Oxygen-Initiated and Regulated Controlled Radical Polymerization under Ambient Conditions

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Abstract: A rapid oxygen-initiated and -regulated controlled radical polymerization was conducted under ambient temperature and atmosphere. The reaction between triethylborane and oxygen provides ethyl radicals, which initiate and mediate the radical polymerization. The controlled radical polymerization was achieved using RAFT chain transfer agents (CTA) without any process of removing oxygen, providing well-defined polymers with almost full conversion (>95%) in a short period (15 min). High-throughput screening was used to discover the suitable conditions for various CTA and monomers. To show the versatility of this method, a polymer library containing 25 well-defined polymers with different compositions (block and statistical copolymers) and molecular weights were synthesized in 1 h via high-throughput synthesis technique. A polymer-painting technique was developed using this method, forming films with spatial control and excellent control in molecular weight and dispersity.

Controlled radical polymerization (CRP, also termed reversible-deactivation radical polymerization, RDRP suggested by IUPAC) has reformed polymer and material science by providing a facile and robust synthesis of well-defined polymers and predesigned complex architectures. Since oxygen molecule is an efficient and undesired radical scavenger, radical polymerization has to be performed in deoxygenated atmosphere (for example, in glove box). The freeze–pump–thaw technique and deoxygenation with inert gas are widely used but time-consuming methods to remove oxygen. Several methods with some degree of oxygen tolerance were developed via consuming oxygen by excess radicals or converting oxygen to non-initiating species, including photoinitiated atom-transfer radical polymerization (photoATRP), photoinduced electron/energy-transfer–reversible addition–fragmentation chain-transfer (PET-RAFT), etc.

Glucose oxidase (GOx) was capable of converting oxygen with D-glucose into hydrogen peroxide; therefore, it was elegantly adopted as oxygen scavenger in RAFT and ATRP under ambient atmosphere. However, the GOx-catalyzed polymerization required the thermal radical initiator to provide free radicals and needed aqueous media to dissolve the enzyme, which has some drawbacks such as limitations in polymerization of hydrophobic monomers and contaminations with enzymatic byproducts.

Based on previous reports and our previous results that triethylborane (Et₃B) with oxygen efficiently initiated radical dehalogenation, we proposed that the combination of oxygen and Et₃B could initiate and regulate the CRP. Et₃B has the unique property of reacting with oxygen molecule to spontaneously generate ethyl radical, which is able to initiate free radical transformation and polymerization at ambient temperature even at ~78°C therefore, conventional thermal radical initiators could be avoided when compared with other oxygen-tolerated CRP methods. External regulated CRP has attracted blooming attention as its allowing spatial and temporal control with current light and mechanical forces as stimuli. Oxygen could be a potential regulator in Et₃B-initiated polymerization process. As a proof-of-concept, we showed that RAFT as a model polymerization method could be initiated and temporally regulated by air (essential oxygen). This initiation system could be potentially extended to other CRP techniques such as ATRP, iodine-transfer polymerization and telluride-mediated polymerization.

The polymerization of methyl acrylate (MA) was conducted using 2-(dodecylthiocarbonothioylthio)-2-methylpropiolic acid (CTA-1) as chain transfer agent in dimethyl sulfoxide (DMSO) under ambient temperature and atmosphere without any pretreatment of removing oxygen, and the results are summarized in Table 1 and the Supporting Information, Tables S1, S2. The tetrahydrofuran solution (1m) of Et₃B was injected into the reaction mixture in the

Table 1: Polymerization of MA under various conditions via Et₃B and oxygen initiated CRP.

| Entry | Solvent | Et₃B | t [min] | Conv [%] | Mₓ,n | Mₓ,w | Mₓ/Iₓ
|-------|--------|------|--------|----------|------|------|------
| 1     | DMSO   | 2.0  | 15     | >95      | 33 000 | 29 200 | 1.15
| 2     | DMSO   | 2.0  | 60     | 32 500   | 28 000 | 1.20
| 3     | DMF    | 2.0  | 15     | 87 302   | 28 000 | 1.20
| 4     | MeCN   | 2.0  | 15     | 71 240   | 23 200 | 1.18
| 5     | DMSO   | 0.5  | 15     | 10 380   | 2000   | 1.12
| 6     | DMSO   | 1.0  | 15     | 77 260   | 19 000 | 1.14
| 7     | DMSO   | 4.0  | 15     | >98 34000 | 20400 | 1.66

[a] Reaction conditions: [MA]₀/[CTA-1]₀/[Et₃B]₀ = 400:1:x. [MA]₀ = 8 m, Et₃B solution injected at once, ambient temperature and atmosphere. [b] Determined by 1H NMR spectroscopy. [c] Calculated on the basis of conversion (that is, Mₓ,n = Mₓ,CTA + 400x conversion × Mₓ,Et3B). [d] Determined by SEC in THF, based on linear PMMA calibration standards. [e] All of the solutions were degassed and kept in nitrogen atmosphere.
vial capped with a needle connecting to the atmosphere. After 15 min of stirring, the conversion of MA reached more than 95%, providing a polymer with $M_n = 29200$ and $M_w/M_n = 1.15$ (entry 1, Table 1). In a control experiment, Et$_3$B was added into the degassed reaction mixture, and no monomer conversion was detected in 1 h (entry 2), indicating oxygen was necessary for the formation of radicals. The polymerization in dimethylformamide (DMF) or acetonitrile (MeCN) was inferior and reached lower conversion (87% or 71%), but still providing the well-defined polymers (entries 3 and 4). The reaction was much less efficient with lower amount of Et$_3$B, stopping at 10% and 77% conversion with only 0.5 and 1.0 equiv Et$_3$B (molar ratio to CTA), respectively (entries 5 and 6). With 4 equiv of Et$_3$B, the reaction reached almost full conversion (entry 7), yielding the polymer with broad distribution and much lower molecular weight compared to the theoretical value, which suggested that excess radicals, formed from Et$_3$B and oxygen, initiated short chains during the late stage of polymerization.

With optimized conditions ([MA]$_0$:[CTA-1]:[Et$_3$B]$_0$ = DP:1:2, [MA]$_0$ = 8 m in DMSO) the polymerization of MA was investigated for various targeted degrees of polymerization (DP = 50, 100, 200, 400, and 800). The polymerization was almost completed (> 95% monomer conversion) in 15 min, and polymers were obtained with low dispersity (ca. 1.20) and predetermined molecular weights (Figure 1a and b). Chain extension of homopolymer PMA showed the high retention of chain end functionality of synthesized polymer (Supporting Information, Figures S5 and S9). The temporal control of this process was investigated by using oxygen as an external regulator (Figure 1c). The kinetic results showed that injecting air (1 mL) into the degassed solution turned on the reaction whereas the polymerization was almost stopped without feeding the fresh air. Re-feeding the air into the solution restarted the reaction, and higher conversion was reached after five successive on/off cycles. The final obtained polymer still showed low dispersity and molecular weight, in agreement with theoretical values (Supporting Information, Figure S6), indicating good control was maintained throughout all these periods.

High-throughput screening was later utilized to discover the suitable combination for five different CTA and five monomers (Figure 2a). Monomers and CTA were firstly mixed in DMSO at low volume (600 μL) in a 5 × 5 matrix in microtiter well plates on the benchtop, and subsequently Et$_3$B was injected. The polymerizations were then evaluated by three factors: conversion of monomers, initiation efficiency ($W_1 = M_{w,SEC}/M_{w,th}$), and molecular weight distribution. To ensure that screening method was reliable, the same polymerizations of MA were evaluated using four CTA. The results showed that the PMA, poly(methyl acrylate), synthesized at low volume in microtiter well plates can be compared with the reaction in the traditional reaction flask (Supporting Information, Table S3). For example, CRP with CTA-1 and MA reached almost full conversion and provided PMA ($M_n = 31600$ and $M_w/M_n = 1.19$) in screening test, which was very similar to the values indicated as entry 1 in Table 1. The 5 × 5 high-throughput screening results are summarized in Figure 2c and the Supporting Information, Table S4. Three acrylates (methyl, ethyl, tert-butyl) had an ideal compatibility with CTA-1, -2, -3, and -4 in Et$_3$B and oxygen-initiated RAFT, while polymerization of NIPAm with CTA-1 was superior to other CTA. Since polymerization of MMA was much slower compared to acrylate, the reaction time was prolonged to 4 h, showing a suitable compatibility between CTA-4 and MMA but with some imperfection in conversion and dispersity.

Besides screening the polymerization conditions, high-throughput concept was also extended to synthesize a library containing various polymers with different DP and composition (for example, statistical and block copolymers). The optimized conditions using CTA-1 was also applied to high-throughput synthesis, and 25 reactions were performed in microtiter well plates simultaneously (see the Supporting Information). The synthesized polymers were analyzed by $^1$H NMR spectroscopy and SEC, showing well-defined polymers with pre-determined MW, low dispersity and full conversion (Supporting Information, Tables S5–S7 and Figures S7–S9).

This technique can also be expanded to have a spatial control by a painting-on-a-surface approach. Monomer MA and CTA-1 were mixed together at 100/1 ratio, and tetra-bromofluorescein was added to visualize the painting process. Triethylborane was added after degassing the reaction.

![Figure 1](image-url)
mixture. The solution was taken out with a syringe and added dropwise to the writing brush. The Chinese characters “Fudan” were written on the flat glass surface with the brush containing the reaction solution (Figure 3). As soon as the reaction mixture was painted on the surface, the excess surrounding oxygen immediately initiated CRP to form a film. Three points were scraped off the painted characters and were dissolved in THF for further characterizations. The painted film was uniform, having similarities in both molecular weights ($M_n = 9600, 10400, \text{and } 10400$) and distributions ($M_w/M_n = 1.14, 1.16, \text{and } 1.18$) for three selected points.

The autoxidation of triethylborane was briefly shown and discussed in Figure 2b.\[2,7,17\] The initial homolytic substitution ($S_H^2$) between triethylborane and oxygen molecule provided ethyl radical (Et) and boryl peroxyl radical (BOO$^\cdot$). The ethyl radical was key initiating radicals. However, it also rapidly reacted with excess oxygen, forming ethylperoxy radical (EtOO$^\cdot$) that was not able to initiate the radical polymerization. The ethylperoxy radical was involved in another $S_H^2$ reaction with triethylborane to form active ethyl radical and corresponding oxidized boron product Et$_2$B(OOEt). The first oxidized boron adduct could be cleaved and rearranged to EtB(OEt)$_2$, and finally formed B(OEt)$_3$. Three key boron intermediates were all detected by $^{11}B$ NMR spectroscopy (Supporting Information, Figure S10).

In summary, the property of autoxidation by triethylborane was utilized in controlled radical polymerization. Without any process of removing oxygen, the polymerization was

Figure 2. a) Structures of selected monomers and RAFT agents; b) mechanism for radical initiation by triethylborane and oxygen; c) results obtained from high-throughput screening test under conditions ([Monomer]:[CTA]:[Et$_3$B] = 400:1.2, [M]$_0$ = 8 m in DMSO, ambient temperature and atmosphere); left pie segment: conversion; right segment: initiation efficiency; bottom segment: molecular weight distributions.

Figure 3. Painting on a surface and characterizations of polymer films.
powerful and rapid to yield well-defined polymers. Regarding to the easy operation of polymerization, high-throughput screening and synthesis were combined with this technique to discover the suitable polymerization conditions and to synthesize a polymer library. To the best of our knowledge, oxygen was first time to behave as an external regulator to have temporal and spatial control in controlled radical polymerization. This process would be next extended to other RDRP methods as well as applied in material and biological areas.

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**Conflict of interest**

The authors declare no conflict of interest.

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