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Mechanistic Features and Radical Intermediates in Atom Transfer Radical Polymerization

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Summary: Fundamental mechanistic features of copper mediated atom transfer radical polymerization (ATRP) are presented together with a discussion on radical intermediates involved in atom transfer process. Rate constants of racemization of optically active methyl 2-bromopropionate, of halogen exchange, of trapping with TEMPO and with methyl methacrylate are very similar, confirming free radical intermediates. Rate constant of reaction of propionate radical with methyl methacrylate under model ATRP conditions at 22 °C ($k = 5.6\ 10^4 mol^{-1}\ L\ s^{-1}$) is nearly identical to that measured by time resolved EPR ($k = 6.0\ 10^4 mol^{-1}\ L\ s^{-1}$).

Introduction

Atom transfer radical polymerization (ATRP) together with other controlled/living radical polymerization (CRP) systems is among the most dynamically developing areas of polymer science.[1] Figure 1 illustrates number of publications in the general field of CRP, ATRP as well as in nitroxide mediated polymerization (NMP) and degenerative transfer processes, including RAFT.

ATRP has its roots in atom transfer radical addition (ATRA), a highly selective process of addition of alkenes across carbon-halogen bond catalyzed by redox active transition metal complexes and proceeding via radical intermediates.[2]

Polymerization systems utilizing this concept have been developed using Cu, Ru, Ni, Pd, Rh and Fe complexes to catalyze the ATRP equilibrium; however, the remainder of this article will focus on copper-based ATRP.[3]

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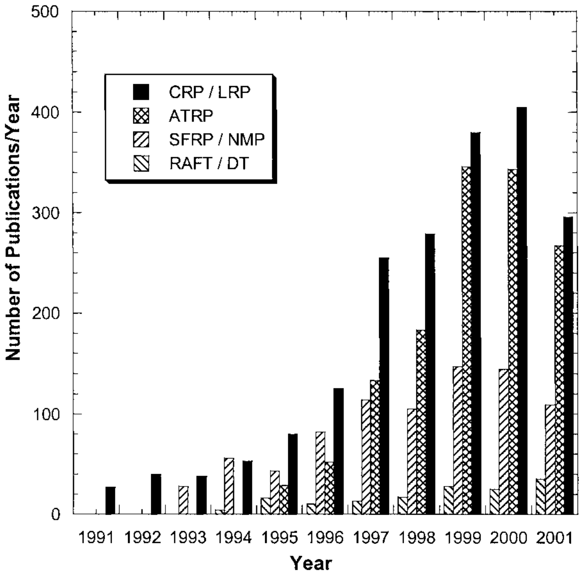
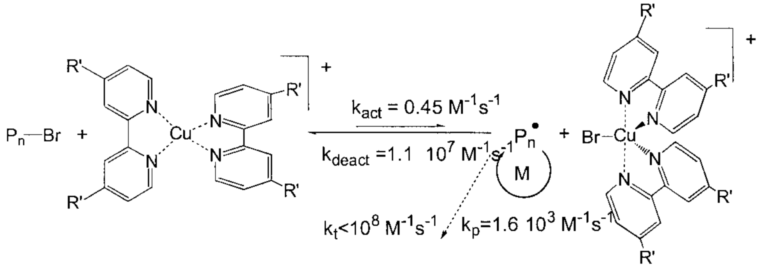


Fig. 1. Number of publications in different areas of controlled/living radical polymerization, according to SciFinder Scholar search from October 14, 2001.

Scheme 1 presents perhaps the most carefully studied system, styrene polymerization initiated by 1-phenylethyl bromide and catalyzed by Cu complexed by 2,2'-bipyridine derivatives: [4, 5]

Scheme 1



A key feature of ATRP is the dynamic equilibration between dormant alkyl halides and propagating free radicals. The control depends on the relative rates of propagation (k_p)

and deactivation (k_{deact}) which affects polydispersity of the obtained polymers. Overall rate (cf. eq. 1) depends on concentration of radicals (P_n^*) which is defined by the ratio of activation and deactivation rate constants and concentrations of initiator/dormant species (P-X) , activator (Cu^I) and deactivator ($X\text{-}Cu^{II}$). In well-controlled systems, contribution of termination (k_t) can be essentially neglected.

General Features of ATRP

A successful ATRP process should meet several requirements:

1. Initiator should be consumed at the early stages and should generate propagating chains leading to polymers with degrees of polymerization predetermined by the ratio of concentrations of converted monomer to the introduced initiator ($DP=\Delta[M]/[I]_o$).
2. The number of monomer molecules added during each activation step should be small, resulting in polymers with low polydispersities.
3. Finally, contribution of chain breaking reactions (transfer and termination) should be negligible to yield polymers with high degrees of end-functionalities and block copolymers.

In order to reach these three goals, it is necessary to select proper structure of reagents and appropriate reaction conditions.

According to the general scheme of ATRP, the rate of the polymerization should be defined by the following equation:

$$R_p = k_p[M]\,[RX]_o\,k_{act}\,[Cu^I] \,/\, (k_{deact}\,[X\text{-}Cu^{II}]) \qquad \text{(eq. 1)}$$

Thus, polymerization should follow internal first order in monomer, external first order in respect to initiator and activator, Cu(I), and external negative first order in respect to deactivator, X-Cu(II).[4] However, the kinetics may be more complex due to spontaneous formation of XCu(II) species via persistent radical effect (PRE). Fractional orders in respect to monomer and other components have been predicted for the idealized system with chain length independent termination rate coefficients.[6] The actual kinetics depends on many factors including solubility of activator and deactivator, their plausible interactions and variations of their structures and reactivities with concentrations and composition of the reaction medium. It should be also noted that the contribution of PRE at the initial stages might be affected by the mixing method, solubility of the metal compound and ligand, etc.

One of the most important parameters in ATRP is the dynamics of exchange and especially relative rate of deactivation. If deactivation process is slow in comparison with propagation, then a classic redox initiation process operates leading to conventional and not controlled radical polymerization. Polydispersities in ATRP are defined by the following equation:

$$M_w/M_n = 1 + \{(k_p\,[RX]_o)/(k_{deact}\,[X\text{-}Cu^{II}])\}\,(2/p - 1) \qquad \text{(eq. 2)}$$

Thus, polydispersities decrease with conversion, p, with the rate constant of deactivation, k_{deact}, and with the concentration of deactivator, [X-Cu(II)]. They, however, increase with the propagation rate constant, k_p, and with the concentration of initiator, $[RX]_o$. This means, that more uniform polymers are obtained at higher conversions and when concentration of deactivator in solution is high and concentration of initiator low.[7] Also, more uniform polymers are formed when deactivator is very reactive (e.g. copper(II) complexed by bipyridine or triamine rather than by water) and monomer propagates slowly (styrene rather than acrylate).

Chain breaking reactions do occur in controlled radical systems. Fortunately, at typical reaction temperatures, contribution of transfer is relatively small. For example, in polymerization of styrene, less than 10% of chains participate in transfer to monomer before reaching M_n=100,000. However, the contribution of transfer progressively increases with the chain length and molecular weights must be limited by the appropriate ratio of monomer to initiator concentrations (for styrene $\Delta[M]/[I]_o<1{,}000$). Termination does occur in radical systems and currently cannot be completely avoided. However, since termination is second order in respect to radicals concentration and propagation is first order, contribution of termination increases with radicals concentration, meaning with the polymerization rate. Thus, most controlled radical polymerizations are designed to be slower than conventional systems. It is possible to generate relatively fast controlled radical polymerization only for the most reactive monomers, such as acrylates and/or for relatively short chains. For short chains, the absolute concentration of terminated chains is still high but their percentile in the total number of chains small enough not to affect end-functionalities and a blocking efficiency. A typical proportion of terminated chains is between 1 and 10%, with the large domination of very short chains. It was possible to measure the evolution of concentration of terminated chains by following the copper(II) species by EPR.[8] Because, termination rate coefficients decrease significantly with chain length and viscosity of the medium, rate of termination dramatically reduces, too, and even more due to PRE.[9]

Radical Nature of ATRP

The simplified picture of the ATRP equilibrium with copper halide complexed by two bipyridine ligands was shown in Scheme 1. Based on the X-ray structures of the corresponding isolated solid Cu(I) cationic complex should be in a slightly distorted tetrahedral coordination and Cu(II) in a trigonal bipyramidal coordination.[10] In solution (EXAFS), structure seems to be similar, although it may be accompanied by linear X-$Cu^{(I)}$-X anion.[11, 12] The rate constants of the exchange process shown in Scheme 1 were determined based on model reactions.[4, 13, 14]

It is possible that not only free radicals but also other species may be involved in propagation. It was demonstrated that ATRP mechanism operates in polymerization of styrene, and (meth)acrylates, catalyzed by copper halides complexed by 2,2'-bipyridine and the corresponding 4,4'-dialkyl substituted bipyridines.[15] This conclusion was reached based on several identical features of ATRP and conventional radical polymerizations. They include:

-chemoselectivity (reactivity ratios, effect of scavengers and additives selective for radical, ionic and organometallic reactions),[5, 16-20]. It has to be realized, that reactivity ratios may depend also on physical phenomena, such as poor compatibility between macromonomer and growing chains, [21, 22] poor solubility, monomer complexation with Lewis acids,[23] etc. Also, some scavengers act very selectively, and e.g. phenols do not inhibit polymerization of methacrylates.[24, 25]

-regioselectivity (end groups, head-to-tail structures),[16] and stereoselectivity (tacticity),[16]

-direct observation of radical coupling products (doubling of molecular weights, crosslinking for multifunctional systems, direct observation of copper(II) by EPR)[8]

-approaching the ATRP equilibria from the opposite site (e.g. AIBN and XCu(II) species), giving direct evidence that copper (II) deactivates growing radicals[26-28]

-increasing rates and polydispersities by reducing concentration of copper(II), e.g. by its lower solubility and by adding copper (0)[29]

- direct EPR detection of propagating free radicals in ATRP of dimethacrylates trapped in glassy matrices [30]

All these experiments strongly indicated that majority of monomer in ATRP is consumed and polymer is predominantly formed by free radicals.

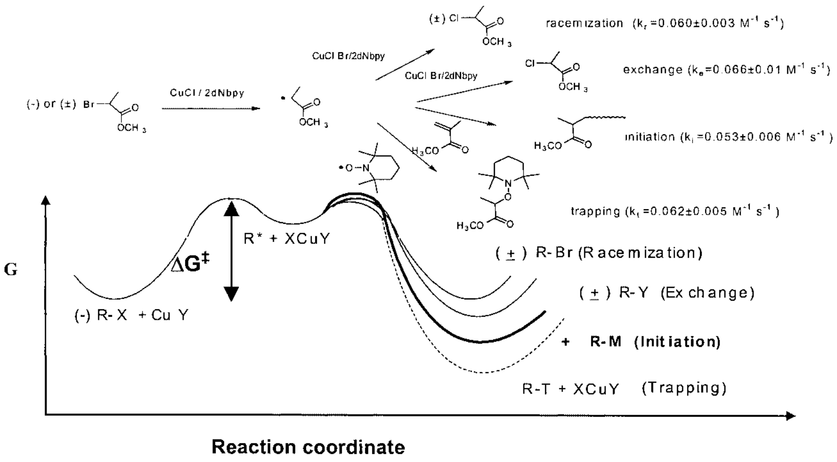
It is possible that under certain conditions, degenerative transfer and reversible formation of organometallic intermediates can supplement ATRP. It is also possible that ATRP may sometimes occur not via concerted process with bridged intermediates but by the two step process with the involvement of radical anions. For some monomers and some metal complexes, either oxidation or reduction of growing radicals to ionic species is possible which will usually induce loss of control due to high reaction temperature and presence of adventitious water. However, it was found, that although degenerative transfer operates with I, it does not with Cl and Br end groups.[31] Also, a negligible effect of Cu(OTf) or $Cu(OTf)_2$ on rates and molecular weights in AIBN initiated polymerization of styrene and acrylates suggests insignificant formation of organometallic intermediates.[32] It is recommended that the radical nature of the metal catalyzed polymerization should be always tested using the above criteria, since even a small change in the monomer, ligand, temperature or solvent may favor other reactions. For example, CuBr/Bpy complex yields a cationic polymerization of p-methoxystyrene,[33] whereas it generates carbanions from diethyl 2-bromomalonate.[34]

Free-radical intermediates in model systems were confirmed by four independent kinetic measurements.[35] The racemization of optically active methyl 2-bromopropionate (MBrP) catalyzed by copper(I) chloride/4,4'-di-(5-nonyl)-2,2'-bipyridine (dNbpy) occurred with the rate constant $k_r = (6.0 \pm 0.3) \times 10^{-2}\ M^{-1}\ s^{-1}$ at 60 °C in toluene, indicating that the intermediate structure allows for the inversion of the chiral center in the alkyl halide during the atom transfer process. The halogen exchange between the MBrP and

Cu(I)Cl/dNbpy to yield methyl 2-chloropropionate and Cu(I)Br complex occurred with the rate constant $k_e = (6.6 \pm 1.1) \times 10^{-2}\ M^{-1}\ s^{-1}$. The consumption of MBrP catalyzed by Cu(I)Cl/dNbpy in the presence of a radical scavenger, 2,2,6,6-tetramethylpiperidinyl-1-oxy (TEMPO) proceeded also with a similar rate constant $k_t = (6.2 \pm 0.5) \times 10^{-2}\ M^{-1}\ s^{-1}$. The generated intermediate was trapped by TEMPO to form an alkoxyamine. Finally, the slow initiation of methyl methacrylate ATRP under similar conditions showed the initiator consumption to occur with slightly smaller rate constant $k_i = (5.3 \pm 0.6) \times 10^{-2}\ M^{-1}\ s^{-1}$

The schematic energy diagram for the racemization, halogen exchange and trapping steps is shown below:

Scheme 2



All four reactions proceed through the same transition rate in which free radical is formed in the rate determining step. Racemization has a "symmetrical" energy diagram, whereas in the exchange and trapping (TEMPO or MMA) some energy may be gained due to the formation of more stable products. The overall energy barrier may be slightly higher for MMA, since it is a much less efficient trap than TEMPO (rate constants of the addition to MMA is $k_{MMA} = 6 \times 10^4\ M^{-1}\ s^{-1}$ and trapping with TEMPO $k_r = \sim 10^9\ M^{-1}\ s^{-1}$ at 25 °C).

Thus for a slower trap (MMA) the deactivation step may not be fully neglected and the apparent rate constant should be expressed as:

$$k^{app} = -d\ln[RX]/dt = k_{act}\,[Cu^{I}] \times k_t\,[T] / (k_{deact}\,[Cu^{II}] + k_t\,[T]) \qquad \text{(eq. 3)}$$

If trapping is fast, i.e. $k_{deact}\,[Cu^{II}] << k_t\,[T]$, this equation reduces to a simple:

$$k^{app} = k_{act}\,[Cu^{I}] \qquad \text{(eq. 4)}$$

However, if trapping is not very efficient ($k_{deact}\,[Cu^{II}] >> k_t\,[T]$), equilibrium radical concentration is established, slowing down the total consumption of RX:

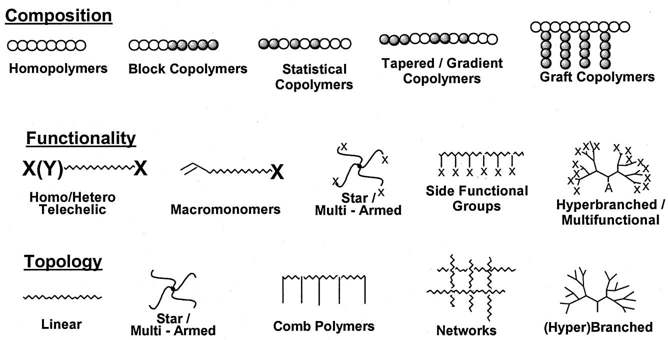
$$k^{app} = k_{act}\,[Cu^{I}] \times k_t\,[T] / k_{deact}\,[Cu^{II}] \qquad \text{(eq. 5)}$$

This corresponds to the pre-equilibrium step and slightly higher energy barrier for the second step, and consequently slower trapping process. Values with MMA are nearly the same indicative that rates of deactivation and trapping are comparable. By varying $[MMA]_o$ and $[Cu^{II}]_o$, it was possible to determine k_{act} and k_{deact}/k_i ratios for trapping with MMA. Evolution of Cu^{II}, in the absence of trap, obeys typical Fischer's kinetics and allows estimates of the ratio k_{act} / k_{deact}, thus allowing to measure independently k_{act} and k_{deact} and k_i. The latter value for the reaction of MMA with tert-butyl 2-bromopropionate at 22 °C was calculated to be $k_i = 5.6\ 10^4 mol^{-1}\ L\ s^{-1}$, which is nearly identical to that measured by time –resolved EPR. ($k_i = 6.0\ 10^4 mol^{-1}\ L\ s^{-1}$)[36].

New Materials by ATRP

Materials prepared by ATRP employ various concepts of macromolecular engineering developed earlier for anionic or cationic processes are schematically shown in Scheme 3: [37, 38] Several structural features are controlled beyond molecular weight and polydispersity and include controlled composition, functionality and chain topology :

Scheme 3



Future Directions in ATRP

It is anticipated that controlled radical polymerization systems will become a commercial reality in a very near future, especially in the areas of specialties, coatings, surfactants, dispersants, etc. ATRP has several advantages but also some limitations in comparison with other LRP processes. The future research should overcome these limitations and expand scope of ATRP. For example, the transition metal catalyst should be removed and, ideally, recycled. In this area some successful approaches include selective absorption, precipitation as well as immobilization techniques.[39-43]

Mechanistically most important areas for future ATRP research will include detail understanding of the process, especially the most crucial atom transfer step and also comprehensive structure – reactivity correlation for initiators, monomers, catalysts with the plausible variation by specific reaction conditions. Synthetically, it is necessary to expand the range of monomers and initiators and better understand limits for range of controlled molecular weights, crosspropagations and end functionalities. Finally, one of the most attractive features is preparation of many new functional polymers with novel and controlled compositions and topologies for structure-property relationship and for better design of novel materials for special applications. ATRP is especially well suited for that purpose due to facile reaction conditions, multitude of polymerizable monomers and accessible chain functionalities.

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