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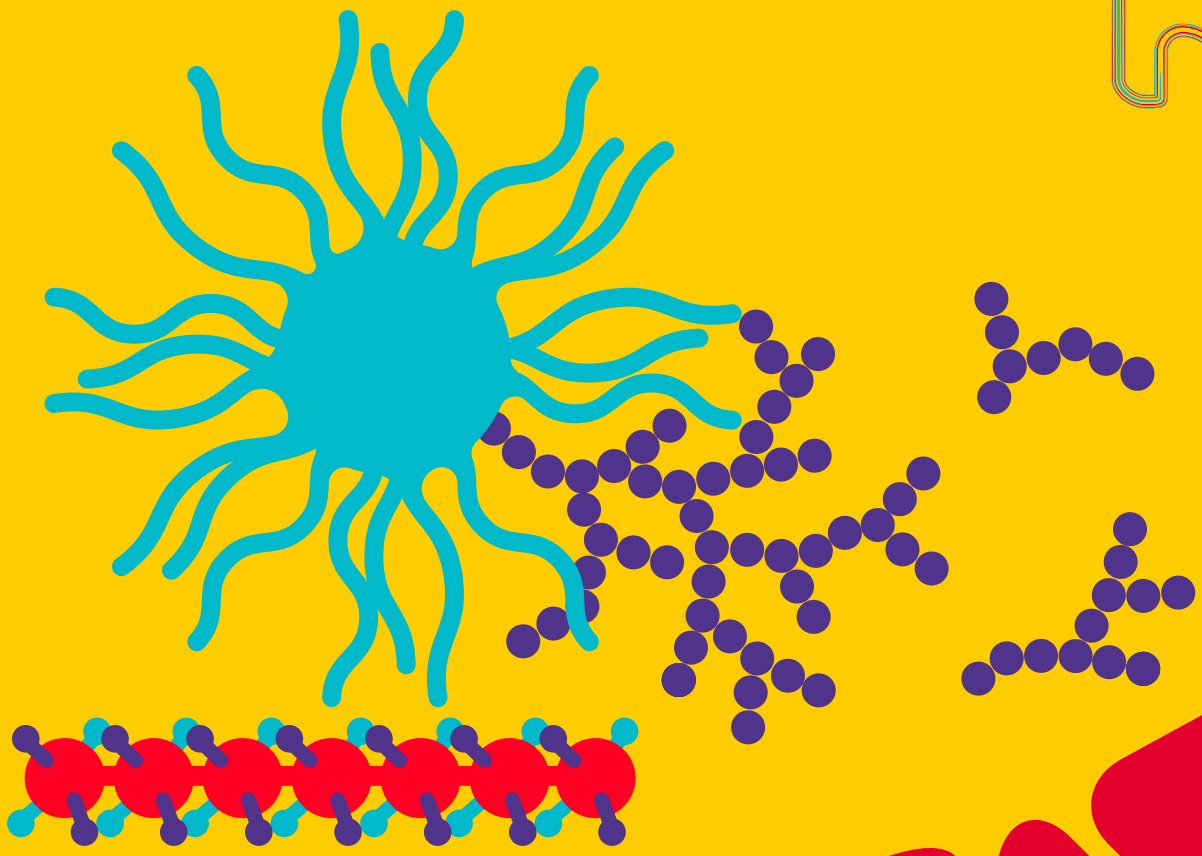
controlled radical polymerization guide

ATRP | RAFT | NMP



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Preface

Chain-growth polymerization has been successfully performed for many decades through conventional free radical, anionic, or cationic polymerization. These polymerization techniques generate many important commodity polymers where their broad range of molecular weight distribution gives rise to important physical properties. While these techniques are useful for a number of applications starting from a wide variety of monomers, several applications benefit from using more precisely controlled polymers. "Living" polymerization pioneered by Michael Szwarc enables control over the polymer architecture, which includes molecular weight, molecular weight distribution (polydispersity), functionality, and composition. The occurrence of premature termination is minimized, and molecular weight proceeds linearly with time until all monomer is consumed or intentionally terminated. In the 1990s, new methods were developed which enabled an adaptation of living ionic polymerization to living radical polymerization (LRP), also referred to as controlled radical polymerization (CRP). Controlled radical polymerization has branched into three fundamental techniques which are listed below.

- Atom Transfer Radical Polymerization (ATRP)
- Reversible Addition/Fragmentation Chain Transfer Polymerization (RAFT)
- Nitroxide-mediated Polymerization (NMP)

CRP can be utilized with a broad range of vinyl monomers for a wide variety of applications. Moreover, CRP enables a new level of materials design and is accessible to all levels of synthetic expertise due to the robustness of the polymerization conditions. **Figure 1** illustrates the trend in literature citations for the main CRP techniques.

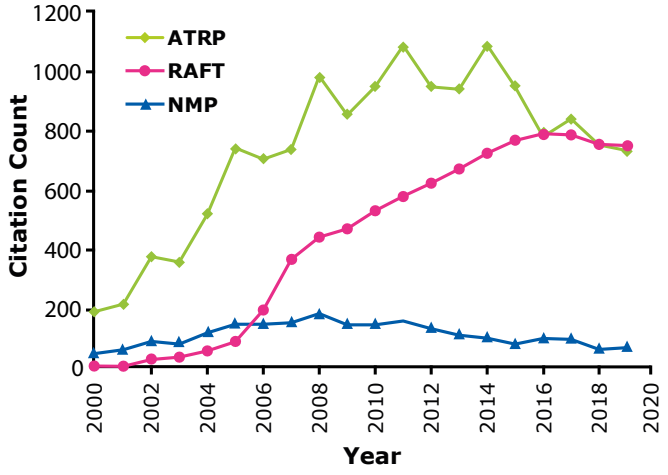

Figure 1. SciFinder search results as of 2011 for ATRP, RAFT, and NMP technologies.

All of these technologies are popular in the research community and are being explored for industrial adoption. ATRP has consistently held the most citations. RAFT technology has gained a substantial increase in publications over the last 5–8 years. NMP remains relevant in research with approximately 150 annual citations since 2005. **Table 1** is a brief summary of benefits and limitations of the different CRP techniques.

Table 1. Benefits and limitations of ATRP, RAFT, and NMP processes.

	ATRP	RAFT	NMP
Primary Benefits	• Versatile • Ability to tailor catalyst to meet specific needs	• Versatile • No use of transition metals	• No use of transition metals • Low potential for odor and discoloration
Primary Limitations	• Use of transition metals • Many variables affecting polymer characteristics	• High potential for odor and discoloration (especially for low molecular weights)	• Least versatile

Polymers generated by controlled radical polymerization are used in many applications. Surface modification, commonly performed through ATRP, enables advancement in many applications which rely on tailored hydrophilicity, adhesive properties, or nanoparticle functionalization. Block copolymers for bio-applications, commonly performed through RAFT or ATRP, enable advancements in drug delivery, bio-mineralization, bio-compatibilization, and hydrogel applications. Block copolymers generated from NMP are used in pigment dispersion, memory devices, composite manufacturing, and many others.

This guide provides a fundamental review of ATRP, RAFT, and NMP techniques, as well as corresponding procedures and product information to utilize these techniques. The guide has been arranged in four sections: the ATRP section contains four articles, two procedures and tables for initiators and catalysts; the RAFT section contains three articles, two procedures and RAFT agent tables; the NMP section contains an article and an NMP agent product table; and the monomer section contains tables of six monomer classes. We hope that this publication will enable chemists and engineers to explore different CRP techniques.

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ATRP for Everyone: Ligands and Initiators for the Clean Synthesis of Functional Polymers

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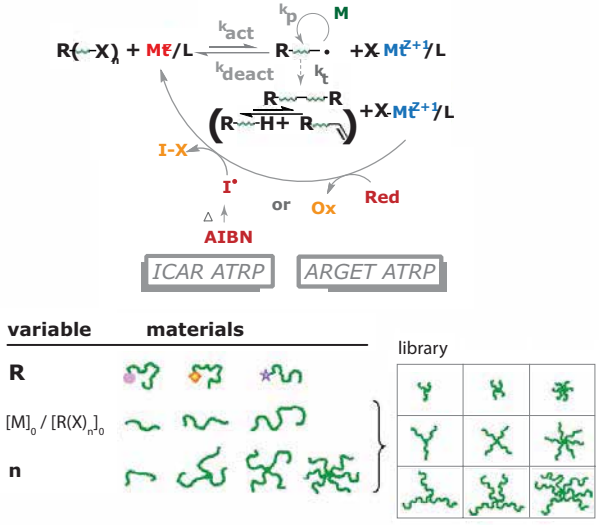
Introduction

Atom transfer radical polymerization (ATRP)[1–4] has emerged as one of the most successful synthetic techniques for the preparation of polymers with predetermined molecular weights, narrow molecular weight distributions, and high degrees of chain end functionalities (**Scheme 1**). The unprecedented control over molecular architecture afforded by the ATRP enables preparation of systematic polymer libraries.[5] **Scheme 1** exemplifies a systematic library of star-shaped polymers, where the polymers in each row have the same arm size and those in each column have the same number of arms. Such libraries can provide important data for understanding the relationships between polymer structure and physical properties or function.

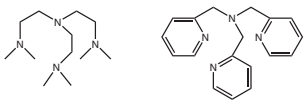


Scheme 1. Schematic illustration of the ATRP process (top) and an example of a star-shaped polymer library.

Catalysts for ATRP

ATRP is a catalytic process using a metal complex, in which the transition metal Mt can exist in two different oxidation states. The lower oxidation state metal complex Mt^z/L (L is a ligand) reacts with the ATRP initiator (alkyl halide RX) to yield a radical R• and the corresponding higher oxidation state metal complex with a coordinated halide anion X-Mt^{z+1}/L, in a process termed activation, proceeding with the rate constant, k_{act}. The latter complex can transfer the halogen atom back to the radical, re-generating the alkyl halide and the lower oxidation state metal complex. The radicals can react with the monomer M (generating polymer with the rate constant of propagation k_p), with each other (termination with the rate constant, k_t) or with X-Mt^{z+1}/L (deactivation with the rate constant, k_{deact}). The last step, which distinguishes ATRP from conventional radical polymerization, yields the halogen-terminated polymeric dormant state, which can be reactivated in a reaction with Mt^z/L. If the deactivation process is efficient (i.e., high value of k_{deact}) and if all polymer chains are initiated within a short period by appropriate selection of the alkyl halide initiator, the resulting polymer will be characterized by a narrow molecular weight distribution. Additionally, it is desirable to use an active catalyst with a high value of the ratio of k_{act}/k_{deact}, termed the ATRP equilibrium constant, K_{ATRP}, to ensure fast polymerization. The rate constants k_{act} and k_{deact} depend on both the transition metal and the ligand. Rules for the rational selection of active catalysts for ATRP for various reaction media and monomers have been developed.[2,6]

Various metals and ligands have been successfully employed as catalysts in ATRP, but the most often used are the catalysts based on copper (the two oxidation states are Cu^I and Cu^{II}) and N-containing ligands. One drawback of the classical ATRP is the use of high amounts of the catalyst.[4] The obtained polymers are well-defined in terms of molecular weight distribution and chain-end functionality but require tedious purification to remove the catalyst. Although various methods for catalyst removal have been developed,[2,7] the extra purification step is associated with longer time needed to obtain the final product, and with generation of waste, both of which increased the cost of the materials prepared by ATRP. However, the use of ligands such as tris[2-(dimethylamino) ethyl]amine (Me_6TREN, Cat. No. 723142) and tris(2-pyridyl-methyl)amine (TPMA, Cat. No. 723134) alleviates this problem (**Figure 1**). These ligands can be used in new techniques called Activators ReGenerated by Electron Transfer (ARGET)[8,9] and Initiators for Continuous Activator Regeneration (ICAR)[10] which allow decreasing the amount of catalyst to only few, often single-digit, ppm. For comparison, 1,000 to 10,000 ppm were used in traditional ATRP. For many applications, in these new systems the residual copper can be left in the final colorless products. Both techniques employ a reducing agent: a radical initiator such as AIBN in ICAR ATRP;[10] and tin(II) ethylhexanoate[8,9,11–13] (Cat. No. S3252), ascorbic acid,[14] glucose,[9] hydrazine,[10] or Cu(0)[15] in ARGET ATRP. These reducing agents allow for regeneration of the lower oxidation state metal complex, which would normally be irreversibly converted to the higher oxidation state complex due to radical termination by a process dubbed "persistent radical effect".[16]



Me_6TREN Cat. No. 723142 | **TPMA** Cat. No. 723134

Figure 1. Ligands for Cu-mediated ATRP using ppm amounts of catalyst.

The ARGET and ICAR ATRP processes allow chemists to reduce the amount of catalyst more than one thousand times and the polymers obtained are white or colorless. These processes also allow preparation of well-defined block copolymers,[12] polymers with high molecular weight,[11,17] high chain-end functionality[11] and adjustable molecular weight distribution.[18]

In addition, since the level of control in ARGET and ICAR ATRP is only weakly affected by an excess of reducing agent, the reactions can be successfully carried out in the presence of limited amounts of air.[13] Reactions can be carried out without deoxygenation, in flasks fitted with rubber septa or even in simple jars. This was demonstrated in our laboratory by placing functionalized wafers in one of these vessels and growing very dense polymer brushes (~0.4 chain/nm^2), including block copolymer brushes, without any deoxygenation. ATRP stops after opening the vessel to air but starts again when a sufficient amount of reducing agent is added to the closed flask. This polymerization process does not require any special skills and is especially well-suited for grafting from larger surfaces, but can also be applied for preparation of any other polymer materials. Only very active catalysts derived from Me_6TREN and TPMA can be used in these new techniques. **Figure 2** presents the kinetic plot, evolution of molecular weights and polydispersities with conversion and GPC traces for polymerization of styrene (St) with 50 ppm of $Cu^{II}Br_2$/TPMA catalyst in the presence of AIBN as reducing agent. Molecular weight control is excellent and follows theoretical values based on quantitative initiation. The polymer, after precipitation in hexane, appeared as a white solid powder containing only 5 ppm of the residual catalyst. If more Cu removal is needed, the *ATRP pure* resin can be used.[5,19]

Typical ICAR ATRP Procedure

The following is a procedure employing very low concentration of copper catalyst that yields well-defined polystyrene macroinitiator (PSt-Br) with degree of polymerization of 100. As shown in **Figure 2**, the polymerization is well-controlled: the linear first order kinetic plot of monomer consumption indicates constant number of active species and the increase of molecular weights with conversion is characteristic of a living process. Moreover, the obtained polymer was virtually colorless without the use of any special purification methods other than simple precipitation in hexane.

- Add $CuBr_2$ (7.8 mg, 3.5 × 10^{-2} mmol, Cat. No. 221775) and TPMA (10.1 mg, 3.49 × 10^{-2} mmol, Cat. No. 723134) to a 10 mL flask equipped with magnetic stirring bar.
- Add DMF (4 mL, Cat. No. D158550) to solubilize $CuBr_2$/TPMA. Stir for 10 min to obtain a homogeneous yellowish solution.
- Add St (80.0 mL, 0.698 mmol, Cat. No. 240869), AIBN (0.153 g, 0.0931 mmol, Cat. No. 441090) and ethyl 2-bromoisobutyrate (0.68 mL, 4.65 mmol, Cat. No. E14403) to a 200 mL round bottom flask equipped with a magnetic stirring bar.
- Transfer the catalyst solution to the 200 mL round bottom flask reactor.
- Close the flask reactor with glass adapter (with glass stopcock and a rubber septum). Stir the solution while purging with nitrogen for 1 h.

Polymerization conditions for ICAR ATRP of styrene:
$[St]_0$/ $[EtBiB]_0$ / $[CuBr_2]_0$ / $[TPMA]_0$ / $[AIBN]_0$ – 100 / 1 / 0.005 / 0.005 / 0.2
T = 70 °C ; DMF as internal standard (5 vol% versus St)

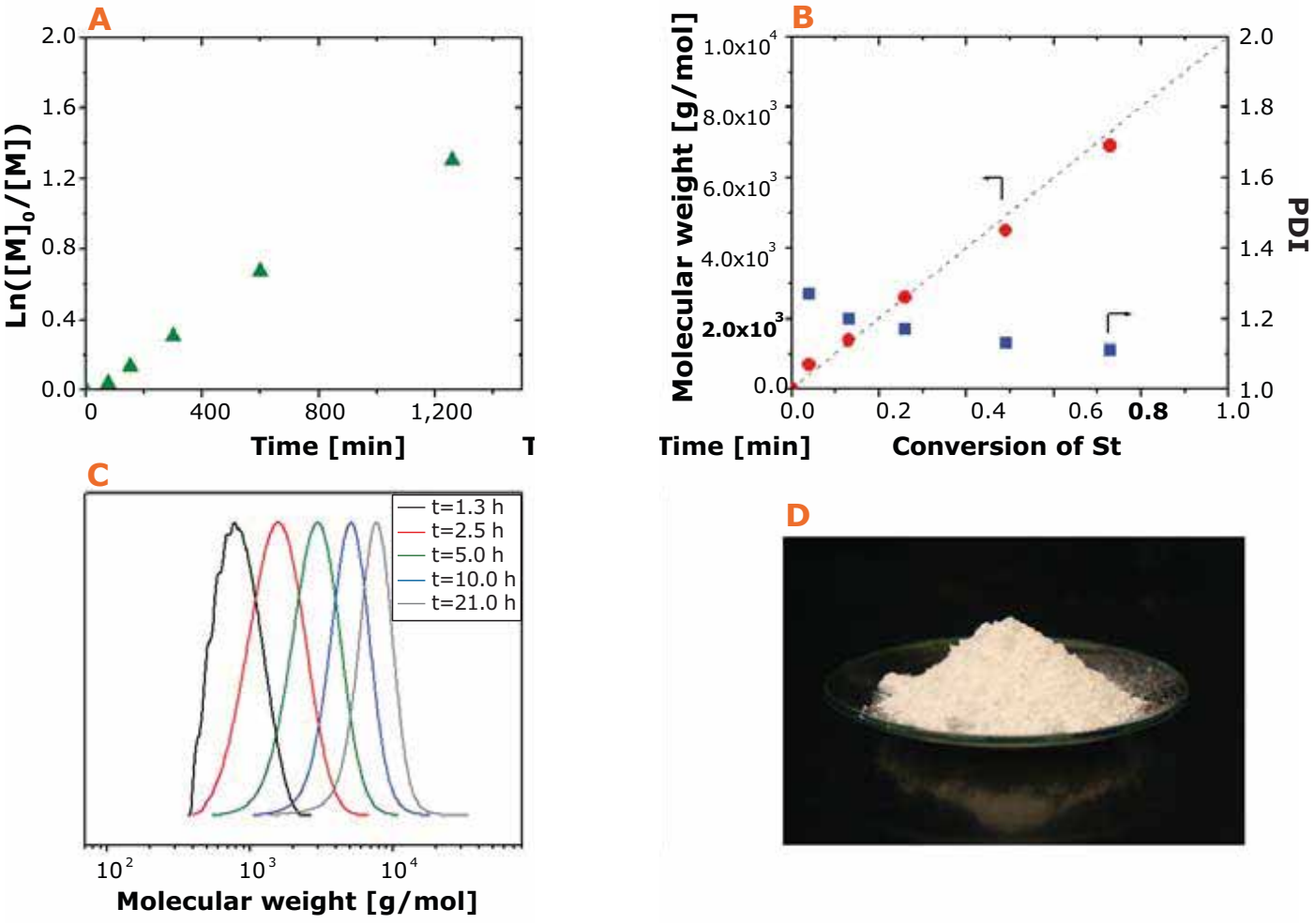


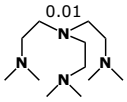
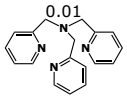
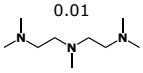
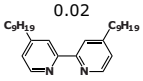
Figure 2. ICAR ATRP of styrene (St) using 50 ppm of catalyst. (**A**) Kinetic plot; (**B**) Molecular weight and polydispersity as a function of conversion; (**C**) Evolution of GPC traces; (**D**) Photograph of polymer after precipitation in hexane

- Place the flask in an oil bath at 70 °C. To follow the progress of the reaction, samples can be withdrawn with a stainless steel needle. The samples can be analyzed by GC or NMR (monomer conversion) and SEC (molecular weight and polydispersity).
- After 20.5 h*, the monomer conversion reaches 69%. M_n = 9,700 g/mol, PDI = 1.11. The reactor is opened to air and allowed to cool to room temperature.
- Dilute the polymer with THF (100 mL) and precipitate into 2 L of hexane.
- Dry the produced polymer at 45 °C to constant weight (ca. 24 h).

***Note:** Time of the reaction may vary depending on a type of used equipment and purity of chemical reagents.

It is interesting to compare the results of ICAR ATRP employing Me_6TREN or TPMA with the process under similar conditions but with other catalysts, derived from ligands, such as the traditionally used derivatives of 2,2-bipyridine (bpy) (ex., Cat. No. 482250) or *N,N,N′,N″,N‴* – pentamethyldiethylenetriamine (PMDETA, Cat. No. 369497). As seen from **Table 1**, only the polymerizations mediated by the complexes of Me_6TREN and TPMA (the first two entries) were well-controlled and yielded polymers with narrow molecular weight distribution.[10] In all cases, only 50 ppm of Cu was employed.

Table 1. ICAR ATRP of St initiated by ethyl 2-bromoisobutyrate (EBiB) in the presence of various Cu-based catalysts.

St / EBiB / CUII / AIBN (60 °C, in anisole, (50 vol % vs. St))	Ligand	Cu (ppm)	Time (min)	Conv. (%)	M_n (theor.)	M_n (SEC)	PDI
200/1/0.01/0.1 Me_6TREN (Cat. No. 723142)	 0.01	50	2760	44	8700	7900	1.12
200/1/0.01/0.1 TPMA (Cat. No. 723134)	 0.01	50	2880	39	7800	6800	1.09
200/1/0.01/0.1 PMDETA (Cat. No. 369497)	 0.01	50	2880	29	5600	4500	1.62
200/1/0.01/0.1 dNbpy (Cat. No. 482250)	 0.02	50	2940	36	7200	5600	1.68

Me_6TREN and TPMA were successfully used in ICAR and ARGET ATRP of various monomers such as styrene,[9–11] methyl acrylate,[15] butyl acrylate,[8] methyl methacrylate,[8,12] butyl methacrylate,[20] dimethylaminoethyl methacrylate,[21] and acrylonitrile.[17,22] They can also be used in classical ATRP of coordinating monomers such as, for example, 4-vinylpyridine (Cat. No. V3204). Rate of ICAR ATRP is not affected by the catalysts but it is defined by the rate of decomposition of the radical initiator and can be significantly accelerated at higher temperatures.

Block Copolymers

Block copolymers continue to remain a subject of intense research and technological interest due to their unusual and useful properties.[23,24] Current and potential high-technology applications of block copolymers are based on their ability to self-assemble, in bulk as well as in selective solvents, into ordered nanostructures. For example, block copolymers with hydrophilic and hydrophobic segments self-assemble, both in the solid state and in solution, to generate a variety of nanoscale structures. The structures range from simple micellar or lamellar to complex gyroid. Recent studies on block copolymer self assembly demonstrated that nanoscale morphology is highly dependent on block chain length, chain length ratios, polydispersity index, and block composition. Therefore, it is essential to precisely control the degree of polymerization of each segment in the block copolymer and achieve narrow molecular weight distribution. ATRP is a convenient technique for preparation of block copolymers because the growing polymer chain contains a stable halogen terminated ω-end that can act as an initiator for chain extension.

Figure 3 presents GPC traces of polystyrene-*b*-poly(*t*-butyl acrylate) (PSt-*b*-P*t*BA) as an example of synthesis of a block copolymer library.[5] In order to synthesize these copolymers ICAR and ARGET ATRP were used with similar conditions as described above. This library can be then converted to polymeric surfactants polystyrene-*b*-poly(acrylic acid) (PSt-*b*-PAA) by deprotection of *t*-butyl groups. PSt-*b*-PAA copolymers may be used as polymeric surfactants in many applications such as particle dispersants (organic, inorganic, and metals), nano-device delivery vehicles, blend compatibilizers, coatings, surface modifiers, detergents, and emulsifiers. The broad range of compositions and molecular weights provided by each polymeric library synthesized by ATRP allows rapid screening and identification of the optimal structure for the particular application. Several systematic polymeric libraries are now commercially available.[19]

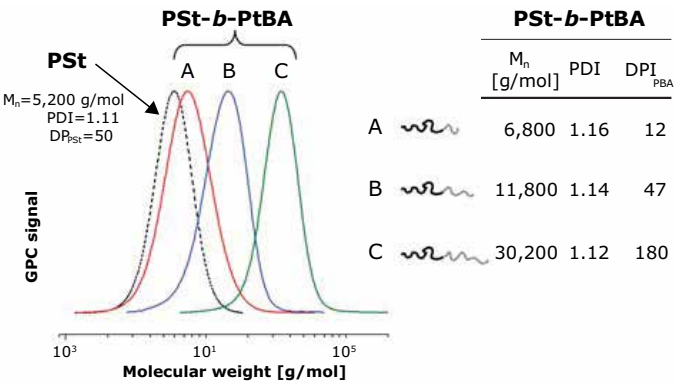


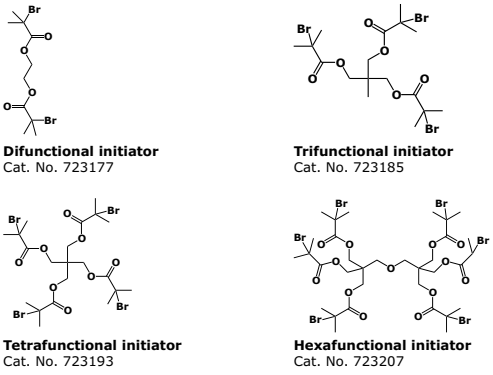
Figure 3. GPC traces and properties of PSt-*b*-PtBA block copolymer library.

Initiators for ATRP

ATRP uses simple initiators, mainly alkyl halides R-X (X = Cl, Br).[1,25,26] The number-average molecular weight Mn of polymers prepared by ATRP depends on the initial concentration ratio of monomer (M) to initiator as well as the monomer conversion:

$$\mathbf{M_n = ([M]_0 \,/\, [RX]_0)\ X\ Conv\ X\ M_W(M)}$$

where $[M]_0$ is the initial monomer concentration, $[RX]_0$ is the initial concentration of alkyl halide, Conv is the monomer conversion, and $M_W(M)$ is the molecular weight of the monomer. The alkyl halides used as initiators can contain either one or numerous halogen atoms. Depending on the exact initiator structure and the number of halogen atoms, the architecture of the prepared polymers can be varied from linear (using alkyl halides with a single halogen atom), to star-like or brush-like (multiple halogen atoms in the initiator). Star polymers can be generated using initiators with alkyl halide groups attached to a single core (**Figure 4**), whereas to obtain brush polymers, the halide groups should be attached along the backbone of a polymer or a large molecule or nanoparticle with a high aspect ratio (e.g., a carbon nanotube).



Difunctional initiator
Cat. No. 723177

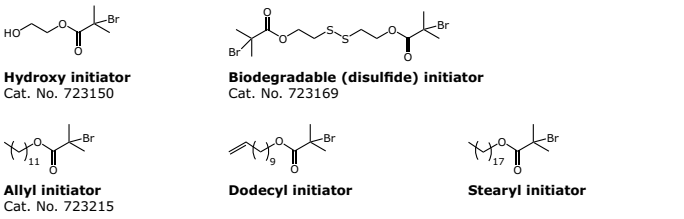
Trifunctional initiator
Cat. No. 723185

Tetrafunctional initiator
Cat. No. 723193

Hexafunctional initiator
Cat. No. 723207

Figure 4. Examples of ATRP initiators yielding polymeric stars.

Four major strategies exist for the synthesis of polymers with functional groups via ATRP: i) direct polymerization of functional monomers, ii) polymerization of "protected" monomers followed by post-polymerization chemical transformations, iii) the use of functional initiators, and iv) substitutions of the terminal halogen atom. The first two approaches yield polymers with multiple functionalities along the backbone, whereas the last two yield end-functionalized polymers. **Figure 5** illustrates structures of alkyl halide functional initiators that yield endfunctionalized polymers. Groups such as hydroxy are suitable for the synthesis of polymers that can react with molecules, or surfaces with carboxylic acid groups. Allyl group-containing initiators yield polymers that can participate in hydrosilylation or ene reactions with polymers or surfaces containing Si-H or S-H bonds, respectively. Trichlorosilyl groups react with surfaces containing hydroxy or amine groups (including Si-OH bonds), such as those on the surface of silica particles or glass. Finally, disulfide-containing difunctional initiators yield polymers containing a functional group able to react with gold surfaces, and also gives the polymers the ability to degrade in reducing environments.



Hydroxy initiator
Cat. No. 723150

Biodegradable (disulfide) initiator
Cat. No. 723169

Allyl initiator
Cat. No. 723215

Dodecyl initiator

Stearyl initiator

Figure 5. Examples of ATRP initiators that can be used to prepare end-functionalized and disulfide containing polymers.

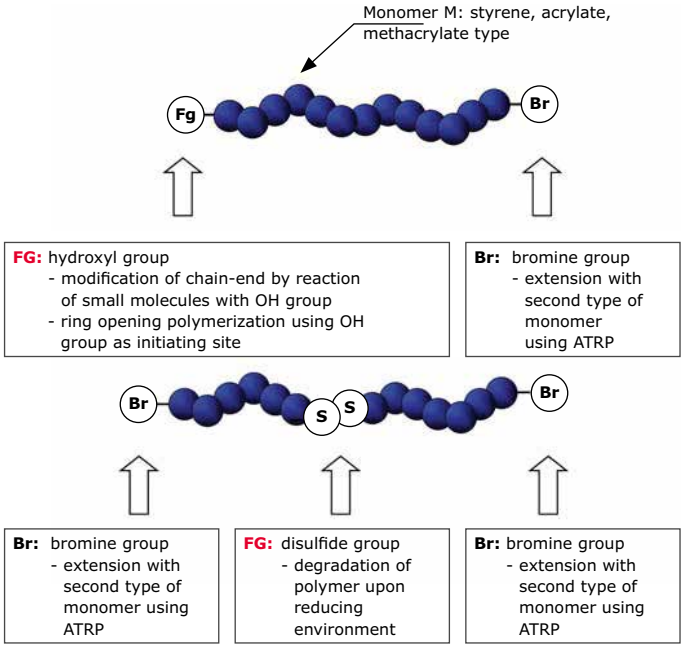


Figure 6. Examples of end-functionalized polymers prepared by ATRP using an initiator with a hydroxy or disulfide functional group (FG).

A much broader variety of functional alkyl halides can be easily custom-synthesized.[1] Several concepts for functional polymer architectures that can be prepared using functionalized ATRP initiators are further illustrated in **Figure 6**. It should be emphasized that the polymers prepared by ATRP contain two chain ends: the -end (FG) derived from the initiator and the ω-end, which is normally a bromine or chlorine atom. Alkyl halides can participate in a number of nucleophilic substitution reactions, which expands significantly the types of endfunctional polymers accessible through ATRP.[25]

Summary

The number of materials and commercial products that use polymers either in a pure form or as a part of more complex mixtures, blends, and composites, is countless. The properties and application of polymers depend not only on the molecular size but also on the molecular shape and composition.[27] Today, ATRP is one of the most powerful polymer synthetic methods which allows control over molecular architecture, as evidenced by over one hundred patent applications, over a thousand journal articles published annually, and also in a number of commercial products made in US, Japan, and Europe. Due to recent advancements in initiation processes (ARGET and ICAR ATRP) it is relatively easy to perform any polymerization reaction and the purification of the final products is now easier, while generating a minimum amount of waste.

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Tools for Performing ATRP

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Introduction

Controlled radical polymerization (CRP) techniques have been reviewed in a number of articles[1,2] and books,[3] and include nitroxide-mediated polymerization (NMP),[4–7] reversible addition fragmentation chain transfer (RAFT),[8–10] and atom transfer radical polymerization (ATRP).[11] All of these CRP techniques operate by rapidly establishing an equilibrium between a small fraction of active polymerizing chains and a majority of dormant moieties. ATRP has proven to be versatile and effective in providing a controlled polymerization environment for a wide range of vinyl monomers including styrenes, (meth)acrylates, acrylonitriles, and dienes.[3] ATRP differs from conventional radical polymerization because of the ability of a metal complex to dictate the rate of monomer addition to the propagating polymer chain end. While the procedure to perform normal ATRP is simple with essentially three components (initiator, catalyst, and monomer) added to solvent, the equilibrium equation describing the reaction is more complex, and is shown in **Figure 1**.

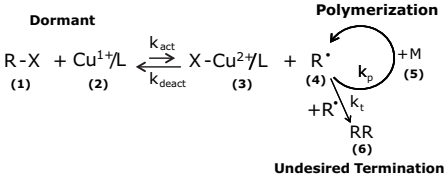

Figure 1. The ATRP equilibrium equation, which resides predominantly to the left/dormant side, includes dormant initiator R-X (1), catalyst composed of a transition metal Cu with ligand L (2), oxidized catalyst (3), active radical or active initiator R• (4), and monomer M (5) and terminated polymer RR (6). The reaction rates are labeled with kx.

This equation may appear to have a high degree of complexity, but its meaning and importance can be illustrated by three situations: a polymer sitting dormant on the left side of the equilibrium; a polymer reacting with monomer on the right side of the equilibrium (and growing in molecular weight); and two radical end-groups combining to terminate and kill the reaction (this is neither reversible nor desired). In ATRP, the reaction resides on the left side of the equation most of the time. This minimizes the likelihood for two radicals to exist near each other at the same time and therefore minimizes termination. This control over termination is the primary benefit of choosing ATRP. Another important feature of ATRP is that only one radical is formed upon activation. This is particularly important if surface-initiated polymerization is desired because this minimizes solution polymerization.

The rate of reaction is marked by rate constants (k_x) where the rate of activation is k_{act}, the rate of deactivation is k_{deact}, the rate of monomer addition is k_p, and the rate of termination is k_t. The control over this equilibrium highly depends on the choice of catalyst.

ATRP: Choosing a Ligand for the Catalyst

The catalyst (complex 2 in **Figure 1**) is a transition metal ion with coordinated ligands, and complex 3 is the oxidized form of the complex. (The difference between the two is that the oxidized complex 3 has the halogen from the initiator and a charge of one higher than complex 2.) A wide variety of transition metals have been reported to work with ATRP, including Ti,[12] Fe,[13–17] Co,[18] Ni,[19–21] Mo,[22–24] Ru,[25–27] Rh,[28] Pd,[29] Re,[30] Os,[31] but the use of Cu dominates the literature. To simplify the discussion, the rest of this article will refer to Cu. The catalyst complex 2 abstracts the halogen from the initiator (or chain end) to activate the polymerization, so it has an important influence on the reaction rates of the equilibrium. The ligand choice will have a profound effect on k_{act} and k_{deact}, which will cause a difference in the rate of polymerization. Several ligands are shown plotted along the ratio of (k_{act}/k_{deact}) in **Figure 2**.

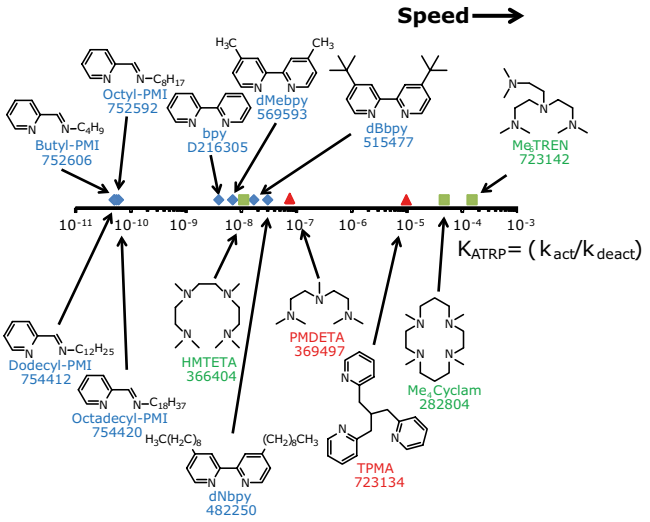

Figure 2. Nitrogen-based ligands plotted against the ATRP equilibrium constant (K_{ATRP}) with initiator EtBibb, in the presence of CuBr in MeCN at 22 °C. Bidentate ligands are blue diamonds, tridentate ligands are red triangles, and tetradentate are green squares. Adapted from Tang, W. et al.[32]

This shows that, in general, the speed of the polymerization in terms of the ligand structure is bidentate < tridentate < tetradentate. This can also be thought of in terms of how much catalyst is needed to perform the reaction. Less catalyst is needed with a large K_{ATRP} value.

Variations of ATRP

Returning to **Figure 1**, the components that are added to the polymerization solution for normal ATRP are initiator 1, catalyst 2, and monomer 5. Catalyst 2 is oxygen-sensitive, so in an effort to minimize handling of this compound, several variations of ATRP have been developed. Newer "variations" of ATRP were developed primarily to generate the air-sensitive catalyst 2 at the start of the reaction rather than requiring it to be handled and added.

- Initiators for Continuous Activator Regeneration (ICAR)
- Activators Generated by Electron Transfer (AGET)
- Activators ReGenerated by Electron Transfer (ARGET)
- Reverse ATRP

Detailing the competing reactions for all of these techniques is beyond the scope of this article; however, the following table summarizes the components added to perform the different ATRP reactions.

Typical Reactants Adde

Table 1. ATRP polymerization type and corresponding identity or concentration of popular reactants added.

Polymerization	Copper(I) Catalyst Concentration (ppm)	Copper(II) Catalyst Concentration (ppm)	Popular Ligands	Reducing Agent	Free Radical Initiator
ATRP	10,000	0-variable	all nitrogen containing ligands	–	–
ICAR	0	10	Me_6TREN and TPMA	–	AIBN
AGET	0	5	Me_6TREN and TPMA	tin(II)ethyl-hexanoate	–
ARGET	0	5	Me_6TREN and TPMA	tin(II)ethyl-hexanoate	–
Reverse ATRP	0	1,000	several	–	–
Simultaneous reverse and normal	0	1,000	several	–	AIBN

All of the newer ATRP variations eliminate the need to handle air sensitive Cu^{1+}. ICAR, AGET, and ARGET methods utilize substantially lower concentrations of Cu catalyst over the other types. **Table 2** summarizes the benefits and limitations of the various ATRP techniques:

Table 2. Benefits and limitations for ATRP techniques.

Polymerization	Benefit	Limitation
Normal ATRP	Versatile	High Cu content, unstable catalyst precursor
ICAR	Low Cu content, catalyst precursors more stable	AIBN might cause side reactions
AGET	Low Cu content, catalyst precursors more stable	High Sn content (FDA approved)
ARGET	Low Cu content, catalyst precursors more stable	High Sn content (FDA approved)
Reverse ATRP	Simple, catalyst precursors more stable	Limited end group functionality; only linear; targeting MW difficult
Simultaneous reverse and normal ATRP	Catalyst precursor more stable	AIBN might cause side reactions

The relatively high levels of residual Cu by traditional ATRP are problematic for biomedical and food packagingapplications where it is required to minimize or eliminate toxins, such as heavy metals. Polymers generated by traditional ATRP contain substantial residual Cu catalyst if not properly purified. ICAR, AGET, and ARGET operate at low levels of Cu during polymerization and therefore need minimal subsequent purification for catalyst removal. These new versions of ATRP enable their utility to prepare well-defined copolymers for these high value applications.

The appropriate ATRP technique can be chosen based on the needs of the application. **Figure 2** can be used to select a ligand based on catalyst activity; however, the effect of the ligand on the resulting molecular weight distribution is not illustrated. The plot of the K_{ATRP} vs. k_{deact} is shown in **Figure 3** and illustrates catalyst activity as a function of control over the polymerization.[32] Wei Tang and co-workers developed this plot which shows the PDI better correlates to the rate of deactivation kdeact rather than the value of K_{ATRP} found in **Figure 2**.[32]

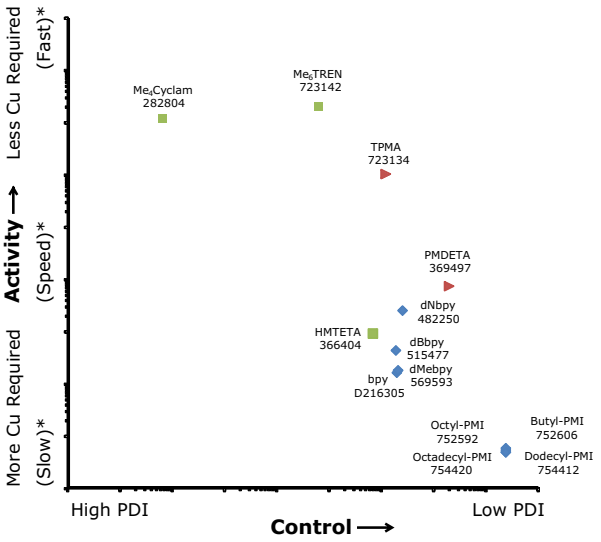

Figure 3. The equilibrium constant K_{ATRP} plotted against k_{deact} illustrates the correlation between catalyst activity and control. This should only be used as a reference, and was adapted from Tang, W. et al.[32] Each ligand is labeled with an acronym as well as the Sigma-Aldrich Cat. No. Bidentate ligands are represented by blue diamonds, red triangles represent tridentate ligands, and green squares represent tetradentate ligands.
*At a given concentration of catalyst, the activity axis shows the relative speed of the polymerization reaction.

The perfect ATRP catalyst would be both fast and well controlled, but this figure can help illustrate the relationship. If minimizing copper concentration is the highest priority, then selecting catalysts from the top of **Figure 3** would be ideal. If a narrow distribution of chain lengths (low PDI) is the highest priority, then the ideal catalyst would be selected from the right side of the **Figure 3**.

The various ATRP techniques provide an opportunity to select a polymerization environment that is well suited to meet applicationspecific needs. When used in combination with the ideal catalyst for a given polymerization, well-defined polymers can be conveniently prepared.

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Copper(I)-mediated Living Radical Polymerization in the Presence of Pyridylmethanimine Ligands

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Background

Emergence of living radical polymerization mediated by transition metal catalysts in 1995 was a seminal piece of work in the field of synthetic polymer chemistry.[1–3] Since this date, many transition metal complexes have been shown to be effective with many different ligands and transition metals. One is left with a number of dilemmas:

- Which system should I use?
- What reaction conditions should I start with?
- Does it make any difference?

As with all effective types of transition metal catalytic processes, the chemistry works due to facile interchange of the oxidation states of the metal, which is controlled by the ligands on the metal.[2] Although the exact mechanism of atom transfer radical polymerization (ATRP) is complex, and more than likely depends on the different ligands employed, it can be simplified to a reversible redox system, whereby the transition metal undergoes a reversible one electron oxidation and reduction process, as shown in **Figure 1**.

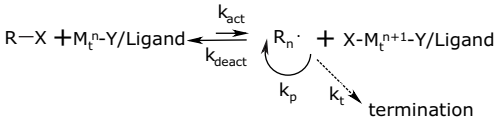

Figure 1. Simplified mechanism for ATRP

Even though many different complexes have been shown to be effective in ATRP, by far the most commonly used chemistry involves copper(I) complexes based on a range of N-donor ligands.[2] The role of these ligands is often described as controlling the solubility of copper(I). Those who have carried out ATRP with an aliphatic amine ligand or bipyridine will know these reactions are quite often heterogeneous and in some cases there is a considerable amount of insoluble material in the reaction flask. However, even though the solubility of the catalyst is very important, the role of the ligand is critical. If the reaction equilibrium lies too far to the left the alkyl halide will be stable and unable to participate in polymerization. Conversely, if the equilibrium is pushed too far to the right, then a high concentration of free radicals will lead to conventional free radical polymerization with termination by normal radical-radical coupling, and in some cases disproportionation. The relative stabilities of copper(I) and copper(II) complexes control the position of this equilibrium and thus the electronic, and often the steric, nature of the ligands in turn allows the synthetic chemist to control the reaction. Copper(II) is usually more stable than copper(I). Copper(II) is d^9 which gives rise to characteristic blue and green complexes.

Note what happens when copper(0) (d^{10} s^1) is left exposed to air on a copper roof or in a bronze statue – it oxidizes to a pale green copper(II). Copper(I) is d^{10} with no readily available d-d transition and thus its compounds are generally colorless, unless there is metal-ligand charge transfer available. The practitioner of ATRP knows very well that even if they purchase 99.999% pure Cu(I)Br from a commercial source it will come as a pale green powder, due to trace oxidation to copper(II) bromide. Also, during the course of a polymerization utilizing an alkyl amine ligand [e.g., TREN (Cat. No. 225630), Me_6TREN (Cat. No. 723142), PMDETA (Cat. No. 369497)] the solution will often be a blue/green color. Since the resulting polymer normally has the desired M_n and narrow PDI, this is often overlooked as the reactions are undoubtedly very successful. However, it is indicative of a build up of copper(II) complexes during the reaction. The second most important part of the equilibrium is the stability of the polymer radical, which changes depending on the electronic and steric environment. For example, in a comparison between a propagating methacrylate and acrylate polymer radicals, the methacrylate has an electron-donating methyl group that also introduces steric effects; these effects are most documented for large differences in propagating rate constants, k_p.

Alkyl Pyridylmethanimine Ligands

Alkyl pyridylmethanimine ligands were first used in 1996[4–11] as work showed that these ligands readily form tetrahedral copper(I) complexes which are unusually stable with regards to oxidation.[12,13] The ligands are very simply prepared by a condensation reaction exemplified by the following procedure; 2-pyridine carboxaldehyde (20 mL, 0.21 mol) and diethyl ether (20 mL) are added to a flask containing dried magnesium sulfate (5 g). The flask is cooled to 0 °C and n-propylamine (19 mL, 0.25 moles) added slowly. The mixture is removed from the ice bath and stirred for two hours at 25 °C prior to filtration. Diethyl ether is removed by rotary evaporation and the resulting yellow oil purified by vacuum distillation. The product is obtained as a straw-colored oil (bp. 43 °C at 7 × 10^{-2} mbar), with a 98% yield (**Figure 2**). The reaction occurs very rapidly under these conditions and a point to note is that the resulting Schiff bases are very stable towards hydrolysis even though the alkyl groups have a primary carbon in the imine. This is contrary to many organic text books that often state secondary or tertiary carbons are required to prevent the reverse reaction. Note that in order to prepare the methyl ligand, a 40% solution of methylamine in water is needed for the reaction to proceed rapidly to completion. This unexpected behavior led us for many months to avoid primary amines, and the use of secondary and tertiary amines leads to ligands that give relatively broad PDI polymers!

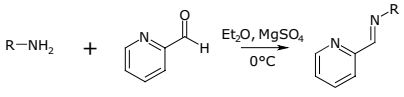

Figure 2. Schematic of the synthesis of alkyl pyridylmethanimine

The alkyl pyridylmethanimine ligands have a very low lying π^* orbital which readily accepts electron density from the copper(I).[13] The implication of this is that when copper(I) is complexed with two alkyl pyridylmethanimine ligands, although the formal oxidation state of copper is +1, in reality this is not the real oxidation state, or electron content of the metal. In addition, the tetrahedral arrangement of the ligand (**Figure 3**) shows that the access to the metal is restricted due to

the steric bulk of the ligands.[14–15] The combination of these effects is to stabilize copper(I) towards oxidation such that it is even possible to bubble air through a solution without causing oxidation.

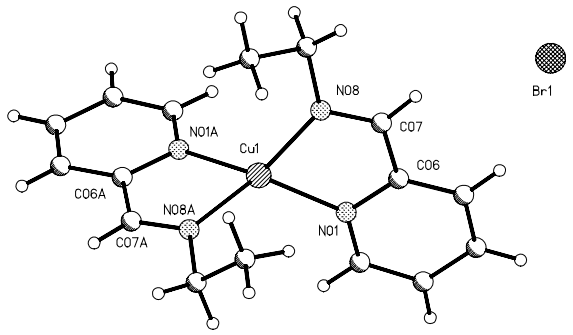

Figure 3. Crystal structure of [L_2Cu]Br, with L = *N*-ethyl 2-pyridylmethanimine.

In addition to the ligands complexing in a tetrahedral way during polymerization, the monomer can act as a competing ligand (**Figure 4**). This will occur for all methacrylates and acrylates, which inherently contain good coordinating groups. This is most profound with tertiary amine-containing ligands which result in competitive binding that can be observed by a small change in reactivity ratios when compared to free radical polymerization values.

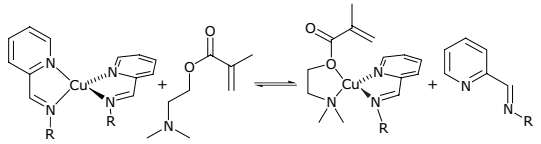

Figure 4. Equilibrium involving DMAEMA (Cat. No. 234907) / *N*-propyl 2-pyridyl methanimine / copper(I) complexes.

It must be remembered that the copper complex formed with all ligand types is always a salt with the transition metal complex forming the cation. This can produce a solubility problem in non-polar solvents. Alkyl pyridylmethanimine ligands help circumvent this by allowing for a facile change in the alkyl group. As the alkyl chain is lengthened, the solubility in non-polar solvents increases. For non-polar monomers such as long chain acrylates and styrene, longer chain ligands need to be used (*n*-butyl, *n*-pentyl, *n*-octyl). However, for polar monomers, it is desirable to use the smallest alkyl chain possible for atom economy, and purification reasons. An interesting, but very useful consequence of this solubility is that during polymerization at high solids the polarity of the reaction medium will decrease markedly. Thus, during the polymerization of methyl methacrylate (MMA) at 30 – 50% solids the polarity decreases and often the catalyst will precipitate from solution, generally as a highly colored oil throughout. This can be avoided by the use of a more non-polar ligand with a longer alkyl group.

However, this potential problem can also have a positive effect with regards to catalyst removal, which can be cited as an unfortunate aspect of ATRP. The solubility of these ligands decreases as the polymerization progresses and upon lowering the temperature from reaction temperature (typically 60 – 80 °C) to ambient. This can result in almost complete precipitation of the catalyst as sticky oil which adheres to the reactor, allowing the catalyst to be removed via trituration/decanting. Alternatively, the reaction mixture can be filtered through a small column/pad of fine filter agents such as Celite®, basic alumina, basic silica which remove the particulate catalyst, ligand and complex, since they adhere to the medium. It is noted that care needs to be taken with certain polymers which might also complex with the filtration medium.

Polymerization is typically carried out under an inert atmosphere with reagents being freeze, pump, thaw degassed. However, on scale-up it is acceptable to bubble nitrogen through the reagents for 15 – 30 minutes or to heat under nitrogen; 100 kg of MMA has been polymerized effectively in this way.

Typical Reaction Conditions

- Up to 66 weight % solids
- Range of solvents from water and alcohols to toluene and cyclic ethers
- 60 – 80 °C
- Inert atmosphere, usually nitrogen
- Robust to many different types of functional group[19–21]

Summary

The family of *N*-alkyl-2-pyridylmethanimines offers an alternative to aliphatic amine ligands and bipyridine for copper(I)-mediated living radical polymerization or ATRP. They yield very stable copper(I) which allows for excellent polymerization of most methacrylate monomers in polar and non-polar solvents. There is little evidence of oxidation or disproportionation even with the most polar monomers and in the most polar solvents[16–17] which is often the case for the aliphatic amine type ligands.[18] Preparation of the ligands and their use in methacrylate polymerization is facile. Typically more than 80% of researchers will achieve polymers with PDI <1.20.

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Typical Procedures for Polymerizing via ATRP

The following two procedures describe two ATRP polymerization reactions as performed by Prof. Dave Hadddleton's research group at the University of Warwick.

Methylmethacrylate (MMA) Polymerization with *N*-propyl-2-pyridylmethanimine

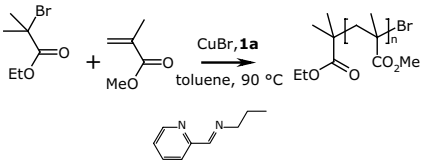

Figure 1. Polymerization of methylmethacrylate (MMA) with *N*-propyl-2-pyridylmethanimine, where 1a = *N*-propyl-2-pyridylmethanimine

The polymerization is carried out under oxygen free conditions. First the transition metal salt is deoxygenated and then the solution, followed by adding initiator to start the polymerization:

1) Cu(I)Br (0.134 g, 9.32 × 10^{-4} moles, Cat. No. 212865) and a dry magnetic stir bar were added to a dry Schlenk flask (or round-bottom flask).
2) The tube is sealed with a rubber septum and deoxygenated with three freeze, pump, thaw cycles using N_2.
3) The polymerization solution was prepared by adding the following reagents/solvents to the flask under N_2:
   - Toluene (10 mL)
   - MMA (10 mL, 9.36 × 10^{-2} moles, Cat. No. M55909)
   - *N*-propyl-2-pyridylmethanimine (0.279 g, 1.87 × 10^{-3} moles)
4) The Schlenk tube is subjected to three additional freeze, pump, thaw cycles and then subsequently heated to 90 °C with constant stirring.
5) Once the reaction temperature is reached the initiator ethyl-2-bromoisobutyrate (0.136 mL, 9.36 × 10^{-4} moles, Cat. No. E14403) is added under N_2 (t = 0) and the polymerization reaction begins.

Samples can be removed at 30 – 60 minute intervals using a degassed syringe and analyzed by GC or NMR to determine the extent of conversion and SEC for molecular weight and polydispersity (PDI). After 300 minutes, the poly(methyl-methacrylate) (PMMA) is isolated with a final conversion of 89.3%. M_n = 8,760 g mol^{-1} (theoretical M_n = 8,930 g mol^{-1}), PDI = 1.20.

Styrene Polymerization with *N*-pentyl 2-pyridyl methanimine

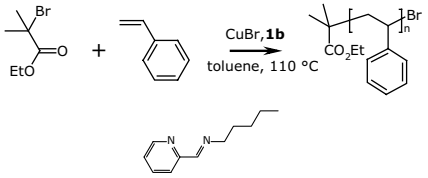

Figure 2. Polymerization of styrene with *N*-pentyl-2-pyridylmethanimine, where 1b = *N*-pentyl-2-pyridylmethanimine

The polymerization is carried out under oxygen free conditions. First the transition metal salt is deoxygenated, and then the monomer and initiator are added to the solution and deoxygenated, followed by adding ligand to start the polymerization:

1) Cu(I)Br (0.131 g, 9.1 × 10^{-4} moles) and a dry magnetic stir bar were added to a dry Schlenk flask (or round-bottom flask).
2) The tube is sealed with a rubber septum and deoxygenated with three freeze, pump, thaw cycles using N_2.
3) The polymerization solution was prepared as follows by adding the following to the flask under N_2:
   - Xylene (20 mL)
   - Styrene (10 mL, 8.73 × 10^{-2} moles, Cat. No. 240869)
   - Ethyl-2-bromoisobutyrate (0.13 mL, 9.1 × 10^{-4} mol)
4) The flask is subjected to an additional three freeze, pump, thaw cycles and subsequently heated to 110 °C with constant stirring.
5) Once the reaction temperature is reached, *N*-pentyl-2-pyridylmethanimine (0.28 mL, 1.8 × 10^{-3} mol) is added under N_2 (t = 0).

Samples can be removed at 30 – 60 minute intervals using a degassed syringe and analysed by GC or NMR for conversion and SEC for molecular weight and polydispersity (PDI). The reaction was stopped after 360 minutes, with a final conversion of 77.9%. M_n = 5,270 (theoretical M_n = 7,900 g mol^{-1}), PDI = 1.29.

Applying ARGET ATRP to the Growth of Polymer Brush Thin Films by Surface-initiated Polymerization

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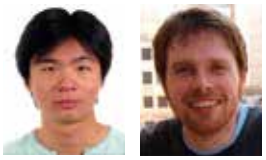

Introduction

In 2006, Matyjaszewski and co-workers first described controlled radical polymerization by Activators ReGenerated by Electron Transfer Atom Transfer Radical Polymerization (ARGET ATRP),[1–3] a development of the very widely used ATRP technology. ARGET ATRP offers two principle advantages over conventional ATRP: improved tolerance of oxygen and significantly reduced heavy metal catalyst concentrations.

Using initiator molecules with specific surface-binding groups (e.g., thiols, silanes, or catechols), monolayers containing a high density of initiator sites can be produced. When polymerization is initiated from a fraction of these sites (the exact fraction depending on the polymerization system and conditions), a layer of densely-packed chains is produced, known as *polymer brushes*. Experimentally, such polymerizations are conducted by immersing an initiator-functionalized surface into bulk monomer or monomer solution, with additional components such as catalysts and free (untethered) initiator added depending on the exact polymerization type.

From an applications perspective, these coatings can be considered as ultra-thin (typically 0 – 500 nm) polymer films with outstanding stability towards solvents due to covalent chain tethering. These films can be immersed in a good solvent for the polymer without fear of damage or dissolution. The coating will reversibly swell in a good solvent, an effect which can be utilized for sensing applications.[5] This solvent stability has been particularly well-exploited in producing robust coatings of hydrophilic polymers, with applications such as non-biofouling/proteinresistant surfaces[6] and antimicrobial coatings[7] for proposed use in biosensors and medical devices. In addition, the "bottom-up" nature of the polymer growth allows thin films to be produced free of pin-hole defects commonly encountered with spin-coating, and makes them suitable for use as dielectric layers in electronic devices.[8] Furthermore, patterning these polymer layers is simple, requiring only that the initiator layer is generated using any of the existing well-developed monolayer patterning techniques (e.g., micro-contact printing).[9]

In this article, we will discuss ARGET ATRP, particularly focusing on the application of this technique to surface-initiated polymerization (SIP). This case study provides an excellent example of how using ARGET ATRP in place of conventional ATRP can help to broaden the applicability and appeal of a polymerization process.

We will first introduce SIP and explore why controlled radical polymerization (CRP) in general, and ATRP in particular, has become such a popular choice of polymerization technology for SIP. After introducing ARGET ATRP, we will discuss how it enables SIP to be more widely applied outside of the synthetic chemistry laboratory.

Surface-initiated Polymerization (SIP) and Polymer Brushes

Chain-growth polymerizations (e.g., radical addition polymerization) frequently use initiators intimately mixed with the monomers either in solution or in bulk. However, if initiators can be tethered to a surface (using established chemistry from the field of self-assembled monolayers),[4] then chains grown from these initiators will also be endtethered (or *grafted*) to the surface. Such a process is termed *surface-initiated polymerization* (SIP). The overall process for SIP is shown in **Figure 1**.

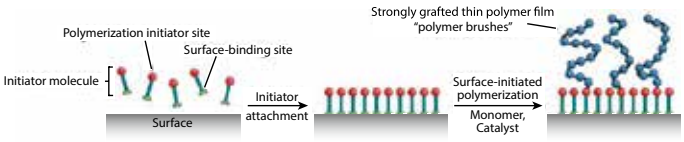

Figure 1. The process for generating a polymer brush. First, initiator molecules are attached to a surface, then in the presence of monomer and catalyst the polymer chains are grown from the surface.

Controlled Radical Polymerization for SIP

Most chain-growth polymerization techniques which have been utilized to synthesize polymers in bulk or in solution have also been applied to growing polymer brushes. However, the vast majority of recent research in coatings has focused on CRP technology such as nitroxide-mediated polymerization (NMP), reversible addition/fragmentation chain transfer polymerization (RAFT) and most notable ATRP. For detailed coverage of the application of CRP to polymer brush growth, see reviews by Edmondson et al.[10] and Barbey et al.[11]

Using CRP allows the molecular weight of the grafted chains to be easily controlled, which in turn controls the thickness of the brush layer. Perhaps the simplest way of achieving this control is to vary the polymerization time — experimentally, this can be realized by simply removing samples from the reaction periodically as required. Very thin uniform films (just a few nanometers thick) can be produced in this way using slow polymerization methods and short growth times, although thicknesses of up to ~500 nm are possible. Gradients of thickness can also be produced by slowly feeding polymerization solution (monomer and catalyst in solvent) into or out of the vessel containing the substrate.[12] Thickness control can also be achieved by adding free (untethered) initiator and allowing the polymerization to run to high conversion, with the molecular weight being determined by the [monomer]/[initiator] ratio. However, this method produces free polymer which can make sample extraction and cleaning difficult.

A wide range of monomers have been utilized to prepare polymer brushes via CRP. Some polymer brushes can also be modified after growth, for example by coupling biomolecules, giving an even wider range of available functionality. Moreover, multi-block copolymers producing multi-layer films can also be made by sequential polymer growth with different monomers (**Figure 2**).

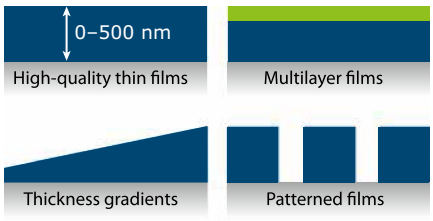

Figure 2. Examples of the diverse film structures which can be produced by surfaceinitiated polymerization.

ATRP has proved to be the most popular CRP technology for the formation of polymer brushes, with hundreds of published examples. The beneficial features of ATRP for solution polymerization (e.g., tolerance to a wide range of functional groups, ability to polymerize at room temperature in environmentally benign solvents with good control) are also applicable to SIP brush growth. A wide range of acrylates, methacrylates, and styrenic monomers have been used to make brush coatings with surface-initiated ATRP. Many diverse classes of polymers have been grown this way, including hydrophobic, hydrophilic, charged (cationic and anionic), stimuli-responsive (pH and temperature), biocompatible, cell-adhesive, antimicrobial, and chemically reactive (for post-growth functionalization or crosslinking).[11]

In addition to the wide range of accessible polymer functionality, the popularity of ATRP for SIP can also be attributed to the ease of synthesis of suitable alkyl halide initiators. An acyl bromide initiator, 2-bromoisobutyryl bromide (BIBB) (**Figure 3**) is commercially available (Cat. No. 252271) and can be used to synthesize a range of surface-reactive initiators such as silanes (for silica and some metal oxides) and catechols (for some metal oxides). A disulfide-functional initiator is also commercially available (Cat. No. 733350 in **Figure 3**) for use with noble metals (e.g., gold) and select oxide-free transition metal surfaces (e.g., copper).

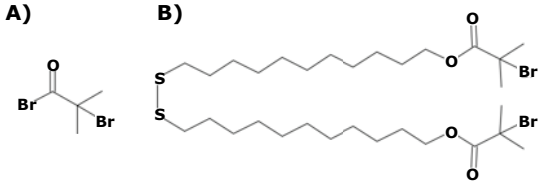

Figure 3. ATRP initiator 2-bromoisobutyryl bromide is commonly used to synthesize functionalized initiators, and bis[2-(2-bromoisobutyryloxy)undecyl] disulfide is an ATRP initiator that is used to functionalize noble metals and oxide-free transition metal surfaces.

Surfaces bearing organic hydroxyl groups (C-OH) can be more directly modified to incorporate initiating sites by directly reacting with BIBB, an approach which has been used to functionalize surfaces such as cellulose[13] and oxidized/activated polymer surfaces (shown in **Figure 4**). Our group has also been working on more general (non-substrate-specific) initiators, based on polyelectrolytes[14] and dopamine polycondensation[15] to further broaden the application of SIP.

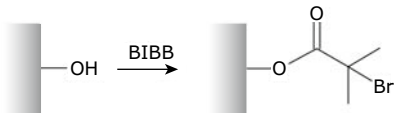

Figure 4. Introduction of ATRP initiator sites onto a hydroxyl-functional surface (e.g., cellulose) using 2-bromoisobutyryl bromide (BIBB).

ARGET ATRP for Robust Brush Growth

ATRP has been very successfully used for surface-initiated polymerization, but suffers one major drawback – the oxygen sensitivity of the Cu(I) complexes typically used for polymerization. This sensitivity necessitates careful deoxygenation of solvents and polymerization vessels. Matyjaszewski and co-workers have recently developed a version of ATRP, termed ARGET ATRP which has greatly reduced sensitivity to oxygen by the introduction of an excess of reducing agent in the reaction.[1–3]

The effect of oxygen in a conventional ATRP polymerization is to oxidize the Cu(I) to Cu(II). Since the polymerization rate is proportional to the ratio [Cu(I)]/[Cu(II)], a small amount of oxygen leads to a large reduction in polymerization rate. ARGET ATRP overcomes this problem by having a reservoir of reducing agent in the reaction mixture. Cu(II) generated by oxidation, or other processes such as termination or disproportionation, is simply reduced back to the active Cu(I) (**Figure 5**).

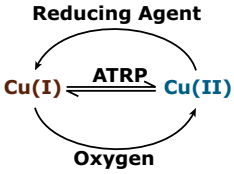

Figure 5. The fundamental reactions of ARGET ATRP. In the normal course of ATRP, the catalyst is shuttled between the two oxidation states. The presence of excess reducing agent counters the effect of oxygen (or other processes such as termination), regenerating lost Cu(I).

ARGET ATRP offers further advantages over conventional ATRP:

- Copper catalyst can be added initially as Cu(II) and generate active Cu(I) *in situ* via reduction at the start of the polymerization. Therefore, only air-stable Cu(II) salts need to be stored and handled in the laboratory, rather than air-sensitive Cu(I) salts.
- The total amount of copper catalyst can be greatly reduced, even down to ppm levels,[1] since the polymerization rate theoretically only depends on the ratio [Cu(I)]/[Cu(II)], not the total amount of copper. Conventional ATRP must employ much greater concentrations of copper than ARGET ATRP to minimize the effects of oxidation and termination.

The controlled synthesis of a range of polymers in solution (i.e., not tethered) using ARGET ATRP have been reported, for example hydrophobic polymers such as polystyrene (PS),[2] poly(methyl methacrylate) (PMMA),[1,3] and poly(n-butyl acrylate) (PnBA),[1,3] as well as hydrophilic poly(2-hydroxyethyl methacrylate) (PHEMA).[16] The high level of control possible with ARGET ATRP has been demonstrated by the synthesis of block copolymers.[1,3] In some cases ARGET ATRP allows the synthesis of polymers that are not accessible by conventional ATRP, such as high molecular weight acrylonitrile homopolymers[17] and copolymers.[18]

Interestingly, some reported ARGET ATRP polymerizations do not require the addition of a reducing agent, for example tertiary amine groups present on the ligand[19] or monomer (2-dimethylaminoethyl methacrylate, DMAEMA)[20] can act as 'intrinsic' reducing agents.

The benefits of ARGET ATRP over conventional ATRP make it a particularly attractive system for the growth of polymer brushes by SIP. The less stringent experimental conditions required make ARGET ATRP ideal for use by scientists and engineers with all levels of synthetic expertise, greatly broadening the application of polymer brush growth. Furthermore, low catalyst concentrations, ambient temperature polymerization conditions (for many monomers) and relatively benign solvents and reducing agents (e.g., methanol/water mixes and ascorbic acid, respectively) make this technique more applicable for use outside the chemistry laboratory, and extendable into industrial settings.

Sample handling with ARGET ATRP is also simplified since it is sufficient for the polymerization to be conducted in a sealed jar under air, because the small amount of oxygen present will be consumed by the excess reducing agent. However, to prepare polymer brush surfaces by conventional ATRP the system must be enclosed in rigorously deoxygenated flasks or entirely conducted in a glove box.

The tolerance of the polymerization to low levels of oxygen also allows samples to be removed from a polymerization vessel during the reaction without terminating the polymerization. Samples can even be analyzed (e.g., ellipsometric thickness) and returned to the polymerization reaction if a thicker layer is required. Conventional ATRP would require an extensive process for re-initiation including transfer to a new deoxygenated reaction flask with fresh polymerization solution.

Research utilizing ARGET ATRP for surface initiated polymerization is continuing to grow. Matyjaszewski and coworkers first demonstrated the technique by synthesizing PnBA brushes and PnBA-*block*-PS copolymer brushes.[21] More recently, chemically functional polymer brushes such as epoxy-functional poly(glycidyl methacrylate)[13] and hydroxyl-functional PHEMA[15] have also been prepared by ARGET ATRP. In addition, PMMA brushes via ARGET ATRP have been grown from a variety of substrate materials including silicon wafers,[15] high-surface-area porous silica,[22] and imogolite nanotubes (an aluminosilicate clay).[23]

Our group has had significant success in simply adapting existing ATRP protocols into ARGET ATRP protocols, especially those run at ambient temperature using polar solvents (e.g., methanol and water), by simply applying the following 'algorithm':

- Monomer and solvents quantities are kept identical
- Replace Cu(I) salts with $CuBr_2$ and greatly reduce the overall copper concentration.
  (Typical [monomer]:[Cu] = 5000:1)
- Keep the same ligand species, but increase the amount of ligand. (Typical [ligand]:[Cu] = 10:1)
- Add reducing agent (typically ascorbic acid or sodium ascorbate), in large excess over copper.
  (Typical [reducing agent]:[Cu] = 10:1)

To conduct ARGET ATRP in the most ideal manner (achieving the best control and the lowest polydispersity), further optimizations need to be made. For example, a stronger chelating ligand (e.g., Me_6TREN or TPMA)[1] may need to be used and the concentration and nature of the reducing agent should be optimized. However, in surface-initiated polymerization a simple recipe produced by the algorithm above is often sufficient to grow a brush layer, where polydispersity and good re-initiation efficiency are not of critical importance. A typical polymerization procedure for PMMA brushes, developed using this algorithm, is given at the end of this article.

It should be noted that if an ARGET ATRP brush growth protocol produces brush layers which are too thin, as measured by ellipsometry or other techniques, this could occur for two quite different reasons:

- The polymerization is too fast, causing high levels of termination. In this case, the polymerization can be slowed by using less polar solvents or less active reducing agents.
- The polymerization is too slow. In this case, the polymerization can be accelerated by using more polar solvents (e.g., adding water to the solvent mix), more active reducing agents, or adopting more rigorous oxygen exclusion.

These two scenarios can be differentiated by growing samples for a range of times, making obvious the difference between early termination (constant thickness with increasing time) and slow propagation (slowly increasing thickness).

Conclusion

In this short article, we have reviewed the fundamental principles of ARGET ATRP and discussed the advantages of this technique over conventional ATRP. We have focused on the application of ARGET ATRP for surface-initiated polymerization to prepare polymer brushes. Using ARGET ATRP in this application reduces the experimental complexity of brush growth, in particular by requiring less rigorous inert atmosphere conditions. The synthesis of a range of useful polymers (both surfacetethered and free) by ARGET ATRP has been demonstrated in literature, and this useful technique is likely to grow in importance for controlled polymer synthesis both inside and beyond the chemistry laboratory.

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ARGET ATRP: Procedure for PMMA Polymer Brush Growth

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Surface Cleaning and Initiator Immobilization

Surface preparation before polymer brush growth consists of two steps: surface cleaning and initiator monolayer deposition.

There are many common techniques for rigorous surface cleaning; however, the choice is dependent on substrate type, the degree of contamination, and the desired cleanliness of the surface. Heavily contaminated inorganic substrates can be cleaned by washing and ultrasonication in aqueous surfactants and solvents, followed by immersion in piranha solution (H_2O + H_2O_2 + H_2SO_4 – warning, extremely hazardous). Silica surfaces (including silicon wafers) can be cleaned using the less hazardous RCA-1 clean (H_2O + H_2O_2 + NH_4OH) in place of piranha solution, which introduces silanol (Si-OH) groups to the wafer surface to allow reaction with silanes. For less heavily contaminated inorganic surfaces, a 'dry' clean using UV/O_3 exposure will often suffice.

Organic surfaces such as polymers or cellulose are often cleaned simply using solvents. If the material does not intrinsically contain nucleophilic amine or hydroxyl groups, the surface can be 'activated' by a variety of means (e.g., UV/O_3 or O_2 plasma to introduce hydroxyl groups, treatment of polyesters with ethylenediamine to introduce amine groups).[24]

After the surface is clean the initiator monolayer can be formed using a method specific to the surface type.

1) **Gold and other noble metals surfaces:** Monolayers of initiator can be formed by simply immersing the surface in a dilute solution of a disulfide initiator (Cat. No. 733350) (1 – 5 mM in ethanol) for 16 – 24 hours under ambient conditions, followed by washing with ethanol.

2) **Organic hydroxyl functional surfaces (e.g., cellulose or activated polymer surfaces):** ATRP initiator sites are introduced by reacting surface hydroxyls or amines with 2-bromoisobutyryl bromide (BIBB, Cat. No. 252271) in anhydrous solvent with an amine base.
A typical procedure for cellulose is given below:
   - Cellulose (fibers or paper) is placed in a test tube sealed with a septum and the tube deoxygenated by nitrogen purging or vacuum/nitrogen cycling.
   - Anhydrous tetrahydrofuran (THF, 10 mL, Cat. No. 401757) is syringed over the cellulose. BIBB (0.26 mL, 2.10 mmol) and anhydrous triethylamine (0.30 mL, 2.10 mmol) are added by syringe and the tube gently agitated to mix. Note: triethylamine should be dried using 4 Å molecular sieves before use.
   - After 1 hour remove the cellulose from the tube, wash with THF, methanol and deionized water and then dry under a nitrogen stream.

3) **Silica/silicon and other metal oxides:** Many publications use presynthesized silane ATRP initiators for these surfaces. However, a procedure suitable for all levels of synthetic expertise is provided below (and illustrated in **Figure 1**), using only commercial reagents:
   - Clean substrates are placed in a vacuum desiccator or vacuum oven with a vial containing 10 drops of (3-aminopropyl)triethoxysilane (APTES, Cat. No. A3648). The chamber is then pumped down to <1 mbar, isolated from the pump and left under vacuum for 30 minutes.
   - Substrates are then annealed at 110 °C in air at atmospheric pressure for 30 minutes. Note: if using the same vacuum oven for both steps, remove the APTES before heating.
   - After annealing, substrates can be reacted directly with BIBB, using the same procedure as for cellulose, above.

Initiator-coated substrates can be stored in air for several weeks without significant loss of activity.

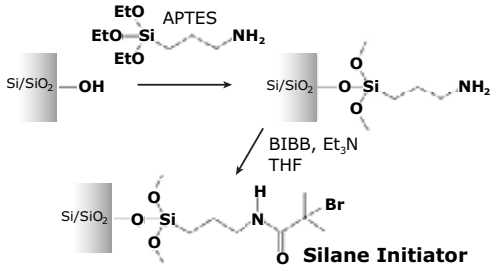


Figure 1. Surface functionalization with silane ATRP initiator.

Polymer Brush Growth by ARGET ATRP

A typical procedure for the growth of PMMA polymer brushes is given below, and illustrated in **Figure 2**.

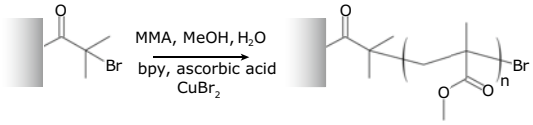


Figure 2. Polymerization of methyl methacrylate from a surface.

Samples can be handled using stringent inert atmosphere with the polymerization taking place in a deoxygenated tube or under less stringent conditions in a screw-top jar (**Figure 3**). Several ARGET ATRP brush growth polymerization methods will work adequately under the less stringent conditions, which also greatly simplifies handling. Under less stringent conditions fresh samples can simply be dipped into the solution and removed when desired, although the jar should be sealed for the majority of the polymerization time.

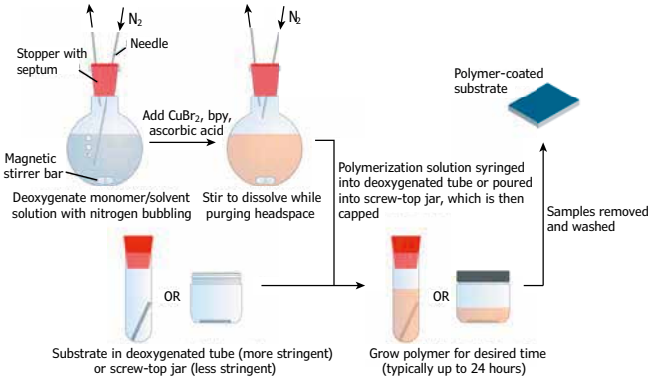


Figure 3. Typical experimental procedure for SIP by ARGET ATRP.

- Initiator-coated substrates are placed in test tubes which are deoxygenated by nitrogen purging or vacuum/nitrogen cycling. Alternatively, they can be placed in a screw-top jar under air.
- In a round-bottomed flask sealed with a septum, methanol (16 mL), water (4 mL) and methyl methacrylate (20 mL, 18.72 g, 187.0 mmol, Cat. No. M55909) are mixed and deoxygenated by bubbling through nitrogen for 10 – 15 minutes.

- $CuBr_2$ (7.4 mg, 0.033 mmol, Cat. No. 221775), 2,2′-dipyridyl (bpy, 51.5 mg, 0.33 mmol, Cat. No. D216305) and sodium L-ascorbate (65.3 mg, 0.33 mmol, Cat. No. A7631) or ascorbic acid (58.1 mg, 0.33 mmol, Cat. No. A0278) are added and the headspace purged with nitrogen. The mixture is stirred to dissolve the solids.
- The solution is syringed over the substrates in the deoxygenated tubes, or simply poured over the substrates in the screw-top jar, which is then resealed. The samples are allowed to polymerize at ambient temperature.
- After the desired polymerization time, samples are removed and washed with methanol and water. If free polymer is observed on the samples, this can be removed by washing with THF or other appropriate solvents for PMMA — the polymer coating will not be damaged by solvent washing.

Typically, this method produces a polymer growth rate of approximately 10 nm/hour (**Figure 4**).

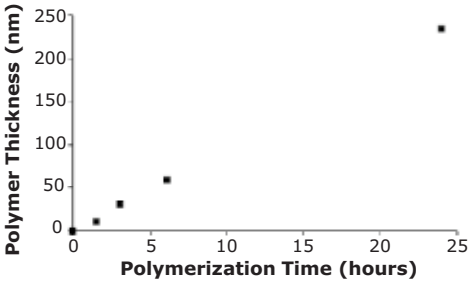
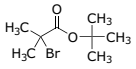
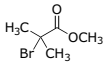
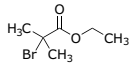
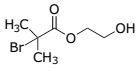
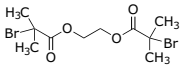
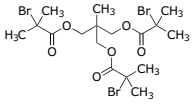
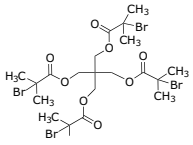
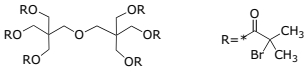
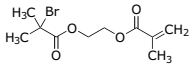
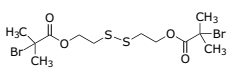
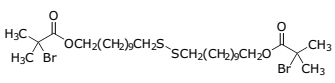
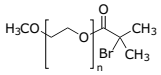
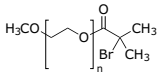
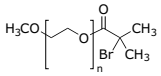


Figure 4. PMMA Polymer brush thickness during polymerization under stringent deoxygenation conditions at 20 °C (measured by ellipsometry).

ATRP Initiators

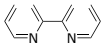
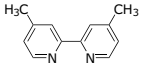
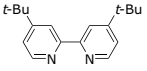
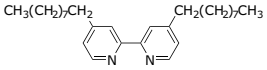
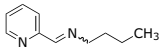
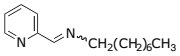
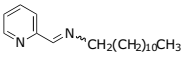
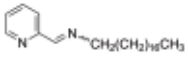
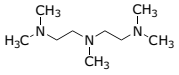
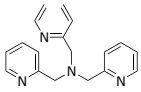
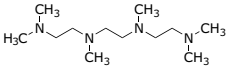
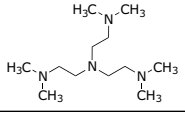
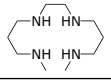
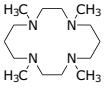
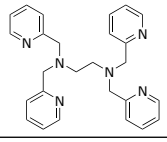
For a complete description of available ATRP initiators including purities, visit SigmaAldrich.com/crp.

Name	Structure	Description	Cat. No.
tert-Butyl α-bromoisobutyrate		Atom Transfer Radical Polymerization (ATRP) initiator with a *tert*-butyl leaving group.	17455-100ML 17455-500ML
Methyl α-bromoisobutyrate		Atom Transfer Radical Polymerization (ATRP) initiator that will generate a polymer with a methyl end group	17457-100ML
α-Bromoisobutyryl bromide		Used to form an *N*-protected halodienamide which provided four- and five-membered lactams in the presence of copper (I) and a tertiary amine. Atom Transfer Radical Polymerization (ATRP) initiator commonly used to functionalize alcohols or oxidized surfaces	252271-100G 252271-500G
Ethyl α-bromoisobutyrate		Atom Transfer Radical Polymerization (ATRP) initiator that will generate a polymer with an ethyl end group.	E14403-5G E14403-100G E14403-500G
2-Hydroxyethyl 2-bromoisobutyrate		Atom Transfer Radical Polymerization (ATRP) initiator for the creation of hydroxy functionalized telechelic polymers. Can be used to modify carboxylate- or isocyanate- modified surfaces, particles, or biomolecules.	723150-1G 723150-5G
Ethylene bis(2-bromoisobutyrate)		Atom Transfer Radical Polymerization (ATRP) initiator for the creation of difunctional polymers. Polymerization will occur at two sites creating a polymer with ester functionality at the center.	723177-1G 723177-5G
1,1,1-Tris(2-bromoisobutyryloxymethyl) ethane		Atom Transfer Radical Polymerization (ATRP) initiator for the creation of trifunctional polymers. Polymerization will occur at three sites creating a three-arm star polymer.	723185-1G 723185-5G
Pentaerythritol tetrakis (2-bromoisobutyrate)		Atom Transfer Radical Polymerization (ATRP) initiator for the creation of tetrafunctional polymers. Polymerization will occur at four sites creating a four-arm star polymer.	723193-1G 723193-5G
Dipentaerythritol hexakis (2-bromoisobutyrate)		Atom Transfer Radical Polymerization (ATRP) initiator for the creation of hexafunctional polymers. Polymerization will occur at six sites creating a six-arm star polymer.	723207-1G 723207-5G
2-(2-Bromoisobutyryloxy)ethyl methacrylate		Atom Transfer Radical Polymerization (ATRP) initiator with a methacrylate functionality for branched polymerization, orthogonal polymerization, or other functionalization.	734586-1G 734586-5G
Bis[2-(2-bromoisobutyryloxy)ethyl] disulfide		Atom Transfer Radical Polymerization (ATRP) initiator for the preparation of biodegradable polymers as well as polymers that adhere to gold surfaces. This can also be used to introduce temperature and light sensitive regions to cleave the polymer.	723169-1G 723169-5G
Bis[2-(2-bromoisobutyryloxy)undecyl] disulfide		Atom Transfer Radical Polymerization (ATRP) initiator commonly used to functionalize noble metal surfaces. This can also be used to introduce temperature and light sensitive regions to cleave the polymer.	733350-500MG

Name	Structure	Description	Cat. No.
Poly(ethylene glycol) methyl ether 2-bromoisobutyrate Average M_n: 2,200		Poly(ethylene glycol)-containing ATRP initiator for generating a block copolymer with a PEG block on one end. The PEG block is terminated with an unreactive methoxy group. Can be used to enhance biocompatibility.	750069-1G 750069-5G
Poly(ethylene glycol) methyl ether 2-bromoisobutyrate Average M_n: 5,000		Poly(ethylene glycol)-containing ATRP initiator for generating a block copolymer with a PEG block on one end. The PEG block is terminated with an unreactive methoxy group.	736333-1G 736333-5G
Poly(ethylene glycol) methyl ether 2-bromoisobutyrate Average M_n: 1,200		Poly(ethylene glycol)-containing ATRP initiator for generating a block copolymer with a PEG block on one end. The PEG block is terminated with an unreactive methoxy group.	739456-1G 739456-5G

Ligands for ATRP Catalysts

For a complete description of available ligands, visit SigmaAldrich.com/crp.

Name	Structure	Cat. No.
2,2′-Bipyridyl		D216305-2.5G D216305-10G D216305-25G D216305-100G D216305-500G D216305-1KG
4,4′-Dimethyl-2,2′-dipyridyl		569593-1G 569593-5G
4,4′-Di-*tert*-butyl-2,2′-dipyridyl		515477-5G 515477-25G
4,4′-Dinonyl-2,2′-dipyridyl		482250-1G 482250-5G
N-Butyl-2-pyridylmethanimine		752606-1G
N-Octyl-2-pyridylmethanimine		752592-1G
N-Dodecyl-*N*-(2-pyridylmethylene)amine		754412-1ML
N-Octadecyl-*N*-(2-pyridylmethylene)amine		754420-1G
N,N,N′,N′′,N′′-Pentamethyldiethylenetriamine		369497-250ML 369497-1L
Tris(2-pyridylmethyl)amine		723134-250MG 723134-1G
1,1,4,7,10,10-Hexamethyltriethylenetetramine		366404-5G 366404-25G
Tris[2-(dimethylamino)ethyl]amine		723142-1ML
1,4,8,11-Tetraazacyclotetra-decane		259160-1G 259160-5G
1,4,8,11-Tetramethyl-1,4,8,11-tetraazacyclotetradecane		282804-1G
N,N,N′,N′-Tetrakis(2-pyridylmethyl)-ethylenediamine		P4413-50MG P4413-100MG

Metal Salts for ATRP Catalysts

For a complete list of available metal salts, visit SigmaAldrich.com/metalsalts.

Name	Formula	Purity	Cat. No.
Copper(I) chloride	CuCl	≥99.995% trace metals basis	229628-10G 229628-100G
Copper(II) chloride	$CuCl_2$	99.999% trace metals basis	203149-10G 203149-50G
Copper(I) bromide	CuBr	99.999% trace metals basis	254185-10G 254185-100G
Copper(II) bromide	$CuBr_2$	99.999% trace metals basis	437867-5G 437867-25G
Titanium(IV) chloride	$TiCl_4$	≥99.995% trace metals basis	254312-10 254312-50G
Iron(II) chloride	$FeCl_2$	98%	372870-25G 372870-250G
Iron(III) chloride	$FeCl_3$	≥99.99% trace metals basis	451649-1G 451649-5G
Iron(II) bromide	$FeBr_2$	98%	400831-10G 400831-50G
Iron(III) bromide	$FeBr_3$	98%	217883-10G 217883-50G
Cobalt(II) chloride	$CoCl_2$	97%	232696-5G 232696-100G 232696-500G
Cobalt(II) bromide	$CoBr_2$	99%	334022-50G 334022-250G
Nickel(II) chloride	$NiCl_2$	99.99% trace metals basis	451193-5G 451193-25G
Nickel(II) bromide	$NiBr_2$	≥99.99% trace metals basis	449156-1G 449156-5G
Molybdenum(III) chloride	$MoCl_3$	99.95% trace metals basis	339334-2G
Molybdenum(V) chloride	$MoCl_5$	99.99% trace metals basis	642452-2G 642452-10G
Ruthenium(III) chloride	$RuCl_3$	–	208523-2G 208523-10G 208523-50G

RAFT

A Micro Review of Reversible Addition/Fragmentation Chain Transfer (RAFT) Polymerization

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Introduction

RAFT (Reversible Addition/Fragmentation Chain Transfer) polymerization is a reversible deactivation radical polymerization (RDRP) and one of the more versatile methods for providing living characteristics to radical polymerization.[1–7] The historical development of RAFT polymerization at CSIRO has been outlined.[1] Advantages of RAFT polymerization include:

- The ability to control polymerization of most monomers polymerizable by radical polymerization. These include (meth)acrylates, (meth)acrylamides, acrylonitrile, styrenes, dienes, and vinyl monomers.
- Tolerance of unprotected functionality in monomer and solvent (e.g., OH, NR_2, COOH, $CONR_2$, SO_3H). Polymerizations can be carried out in aqueous or protic media.
- Compatibility with reaction conditions (e.g., bulk, organic or aqueous solution, emulsion, mini-emulsion, suspension).
- Ease of implementation and inexpensive relative to competitive technologies.

In an ideal living polymerization, all chains are initiated at the begi nning of the reaction, grow at a similar rate, and survive the polymerization: there is no irreversible chain transfer or termination. If initiation is rapid with respect to propagation, the molecular weight distribution is very narrow and chains can be extended by further adding monomers into the reaction. In a radical polymerization all chains cannot be simultaneously active. In RDRP, such as RAFT polymerization, these attributes are displayed in the presence of reagents that are capable of reversibly deactivating propagating radicals such that the majority of living chains are maintained in a dormant form, and reaction conditions that support a rapid equilibrium between the active and dormant chains (**Figure 1**).

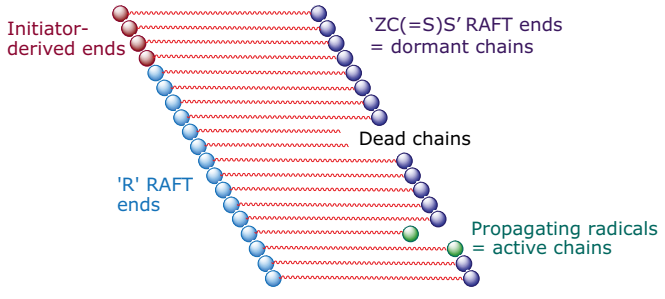


Figure 1. RAFT Polymerization Schematic.[4] The number of chains of each type shown here is not in proportion to that expected for a well-designed experiment. On average, all living chains grow simultaneously and have equal chain length because equilibration of the dormant and active chain ends is rapid with respect to propagation. A RAFT agent is represented as 'ZC(=S)S'.

Under these conditions, molecular weights can increase linearly with conversion, molecular weight distributions can be very narrow (**Figure 2**) and the majority of the polymerization product should be comprised of dormant chains.

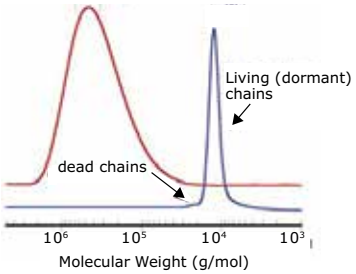
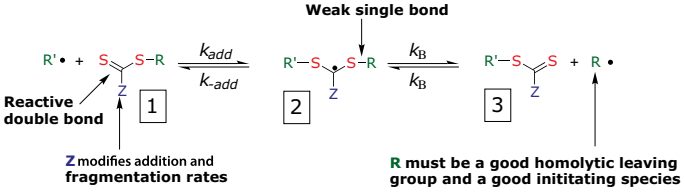


Figure 2. Typical molecular weight distributions for a conventional and a RAFT polymerization of styrene under similar experimental conditions.[4]

The mechanism of chain activation/deactivation in RAFT is shown in **Scheme 1**. The reactions associated with RAFT equilibria are in addition to those (i.e., initiation, propagation, and termination) that occur during conventional radical polymerization. In an ideal RAFT process, the RAFT agent should behave as a transfer agent. Termination is not suppressed by the RAFT process. Retention of the thiocarbonylthio groups in the polymeric product is responsible for the living character of RAFT polymerization and renders the process suitable for synthesizing block copolymers and end functional polymers. Removal or transformation of the thiocarbonylthio group may be required for some applications. A number of methods to accomplish the end group removal have been devised and can be readily incorporated into polymer syntheses.[10,12–16]



Scheme 1. Mechanism for reversible addition-fragmentation chain transfer (RAFT)

Selection of the RAFT agent (ZC(=S)SR) for the monomers and reaction conditions is crucial for the success of a RAFT polymerization experiment. However, this should not be a daunting task. The effectiveness of RAFT agents is determined by the substituents R and Z and guidelines for selection have been proposed (**Figure 3**).[1,3] Polymerization of most monomers can be well-controlled to provide minimal retardation and a high fraction of living chains by using one of just two RAFT agents. The first class is suited to more activated monomers (MAM) such as methacrylics, e.g., methyl methacrylate (MMA, Cat. No. M55909), methacrylic acid (MAA, Cat. No. 155721), hydroxypropyl methacrylamide (HPMAM) and acrylics, e.g., methyl acrylate (MA, Cat. No. M27301), acrylic acid (Cat. No. 147230), acrylamide (AM, Cat. No. 148660), acrylonitrile (AN, Cat. No. 320137), and styrene (St, Cat. No. S4972). The second class of RAFT agents is suited to less activated monomers (LAM) such as vinyl acetate (VAc, Cat. No. V1503), *N*-vinylpyrrolidone (NVP), or *N*-vinylcarbazole (NVC).

Recently, a switchable RAFT agent that can be used to control polymerization of both MAMs and LAMs has been described.[8,9] Requirements for specific end-functionality or polymer architecture may dictate the use of other RAFT agents.[10,11]

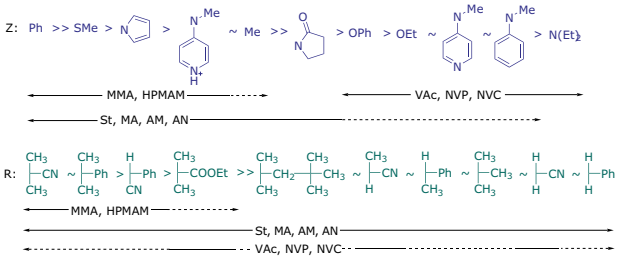


Figure 3. Guidelines for selection of RAFT agents (Z-C(=S)S-R) for various polymerizations.[1,3] For 'Z', addition rates and transfer constants decrease and fragmentation rates increase from left to right. For 'R', fragmentation rates decrease from left to right. A dashed line indicates limited control (e.g., retardation, high dispersity likely).

With appropriate choice of reagents and polymerization conditions RAFT polymerization can be used in the synthesis of well-defined homo, gradient, diblock, triblock, and star polymers, as well as more complex architectures including microgels and polymer brushes. Applications now being reported range from novel surfactants, dispersants, coatings, and adhesives, to biomaterials, membranes, drug delivery media, electroactive materials, and other fields falling under the nanotechnology umbrella.

RAFT Polymerization of 'More-Activated Monomers' (MAMs)

Good control over polymerization of a MAM is observed with trithiocarbonates (Z = S-alkyl, e.g., **4 – 6**). Z is preferably based on a thiol with low volatility. Aromatic dithioesters (Z = aryl, e.g., **9, 10**) are amongst the most active RAFT agents and show general utility in the polymerization of MAMs.[1,2] However, the aromatic substituted RAFT agents may give retardation when used in high concentrations and are more sensitive to hydrolysis and decomposition induced by Lewis acids.[17,18] Alkyl-substituted RAFT agents (**4 – 6**) can be tried if hydrolysis is a concern. The bis(thiocarbonyl) disulfides **7** and **8** are useful as precursors to the tertiary RAFT agents and can be used to form a RAFT agent in situ during polymerization.[19]

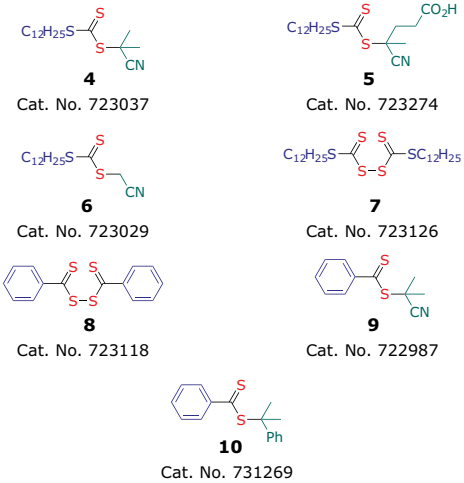


Figure 4. A series of RAFT agents that show good polymerization control for MAMs.

R must efficiently reinitiate polymerization and must be a good homolytic leaving group with respect to the propagating radical.[20] R* must also be efficient in reinitiating polymerization: it should add to monomer rapidly with respect to the rate of propagation. A good choice for the case of acrylates and acrylamides is the RAFT agent **6** with R = cyanomethyl. The choice of 'R' is critical in the case of methacrylates. In some of the most effective RAFT agents R is tertiary cyanoalkyl (e.g., **4, 5, 9**). The utility of the RAFT process is illustrated by the following example of RAFT polymerization of methyl methacrylate (MMA). A series of high (80 – 100%) conversion MMA polymerizations were carried out at 90 °C with 1,1'-azobis(1-cyclohexanecarbonitrile) initiator, and using an ~60-fold range of concentrations of *S*-dodecyl *S*-(2-cyano-4-carboxy)but-2-yl trithiocarbonate **5**.[10] The molecular weight distributions observed after six hours are shown in **Figure 5**. The molecular weights, ranging from 2,600 to 125,000, agree with expectation based on the concentrations of RAFT agent and initiator used.[10] All samples have narrow molecular weight distributions (PDI <1.2).

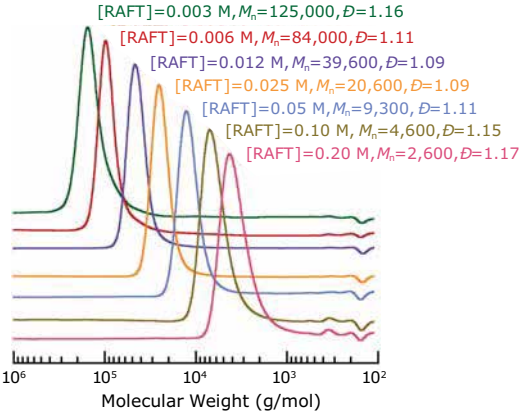


Figure 5. Molecular weight distributions for PMMA formed by high conversion RAFT polymerization of MMA (6.55 M in benzene) with 1,1'-azobis(1-cyclohexane-carbonitrile) (0.0018 M) as initiator and various concentrations of RAFT agent 5 for 6 h at 90 °C.[10]

RAFT Polymerization of 'Less-Activated Monomers' (LAMs)

The less active RAFT agents with Z = NR'2 (dithiocarbamates), Z = OR' (xanthates) and R' = alkyl or aryl offer good control. The more active RAFT agents Z = R (dithioesters) or SR (trithiocarbonates) inhibit polymerization of a LAM. The choice of R group is also critical because most monomers in the class have a high propagation rate constant. Inhibition periods due to slow reinitiation are expected for RAFT agents such as **12** and **13**. One preferred RAFT agent is **11**. Examples of VAc polymerization with **11** are shown in **Table 1**.[7]

Table 1. RAFT Polymerization of Vinyl Acetate[7]

Monomer (M)	RAFT Agent (M×10²)	Initiator[a] (M×10³)/ Conditions	Conv %	M_n[b]	M_n (calc)[c]	*PDI*
10.86	11 (4.98)	AIBN (61) 60 °C 16 h	96	22,700	18,000	1.24
7.24	11 (5.06)	ACHN (28) 75 °C 16 h	93	13,400	11,440	1.29
7.24	11 (10.06)	ACHN (28) 75 °C 16 h	95	7,100	5,880	1.25

[a]AIBN: 2,2'-azobis(isobutyronitrile) (**Cat. No. 441090**); ACHN: 1,1'-azobis(cyclohexanecarbonitrile) (**Cat. No. 380210**)
[b]number average molecular weight in polystyrene equivalents.
[c]calculated molecular weight based on complete consumption of RAFT agent

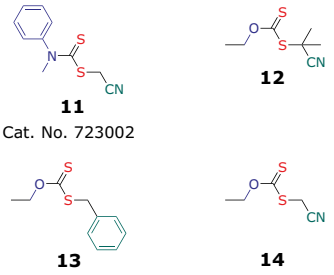
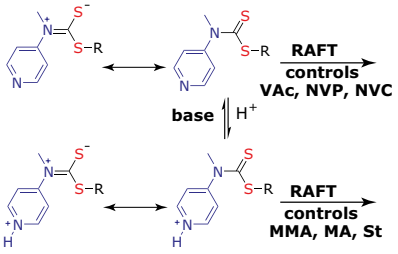


Figure 6. A series of RAFT agents that show good polymerization control for MAMs.

Switchable RAFT Agents

We recently reported on a new class of stimuli-responsive RAFT agents that can be "switched" to offer good control over polymerization of both MAMs and LAMs, and thus a more convenient route to polyMAM-*block*-polyLAM polymers with narrowed molecular weight distributions.[9] This approach was demonstrated with the use of 4-pyridinyl-*N*-methyldithiocarbamate derivatives to prepare PMMA-*block*-PVAc and PMA-*block*-PNVC. The *N*-4-pyridinyl-*N*-methyldithiocarbamates provide effective control over polymerization of LAMs (**Scheme 2**) and when protonated also provide excellent control over the polymerization of MAMs.[9]



Scheme 2. RAFT Agent capable of polymerization of both LAMs and MAMs controlled by pH.

Conclusions

Reversible Addition/Fragmentation Chain Transfer (RAFT) has emerged as one of the most important methods for controlling radical polymerization. RAFT has been shown to be robust and versatile, and applicable to the majority of monomers subject to radical polymerization. However, selection of the appropriate RAFT agent for the monomers in tandem with the proper reaction conditions is crucial for successful polymerization.

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Concepts and Tools for RAFT Polymerization

Adapted from contributions by researchers at CSIRO
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The RAFT Process

RAFT or **R**eversible **A**ddition/**F**ragmentation Chain **T**ransfer is a form of living radical polymerization. RAFT polymerization was discovered at CSIRO in 1998.[1] It soon became the focus of intensive research, since the method allows synthetic tailoring of macromolecules with complex architectures including block, graft, comb, and star structures with controlled molecular weight.[2] RAFT polymerization is applicable to a very wide range of vinyl monomers under a variety of experimental conditions, including the preparation of water-soluble materials.[3]

The RAFT process involves conventional free radical polymerization of a substituted monomer in the presence of a suitable chain transfer agent (RAFT agent or CTA). Commonly used RAFT agents include thiocarbonylthio compounds such as dithioesters,[1] dithiocarbamates,[4,5] trithiocarbonates,[6] and xanthates,[7] which mediate the polymerization via a reversible chain-transfer process. Use of a proper RAFT agent allows synthesis of polymers with a high degree of functionality and narrow distribution of molecular weights also referred to as a low polydispersity index (PDI) as shown in **Figure 1**.

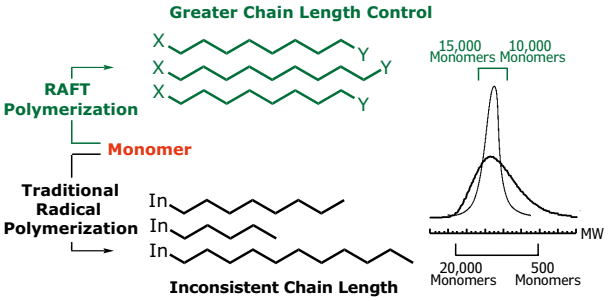

Figure 1. General comparison of polymers made with traditional radical polymerization against those made using RAFT process.

A RAFT CTA typically has a thiocarbonylthio group (S = C–S) with substituents R and Z that impact the polymerization reaction kinetics and therefore, the degree of structural control. Initiation of the polymerization reaction is accomplished utilizing conventional thermal, photochemical, or redox methods, and the success of the RAFT polymerization experiment is dependent upon selecting the appropriate RAFT reagent for a particular monomer and reaction medium. This general concept is depicted in **Figure 2**.

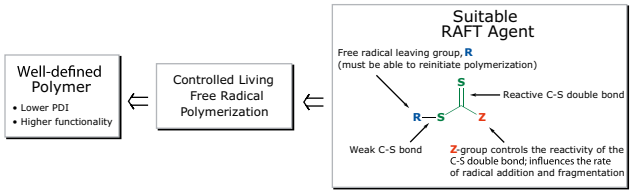

Figure 2. General structure of a RAFT agent, where the R and Z subtituents impact reaction kinetics. The choice of the RAFT agent is critical to obtain polymers with low PDI and controlled architecture.

Classes of RAFT Agents

Solubility and reactivity of a RAFT agent depend on the R and Z groups; as a result, different RAFT agents are more suitable for specific classes of monomers. The main classes of RAFT agents are:

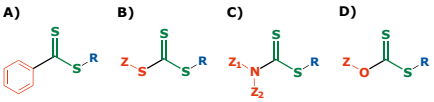

Figure 3. Four classes of RAFT agents: **A)** Dithiobenzoates, **B)** Trithiocarbonates, **C)** Dithiocarbamates, and **D)** Xanthates.

A) Dithiobenzoates

- Very high transfer constants
- Prone to hydrolysis
- May cause polymerization retardation under high concentrations

B) Trithiocarbonates

- High transfer constants
- More hydrolytically stable (than dithiobenzoates)
- Cause less retardation

C) Dithiocarbamates

- Activity determined by substituents on *N*
- Effective with electron-rich monomers

D) Xanthates

- Lower transfer constants
- More effective with less activated monomers
- Made more active by electron-withdrawing substituents

RAFT Agent to Monomer Compatibility Table

The application of RAFT agents with common monomers used in polymerizations is shown in **Table 1**. The plus and minus symbols represent the degree of compatibility between monomer classes and a RAFT agent. For example, Cat. No. 723037 (fifth item down in **Table 1**) is very useful in polymerizing styrenes, methacrylates and methacrylamides, shows moderate activity for acrylates and acrylamides but cannot polymerize vinyl esters or vinyl amides. This table can be used as a guide for selecting the most appropriate RAFT agent for your needs.

Table 1. RAFT agents suitability for various monomer types. (Adapted from CSIRO's RAFT agent Monomer Matching guide).

	styrenes	acrylates	acrylamides	methacrylates	methacrylamides	vinyl esters	vinyl amides
723002	–	–	–	–	–	+++	+++
723029	+++	+++	+++	–	–	–	–
722987	++	+	–	+++	+++	–	–
722995	++	+	+	+++	+++	–	–
723037	+++	++	++	+++	+++	–	–
723274	+++	++	++	+++	+++	–	–
723010	+++	+++	+++	+	+	–	–

+++= Well-suited ++= Moderately suited += Variable results –= Poorly suited

Please see the fold out compatibility table at the end of the book for more information.

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Typical Procedures for Polymerizing via RAFT

The following procedures describe polymerization of methyl methacrylate and vinyl acetate homopolymers and a block copolymer as performed by researchers at CSIRO.

Introduction

RAFT (Reversible Addition/Fragmentation Chain Transfer) is a form of living radical polymerization involving conventional free radical polymerization of a substituted monomer in the presence of a suitable chain transfer (RAFT) reagent. Use of the appropriate RAFT agent and polymerization conditions allows for the synthesis of polymers with low PDI and high functionality. For a further explanation of RAFT technology and its advantages, please read the review by researchers at CSIRO on page 21.

Reagents

RAFT Agent (Cat. No.)

- 2-Cyano-2-propyl benzodithioate (722987)
- 4-Cyano-4-[(dodecylsulfanylthiocarbonyl)sulfanyl]pentanoic acid (723274)
- Cyanomethyl methyl(phenyl) carbamodithioate (723002)
- 4-Cyano-4-(phenylcarbonothioylthio) pentanoic acid (722995)
- 2-Cyano-2-propyl dodecyl trithiocarbonate (723037)
- 2-(Dodecylthiocarbonothioylthio)-2-methylpropionic acid (723010)
- Cyanomethyl dodecyl trithiocarbonate (723029)

Storage/Stability

- 723274 — Store the product at -20 °C and keep tightly closed. The product is light sensitive.
- 722995 and 723037 — Store the products at 2–8 °C and keep tightly closed.
- 722987, 723002, 723010, and 723029 — Store the products at 2–8 °C and keep tightly closed. The products are light sensitive.

Note: Please consult the Material Safety Data Sheet for information regarding hazards and safe handling practices.

RAFT Polymerization Procedures

1) Methyl Methacrylate Polymerization: using methyl methacrylate (MMA, Cat. No. M55909) as the monomer, AIBN (Cat. No. 441090) as the initiator, and a RAFT agent (Cat. No. 722987 or 723274).

- Prepare stock solution of methyl methacrylate (15 mL, 0.14 mol) and AIBN (20.1 mg, 0.122 mmol) in 5 mL of benzene.
- Aliquot 2 mL samples of stock solution into ampules containing Cat. No. 722987 (12.3 mg, 0.056 mmol) or Cat. No. 723274 (22.5 mg, 0.056 mmol). **Note:** Other glassware suitable for handling air sensitive reactions, such as a Schlenk reaction tube (Cat. No. Z515981), may be used as an alternative to a sealed ampule.
- De-gas contents of ampules by three repeated freeze-evacuate-thaw cycles (0.05 mm Hg) and seal under vacuum.
- Polymerize by placing sealed ampule in heated oil bath (60 °C) for 15 hours.

Characterization of Poly(methyl methacrylate)

Table 1. Characteristics of poly(methyl methacrylate) synthesized by RAFT polymerization

RAFT Agent	Polymerization Time	M_n	PDI	% Conv. (NMR)
722987	4 hours	8468	1.14	24.5
722987	15 hours	30032	1.07	93.6
723274	15 hours	25959	1.08	98.5

2) Vinyl Acetate Polymerization:
using vinyl acetate (Cat. No. V1503) as the monomer, AIBN (Cat. No. 441090) as the initiator, and a RAFT agent (Cat. No. 723002).

- Prepare solution of vinyl acetate (2.0 mL, 23.23 mmol), AIBN (2.0 mg, 0.012 mmol), and Cat. No. 723002 (26.64 mg, 0.12 mmol) in an ampule. Note: Other glassware suitable for handling air sensitive reactions, such as a Schlenk reaction tube (Cat. No. Z515981), may be used as an alternative to a sealed ampule.
- De-gas contents of the ampule by three repeated freeze-evacuatethaw cycles (0.05 mm Hg) and seal under vacuum.
- Polymerize by placing sealed ampule in heated oil bath (60 °C) for 16 hours.

Researchers at CSIRO have tested select Sigma-Aldrich RAFT agents in the polymerization of vinyl acetate and analyzed the resulting polymer. The data are presented in **Table 2** and **Figure 1**.

Characterization of Poly(vinyl acetate)

Table 2. Characteristics of poly(vinyl acetate) synthesized by RAFT polymerization.

RAFT Agent	Polymerization Time	M_n	PDI	% Conv. (NMR)
723002	16 hours	16,400	1.25	91

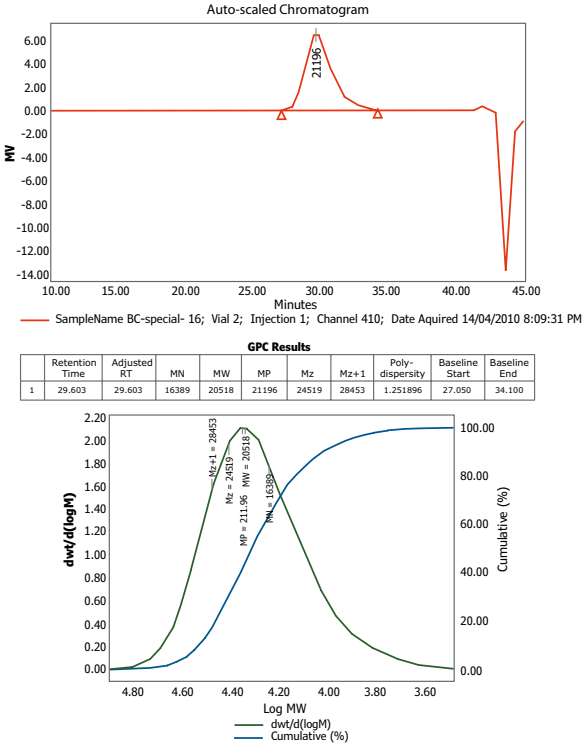

Figure 1. GPC analysis of poly(vinyl acetate) polymerized for 16 hours using Cat. No. 723002 as a RAFT agent.

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Universal/Switchable RAFT Agents for Well-defined Block Copolymers: Agent Selection and Polymerization

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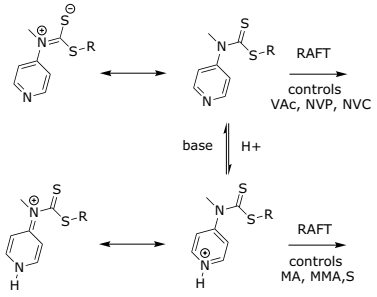
Introduction to Switchable RAFT Agents

Reversible Addition/Fragmentation Chain Transfer (RAFT) polymerization is a versatile controlled radical polymerization method.[1–3] For example, most vinyl monomers which are polymerizable by radical polymerization can be polymerized via RAFT.[4] However, due to reactivity differences, the appropriate RAFT agent must be selected for a given monomer type in order to obtain living polymerization characteristics. In general, RAFT agents such as dithioesters[2] and trithiocarbonates[5] work well with controlling the polymerization of "more-activated" monomers (MAMs), such as styrene (Sty), methyl acrylate (MA), and methyl methacrylate (MMA), meanwhile dithiocarbamates[6,7] and xanthates[8] must be used to control the polymerization of "less activated" monomers (LAMs), such as vinyl acetate (VAc), *N*-vinylpyrrolidone (NVP), and *N*-vinylcarbazole (NVC). Improper pairing (e.g., dithiocarbamate RAFT agent with MMA monomer) will inhibit or significantly limit the polymerization.[5]

Differences in the reactivity of vinyl monomers have historically limited the ability to form block copolymers comprised of MAMs and LAMs (poly(MAM)-*block*-poly(LAM)) with a narrow molecular weight distribution. In an effort to overcome this limitation, CSIRO scientists have recently reported switchable (universal) RAFT agents.[1] These specialty RAFT agents are dithiocarbamates that are able to control the polymerization of MAMs when the pyridyl nitrogen is protonated and then readily control the polymerization of LAMs when deprotonated (**Scheme 1**).



Scheme 1. Differences in the canonical forms of protonated and deprotonated *N*-methyl, *N*-(4-pyridyl)dithiocarbamates. When protonated the agents can control polymerization of MAMs (such as Sty, MA, MMA) and then when deprotonated, the RAFT agents can effectively control polymerization of LAMs (such as VAc, NVP and NVC).[1,9]

Practical Considerations

The synthesis of poly(MAM)-*block*-poly(LAM) can be performed *in situ* via direct solution polymerization and is rapid and reversible. The highest level of control over the polymerization is achieved by protonation of the 4-pyridyl group with a stoichiometric amount of a strong organic acid (e.g., *p*-toluenesulfonic acid, trifluoromethanesulfonic acid, etc).[10] Alternatively, coordination of the 4-pyridyl group with Lewis acids such as $Al(OTf)_3$ will also work.[10] Deprotonation can be performed *in situ* using organic bases such as *N,N*-dimethylaminopyridine (DMAP),[1] or can be achieved by passing a polymer solution through a bed of crushed sodium carbonate.

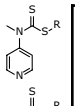
In order to prepare well-defined block copolymers using switchable RAFT agents, the MAM block segment should be polymerized first with a protonated RAFT agent, followed by deprotonation and subsequent polymerization of the LAM block(s).[1,9,10] This is primarily due to the fact that terminal LAM groups are poor radical leaving groups, leading to poor blocking efficiency in the presence of MAMs, whereas poly(MAM)s tend to have high chain transfer constants relative to LAMs. In certain cases, it is strongly recommended (particularly when initiating the polymerization of a vinyl acetate block from a polystyrene macro chain transfer agent) that all traces of residual MAM are removed (either by precipitation or vacuum distillation). Trace MAM in the reaction solution could lead to inhibition of future polymerization events. Additionally, in some cases addition of an intermediate monomer may be required in order to bridge the reactivity between MAM and LAM units. In the case of styrene and vinyl acetate, a small amount of methyl acrylate (~5%) can be added, after all Sty monomer is consumed or removed, to a solution of the polystyrene macroCTA and vinyl acetate. The polystyrene macroCTA will incorporate the methyl acrylate and the vinyl acetate in a gradient fashion before leading to a true vinyl acetate block once all methyl acrylate is consumed.

A technical protocol describing the synthesis of poly(MAM)-*block*-poly (LAM) via switchable RAFT agents is included on page 27.

Switchable RAFT Agent to Monomer Compatibility Table

The compatibility of switchable RAFT agents with common monomers is shown in **Table 1**. The check and dash symbols represent the compatibility and incompatibility, respectively, between monomer classes and a protonated and neutral form of switchable RAFT agent. For example, 2-Cyanopropan-2-yl *N*-methyl-*N*-(pyridin-4-yl)carbamodithioate, Cat. No. 736236, is very useful in polymerizing styrenes, methacrylates and methacrylamides when protonated, but shows poor activity in controlling vinyl esters or vinyl amides.

Table 1. The neutral and protonated switchable RAFT agents with their suitability for selected monomer types (✔ = compatible; – = incompatible).

	Styrenes	Acrylates	Methacrylates	Vinyl esters/amides
	–	–	–	✔
	✔	✔	✔	–

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Polymerization Procedure with Universal/Switchable RAFT Agents

The following procedure describes polymerizations as performed by researchers at CSIRO and researchers at Sigma-Aldrich.[1]

Product Description

RAFT (Reversible Addition/Fragmentation Chain Transfer) is a form of living radical polymerization involving conventional free radical polymerization of a monomer in the presence of a suitable chain transfer (RAFT) reagent. RAFT technology can be used with a wide range of monomers by all modes of free radical polymerization (solution, emulsion, and suspension). The appropriate RAFT agent must be selected for the monomer of interest. Historically there have been no "universal" RAFT agents capable of preparing block copolymers comprised of both lower activity monomers (LAMs; e.g., *N*-vinylpyrrolidone (Cat. No. V3409), vinyl acetate (Cat. No. V1503), etc.), along with more active monomers (MAMs; e.g., acrylates, methacrylates, styrenes, etc.). However, with the development of a new class of stimuli responsive, "pH-switchable/Universal" RAFT agents, the synthesis of poly(MAM)-*block*-poly(LAM) can be performed *in situ* via direct solution polymerization, and is rapid and reversible. The highest level of control over the polymerization is achieved by protonation of the 4-pyridyl group with a stoichiometric amount of a strong organic acid (e.g., *p*-toluenesulfonic acid, trifluoromethanesulfonic acid, etc).[2] Alternatively, coordination of the 4-pyridyl group with Lewis acids such as Al(OTf)$_3$ will also work.[2] Deprotonation can be performed *in situ* using organic bases such as *N,N*-dimethylaminopyridine (DMAP),[1] or can be achieved by passing a polymer solution through a bed of crushed sodium carbonate. For a further explanation of RAFT technology and its advantages, please read the review by researchers at CSIRO on page 21.

Reagents

Switchable RAFT Agent (**Cat. No.**)

- Methyl 2-propionate methyl(4-pyridinyl)carbamodithioate (735639)
- 2-Cyanopropan-2-yl *N*-methyl-*N*-(pyridin-4-yl) carbamodithioate (736236)
- *S*-cyanomethyl-*N*-methyl-*N*-(pyridin-4-yl)carbamodithioate (738689)
- *N,N′*-Dimethyl *N,N′*-di(4-pyridinyl)thiuram disulfide (735973)

Storage/Stability

The products are light sensitive. Store the products at 2 – 8 °C and keep tightly closed.

Switchable RAFT Polymerization Procedures

Example procedures of RAFT polymerization utilizing "Switchable" RAFT reagents (as performed by researchers at CSIRO):

1) Poly(methyl methacrylate) homopolymer
2) Poly(vinyl acetate) homopolymer
3) Poly(methyl methacrylate)-*block*-poly(vinyl acetate) copolymer

1) Methyl Methacrylate Polymerization: using methyl methacrylate (MMA, Cat. No. M55909) as the monomer, 2,2′-Azobis (2-methylpropionitrile) (AIBN) (Cat. No. 441090) as the initiator, and a Switchable RAFT agent 2-Cyanopropan-2-yl *N*-methyl-*N*-(pyridin-4-yl)carbamodithioate (Cat. No. 736236).

- A stock solution (A) of trifluoromethanesulfonic acid (100 µL or 170 mg, Cat. No. 347817) in acetonitrile (5.0 mL) was prepared.
- A second stock solution (B) was prepared containing methyl methacrylate (7.0 mL), AIBN (10 mg), 2-Cyanopropan-2-yl *N*-methyl-*N*-(pyridin-4-yl)carbamodithioate (50.02 mg), acetonitrile (2.0 mL) and stock solution A (1.0 mL) from previous step.
- 2.0 mL of stock solution B was transferred to an ampule, degassed by three repeated freeze-evacuate-thaw cycles and sealed. Other glassware suitable for handling air sensitive reactions, such as a Schlenk reaction tube, may be used as an alternative to a sealed ampule.
- The ampule was polymerized at 60 °C for 16 hours. Characterization data for this polymerization is presented in **Table 1**.
- To remove color from the final product the polymer was dissolved in excess dichloromethane and passed through a crushed sodium carbonate bed. A color change from yellow to colorless occurs.

Table 1. Characteristics of PMMA synthesized by switchable RAFT polymerization using Cat. No. 736236.

Reaction Time	M_n	PDI	% Conv.
3 hours	15,500	1.56	27.6%
6 hours	19,200	1.58	51.1%
16 hours	33,050	1.25	98.0%

2) Vinyl Acetate Polymerization: using vinyl acetate (Cat. No. V1503) as the monomer, 1,1′-Azobis (cyclohexanecarbonitrile) (ACHN) (Cat. No. 380210) as the initiator, *S*-cyanomethyl *N*-methyl, *N*-(pyridin-3-yl) carbamodithioate (Cat. No. 738689) as the Switchable RAFT agent, and ethyl acetate as solvent (Cat. No. 270989).

- A solution of ACHN (10.3 mg), vinyl acetate (10 mL) and ethyl acetate (5.0 mL) was prepared. An aliquot (3.0 mL) of this stock solution was transferred into an ampule containing *S*-cyanomethyl *N*-methyl,*N*-(pyridin-3-yl) carbamodithioate (35.0 mg), which was degassed by three repeated freeze-evacuate-thaw cycles and sealed.
- The ampule was heated at 75 °C for 3 days. After the reaction, the unreacted monomer was removed on rotary evaporator. The resulting poly(vinyl acetate) displayed a low polydispersity as shown in **Table 2**.

Table 2. Characteristics of poly(vinyl acetate) synthesized by switchable RAFT polymerization using Cat. No. 738689.

Reaction Time	M_n	PDI	% Conv.
3 days	8,900	1.24	54.8%

3) Poly(methyl methacrylate)-*block*-poly(vinyl acetate) copolymer: was prepared by essentially combining the previous two procedures. The PMMA polymer from the PMMA polymerization procedure is now the macro chain transfer agent (macroCTA) for controlling the second vinyl acetate block. The last step of the PMMA polymerization was passing the polymer over a crushed bed of sodium carbonate, which deprotonated the RAFT functionality and prepared the macroCTA for polymerization of vinyl acetate.

PMMA-*block*-PVac was prepared by using vinyl acetate (Cat. No. V1503) as the monomer, ACHN (Cat. No. 380210) as the initiator, and the PMMA macro chain transfer agent (macroCTA) prepared in the previous Procedure 1 (PMMA, 33,050 Da, PDI = 1.25). The poly(methyl methacrylate)-*block*-poly(vinyl acetate) copolymer was synthesized under reaction conditions similar to Procedure 2.

- A solution of ACHN (10.3 mg), vinyl acetate (10 mL) and ethyl acetate (5.0 mL) was prepared. An aliquot (3.0 mL) of this stock solution was transferred into an ampule containing the macroCTA, the mass of which depends on the molecular weight obtained. This was degassed by three repeated freeze, pump, thaw cycles and sealed.
- The ampule was heated at 75 °C for 3 days. After the reaction, the unreacted monomer was removed with a rotary evaporator. The resulting poly(methyl methacrylate)-block-poly(vinyl acetate) copolymer displayed a low polydispersity as shown in **Table 3**.

Table 3. Characteristics of poly(methyl methacrylate)-*block*-poly(vinyl acetate) copolymer synthesized by switchable RAFT technology.

Reaction Time	M_n	PDI	% Conv.
3 days	55,900	1.39	80%

The Switchable RAFT agents are able to successfully polymerize monomers of different reactivity and achieve narrow molecular weight distributions as shown in **Figure 1**.

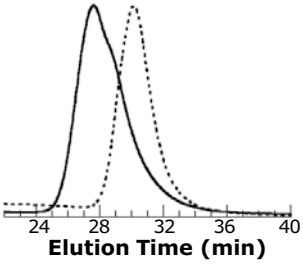


Figure 1. GPC analysis of poly(methyl methacrylate)-block-poly(vinyl acetate) polymerized for 16 hours using PMMA as a macroCTA.[1] Reprinted with permission from the American Chemical Society.

Gel permeation chromatography (GPC) method: Waters Associates liquid chromatograph equipped with differential refractometer and 3×mixed C and 1 mixed E PLgel column. Tetrahydrofuran (flow rate of 1.0 mL/min) was used as eluent at 22 ± 2 °C. The columns were calibrated with narrow polydispersity polystyrene standards. The molecular weights are reported as polystyrene equivalents.

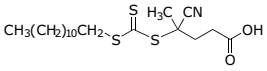
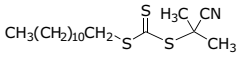
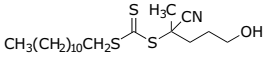
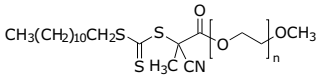
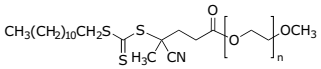
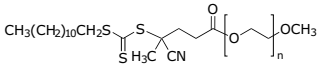
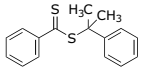
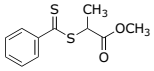
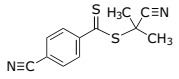
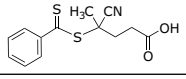
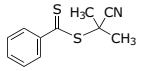
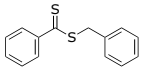
RAFT agents are sold for research purposes only. For patent information, see SigmaAldrich.com/raftlicense.

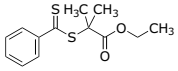
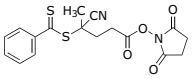
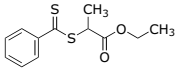
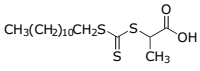
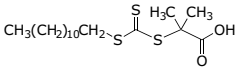
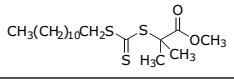
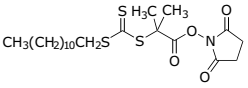
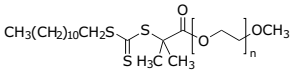
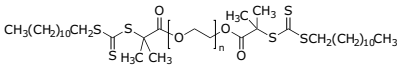
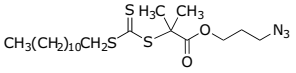
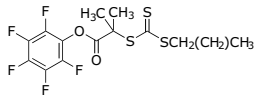
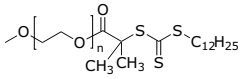
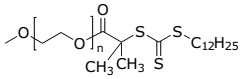
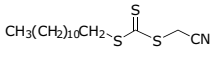
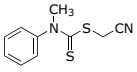
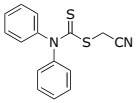
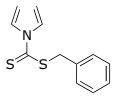
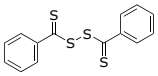
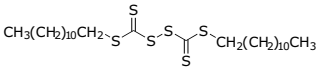
References

1 Benaglia, M.; Chiefari, J.; Chong, Y.K.; Moad, G.; Rizzardo, E.; Thang, S. H. *J. Am. Chem. Soc.* **2009**, *131*, 6914.
2 Keddie, D.J.; Guerrero-Sanchez, C.; Moad, G.; Rizzardo, E.; Thang, S. H. *Macromolecules*, **2011**, *44* , 6738.

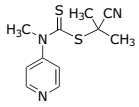
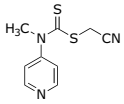
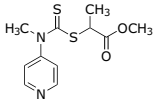
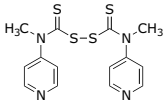
Reversible Addition/Fragmentation

For a complete list of available RAFT agents, visit SigmaAldrich.com/raftagent.

Name	Structure	Description	Cat. No.
4-Cyano-4-[(dodecylsulfanylthiocarbonyl) sulfanyl]pentanoic acid		RAFT agent for controlled radical polymerization; especially suited for the polymerization of methacrylate, methacrylamide and styrene monomers. Chain Transfer Agent (CTA)	723274-1G 723274-5G
2-Cyano-2-propyl dodecyl trithiocarbonate		RAFT agent for controlled radical polymerization; especially suited for the polymerization of methacrylate, methacrylamide and styrene monomers. Chain Transfer Agent (CTA)	723037-1G 723037-5G
4-Cyano-4-[(dodecylsulfanylthiocarbonyl) sulfanyl]pentanol		RAFT agent for controlled radical polymerization; This alcohol-functionalized RAFT CTA would allow wide variety of pre- and post-polymerization functionalization; including standard coupling reactions and even ringopening polymerization; allowing for poly(vinyl)-*block*-poly(ROP) polymers (e.g. Polystyrene-*block*-poly(L-lactide); etc). This is best suited for methacrylate/methacrylamide/styrenic monomers.	760110-1G 760110-5G
Poly(ethylene glycol) methyl ether 4-cyano-4-[(dodecylsulfanylthiocarbonyl) sulfanyl]pentanoate, average M_n 10,400		RAFT agent for controlled radical polymerization; especially suited for the polymerization of styrene, acrylate and acrylamide monomers to make lithographically and biologically important PEG-block copolymers. Chain Transfer Agent (CTA)	753033-1G
Poly(ethylene glycol) methyl ether (4-cyano-4-pentanoate dodecyl trithiocarbonate), average M_n 5,400		RAFT agent for controlled radical polymerization; especially suited for the polymerization of styrene; acrylate and acrylamide monomers to make lithographically and biologically important PEG-block copolymers. Chain Transfer Agent (CTA)	751626-5G 751626-1G
Poly(ethylene glycol) methyl ether (4-cyano-4-pentanoate dodecyl trithiocarbonate), average M_n 2,400		RAFT agent for controlled radical polymerization; especially suited for the polymerization of styrene; acrylate and acrylamide monomers to make lithographically and biologically important PEG-block copolymers. Chain Transfer Agent (CTA)	751634-5G 751634-1G
2-Phenyl-2-propyl benzodithioate		RAFT agent for controlled radical polymerization; especially suited for the polymerization of methacrylates/methacrylamides, and to a lesser extent acrylates/acrylamides and styrenes; Chain Transfer Agent (CTA)	731269-1G 731269-5G
1-(Methoxycarbonyl)ethyl benzodithioate		RAFT agent for controlled radical polymerization; wellsuited for polymerization of methacrylates, methacrylamides, and to a lesser extent styrenes, acrylates, and acrylamides. Chain Transfer Agent (CTA)	751138-1G
2-Cyano-2-propyl 4-cyanobenzodithioate		RAFT agent for controlled radical polymerization; especially suited for the polymerization of methyl methacrylate and styrene monomers. Chain Transfer Agent (CTA)	731277-1G 731277-5G
4-Cyano-4-(phenylcarbonothioylthio) pentanoic acid		RAFT agent for controlled radical polymerization; especially suited for the polymerization of methacrylate and methacrylamide monomers. Chain Transfer Agent (CTA)	722995-1G 722995-5G
2-Cyano-2-propyl benzodithioate		RAFT agent for controlled radical polymerization; especially suited for the polymerization of methacrylate and methacrylamide monomers. Chain Transfer Agent (CTA)	722987-1G 722987-5G
Benzyl benzodithioate		RAFT agent for controlled radical polymerization; Chain Transfer Agent (CTA) well-suited for methacrylates, methacrylamides, and styrenes.	760439-1G 760439-5G

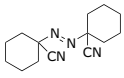
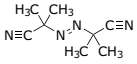
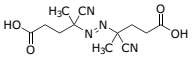
Name	Structure	Description	Cat. No.
Ethyl 2-methyl-2-(phenylthiocarbonylthio) propionate		RAFT agent for controlled radical polymerization; wellsuited for polymerization of methacrylates, methacrylamides, and to a lesser extent styrenes, acrylates, and acrylamides. Chain Transfer Agent (CTA)	741701-1G
4-Cyano-4-(phenylcarbonothioylthio) pentanoic acid *N*-succinimidyl ester		RAFT agent for controlled radical polymerization; This is the NHS protected version of 722995; well suited for methacrylates and methacrylamides; Chain Transfer Agent (CTA)	758353-1G
Ethyl 2-(phenylcarbonothioylthio) propionate		RAFT agent for controlled radical polymerization; especially suited for methacrylates and methacrylamides; Chain Transfer Agent (CTA)	760455-1G
2-(Dodecylthiocarbonothioylthio) propionic acid		RAFT agent for controlled radical polymerization; especially suited for the polymerization of styrene, acrylate and acrylamide monomers. Chain Transfer Agent (CTA)	749133-1G 749133-5G
2-(Dodecylthiocarbonothioylthio)-2-methylpropionic acid		RAFT agent for controlled radical polymerization; especially suited for the polymerization of styrene, acrylate and acrylamide monomers. Chain Transfer Agent (CTA)	723010-1G 723010-5G
Methyl 2-(dodecylthiocarbonothioylthio)-2-methylpropionate		RAFT agent for controlled radical polymerization; especially suited for the polymerization of styrene; acrylate and acrylamide monomers. Chain Transfrer Agent (CTA)	740497-1G 740497-5G
2-(Dodecylthiocarbonothioylthio)-2-methylpropionic acid *N*-hydroxysuccinimide ester		Functionalized RAFT agent for controlled radical polymerization; especially suited for the polymerization of styrene; acrylate and acrylamide monomers. NHS ester terminus can be used to conjugate to a variety of biomolecules. Chain Transfer Agent (CTA)	741035-1G 741035-5G
Poly(ethylene glycol) methyl ether (2-methyl-2-propionic acid dodecyl trithiocarbonate), average M_n 10,400		RAFT agent for controlled radical polymerization; especially suited for the polymerization of styrene; acrylate; and acrylamide monomers to make lithographically and biologically important PEG-block copolymers. Chain Transfer Agent (CTA)	752495-1G
Poly(ethylene glycol) bis[2-(dodecylthiocarbonothioylthio)-2-methylpropionate], average M_n 10,800		RAFT agent for controlled radical polymerization; especially suited for the polymerization of styrene; acrylate; and acrylamide monomers to make lithographically and biologically important PEG-block copolymers. Chain Transfer Agent (CTA)	753025-1G
2-(Dodecylthiocarbonothioylthio)-2-methylpropionic acid 3-azido-1-propanol ester		Functionalized RAFT agent for controlled radical polymerization; especially suited for the polymerization of styrene, acrylate and acrylamide monomers. Azide group can be used to conjugate to a variety of alkynefunctionalized biomolecules. Chain Transfer Agent (CTA).	741698-1G 741698-5G
2-(Dodecylthiocarbonothioylthio)-2-methylpropionic acid pentafluorophenyl ester		RAFT agent for controlled radical polymerization; especially suited for the polymerization of styrene; acrylate and acrylamide monomers. Chain Transfer Agent (CTA)	740810-1G 740810-5G
Poly(ethylene glycol) methyl ether 2-(dodecylthiocarbonothioylthio)-2-methylpropionate, average M_n 1,100		RAFT agent for controlled radical polymerization; especially suited for the polymerization of styrene; acrylate and acrylamide monomers to make lithographically and biologically important PEG-block copolymers. Chain Transfer Agent (CTA)	740705-1G
Poly(ethylene glycol) methyl ether 2-(dodecylthiocarbonothioylthio)-2-methylpropionate, M_n 5,000		RAFT agent for controlled radical polymerization; especially suited for the polymerization of styrene, acrylate, and acrylamide monomers to make lithographically and biologically important PEG-block copolymers. Chain Transfer Agent (CTA)	736325-1G
Cyanomethyl dodecyl trithiocarbonate		RAFT agent for controlled radical polymerization; especially suited for the polymerization of styrene, acrylate and acrylamide monomers. Chain Transfer Agent (CTA)	723029-1G 723029-5G
Cyanomethyl methyl(phenyl) carbamodithioate		RAFT agent for controlled radical polymerization; especially suited for the polymerization of vinyl ester and vinyl amide monomers. Chain Transfer Agent (CTA)	723002-1G 723002-5G
Cyanomethyl diphenylcarbamodithioate		RAFT agent for controlled radical polymerization; wellsuited for vinyl acetates and vinyl benzoates. Chain Transfer Agent (CTA)	751200-1G 751200-5G
Benzyl 1*H*-pyrrole-1-carbodithioate		RAFT agent for controlled radical polymerization; wellsuited for polymerization of vinyl esters and vinyl amides (LAMs)	753106-5G 753106-1G
Bis(thiobenzoyl) disulfide		Precursor for the synthesis of RAFT agents for controlled radical polymerization.	723118-5G
Bis(dodecylsulfanylthiocarbonyl) disulfide		Precursor for the synthesis of RAFT agents for controlled radical polymerization.	723126-5G

Switchable RAFT Agents

Name	Structure	Description	Cat. No.
2-Cyanopropan-2-yl Nmethyl-*N*-(pyridin-4-yl)carbamodithioate		Switchable RAFT agent for controlled radical polymerization. The neutral form is well-suited for polymerization of vinyl esters and vinyl amides (LAMs), and the protonated form is well-suited for styrenes acrylates and methacrylates (MAMs). Chain Transfer Agent (CTA)	736236-1G 736236-5G
Cyanomethyl methyl(4-pyridyl) carbamodithioate		Switchable RAFT agent for controlled radical polymerization. The neutral form is well-suited for polymerization of vinyl esters and vinyl amides (LAMs), and the protonated form is well-suited for styrenes acrylates and methacrylates (MAMs). Chain Transfer Agent (CTA)	738689-1G 738689-5G
Methyl 2-propionate methyl(4-pyridinyl)carbamodithioate		Switchable RAFT agent for controlled radical polymerization. The neutral form is well-suited for polymerization of vinyl esters and vinyl amides (LAMs), and the protonated form is well-suited for styrenes acrylates and methacrylates (MAMs). Chain Transfer Agent (CTA)	735639-1G 735639-5G
N,N′-Dimethyl *N,N′*-di(4-pyridinyl) thiuram disulfide		Precursor for the synthesis of novel switchable RAFT agents for controlled radical polymerization. Chain Transfer Agent (CTA)	735973-5G

Radical Initiators

For a complete list of available radical initiators, visit SigmaAldrich.com/crp.

Name	Structure	Purity	Cat. No.
1,1′-Azobis(cyclohexanecarbonitrile)		98%	380210-25G 380210-100G
2,2′-Azobis(2-methylpropionitrile)		98%	441090-25G 441090-100G
4,4′-Azobis(4-cyanovaleric acid)		≥98.0%, T	11590-25G 11590-100G

NMP

Block Copolymer Synthesis Using a Commercially Available Nitroxide-mediated Radical Polymerization (NMP) Initiator

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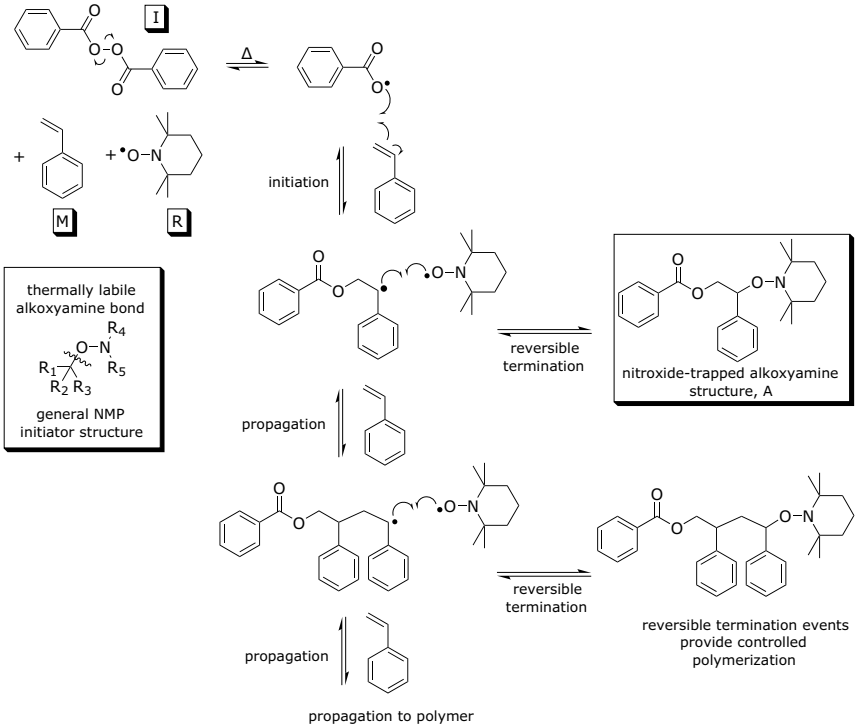
Introduction

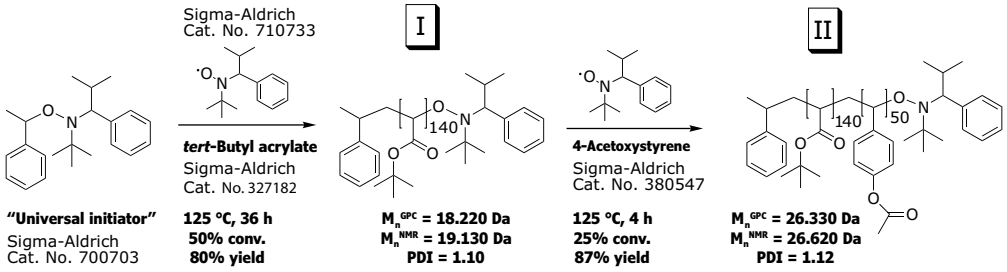
Controlled radical polymerization, which provides exquisite tuning of macromolecular size, structure, composition, and architecture, with experimental convenience, has become one of the most indispensible tools for polymer chemists. Its emergence in the mid-1990s has greatly advanced the fields of nanoscience and nanotechnology, by providing ready access to complex polymers that serve as building blocks for functional nanostructures with predictable parameters such as the size, morphology, regioselective placement of functionalities, etc. This exceptional polymerization control is due to reversible termination events that mediate the radical concentration and reactivity. The living character of this type of polymerization provides an ability to produce polymers with controlled molecular weight and narrow molecular weight distribution, and, moreover, to chain extend with different monomers and obtain multi-block copolymers. Nitroxide-mediated radical polymerization (NMP) is one of these controlled radical polymerizations that also includes atom transfer radical polymerization (ATRP), and reversible addition/fragmentation chain transfer (RAFT) polymerization. NMP stands out due to its simplicity: the polymerization is thermally initiated in the absence of an external radical source or a metal catalyst. As illustrated in **Scheme 1**, NMP involves a combination of radical initiator (I), monomer (M) and nitroxide radical (R), for trapping of intermediate radical species. For instance, the thermally-promoted homolysis of benzoyl peroxide (Cat. No. 179981) produces radicals that are capable of initiating the polymerization of styrene monomer. Propagation proceeds to produce polymer chains, while reversible termination events, involving reactions with nitroxide radicals to afford thermally-labile alkoxyamines, mediate the availability of the reactive radical species and, thereby, provide control over the polymerization. It is important that the stable nitroxide radicals are capable of the reversible termination reactions, but do not initiate polymerizations.



Scheme 1. Overall mechanism for NMP, illustrated for styrene monomer (M) polymerization initiated by benzoyl peroxide initiator (I) and mediated by TEMPO nitroxide radicals (R). Also shown is the general structure for alkoxyamine-based unimolecular NMP initiators.

One of the most significant advances with NMP was the isolation of an alkoxyamine that could act as a unimolecular agent, providing both the reactive, initiating radical, and the stable, mediating nitroxide radical.[1] Initially, nitroxides were employed as additives to reversibly terminate polymer chains initiated by a separate radical source.[2] By using TEMPO to trap a styrenyl radical initiated by benzoyl peroxide (as shown by structure A of **Scheme 1**), Hawker demonstrated an ability to tune the molecular weight, define the end groups, and extend to block copolymers, while maintaining narrow molecular weight distributions. He later developed a universal initiator, which has received broad application in laboratories around the world.[3] A key limitation to the use of this universal initiator remained the challenge of its synthesis. With it now being offered commercially by Sigma-Aldrich Materials Science, it is expected NMP will experience a renewed vigor of investigation.

With our interest in the construction of nanoscopic objects via the self-assembly of amphiphilic block copolymers in water, we have used the universal initiator (Cat. No. 700703), in the presence of less than 5 equivalent percent of the corresponding nitroxide (added to assist with capping the propagating chain ends during polymerization), to prepare an amphiphilic diblock copolymer precursor, poly(*tert*-butyl acrylate)-*b*-poly(4-acetoxystyrene) with a controlled molecular weight and a narrow molecular weight distribution (**Scheme 2**).[4]



Scheme 2. Synthesis of poly(*tert*-butyl acrylate) (I) continuing on to create poly(*t*-butyl acrylate)-*b*-poly(4-acetoxystyrene) (II) using the universal NMP initiator.

Synthesis of poly(*t*-butyl acrylate)$_{140}$ (I)

^{1}H NMR and ^{13}C NMR spectra were recorded at 300 MHz and 75 MHz, respectively, as solutions with the solvent proton as a standard. To a flame-dried 50 mL Schlenk flask equipped with a magnetic stir bar and under N_2 atmosphere, at room temperature, was added (124 mg, 0.381 mmol, Cat. No. 700703), 2,2,5-trimethyl-4-phenyl-3-azahexane-3-nitroxide (4.19 mg, 0.019 mmol, Cat. No. 710733), and *tert*-butyl acrylate (10.16 g, 79.6 mmol, Cat. No. 327182). The reaction flask was sealed and stirred for 10 min at rt. The reaction mixture was degassed through three cycles of freezepump- thaw. After the last cycle, the reaction mixture was recovered back to rt and stirred for 10 min before being immersed into a pre-heated oil bath at 125 °C to start the polymerization. After 36 h (kinetic data for conversion shown in **Figure 1**), ^{1}H NMR analysis showed 50% monomer conversion had been reached (**Figure 3**). The polymerization was quenched by quick immersion of the reaction flask into liquid N_2. The reaction mixture was dissolved in THF (Cat. No. 401757) and precipitated into H_2O/MeOH (v:v, 1:4) three times to afford PtBA as a white powder, (4.1 g, 80% yield based upon monomer conversion); M_n ^{NMR} = 19,130 g/mol, M_n ^{GPC} = 18,220 g/mol, PDI = 1.10. ^{1}H NMR (CD_2Cl_2, ppm): δ 1.43 (br, 1290 H), 1.80 (br, 70 H), 2.21 (br, 160 H), 7.14-7.26 (m, 10 H). 13C NMR (CD_2Cl_2, ppm): δ 28.4, 36.5, 38.0, 42.5, 80.9, 174.4. The GPC data can be seen in **Figure 2**.

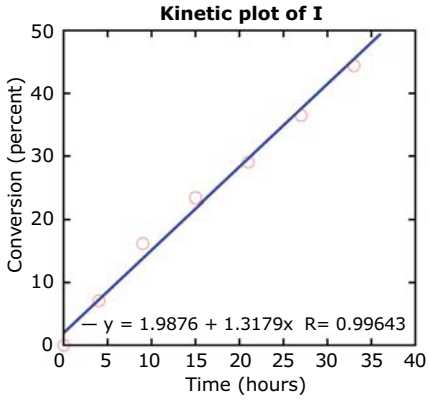


Figure 1. Percent conversion of monomers vs. time

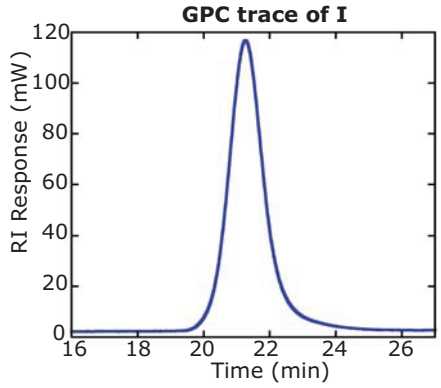


Figure 2. Molecular weight distribution of I. M_n = 18,220 g/mol, PDI = 1.10

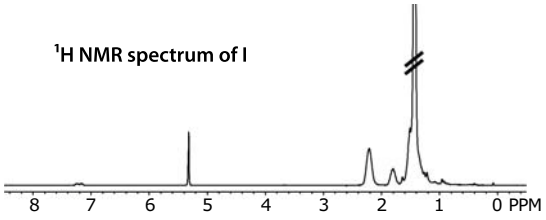


Figure 3. ^{1}H NMR spectrum of I

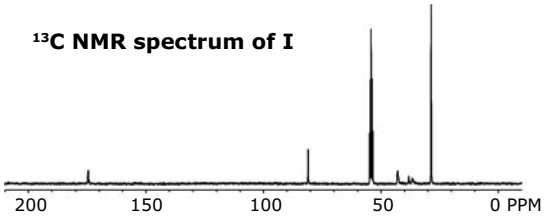


Figure 4. ^{13}C NMR spectrum of I

Synthesis of poly(t-butyl acrylate)$_{140}$-*b*-poly(acetoxystyrene)$_{50}$ (II)

^{1}H NMR and ^{13}C NMR spectra were recorded at 300 MHz and 75 MHz, respectively, as solutions with the solvent proton as a standard. To a flame-dried 50 mL Schlenk flask equipped with a magnetic stir bar and under N_2 atmosphere, at room temperature, was added **I** (124 mg, 0.381 mmol), 2,2,5-trimethyl-4-phenyl-3-azahexane-3-nitroxide (4.19 mg, 0.019 mmol), and 4-acetoxystyrene (10.16 g, 79.6 mmol, Cat. No. 380547). The reaction flask was sealed and stirred for 10 min at rt. The reaction mixture was degassed through three cycles of freeze-pump-thaw. After the last cycle, the reaction mixture was recovered back to rt and stirred for 10 min before being immersed into a pre-heated oil bath at 125 °C to start the polymerization. After 4 h (kinetic data for conversion shown in **Figure 5**), ^{1}H NMR analysis showed 25% monomer conversion had been reached (**Figure 7**). The polymerization was quenched by quick immersion of the reaction flask into liquid N_2. The reaction mixture was dissolved in THF and precipitated into H_2O / MeOH (v:v, 1:4) three times to afford P*t*BA-*b*-PAS as a white powder, (4.62 g, 87% yield based upon monomer conversion); M_n^{NMR} = 26,620 g/mol, M_n^{GPC} = 26,330 g/mol, PDI = 1.12. ^{1}H NMR (CD_2Cl_2, ppm): δ 1.43 (br, 1500 H), 1.80 (br, 100 H), 2.21 (br, 290 H), 6.36–6.82 (m, 190 H), 7.14–7.26 (m, 10 H). ^{13}C NMR (CD_2Cl_2, ppm, **Figure 8**): δ 21.5, 28.4, 36.5, 38.0, 40.5, 42.6, 80.9, 121.8, 128.9, 143.0, 149.4, 169.7, 174.7. The GPC data can be seen in **Figure 6**.

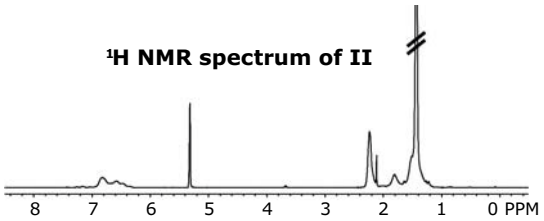


Figure 7. 1H NMR spectrum of II

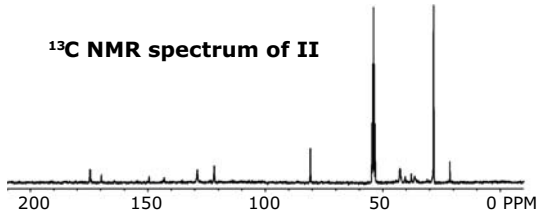


Figure 8. ^{13}C NMR spectrum of II

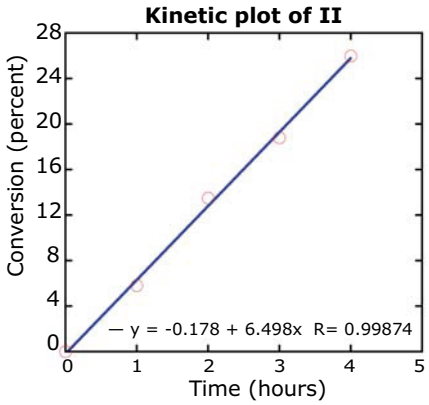


Figure 5. Percent conversion of monomers vs. time

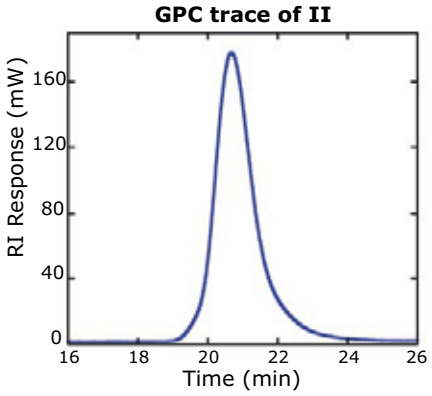


Figure 6. Molecular weight distribution of II. M_n = 26,330 g/mol, PDI = 1.12

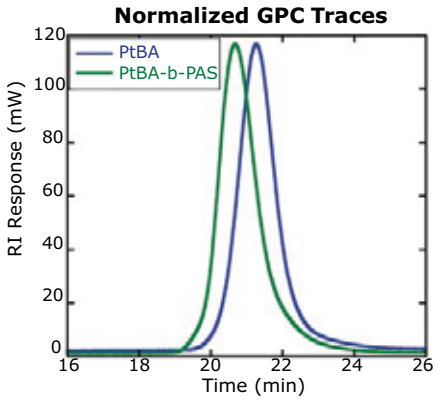


Figure 9. Normalized GPC traces showing molecular weight distributions of polymers I and II.

Conclusions

We have demonstrated a facile preparation of an amphiphilic diblock copolymer precursor with a controlled molecular weight and a low PDI using the universal NMP initiator (Cat. No. 700703). This required no special apparatus nor technique, beyond those employed for standard radical polymerizations, but only synthesis of the corresponding nitroxide (Cat. No. 710733). The final block copolymer was purified by precipitation to remove excess monomers, and was then deprotected. The morphology and size of the subsequent supramolecularly assembled nanostructures in water depend on the polymer block length and the ratio of the block lengths, each carefully manipulated through monomer conversions, the control over which arises from the universal NMP initiator. With the simplicity of this system, it is expected that NMP will experience a dramatic increase in breadth of application.

Acknowledgments

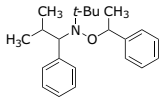
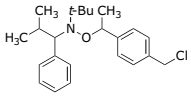
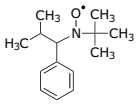
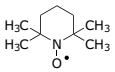
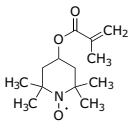
This material is based upon work supported by the National Heart Lung and Blood Institute of the National Institutes of Health as a Program of Excellence in Nanotechnology (HL080729). N. S. Lee thanks GlaxoSmithKline for their financial support through the ACS Division of Organic Chemistry Graduate Fellowship 2008 – 2009.

References

1. Hawker, C. J. *J. Am. Chem. Soc.* **1994**, *116*, 11185.
2. Moad, G.; Solomon, D. H.; Johns, S. R.; Willing, R. I. *Macromolecules* **1982**, *15*, 909; Rizzardo, E. *Chem. Aust.* **1987**, *54*, 32; Georges, M. K.; Veregin, R. P. N.; Kazmaier, P. M.; Hamer, G. K. *Macromolecules* **1993**, *26*, 2987.
3. Benoit, D.; Chaplinski, V.; Braslau, R.; Hawker, C. J. *J. Am. Chem. Soc.* **1999**, *121*, 3904.
4. Lee, N. S.; Li, Y.; Ruda, C. M.; Wooley, K. L. *Chem. Commun.* **2008**, *42*, 5339.

NMP Initiators

For a complete description of available free radical initiators, visit SigmaAldrich.com/crp.

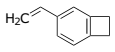
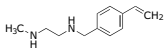
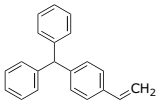
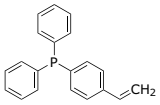
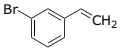
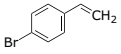
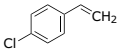
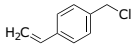
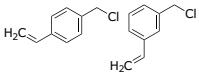
Name	Structure	Description	Cat. No.
N-tert-Butyl-*N*-(2-methyl-1-phenylpropyl)-*O*-(1-phenylethyl) hydroxylamine		Universal alkoxyamine initiator for nitroxide-mediated living radical polymerization (NMP initiator). Particularly useful for synthesis of styrene and acrylate polymers and co-polymers.	700703-250MG 700703-1G
N-tert-Butyl-*O*-[1-[4-(chloromethyl) phenyl]ethyl]-*N*-(2-methyl-1-phenylpropyl)hydroxylamine		Functional alkoxyamine initiator for nitroxide-mediated living radical polymerization (NMP initiator). Particularly useful for synthesis of styrene and acrylate polymers and co-polymers.	711268-250MG
2,2,5-Trimethyl-4-phenyl-3-azahexane-3-nitroxide		Stable nitroxide radical useful in controlling living radical polymerizations	710733-250MG 710733-1G
TEMPO		Stable nitroxide radical useful in controlling living polymerizations	426369-1G 426369-5G
TEMPO methacrylate		Stable nitroxide radical useful in controlling living radical polymerizations, with a methacrylate functionality for cross-linking or orthogonal polymerization.	730297-1G

Monomer Index

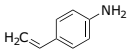
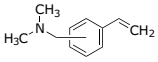
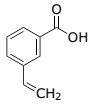
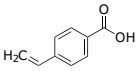
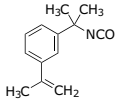
Styrene Monomers

For a complete list of available styrene, functionalized styrene, and substituted styrene monomers, visit SigmaAldrich.com/monomers.

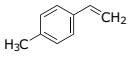
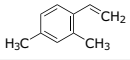
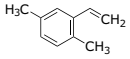
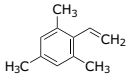
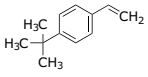
Functionalized Styrene Monomers

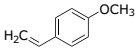
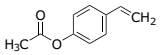
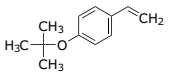
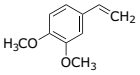
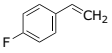
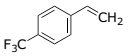
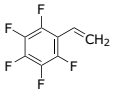
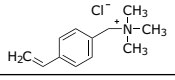
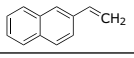
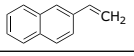
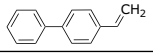
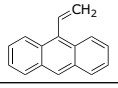
Name	Structure	Purity	Additive	Cat. No.
4-Vinylbenzocyclobutene		97%	–	733377-1G
4-[*N*-(Methylaminoethyl)aminomethyl] styrene		>90%	–	725609-1G
4-Benzhydrylstyrene		96%	–	725595-1G
4-(Diphenylphosphino)styrene		97%	–	708127-1G 708127-5G 708127-25G
3-Vinylaniline		97%	KOH as inhibitor	560839-1G 560839-5G
α-Bromostyrene		90%	–	292273-5G 292273-25G
2-Bromostyrene		97%	3,5-di-*tert*-butylcatechol 0.1% as inhibitor	132683-1G 132683-5G
3-Bromostyrene		97%	3,5-di-*tert*-butylcatechol 0.1% as inhibitor	132675-5G
4-Bromostyrene		98%	3,5-di-*tert*-butylcatechol 0.1% as inhibitor	124141-10G 124141-25G
2-Chlorostyrene		97%	hydroquinone 0.1% as stabilizer	160679-5G 160679-25G
3-Chlorostyrene		98%	3,5-di-*tert*-butylcatechol 0.1% as stabilizer	C71009-1G
4-Chlorostyrene		97%	4-*tert*-butylcatechol 500 ppm as inhibitor	C71203-10G C71203-50G
2,6-Dichlorostyrene		99%	–	D74509-2.5G D74509-10G
4-Vinylbenzyl chloride		90%	*tert*-butylcatechol 500 ppm as inhibitor	436887-25ML 436887-100ML
Vinylbenzyl chloride		97%	*tert*-butylcatechol 50 – 100 ppm as inhibitor nitromethane 700 – 1,100 ppm as inhibitor	338729-25G 338729-100G

Monomer Index

Name	Structure	Purity	Additive	Cat. No.
2-Isopropenylaniline		≥98%	–	194212-5G 194212-25G
3-Vinylaniline		97%	KOH as inhibitor	560839-1G 560839-5G
4-Vinylaniline		97%	–	536180-1G 536180-5G
N,N-Dimethylvinyl-benzylamine, mixture of isomers		97%	–	476382-1G 476382-10G
3-Vinylbenzoic acid		96%	–	523089-5G
4-Vinylbenzoic acid		97%	–	254738-1G 254738-5G
3-Isopropenyl-α,α-dimethylbenzyl isocyanate		95%	BHT ≤200 ppm as inhibitor	361771-250ML 361771-1L

Substituted Styrene Monomers

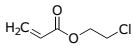
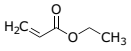
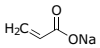
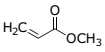
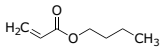
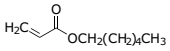
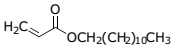
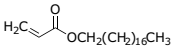
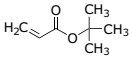
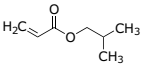
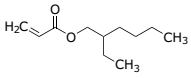
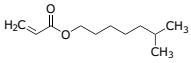
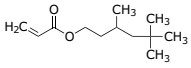
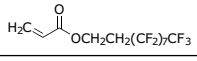
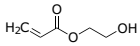
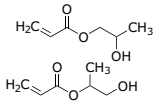
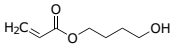
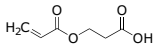
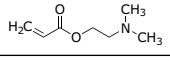
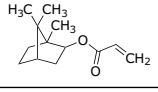
Name	Structure	Purity	Additive	Cat. No.
α-Methylstyrene		99%	*p-tert*-butylcatechol 15 ppm as inhibitor	M80903-5ML M80903-100ML M80903-1L
Methylstyrene		99%	4-*tert*-butylcatechol ≤50 ppm as inhibitor	522864-250ML 522864-1L
3-Methylstyrene		99%	3,5-di-*tert*-butylcatechol 0.1% as inhibitor	184675-5G
4-Methylstyrene		96%	3,5-di-*tert*-butylcatechol as inhibitor	M80806-10ML M80806-100ML M80806-500ML
2,4-Dimethylstyrene		97%	*tert*-butylcatechol 100 ppm as inhibitor	262633-5G
2,5-Dimethylstyrene		98%	*tert*-Butylcatechol 500 ppm as stabilizer	361135-5G
2,4,6-Trimethylstyrene		95%	*tert*-butylcatechol <0.05% as inhibitor	259780-5G
4-*tert*-Butylstyrene		93%	*tert*-butylcatechol ≤100 ppm as inhibitor	523933-250ML 523933-1L

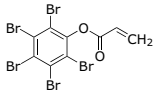
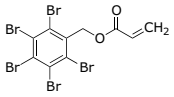
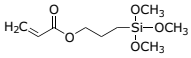
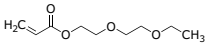
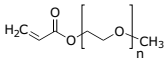
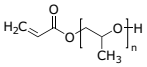
Name	Structure	Purity	Additive	Cat. No.
4-Vinylanisole		97%	–	141003-5G 141003-25G
4-Acetoxystyrene		96%	monomethyl ether hydroquinone 200 – 300 ppm as inhibitor	380547-5ML 380547-25ML
4-*tert*-Butoxystyrene		99%	4-*tert*-butylcatechol 200 ppm as inhibitor	455644-50ML
3,4-Dimethoxystyrene		technical grade	hydroquinone 1% as inhibitor	154466-5G 154466-10G
2-Fluorostyrene		98%	4-*tert*-butylcatechol as inhibitor	290505-5G
3-Fluorostyrene		>99%	–	219452-1G
4-Fluorostyrene		99%	*tert*-butylcatechol as inhibitor	155799-1G 155799-10G
2-(Trifluoromethyl)styrene		99%	4-*tert*-butylcatechol 0.1% as inhibitor	369594-1G
3-(Trifluoromethyl)styrene		99%	4-*tert*-butylcatechol as inhibitor	366692-1G
4-(Trifluoromethyl)styrene		98%	4-*tert*-butylcatechol 0.1% as inhibitor	369608-1G
2,6-Difluorostyrene		99%	4-*tert*-butylcatechol 0.25% as inhibitor	374407-250MG 374407-1G
2,3,4,5,6-Pentafluorostyrene		99%	*p*-*tert*-butylcatechol 0.1% as inhibitor	196916-25G
3-Nitrostyrene		96%	–	N26601-2.5G N26601-10G
(Vinylbenzyl)trimethylammonium chloride		99%	–	458694-100G 458694-250G
2-Vinylnaphthalene		98%, optical grade	–	453870-1G
2-Vinylnaphthalene		95%	–	V2909-5G V2909-25G
4-Vinylbiphenyl		–	–	V1805-1G V1805-10G
9-Vinylanthracene		97%	–	V1708-1G V1708-5G

Acrylate Monomers

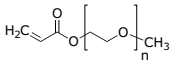
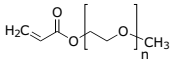
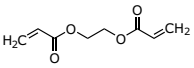
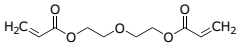
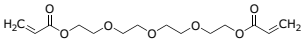
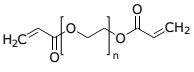
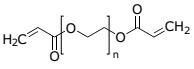
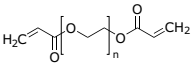
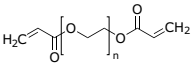
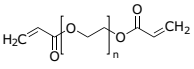
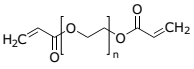
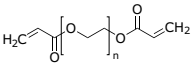
For a complete list of available acrylate monomers, visit SigmaAldrich.com/acrylic.

Monofunctional Acrylate Monomers

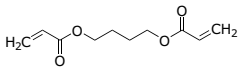
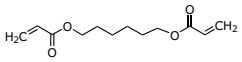
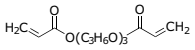
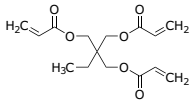
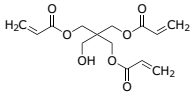
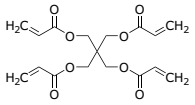
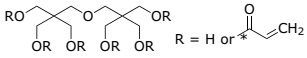
Name	Structure	Purity	Additive	Cat. No.
2-Chloroethyl acrylate		97%	MEHQ, >100 ppm as inhibitor	729817-5G
Sodium acrylate		97%	–	408220-25G 408220-100G
Methyl acrylate		99%	monomethyl ether hydroquinone, ≤100 ppm as inhibitor	M27301-5ML M27301-250ML M27301-1L M27301-2L M27301-18L
Ethyl acrylate		99%	MEHQ 10 – 20 ppm as inhibitor	E9706-100ML E9706-1L E9706-2L
Butyl acrylate		≥99%	monomethyl ether hydroquinone, 10 – 60 ppm as inhibitor	234923-100ML 234923-1L 234923-18L
Hexyl acrylate		98%	hydroquinone 100 ppm as inhibitor	408905-25ML 408905-100ML
Lauryl acrylate		90%, technical grade	monomethyl ether hydroquinone 60 – 100 ppm as inhibitor	447315-100ML 447315-500ML
Octadecyl acrylate		97%	MEHQ 200 as inhibitor	409693-250G 409693-1KG
tert-Butyl acrylate		98%	monomethyl ether hydroquinone 10 – 20 ppm as inhibitor	327182-5ML 327182-100ML 327182-1L
Isobutyl acrylate		≥99%	monomethyl ether hydroquinone 10 – 20 ppm as inhibitor	436305-250ML 436305-1L
2-Ethylhexyl acrylate		98%	monomethyl ether hydroquinone ≥0.001 – ≤0.11% as stabilizer	290815-25ML 290815-1L 290815-3L 290815-18L
Isooctyl acrylate		>90%	monomethyl ether hydroquinone 75 – 125 ppm as inhibitor	437425-100ML
3,5,5-Trimethylhexyl acrylate		technical grade	monomethyl ether hydroquinone 15 – 20 ppm as inhibitor	424021-25ML
1*H*,1*H*,2*H*,2*H*-Perfluorodecyl acrylate		97%	monomethyl ether hydroquinone 100 ppm as inhibitor	474487-5ML 474487-25ML
2-Hydroxyethyl acrylate		96%	monomethyl ether hydroquinone 200 – 650 ppm as inhibitor	292818-250ML 292818-1L 292818-18L
Hydroxypropyl acrylate, mixture of isomers		95%	hydroquinone monomethyl ether 200 – 650 ppm as inhibitor	370932-1L 370932-18L
4-Hydroxybutyl acrylate		90%	hydroquinone 300 ppm as inhibitor monomethyl ether hydroquinone 50 ppm as inhibitor	275573-25G
2-Carboxyethyl acrylate		–	MEHQ, 900 – 1,100 ppm as inhibitor	552348-50ML 552348-500ML
2-(Dimethylamino)ethyl acrylate		98%	MEHQ, 2,000 ppm as inhibitor	330957-100ML 330957-500ML
Isobornyl acrylate		technical grade	monomethyl ether hydroquinone 200 ppm as inhibitor	392103-100ML 392103-500ML 392103-1L

Name	Structure	Purity	Additive	Cat. No.
Pentabromophenyl acrylate		96%	–	592552-5G
Pentabromobenzyl acrylate		98%	–	640263-1G 640263-5G
3-(Trimethoxysilyl)propyl acrylate		92%	BHT 100 ppm as inhibitor	475149-5ML 475149-25ML
Di(ethylene glycol) ethyl ether acrylate		≥90%, technical grade	monomethyl ether hydroquinone 1,000 ppm as inhibitor	408298-250ML
Poly(ethylene glycol) methyl ether acrylate		–	BHT 100 ppm as inhibitor MEHQ 100 ppm as inhibitor	454990-250ML 454990-1L
Poly(propylene glycol) acrylate		–	monomethyl ether hydroquinone 200 – 400 ppm as inhibitor	469815-100ML 469815-500ML

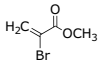
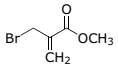
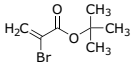
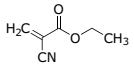
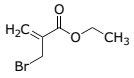
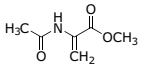
PEG Acrylate and Diacrylate Monomers

Name	Structure	Average M_n	Additive (ppm)	Cat. No.
Poly(ethylene glycol) methyl ether acrylate		2,000	MEHQ ≤3,500 as inhibitor (may contain)	730270-1G
Poly(ethylene glycol) methyl ether acrylate		5,000	MEHQ ≤5,500 as inhibitor (may contain)	730289-1G
Ethylene glycol diacrylate		170.16	–	480797-5ML 480797-25ML
Di(ethylene glycol) diacrylate		214.22	HQ 60 – 100 as inhibitor MEHQ 90 – 150 as inhibitor	437433-100ML
Tetra(ethylene glycol) diacrylate		302.32	HQ 100 – 150 as inhibitor MEHQ 150 – 200 as inhibitor	398802-250ML 398802-1L
Poly(ethylene glycol) diacrylate		258	MEHQ 100 as inhibitor	475629-100ML 475629-500ML
Poly(ethylene glycol) diacrylate		575	MEHQ 400 – 600 as inhibitor	437441-100ML 437441-500ML
Poly(ethylene glycol) diacrylate		700	BHT 300 as inhibitor MEHQ 100 as inhibitor	455008-100ML 455008-500ML
Poly(ethylene glycol) diacrylate		1,000	MEHQ ≤1,500 as inhibitor (may contain)	729086-1G
Poly(ethylene glycol) diacrylate		2,000	MEHQ ≤1,500 as inhibitor (may contain)	701971-1G
Poly(ethylene glycol) diacrylate		6,000	MEHQ, ≤1,500 as inhibitor	701963-1G
Poly(ethylene glycol) diacrylate		10,000	MEHQ ≤1,500 as inhibitor (may contain)	729094-1G

Polyfunctional Acrylate Monomers

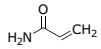
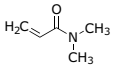
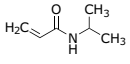
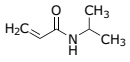
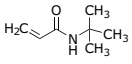
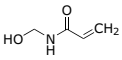
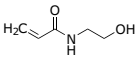
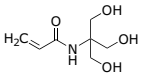
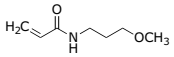
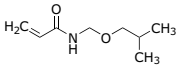
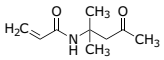
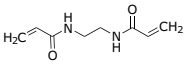
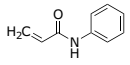
Name	Structure	Additive	Cat. No.
1,4-Butanediol diacrylate		hydroquinone, ~75 ppm as inhibitor	411744-25ML 411744-100ML
1,6-Hexanediol diacrylate		monomethyl ether hydroquinone 100 ppm as inhibitor	246816-100G 246816-500G
Tri(propylene glycol) diacrylate, mixture of isomers		monomethyl ether hydroquinone 250 ppm as inhibitor	246832-100G 246832-500G
Trimethylolpropane triacrylate		monomethyl ether hydroquinone 100 ppm as inhibitor	246808-100G 246808-500G
Pentaerythritol triacrylate		monomethyl ether hydroquinone 300 – 400 ppm as inhibitor	246794-100G 246794-500G
Pentaerythritol tetraacrylate		monomethyl ether hydroquinone 350 ppm as inhibitor	408263-100ML 408263-250ML
Dipentaerythritol penta-/ hexa-acrylate		monomethyl ether hydroquinone 500 ppm as inhibitor	407283-100ML 407283-500ML

α-Substituted Acrylate Monomers

Name	Structure	Purity	Cat. No.
Methyl α-bromoacrylate		98%	588466-1G
Methyl 2-(bromomethyl)acrylate		97%	302546-1G 302546-5G
tert-Butyl 2-bromoacrylate		95%	588458-1G
Ethyl 2-cyanoacrylate		–	E1505-5G E1505-10G
Ethyl 2-(bromomethyl)acrylate		98%	425222-1G 425222-5G
Methyl 2-acetamidoacrylate		98%	317519-1G 317519-5G

Acrylamide Monomers

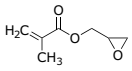
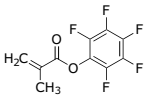
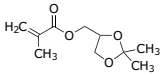
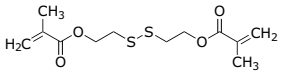
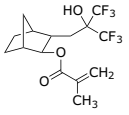
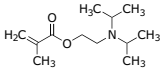
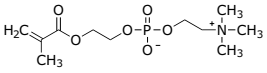
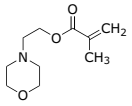
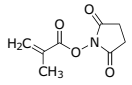
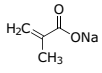
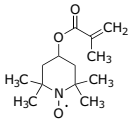
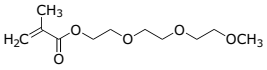
For a complete list of available acrylamide and methacrylamide monomers, visit SigmaAldrich.com/acrylic.

Name	Structure	Purity	Additive (ppm)	Cat. No.
Acrylamide		≥99%	–	A8887-100G A8887-500G A8887-1KG A8887-2.5KG
N,N-Dimethylacrylamide		99%	monomethyl ether hydroquinone 500 as inhibitor	274135-5ML 274135-100ML 274135-500ML
N-Isopropylacrylamide		97%	–	415324-10G 415324-50G
N-Isopropylacrylamide		≥99%	–	731129-5G 731129-25G
N-*tert*-Butylacrylamide		97%	–	411779-100G
N-(Hydroxymethyl)acrylamide solution		–	monomethyl ether hydroquinone 30 as inhibitor	245801-100G 245801-1KG
N-Hydroxyethyl acrylamide		97%	monomethyl ether hydroquinone 3,000 as stabilizer	697931-100ML
N-[Tris(hydroxymethyl)methyl] acrylamide		93%	–	364959-5G 364959-25G
N-(3-Methoxypropyl)acrylamide		95%	MEHQ as inhibitor	730149-25G
N-(Isobutoxymethyl)acrylamide		technical grade	monomethyl ether hydroquinone 200 as inhibitor	436534-100ML
Diacetone acrylamide		99%	–	222348-100G 222348-500G
N,N′-Ethylenebis(acrylamide)		technical grade	–	358878-5G
N-Phenylacrylamide		99%	–	530042-10G

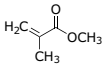
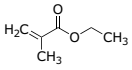
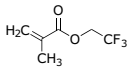
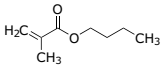
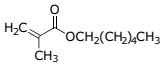
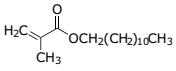
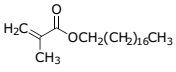
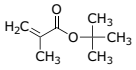
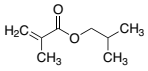
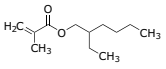
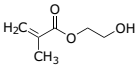
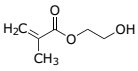
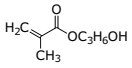
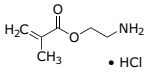
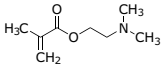
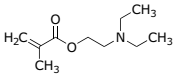
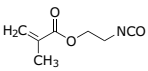
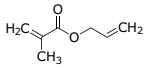
Methacrylate Monomers

For a complete list of available methacrylate monomers, visit SigmaAldrich.com/acrylic.

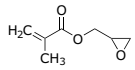
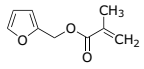
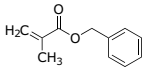
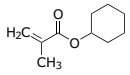
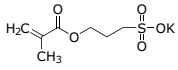
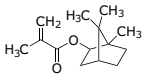
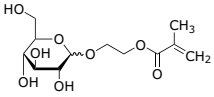
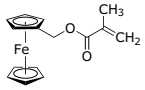
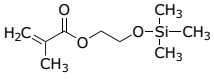
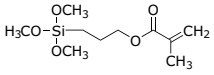
Monofunctional Methacrylate Monomers

Name	Structure	Purity	Additive	Cat. No.
Glycidyl methacrylate		≥97.0%, GC	hydrochinone monomethylether ~0.01% (w/v) as stabilizer	779342-100ML 779342-500ML
Pentafluorophenyl methacrylate		95%	MEHQ 1,500 ppm as inhibitor	741108-5G 741108-1G
Solketal methacrylate		–	4-*tert*-Butylcatechol ~280 ppm as inhibitor	740950-5ML 740950-25ML
Bis(2-methacryloyl)oxyethyl disulfide		–	hydroquinone, ≤6,000 ppm as stabilizer	735094-5G
2-[(1′,1′,1′-Trifluoro-2′-(trifluoromethyl)-2′-hydroxy)propyl]-3-norbornyl methacrylate		>97%	–	733660-1G 733660-5G
2-(Diisopropylamino)ethyl methacrylate		97%	monomethyl ether hydroquinone ~100 ppm as inhibitor	730971-25G
Methacrylic acid *N*-hydroxysuccinimide ester		98%	–	730300-1G 730300-5G
TEMPO methacrylate		98%	–	730297-1G
2-Methacryloyloxyethyl phosphoryl-choline		97%	4-methylphenol ≤100 ppm as inhibitor	730114-5G
Triethylene glycol methyl ether methacrylate		95%	MEHQ, >1,000 ppm	729841-25G
2-*N*-Morpholinoethyl methacrylate		95%	MEHQ ppm as inhibitor	729833-25G
Methacryloyl chloride		97%	monomethyl ether hydroquinone, ~200 ppm as stabilizer	523216-100ML 523216-1L
Sodium methacrylate		99%	–	408212-50G 408212-250G

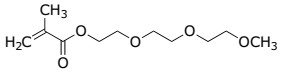
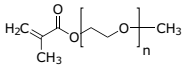
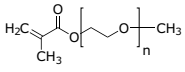
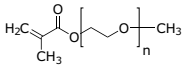
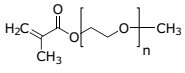
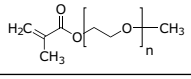
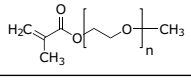
Monomer Index

Name	Structure	Purity	Additive	Cat. No.
Methacrylic acid		99%	MEHQ, 250 ppm as inhibitor	155721-5G 155721-100G 155721-500G 155721-2KG 155721-3KG 155721-18KG
Methyl methacrylate		99%	MEHQ, ≤30 ppm as inhibitor	M55909-25ML M55909-500ML M55909-1L M55909-2L M55909-17L
Ethyl methacrylate		99%	monomethyl ether hydroquinone, 15 – 20 ppm as inhibitor	234893-100ML 234893-500ML 234893-1L
2,2,2-Trifluoroethyl methacrylate		99%	MEHQ 100 ppm as inhibitor	373761-5G 373761-25G
Butyl methacrylate		99%	monomethyl ether hydroquinone 10 ppm as inhibitor	235865-5ML 235865-100ML 235865-1L 235865-18L
Hexyl methacrylate		98%	MEHQ, 100 ppm	462373-500G 462373-1KG
Lauryl methacrylate		96%	MEHQ 500 ppm as inhibitor	291811-100ML 291811-500ML
Stearyl methacrylate		technical grade	monomethyl ether hydroquinone 300 – 500 ppm as inhibitor	411442-250ML 411442-1L
tert-Butyl methacrylate		98%	monomethyl ether hydroquinone 200 ppm as inhibitor	463353-100ML 463353-250ML
Isobutyl methacrylate		97%	monomethyl ether hydroquinone ≤15 ppm as inhibitor	169919-1L 169919-18L
2-Ethylhexyl methacrylate		98%	monomethyl ether hydroquinone ~50 ppm as stabilizer	290807-25ML 290807-1L
2-Hydroxyethyl methacrylate		≥99%	monomethyl ether hydroquinone ≤50 ppm as inhibitor	477028-25ML 477028-100ML
2-Hydroxyethyl methacrylate		97%	monomethyl ether hydroquinone 200 – 220 ppm as inhibitor	128635-5G 128635-500G 128635-1KG 128635-18KG
Hydroxypropyl methacrylate		97%	monomethyl ether hydroquinone 250 – 350 ppm as inhibitor	268542-100ML 268542-1L 268542-18L
2-Aminoethyl methacrylate hydrochloride		90%	phenothiazine ~500 ppm as stabilizer	516155-5G 516155-25G
2-(Dimethylamino)ethyl methacrylate		98%	monomethyl ether hydroquinone 2,000 ppm as inhibitor	234907-100ML 234907-1L
2-(Diethylamino)ethyl methacrylate		99%	phenothiazine 100 ppm as inhibitor	408980-250ML 408980-1L
2-Isocyanatoethyl methacrylate		98%	BHT <0.1% (w/v) as inhibitor	477060-5ML 477060-50ML
Allyl methacrylate		98%	MEHQ 50 – 185 ppm as inhibitor	234931-100ML 234931-500ML

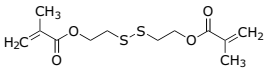
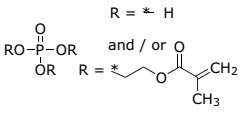
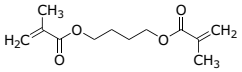
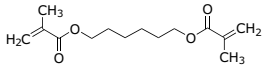
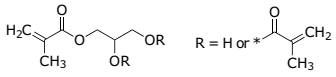
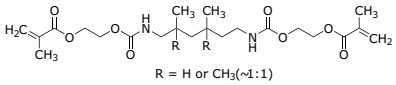
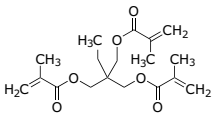
Monomer Index

Name	Structure	Purity	Additive	Cat. No.
Glycidyl methacrylate		97%	monomethyl ether hydroquinone 100 ppm as inhibitor	151238-100G 151238-500G
Furfuryl methacrylate		97%	monomethyl ether hydroquinone 200 ppm as inhibitor	411760-25ML 411760-100ML
Benzyl methacrylate		96%	monomethyl ether hydroquinone 50 ppm as inhibitor	409448-250ML 409448-1L
Cyclohexyl methacrylate		≥97%	monomethyl ether hydroquinone ~60 ppm as inhibitor	408964-100ML 408964-250ML
3-Sulfopropyl methacrylate potassium salt		98%	–	251658-100G 251658-500G
Isobornyl methacrylate		technical grade	monomethyl ether hydroquinone 150 ppm as inhibitor	392111-100ML 392111-500ML 392111-1L
Glycosyloxyethyl methacrylate solution 5% (w/v) in ethanol		–	–	659576-25ML
Ferrocenylmethyl methacrylate		95%, NMR	Ionol® 46 (Raschig GmbH) as inhibitor	700479-1G
2-(Trimethylsilyloxy)ethyl methacrylate		96%	–	347485-25G 347485-100G
3-(Trimethoxysilyl)propyl methacrylate		98%	–	440159-100ML 440159-500ML

PEG Methacrylate Monomers

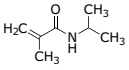
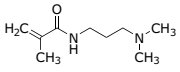
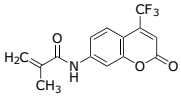
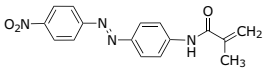
Name	Structure	Average M_n	Additive (ppm)	Cat. No.
Triethylene glycol methyl ether methacrylate		232.27	MEHQ, >1,000	729841-25G
Poly(ethylene glycol) methyl ether methacrylate		300	BHT 300 as inhibitor MEHQ 100 as inhibitor	447935-100ML 447935-500ML
Poly(ethylene glycol) methyl ether methacrylate		475	BHT 200 as inhibitor MEHQ 100 as inhibitor	447943-100ML 447943-500ML
Poly(ethylene glycol) methyl ether methacrylate		950	BHT 300 as inhibitor MEHQ 100 as inhibitor	447951-100ML 447951-500ML
Poly(ethylene glycol) methyl ether methacrylate		2,000	MEHQ ≤3,000 as inhibitor	730319-1G
Poly(ethylene glycol) methyl ether methacrylate		5,000	MEHQ ≤5,000 as inhibitor	730327-1G
Poly(ethylene glycol) methyl ether methacrylate		~2,080	–	457876-250ML 457876-1L

Polyfunctional Methacrylate Monomers

Name	Structure	Purity	Additive (ppm)	Cat. No.
Bis(2-methacryloyl)oxyethyl disulfide		–	hydroquinone, ≤6,000 as stabilizer	735094-5G
Phosphoric acid 2-hydroxyethyl methacrylate ester		90%	monomethyl ether hydroquinone 700 – 1,000	695890-100ML 695890-250ML
1,4-Butanediol dimethacrylate		95%	monomethyl ether hydroquinone 100 as inhibitor	234958-100G 234958-500G
1,6-Hexanediol dimethacrylate		≥90%	hydroquinone 100 as inhibitor	411736-100ML
Glycerol dimethacrylate, mixture of isomers		85%, technical grade	monomethyl ether hydroquinone 200 as inhibitor	436895-100ML 436895-500ML
Diurethane dimethacrylate, mixture of isomers		≥97%	topanol 225±25 as inhibitor	436909-100ML 436909-500ML
Trimethylolpropane trimethacrylate		technical grade	monomethyl ether hydroquinone 250 as inhibitor	246840-100G 246840-500G

Methacrylamide Monomers

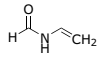
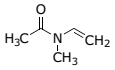
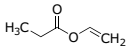
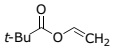
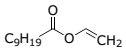
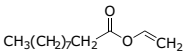
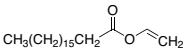
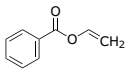
For a complete list of available acrylamides and methacrylamide monomers, visit SigmaAldrich.com/acrylic.

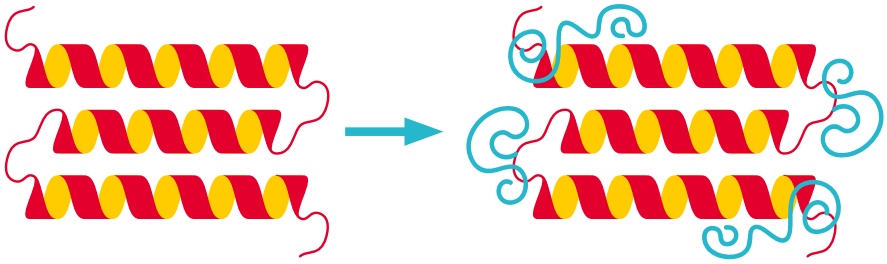
Name	Structure	Purity	Cat. No.
Methacrylamide		98%	109606-5G 109606-250G 109606-500G
N-Isopropylmethacrylamide		97%	423548-25G
N-[3-(Dimethylamino)propyl] methacrylamide		99%	409472-250ML 409472-1L
7-[4-(Trifluoromethyl)coumarin] methacrylamide		98%	566225-100MG 566225-500MG
Disperse Orange 3 methacrylamide		–	595845-1G

Monomer Index

Vinyl Amide and Vinyl Ester Monomers

For a complete list of available vinyl monomers, visit SigmaAldrich.com/monomers.

Name	Structure	Purity	Additive	Cat. No.
N-Vinylformamide		98%	4-Hydroxy-TEMPO 25 – 55 ppm as stabilizer	447331-100ML 447331-500ML
N-Methyl-*N*-vinylacetamide		98%	–	255130-100ML 255130-500ML
Vinyl propionate		98%	monomethyl ether hydroquinone <100 ppm as inhibitor	401714-500ML
Vinyl pivalate		99%	monomethyl ether hydroquinone 6 – 15 ppm as stabilizer	124400-250ML 124400-1L
Vinyl neodecanoate, mixture of isomers		–	monomethyl ether hydroquinone 5 ppm as inhibitor	134481-1L
Vinyl decanoate		>99%	–	411795-10G
Vinyl stearate		95%	MEHQ 20 ppm as inhibitor	436208-50G 436208-250G
Vinyl benzoate		≥99%	hydroquinone 20 ppm as stabilizer	403091-100ML 403091-500ML



MilliporeSigma

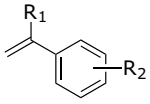
FUNCTIONALIZED PEGS FOR BIOCONJUGATION

Monofunctional PEGs are linear polymers that contain one reactive terminal group and one unreactive, methyl ester terminal group. These PEGs are used for a variety of conjugation strategies, including:

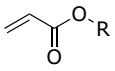
- Click Chemistry
- N-terminal amine PEGylation
- Thiol and surface conjugation

For a complete list of available monofunctional PEGs, visit **SigmaAldrich.com/monofunctionalPEGs**

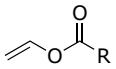
RAFT Agent to Monomer Compatibility Table



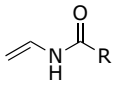
Styrenes



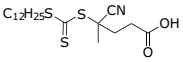
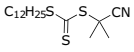
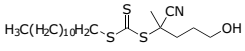
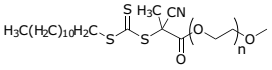
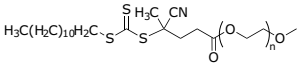
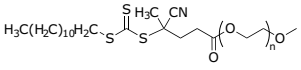
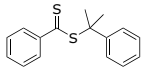
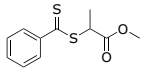
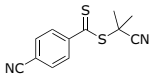
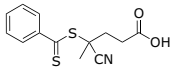
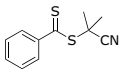
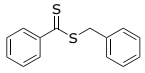
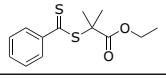
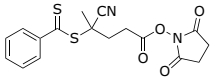
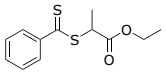
Acrylates



Vinyl Esters

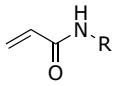


Vinyl Amides

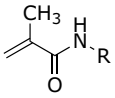
Cat. No.	Structure	Styrenes	Acrylates	Acrylamides	Meth-acrylates	Meth-acrylamides	Vinyl Esters	Vinyl Amides
723274		+++	++	++	+++	+++	–	–
723037		+++	++	++	+++	+++	–	–
760110		+++	++	++	+++	+++	–	–
753033		+++	++	++	+++	+++	–	–
751634		+++	++	++	+++	+++	–	–
751626		+++	++	++	+++	+++	–	–
731269		++	++	++	+++	+++	–	–
751138		++	++	++	+++	+++	–	–
731277		+++	+	–	+++	+++	–	–
722995		++	+	+	+++	+++	–	–
722987		++	+	–	+++	+++	–	–
760439		++	+	–	+++	+++	–	–
741701		++	+	+	+++	+++	–	–
758353		++	+	+	+++	+++	–	–
760455		++	+	+	+++	+++	–	–

+++ = Well suited
++ = Moderately suited
+ = Variable results
– = Poorly suited

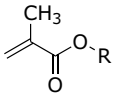
RAFT Agent to Monomer Compatibility Table



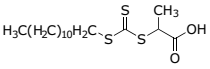
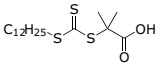
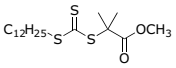
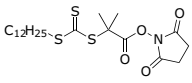
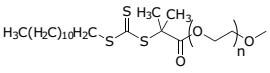
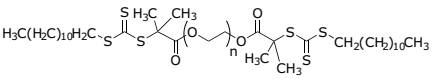
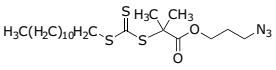
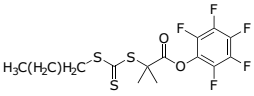
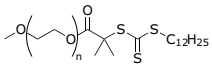
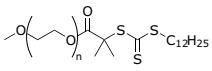
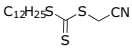
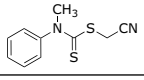
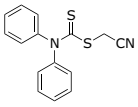
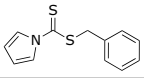
Acrylamides



Methacrylamides



Methacrylates

Cat. No.	Structure	Styrenes	Acrylates	Acrylamides	Meth-acrylates	Meth-acrylamides	Vinyl Esters	Vinyl Amides
749133		++	+	+	+++	+++	–	–
723010		+++	+++	+++	+	+	–	–
740497		+++	+++	+++	+	+	–	–
741035		+++	+++	+++	+	+	–	–
752495		+++	+++	+++	+	+	–	–
753025		+++	+++	+++	+	+	–	–
741698		+++	+++	+++	+	+	–	–
740810		+++	+++	+++	+	+	–	–
740705		+++	+++	+++	+	+	–	–
736325		+++	+++	+++	+	+	–	–
723029		+++	+++	+++	–	–	–	–
723002		–	–	–	–	–	+++	+++
751200		–	–	–	–	–	+++	+++
753106		–	–	–	–	–	+++	+++

+++ = Well suited
++ = Moderately suited
+ = Variable results
– = Poorly suited

Notes:

Notes:

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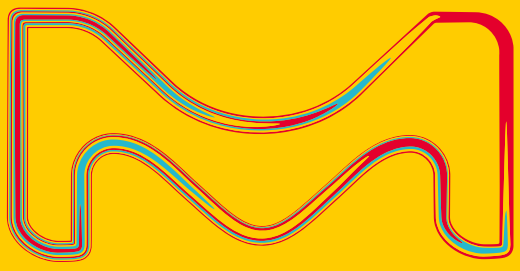

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