European Polymer Journal 119 (2019) 344–351

Contents lists available at ScienceDirect

European Polymer Journal

journal homepage: www.elsevier.com/locate/europolj

Synthetic approaches on conjugation of poly(2-oxazoline)s with vinyl based polymers

Ben A. Drain[a,b], C. Remzi Becer[a,*]

[a] Department of Chemistry, University of Warwick, Coventry CV4 7AL, United Kingdom
[b] School of Engineering and Materials Science, Queen Mary University of London, London E1 4NS, United Kingdom

ABSTRACT

2-oxazoline based polymers are attracting more and more attention in the last decade owing to their unique properties not only in biomedical applications but also in lubrication. Their combination with widely used polymers that are usually synthesized via controlled/"living" polymerisation techniques allows the design of novel polymer architectures and further increases the range of properties accessible from poly(2-oxazoline) based materials. However, there are several synthetic challenges to achieve a successful combination of these polymers and various techniques, such as click reactions, macromonomers, and heterobifunctional initiators have been reported in the literature to overcome these challenges. In this review, various synthetic methods to combine poly(2-oxazoline)s with vinyl based polymers have been discussed including the pros and cons of each method.

1. Introduction

Poly(2-oxazoline)s are an important class of polymers formed from the cationic ring opening polymerisation (CROP) of 2-oxazolines [1–4]. Their use in biomedical fields are extensive due to their comparable or superior performance over commonly used polymers such as poly (ethylene glycol) [5–14]. Moreover, by creating amphiphilic copolymers their solution behaviour is drastically changed by the formation of micelles [15–17] or by introducing or modifying thermoresponsive properties [18–21]. Whilst it is possible to form these copolymers by using a hydrophobic and hydrophilic 2-oxazoline, this is not the main focus of this review [22]. Rather, this mini-review will explore the synthetic methods, currently reported in the literature, to form copolymers between 2-oxazolines and vinyl polymers, such as poly(acrylate)s, poly(methacrylate)s, poly(acrylamide)s, poly(methacrylamide)s, poly (styrene) and their derivatives [23,24]. The most widely used synthetic approaches such as polymer-polymer coupling and a macroinitiator route will be highlighted. All possible synthetic combinations to obtain copolymers are listed in Table 1 with the associated sections and reference. It should be noted at this stage that in many cases a specific example has been selected and this is not exhaustive. Notes have been provided to illustrate potential scope, at a glance.

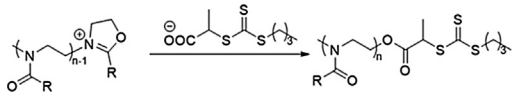
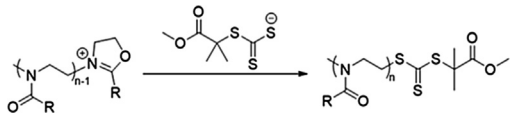
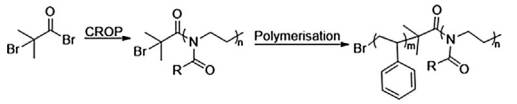
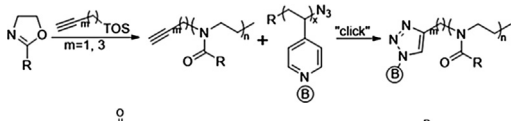
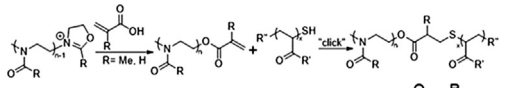
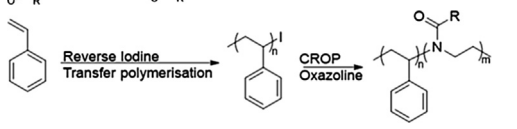
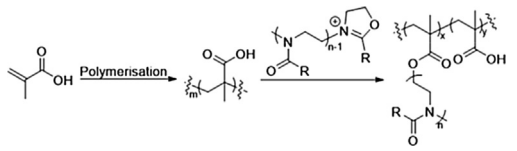
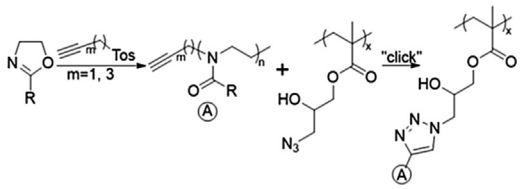
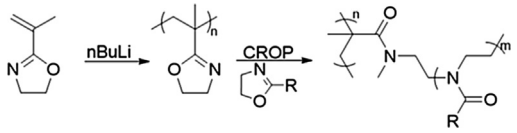
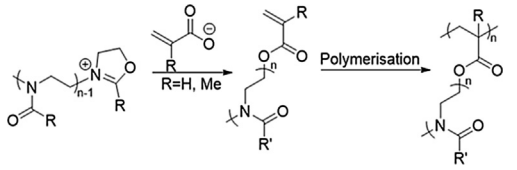
Before moving onto the main body of this mini-review, it is useful to reconsider the CROP mechanism. Scheme 1 shows the CROP of a generic 2-oxazoline, although all 2-oxazolines polymerise in a similar manner, albeit at different rates based on the substituent on the monomer, as well as the choice of initiator and solvent [4,25–27]. Under ideal conditions, the cationic polymerisation of 2-oxazolines proceeds via a living mechanism, that is, with the absence of termination reactions. In the first step, which is initiation, the polymerisation is initiated by an electrophilic species, for example, a tosylate, alkyl halide or triflate, among others [4,27]. These initiators can also bear a functional group, such as propargyl tosylate. This forms a cationic species, an oxazolinium ion, which then undergoes nucleophilic attack by another 2-oxazoline to propagate the chain. This continues until all monomer is consumed or the polymerisation is terminated by any nucleophilic species. Functional initiators and terminating agents will prove crucial in this review for the combination of vinyl polymers and poly(2-oxazolines). Although beyond the scope of this review, a review by Hoogenboom et al. provides a convenient summary of the various terminators that can be used [28].

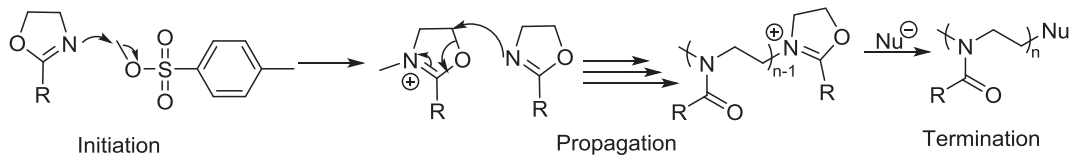
One disadvantage of the CROP, as already touched upon, is the requirement to avoid nucleophiles or use protection chemistry. Conversely, this is not a limitation of vinyl monomers polymerised via reversible deactivation radical polymerisation (RDRP) techniques. Additionally, the wide range of commercially available monomers with varying functionality that are available for RDRP makes this type of polymerisation attractive. Therefore, by combining CROP and RDRP techniques, one can introduce functionality into the polymer that otherwise would have required protection chemistry. Moreover, the inclusion of polymers from differing techniques often leads to a number of applications from anti-fouling coatings [29] to hydrogels [30] as well as interesting thermoresponsive behaviours [28,31–34], among other properties.

* Corresponding author.
E-mail address: Remzi.Becer@warwick.ac.uk (C.R. Becer).

https://doi.org/10.1016/j.eurpolymj.2019.07.047
Received 20 June 2019; Received in revised form 16 July 2019; Accepted 31 July 2019
Available online 07 August 2019
0014-3057/

Table 1
Table indicating the possible route to combining vinyl monomers with 2-oxazolines. Also included is a notes column with scope and advantages/disadvantages. Note that the schemes included in the table are specific cases.

Reaction Scheme	Method	Pros and Cons of the Method	Section	Refs
Block copolymers				
	Macroinitiator for RAFT block copolymerisation	• Works with acrylates and acrylamides. • Gives narrow dispersed polymers • Good purity of macroinitiator required • Good end group fidelity required	4.1	[46]
	Macroinitiator for RAFT block copolymerisation	• Works with acrylates and acrylamides • One-pot reaction possible • Good end group fidelity required • Making CTA required use of CS_2	4.1	[48]
	Heterofunctional initiator to give a block polymer	• Only suitable for SET-LRP/ATRP polymerisation • Initiator requires orthogonal reactivity	3	[15]
	Functional initiator for block copolymers	• Works with acrylates, styrenics and acrylamides • Low DPs are favoured	2.1.2	[37,38]
	End capping to give block copolymers via thiol-ene click	• Only suitable for RAFT polymers • Reduction of RAFT polymer conducted in-situ to the thiol-ene click reaction	2.1.1	[36]
	Macroinitiator for the formation of diblock polymers	• Difficult to purify final polymer • Requires high degree of iodine functionality • Works with other vinyl monomers	4.2	[49]
Graft copolymers				
	Grafting onto to give a graft polymer	• Shorter grafting reaction time compared to macromonomer approach • Determining grafting density challenging	2.2	[44]
	Functional initiator to give graft polymers via CuAAC	• Easy to tune backbone/side chain lengths • Grafting efficiency varies due to sterics	2.1.2	[39]
	Bifunctional monomer to form a macroinitiator	• Compatible with RAFT, FRP and anionic polymerisation • High DPs with narrow dispersity achievable	4.3	[50]
	End-capping to give a macromonomer for graft polymer synthesis	• Can be polymerised by RAFT, NMP, free radical techniques and ATRP • Requires a high degree of functionalisation • Both acrylic and methacrylic acid can be used as the terminator	5	[5758]



Scheme 1. General reaction scheme for the cationic ring opening polymerisation (CROP) of a generic 2-oxazoline initiated by methyl tosylate, as an example.

2. Combination by polymer-polymer coupling reactions

Polymer-polymer coupling reactions are potentially the most practical way to join together two polymers polymerised by different synthetic techniques. The chemistry employed is often of a facile nature and the purification is normally minimal. In this section, click chemistry to synthesise block copolymers as well as graft polymers will be presented.

2.1. Click chemistry for coupling polymers

The advent of "click" chemistry primarily by Sharpless et al. [35] in 2001 opened a new field of chemistry that allows for efficient reactions with good yields. Here, the methodology of using click chemistry to form block copolymers as well as brush polymers will be discussed and explored. Both copper catalysed azide-alkyne cycloadditions (CuAAC) and thiol-ene reactions will be presented. Although there is some disparity in the published literature about whether the thiol-ene click reaction is a "true" click reaction this is beyond the scope of this review. For the purposes of this review, the thiol-ene reaction will be treated as a click reaction.

In the case of poly(2-oxazoline)s there are three areas of functionality; the initiator end, the side chain, and the terminator end. This allows a range of functionalities to be incorporated within the polymer. Although it is important to mention that any side chain or initiator groups are non-nucleophilic so that they do not interfere with the CROP. However, nucleophilic groups can be introduced as long as adequate protection chemistry is employed.

2.1.1. Coupling polymers via thiol-ene click chemistry

To utilise thiol-ene click reactions, the living end of the poly(2-oxazoline) chain can be terminated with (meth)acrylic acid in the presence of a base, giving rise to a terminal double bond. This double bond can then be subsequently polymerised (discussed later) or in the case of the article by Y. Zhou and P. Wu, reacted with a thiol in a thiol-ene click reaction via a 1,4 Michael addition [36]. In this case the thiol employed was poly(*N*-isopropylacrylamide) (poly(NIPAM)) polymerised via reversible addition fragmentation chain transfer (RAFT) polymerisation with a subsequent *in-situ* aminolysis reduction to give the corresponding thiol (Scheme 2). In this way a block polymer of poly(2-oxazoline) and poly(NIPAM) is formed. Although, this is a useful technique to form block polymers, there are some limitations as well. For example, only polymers that are polymerised via RAFT polymerisation are suitable and a high chain end fidelity is required for the end-capping of the poly (2-oxazoline). Nevertheless, this technique is a reasonably facile way of forming a block copolymer. Additionally, the polymer backbone(s) (depicted as n and x in Scheme 2) can be altered to induce and alter the phase transition behaviour of the coupled polymer [36].

2.1.2. Coupling polymers via CuAAC

Having discussed the thiol-ene approach to form block polymers, attention now turns to using the copper catalysed azide-alkyne cycloaddition (CuAAC) reaction as a useful synthetic tool to form block polymers. In the case of thiol-ene click, a functional terminating agent was used. However, by using a functional initiator, such as propargyl tosylate, a terminal alkyne group is introduced which can then undergo a CuAAC reaction. By utilising a polymer that has been polymerised via atom transfer radical polymerisation (ATRP) or single electron transfer – living radical polymerisation (SET-LRP) one obtains a polymer with terminal bromine groups which can be easily transformed to an azide by treatment with sodium azide. By combining the propargyl initiated poly(2-oxazoline) with the azide terminated polymer it is possible to couple them together via CuAAC to yield a well-defined block [37,38]. Scheme 3 shows the reaction pathway for the formation of these block copolymers utilising this method. It is important to note that although the scheme depicts the example of 4-vinylpyridine [37], this method is also suitable for acrylates and acrylamides [38].

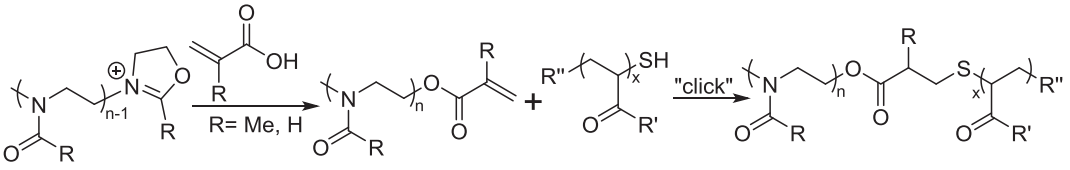
It is important to briefly mention the properties and applications of these block copolymers. The ease at which a block polymer can be synthesised gives rise to polymers of an amphiphilic nature. Such polymers can undergo micellisation in aqueous media [38]. Moreover, polymers from this type of coupling have also found use as a precursor to anti-fouling coatings [37].

In much the same way as the thiol-ene click reaction, this reaction does have some limitations. For example, mostly polymers synthesised via Cu mediated polymerisation techniques (i.e. ATRP/SET-LRP) can utilise this technique and low degrees of polymerisation (DP) were obtained for the vinyl polymer block due to unfavourable coupling between a highly hydrophilic block and a hydrophobic block [37,38]. It is important to note here that the poly(2-oxazoline) chain can also be terminated with sodium azide (and initiated with, for example, methyl tosylate). However, this would require introduction of an alkyne bond to the vinyl-based polymer. Although, this could be achieved via nucleophilic substitution with propargyl amine, the method described previously is more facile and in any case provides a very similar product.

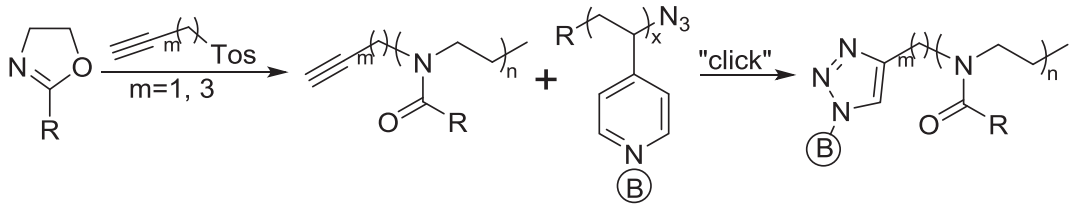
Having considered the linear approaches with click chemistry coupling, the graft polymer alternatives will now be discussed (Scheme 4). As discussed, it is possible to use a functional initiator such as propargyl or pent-4-ynyl tosylate to initiate the CROP polymerisation to give a polymer suitable for click reactions. Chu et al. synthesised a polymer with an azide containing side chain by epoxide ring opening of poly (glycidyl methacrylate) with sodium azide [39]. This was then coupled via CuAAC with a pent-4-ynyl tosylate initiated poly(2-oxazoline) forming a graft polymer. Note that the authors also employed propargyl tosylate, which was found to have a much higher initiation efficiency than the corresponding pent-4-ynyl tosylate. The grafting density is dependent on both the alkyl chain length (R in Scheme 4) and the degree of polymerisation (n in Scheme 4) with densities of 47.3–85.2% reported [39]. As expected, the shorter R and n, the higher the grafting density due to the reduction of steric hindrance. In an important contrast to the linear method, well defined, high DP brush polymers have been reported [39].

It is important to note that the reverse, polymerising propargyl acrylate, for example, is less facile. This is because to polymerise this acrylate one would first need to protect the triple bond and then deprotect to carry out the click reaction. Conversely, one could do the click reaction with a poly(2-oxazoline) and then polymerise the double bond as a subsequent step as carried out by Bouilhac and coworkers; an analogous method to end-capping poly(2-oxazoline) with (meth)acrylic acid (discussed in subsequent sections) [40]. Whilst a 2-oxazoline monomer (Scheme 5) has been polymerised to form a poly(2-oxazoline) containing a methacrylate group within each side chain, no examples of the acrylate subsequently being polymerised were found [41]. Additionally, examples of poly(2-oxazoline)s with azide [42] and terminal alkyne [43] groups on the side chain have been reported. To the best of our knowledge the combination with vinyl polymers has not been reported.

As discussed, click chemistry is a rather versatile technique to couple poly(oxazoline) with poly(acrylate)/(acrylamide)s etc., however each method has its own limitations. Both polymers polymerised via



Scheme 2. General scheme showing the end functionalisation of an active chain end of poly(2-oxazoline) with (meth)acrylic acid and the subsequent thiol-ene click reaction with a thiol terminated polymer synthesised via RAFT.



Scheme 3. Reaction scheme showing the copper catalysed azide-alkyne cycloaddition (CuAAC) between an alkyne functionalised initiated poly(2-oxazoline) and an azide terminated poly(4-vinylpyridine) **(B)** to form a diblock copolymer with a 1,4-triazole linker.

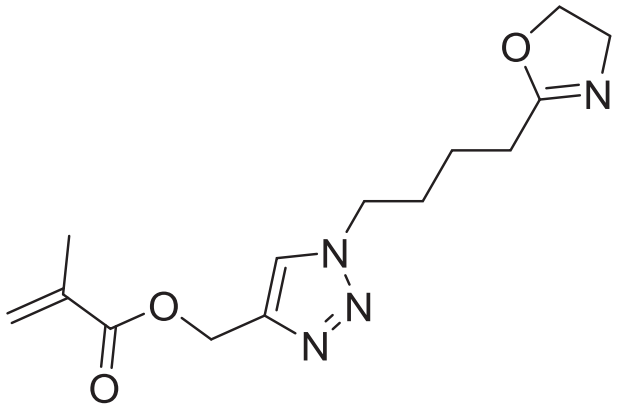
RAFT and ATRP/SET-LRP can be clicked together with poly(oxazoline)s by thiol-ene to form linear polymers or CuAAC to form graft or linear polymers. The choice therefore comes down to experimental constraints, the type of architecture (graft or block copolymers) and the linker in between. For example, for a particular application having a less stable thio-ether bond may not be desirable, so therefore CuAAC method could be selected and vice versa if a weaker bond is desired for an application.

2.2. Grafting onto via poly(methacrylic acid) end capping

Scheme 6 shows the grafting onto reaction of a poly(2-oxazoline) onto the back bone of poly(methacrylic acid). By utilising the living nature of the CROP one can terminate the polymer with a macromolecule, in this case poly(methacrylic acid) [44,45]. In this reaction, a poly(2-oxazoline) is formed via CROP and to this poly(methacrylic acid) is added in the presence of a non-nucleophilic base, for example, triethylamine. This, in effect, terminates the polymerisation via a carboxylate anion, which in this case makes up the back bone of the polymer. This gives a well defined graft polymer with grafting densities of up to 92% reported [44]. It should be noted here that calculating the grafting density is problematic given that the OH of the carboxylic acid undergoes proton exchange in ^{1}H NMR. However, for water soluble polymers an acid/base titration provides a convenient analytical method [44].

It is important to mention the potential applications of such polymerisation techniques. Weber et al. reported that by varying the grafting density and the pH of the solution LCST behaviour can be introduced and modified [44]. Moreover, by employing RAFT as the polymerisation technique to form the backbone upon which the poly(2-oxazoline) is grafted, additional avenues of functionalisation are opened via the reduction of the terminus to a thiol. This could be used for a further thiol-ene click reaction or, as is the case in the paper by Zheng et al., used as an antifouling coating on a gold surface [29].

This method of grafting onto allows the full analysis of both the back bone and poly(2-oxazoline) side chains, although as noted, the grafting density determination is not always facile. It is also possible to end cap the chain of the poly(2-oxazoline) with (meth)acrylic acid to give a macromonomer that gives the same structure as formed in this technique. However, this will be discussed in a subsequent section.



Scheme 5. 2-oxazoline monomer formed via the CuAAC reaction between azidopentyl-2-oxazoline and propargyl methacrylate.

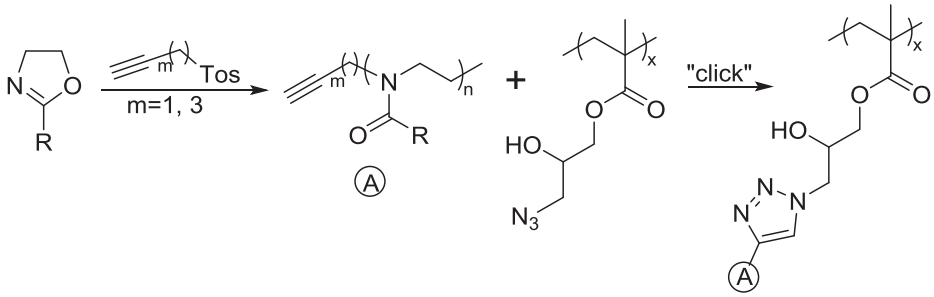
3. Combination via heterofunctional initiator – ATRP/SET-LRP

Initiating CROP on one hand but another polymer on the other gives rise to a versatile technique. Scheme 7 shows one such example of initiating the polymerisation of a 2-oxazoline with α-bromoisobutyryl-bromide on the acyl bromide side and then using the tertiary bromide on the other side to initiate a polymerisation of styrene [15]. The technique is compatible with a wide range of vinyl monomers and the 2-oxazoline polymerisation can be carried out to high molecular weights whilst still maintaining low dispersity. Moreover, the styrene block can also reach to high molecular weights whilst still maintaining relatively low dispersity. It therefore provides an efficient technique to get functional diblock polymers.

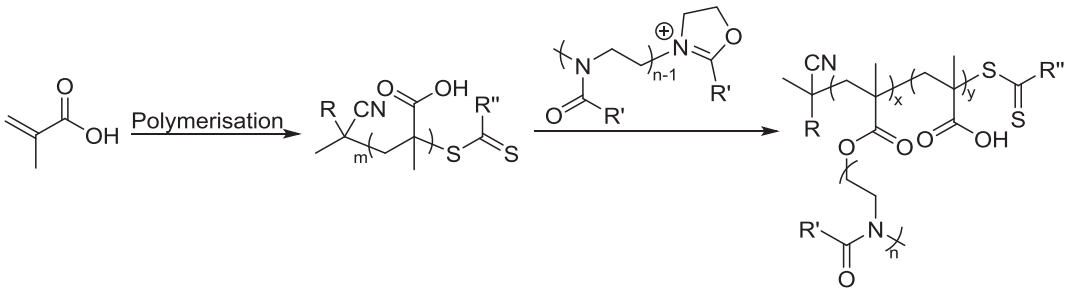
There are a few examples of using a heterofunctional initiator, likely because of the increased difficulty with obtaining groups that are compatible and do not interfere with either polymerisation technique. Nevertheless, the heterofunctional initiator route is also facile in terms of the experimental conditions and provides well defined polymers with high molar mass.

4. Combination via macroinitiators

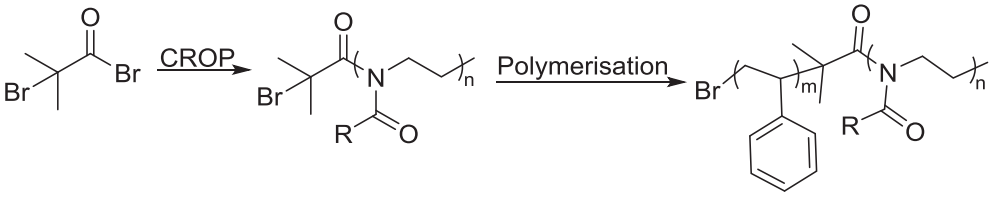
In this section, techniques to form a macroinitiator for the



Scheme 4. Reaction pathway showing the CuAAC reaction between a functionalised poly(2-oxazoline) and poly(3-azido-2-hydroxypropyl methacrylate) formed via the epoxide ring opening of poly(glycidyl methacrylate) to give a graft polymer.



Scheme 6. Polymerisation of methacrylic acid and subsequent grafting of poly(2-oxazoline) via end capping the active chain end.



Scheme 7. Hetereofunctional initiator route. α-bromoisobutyrylbromide initiates the CROP. The tertiary bromine then initiates the ATRP/SET-LRP polymerisation.

subsequent polymerisation of vinyl monomers will be discussed. It is worth noting the contrast between this and, for example, the polymer-polymer coupling reaction methods in Section 2. Previously, the polymers were formed separately then joined together, whereas in this case the vinyl polymer is initiated and propagated from the poly(2-oxazoline). The examples of this type of methodology are more limited, which is likely due to the increased difficulty in obtaining compatible initiators/terminators.

4.1. End functionalisation with an initiator for RAFT

In a previous part of this review (Section 2.1), the method of using the reduction of the terminal group of a RAFT polymer to a thiol and the subsequent thiol-ene click reaction was explored. In this section a macroinitator method will be discussed for the polymerisation of monomers via RAFT polymerisation and hence the formation of a diblock polymer with poly(2-oxazoline). Note that there are two distinct methods, which will be discussed separately, although the general chemistry principles are similar.

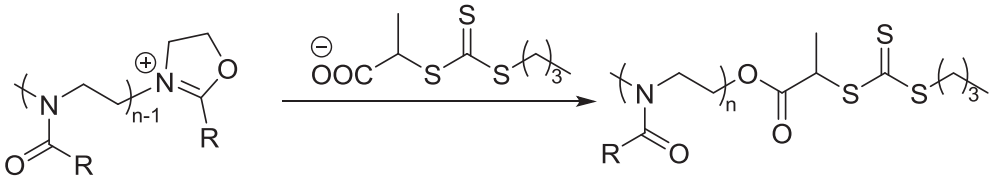
As discussed previously, the chain end of a poly(oxazoline) is susceptible to a nucleophilic attack. This coupled with the living nature of the polymerisation allows for the formation of functionally terminated polymers. Carboxylic acids are one such nucleophilic species that can be exploited. In 2012, Becer et al. presented a method whereby they utilised the living chain end of a poly(2-oxazoline) to form a macroinitiator by terminating the polymerisation with a carboxylic acid functionalised chain transfer reagent (CTA) (Scheme 8) [46]. The obtained macroinitiators were all narrowly dispersed and had a high degree of functionalisation; crucial for the subsequent RAFT polymerisation. The subsequent polymerisation was carried out with styrene, acrylates and acrylamides demonstrating the versatility of this reasonably straightforward technique. In this work methyl, ethyl and nonyl 2-oxazolines were used but this method would likely be suitable for a wide range of 2-oxazolines. It is worth noting that poly(2-methyl 2-oxazoline) had the lowest degree of functionalisation but this could be due to the increased reactivity of the 2-methyl 2-oxazoline monomer leading to more side reactions [4]. Recently, Delaittre et al, utilised two routes to form a macro-CTA, the route described by Becer et al., and a route whereby they end-capped the chain end of the poly(2-oxazoline) with sodium azide and then subsequently introduced the CTA via a CuAAC [47].

This technique is not only limited to forming diblock copolymers but also triblock polymers. By using a bis-initiator for the CROP for example, 4,4′-Bis(bromomethyl)biphenyl, the CROP can be initiated on both sides forming two living chain ends [23,33]. Then, in the same way as before, the chain end is terminated with a carboxylic acid containing CTA. This then allows the polymerisation of the same range of monomers as previously discussed. Finally, by forming di/tri block copolymers the lower critical solution temperature (LCST) is modified depending on the monomer composition [23,33,46].

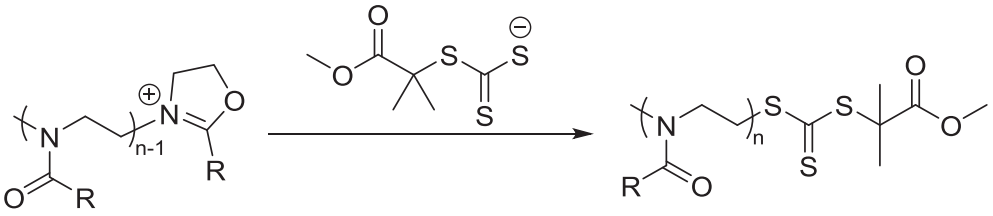
The methodology of endcapping with a carboxylic acid functionalised CTA is not the only technique to incorporate a CTA at the chain end of a poly(2-oxazoline). Another method was recently reported of using a carbonotrithioate to terminate the reaction (Scheme 9) [48]. The resulting macro-CTA can then be applied to polymerise acrylates, styrenics and acrylamides, as previously mentioned. Given that a convenient and facile method exists to form a macro-CTA, as discussed previously, attention now turns as to the merits of the method in Scheme 9. The major advantage is that no purification is required and therefore allows the formation of diblock polymers in a one-pot fashion. Despite this clear benefit, it is important to note that the formation of the terminator, in this case, requires the use of CS_2, which is known to have a relatively high toxicity.

4.2. Macroinititator via reverse iodine transfer polymerisation

In Section 3, a heterofunctional initiator approach to form poly(2-oxazoline) block copolymers with vinyl polymers via SET-LRP/ATRP was introduced. Here, a not dissimilar approach will be highlighted. In Scheme 10, an approach is shown whereby styrene is polymerised via reverse iodine transfer polymerisation (RITP), which yields a terminal iodine group [49]. The resulting polymer is now effectively a macro-



Scheme 8. End capping the poly(2-oxazoline) chain end with a carboxylic acid containing chain transfer agent for the subsequent RAFT polymerisation.



Scheme 9. End capping the poly(2-oxazoline) chain end with a carbonotrithioate chain transfer agent for the subsequent RAFT polymerisation to form a block polymer. Note that no purification is required in this method.

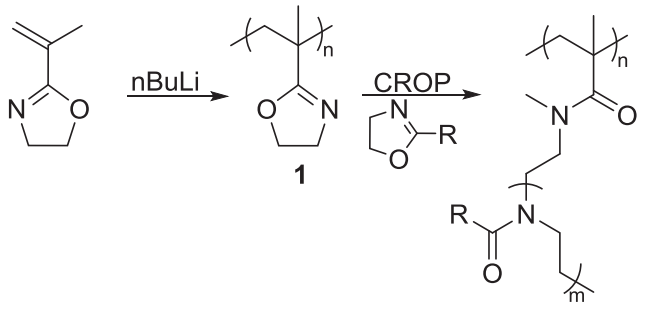
alkyl halide and can initiate the polymerisation of 2-oxazolines forming a di-block copolymer in a one pot fashion. Whilst noting that RITP is a versatile technique capable of polymerising a range of monomers, there are some limitations to this method. Although capable of a one-pot process, the final purification is not straightforward with a mixture of vinyl monomer as well as homopolymer of the 2-oxazoline monomer. Due to this, in the example presented by Rayeroux et al. three consecutive precipitations and a dialysis were required for purification [49]. The macroinitiatior, unsurprisingly, also has to have a high degree of iodine functionality. Given the other methods described to form block copolymers described in this review both previously and going forward, this method is likely to remain niche in use and application.

4.3. Combination via a bifunctional monomer

In 2009, Jordan et al. polymerised the double bond of 2-isopropenyl 2-oxazoline via anionic polymerisation and then subsequently the 2-oxazoline component (Scheme 11) via cationic polymerisation [50]. By treating the formed polymer (**1** in Scheme 11) with methyl triflate a positively charged species is formed. In effect, a macroinitiator is formed, which can initiate the polymerisation of 2-oxazolines from each repeating unit. In doing so, a copolymer with 2-oxazoline brushes is obtained via a grafting from approach. The structure is similar to the one formed via the grafting through (macromonomer approach) and grafting onto method albeit it with an amide linker rather than an ester. Unsurprisingly, the monomer used must have orthogonal polymerisation methods for this approach to be successful, which probably explains the limited number of examples. The initial polymerisation can be carried out via ionic polymerisation [50], free radical polymerisation [50] and RAFT polymerisation [51]. It is important to mention that the initial polymerisation has not yet been reported using ATRP or SET-LRP due to strong complexation from 2-oxazolines with transition metals. Nevertheless, the brushes can be formed in an easy, controlled manner, with narrow distributions even at high chain lengths providing for a convenient technique for the formation of graft polymers.

Furthermore, the polymerisation kinetics of the macroinitiator were investigated and found to be similar to methyl triflate and the chain length had no effect on the polymerisation rate of the oxazoline brush, following first order kinetics [52]. This was attributed to the polycation nature of the macroinitiator which causes stretching of the backbone and therefore an increase in accessibility. In contrast, LCST turbidity measurements were found to be dependent on side chain length, backbone length as well as the composition of the side chain, as expected [50,52].

Whilst not explicitly related to the title of this section another



Scheme 11. Ionic polymerisation of 2-isopropenyl-2-oxazoline followed by the polymerisation of a 2-oxazoline via formation of a macroinitiator.

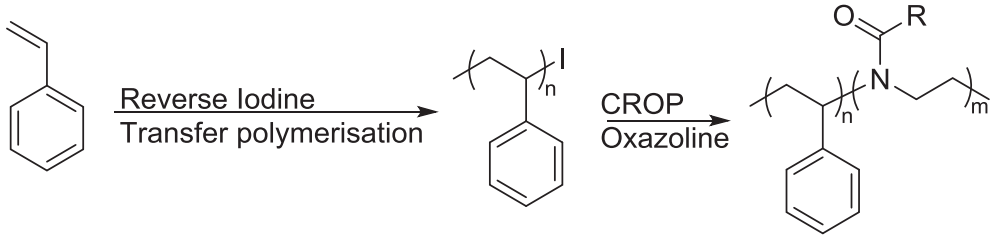
method of forming a graft co-polymer via a grafting from approach should be discussed, albeit briefly. By utilising the polymerisation of chloromethylstyrene, a macroinitiator is then formed, which can initiate an oxazoline polymerisation via the chloromethyl bond with yields up to 94% reported [31,53–55]. This technique is capable, by combination with appropriate comonomer in the first polymerisation of creating graft polymers with interesting thermoresponsive behaviours [31,53]. Moreover, star type architectures have been also reported in the literature [56].

5. Combination via grafting through (macromonomer approach)

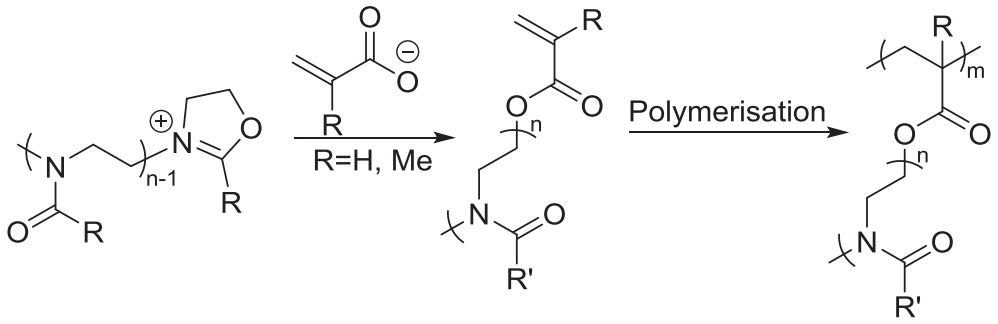
As explained previously, the CROP of poly(2-oxazoline)s proceeds in a living manner, that is, in the absence of termination. On the living end of the chain, an oxazolinium ion is formed which is susceptible to nucleophilic attack and can be used to introduce additional functionality. Furthermore, as discussed, functionality can also be introduced via a functional initiator.

In 2009, Weber et al. showed that the poly(oxazoline) chain can be initiated using methacryloyl chloride introducing a radically polymerisable group at one end [57,58]. However, they found that the degree of functionalisation was low at 21% due to a large number of hydrogen initiated chains. Given the low functionalisation, introducing methacrylate functionality by end-capping the active chain end with the methacrylate anion formed in-situ from methacrylic acid and a suitable base was explored. In addition to this, the polymer was end-capped with aqueous sodium carbonate and then subsequently reacted with methacryloyl chloride to introduce the radically polymerisable group. These two approaches described here demonstrates the versatility of this method of functionalisation.

By end capping the chain with (meth)acrylic acid, a macromonomer



Scheme 10. Reverse iodine transfer polymerisation (RITP) followed by a subsequent polymerisation of a 2-oxazoline.



Scheme 12. End capping the reaction with (meth)acrylic acid to form a macromonomer (grafting from approach) followed by the subsequent radical polymerisation to form a brush polymer.

is then formed. This therefore allows the formation of graft polymers via radical polymerisation of the (meth)acrylate end group, a grafting through approach as shown in Scheme 12 [34,57,59–67]. It is important to note at this stage that the radical polymerisation can proceed under reversible addition-fragmentation chain transfer (RAFT) polymerisation, nitroxide mediated polymerisation (NMP) and free radical polymerisation (FRP) techniques [60]. Moreover, the polymerisation of these macromonomers via ATRP has also been reported [65,66].

Notwithstanding the homopolymerisation of the macromonomers, it is also possible to combine different macromonomers containing different poly(2-oxazolines). In this way, by combining poly(2-ethyl 2-oxazoline) and poly(2-nonyl 2-oxazoline) macromonomers, for example, one can form amphiphilic brush polymers in a relatively easy manner [61]. Whilst in the specific given case the poly(2-oxazoline) macromonomers had a DP of only 5, DPs of over 20 have also been reported in the literature [34]. It is worth considering at this stage that the copolymerisation need not only be carried out with differing poly(2-oxazoline) macromonomers but also can be copolymerised with acrylates [63] and 4-vinylpyridine [62], which both have been shown to successfully copolymerise with poly(2-oxazoline) macromonomers.

This grafting through approach via a meth(acrylate) poly(2-oxazoline) macromonomer is by far the most common employed technique as discussed within this review. This is due to the ability to polymerise these macromonomers via widely applied free/controlled radical polymerisation techniques, the versatility of forming copolymers and the synthetic ease that comes with end capping the polymer. They allow a wide range of graft polymers of varying composition to be synthesised in a controlled and well defined manner owing to the properties described here. Finally, applications of these functional polymers include anti-fouling coatings [62,63] as well as cross-linked hydrogels [68,69].

6. Conclusion and outlook

In this review, several methods were discussed to form both di/triblock copolymers as well as brush copolymers. In the case of di/triblock copolymers, methods such as polymer-polymer coupling and macroinitiators were discussed. Brush polymers were demonstrated by the macromonomer approach as well as polymer-polymer coupling. Perhaps the most versatile of these techniques was found to be click chemistry, having the capability of forming brush or block copolymers in a relatively facile manner, depending on the set up. Although it is noteworthy that the macromonomer approach was the most versatile in the specific case of brush copolymers.

One common theme with the brush polymers was having the backbone as the vinyl polymer and the side chain as poly(2-oxazoline). Accordingly, it would be beneficial to the literature to have more methods to, in effect, reverse the functionality. This is especially valid given that in the majority of cases these polymers have interesting solution behaviours. By altering the structure and architecture of poly(2-oxazoline)/vinyl copolymers, polymers with unique physical properties could be further explored and adapted.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.eurpolymj.2019.07.047.

References

[1] P. Wilson, P.C. Ke, T.P. Davis, K. Kempe, Eur. Polym. J. 88 (2017) 486–515.
[2] E. Vlassi, A. Papagiannopoulos, S. Pispas, Eur. Polym. J. 88 (2017) 516–523.
[3] K. Lava, B. Verbraeken, R. Hoogenboom, Eur. Polym. J. 65 (2015) 98–111.
[4] B. Verbraeken, B.D. Monnery, K. Lava, R. Hoogenboom, Eur. Polym. J. 88 (2017) 451–469.
[5] R. Hoogenboom, Angew. Chem. Int. Ed. 48 (2009) 7978–7994.
[6] N. Adams, U.S. Schubert, Adv. Drug Deliv. Rev. 59 (2007) 1504–1520.
[7] O. Sedlacek, B.D. Monnery, S.K. Filippov, R. Hoogenboom, M. Hruby, Macromol. Rapid Commun. 33 (2012) 1648–1662.
[8] V.R. de la Rosa, J. Mater. Sci. Mater. Med. 25 (2014) 1211–1225.
[9] G.K. Abilova, D.B. Kaldybekov, E.K. Ozhmukhametova, A.Z. Saimova, D.S. Kazybayeva, G.S. Irmukhametova, V.V. Khutoryanskiy, Eur. Polym. J. 116 (2019) 311–320.
[10] E. Cagli, E. Ugur, S. Ulusan, S. Banerjee, I. Erel-Goktepe, Eur. Polym. J. 114 (2019) 452–463.
[11] A.K. Blakney, G. Yilmaz, P.F. McKay, C.R. Becer, R.J. Shattock, Biomacromolecules 19 (2018) 2870–2879.
[12] G. Yilmaz, V. Uzunova, M. Hartweg, V. Beyer, R. Napier, C.R. Becer, Polym. Chem. 9 (2018) 611–618.
[13] N. Ahmad, B. Colak, M.J. Gibbs, D.-W. Zhang, J.E. Gautrot, M. Watkinson, C.R. Becer, S. Krause, Biomacromolecules 20 (2019) 2506–2514.
[14] T.X. Viegas, M.D. Bentley, J.M. Harris, Z. Fang, K. Yoon, B. Dizman, R. Weimer, A. Mero, G. Pasut, F.M. Veronese, Bioconjug. Chem. 22 (2011) 976–986.
[15] C.R. Becer, R.M. Paulus, S. Höppener, R. Hoogenboom, C.-A. Fustin, J.-F. Gohy, U.S. Schubert, Macromolecules 41 (2008) 5210–5215.
[16] R.A. Young, E.L. Malins, C.R. Becer, Aust. J. Chem. 65 (2012) 1132–1138.
[17] S.K. Filippov, B. Verbraeken, P.V. Konarev, D.I. Svergun, B. Angelov, N.S. Vishnevetskaya, C.M. Papadakis, S. Rogers, A. Radulescu, T. Courtin, J.C. Martins, L. Starovoytova, M. Hruby, P. Stepanek, V.S. Kravchenko, I.I. Potemkin, R. Hoogenboom, J. Phys. Chem. Lett. 8 (2017) 3800–3804.
[18] B. D. Monnery and R. Hoogenboom, Polym. Chem., 2019, Advance Article.
[19] C. Weber, A. Krieg, R.M. Paulus, H.M.L. Lambermont-Thijs, C.R. Becer, R. Hoogenboom, U.S. Schubert, Macromol. Symp. 308 (2011) 17–24.
[20] M. Divandari, G. Morgese, S.N. Ramakrishna, E.M. Benetti, Eur. Polym. J. 110 (2019) 301–306.
[21] M. Schmidt, T. Raidt, S. Ring, S. Gielke, C. Gramse, S. Wilhelm, F. Katzenberg, C. Krumm, J.C. Tiller, Eur. Polym. J. 88 (2017) 562–574.
[22] J.H. Joe, J.M. Park, H. Lee, W.-D. Jang, Eur. Polym. J. 118 (2019) 320–326.
[23] M. Sahn, L.M. Stafast, M. Dirauf, D. Bandelli, C. Weber, U.S. Schubert, Eur. Polym. J. 100 (2018) 57–66.
[24] M. Sahn, C. Weber, U.S. Schubert, Polym. Rev. 59 (2019) 240–279.
[25] F. Wiesbrock, R. Hoogenboom, M. Leenen, S.F. van Nispen, M. van der Loop, C.H. Abeln, A.M. van den Berg, U.S. Schubert, Macromolecules 38 (2005) 7957–7966.
[26] R.M. Paulus, T. Erdmenger, C.R. Becer, R. Hoogenboom, U.S. Schubert, Macromol. Rapid Commun. 28 (2007) 484–491.
[27] R.M. Paulus, C.R. Becer, R. Hoogenboom, U.S. Schubert, Macromol. Chem. Phys. 209 (2008) 794–800.
[28] M. Glassner, M. Vergaelen, R. Hoogenboom, Polym. Int. 67 (2018) 32–45.
[29] X. Zheng, C. Zhang, L. Bai, S. Liu, L. Tan, Y. Wang, J. Mater. Chem. B 3 (2015) 1921–1930.
[30] J.C. Rueda, H. Komber, J.C. Cedrón, B. Voit, G. Shevtsova, Macromol. Chem. Phys. 204 (2003) 947–953.
[31] S. Zschoche, J.C. Rueda, M. Binner, H. Komber, A. Janke, K.-F. Arndt, S. Lehmann, B. Voit, Macromol. Chem. Phys. 213 (2012) 215–226.
[32] J. Rueda, S. Zschoche, H. Komber, A. Dirk Schmaljohann, B. Voit, Macromolecules 38 (2005) 7330–7336.

[33] M. Sahn, T. Yildirim, M. Dirauf, C. Weber, P. Sungur, S. Hoeppener, U.S. Schubert, Macromolecules 49 (2016) 7257–7267.
[34] I. Muljajew, C. Weber, I. Nischang, U. Schubert, I. Muljajew, C. Weber, I. Nischang, U.S. Schubert, Materials (Basel) 11 (2018) 528.
[35] H.C. Kolb, M.G. Finn, K.B. Sharpless, Angew. Chem. Int. Ed. Engl. 40 (2001) 2004–2021.
[36] Y. Zhou, P. Wu, Polymer (Guildf) 153 (2018) 250–261.
[37] L. Tan, L. Bai, H. Zhu, C. Zhang, L. Chen, Y. Wang, H. Cheradame, J. Mater. Sci. 50 (2015) 4898–4913.
[38] B. Guillerm, S. Monge, V. Lapinte, J.-J. Robin, J. Polym. Sci. Part A Polym. Chem. 51 (2013) 1118–1128.
[39] Y. Chu, H. Li, H. Huang, H. Zhou, Y. Chen, B. Andreas, L. Liu, Y. Chen, J. Polym. Sci. Part A Polym. Chem. 56 (2018) 174–183.
[40] D. Rayeroux, C. Travelet, V. Lapinte, R. Borsali, J.-J. Robin, C. Bouilhac, Polym. Chem. 8 (2017) 4246–4263.
[41] A.-L. Kampmann, T. Grabe, C. Jaworski, R. Weberskirch, RSC Adv. 6 (2016) 99752–99763.
[42] G. Le Fer, C. Amiel, G. Volet, Eur. Polym. J. 71 (2015) 523–533.
[43] R. Luxenhofer, R. Jordan, Macromolecules 39 (2006) 3509–3516.
[44] C. Weber, C. Remzi Becer, W. Guenther, R. Hoogenboom, U.S. Schubert, Macromolecules 43 (2010) 160–167.
[45] G. Morgese, E.M. Benetti, Eur. Polym. J. 88 (2017) 470–485.
[46] A. Krieg, C. Weber, R. Hoogenboom, C.R. Becer, U.S. Schubert, ACS Macro Lett. 1 (2012) 776–779.
[47] D. Le, F. Wagner, M. Takamiya, I.-L. Hsiao, G. Gil Alvaradejo, U. Strähle, C. Weiss, G. Delaittre, Chem. Commun. 55 (2019) 3741–3744.
[48] A.-K. Trützschler, M.N. Leiske, M. Strumpf, J.C. Brendel, U.S. Schubert, Macromol. Rapid Commun. 40 (2019) 1800398.
[49] D. Rayeroux, V. Lapinte, P. Lacroix-Desmazes, J. Polym. Sci. Part A Polym. Chem. 50 (2012) 4589–4593.
[50] N. Zhang, S. Huber, A. Schulz, R. Luxenhofer, R. Jordan, Macromolecules 42 (2009) 2215–2221.
[51] C. Weber, T. Neuwirth, K. Kempe, B. Ozkahraman, E. Tamahkar, H. Mert, C.R. Becer, U.S. Schubert, Macromolecules 45 (2012) 20–27.
[52] N. Zhang, R. Luxenhofer, R. Jordan, Macromol. Chem. Phys. 213 (2012) 973–981.
[53] J.C. Rueda, S. Zschoche, H. Komber, F. Krahl, K.-F. Arndt, B. Voit, Macromol. Chem. Phys. 211 (2010) 706–716.
[54] O. Nuyken, J. Rueda-Sanchez, B. Voit, Polym. Bull. 38 (1997) 657–664.
[55] O. Nuyken, J.R. Sanchez, B. Voit, Macromol. Rapid Commun. 18 (1997) 125–131.
[56] R. Weberskirch, R. Hettich, O. Nuyken, D. Schmaljohann, B. Voit, Macromol. Chem. Phys. 200 (1999) 863–873.
[57] C. Weber, R.C. Becer, A. Baumgaertel, R. Hoogenboom, U.S. Schubert, Des. Monomers Polym. 12 (2009) 149–165.
[58] C. Weber, C.R. Becer, R. Hoogenboom, U.S. Schubert, Macromolecules 42 (2009) 2965–2971.
[59] S. Kobayashi, M. Kaku, S. Sawada, T. Saegusa, Polym. Bull. 13 (1985) 447–451.
[60] C. Weber, K. Babiuch, S. Rogers, I.Y. Perevyazko, R. Hoogenboom, U.S. Schubert, Polym. Chem. 3 (2012) 2976.
[61] C. Weber, M. Wagner, D. Baykal, S. Hoeppener, R.M. Paulus, G. Festag, E. Altuntas, F.H. Schacher, U.S. Schubert, Macromolecules 46 (2013) 5107–5116.
[62] H. Zhu, F. Mumtaz, C. Zhang, L. Tan, S. Liu, Y. Zhang, C. Pan, Y. Wang, Appl. Surf. Sci. 426 (2017) 817–826.
[63] K. Kempe, S.L. Ng, K.F. Noi, M. Müllner, S.T. Gunawan, F. Caruso, ACS Macro Lett. 2 (2013) 1069–1072.
[64] C. Weber, S. Rogers, A. Vollrath, S. Hoeppener, T. Rudolph, N. Fritz, R. Hoogenboom, U.S. Schubert, J. Polym. Sci. Part A Polym. Chem. 51 (2013) 139–148.
[65] J. Collins, S.J. Wallis, A. Simula, M.R. Whittaker, M.P. McIntosh, P. Wilson, T.P. Davis, D.M. Haddleton, K. Kempe, Macromol. Rapid Commun. 38 (2017) 1600534.
[66] D. Gieseler, R. Jordan, Polym. Chem. 6 (2015) 4678–4689.
[67] S. Kobayashi, H. Uyama, J.H. Choi, Y. Matsumoto, Polym. Int. 30 (1993) 265–270.
[68] D. Christova, R. Velichkova, E.J. Goethals, Macromol. Rapid Commun. 18 (1997) 1067–1073.
[69] D. Christova, R. Velichkova, W. Loos, E.J. Goethals, F. Du Prez, Polymer (Guildf) 44 (2003) 2255–2261.