The Republic of Iraq
Ministry of Higher Education
and Scientific Research
University of Misan
College of Science
Department of Chemistry

RAFT agents

submitted by

Sarah Karim Shajar **Tabarak Rahim Hassan**

To the Council of the College of Science - Department of Chemistry / University of Maysan as part of the requirements for obtaining a Bachelor's degree in Chemistry

Supervised by

Dr. Maan Abdel Dayem Hassan

٢٠٢٤ AD ١٤٤٥ AH

بسم الله الرحمن الرحيم

﴿ يَرْفَعِ اللَّهُ الَّذِينَ آمَنُوا مِنكُمْ وَالَّذِينَ أُوتُوا الْعِلْمَ دَرَجَاتٍ ﴾

(المجادلة: ١١)

- صدق الله العلي العظيم -

Dedication…

(And our last supplication is: Praise be to God, Lord of the worlds)

To my very ambitious self, I thought I couldn't, but whoever said we have it has achieved it.

And if she refused, against her will, I brought her, and here I am today gently continuing my steps, and today I am writing my graduation thesis for the bachelor’s degree. After I spent a long time running for fear of missing out on something, I realized that I would not miss out on anything that God had written for me. It was a dream that we did not think would happen, but the grace of God was great. I hoped. Generous people have trusted in his workmanship, and whoever hopes for generous people will never be disappointed.

To the dear one, whose name I carry with pride, my name is repeated high in the sky, carrying the honor of your title, and with all pride that this man has the daughter of the one who took my hand to complete my path, who harvested the ash from my path, my firm side and the source of my strength.. (My dear father)

To the one whose feet God made Paradise a footstool, whose heart embraced me before its hands, and made adversity easy for me with its supplications to the compassionate heart and the candle that was for me in the dark nights.. (My beloved mother)

To those who are happy with my success, and to everyone who has been a help and support on this path, to my brothers and sisters, to friends and companions for years, and to those who have faced adversity and crises.

Acknowledgment

After thanking God Almighty for taking the trouble to complete this humble research, I would like to extend my partial thanks and gratitude to the distinguished professor.

Dr. Maan Abdel Dayem Hassan

For kindly agreeing to supervise this, and for the advice and guidance he gave me. Nebras Mounir’s kindness was enlightening in my steps, as well as my thanks and gratitude to all my honorable teachers who helped me, from near or far, in reaching this stage.

Thank you all

Content

Chapter One

Introduction, Definition, and Classification of RAFT agents

Introduction:

RAFT (Reversible Addition-Fragmentation chain Transfer) polymerization is a powerful technique (using **controlled radical polymerization)** for controlling polymer architecture and properties. The reversible addition-fragmentation chain transfer (RAFT) process, developed by the Commonwealth Scientific and Industrial Research Organization (CSIRO) in Australia in ١٩٩٨, is a significant advancement in the field of free radical polymerization. It allows for controlled polymer synthesis and has revolutionized the way polymers are designed and utilized in various industrial applications. (١)

Almost simultaneously, a group of researchers in France patented a similar process called macromolecular design via the interchange of xanthates (MADIX), which also utilizes xanthates as controlling agents but follows an identical mechanism to the RAFT process. Both processes are based on earlier chemistries, such as small radical reactions pioneered by Zard and colleagues.

Traditional radical polymerization: (٢) Initiators create free radicals that attack monomers, forming chains that grow uncontrollably, leading to a wide range of polymer sizes and properties. We can say that traditional radical polymerization is a Chaotic Chain Reaction. Unlike the controlled approach of RAFT, traditional radical polymerization relies on a cascade of uncontrolled reactions to form polymers. While this might sound messy, it has been the workhorse of the polymer world for decades, offering several steps of mechanism:

١. Initiation: Similar to RAFT, the process starts with an initiator generating free radicals.

٢. Propagation: These radicals react with monomers, adding them to the growing chain, building longer and longer polymer chains.

٣. Termination: Unfortunately, this is where things get wild. Growing chains can encounter each other in two ways:

-Combination: Two chains simply combine, ending their growth and forming a larger, less desirable polymer.

-Disproportionation: One radical abstracts a hydrogen from another chain, creating two saturated (non-radical) polymer ends.

However, the lack of control leads to several key drawbacks:

-Broad molecular weight distribution: Chains grow at different rates due to random termination, resulting in a mix of large and small polymers, affecting material properties.

-Limited control over architecture: Mainly linear chains are formed, restricting access to complex structures like block copolymers.

- Monomer specificity: Not all monomers are compatible with uncontrolled systems, limiting material diversity. (٣)

Despite its chaotic nature, traditional radical polymerization offers distinct advantages: (٤)

- Simple setup: Requires fewer specialized reagents and techniques compared to controlled methods like RAFT.

- Fast and efficient: Often faster than controlled methods, making it suitable for high-volume production.

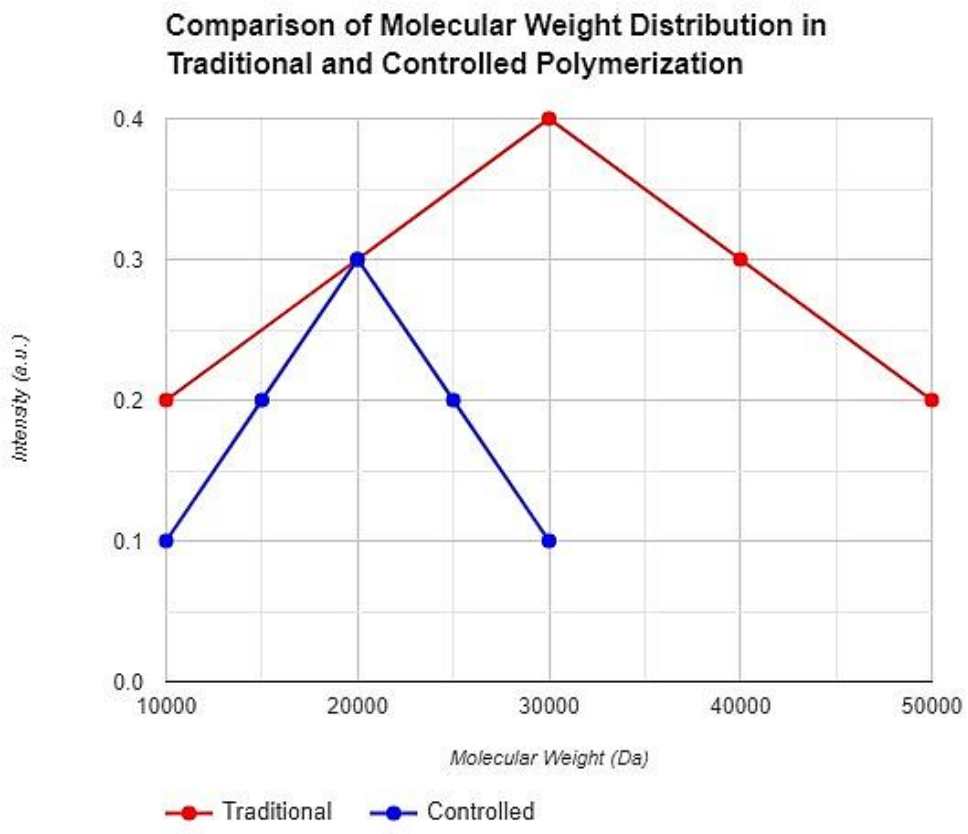
- Cost-effective: Often uses cheaper reagents, making it cost-efficient for some applications.

Even though, nowadays, some applications are used by traditional radical polymerization, such as:

- Commodity plastics: Polyethylene, polypropylene, polystyrene, etc.

- Paints and coatings: Provides durable and versatile coatings.

- Adhesives: Ensures strong bonding between materials.



The choice between traditional and controlled polymerization depends on your specific needs. If precise control over polymer size and architecture is crucial, RAFT is preferred. However, for simple, cost-effective production of standard polymers, traditional methods remain relevant. Both methods have their place, and understanding their strengths and weaknesses is key to selecting the optimal approach for your desired polymer material. (°)

Feature	Traditional Radical Polymerization	Controlled Radical Polymerization (RAFT)
Mechanism	Uncontrolled chain growth and termination	Reversible capping and activation of growing chains
Molecular weight distribution	Broad	Narrow
Control over architecture	Limited	High
Monomer specificity	Limited	More compatible with diverse monomers
Setup	Simple	More complex, requires specialized reagents and techniques
Speed and efficiency	Fast	Can be slower than traditional methods
Cost	Cost-effective	Can be more expensive due to specialized reagents
Applications	Commodity plastics, paints, coatings, adhesives	Advanced materials, biomedical applications, specialty polymers

RAFT polymerization: Uses special "RAFT agents" that act as temporary stoppers for growing polymer chains. These agents can reversibly capture and release the growing chain, allowing for more controlled growth and ultimately, polymers with well-defined sizes and architectures. (٦)

This controlled nature of RAFT offers several advantages:

Narrow molecular weight distribution: Polymers have similar sizes, leading to more consistent properties.

Tailored architectures: Can create complex polymer structures like block copolymers, star polymers, and more.

Wide range of compatible monomers: Works with many different types of monomers.

Therefore, RAFT is used in various applications:

Advanced materials: Drug delivery systems, membranes, sensors, energy storage devices.

Biomedical applications: Tissue engineering, gene delivery, targeted drug delivery.

Coatings and adhesives: Tailoring surface properties and adhesion strength.

The RAFT process employs a fundamentally different conceptual approach compared to other living polymerization methods such as nitroxide-mediated polymerization (NMP) and atom transfer radical polymerization (ATRP). (٧)

Controlled radical polymerization (CRP) techniques are indeed classified into three major methods: nitroxide-mediated polymerization (NMP), atom transfer radical polymerization (ATRP), and reversible addition-fragmentation chain transfer polymerization (RAFT). Each method has its own advantages and requirements.

١-Nitroxide-Mediated Polymerization (NMP): NMP is a CRP technique that involves the use of nitroxide radicals to control the polymerization process. It typically requires high reaction temperatures. (٨)

٢-Atom Transfer Radical Polymerization (ATRP): ATRP is a CRP technique that utilizes a transition metal catalyst to control the polymerization process. It is known for its ability to produce polymers with well-defined structures. However, it does require the use of a metal catalyst. (٩)

٣-. Reversible Addition-Fragmentation Chain Transfer Polymerization (RAFT): RAFT is a CRP technique that has gained significant popularity due to its simplicity and versatility. It does not require a metal catalyst, operates at relatively low temperatures, and can be used with a wide range of monomers. These features make RAFT particularly attractive for various polymerization applications. In summary, while all three CRP techniques have their advantages, RAFT stands out for its simplicity, versatility, and lack of metal catalyst, making it a widely used method in the field of controlled radical polymer. (١٠)

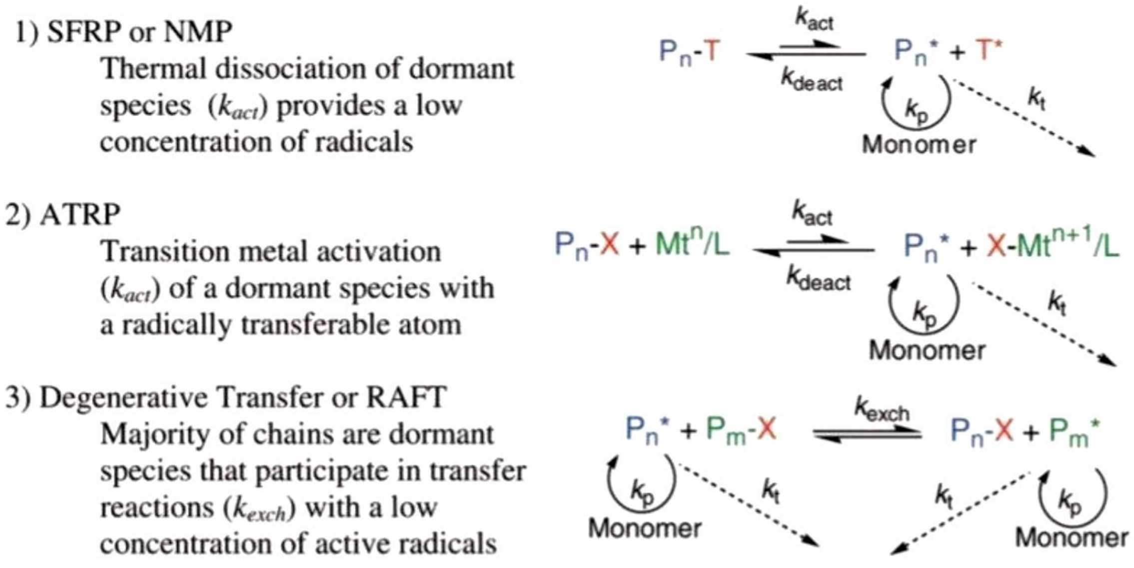


Figure: The three main CRP methods.

One of the unique features of the RAFT process is its high tolerance to functional monomers, allowing for the polymerization of substances like vinyl acetate and acrylic acid with living characteristics. Additionally, the RAFT process is a powerful tool for constructing complex macromolecular architectures using variable approaches, such as Z- and R-group designs, which offer almost limitless possibilities in synthetic protocols. (١١)

Since its first report in ١٩٩٨, the popularity of the RAFT process has steadily increased due to its ability to provide precise control over polymer synthesis, enabling the development of tailored polymers with specific properties for various applications.

RAFT agents

There are several types of RAFT (Reversible Addition-Fragmentation Chain Transfer) agents that are commonly used in controlled radical polymerization processes. These RAFT agents vary in their chemical structures and properties, allowing for flexibility in designing and synthesizing polymers with specific characteristics. Some of the commonly used types of RAFT agents include: (١٢،١٣)

١-Dithioesters: These are one of the most widely used types of RAFT agents. Dithioesters contain a sulfur-sulfur bond and are often derived from carboxylic acids and dithiols. They have been extensively used in various controlled radical polymerization reactions due to their effectiveness in controlling the polymerization process.

٢-Trithiocarbonates: Trithiocarbonates are another important class of RAFT agents. They contain a central carbon atom bonded to three sulfur atoms and are derived from the reaction of a suitable alcohol with carbon disulfide. Trithiocarbonates have been used in the synthesis of a wide range of polymers with controlled architectures and properties.

٣-Dithiocarbamates: Dithiocarbamates are RAFT agents that contain a nitrogen atom coordinated to a sulfur atom, forming a dithiocarbamate linkage. They have been employed in various controlled radical polymerization processes to produce well-defined polymers with controlled molecular weights and end-groups.

٤-Xanthates: Xanthates are RAFT agents that contain a carbonyl sulfur group attached to an alkyl or aryl group. They have been used in controlled radical polymerization reactions, particularly in the synthesis of polymers with specific end-group functionalities.

٥-Trithiocarbonates: Trithiocarbonates are another important class of RAFT agents. They contain a central carbon atom bonded to three sulfur atoms and are derived from the reaction of a suitable alcohol with carbon disulfide. Trithiocarbonates have been used in the synthesis of a wide range of polymers with controlled architectures and properties.

These types of RAFT agents, along with others, provide researchers and polymer chemists with a diverse toolkit for controlling the polymerization process and tailoring the properties of the resulting polymers for various applications.

Chapter Two

Mechanism, Response, Functionality, and Types of RAFT agents

Mechanism

The RAFT (Reversible Addition-Fragmentation Chain Transfer) process involves the use of a control agent, known as the RAFT agent, to regulate the polymerization process. The RAFT agent is typically a dithioester compound that allows for the reversible trapping of the growing polymeric radical as a dormant species. This is achieved by the propagating radical adding to the thiocarbonyl sulfur center of the dithioester, resulting in an intermediate carbon-centered radical. This carbon-centered radical can then undergo ß-scission, either to re-form the propagating radical or to release a new carbon-centered radical (the leaving group). (١٤)

The choice of R group in the RAFT agent is crucial, as it determines the preference for ß-scission from the RAFT-adduct radical over the propagating species, while still enabling reinitiation of polymerization. As a result, the initial RAFT agent (S=C(Z)SR) is rapidly converted to the poly-RAFT agent R, which leads to more propagating species. Eventually, an equilibrium is established between the propagating radical and the dormant poly-RAFT agent. (١٥)

By carefully controlling the equilibrium between the propagating radical and the dormant poly-RAFT agent, the RAFT process allows for precise control over the molecular weight and architecture of the resulting polymer. This enables the production of polymers with specific properties and complex designs. (١٦)

Here's a deeper dive into the mechanism:

١. **Initiation:** The polymerization reaction is initiated using a radical suitable initiator, which generates active radicals.

٢. **Monomer addition:** Active radicals attack monomers, adding them to the growing chain, leading to the growth of polymer chains.

٣. **Chain transfer:** The chain encounters a RAFT agent, transferring the radical and forming a dormant chain capped by the agent.

٤. **Fragmentation:** The RAFT agent breaks, releasing a new radical and reactivating the dormant chain.

٥. **Re-initiation:** The released radical attacks more monomers, continuing chain growth.

Where the RAFT agent interacts with the growing polymer chains, reversibly trapping and controlling the active radicals. This reversible trapping process allows for precise control over the polymerization.

٦. **Equilibrium:** This cycle of chain transfer and fragmentation establishes an equilibrium, controlling the number of growing chains and ultimately the polymer size. A dynamic equilibrium is established between the active radicals and the dormant species formed by the RAFT agent, ensuring a controlled and regulated polymerization process.

٧. Termination: The polymerization reaction can be terminated when desired, resulting in the production of polymers with well-defined molecular weights and architectures.

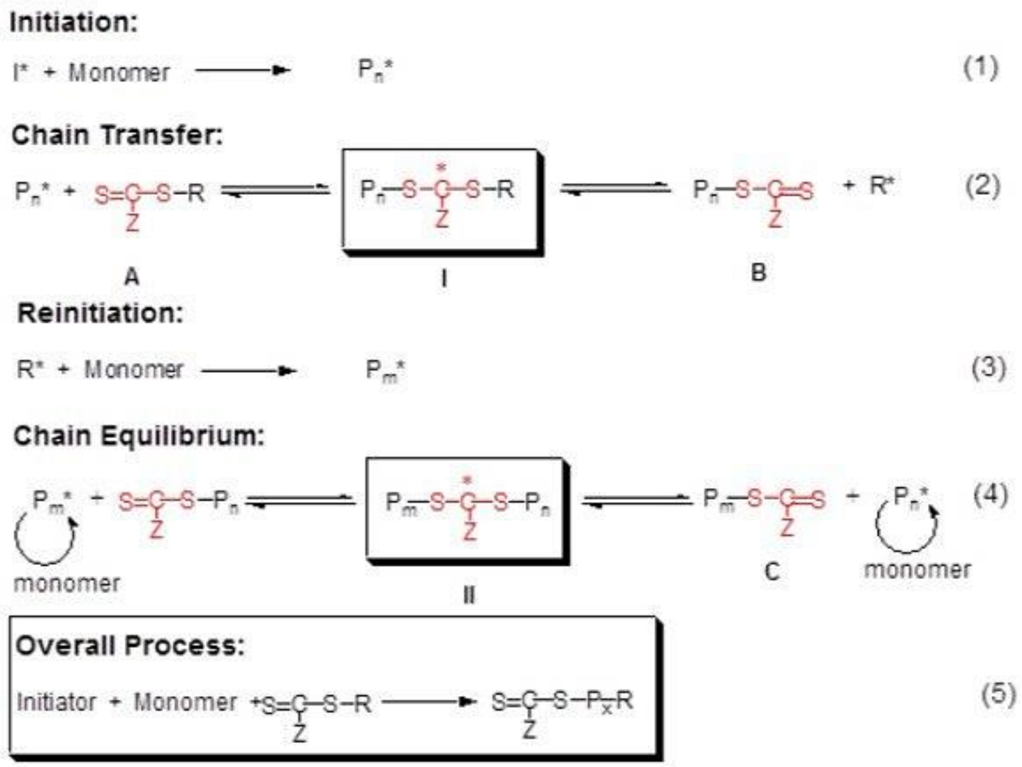


Figure ٢،١: General mechanism of Raft polymerization

RAFT "Reversible Addition-Fragmentation Chain Transfer" agents, are constantly being developed to address limitations and improve the efficiency of polymer synthesis. Here are some novel RAFT agents that used in different areas of researches:

Noval Initiation Mechanism of RAFT polymerization

Traditional RAFT relies on thermal initiators, which can have drawbacks like side reactions. This technique allows for the precise control of polymer chain length, composition, and functionality, making it a valuable tool in polymer science. The RAFT technique involves the use of a chain transfer agent (CTA), which creates and participates in a chain equilibrium to control the polymerization process. Commonly used CTAs include dithioesters, dithiocarbamates, and trithiocarbonates, also known as RAFT agents, which contain specific R and Z groups that are responsible for regulating the polymerization. The structure of the monomer and the R and Z groups of the CTA are key factors that determine the level of control achieved in the polymerization process. The general proposed mechanism for RAFT polymerization is shown in Figure ٢،١. It begins with the conventional initiation process, where a free radical initiator undergoes homolysis. This creates propagating radical species (Pn*) which then reacts with the RAFT agent (A) to form the intermediate (I). The intermediate can then fragment into a dithioester (B) and a new radical (R*). This new radical (R*) can then initiate the polymerization process by reacting with more monomer to form a new propagating radical species (Pm*). The cycle continues until all the monomers are consumed, resulting in the formation of the desired polymer. The equilibrium between two propagating radical species (Pn*, Pm*) will be established when using RAFT polymerization. This allows for the chain end of RAFT CTA to remain active, facilitating the addition of more monomers for the synthesis of block copolymers or other advanced polymer architectures. It is important to maintain a high ratio of RAFT agent to initiator in the polymerization process to ensure the equilibrium between active radical species is maintained and to avoid termination between propagating radical species (Pn*, Pm*). Failure to maintain this equilibrium can result in a large number of active species, which can lead to premature termination of the reaction. Controlling the polymerization reaction, while the R group plays a crucial role in determining the rate of monomer addition. By altering the Z and R groups, the equilibrium between active radical species and the rate of monomer addition can be adjusted, allowing for control over the polymerization process. This is essential for producing polymers with specific properties and characteristics. (١٨)

Researchers are exploring alternative initiation methods like:

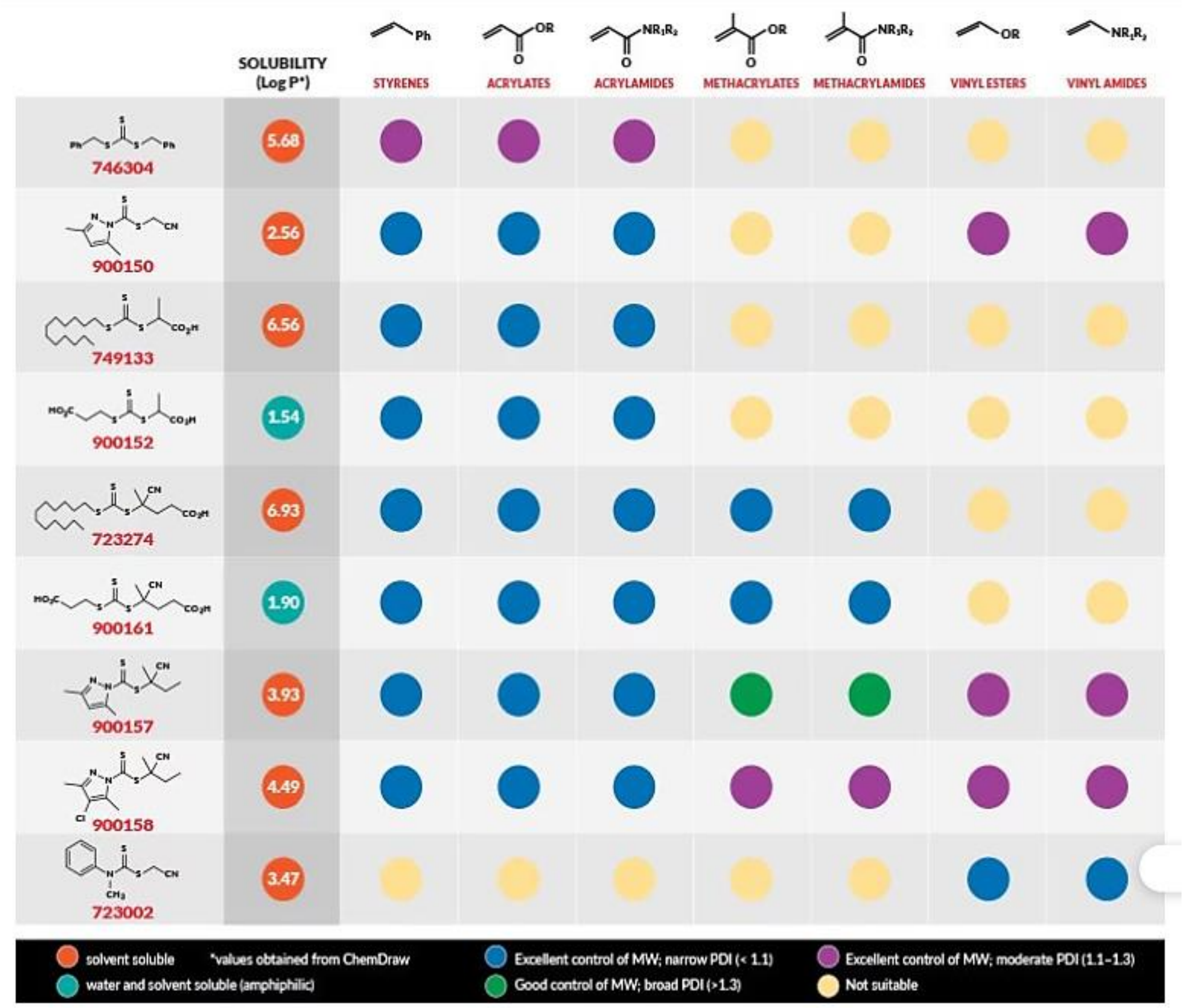
- **Photo-initiation:** Light-induced radical generation for better control in specific areas.
- **Metal-mediated:** Using metal complexes for controlled polymerization at lower temperatures.
- **Enzymatic:** Utilizing enzymes for biocompatible and environmentally friendly processes.

Functionalized RAFT agents: (١٨)

A- α-Functional groups can be introduced via the R group of the chain transfer agent (CTA). The R group of the RAFT agent is a free radical leaving group that must also be able to reinitiate the polymerization. Although there is always a proportion of polymeric chains formed during the RAFT process that are initiated by radicals derived from the free radical initiator, these are usually kept very low due to the high CTA-to-initiator ratios utilized. It follows that most polymeric chains produced via RAFT will show an α-functionality provided by the R group of the initial CTA.

B- ω-Functional groups can be introduced via the Z group. The Z group is responsible for the stabilization of the intermediate radicals that are produced during the polymerization. Although the chains that terminate during polymerization will lose the thiocarbonylthio end group and therefore the Z functionality, the ratio of living chains (with Z group) to dead chains is usually kept very high (typically above ٩٠٪), thus ensuring that most chains retain their Z-group functionality. This approach is unique to the RAFT process and cannot be achieved by other living radical polymerization techniques. Problems arise, however, for applications in which the terminal C-S bond may be broken under certain conditions, thus leading to the loss of the ω-functionality.

C- ω-Functional groups can also be introduced via the modification of the thiocarbonylthio group post polymerization. The modification of thiocarbonylthio groups is well known, and a few methodologies have been applied to RAFT-synthesized polymers to remove this group and modify it into an alternative functional group



	SOLUBILITY (Log P*)	STYRENES	ACRYLATES	ACRYLAMIDES	METHACRYLATES	METHACRYLAMIDES	VINYL ESTERS	VINYL AMIDES
746304	🟠 5.68	🟣	🟣	🟣	🟡	🟡	🟡	🟡
900150	🟠 2.56	🔵	🔵	🔵	🟡	🟡	🟣	🟣
749133	🟠 6.56	🔵	🔵	🔵	🟡	🟡	🟡	🟡
900152	● 1.54	🔵	🔵	🔵	🟡	🟡	🟡	🟡
723274	🟠 6.93	🔵	🔵	🔵	🔵	🔵	🟡	🟡
900161	● 1.90	🔵	🔵	🔵	🔵	🔵	🟡	🟡
900157	🟠 3.93	🔵	🔵	🔵	🟢	🟢	🟣	🟣
900158	🟠 4.49	🔵	🔵	🔵	🟣	🟣	🟣	🟣
723002	🟠 3.47	🟡	🟡	🟡	🟡	🟡	🔵	🔵

🟠 solvent soluble *values obtained from ChemDraw
● water and solvent soluble (amphiphilic)
🔵 Excellent control of MW; narrow PDI (< 1.1)
🟢 Good control of MW; broad PDI (>1.3)
🟣 Excellent control of MW; moderate PDI (1.1–1.3)
🟡 Not suitable

We review the various methodologies that have been used to produce polymers with well-defined end groups via the RAFT process. We highlight the introduction of chain-end groups via the R and Z groups of CTAs. This is devoted to the use of functionalities in the CTA and/or the telechelic polymer that can initiate polymerizations proceeding via an alternative mechanism to radical polymerization (e.g. ring-opening polymerization (ROP)). Another part of the chapter is concerned with the removal of the thiocarbonylthio groups, its effect on the stability of RAFT-synthesized polymers and its use to introduce ω-functionality.

Responsive RAFT agents:

a wide range of potential applications in fields like drug delivery, sensors, and smart materials. Stimuli-responsive polymers are indeed fascinating materials that can adapt to various external signals. The ability to respond to stimuli such as light, temperature, pH, and more.

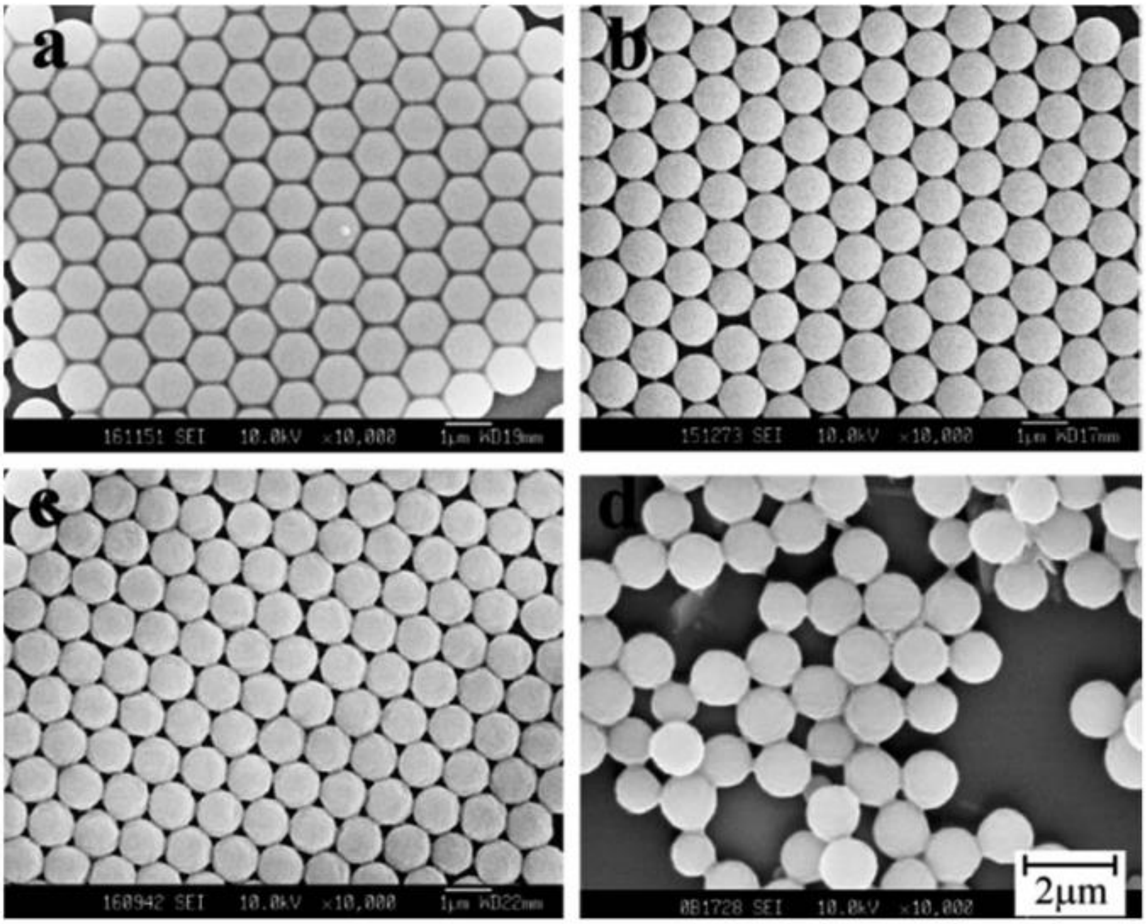
This controlled polymerization technique allows for the synthesis of polymers with well-defined structures and properties. By incorporating stimuli-responsive elements into the polymer chains, researchers can create materials that exhibit reversible responses to specific triggers (١٩).

Overall, the study of stimuli-responsive polymers and their synthesis methods like RAFT polymerization holds great promise for developing advanced materials with tailored functionalities for various applications. Responsive RAFT refers to RAFT polymerization methods that enable the creation of stimuli-responsive polymers by incorporating specific monomers or functional groups that can respond to external stimuli.

In responsive RAFT, the choice of monomers and reaction conditions can be tailored to create polymers that exhibit responsiveness to various stimuli such as temperature, pH, light, ions, or other environmental changes. By carefully designing the polymer structure and composition, researchers can control the polymer's behavior and properties in response to specific triggers.

For example, temperature-responsive RAFT polymers can undergo reversible changes in their conformation or solubility in response to changes in temperature, leading to applications in drug delivery, tissue engineering, and smart coatings. PH-responsive RAFT polymers can change their charge or hydrophilicity in response to pH variations, making them useful for drug release systems, sensors, and separation processes (٢٠).

By combining the principles of RAFT polymerization with stimuli-responsive design strategies, researchers can create a wide range of functional materials with tailored properties for specific applications. Responsive RAFT provides a versatile platform for the development of smart materials that can adapt to changing environmental conditions and stimuli, opening up new possibilities in fields such as biomedicine, nanotechnology, and advanced materials science.


a
161151 SEI 10.0kV ×10,000 1μm WD19mm
b
151273 SEI 10.0kV ×10,000 1μm WD17mm
c
160942 SEI 10.0kV ×10,000 1μm WD22mm
d
0B1728 SEI 10.0kV ×10,000
2μm

PH-Responsive polymers:

PH-responsive polymers are a class of materials that exhibit reversible changes in their properties in response to variations in pH levels. These polymers can undergo alterations in solubility, configuration, conformation, or volume when exposed to different pH environments. This responsiveness to pH stimuli is particularly relevant in biomedical applications, as many biological compartments exhibit distinct pH levels.

The ability of pH- responsive polymers to adapt to specific pH conditions makes them promising candidates for targeted drug delivery, tissue engineering, and other biomedical applications. By designing polymers that can respond to the pH levels found in specific tissues or cellular compartments, researchers can create materials that exhibit tailored behaviors and functions in these environments.

Overall, pH-responsive polymers offer exciting opportunities for developing advanced biomaterials that can respond dynamically to changes in pH, making them valuable tools for targeted therapeutic interventions and biomedical research. (٢١)

Ion–responsive Polymers:

Ion-responsive polymers are a versatile class of macromolecules that contain ionizable groups attached to their polymer backbone. These polymers play a crucial role in various applications such as enhanced oil recovery, water treatment, and the formulation of personal care products and pharmaceuticals. Ion-responsive polymers can be categorized into two main groups: polyelectrolytes and polyzwitterions.

Polyelectrolytes are ionic polymers that possess either anionic or cationic functionalities, while polyzwitterions contain both anionic and cationic groups. Polyzwitterions can be further classified as polyampholytes or polybetaines based on the distribution of ionic groups within the polymer structure. Polyampholytes have ionic groups on different repeat units, whereas polybetaines have both anionic and cationic groups on the same repeat unit.

In dilute aqueous solutions, polyelectrolytes exhibit a highly expanded coil conformation due to Coulombic repulsions between the charged groups along the polymer chains. However, the addition of small molecule electrolytes like NaCl leads to a significant decrease in hydrodynamic volume and solution viscosity due to Coulombic shielding effects caused by the salt.

On the other hand, polyzwitterions display a compact hydrodynamic volume in the absence of salt, resulting from Coulombic interactions between the positively and negatively charged groups within the polymer structure. When small molecule electrolytes are introduced, such as NaCl, the hydrodynamic volume increases, leading to a rise in solution viscosity.

Overall, ion-responsive polymers offer unique properties and behaviors that make them valuable in a wide range of industrial and scientific applications, show casing their versatility and potential for diverse uses. (٢٢)

Thermo-responsive Polymers:

Thermo-responsive polymers, also known as temperature-sensitive polymers, are a type of polymer that undergoes a change in its solubility or physical properties in response to changes in temperature. This can either be a lower critical solution temperature (LCST) where the polymer becomes insoluble upon heating or an upper critical solution temperature (UCST) where the polymer becomes insoluble upon cooling. While most research focuses on polymers with LCST behavior, there are some polymers that exhibit UCST behavior. These polymers are typically used in applications such as drug delivery, tissue engineering, and smart materials. Examples of thermo-responsive polymers include P (NIPAm) and P(OEGMA), both of which are commonly synthesized using the RAFT technique. LCST behavior, or lower critical solution temperature behavior, is a common characteristic of many acrylamide and methacrylamide homo- and copolymers. These polymers can be easily synthesized using the RAFT polymerization method. Other types of polymers that display LCST behavior include copolymers of poly (vinyl alcohol), poly (vinyl chloride), and poly (diallyl dimethyl ammonium chloride), as well as some polymer ionic liquids. There is significant interest in utilizing thermos-responsive behavior in materials such as blocks, biopolymer conjugates, particles, and surfaces, as it can serve as a trigger for therapeutic release. (٢٣)

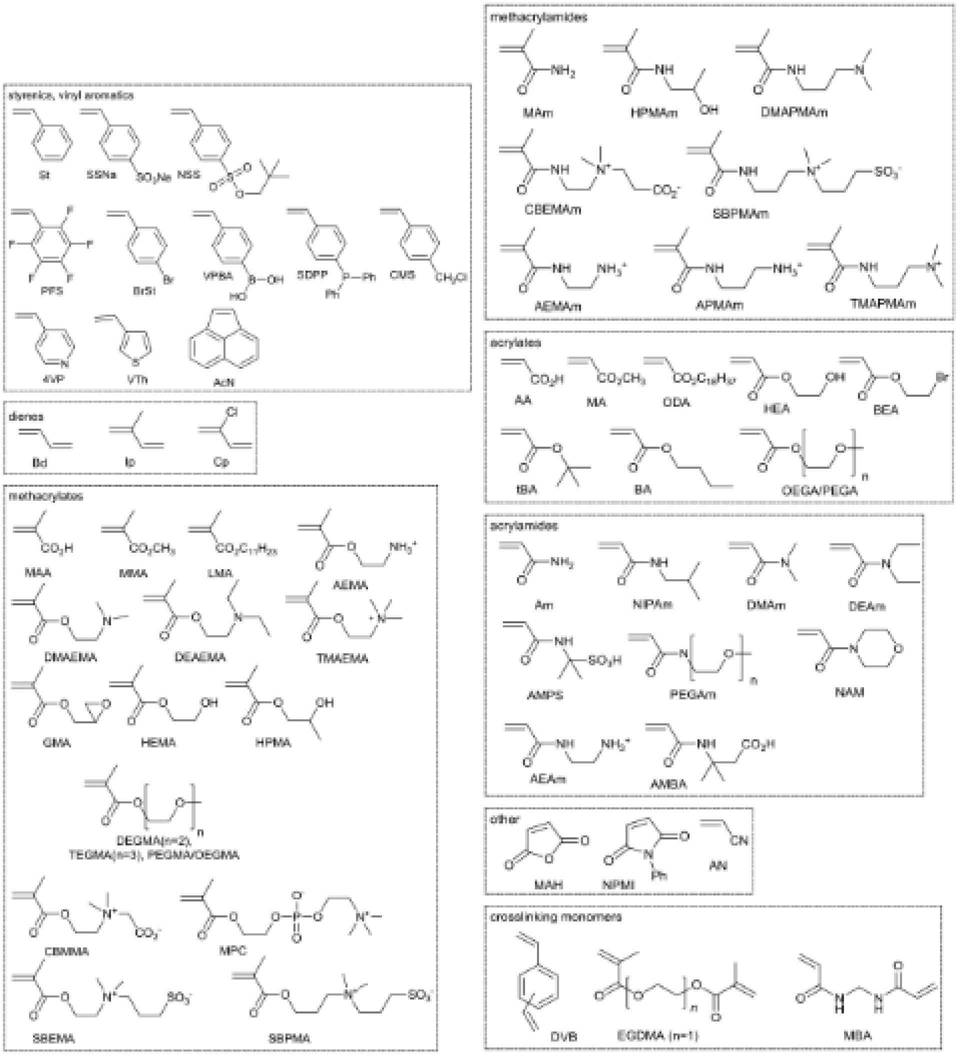
Monomers used with RAFT agents

In polymer chemistry, a wide variety of monomers can be used in RAFT polymerization, offering great versatility in creating different polymer types. However, the success of RAFT polymerization depends on the relative reactivity of the chosen monomer and the RAFT agent.

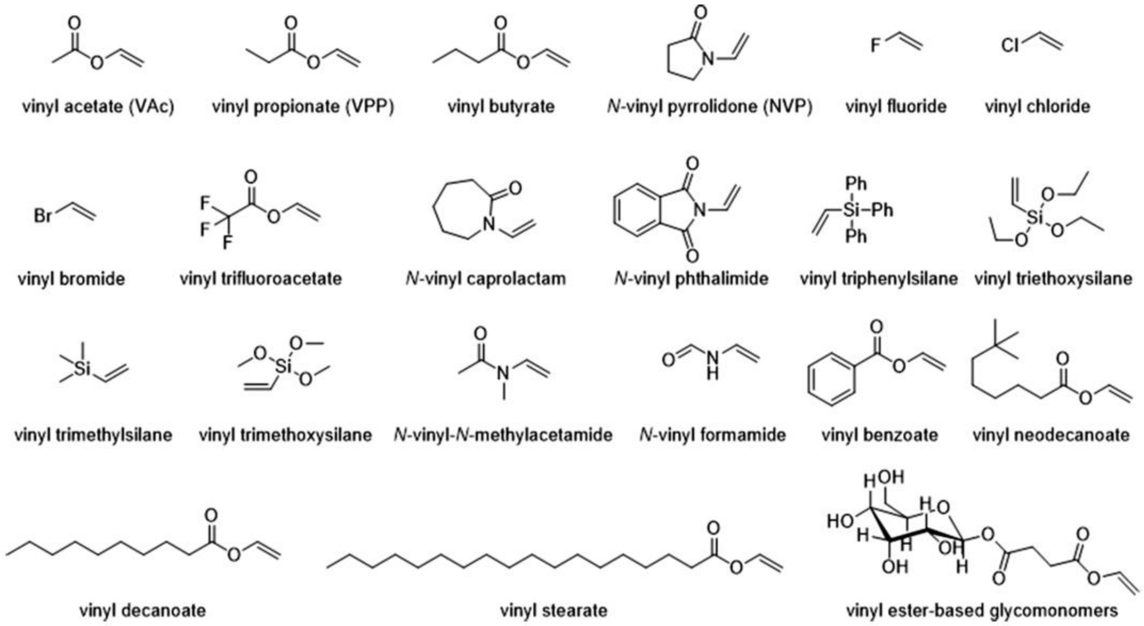
Here's a breakdown of the commonly used monomer systems: **More-Activated Monomers (MAMs)** and **Less-Activated Monomers (LAMs)**

The distinction between MAMs and LAMs plays a crucial role in determining the reactivity and properties of the resulting polymers .(٢٤)

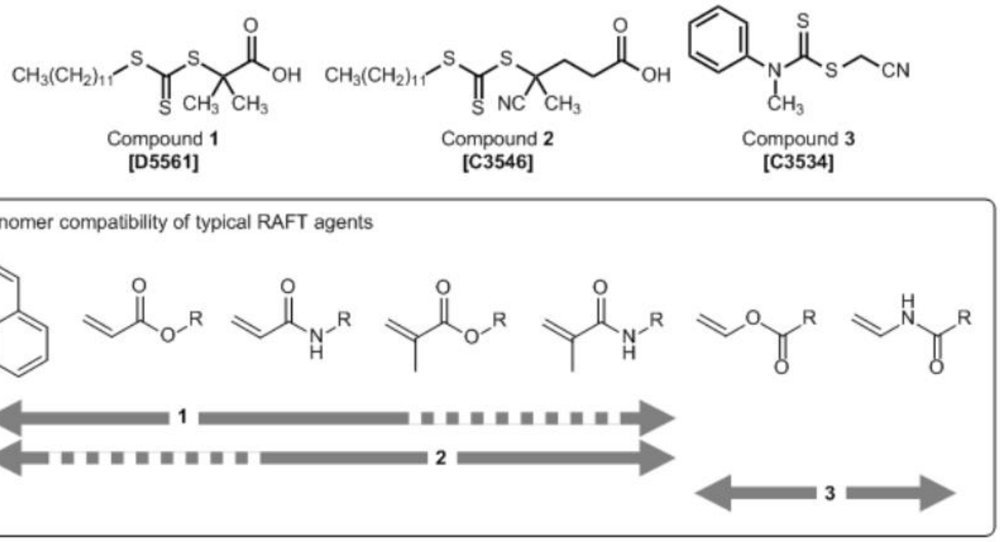
MAMs (more activated monomers) have a double bond adjacent to an electron-withdrawing group like carbonyl, nitrile, or nitro. Examples of MAMs include acrylonitrile, acrolein, methacrylic acid, and acrylamide. MAMs exhibit higher reactivity and stability compared to LAMs due to their chemical structure. Radical polymerization of MAMs can be effectively controlled using RAFT agents like dithioesters and trithiocarbonates. (٢٥)



LAMs (less activated monomers) lack conjugation to aromatic rings, double bonds, carbonyl groups, or nitriles. Examples of LAMs include N-vinylcarbazole and vinyl esters like vinyl acetate and vinyl propionate. LAMs are generally less reactive and stable than MAMs but still contribute to polymerization processes. RAFT agents favoring LAMs, such as N-alkyl-N-aryl dithiocarbamates and O-alkyl xanthates, are less effective with MAMs. (٢٦)



Understanding the distinction between MAMs and LAMs is essential for designing polymerization reactions and controlling the properties of polymers based on the monomer structure. RAFT agents play a key role in regulating the polymerization of both MAMs and LAMs, offering opportunities to tailor polymer properties for specific applications.



Types of RAFT agents

The RAFT process offers several advantages, including the ability to synthesize polymers with narrow molecular weight distributions, controlled end-group functionality, and complex architectures such as block copolymers and star polymers. This level of control makes the RAFT process valuable in various applications, including materials science, biomedical engineering, and nanotechnology.

The desired polymers that are commonly synthesized in RAFT polymerization

RAFT polymerization excels at creating various polymer architectures due to its controlled nature and ability to manipulate the growing polymer chain. Here are some desired polymer architectures that work effectively with RAFT agents (٢٧).

١-Linear Homo-polymers:

Linear homo-polymers are polymers composed of repeating units of a single type of monomer. These polymers have a simple molecular structure where the monomer units are linked together in a linear fashion without any branching or side chains. This results in a linear chain structure with a high degree of symmetry and regularity.

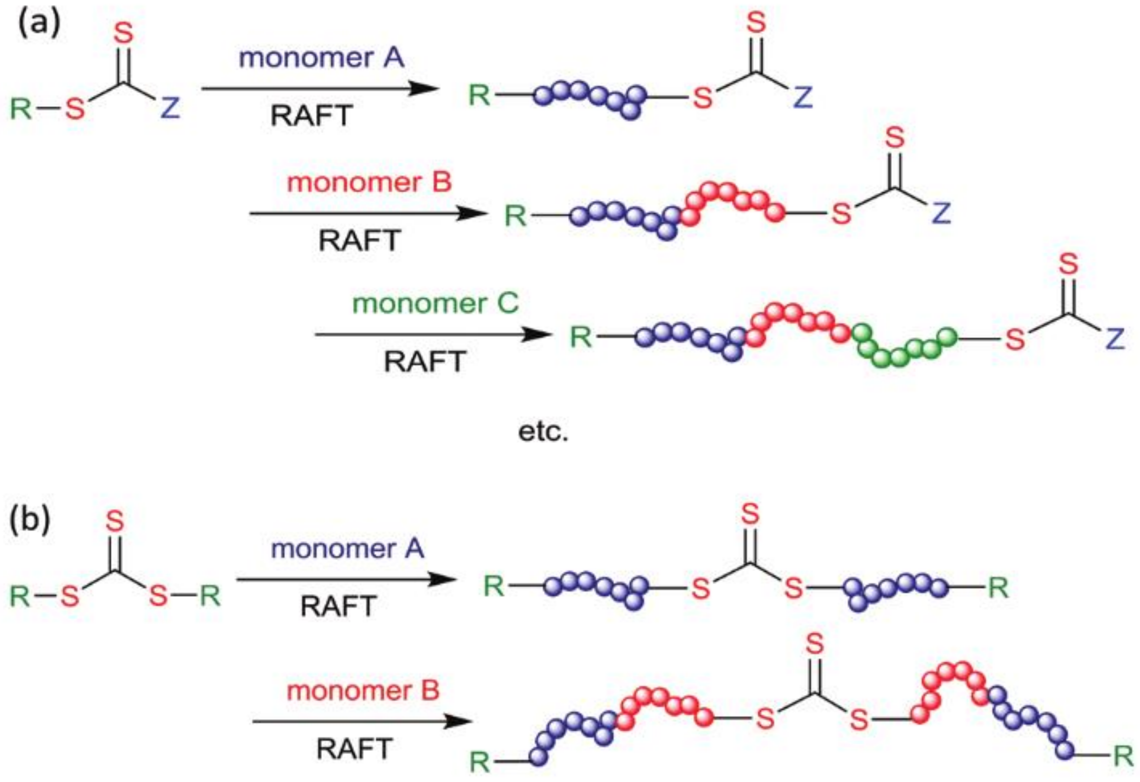
Linear homo-polymers are known for their uniformity and purity, as all the monomer units in the polymer chain are the same. This leads to consistent properties throughout the material, making them ideal for applications where uniformity is critical. Additionally, the absence of branching in linear homo-polymers contributes to their mechanical strength and process ability.

Common examples of linear homo-polymers include polyethylene, polypropylene, polystyrene, and polyvinyl chloride (PVC). These polymers are widely used in various industries due to their versatility, ease of processing, and desirable properties such as chemical resistance, thermal stability, and electrical insulation.

Overall, linear homo-polymers play a significant role in the polymer industry and find applications in areas such as packaging, construction, automotive, textiles, and medical devices. Their well-defined structure and properties make them valuable materials for a wide range of industrial and commercial applications.

٢-Block Copolymers:

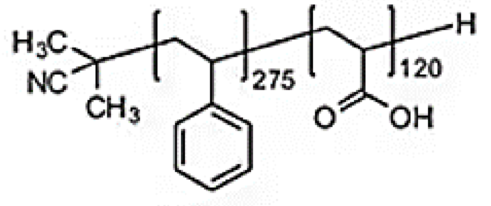
RAFT polymerization is indeed a versatile method for synthesizing block copolymers with well-defined structures. The ability to retain the thio-carbonylthio group during polymerization allows for the sequential addition of different monomers to create block copolymers with various architectures, such as AB diblock copolymers, ABA triblock copolymers, ABC triblock copolymers, and so on. (٢٨)



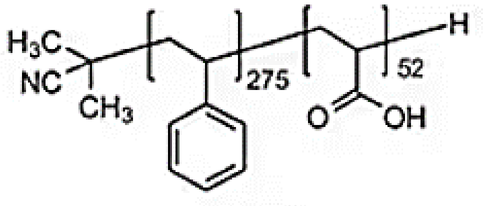
The order in which the blocks of a block copolymer are constructed is crucial in RAFT polymerization. It is important to consider the reactivity of the propagating radicals of each monomer to ensure efficient block formation. For example, in the synthesis of a methacrylate–acrylate or methacrylate–styrene diblock copolymer, it is recommended to prepare the methacrylate block first due to the differences in leaving group capabilities of the propagating radicals.

Reverse addition protocols can also be employed to synthesize block copolymers in a different order. By carefully controlling the monomer concentration relative to the RAFT agent, it is possible to grow blocks in a desired sequence. Additionally, block copolymers based on polymers synthesized by other methods can be prepared by using a prepolymer containing thiocarbonylthio groups as a macro-RAFT agent.

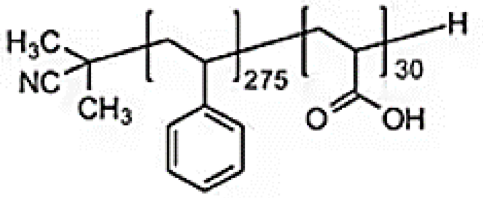
Overall, RAFT polymerization offers a powerful tool for designing and synthesizing a wide range of block copolymers and complex polymer architectures with tailored properties for various applications in materials science and nanotechnology.



746983



746991



747009

٣-Graft Copolymers:

Graft copolymers are a kind of copolymer that combines the features of physical blends and random copolymers. They can be thought of as chemically bonded pairs of homopolymers, similar to block copolymers. Milled copolymers consist of a backbone polymer “A” onto which the “B” sequences are grafted. The chemical nature of the backbone and grafted parts can vary, and there are different techniques for bonding them.

This class of polymers is used in the production of many commercially important materials such as impact-resistant polystyrene, ABS, and methacrylate butadiene styrene (MBS). (٢٩)

٤-Star polymers:

Star polymers are branched polymer molecules characterized by a single branch point from which multiple linear chains or arms extend. When the arms are identical, the star polymer is considered regular, while if adjacent arms have different repeating units, it is termed variegated. These polymers are of interest due to their unique rheological and dilute solution properties. Compared to linear polymers of the same molecular weight, star polymers exhibit enhanced segmental density and compactness, resembling the hard sphere model, especially as the number of arms increases.

The shape and properties of star polymers are influenced by their high segmental density and reduced degree of dynamic entanglement compared to linear polymers. This results in lower intrinsic viscosity for star polymers. A typical star-shaped polymer consists of at least three linear polymeric chains of similar lengths radiating from a central branched point known as the core. The core size is significantly smaller than the arm dimensions, distinguishing star-shaped polymers from nanoparticles.

Star-shaped polymers can be homo-stars, where all arms have the same chemical structure, or hetero-stars with arms composed of different structures. By varying the chemical composition of the arms and core, different types of star polymers such as star-block copolymers and hetero-star copolymers can be synthesized for specific applications. Star polymers can be further classified into homo-arm (regular) star polymers with identical arms and mikto-arm (hetero-arm) star copolymers containing arms with different compositions, molecular weights, or functionalities. (٣٠)

٥- Brush Polymers:

A brush polymer molecule consists of a main chain with linear, unbranched side chains where one or more of the branch points has at least a four-way functionality. A polymer brush consists of end-tethered (grafted, anchored) polymer chains stretched away from the substrate due to the volume-excluded effect. In mixed brushes, two or more different polymers grafted to the same substrate constitute the brush. Unlike unmixed brush polymers, different polymers in the mixed brush segregate into nano-scopic phases. The phase segregation is a lateral segregation process in a nonselective solvent in which different polymers form spherical or elongated clusters. Both polymers are exposed on the top of the brush.

In selective solvents, the mixed brush structure may be seen as a combination of lateral and layered segregation mechanisms. In the latter case, one polymer preferentially segregates to the top of the brush, while another polymer forms clusters segregated onto the grafting surface. The most important difference of the mixed brush compared to the homopolymer brush is that not only the height and density profile but also the composition profile depends on the solvent quality. In other words, the surface composition of the brush is switched by a change in its environment. (٣١)

٦- Hyper-branched Polymers:

Hyper-branched polymers belong to a class of synthetic tree-like macromolecules called dendritic polymers, which also include dendrimers. Hyperbranched polymers have a densely branched structure with a large number of end groups, while dendrimers have completely branched star-like topologies. Both types of molecules are composed of repeating units emanating from a central core, with the core's functionality determining the number of chemical bonds through which it can be connected to the external parts of the molecule.

The functionality of the core is typically three or four, such as amine or ethylenediamine, respectively. Linear units are attached to the core through these bonds, and each arm is terminated with a multifunctional branched unit. By adding shells of linear units to the end groups of the layer beneath, larger molecules are created. Perfect attachment of all units results in a dendrimer, while the absence of any unit leads to a hyperbranched polymer structure.

Due to their unique properties and easy synthesis, hyperbranched polymers have a wide range of potential applications. They can be used as nanomaterials for host-guest encapsulation, fabrication of organic-inorganic hybrids, and as nanoreactors. The low cost, well-defined architecture with multifunctional terminal groups, and narrow polydispersity make hyperbranched polymers increasingly attractive for various applications in materials science and nanotechnology. (٣٢)

٧- Dendrimers:

Dendrimers are highly structured, branched polymer molecules that are often referred to as arborols or cascade molecules. They are typically symmetrical around a central core and commonly exhibit a spherical three-dimensional shape. The term "dendron" is also frequently used, referring to a unit within a dendrimer that contains a chemically addressable group known as the focal point or core.

Dendrimers and dendrons belong to the same category, with the former being individual molecules and the latter encompassing dendronized polymers, hyperbranched polymers, and polymer brushes. The properties of dendrimers are primarily influenced by the functional groups present on their surface, although some dendrimers may also have internal functionality.

One significant advantage of dendrimers is their ability to encapsulate functional molecules, isolating them in a manner similar to active sites found in biological systems. Additionally, dendrimers can be made water-soluble by modifying their outer shell with charged or hydrophilic groups, a feature not commonly seen in other polymers. Other controllable properties of dendrimers include toxicity, crystallinity, formation of tecto-dendrimers, and chirality.

Dendrimers are classified by generation, which indicates the number of branching cycles performed during their synthesis. Higher-generation dendrimers have increased molecular weight and more exposed functional groups on their surface, allowing for customization based on specific applications. They can possess single or multiple surface functional groups depending on the desired functionality. (٣٣)

Dendrimers are polymers that have garnered significant attention and application across diverse fields due to their distinctive and precisely defined structure. Their versatility lies in their ease of modification and functionalization, rendering them highly suitable for a wide array of uses. Noteworthy physicochemical attributes of dendrimers encompass their size, shape, and capacity to form compartmentalized structures akin to biomolecules. Moreover, their properties can be finely tuned by manipulating solvent pH and polarity, rendering them adaptable to different environments.

The biocompatibility of dendrimers further enhances their utility in biological systems, particularly in drug delivery, bio-sensing, and targeted therapy. Nonetheless, thorough investigation is imperative to comprehend potential risks and side effects like cytotoxicity and immunogenicity prior to widespread medical application. Dendrimers have also served as ligands in bio-specific recognition, inhibition, and targeting, playing pivotal roles in drug delivery, gene therapy, and acting as agents against bacteria, viruses, and tumors.

Their unique architecture enables the controlled presentation of biomolecules, making them invaluable for targeted drug delivery and diagnostic purposes. For instance, dendrimers have been instrumental in presenting carbohydrates for precise tissue targeting in malignant diseases and as frameworks for vaccine antigens. Overall, dendrimers exhibit immense promise in the realm of medicine and remain a focal point of research for their diverse applications. (٣٤)

References

(١) Tian X, Ding J, Zhang B, Qiu F, Zhuang X, Chen Y. Recent Advances in RAFT Polymerization: Novel Initiation Mechanisms and Optoelectronic Applications. Polymers (Basel). ٢٠١٨ Mar ١٤; ١٠(٣):٣١٨.

(٢) Destarac, Mathias, et al. "Macromolecular design via the interchange of xanthates (MADIX): polymerization of styrene with o-ethyl xanthates as controlling agents." Macromolecular Chemistry and Physics ٢٠٣,١٦ (٢٠٠٢): ٢٢٨١-٢٢٨٩.

(٣) López-Alarcón, Camilo, et al. "Azocompounds as generators of defined radical species: Contributions and challenges for free radical research." Free Radical Biology and Medicine ١٦٠ (٢٠٢٠): ٧٨-٩١.

(٤) Ramsey, Bonnie L., et al. "Photoinduced organocatalyzed atom transfer radical polymerization using continuous flow." Macromolecules ٥٠,٧ (٢٠١٧): ٢٦٦٨-٢٦٧٤.

(٥) Su, Wei-Fang, and Wei-Fang Su. "Radical chain polymerization." Principles of Polymer Design and Synthesis (٢٠١٣): ١٣٧-١٨٣.

(٦) Lowe, Andrew B., and Charles L. McCormick. "RAFT polymerization in homogeneous aqueous media: initiation systems, RAFT agent stability, monomers and polymer structures." Handbook of RAFT Polymerization (٢٠٠٨): ٢٣٥-٢٨٤.

(٧) Barner-Kowollik, Christopher, ed. Handbook of RAFT polymerization. John Wiley & Sons, ٢٠٠٨.

(٨) Hawker, Craig J. "“Living” free radical polymerization: a unique technique for the preparation of controlled macromolecular architectures." Accounts of chemical research ٣٠,٩ (١٩٩٧): ٣٧٣-٣٨٢.

(٩) Coessens, Veerle, Tomislav Pintauer, and Krzysztof Matyjaszewski. "Functional polymers by atom transfer radical polymerization." Progress in polymer science ٢٦,٣ (٢٠٠١): ٣٣٧-٣٧٧.

(١٠) Semsarilar, Mona, and Sébastien Perrier. "'Green'reversible addition-fragmentation chain-transfer (RAFT) polymerization." Nature chemistry ٢,١٠ (٢٠١٠): ٨١١-٨٢٠ .

(١١) Nicholas, Carmean R. "Expanding the Scope of RAFT Polymerization: Recent Advances and New Horizons." (٢٠١٥ .

(١٢) Tan, Ruwen, Jin Yoo, and Yeongseon Jang. "Engineering approaches to create antibacterial surfaces on biomedical implants and devices." Racing for the Surface: Pathogenesis of Implant Infection and Advanced Antimicrobial Strategies (٢٠٢٠): ٣١٣-٣٤٠.

(١٣) Tan, Ruwen, Jin Yoo, and Yeongseon Jang. "Engineering approaches to create antibacterial surfaces on biomedical implants and devices." Racing for the Surface: Pathogenesis of Implant Infection and Advanced Antimicrobial Strategies (٢٠٢٠): ٣١٣-٣٤٠.

(١٤) Barner-Kowollik, Christopher, and Sébastien Perrier. "The future of reversible addition fragmentation chain transfer polymerization." Journal of Polymer Science Part A: Polymer Chemistry ٤٦,١٧ (٢٠٠٨): ٥٧١٥-٥٧٢٣.

(١٥) Coote, Michelle L., and David J. Henry. "Computer-aided design of a destabilized RAFT adduct radical: Toward improved RAFT agents for styrene-block-vinyl acetate copolymers." Macromolecules ٣٨,١٣ (٢٠٠٥): ٥٧٧٤-٥٧٧٩.

(١٦) Semsarilar, Mona, and Volker Abetz. "Polymerizations by RAFT: Developments of the Technique and Its Application in the Synthesis of Tailored (Co) polymers." Macromolecular Chemistry and Physics ٢٢٢,١ (٢٠٢١): ٢٠٠٠٣١١.

(١٧) Hawker, Craig J. "“Living” free radical polymerization: a unique technique for the preparation of controlled macromolecular architectures." Accounts of chemical research ٣٠,٩ (١٩٩٧): ٣٧٣-٣٨٢.

(١٨) Al-Ali, Maan Abduldiyem Hassan. "Synthesis and Design of Novel Polymer Grafted Nanoparticles Relevant to Drug Delivery Vehicles for Biomedical Applications." (٢٠٢٠.

(١٩) Barner-Kowollik, Christopher, ed. Handbook of RAFT polymerization. John Wiley & Sons, ٢٠٠٨.

(٢٠) Moad, Graeme. "RAFT polymerization to form stimuli-responsive polymers." Polymer Chemistry ٨،١ (٢٠١٧): ١٧٧-٢١٩.

(٢١) Singh, Jagtar, and Pallavi Nayak. "pH-responsive polymers for drug delivery: Trends and opportunities." Journal of Polymer Science ٦١،٢٢ (٢٠٢٣): ٢٨٢٨-٢٨٥٠.

(٢٢) González-Sálamo, Javier, et al. "Application of stimuli-responsive materials for extraction purposes." Journal of Chromatography A ١٦٣٦ (٢٠٢١): ٤٦١٧٦٤.

(٢٣) Schneiderman, Deborah K., and Marc A. Hillmyer. "٥٠th anniversary perspective: there is a great future in sustainable polymers." Macromolecules ٥٠،١٠ (٢٠١٧): ٣٧٣٣-٣٧٤٩.

(٢٤) Barner-Kowollik, Christopher, ed. Handbook of RAFT polymerization. John Wiley & Sons, ٢٠٠٨.

(٢٥) Moad, Graeme, Ezio Rizzardo, and San H. Thang. "RAFT polymerization and some of its applications." Chemistry–An Asian Journal ٨،٨ (٢٠١٣): ١٦٣٤-١٦٤٤.

(٢٦) Tilottama, Baisakhi, et al. "A short review on RAFT polymerization of less activated monomers." Journal of Macromolecular Science, Part A ٥٩،٣ (٢٠٢٢): ١٨٠-٢٠١.

(٢٧) Barner-Kowollik, Christopher, ed. Handbook of RAFT polymerization. John Wiley & Sons, ٢٠٠٨.

(٢٨) Efron, Nathan. Contact Lens Practice-E-Book. Elsevier Health Sciences, (٢٠٢٣).

(٢٩) Keddie, Daniel J. "A guide to the synthesis of block copolymers using reversible-addition fragmentation chain transfer (RAFT) polymerization." Chemical Society Reviews ٤٣,٢ (٢٠١٤) ٤٩٦-٥٠٥.

(٣٠) Rzayev, Zakir MO. "Graft copolymers of maleic anhydride and its isostructural analogues: high performance engineering materials." arXiv preprint arXiv:١١٠٥,١٢٦٠ (٢٠١١)

(٣١) Aloorkar, N. H., et al. "Star polymers: an overview." Int. J. Pharm. Sci. Nanotechnol ٥ (٢٠١٢): ١٦٧٥-١٦٨٤.

(٣٢) Driving Polymer Brushes from Synthesis to Functioning

(٣٣) Hult, Anders, Mats Johansson, and Eva Malmström. "Hyperbranched polymers." Branched Polymers II (١٩٩٩): ١-٣٤.

(٣٤) Kesharwani, Prashant, Keerti Jain, and Narendra Kumar Jain. "Dendrimer as nanocarrier for drug delivery." Progress in Polymer Science ٣٩,٢ (٢٠١٤): ٢٦٨-٣٠٧ .