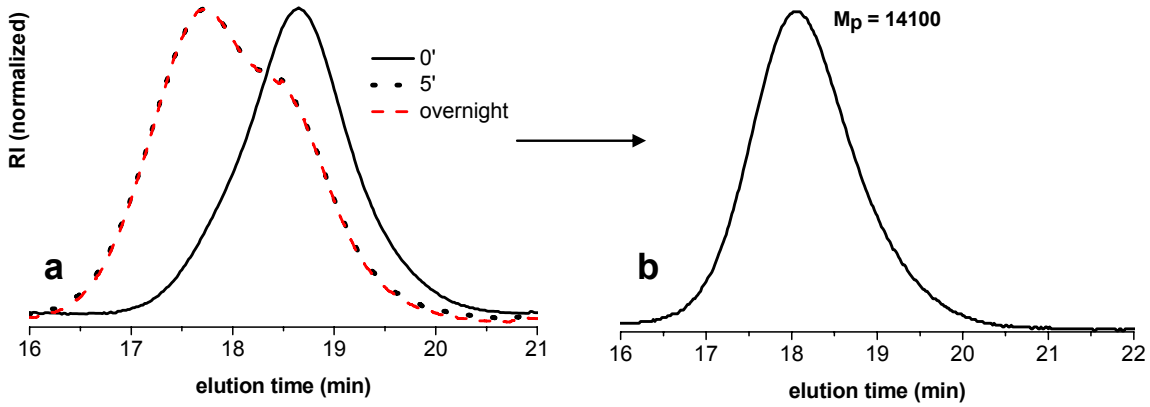


**Figure VIII-13** **(a) GPC traces of "click" coupling reaction CLC1 of a PiBA-$N_3$ and a PEEA-≡ polymer, before the coupling reaction (0', mixture of start products), after 5 minutes (5'), and overnight. (b) GPC trace of the "click" coupling reaction CLC1 after removal of the excess PEEA-≡ by selective precipitation in methanol.**

The $^1$H NMR spectrum of the purified "click" coupled product clearly shows the signals of the triazole link at 5.0-5.1, 5.15-5.3 and 7.65-7.75 ppm that have been formed starting from PiBA-$N_3$ and PEEA-≡ (see Figure VIII-14).

TGA analysis of the purified poly(iBA-*b*-EEA) sample showed an experimental weight loss of 18 % (see Figure VIII-15, solid line). The weight loss arises from the loss of ethyl vinyl ether during the deprotection of poly(iBA-*b*-EEA) to poly(iBA-*b*-AA) (see also Chapter V). Ethyl vinyl ether is a gaseous compound at elevated temperatures (boiling point = 33 °C). Integration of characteristic $^1$H NMR signals of PiBA (at 4.4-4.8 ppm) and PEEA (at 5.8-6.1 ppm) revealed a relative composition of PiBA/PEEA of 1 to 0.86. Taking into account the molar mass of PiBA, the relative composition of iBA and EEA in the block copolymer and the respective molecular weight of the monomers, the theoretical weight loss is 18.6 %. It can thus be concluded that the experimental and theoretical weight loss are in good agreement.

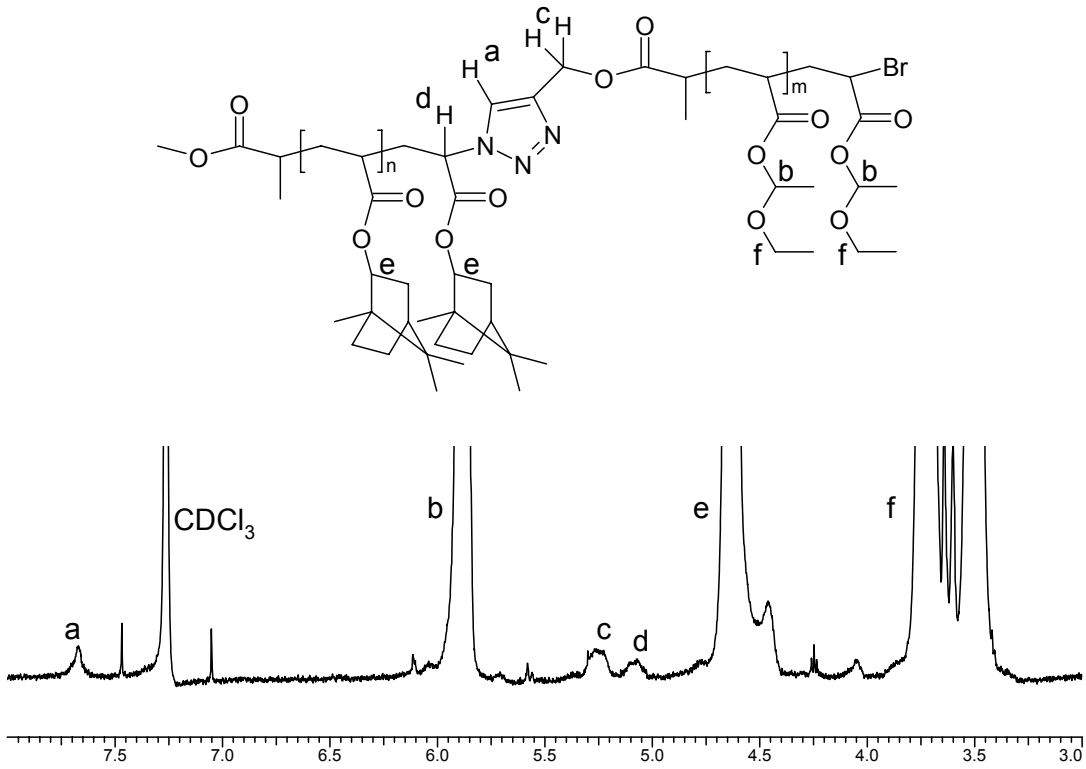


**Figure VIII-14** **$^1$H NMR spectrum of the product of “click” coupling reaction (CLC1) of PiBA-$N_3$ (HP14I4) and PEEA-≡ (HP7Q3) to yield a poly(iBA-*b*-EEA) block copolymer. (in $CDCl_3$, 500 MHz)**

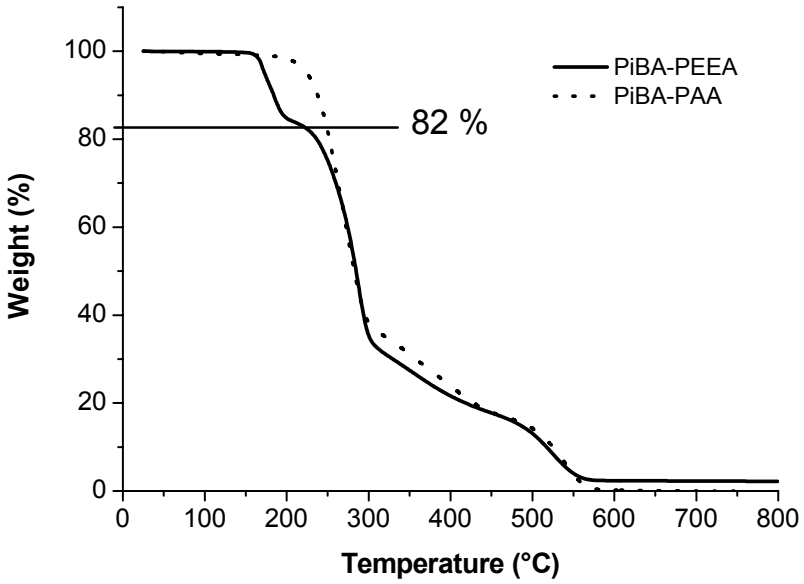


**Figure VIII-15** **TGA analysis of the “click” coupled poly(iBA-*b*-EEA) block copolymer before (solid line) and after deprotection (dotted line) by a heating process at 80 °C during 24 hours (reaction CLC1). Heating rate: 10 °C/min; air atmosphere.**

To obtain the amphiphilic block copolymer, deprotection of the PEEA segment to the desired PAA segment with loss of ethyl vinyl ether was carried out by a heating step. The polymer was spread out on a glass plate and was put in an oven at 80 °C during 24 hours. Complete deprotection of the poly(iBA-*b*-EEA) to poly(iBA-*b*-AA) is confirmed by TGA analysis of the obtained poly(iBA-*b*-AA), as no weight loss arising from deprotection could be observed (see Figure VIII-15, dotted line).

It can be concluded that the "click" chemistry approach is an easy, fast and straight forward strategy to synthesize block copolymers.

### VIII.4.2. Formation of comb/brush copolymers

Comb or brush copolymers can also be prepared *via* the "click" chemistry approach. In this case, the procedure consists of "clicking" a linear polymer that contains one alkyne functionality (this is the "side chain" of the brush) with another polymer that contains multiple azide functionalities (this is the "backbone" of the brush), as illustrated in Figure VIII-1.

In our case, poly(1-ethoxyethyl acrylate) with a terminal alkyne (PEEA-≡ , see §VIII.2.2) will be "click" coupled with a copolymer of isobornyl acrylate (iBA) and 3-azidopropyl methacrylate (AzMA) (see §VIII.3.2.2). After the "click" reaction, deprotection of the PEEA segments to the corresponding PAA segments by a simple heating procedure will provide the desired amphiphilic comb/brush copolymer structures, making use of the modular "click" chemistry approach.

Table VIII-6 summarizes the data and results of the performed "click" coupling reaction of a copolymer consisting of iBA and AzMA, and PEEA-≡ . The same reaction conditions were applied as for the "click" coupling reaction to form a block copolymer (see §VIII.4.1). The poly(iBA-*co*-AzMA) copolymer was mixed with 2 equivalents of PEEA-≡ with regard to the amount of azide groups (from AzMA) in the poly(iBA-*co*-AzMA) copolymer. Again, PMDETA was used as the ligand and a 3 times excess of Cu(I)Br relative to alkyne end groups was used.[25] After taking a sample of the starting mixture (time = 0') for GPC analysis, Cu(I)Br was added to start the coupling reaction.

**Table VIII-6 Summary of the results of the "click" coupling reaction between poly(iBA-*co*-AzMA) copolymer and PEEA-≡ , yielding a brush/comb copolymer.**

| Entry | $M_n/M_p/PDI^a$ copolymer poly(iBA-*co*-AzMA)[b] | $M_n/M_p/PDI^a$ PEEA-≡[c] | $M_n/M_p/PDI^a$ coupled product[d] | Composition coupled product[d, e] |
|---|---|---|---|---|
| CLD1 | 5000/6000/1.32 | 4700/5600/1.22 | 14400/16300/1.23 | $iBA_{24}/AzMA_{12}/(EEA_{32})_2$ |

[a.] relative to polystyrene standards. [b.] CPA2. [c.] HP7Q3. [d.] after purification (removal of excess PEEA). [e.] Determined *via* $^1$H NMR analysis of the purified product by comparing the integration of PiBA and PEEA signals. $DP_n$ of PiBA was found by GPC analysis (applying a conversion factor of 1.4 (calibration of GPC was done with polystyrene standards)).

GPC analysis proved coupling of the starting polymers, as the coupled product reveals a shift towards higher molecular weight in comparison to the start products (see data in Table VIII-6). The "click" coupling reaction was completed in 5 minutes. However, the GPC trace of the coupled product shows a bimodal shape as a result of the excess of PEEA-≡ that was used (see Figure VIII-16, dotted line). The excess of PEEA-≡ was removed by selective precipitation in cold methanol. GPC analysis proves the successful removal of the excess PEEA (Figure VIII-16, solid line).

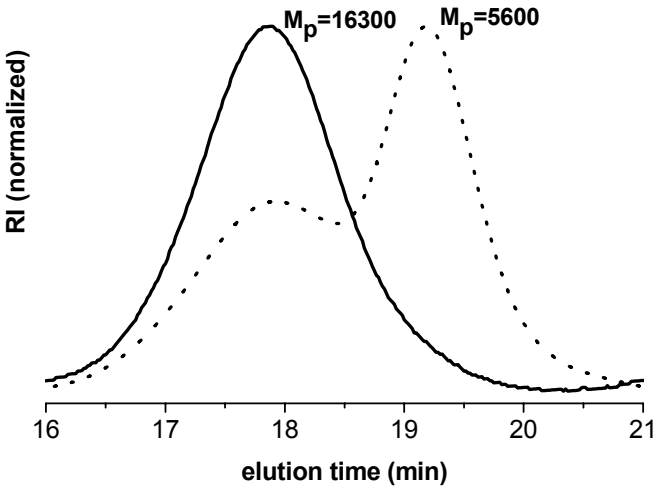


**Figure VIII-16 GPC trace of the "click" coupling reaction CLD1 before (dotted line) and after removal of the excess PEEA-≡ by selective precipitation in methanol (solid line).**

Taking into account the number of azide groups in the poly($iBA_{24}$-*co*-$AzMA_{12}$) copolymer, the molecular weight of the coupled product is lower than expected, although it is known that the molecular weight as obtained by GPC analysis is often underestimated

for brush/comb copolymers because of their lower hydrodynamic volume in comparison to linear polymers.

$^1$H NMR analysis of the purified coupled product revealed relative integrations for iBA and EEA of 1 to 2.7 (see Figure VIII-17). Taking into account the composition and the molecular weight of the poly(iBA$_{24}$-*co*-AzMA$_{12}$) copolymer and PEEA$_{32}$-≡ , this means that only an average of 2 PEEA$_{32}$-≡ chains are "click" coupled to the poly(iBA$_{24}$-*co*-AzMA$_{12}$) backbone.

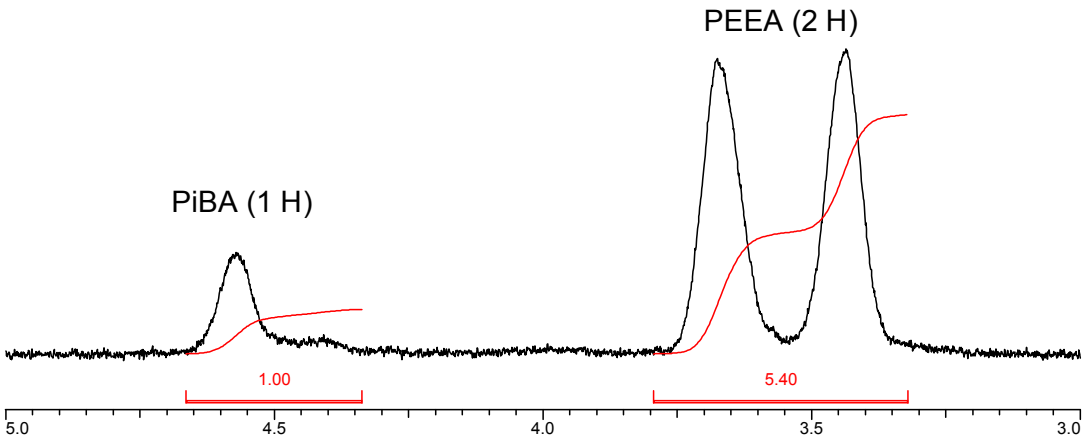


**Figure VIII-17 $^1$H NMR spectrum of the purified "click" coupled product of PEEA-≡ (HP7Q3) and poly(iBA$_{24}$-*co*-AzMA$_{12}$) (CPA2) copolymer (reaction CLD1).**

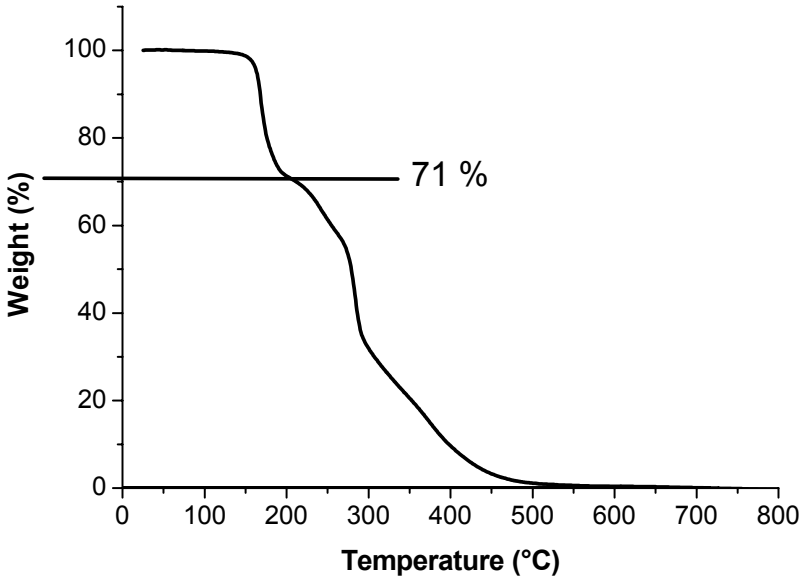


**Figure VIII-18 TGA analysis of the "click" coupled PiBA-PEEA comb/brush copolymer (CLD1). Heating rate: 10 °C/min.**

Further analysis of the coupled product with TGA shows an experimental weight loss of about 29 %, corresponding to the deprotection of the PEEA segments to PAA (see Figure VIII-18). Supposing that 2 $PEEA_{32}$-≡ chains have "click" coupled to the poly($iBA_{24}$-*co*-$AzMA_{12}$) backbone, a theoretical weight loss of 28.6 % is calculated (= residual weight of 71.4 %).

From the good agreement of the results of both NMR and TGA analysis, and from the molecular weight of the coupled product that turned out to be lower than expected, it can be concluded that the "click" coupling reaction of $PEEA_{32}$-≡ to a poly($iBA_{24}$-*co*-$AzMA_{12}$) copolymer to yield a brush/comb copolymer was not successful.

The fact that only 2 PEEA-≡ chains have attached to the poly($iBA_{24}$-*co*-$AzMA_{12}$) copolymer backbone could be an indication for a strongly limited accessibility of the $N_3$ functionalities, which would explain the fact that only 2 PEEA-≡ polymer chains have "clicked" to the poly($iBA_{24}$-*co*-$AzMA_{12}$) backbone.

Two plausible reasons for this unexpected result could be considered:

- Because of the higher reactivity of AzMA compared to iBA (see §VIII.3.2.2), AzMA is incorporated more into the copolymer during the early stages of the copolymerization reaction. As a result, the azide functions are concentrated at one chain end of the poly($iBA_{24}$-*co*-$AzMA_{12}$) backbone, which possibly limits the accessibility of the azide functions. If one PEEA-≡ chain is already attached in this region, one could expect further loss of accessibility because of additional steric hindrance.
- The accessibility of the azide functionalities is limited because of the bulkyness of the isobornyl side group of iBA itself.

To check if these assumptions are right, a copolymer of MMA and AzMA was synthesized (reaction CPC1, see Table VIII-7). The same conditions that were applied for the synthesis of the poly(iBA-*co*-AzMA) copolymer were used (see CPA1/2, Table VIII-4). With the copolymerization of MMA and AzMA, a more equally distribution of AzMA along the PMMA backbone is obtained, as the monomers are both methacrylate monomers, having a similar reactivity. The equal reactivity of both methacrylate monomers is confirmed by the similar conversion that was obtained for both monomers

(see Table VIII-7). On the other hand, the methyl group of MMA, which is less bulky than the isobornyl group of iBA, is supposed to give rise to a highly increased accessibility of the azide functionalities of the poly(MMA-*co*-AzMA) backbone.

**Table VIII-7 Summary of the reaction conditions and results of the copolymerization of MMA and AzMA by ATRP.**

| Entry[a] | $[MMA]_0/[AzMA]_0/[In]_0/[Cu]_0/[ligand]$[b] | Temp. (°C) | Time (min) | Conv.[c] MMA (%) | Conv.[c] AzMA (%) | Composition[d] | $M_{n,exp}$[e] ($g.mol^{-1}$) | $M_w/M_n$ |
|---|---|---|---|---|---|---|---|---|
| CPC1 | 60/15/1/0.5/0.5 | 50 | 60 | 48 | 47 | $MMA_{39}$/ $AzMA_9$ | 7000 | 1.25 |

[a.] Polymerization was performed in 25 v% of acetone as solvent, with ethyl 2-bromoisobutyrate as initiator, Cu(I)Br as catalyst and PMDETA as ligand. [b.] $[MMA]_0$, $[AzMA]_0$, $[In]_0$, $[Cu]_0$ and [ligand] = initial concentration of methyl methacrylate, 3-azidopropyl methacrylate, initiator, Cu catalyst and ligand respectively. [c.] Calculated from $^1H$ NMR. [d.] Composition was determined from $^1H$ NMR analysis of the purified product, taking into account an initiator efficiency of 75 %. [e.] relative to polystyrene standards.

Subsequently, "click" coupling reaction CLE1 was performed to "click" the PEEA-≡ polymer with the poly($MMA_{39}$-co-$AzMA_9$) backbone, under similar conditions as the previous reactions. Table VIII-8 shows the data of the starting products and the coupled product of reaction CLE1. From a comparison of the $M_n$ or $M_p$ values of the poly($MMA_{39}$-co-$AzMA_9$) copolymer, the PEEA-≡ and the coupled product, it can be concluded that the "click" coupling reaction proceeded successfully. Moreover, the high molecular weight of the coupled product proves that, in contrast to the coupling reaction with poly(iBA-*co*-AzMA), the coupling of PEEA-≡ with the azide groups of poly($MMA_{39}$-co-$AzMA_9$) was nearly quantitative. It can be concluded that the azide groups did not show a limited accessibility in this case. Figure VIII-19 proves that the reaction was again completed in a very short time interval of less than 5 minutes, as evidenced by comparison of the GPC analysis of a sample taken just before addition of Cu(I)Br to the reaction mixture (0') and samples taken at 5 and 60 minutes (5', 60') after addition of Cu(I)Br.

**Table VIII-8** **Summary of the results of the "click" coupling reaction between poly(MMA-*co*-AzMA) and PEEA-≡ , yielding a brush/comb copolymer.**

| Entry | $M_n/M_p/PDI^a$ copolymer poly(MMA-*co*-AzMA)[b] | $M_n/M_p/PDI^a$ PEEA-≡ [c] | $M_n/M_p/PDI^a$ coupled product |
|---|---|---|---|
| CLE1 | 7000/9900/1.25 | 4600/5400/1.21 | 37100/46900/1.27 |
| CLF1 | 7000/9900/1.25 | 4600/5400/1.21 | 35200/41500/1.27 |

[a.] relative to polystyrene standards. [b.] CPC1. [c.] HP7Q4.

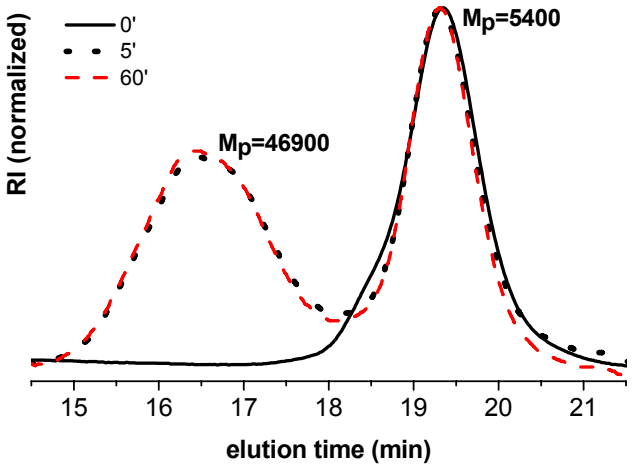


**Figure VIII-19** **GPC traces of "click" coupling reaction CLE1 of a poly(MMA-*co*-AzMA) copolymer (CPC1) and a PEEA-≡ polymer (HP7Q4), before the coupling reaction (0'), after 5 minutes (5'), and after 60 minutes (60').**

In a next experiment "click" coupling reaction CLF1 (see Table VIII-8), the copper concentration was lowered 10 times in comparison to reaction CLE1, while the experiment was still performed at room temperature. Figure VIII-20 shows the GPC analysis of the samples taken during the reaction. No significant difference between the molecular weights of the 2 coupled products could be observed. However, it seems that after five minutes, the coupling reaction is not yet fully completed with this lower concentration of copper, as a (small) additional increase of the peak molecular weight ($M_p$) can be noted in the analysis of the samples taken at a longer reaction time. Anyhow, GPC analysis indicates very similar molecular weights for both reactions (Table VIII-8). Also in this case, a bimodal GPC curve is obtained after the coupling reaction because an excess of PEEA-≡ was used. Unfortunately, because of the high PEEA content of the resulting comb/brush copolymer,

selective precipitation to seperate the comb/brush copolymer from the PEEA-≡ was not possible.

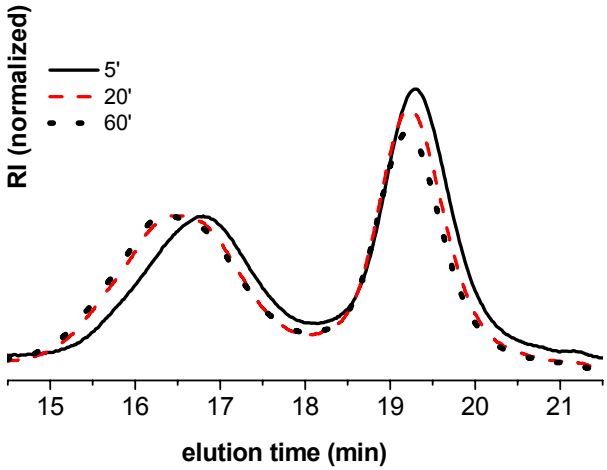


**Figure VIII-20** **GPC traces of “click” coupling reaction CLF1 of poly(MMA-*co*-AzMA) (CPC1) and a PEEA-≡ polymer (HP7Q4) at 5, 20 and 60 minutes (5’, 20’, 60’).**

To our knowledge, this is the first example of the controlled synthesis of a comb/brush copolymer using ATRP and the “click” coupling strategy. The only report found on the combination of “click” chemistry and controlled synthesis of comb/brush copolymers was published by Parrish *et al*[16]. His research group reported on the preparation of poly(ethylene glycol) and peptide-grafted aliphatic polyesters. Novel aliphatic polyesters with pendant acetylene groups were synthesized by controlled ring-opening polymerization that were subsequently used for grafting poly(ethylene glycol) and oligopeptide moieties by Cu(I) catalyzed addition of azides and alkynes.[16] With regard to this report, using ATRP significantly broadens the range of accessible comb/brush copolymers, as only a strictly limited number of monomers are polymerizable *via* the ring opening polymerization technique. Moreover, using ATRP for the preparation of the sidechain polymer not only offers the opportunity to graft polymers with different properties onto the backbone but also to introduce various architectures (e.g. block copolymers) into the side chain of the graft copolymers.

## VIII.5. Conclusion

In this chapter, the combination of ATRP of EEA and the copper(I) catalyzed "click" 1,3-dipolar cycloaddition reaction of azides and terminal alkynes was evaluated as a method to synthesize amphiphilic polymer structures, using a modular approach.

First, it was demonstrated that ATRP is a particularly suitable polymerization technique for combination with the "click" 1,3-dipolar cycloaddion reaction of azides and terminal alkynes, as it permits to introduce both alkyne and azide functionalities into a polymer chain. Alkyne functionalities were introduced *via* an alkyne containing initiator, while azide functionalities can be obtained either *via* nucleophilic substitution of the bromine end group into an azide, the use of an azide containing initiator or copolymerization with an azide containing monomer. The controlled behaviour of the polymerization reactions was demonstrated. The azide containing monomer AzMA was copolymerized with either iBA or MMA. In the first case, a spontaneous gradient copolymer was obtained, while the latter case yielded a statistically random copolymer.

Block copolymers were obtained by "clicking" PEEA-≡ with PiBA-$N_3$. The reaction showed to be both quantitative and fast. After selective precipitation (PEEA-≡ was used in excess) and deprotection of the PEEA segment to PAA, the desired amphiphilic block copolymer was obtained.

Amphiphilic comb/brush copolymers were successfully prepared by "clicking" linear PEEA-≡ onto a polymer containing multiple azide functions. In case of a poly(iBA-co-AzMA) copolymer, only a limited amount of PEEA-≡ chains were able to "click" onto the Poly(iBA-co-AzMA) copolymer, which was attributed to sterical hindrance of the attached PEEA chains as a result of the distinct reactivity of iBA and AzMA in the ATRP copolymerization. When PEEA-≡ chains were "clicked" onto a poly(MMA-*co*-AzMA) copolymer, quantitative coupling was observed. In addition, the "click" coupling reactions were found to be surprisingly fast (about 5 minutes reaction time), even at low copper concentration (0.3 equivalent to alkyne functions).

It has been shown that the combination of ATRP and the copper(I) catalyzed "click" 1,3 dipolar cycloaddion reaction of azides and terminal alkynes is a powerful tool for the modular synthesis of block copolymers and comb/brush copolymers. Using our EEA strategy, the application field was broadened with the synthesis of amphiphilic polymer

structures with PAA segments. For the first time, comb/brush copolymers were synthesized by a combination of ATRP and "click" chemistry.

## VIII.6. Acknowledgement

Thanks to L. Mespouille, P. Degée and P. Dubois for their kind donation of 2-(2-azidoethoxy)ethyl bromoisobutyrate.

## VIII.7. Experimental part

### VIII.7.1. Materials

Isobornyl acrylate (iBA, Aldrich, tech.) was purified by vacuum distillation (121 °C/18 mmHg). 1-Ethoxyethyl acrylate (EEA) was synthesized by the acid catalyzed addition reaction of acrylic acid to ethyl vinyl ether as described previously[42-44], and purified by vacuum distillation (30 °C/7 mbar). Cu(I)Br (Aldrich, 98 %) was purified by stirring with acetic acid, then by filtering and washing with ethanol and diethylether, and finally by drying in a vacuum oven at 70 °C.[45] *N,N,N′,N″,N″*-pentamethyldiethylenetriamine (PMDETA, Acros, 99 +%) was distilled (85-86 °C/12 mmHg). Methyl-2-bromopropionate (MBP, Acros, 99 %), ethyl 2-bromoisobutyrate (Aldrich, 98 %), dimethyl 2,6-dibromoheptanedioate (BHD, Aldrich, 97 %), propargyl alcohol (Aldrich, 99 %), 2-bromopropionic acid (Acros, 99 %), *N, N'*-dicyclohexylcarbodiimide (DCC, Acros, 99 %), 4-dimethylaminopyridine (4-DMAP, Acros, 99 %), azidotrimethyl silane (Acros, 97 %), tetrabutyl ammoniumfluoride (1.0 M solution in THF, 99 %), sodium azide (Aldrich, 99.5 %), tetrabutyl ammonium hydrogen sulphate (Acros, 98 %), hydroquinone (Fluka, 99 %) and (trimethylsilyl)diazomethane (2.0 M solution in diethyl ether, Aldrich) were used as received. Solvents were purchased from Aldrich (HPLC grade) and used without purification. All other chemicals were used as received.

### VIII.7.2. Characterization

**$^1$H NMR** spectra were recorded in $CDCl_3$ at room temperature, with a Bruker AM500 or a Bruker Avance 300 spectrometer.

**GPC analysis** was performed on a Waters instrument, using a refractive index detector (2410 Waters), equipped with Waters Styragel $10^3$-$10^4$-$10^5$ Å serial columns (5 μm particle size) at 35 °C. Polystyrene standards were used for calibration and $CHCl_3$ as eluent at a flow rate of 1.5 mL/min. GPC samples were injected using a Gilson autoinjector type 234.

**Infrared** spectra were obtained with React-IR 4000 instrument from Mettler Toledo.

**Thermogravimetric analysis** (TGA) was performed with a Mettler Toledo TGA/SDTA851e instrument under air atmosphere at a heating rate of 10 °C/min from 25 °C-800 °C.

### VIII.7.3. Synthesis of propargyl 2-bromopropionate: alkyne-containing initiator

10 mL (9.6 g, 0.17 mol) propargyl alcohol and 15.46 mL (26.3 g, 0.17 mol) 2-bromopropionic acid are dissolved in 100 mL of THF. The reaction mixture is cooled in an ice bath. A solution of 34.8 g DCC (0.17 mol) in 40 mL of THF is added slowly under continuous stirring. Next, a solution of 1.2 g 4-DMAP in 40 mL of THF is added during 10 minutes. The mixture is stirred during 1 hour at 0 °C and followed by 24 hours at room temperature. During the reaction, dicyclohexyl ureum is formed and precipitates. After the reaction time is completed, the dicyclohexyl ureum is filtered off and washed with THF. The solvent THF was removed, and propargyl 2-bromopropionate was obtained as a yellow viscous oil. Yield is 74 %.

### VIII.7.4. ATRP of EEA with propargyl 2-bromopropionate as the initiator

A typical polymerization procedure is as follows (e.g. reaction HP7Q1, Table VIII-1). A mixture of 0.0624 mol (9.0 mL) of the monomer EEA and $0.624 .10^{-3}$ mol (0.130 mL) of PMDETA as the ligand was added to a reaction flask and was bubbled with $N_2$ for 1h to remove oxygen from the reaction mixture. After that, Cu(I)Br ($0.624 .10^{-3}$ mol, 0.090 g) was added and the reaction flask was placed in an oil bath at 70 °C. When the reaction mixture reached the desired reaction temperature, the polymerization was started by adding $0.624 .10^{-3}$ mol (0.086 mL) of propargyl 2-bromopropionate as the initiator. Samples were withdrawn periodically to monitor the monomer conversion (by $^1$H NMR) and the average molecular weight (by GPC). The reaction was ended by cooling the reaction mixture in liquid nitrogen. The resulting polymer was dissolved in THF and the copper catalyst was

removed by passing the diluted reaction mixture over a column of neutral $Al_2O_3$. After evaporating the excess solvent, the residual monomer was removed by high vacuum.

## VIII.7.5. Nucleophilic substitution of the Br end group of polymers into an azide function

### VIII.7.5.1. Synthesis of PiBA-Br

A typical polymerization procedure is as follows (e.g. reaction AzHP14I4, Table VIII-2). A mixture of 0.1136 mol (24.0 mL) of the monomer iBA and 2.84 $.10^{-4}$ mol (0.059 mL) of PMDETA as the ligand was bubbled with $N_2$ for 1 h to remove oxygen. Ethyl acetate as the solvent was also bubbled with $N_2$ for 1 h to remove oxygen and 8 mL (25 v%) ethyl acetate was added to the reaction flask. Cu(I)Br (2.84 $.10^{-4}$ mol, 0.0407 g) was added under $N_2$ atmosphere, and the reaction flask was placed in an oil bath at 90 °C. When the reaction mixture reached the desired temperature, the polymerization was started by adding 5.68 $.10^{-4}$ mol (0.063 mL) of methyl-2-bromopropionate as the initiator. Samples were withdrawn periodically to monitor the monomer conversion (by $^1$H-NMR) and the average molecular weight $M_n$ (by GPC). The reaction was ended by cooling the reaction mixture in liquid nitrogen. The resulting polymer was dissolved in THF and the copper catalyst was removed by passing the diluted reaction mixture over a column of neutral $Al_2O_3$. After evaporating the excess solvent, the polymer was precipitated in methanol (10-fold excess).

### VIII.7.5.2. Substitution of PiBA-Br to PiBA-$N_3$

A typical substitution procedure is as follows. PiBA is dissolved in THF. 10 equivalents of azidotrimetylsilane ($Me_3SiN_3$) and 10 equivalents of tetrabutylammonium fluoride (TBAF) relative to the amount of Br end groups are added to the polymer solution. The reaction mixture is then stirred for 48 hours at room temperature. Purification of the product is done by precipitation into a 10-fold excess of cold methanol. The precipitated polymer is filtered off, washed with cold methanol. This precipitation procedure was done twice. Finally the PiBA-$N_3$ was dried at room temperature under vacuum.

## VIII.7.6. ATRP of acrylates with 2-(2-azidoethoxy)ethyl bromoisobutyrate as the initiator

The polymerization procedure is identical to the one described in §VIII.7.4.

### VIII.7.7. Synthesis of 3-azidopropyl methacrylate: azide-containing monomer

***Step 1: synthesis of 3-azidopropanol.***

30.0 mL (33.9 g, 0.358 mol) of 3-chloropropanol is added to a mixture of 40 mL water, 47 g (0.716 mol) sodium azide and 1 g tetrabutyl ammonium sulphate. The reaction flask is equipped with a reflux condenser and the reaction mixture is stirred at 80 °C during 24 hours. Then it was stirred at room temperature during 14 hours. The product is then extracted with diethyl ether (3 times 100 mL) and the organic phase is dried using sodium sulphate. 3-azidopropanol is obtained as a colorless liquid by vacuum distillation. Boiling point is 62 °C at 3-4 mbar.

***Step 2: synthesis of 3-azidopropyl methacrylate.***

A mixture of 23.5 mL (0.253 mol) 3-azidopropanol, 45 mL (0.323 mol) triethylamine (dried with sodium sulphate), 0.1 g hydroquinone and 100 mL of diethyl ether (dried with sodium sulphate) is cooled to 0 °C in an ice bath. 29.0 mL (0.300 mol) of methacryloyl chloride is added dropwise during a period of 20 minutes. The reaction mixture is stirred at 0 °C for one more hour and stirring was continued for 14 hours at room temperature. 100 mL of diethyl ether is added to the reaction mixture and the mixture is extracted subsequently with an aqueous solution of HCl (10 vol%, 2 times 100 mL), water (2 times 100 mL), an aqueous solution of NaOH (10 weight%, 2 times 100 mL), and again with water (2 times 100 mL). The diethyl ether phase is dried with sodium sulphate. After removal of sodium sulphate and the solvent diethyl ether, 3-azidopropyl methacrylate was obtained as a yellow oil. No further purification was done. Yield is 70 %.

### VIII.7.8. Copolymerization of AzMA and iBA

A typical polymerization procedure is as follows (e.g. reaction CPA2, Table VIII-1). 0.0473 mol (10.0 mL) of iBA, 0.0118 mol (1.87 mL) of AzMA and 1.58 $.10^{-3}$ mol (0.329 mL) of PMDETA as ligand were added to a reaction flask and the mixture was bubbled with $N_2$ for 1h to remove oxygen from the reaction mixture. Acetone was degassed separately by bubbling with $N_2$ and 25 volume % (3.96 mL) of acetone was added to the reaction flask. After that, Cu(I)Br (1.58 $.10^{-3}$ mol, 0.227 g) was added and the reaction flask was placed in an oil bath at 50 °C. When the reaction mixture reached the desired reaction temperature, the polymerization was started by adding dropwise during 20

seconds 0.789 $.10^{-3}$ mol (0.088 mL) of methyl 2-bromopropionate as the initiator. Samples were withdrawn periodically to monitor the monomer conversion (by $^{1}$H-NMR) and the average molecular weight (by GPC). The reaction was ended by cooling the reaction mixture in liquid nitrogen. The resulting polymer was dissolved in THF and the copper catalyst was removed by passing the diluted reaction mixture over a column of neutral $Al_2O_3$. After evaporating the excess solvent, the polymer was precipitated in cold methanol, and dried under vacuum.

### VIII.7.9. Formation of block copolymer by "click" reaction

A typical "click" coupling procedure for the formation of a poly(iBA-*b*-EEA) block copolymer is as follows (e.g. reaction CLC1, Table VIII-5). The bromine end group of PiBA ($M_n$=10600 g.mol$^{-1}$) was substituted to an azide end group as described in §VIII.7.5. Then, PiBA-$N_3$ (0.4 g, 3.77 $.10^{-5}$ mol) and PEEA-≡ (0.5 g, 7.46 $.10^{-5}$ mol, 2 equivalents to PiBA- $N_3$) were dissolved in 4 mL of THF. PMDETA (2.23 $.10^{-4}$ mol, 0.047 mL, 3 eq. to alkyne functions) was added and the mixture was bubbled with $N_2$ for 30 minutes. The "click" coupling reaction was started by adding Cu(I)Br (2.23 $.10^{-4}$ mol, 0.0319 g, 3 eq. to alkyne functions). After completion of the "click" reaction, the resulting solution was further diluted in THF and the copper catalyst was removed by passing the reaction mixture over a column of neutral $Al_2O_3$. After evaporating the excess solvent, the excess of PEEA-≡ was removed by selective precipitation in cold methanol. The coupled product poly(iBA-*b*-EEA) was filtered off, washed with cold methanol, and dried under vacuum.

### VIII.7.10. Formation of comb/brush copolymer by "click" reaction

#### VIII.7.10.1. "Click" reaction of poly(iBA-*co*-AzMA) with PEEA-≡

The "click" coupling procedure for the formation of a poly(iBA-*g*-EEA) comb/brush copolymer is as follows (reaction CLD1, Table VIII-6). Poly($iBA_{24}$-*co*-$AzMA_{12}$) copolymer (0.025 g, 3.55 $.10^{-6}$ mol, 4.26 $.10^{-5}$ mol of $N_3$ groups) and PEEA-≡ (2 equivalents to $N_3$ groups, 8.52 $.10^{-5}$ mol, 0.41 g) were dissolved in 5 mL of THF. PMDETA (2.55 $.10^{-4}$ mol, 0.053 mL, 3 eq. to alkyne functions) was added and the mixture was bubbled with $N_2$ for 30 minutes. The "click" coupling reaction was started by adding Cu(I)Br (2.55 $.10^{-4}$ mol, 0.0366 g, 3 eq. to alkyne functions). After completion of the

"click" reaction, the resulting solution was further diluted in THF and the copper catalyst was removed by passing the reaction mixture over a column of neutral $Al_2O_3$. After evaporating the excess solvent, the excess of PEEA-≡ was removed by selective precipitation in cold methanol. The coupled product poly(iBA-*g*-PEEA) was filtered off, washed with cold methanol, and dried under vacuum.

### VIII.7.10.2. Copolymerization of MMA and AzMA

The copolymerization procedure of MMA and AzMA is as follows (reaction CPC1, Table VIII-7). 0.0928 mol (10.0 mL) of iBA, 0.02322 mol (3.93 g, 3.67 mL) of AzMA and $0.774 .10^{-3}$ mol (0.134 g, 00.162 mL) of PMDETA as the ligand was added to a reaction flask and the mixture was bubbled with $N_2$ for 1h to remove oxygen from the reaction mixture. Acetone was degassed separately by bubbling with $N_2$ and 25 volume % (4.55 mL) of acetone was added to the reaction flask. After that, Cu(I)Br (0.5 eq. to initiator, $0.774 .10^{-3}$ mol, 0.111 g) was added and the reaction flask was placed in an oil bath at 50 °C. When the reaction mixture reached the desired reaction temperature, the polymerization was started by adding dropwise during 20 seconds $1.548 .10^{-3}$ mol (0.3019 g, 0.227 mL) of ethyl 2-bromoisobutyrate as the initiator. Samples were withdrawn periodically to monitor the monomer conversion (by $^1$H-NMR) and the average molecular weight $M_n$ (by GPC). The reaction was ended by cooling the reaction mixture in liquid nitrogen. The resulting polymer was dissolved in THF and the copper catalyst was removed by passing the diluted reaction mixture over a column of neutral $Al_2O_3$. After evaporating the excess solvent, the polymer was precipitated in cold hexane, and dried under vacuum.

### VIII.7.10.3. "Click" reaction of poly(MMA-*co*-AzMA) with PEEA-≡

The "click" coupling procedure for the formation of a poly(MMA-*g*-EEA) comb/brush copolymer is as follows (reaction CLE1, Table VIII-8). Poly($MMA_{39}$-*co*-$AzMA_9$) copolymer (0.046 g, $8.36 .10^{-6}$ mol, $7.53 .10^{-5}$ mol of $N_3$ groups) and PEEA-≡ (1.5 equivalents to $N_3$ groups, $1.17 .10^{-4}$ mol, 0.54 g) were dissolved in 4 mL of THF. PMDETA ($3.52 .10^{-4}$ mol, 0.074 mL, 1 eq. to Cu(I)Br) was added and the mixture was bubbled with $N_2$ for 30 minutes. The "click" coupling reaction was started by adding Cu(I)Br ($3.52 .10^{-4}$ mol, 0.0505 g, 3 eq. to alkyne functions). After completion of the

"click" reaction, the resulting solution was further diluted in THF and the copper catalyst was removed by passing the reaction mixture over a column of neutral $Al_2O_3$.

## VIII.8. References


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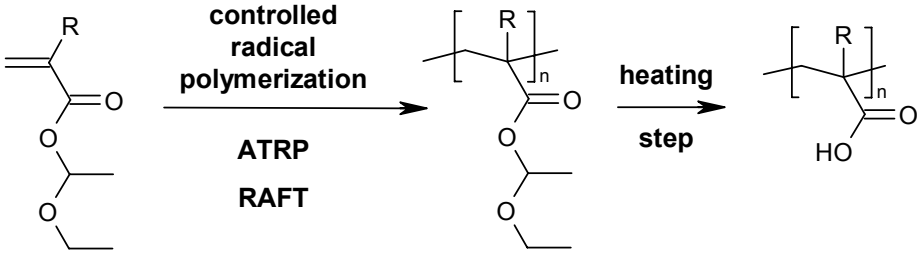
# *Chapter IX*
# *Summary and conclusions*

# IX
# Summary and conclusions

In this thesis, we have developed a novel strategy for the preparation of amphiphilic poly((meth)acrylic acid) (P(M)AA) containing polymer architectures by controlled radical polymerization. A general applicable precursor strategy that makes use of the 1-ethoxyethyl protecting group was developed. This approach not only prevents direct polymerization of (meth)acrylic acid, which is often undesired because of the requirement of a polar reaction medium, but also allows the use of the atom transfer radical polymerization (ATRP) technique which is of great importance for the synthesis of functional and/or complex polymer structures. Poly(1-ethoxyethyl acrylate) and poly(1-ethoxyethyl methacrylate) are novel precursor polymers for poly(acrylic acid) and poly(methacrylic acid) polymers, respectively. It was shown that deprotection of the precursor polymer (segment) to poly((meth)acrylic acid) proceeds *via* a general applicable and simple procedure, without the need for any additional purification step.




**Controlled radical polymerization (ATRP, RAFT) of EE(M)A to yield PEE(M)A, and subsequent deprotection to P(M)AA by a heating step. (R=H or $CH_3$ for EEA and EEMA, respectively).**

In order to be able to further improve and adjust the properties of the current P(M)AA containing materials, the ability to synthesize these polymers with good control over the molar mass, chain architecture and polydispersity is of great importance. It is clear that controlled polymerization techniques are a prerequisite for their successful synthesis. **Chapter II** gives an introduction on the controlled radical polymerization (CRP). It is

concluded that the development of various CRP methods and all advances made in the field have provided synthetic chemists with the ability to prepare materials that were impossible to synthesize a decade ago. Numerous corporations in a broad range of markets are preparing a spectrum of new materials as they now have the capability to tailor the properties of their products to their customers' needs.

As the synthesis of well-defined P(M)AA containing polymers by CRP techniques is not straightforward and is still an ongoing challenge, **Chapter III** describes the current state-of-the-art in the field. Reversible addition-fragmentation chain transfer (RAFT) polymerization and nitroxide mediated polymerization (NMP) have shown to be methods for the direct polymerization of acrylic acid. However, direct polymerization of acrylic acid was not found to be a complete solution, because this approach requires a rather polar reaction medium, which limits the choice of other monomers and/or segments. Another challenge that remains is the synthesis of more complex architectures such as graft, star or brush copolymers. For these architectures, atom transfer radical polymerization (ATRP) has proven to be the most versatile CRP method. Unfortunately, this method is not compatible with (meth)acrylic acid, due to side reactions. Therefore, protected derivatives of (meth)acrylic acid have been widely explored. This requires however a postpolymerization deprotection and purification step, which is quite labour intensive.

**Chapter IV** overviews the possibilities of “click” chemistry in the world of polymers, which has become a hot topic in polymer synthesis during the last 3 years. It was shown that the copper(I) catalyzed Huisgen 1,3 dipolar cycloaddition of azides and terminal alkynes is a highly attractive “click” coupling reaction because of its near quantitative yields and absence of side reactions, while it is performed under mild reaction conditions. As a conclusion, “click” chemistry has provided synthetic polymer chemists with a powerful tool for further broadening the possibilities of controlled polymerization techniques, especially in the field of functionalization of macromolecules, and preparing a range of polymer architectures and materials.

In **Chapter V**, the ATRP of 1-ethoxyethyl (meth)acrylate (EE(M)A) is investigated, which is evaluated as a novel route towards the synthesis of P(M)AA containing polymers. It has been demonstrated that ATRP is a suitable technique to polymerize 1-ethoxyethyl methacrylate (EEMA) and 1-ethoxyethyl acrylate (EEA), resulting in polymers with a good control of average molar mass ($M_n$) and narrow molecular weight distribution.[1, 2] It was shown that deprotection is easily carried out by a heating step, with the loss of ethyl

vinyl ether (boiling point: 33 °C) as a gas, preventing the need of an additional purification step after deprotection. Common initiators as well as "tailor-made" initiators have been used, as demonstrated with the use of a disulfide containing initiator. Using "tailor-made" initiators, it was shown that the polymer properties can be adjusted to specific applications. In our case, a disulfide containing initiator was used for the preparation of PAA with a disulfide bond, which allowed us to create pH-responsive gold surfaces. The pH-switchable properties of the PAA-functionalized gold surfaces were characterized by atomic force microscopy in water. The thickness of the polymer chains in their swollen state (at pH 9) was estimated to be at least 5 times the thickness of the polymer chains in their collapsed state (at pH 5).

Moreover, to illustrate the general applicability of EEA, various PEE(M)A containing polymers were prepared successfully, including block copolymers, "block-like" copolymers, and random copolymers.

In **Chapter VI** the ATRP of EEA was applied to synthesize a variety of poly(isobornyl acrylate)-*b*-poly(acrylic acid) block copolymers (poly(iBA-*b*-AA)). The controlled behaviour of the synthesis of the PiBA homopolymer as well as of the poly(iBA-*b*-AA) block copolymers was demonstrated. Preliminary results about these poly(iBA-*b*-AA) polymers acting as pigment stabilizing polymers are reported as well. It was found that PiBA-PAA block copolymers with a long PAA block showed good stabilization for aqueous dispersions of hydrophilic pigment $TiO_2$, whereas for aqueous dispersions of hydrophobic CuPc pigment, poly(iBA-*b*-AA) block copolymers with a ratio of PiBA/PAA of ± 2 revealed the best result.

In **Chapter VII**, the polymerization of EEA using the RAFT polymerization technique is investigated to further illustrate the versatility of the use of the 1-ethoxyethyl acrylate strategy.[3] Temperature optimization revealed an optimal polymerization temperature of 70 ºC providing an optimal balance between control over the polymerization and reaction speed without significant deprotection. The direct synthesis in toluene of block copolymer structures with an EEA second block, without purification of the first block, was demonstrated. As a conclusion, the successful (co)polymerizations of EEA utilizing RAFT offer many possibilities for the straightforward synthesis of PAA containing copolymers without the need for polar solvents or labor-intensive deprotection steps. All investigations were performed using a high-throughput workflow equipped with synthesis robots and fast analysis equipment demonstrating the added value in polymer research.

**Chapter VIII** evaluates the combination of ATRP of EEA and the copper(I) catalyzed "click" 1,3-dipolar cycloaddition reaction of azides and terminal alkynes as a method to synthesize amphiphilic polymer structures. Using our EEA strategy, we have broadened the application field with the synthesis of polymer structures containing PAA segments. It was demonstrated that ATRP is a particularly suitable polymerization technique for combination with the "click" 1,3-dipolar cycloaddion reaction of azides and terminal alkynes, as it permits to introduce in an easy way both alkyne and azide functionalities into a polymer chain. Then, the "click" coupling reaction of these polymers was investigated to obtain block copolymers. The "click" reaction showed to be both quantitative and fast. After selective precipitation and deprotection of the PEEA segment to PAA, the desired amphiphilic block copolymer was obtained. Also comb/brush copolymers were successfully prepared by "clicking" linear PEEA with a terminal alkyne function onto a polymer containing multiple azide functions. For the first time, comb/brush copolymers were synthesized by a combination of ATRP and "click" chemistry.

As a general conclusion, it has been shown that the EE(M)A strategy is an easy and general applicable strategy for the synthesis of a wide variety of P(M)AA containing polymer structures by controlled radical polymerization.[4]

With regard to future developments based on the reported EE(M)A strategy, we expect opportunities for specific applications as well as concerning the further research towards sophisticated materials design.

Considering the still on-going developments in polymer chemistry (see Chapter II), it is clear that modern materials design is intrinsically linked to the synthesis of increasingly complex polymer architectures. As with increased complexity of the materials, the simplicity of the synthesis and purification steps are defining the applicability of the synthetic strategy towards P(M)AA containing polymers, controlled radical polymerization of EE(M)A (by ATRP and RAFT) provides chemists with a valuable alternative to the commonly established methods. Also the utilization of nitroxide mediated polymerization (NMP) for the synthesis of EE(M)A containing (co)polymers can be expected. Although the applied temperature is nowadays too high for the application of our EE(M)A strategy, this polymerization technique shows a continuously evolution towards the application of

lower polymerization temperatures. Recently, the polymerization temperature could be decreased to < 90 °C using a novel alkoxyamine.[5] Further on, as can be concluded from the description in Chapter III, the possibilities of the combination of "click" chemistry and controlled radical polymerization are being rapidly explored. As for many applications, P(M)AA containing polymers are of great interest, we expect this combination may lead to new opportunities.

Another field which offers new possibilities and is worthy to be further explored, is the property switch that is inherent to the developed EE(M)A technology. Especially in the field of lithographic applications, photoresist and printing plate technology, we expect that this property switch might be useful.

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# *Hoofdstuk X*
# *Samenvatting en besluit*

***Nieuwe routes voor de synthese van poly((meth)acrylzuur) bevattende polymeerstructuren via gecontroleerde radicalaire polymerisatie***

# X
# Samenvatting en besluit

## *Nieuwe routes voor de synthese van poly((meth)acrylzuur) bevattende polymeerstructuren via gecontroleerde radicalaire polymerisatie*

Deze thesis behandelt de synthese van amfifiele poly((meth)acrylzuur) (P(M)AA) bevattende polymeerstructuren. P(M)AA bevattende polymeren zijn belangrijk voor tal van toepassingen omwille van hun pH-gevoeligheid, hun hydrofiele en waterabsorberende eigenschappen, en omwille van hun interactie met metaalionen[1-4]. De wereldmarkt voor poly(acrylzuur) en poly(methacrylzuur) is enorm (5-10.000.000 ton/jaar; 10-20 miljoen euro). Hoofdrolspelers op de markt zijn bijvoorbeeld Arkema, BASF, Du Pont, ...

Stimulusgevoelige amfifiele blokcopolymeren zijn een bekende klasse intelligente polymeren met een waaier van toepassingen, zoals immobilisatie van milieuvervuilende deeltjes[5] (vb. metalen), katalyse[6], stabilisatoren in emulsiepolymerisatie[7], geneesmiddelendragers[8], nanoreactors[9] en polymeersurfactanten[10, 11]. P(M)AA bevattende amfifiele copolymeren worden bijvoorbeeld gebruikt als emulgatoren, stabilisatoren[7], surfactanten, dispergeermiddelen[12-14], bevochtigers, enz… Hun toepassingsgebieden omvatten cosmetica, verven, coatings, textiel, waterzuivering, papierindustrie[12-14], bio-toepassingen[15] en geneesmiddelenafgiftesystemen, enz…

Om de eigenschappen van de bestaande materialen te verbeteren, is het zeer belangrijk dat deze polymeren gesynthetiseerd kunnen worden met goede controle over het moleculair gewicht, met een gecontroleerde ketenarchitectuur en nauwe polydispersiteit. Het is duidelijk dat om aan deze voorwaarden te kunnen voldoen de synthese van deze materialen met gecontroleerde polymerisatietechnieken moet gebeuren. Traditionele

polymerisatiemethoden voor de synthese van goed-gedefinieerde P(M)AA bevattende polymeren omvatten levende anionische[16] en groep-transfer[17] polymerisatietechnieken, die beide gebruik maken van beschermde derivaten van (meth)acrylzuur monomeren. Deze ionische polymerisatiemethoden hebben enkele specifieke praktische nadelen, en de combinatiemogelijkheden met andere monomeren of polymeersegmenten zijn beperkt.

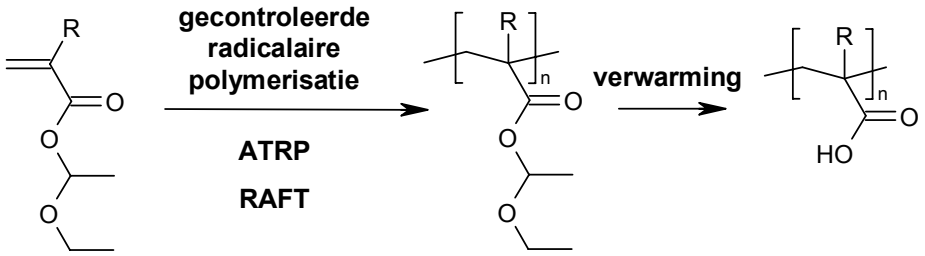
Omdat radicalaire polymerisatie vele voordelen heeft in vergelijking met andere polymerisatieprocessen zoals ionische polymerisatie, zijn in de laatste 10-15 jaar verschillende methodes ontwikkeld om controle over het radicalaire polymerisatieproces te verkrijgen.[18-26] **Hoofdstuk II** bevat een inleiding over gecontroleerde radicalaire polymerisatie (CRP), beschrijft de fundamentele karakteristieken van CRP en gaat dieper in op de belangrijkste types van gecontroleerde radicalaire polymerisatie (meer bepaald atoomtransfer radicalaire polymerisatie (ATRP), reversibele additie-fragmentatie ketentransfer (RAFT) polymerisatie, en nitroxide-gecontroleerde polymerisatie (NMP)). Verder wordt de toepasbaarheid van de verschillende CRP methoden besproken met betrekking tot hun relatieve voordelen en beperkingen. Ten slotte wordt een overzicht gegeven van de huidige industriële implementaties van CRP, wat het belang van CRP voor de industrie aantoont. Het voorgaande toont aan dat de ontwikkeling van diverse CRP methoden en alle vooruitgang die geboekt werd op dit domein heeft geleid tot de mogelijkheid om materialen te synthetiseren die 10 jaar geleden onmogelijk te bereiden waren. Verschillende bedrijven in uiteenlopende marktsegmenten zijn bezig met de ontwikkeling van een breed spectrum aan nieuwe materialen. Dankzij CRP technieken hebben zij nu de mogelijkheid om de eigenschappen van hun producten verder af te stemmen op de wensen en eisen van hun klanten.

Omdat de synthese van goed-gedefinieerde P(M)AA bevattende polymeren via CRP technieken niet zo gemakkelijk is en daarom nog steeds een uitdaging blijft, beschrijft **hoofdstuk III** de huidige stand van zaken op dit gebied. Zowel de ATRP, RAFT als NMP techniek wordt besproken en er wordt een overzicht gegeven met betrekking tot de synthese van goed-gedefinieerde P(M)AA bevattende polymeren. Elke van deze technieken heeft echter zijn beperkingen (zie hoofdstuk V).

**Hoofdstuk IV** geeft een overzicht van de mogelijkheden van “klik” chemie in de polymeerwereld, wat een “hot topic” in de polymeersynthese is geworden gedurende de laatste 3 jaar. Omdat ATRP één van de meest veelzijdige en meest gebruikte polymerisatiemethoden in de moderne materiaalwetenschap is, wordt een gedetailleerd

overzicht gegeven over de combinatie van “klik” chemie en ATRP. Er werd aangetoond dat de koper(I) gekatalyseerde Huisgen 1,3 dipolaire cycloadditie van azides en eindstandige alkynen een zeer aantrekkelijke “klik” koppeling reactie is omwille van de kwantitatieve rendementen en de afwezigheid van nevenreacties, terwijl de reactie doorgaat onder milde reactiecondities. Er kon besloten worden dat “klik” chemie een krachtige en veelzijdige strategie is die leidt tot een verbreding van de mogelijkheden van CRP technieken, zowel op het gebied van functionalisatie van macromoleculen als voor de bereiding van een waaier van polymeerarchitecturen en materialen.

**Hoofdstuk V** beschrijft de ATRP van 1-ethoxyethyl (meth)acrylaat (EE(M)A), en deze strategie werd geëvalueerd als een nieuwe route voor de synthese van P(M)AA bevattende polymeren.[27]




**Gecontroleerde radicalaire polymerisatie (ATRP, RAFT) van EE(M)A to PEE(M)A, en ontscherming tot P(M)AA door verwarming. (R=H of $CH_3$ voor respectievelijk EEA and EEMA).**

ATRP van EE(M)A biedt een oplossing aan de uitdagingen die blijven voor de synthese van goed-gedefineerde P(M)AA bevattende polymeren via CRP technieken (zie ook hoofdstuk III). Alhoewel het mogelijk is om acrylzuur direct te polymeriseren via RAFT[28, 29] of NMP[30], is hun toepasbaarheid voor de synthese van (blok)copolymeren met een waaier van apolaire monomeren sterk gelimiteerd omwille van de polaire reactiecondities die vereist zijn. Bovendien zijn deze twee technieken, vanuit synthetisch oogpunt, niet de meest veelzijdige wanneer de synthese van meer complexe polymeerarchitecturen zoals ster-, graft- en kamcopolymeren is gewenst. ATRP is hiervoor de meest geschikte techniek. (Meth)acrylzuur kan echter niet met ATRP gepolymeriseerd worden wegens een nevenreactie van het monomeer met het metaalcomplex.[31] Strategieën om deze incompatibiliteit te overwinnen zijn het gebruik van het natriumzout van methacrylzuur[32], of het gebruik van beschermde derivaten van (meth)acrylzuur, zoals tert-

butyl (meth)acrylaat[33-35] of benzyl (meth)acrylaat[36]. In al deze gevallen is echter na de polymerisatie een ontschermings- en zuiveringsstap vereist om het P(M)AA te genereren. Bovendien is deze ontschermingsstap niet altijd vrij van nevenreacties.

Om deze extra zuiveringsstap te vermijden beschrijft **hoofdstuk V** het gebruik van 1-ethoxyethyl als de beschermende groep voor (meth)acrylzuur. Het werd aangetoond dat ATRP een geschikte techniek is om 1-ethoxyethyl methacrylaat (EEMA) en 1-ethoxyethyl acrylaat (EEA) te polymeriseren. Polymeren met een gecontroleerd moleculair gewicht en en nauwe moleculair gewichtsdistributie konden worden bereid. Deze PEE(M)A polymeren zijn nieuwe precursoren voor respectievelijk polymethacrylzuur en polyacrylzuur. Er werd aangetoond dat ontscherming eenvoudig kan worden uitgevoerd door een verwarmingsstap, met de uitstoot van ethyl vinyl ether (kookpunt: 33 °C) als een gas, hetgeen betekent dat na de ontschermingsstap geen extra zuiveringsstap noodzakelijk is. Dit gedeelte van het onderzoek werd uitgevoerd in samenwerking met de onderzoeksgroep van Dr. S. Bon (Warwick University, Engeland).

Zowel conventionele als “op maat gemaakte” initiatoren werden gebruikt voor de polymerisatie van EE(M)A. Hiermee werd aangetoond dat de polymeereigenschappen aangepast kunnen worden naargelang de beoogde specifieke toepassingen. Als voorbeeld werd een disulfide-bevattende initiator gesynthetiseerd voor de bereiding van pH-gevoelige goudoppervlakken. De pH-gevoelige eigenschappen van de met PAA gefunctionaliseerde goudoppervlakken werden gekarakteriseerd met behulp van atomaire kracht microscopie (AFM) in water, in samenwerking met de onderzoeksgroep van Dr. S. Demoustier-Champagne (Université Catholique de Louvain, UCL, België). De dikte van de polymeerketens in hun gezwollen toestand (bij pH = 9) bleek minstens 5 keer dikker dan in de samengevouwen toestand (bij pH = 5), wat een belangrijk gegeven is voor verdere toepassingen. Om de algemene toepasbaarheid van EEA te illustreren werden diverse PEE(M)A bevattende polymeren bereid, waaronder blokcopolymeren, “blokachtige” copolymeren, statistische copolymeren, enz…[37, 38]

In **hoofdstuk VI** werd de ATRP van EEA toegepast om een waaier van poly(isobornyl acrylaat)-poly(acrylzuur) blokcopolymeren (poly(iBA-*b*-AA)) te bereiden. Alhoewel PiBA een polyacrylaat is met enkele interessante eigenschappen zoals o.a. een hoge glastransitietemperatuur, werd de gecontroleerde synthese van PiBA via ATRP nog niet eerder in detail beschreven. Daarom werd eerst een studie van de homopolymerisatie uitgevoerd, hetgeen een vereiste is voor de synthese van goed-gedefinieerde

blokcopolymeren. Het gecontroleerde verloop van zowel de homopolymerisatie als de synthese van de poly(iBA-*b*-AA) blokcopolymeren werd aangetoond. Verder werden deze poly(iBA-*b*-AA) blokcopolymeren onderzocht als stabilisatoren voor waterige dispersies van pigmenten. Voorlopige resultaten toonden aan dat poly(iBA-*b*-AA) blokcopolymeren met een lang PAA segment goede stabilisatie vertoonden van waterige dispersies van het hydrofiele $TiO_2$ pigment, terwijl voor waterige dispersies van het hydrofobe CuPc (koper phtalocyanine) pigment de beste resultaten werden bekomen voor poly(iBA-*b*-AA) blokcopolymeren met een PiBA/PAA verhouding van ± 2/1. Deze studie werd uitgevoerd in een samenwerking met Prof. Eisenbach (Universiteit van Stuttgart, Duitsland) and Prof. Zubov (Lomonosov Moscow State Academy of Fine Chemical Technology, Rusland)

In **hoofdstuk VII** werd de polymerisatie van EEA met de RAFT techniek onderzocht om de algemene toepasbaarheid en het universele karakter van het gebruik van de 1-ethoxyethylacrylaat strategie aan te tonen.[39] Dit onderzoek werd gedaan in samenwerking met Dr. R. Hoogenboom and Prof. U. Schubert (Technische Universiteit Eindhoven, Nederland). Alhoewel het mogelijk is om met RAFT acrylzuur rechtstreeks te polymeriseren, kunnen (blok)copolymeren met een waaier aan apolaire monomeren/segmenten niet eenvoudig gepolymeriseerd worden aangezien rechtstreekse polymerisatie van acrylzuur polaire reactiecondities vereist. RAFT polymerisatie van EEA vermijdt dit probleem. Temperatuuroptimalisatie toonde aan dat 70 °C de optimale polymerisatietemperatuur is, met een optimale balans tussen controle over de polymerisatie en een goede reactiesnelheid, terwijl geen significante ontscherming werd waargenomen. De synthese in tolueen van diverse blokcopolymeerstructuren met een PEEA segment als 2$^{e}$ blok, zonder voorafgaande zuivering van de 1$^{e}$ blok, werd succesvol uitgevoerd. Als besluit kan gesteld worden dat de succesvolle (co)polymerisatie van EEA met RAFT een goede strategie is voor de eenvoudige synthese van PAA-bevattende copolymeren zonder de nood aan polaire reactiecondities of arbeidsintensieve ontschermingsstappen. Alle reacties werden uitgevoerd met syntheserobotten en snelle analyseapparatuur, waarmee de toegevoegde waarde van deze apparatuur in polymeersynthese werd geïllustreerd.

**Hoofdstuk VIII** evalueert de combinatie van ATRP van EEA en de koper(I) gekatalyseerde “klik” 1,3 dipolaire cycloadditiereactie van azides en eindstandige alkynen als een methode om amfifiele polymeerstructuren te bereiden. Gebruikmakende van de ontwikkelde EEA strategie werd het toepassingsgebied uitgebreid met de synthese van polymeerstructuren met PAA segmenten. Er werd een modulaire benadering toegepast:

zowel de synthese van polymeren met alkynfunctionaliteiten als polymeren met azidefunctionaliteiten werd geëvalueerd. Er werd aangetoond dat ATRP een bij uitstek geschikte polymerisatietechniek is voor combinatie met de "klik" 1,3 dipolaire cycloadditiereactie van azides en alkynen, aangezien met ATRP zowel alkyn als azide functionaliteiten eenvoudig kunnen worden geïntroduceerd in de polymeerketens. Vervolgens werd de bereiding van blokcopolymeren door "klik" koppeling van deze polymeren onderzocht. De "klik" reactie bleek zowel snel als kwantitatief door te gaan. Ook kamcopolymeren werden succesvol gesynthetiseerd door PEEA met een eindstandig alkyn te "klikken" op een polymeer dat meerdere azide-zijketens bevat. Zo werden voor de eerste maal kamcopolymeren bereid met een combinatie van ATRP en "klik" chemie.

Als algemeen besluit kan gesteld worden dat de EE(M)A strategie een eenvoudige en algemeen toepasbare strategie is voor de synthese van een brede waaier van P(M)AA bevattende polymeerstructuren.

Met het oog op toekomstige ontwikkelingen gebaseerd op de hier beschreven EE(M)A strategie verwachten we zowel mogelijkheden voor specifieke toepassingen als voor verder onderzoek naar steeds meer complexe materialen.

Gesteund door de voortdurende vooruitgang op het vlak van polymeersynthese (zie ook hoofstuk II), vertonen moderne materialen een steeds complexere polymerenarchitectuur. Omdat met een toenemende complexiteit van de materialen de eenvoud van de synthese- en zuiveringsstappen steeds meer bepalend zijn voor de synthetische strategie voor de bereiding van P(M)AA bevattende polymeren, biedt de gecontroleerde radicalaire polymerisatie van EE(M)A (met ATRP en RAFT) een eenvoudig alternatief voor de gekende methoden. Ook kan met het gebruik van nitroxide gecontroleerde polymerisatie (NMP) voor de synthese van EE(M)A bevattende polymeren verwachten. Alhoewel de gebruikelijk polymerisatietemperatuur vandaag de dag nog te hoog is om de EE(M)A strategie te kunnen toepassen, vertoont deze polymerisatietechniek een voordurende evolutie naar lagere polymerisatietemperaturen. Recent kon de temperatuur verlaagd worden tot beneden 90 °C door het gebruik van een nieuw alkoxyamine.[40]

Zoals besloten kan worden uit de beschrijving in hoofdstuk III, worden de mogelijkheden van de combinatie van "klik" chemie en gecontroleerde radicalaire

polymerisatie in een sneltempo verkend. Omdat voor tal van toepassingen P(M)AA bevattende polymeren van groot belang zijn, verwachten we dat deze combinatie zal leiden tot nieuwe mogelijkheden.

Een ander aspect dat nieuwe toepassingsmogelijkheden biedt en interessant is om verder te onderzoeken, is de eigenschappenovergang (hydrofoob naar hydrofiel) die inherent is aan de ontwikkelde EE(M)A strategie. Bijvoorbeeld op het vlak van lithografische toepassingen en drukplaattechnologie wordt verwacht dat deze eigenschappenovergang nuttig kan zijn.

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# *Publication List*

## Publications with international referee system

- Van Camp, W.; Du Prez, F. E.; Bon, S. A. F. "Atom Transfer Radical Polymerization of 1-Ethoxyethyl (Meth)acrylate: Facile Route toward Near-Monodisperse Poly((meth)acrylic acid)", *Macromolecules* **2004**, *37*, 6673.
- Hoogenboom, R.; Schubert U. S.; Van Camp, W.; Du Prez, F. E. "RAFT Polymerization of 1-Ethoxyethyl Acrylate: A Novel Route toward Near-Monodisperse Poly(Acrylic Acid) and Derived Block Copolymer Structures", *Macromolecules* **2005**, *38*, 7653.
- Bernaerts, K. V.; Willet, N.; Van Camp, W.; Jérôme, R.; Du Prez, F. E. "pH-Responsive Diblock Copolymers Prepared by the Dual Initiator Strategy" *Macromolecules* **2006**, *39*, 3760.
- Van Camp, W.; Dervaux, B., Van Renterghem, L.; Lammens, M.; Du Prez, F. E. "Synthesis of well-defined amphiphilic poly(isobornyl acrylate) and poly(acrylic acid) containing polymer structures by ATRP", *manuscript in preparation.*
- Van Camp, W.; Bulichev, N.; Dervaux, B.; Eisenbach, C. D.; Du Prez, F. E. "Pigment stabilization by amphiphilic poly(isobornyl acrylate) and poly(acrylic acid) containing block and blocky gradient copolymers synthesized by ATRP", *manuscript in preparation*.
- Van Camp, W.; Du Prez, F. E. "Modular synthesis of amphiphilic poly(acrylic acid) containing graft copolymers using "click" chemistry", *manuscript in preparation.*

## Book Chapter

- "Controlled Radical Polymerization of 1-Ethoxyethyl (Meth)acrylate: Novel Route for the Synthesis of Poly((meth)acrylic acid) Containing Polymer Structures", in "Controlled/Living Radical Polymerization: From Synthesis to Materials", Ed. Matyjaszewski K., ACS Symposium Series 944, American Chemical Society Washington, D.C., **2006** : Chapter 13, p. 171 – 184.

## Patent Application

- "Monodisperse polymers containing (alkyl)acrylic acid moieties, precursors and methods for making them and their applications", Van Camp W., Du Prez F. E., Bon S. A. F., PCT/BE2005/000106 (30 june 2005).

# *International Oral Presentations*

**European Polymer Federation Polymer Congress, Moscow, Russia**
**27/06 - 01/07/2005**

"Novel Route toward Monodisperse Poly((meth)acrylic acid) Containing Polymer Architectures by Atom Transfer Radical Polymerization"

**Selected for YES 2005, Cracow, Poland**
**13 - 19/09/2005**

(2nd Young European Scientists Workshop, organized by the European Polymer Federation)

"Novel Routes toward Near-Monodisperse Poly((meth)acrylic acid) Containing Polymer Architectures"

**STIPOMAT Conference 2005, Obernai, France**
**27 – 30/10/2005**

"Novel Way toward Well-Defined pH-Responsive Polymer Structures via Controlled Radical Polymerization Techniques"

**Macro Group UK International Conference on Polymer Synthesis, Warwick, UK**
**31/07 – 03/08/2006**

"How to Deal with Challenges to Prepare Well-defined Poly((meth)acrylic acid) Containing Polymer Structures by Controlled Radical Polymerization?"

Iedereen weet dat dit doctoraatswerk er niet alleen door mijn inzet is gekomen.
Talrijke mensen hebben rechtstreeks of onrechtstreeks iets aan dit werk bijgedragen.

Ik wil mijn collega's in Gent en daarbuiten, mijn promotor, het personeel van de vakgroep, mijn vrienden, mijn familie, mijn broer en mijn ouders dan ook nog eens oprecht bedanken voor alles wat ze hebben gedaan of betekend hebben, voor hun inzet, hulp, steun, vriendschap, en ook gewoon om te zijn wie ze zijn.
Jullie zijn een deel van mijn doctoraat!

Bedankt voor alle toffe momenten gedurende de afgelopen vier jaar!

Wim


Tom Van Camp