1
Introduction

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The *reversible addition–fragmentation chain transfer* (RAFT) process is the most recent of the living/controlled free radical methodologies that have revolutionized the field of free radical polymerization. It was invented in 1998 by the Commonwealth Scientific and Industrial Research Organization (CSIRO) in Melbourne, Australia, by a team of several researchers [1]. Almost simultaneously, a group of researchers in France patented a process they termed *macromolecular design via the interchange of xanthates* (MADIX) [2], which employed xanthates as controlling agents but proceeds by an identical mechanism as the CSIRO-reported RAFT process. Both processes are based on earlier developed chemistries, such as the small radical reactions pioneered by Zard and coworkers [3]. Equally, polymerizations employing reversible addition–fragmentation chain transfer principles, which showed some of the characteristics of living polymerization, were first reported in 1995 by the CSIRO group [4]. The RAFT process employs a fundamentally different conceptual approach compared to nitroxide-mediated polymerization (NMP) and atom transfer radical polymerization (ATRP) in that it relies on a degenerative chain transfer process and does not make use of a persistent radical effect to establish control. Such an approach has the important consequence that the RAFT process features quasi-identical rates of polymerization – apart from deviations caused by the chain length dependence of some rate coefficients – as the respective conventional free radical polymerization processes. Among the other unique features of the RAFT process is its high tolerance to functional monomers – such as vinyl acetate and acrylic acid – which can be polymerized with living characteristics with ease. The RAFT process is an equally powerful tool for the construction of complex macromolecular architectures via variable approaches – i.e. the so-called Z- and R-group designs – that allow for almost limitless possibilities in the synthetic protocols in terms of the low molecular weight scaffolds that support the complex structure.

The popularity of the RAFT process has steadily increased since the first report in 1998. Figure 1.1 gives the number of RAFT-related papers as function of the year (up to April 2007). It is clear that the research interest in the RAFT process continues to be very strong. The present book aims at collating the current state of the art

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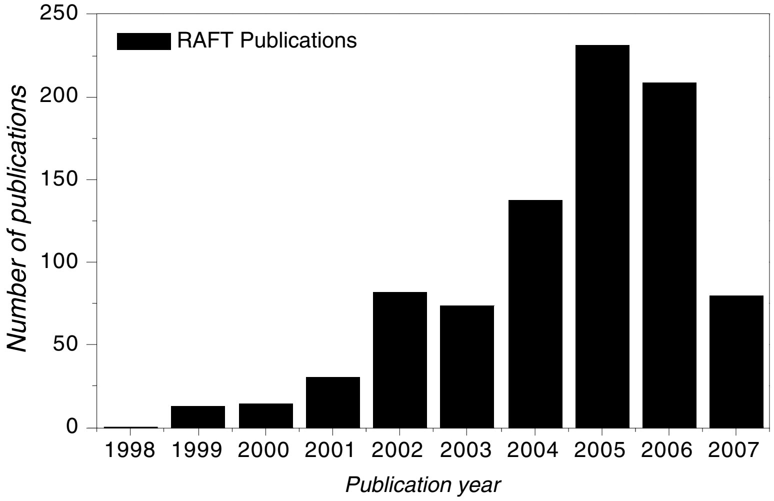

Fig. 1.1 RAFT publications as function of publication year (ISI Web of Science Database, 24.04.2007, search for 'reversible addition fragmentation chain transfer polymerization').

in RAFT and MADIX. It assembles a cross-section of the world's leading experts on the RAFT/MADIX process, with the view of providing an encompassing picture. It ranges from the underpinning fundamental rate coefficients and equilibrium constants obtained via high-level quantum chemical approaches (Chapter 2) as well as the – sometimes complex – kinetics and mechanism of RAFT and its employment as a powerful kinetic tool (Chapters 3 and 4) to the uses of the process for the formation of simple, yet well-defined polymers in bulk (Chapter 6) to the synthesis of highly complex star and block copolymer structures (Chapter 9). As the MADIX process – although essentially identical to RAFT from a mechanistic perspective – was developed simultaneously, it seems apt to cover its particular strengths and applications in a separate chapter (Chapter 10) accompanied by a contribution on the small radical chemistry of thiocarbonylthio compounds (Chapter 5). The rationale for including a chapter solely on small radical chemistry early in the book is to provide synthetic depths and insight into thiocarbonylthio chemistry from the perspective of an organic chemist. Further chapters highlight the strengths and limitations of RAFT in the context of emulsion and miniemulsion polymerization (Chapter 8) and in homogeneous aqueous systems (Chapter 7). The RAFT process has also been frequently employed to successfully functionalize surfaces as well as micro- and nanoparticles, and Chapter 11 is dedicated to this topic. The controlled functionalization of surfaces is of high importance for a range of applications, including diagnostic kits and tissue engineering. Chapter 12 examines the functional variety that is achievable in RAFT-controlled end groups as well as the stability of RAFT-made polymers. One of the most outward looking chapters aims to examine the materials that have been prepared via the RAFT process for applications ranging from drug delivery to optoelectronics (Chapter 13).

The reader may ask: where to from here? Synthetically, further improvements can be made, especially with a view to generating (complex) block copolymers of monomers with very disparate reactivities, such as styrene and vinyl acetate. While theoretical and some practical advances have been made toward a universal RAFT agent, more research is required in this area. Alternatively, the fusion of RAFT chemistry with highly orthogonal pericyclic reactions (*click* chemistry) is only now emerging and further combination and clever exploitation of these concepts will allow for the construction of extremely well-defined complex polymer systems. Kinetically, the ongoing fruitful discussions about the mechanism of the RAFT process – stimulated by the formation of an IUPAC working party on its mechanism – have led to some clarifications, yet important questions remain to be more fully investigated: How does the size of the equilibrium constant vary with chain length and substitution? If cross-terminations occur, are they reversible and what is the value of the associated termination rate coefficient? Are such side reactions a consequence of slowly fragmenting intermediates or do short-lived adduct radicals react with large termination rate coefficients? Some of the answers to these questions are emerging now and it will be fascinating to follow the progress in this field. However, it is important to note that complex kinetic situations – including the often-quoted rate retardation and inhibition effects – do not occur in the majority of RAFT processes. Ultimately, the application of the RAFT process in materials that benefit society has yet to come to full fruition. We are seeing encouraging trends where RAFT chemistry is employed in variable areas including drug and gene delivery, diagnostic applications, tissue engineering and regenerative medicine, membrane science, bioconjugation as well as the preparation polymers with optoelectronic properties. Yet, more work is required to enhance the existing materials and enable RAFT chemistry to deliver tangible benefits for society.

It is an interesting observation that the RAFT process – although it is in many aspects an extremely powerful living/controlled free radical technique – has still not attracted the overall popularity of living/controlled polymerization based on atom transfer concepts. It is a sometimes advanced notion that this is correlated with the fact that RAFT/MADIX agents are (as of April 2007) not commercially available (except one) and have to be synthesized prior to polymerization. Although this is largely correct, read in Chapter 3 of this book: “While a wide variety of RAFT agents have been made featuring variable Z and R groups, it is important to point out that in principle it should be possible to control polymerization of all monomers using just two RAFT agent structures (e.g. a cyanoisopropyl dithiobenzoate) for styrenics, acrylates, methacrylates, acrylamides and a xanthate or dithiocarbamate (e.g. *O*-ethyl-*S*-cyanomethyl xanthate) for vinyl acetate, *N*-vinyl pyrrolidone and similar monomers.”

The current compilation of fascinating RAFT chemistry will further widen its use as a versatile tool in the toolbox of living/controlled polymerization and enhance further collaborative efforts between theoreticians, organic chemists, kineticists, polymer chemists, physical chemists, material scientists and industry. Concomitantly, the current book aims at advancing applications of RAFT for the generation of advanced materials that will positively impact on the lives of all of us.

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