<table>
<thead>
<tr>
<th>Title</th>
<th>Solvent-Selective Reactions of Alkyl Iodide with Sodium Azide for Radical Generation and Azide Substitution and Their Application to One-Pot Synthesis of Chain-End-Functionalized Polymers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Author(s)</td>
<td>Wang, Chen-Gang; Goto, Atsushi</td>
</tr>
<tr>
<td>Date</td>
<td>2017</td>
</tr>
<tr>
<td>URL</td>
<td><a href="http://hdl.handle.net/10220/44315">http://hdl.handle.net/10220/44315</a></td>
</tr>
<tr>
<td>Rights</td>
<td>© 2017 American Chemical Society (ACS). This is the author created version of a work that has been peer reviewed and accepted for publication by Journal of the American Chemical Society, American Chemical Society (ACS). It incorporates referee’s comments but changes resulting from the publishing process, such as copyediting, structural formatting, may not be reflected in this document. The published version is available at: [<a href="http://dx.doi.org/10.1021/jacs.7b05879">http://dx.doi.org/10.1021/jacs.7b05879</a>].</td>
</tr>
</tbody>
</table>
Solvent-Selective Reactions of Alkyl Iodide with Sodium Azide for Radical Generation and Azide Substitution and Their Application to One-Pot Synthesis of Chain-End Functionalized Polymers

Chen-Gang Wang, Atsushi Goto*

Division of Chemistry and Biological Chemistry, School of Physical and Mathematical Sciences, Nanyang Technological University, 21 Nanyang Link, 637371 Singapore

ABSTRACT: Herein, a new reaction of an alkyl iodide (R–I) with an azide anion (N₃⁻) to reversibly generate the corresponding alkyl radical (R·) is reported. Via this new reaction, N₃⁻ was used as an efficient catalyst in living radical polymerization, yielding a well-defined polymer-iodide. A particularly interesting finding was the solvent selectivity of this reaction; namely, R–I and N₃⁻ generated R· in non-polar solvents, while the substitution product R–N₃ was generated in polar solvents. Exploiting this unique solvent selectivity, a one-pot synthesis of polymer–N₃ was attained. A particularly interesting finding was the solvent selectivity of this reaction; namely, R–I and N₃⁻ generated R· in non-polar solvents, while the substitution product R–N₃ was generated in polar solvents. Using the chain-end N₃⁻, the obtained linear and brush polymers were connected to functional molecules via an azide-alkyne click reaction. The attractive features of this system include facile operation, access to unique polymer designs, and no requirement for using excess NaN₃. In addition to N₃⁻, thiocyanate (–SCN) and cyanate (–OCN) anions were also studied.

INTRODUCTION

Solvent-selective reactions offer unique synthetic approaches in organic chemistry.¹⁻⁴ In different solvents, different products are selectively generated from the same reactant. Solvent is one of the most useful stimuli that can switch the reactions from one to another. Thus, multiple reactions may be regulated in one pot by simply altering the solvent qualities.

A reaction of an alkyl halide (R–X) with sodium azide (NaN₃) is useful for synthesizing an alkyl azide (R–N₃).⁵ The subsequent copper-catalyzed cycloaddition of R–N₃ and an alkyne is a so-called “click” reaction and is extensively exploited to connect various molecules to R.⁶,⁷

Our research group is interested in the generation of a carbon-centered radical (R·) from an alkyl iodide (R–I) using a catalyst.⁸⁻¹² In this paper, we report the unprecedented finding that the reaction of R–I with NaN₃ generated not only R–N₃ but also R· with a catalytic role of NaN₃. A particularly interesting finding was the solvent selectivity of this reaction. Namely, R· was generated in non-polar solvents, and R–N₃ was generated in polar solvents selectively. This finding inspired us with a unique application, i.e., the one-pot synthesis of azide-chain-end-functionalized polymers by selectively controlling the two reactions with solvents (Scheme 1), as described below.

Chain-end-functionalized polymers are employed in many applications.¹³,¹⁴ Because chain-end-functionalized polymers can be connected with other polymers, they are used as building blocks for synthesizing novel block copolymers as well as star, comb, and network polymers. They can also be connected to small molecules and biomolecules and also onto solid surfaces to generate polymer brushes on the surfaces. Chain-end-functionalized polymers can thus create novel materials.

Scheme 1. One-pot synthesis of N₃⁻-chain-end functionalized polymer via solvent-dependent dual works of NaN₃.

(a) Reversible activation (general scheme)

(b) Catalysis with I⁻

(c) Catalysis with N₃⁻

Living radical polymerization (LRP) is a useful method for synthesizing low-polydispersity polymers with well-defined structures.¹⁵⁻⁵⁰ LRP is based on the reversible activation of a dormant species (polymer–X) to a propagating radical (polymer·) (Scheme 2a). A range of chain-end functionalized poly-
mers are synthesized by the post- transformation of the capping agent X to functional groups.

Atom transfer radical polymerization (ATRP) utilizes chloride and bromide as X and yields polymer-chloride and polymer-bromide chains. The post- transformation of these polymer chains with NaN₃ efficiently provides polymer-azide (polymer–N₃), and applications of polymer–N₃ have been extensively developed. Polyacrylates and polyacrylates are used in most cases. Polymethacrylates are rarely used, likely because of the low reactivity of the nucleophilic substitution of N₃ for the tertiary alkyl chloride and bromide. A literature used a 10-fold excess of NaN₃ to convert polymethacrylate-bromide to polyacrylate-N₃. The use of a large amount of azide causes potential safety problems and limits the synthesis of polymethacrylate-N₃. Polymethacrylate-N₃ is highly desirable but its synthesis is still challenging.

We previously reported that R–I reversibly generates R* in the presence of iodide anion (I−) as a catalyst. Several organic and alkali-metal salts such as tetrabutylammonium iodide (Bu₄N+I−) and sodium iodide (NaI) were employed as catalysts. Such a role of I− had been unprecedented in chemistry. We utilized this reaction to the reversible activation of polymer–I to polymer* and developed a new LRP system (Scheme 2b), where X is iodide and the catalyst is I−. This LRP system is attractive because no special capping agents or expensive catalysts are required.

Based on our previous study, we wondered whether pseudo-halides such as an azide anion (N₃−) could also work as catalysts for the reversible generation of R* from R–I (Scheme 2c). The use of N₃− in such a manner is new in chemistry. We suppose that N₃− coordinates the iodide of R–I to form an R–I/N₃− complex and that R–I/N₃− subsequently releases R* and I*/N₃−. This is the first use of halogen bonding (non-covalent bonding of halogen and nitrogen) between R–I and N₃− to generate R*. The concept of halogen bonding has gained increased recognition, particularly in crystal engineering.

While our system is reversible, the irreversible generation of R* from alkyl halides using organic radical anions through single electron transfer (SET) was reported. The SO₂ radical system was used to initiate SET-degenerate chain transfer (SET-DT) polymerization.

In this paper, we report the unique reaction of R–I with N₃− to reversibly generate R* and the application of N₃− as a useful catalyst in LRP. We found that not only N₃− but also thiocyanate (SCN) and cyanate (OCN) anions work as catalysts. The catalysts are amenable to a range of monomers encompassing methacrylates, acrylates, and functional monomers. A particularly significant finding was the solvent selectivity of this reaction; namely, R–I and the pseudo-halides can generate R* in non-polar solvents and substitution products (R–N₃ and R–SCN) in polar solvents. The radical generation and substitution reactions can be switched by simply altering the solvent polarity. A unique application of this solvent selective reaction presented in this paper is the one-pot synthesis of N₃-chain-end-functionalized polymers with the dual use of N₃− for conducting the LRP in “non-polar” solvents (catalyst) and the subsequent chain-end transformation in “polar” solvents (substitution agent) by simply adding polar solvents after the LRP. The one-pot synthesis was further applied to obtain N₃-chain-end-functionalized polymer brushes on a surface, enabling unique control of the N₃ coverage (number density). Notably, this approach also enabled us to synthesize N₃-chain-end polymethacrylates without using a large excess of azide, overcoming the challenge mentioned above.

RESULTS AND DISCUSSION

Experimental Proof of the Generation of R* from R–I Using NaN₃. A radical trap experiment was performed to confirm the generation of R* from R–I catalyzed by NaN₃. The radical CP* is trapped by TEMPO, thereby yielding CP–TEMPO. Figure 2a shows the 1H NMR spectrum of the reaction mixture. After 3 h, new signals appeared and matched those of pure CP–TEMPO that was independently prepared. No substitution product, CP–N₃, was generated. (Figures 2c and 2d show the spectrum of pure CP–I and CP–N₃, respectively, for reference.) The result clearly demonstrates the generation of R* from R–I using NaN₃ in a selective manner in the non-polar solvent.

**Figure 1.** Structures of alkyl iodides, catalysts & substitution agents, and crown ether used in this work.

**Figure 2.** 1H NMR (500 MHz) spectra of toluene-d₈ solutions. (a) CP-I (20 mM), NaN₃ (20 mM), crown-ether (20 mM), and TEMPO (40 mM) heated at 70 °C for 3 h, (b) CP-I (20 mM), Na₂CO₃ (20 mM), and crown-ether (20 mM) heated at 70 °C for 3 h, (c) pure CP-I, and (d) pure CP-N₃.
Figure 2b shows the same reaction but without TEMPO. Virtually 100% of the CP−I remained. This result means that the generation of CP• from CP−I with NaN3 is reversible. Again, no CP−N3 was generated. Taking advantage of this reversible nature, we utilized NaN3 as a catalyst for the polymerization (LRP), as described later.

Solvent-Selective Reaction of R−I with NaN3. We found that the reaction of R−I with NaN3 selectively yields R−N3 in polar solvents and R• in non-polar solvents. We used ethyl 2-iodo-2-methylpropanoate (EMA−I (Figure 1)) as an R−I, which is a unimer model of polymethacrylate-iodide. We heated EMA−I (20 mM), NaN3 (20 mM), and 18-crown-6-ether (20 mM). Dimethyl sulfoxide (DMSO)-d6 was used as a polar solvent, while a mixture of toluene-d8 (70%) and acetone-d6 (30%) was used as a non-polar solvent. This mixture of toluene-d8 (dielectric constant ε = 2.4) and acetone-d6 (ε = 20.7) is a model of methyl methacrylate (MMA) medium (ε = 7.9).

Figure 3a shows the reaction in DMSO-d6 heated at 50 °C for 1 h. EMA−I was quantitatively (100%) converted to EMA−N3 (Figure 3c), and no EMA−I (Figure 3b) remained. Figure 3d shows the reaction in the toluene-d8/acetone-d6 mixture at 50 °C for 1 h. Only 11% of EMA−I was converted to EMA−N3 (Figure 3i), and most (89%) of EMA−I (Figure 3e) remained. The remaining EMA−I underwent only a reversible generation of EMA•. (Virtually no radical-radical termination product of EMA• was observed, because of the low concentration of EMA•.) These results demonstrate that the reaction of R−I with NaN3 can be selectively controlled to generate EMA−N3 in polar solvents and R• in non-polar solvents.

Polymerizations of MMA Using NaN3 as a Catalyst. We exploited the catalytic role of NaN3 (to reversibly generate R• from R−I) in the LRP of MMA. MMA is a non-polar medium. We heated a mixture of MMA (8 M), CP−I (80 mM) as a low-mass dormant species (alkyl iodide initiator), NaN3 (40 mM) as a catalyst, and 18-crown-6-ether (40 mM) for the dissolution of NaN3 at 70 °C.

Although the exact mechanism for the reversible activation with NaN3 remains unclear, we suppose the following scheme. Na+′N3− activates polymer−I, thereby generating polymer∗ and Na+(N3•−) (Scheme 3a). A few monomers are added to polymer∗ until polymer∗ is deactivated to regenerate polymer−I. Because Na+′(N3•−) is not a stable radical, two Na+(N3•−) species may react with each other to produce Na′N3− and Na′(I2N3−) as stable species (Scheme 3b). Na′N3− acts as an activator, whereas Na′(I2N3−) acts as a deactivator (Scheme 3c). Polymer∗ can thus be deactivated by either Na′(N3•−) (Scheme 3a) or Na′(I2N3−) (Scheme 3c). The activation-deactivation cycles are repeated, and hence the polymer chain grows little by little, yielding a low-polydispersity polymer. Again, this supposed mechanism is not definitive, and the exact mechanism needs be clarified.

Scheme 3. Possible mechanism of reversible activation with N3− catalyst.

\[
\text{polymer-I} + \text{Na}^+\text{N}_3\text{O} \rightleftharpoons \text{polymer}^* + \text{Na}^+\text{IN}_3\text{O} \quad (a)
\]
\[
2 \text{Na}^+\text{IN}_3\text{O} \rightarrow \text{Na}^+\text{N}_3\text{O} + \text{Na}^+\text{I}_2\text{N}_3\text{O} \quad (b)
\]
\[
\text{polymer}^* + \text{Na}^+\text{I}_2\text{N}_3\text{O} \rightarrow \text{polymer-I} + \text{Na}^+\text{IN}_3\text{O} \quad (c)
\]
Table 1. Bulk Polymerizations of MMA with R–I, Catalyst, and Crown Ether.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Target DP</th>
<th>R–I</th>
<th>Catalyst</th>
<th>[MMA]0([CP–I]0/[catalyst]0/[crown ether]0/[I2]0) (mM)</th>
<th>T (°C)</th>
<th>t (h)</th>
<th>Conv (%)</th>
<th>Mn (Mn,th)</th>
<th>PDI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>100</td>
<td>CP–I</td>
<td>NaN3</td>
<td>8000/80/40/40/0</td>
<td>70</td>
<td>5</td>
<td>80</td>
<td>7900 (8000)</td>
<td>1.26</td>
</tr>
<tr>
<td>2</td>
<td>100</td>
<td>CP–I</td>
<td>NaN3</td>
<td>8000/80/40/40/1</td>
<td>70</td>
<td>6</td>
<td>91</td>
<td>9400 (9100)</td>
<td>1.24</td>
</tr>
<tr>
<td>3</td>
<td>100</td>
<td>CP–I</td>
<td>NaN3</td>
<td>8000/80/40/40/1</td>
<td>70</td>
<td>10</td>
<td>78</td>
<td>8000 (7800)</td>
<td>1.15</td>
</tr>
<tr>
<td>4</td>
<td>100</td>
<td>CP–I</td>
<td>BNSCN</td>
<td>8000/80/40/0/0</td>
<td>70</td>
<td>10</td>
<td>75</td>
<td>7300 (7500)</td>
<td>1.24</td>
</tr>
<tr>
<td>5</td>
<td>100</td>
<td>CP–I</td>
<td>NaN3</td>
<td>8000/80/160/160/1</td>
<td>70</td>
<td>8</td>
<td>75</td>
<td>8000 (7500)</td>
<td>1.28</td>
</tr>
<tr>
<td>6</td>
<td>200</td>
<td>CP–I</td>
<td>NaN3</td>
<td>8000/80/40/40/1</td>
<td>70</td>
<td>10</td>
<td>84</td>
<td>20000 (17000)</td>
<td>1.33</td>
</tr>
<tr>
<td>7</td>
<td>400</td>
<td>CP–I</td>
<td>NaN3</td>
<td>8000/20/40/40/1</td>
<td>70</td>
<td>24</td>
<td>88</td>
<td>42000 (36000)</td>
<td>1.42</td>
</tr>
<tr>
<td>8</td>
<td>100</td>
<td>EPh–I</td>
<td>NaN3</td>
<td>8000/80/40/0/0</td>
<td>70</td>
<td>5</td>
<td>92</td>
<td>10300 (9200)</td>
<td>1.30</td>
</tr>
<tr>
<td>9</td>
<td>100</td>
<td>EMA–I</td>
<td>NaN3</td>
<td>8000/80/40/40/0</td>
<td>70</td>
<td>8</td>
<td>79</td>
<td>17000 (7900)</td>
<td>1.70</td>
</tr>
<tr>
<td>10</td>
<td>100</td>
<td>EMA–I</td>
<td>NaN3</td>
<td>8000/80/40/40/3</td>
<td>70</td>
<td>24</td>
<td>91</td>
<td>9100 (9600)</td>
<td>1.39</td>
</tr>
<tr>
<td>C1</td>
<td>100</td>
<td>CP–I</td>
<td>BNI</td>
<td>8000/80/40/0/0</td>
<td>70</td>
<td>4</td>
<td>91</td>
<td>9400 (9100)</td>
<td>1.21</td>
</tr>
</tbody>
</table>

* Target degree of polymerization at 100% monomer conversion (calculated by [MMA]0/[CP–I]0). † Theoretical Mn calculated with [MMA]0/[CP–I]0, and monomer conversion.

Figure 4. Plots of (a) ln([M]0/[M]) vs t and (b) Mn and Mw/Mn vs conversion for the MMA/CP–I/NaN3 systems (70 °C): [MMA]0 = 8 M; [CP–I]0 = 80 mM; [NaN3]0 = 40 mM; [crown ether]0 = 40 mM; [I2]0 = 0 or 1 mM, or [MMA]0 = 8 M; [CP–I]0 = 80 mM. The symbols are indicated in the figure.

Figure 5. Plots of (a) ln([M]0/[M]) vs t and (b) Mn and Mw/Mn vs conversion for the MMA/CP–I/catalyst (crown ether)/I2 systems (70 °C): [MMA]0 = 8 M; [CP–I]0 = 80 mM; [crown ether]0 = 40 or 160 mM, [crown ether]0 = 0, 40, 160 mM; [I2]0 = 1 mM. The symbols are indicated in the figure.

Figure 4 (filled circles) and Table 1 (entry 1) show the polymerization result. The polymerization proceeded up to 80% monomer conversion in 5 h, confirming the generation of the carbon-centered radical (the propagating radical) from CP–I and NaN3. No polymerization proceeded without CP–I or NaN3, again confirming that the radical was generated by the combination of CP–I and NaN3. However, the polydispersity index (PDI) (= Mn/Mw) was larger than 1.5 at an early stage of polymerization (Figure 4 (filled circles)), where Mn and Mw were the weight- and number-average molecular weights, respectively. This is because a sufficient amount of the deactivator Na(I2N3) did not accumulate at an early stage of polymerization, at which many monomers added to polymer chains.

Therefore, we added a small amount of molecular iodine (I2), which forms Na(I2N3) with NaN3. In fact (Figure 4 (squares) and Table 1 (entry 2)), with the addition of 1 mM of I2 (as little as 1/40 equivalent to NaN3), Mn agreed with the theoretical value (Mn,th) and PDI was approximately 1.3 from an early stage of polymerization. In this case, the degree of polymerization (DP) expected at full (100%) monomer conversion was 100, because the [MMA]0/[CP–I]0 ratio was set to 100. Importantly, PDI also remained small (approximately 1.2) up to high conversions (nearly 90%), thereby illustrating the success of this LRP. Figure 4 (open circles) and Table 1 (entry C1) show the same polymerization but using BNI (Bu4N+I–) which is one of the most effective catalysts previously used in the LRP. NaN3 led to a slower polymerization than BNI but provided control of the molecular weight and PDI as efficiently as BNI, demonstrating the usefulness of the NaN3 catalyst. We were able to reduce the amount of NaN3 from 40 mM (Table 1 (entry 2)) to 5 mM (Supporting Information (Table S1 and Figure S6)) to control PDI, although the polymerization rate decreased with a reduced amount of NaN3 as expected from the equilibrium in Scheme 2c.

Polymers of MMA Using Different Catalysts. Instead of NaN3, we used SCN and OCN as catalysts. Figure 5 and Table 1 (entries 3–5) show the results with NaSCN, Bu4N+(SCN) (BNSCN) and NaOCN. In all cases, the polymerization proceeded smoothly, Mn well agreed with Mn,th and PDI was small, i.e., approximately 1.2. The cationic counterpart of BNSCN is organic, and hence the polymerization system is completely metal-free. Crown-ether is also unnecessary for BNSCN. Thus, NaN3, SCN, and OCN are all efficient catalysts of LRP.

Toward Higher Molecular Weights. We targeted higher DPs of 200 and 400 (expected at 100% monomer conversion) using NaN3 (Table 1 (entries 6 and 7) and Supporting Information (Figures S7 and S8)). We obtained low-polydispersity polymers.
Other Alkyl Iodide Initiators. Besides CP-I, we used ethyl α-iodophenylacetate (EPh-I) and EMA-I as alkyl iodide initiators (Figure 1) with NaN₃ as a catalyst for the MMA polymerization (Figure 6 and Table 1 (entries 8-10)). A mixture of MMA (8 M), an alkyl iodide (80 mM), NaN₃ (40 mM) and 18-crown-6-ether (40 mM) was heated at 70 °C. EPh-I was a highly efficient alkyl iodide initiator (Figure 6 (circles) and Table 1 (entry 8)). The $M_n$ agreed with the theoretical value ($M_{n, theo}$), and the PDI was small (1.1-1.2) from an early stage of polymerization, suggesting the fast initiation from EPh-I. EMA-I exhibited a deviation of $M_n$ from $M_{n, theo}$ and large PDI values (approximately 1.7) (Figure 6 (squares) and Table 1 (entry 9)). In this system, the addition of a small amount (3 mM) of I₂ led to good control of $M_n$ and PDI (≈ 1.2-1.4) (Figure 6 (triangles) and Table 1 (entry 10)). Thus, EPh-I and EMA-I can also be used with the NaN₃ catalyst.

Acrylate and Other Methacrylates. The monomer scope of the NaN₃ catalyst encompassed other hydrophobic methacrylates with butyl (BMA), lauryl (LMA), and benzyl (BzMA) groups as well as MMA (Figure 2 (entries 1-3)). A methacrylate with an amphiphilic poly(ethylene glycol) (PEGMA) group (Table 2 (entry 4)) was also successfully used in a hydrophobic solvent (50% of toluene).

Besides methacrylates, the NaN₃, BNSCN, and NaOCN catalysts were amenable to an acrylate, butyl acrylate (BA), attaining low polydispersity ($PDI = 1.2-1.3$) (Figure 7 and Table 2 entries 5-7)). Because the carbon–iodine bond in an acrylate polymer (with a secondary alkyl chain end) is stronger than that in a methacrylate polymer (with a tertiary alkyl chain end), highly reactive catalysts are necessary for controlling the polymerization of acrylate. The successful use of these catalysts to BA demonstrates their high reactivity. The relatively slow polymerization of BA is attributed to the addition of I₂ for controlling the polydispersity.

One-Pot Synthesis of N₃-Chain-End Functionalized Polymers. We carried out a one-pot synthesis of poly(methyl methacrylate)-azide (PMMA–N₃) via the polymerization of MMA in a non-polar solvent (toluene) followed by the addition of a polar solvent (DMF) for the chain-end transformation. We heated a mixture of MMA (8 M), CP-I (270 mM), NaN₃ (300 mM), 18-crown-6-ether (300 mM), I₂ (3 mM), and toluene (toluene/MMA = 25/75%) at 70 °C for 3 h (Table 3 (entry 1)). To clearly characterize the chain end, we targeted a relatively short chain and obtained a PMMA–I with $M_n = 3100$ and PDI = 1.17 at 79% monomer conversion. Without purifying the polymer, we directly added the polar solvent DMF (DMF/polymerization solution = 2/1) to the polymerization solution for the chain-end transformation. PMMA–N₃ was obtained after 12 h at room temperature without significant change of $M_n (= 3400)$ and PDI (= 1.16) through the transformation.

**Table 2. Bulk Polymerizations of Several Monomers with CP–I, Catalyst, and Crown Ether.**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Monomer</th>
<th>Target DP*</th>
<th>Catalyst</th>
<th>$[M_J]/[CP–I]/[crown ether]/[I_2]$ (mM)**</th>
<th>$T$ (°C)</th>
<th>$t$ (h)</th>
<th>Conv (%)</th>
<th>$M_n$ (PMMA-calibrated GPC)</th>
<th>$PDI^f$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>BMA</td>
<td>100</td>
<td>NaN₃</td>
<td>8000/80/40/40/0</td>
<td>70</td>
<td>24</td>
<td>78</td>
<td>12000 (11000)</td>
<td>1.32</td>
</tr>
<tr>
<td>2</td>
<td>LMA</td>
<td>100</td>
<td>NaN₃</td>
<td>8000/80/40/40/0</td>
<td>70</td>
<td>90</td>
<td>51</td>
<td>17000 (13000)</td>
<td>1.29</td>
</tr>
<tr>
<td>3</td>
<td>BzMA</td>
<td>100</td>
<td>NaN₃</td>
<td>8000/80/40/40/0</td>
<td>70</td>
<td>12</td>
<td>72</td>
<td>13000 (13000)</td>
<td>1.33</td>
</tr>
<tr>
<td>4</td>
<td>PEGMA</td>
<td>100</td>
<td>NaN₃</td>
<td>8000/80/80/80/2</td>
<td>70</td>
<td>48</td>
<td>100</td>
<td>29000 (30000)</td>
<td>1.45</td>
</tr>
<tr>
<td>5</td>
<td>BA</td>
<td>100</td>
<td>BNSCN</td>
<td>8000/80/40/40/10</td>
<td>110</td>
<td>48</td>
<td>43</td>
<td>7400 (5600)</td>
<td>1.24</td>
</tr>
<tr>
<td>6</td>
<td>BA</td>
<td>100</td>
<td>NaOCN</td>
<td>8000/80/20/0/2</td>
<td>110</td>
<td>40</td>
<td>65</td>
<td>8600 (8300)</td>
<td>1.35</td>
</tr>
<tr>
<td>7</td>
<td>BA</td>
<td>100</td>
<td>NaN₃</td>
<td>8000/80/80/80/2</td>
<td>110</td>
<td>48</td>
<td>65</td>
<td>7300 (8300)</td>
<td>1.30</td>
</tr>
</tbody>
</table>

*Target degree of polymerization at 100% monomer conversion (calculated by $[M_J]/[CP–I]$). **$M = $ monomer. *PMMA-calibrated GPC values. †Theoretical $M_n$ calculated with $[M_J]$, [CP–I], and monomer conversion. ‡Diluted with toluene (50% PEGMA and 50% toluene).
Table 3. One-Pot Synthesis of Chain-End Functionalized Polymers.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Target</th>
<th>Catalyst</th>
<th>[MMA]₀/[CP−I]₀/[catalyst]₀/[crown ether]₀/[I₂]₀ (mM)</th>
<th>Solvent</th>
<th>T (°C)</th>
<th>t (h)</th>
<th>Conv (%)</th>
<th>Mₙ (Mₙ,tho)</th>
<th>PDID</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>30</td>
<td>NaN₃</td>
<td>8000/270/300/300/3</td>
<td>toluene</td>
<td>70</td>
<td>3</td>
<td>79</td>
<td>3100 (2400)</td>
<td>1.17</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>+ DMF</td>
<td></td>
<td>rt</td>
<td>12</td>
<td>–</td>
<td>3400</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>50</td>
<td>NaN₃</td>
<td>8000/160/180/180/2</td>
<td>toluene</td>
<td>70</td>
<td>5</td>
<td>84</td>
<td>5000 (4200)</td>
<td>1.17</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>+ DMF</td>
<td></td>
<td>rt</td>
<td>12</td>
<td>–</td>
<td>5300</td>
<td>1.15</td>
</tr>
<tr>
<td>3</td>
<td>100</td>
<td>NaN₃</td>
<td>8000/80/90/90/1</td>
<td>toluene</td>
<td>70</td>
<td>10</td>
<td>83</td>
<td>8400 (7600)</td>
<td>1.16</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>+ DMF</td>
<td></td>
<td>rt</td>
<td>12</td>
<td>–</td>
<td>8200</td>
<td>1.19</td>
</tr>
<tr>
<td>4</td>
<td>30</td>
<td>BNSCN</td>
<td>8000/270/330/0/3</td>
<td>toluene</td>
<td>70</td>
<td>8</td>
<td>74</td>
<td>2600 (2200)</td>
<td>1.19</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>+ DMF</td>
<td></td>
<td>60</td>
<td>12</td>
<td>–</td>
<td>2700</td>
<td>1.21</td>
</tr>
</tbody>
</table>

a Target degree of polymerization at 100% monomer conversion (calculated by [MMA]₀/[CP−I]₀).

b Theoretical Mₙ calculated with [MMA]₀, [CP−I]₀, and monomer conversion.

c Solution polymerization with toluene (25%) and MMA (75%).

d Addition of DMF to the polymerization solution (DMF/polymerization solution = 2/1). The Mₙ and PDI values are those after purification by reprecipitation.

The infrared (IR) spectrum of the polymer after the chain-end transformation showed a characteristic absorption band for N₃ at 2120 cm⁻¹ (Figure 8c), demonstrating the successful generation of PMMA−N₃. The polymer obtained after the polymerization showed virtually no absorption of N₃ (Figure 8b), and the spectrum matched that of a PMMA−I independently synthesized using the BNI catalyst under an azide-free condition (Figure 8a). Thus, the chain-end transformation occurred only after the addition of DMF (a polar solvent). Substitution may occur by an SN₂ mechanism or be mediated by DMF via an Sₛ₂2 mechanism or be mediated by DMF via an Sₛ₁ or SET mechanism.

The obtained polymers were further analyzed by ¹H NMR (Figure 9). The methyl protons at the side chain appeared at 3.52-3.80 ppm. After the polymerization (Figure 9a), a downfield peak at 3.73-3.76 ppm appeared and is assigned to the o-terminal chain-end unit (a’) adjacent to iodide. This assignment was previously confirmed with a PMMA−I synthesized in an azide-free condition. After the chain-end transformation (Figure 9b), the peak was shifted further downfield to 3.74-3.80 ppm, which is most likely assigned to the chain-end unit (a”) adjacent to N₃. Although this assignment is not definitive, the observed peak shift suggests the transformation of the chain end. The polymer after the polymerization (Figure 9a) displayed a minor peak at 3.74-3.80 ppm for N₃, but the peak was rather small, confirming high fidelity of iodide chain-end during the polymerization.

We attempted to use matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF-MS) for further analysis. However, the carbon-iodide and carbon-azide bonds were so weak that the bonds could be cleaved during the MALDI-TOF-MS analysis, and useful spectra were not obtained.

Figure 8. IR spectra of PMMA-I obtained with (a) BNI and (b) NaN₃ catalysts, (c) PMMA-N₃, (d) PMMA-SCN, and (e) PMMA-PEG. The reaction conditions are given in Tables 3 and 4.

Figure 9. ¹H NMR spectrum (CDCl₃) of (a) PMMA-I obtained after the polymerization in toluene and (b) PMMA-N₃ obtained after the addition of DMF, and (c) PMMA-PEG obtained after click reaction. The reaction conditions for (a) and (b) are given in Table 3 (entry 1). The reaction condition for (c) is given in Table 4 (entry 1).
For quantitative characterization, the polymer after the transformation was studied by elemental analysis (EA) (Table 4 (entry 1)). N(exp) is the nitrogen content experimentally determined by EA. N(theo) is the nitrogen content theoretically calculated from the Mn determined by GPC and on the assumption that all of the polymer chains possess N3 at the growing chain end and a cyano-containing CP group at the initiating chain end. The fraction of N3 at the chain end (Table 4) was calculated by \((N(\text{exp}) - N(\text{theo}) \times 1/4)/(N(\text{theo}) \times 3/4)\) to be 90% (with 10% experimental error), confirming a high yield of PMMA–N3.

A chain-extension experiment was conducted with the polymers after the polymerization (PMMA–I) and the chain-end transformation (PMMA–N3). These polymers were used as macroinitiators in the polymerization of MMA with a tetroctylammonium iodide (ONI) catalyst at 60 °C. Figure 10 shows the GPC chromatograms at 0 and 3 h. A large fraction of the PMMA–I macroinitiator (Figure 10a) extended to a high molecular weight. Only a minor peak remained for the starting peak and is attributed to terminated chains and PMMA–N3 generated during the polymerization. Upon the peak resolution, we estimated these inactive polymers (terminated chains and PMMA–N3) to be at most 10%, again confirming the high fidelity of the iodide chain-end during the polymerization. In contrast, the chain did not extend with the polymer after the chain-end transformation (Figure 10b), indicating that all of the PMMA–I was converted to PMMA–N3 after the chain-end transformation.

We prepared PMMA–N3 with higher DPs (= 51 and 80), as shown in Tables 3 and 4 (entries 2 and 3) (Supporting Information (Figures S9 and S10)). The fraction of N3 at the chain end was 93% and 99% (with 10% experimental error), respectively, showing high yields of PMMA–N3. These results clearly demonstrate the successful one-pot synthesis of PMMA–N3 in high yields (90-99%) by simply altering the solvent quality.

The amount of NaN3 used in the present experiments was 1.1 equivalent to PMMA–I. This amount is much smaller than the previously reported amount (10-fold excess of NaN3) used to convert polymethacrylate-bromide to polymethacrylate-N3. The dramatic reduction of NaN3 in the present case would be attributed to the use of iodide (PMMA–I), offering a practically attractive route for synthesizing polymethacrylate-N3.

Besides N3, we also used BNSCN to carry out a one-pot synthesis of PMMA–SCN (Table 3 (entry 4)) (Supporting Information (Figure S10)). We obtained a PMMA–SCN with \(M_n = 2700\) and PDI = 1.21. For the chain-end transformation, we used a higher temperature for SCN (60 °C) than N3 (room temperature), because the nucleophilicity of SCN is weaker than that of N3. SCN was observed in the IR spectrum at 2155 cm\(^{-1}\) (Figure 8d).

Alkyl thiocyanates (R–SCN) are used as important precursors for synthesizing various sulfur-containing compounds such as thiols, thioesters, disulfides, and sulfur-containing heterocycles.45,46 R–SCN also undergoes an addition reaction to alkynes, enabling R to connect various molecules.45 Thus, the obtained polymer–SCN is an attractive precursor for designing functional polymers.

The SCN anion is an ambident nucleophile taking SCN and NCS forms. Therefore, R–SCN and R–NCS are obtainable through the nucleophilic substitution. R–NCS is thermodynamically more stable and could be obtained at high temperatures.45 However, because the nucleophilicity of the sulfur (SCN) is higher than that of the nitrogen (NCS), R–SCN is exclusively obtainable under mild reaction conditions, under which the isomerization of R–SCN to R–NCS is avoided.45 Under the present mild condition, the formation of PMMA–NCS would be negligible.

**Synthesis of Block Copolymers via Azide-Alkyne Click Reaction.** Using an azide-alkyne cycloaddition click reaction, we synthesized an amphiphilic block copolymer. PMMA–N3 \((M_n = 3400\) and PDI = 1.16) (Table 3 (entry 1)) (1 eq) was reacted with an alkynbearing polyethylene glycol (PEG) \((M_n = 1000\) and PDI = 1.06) (1.5 eq) in the presence of a copper (CuBr) catalyst (1.5 eq) in tetrahydrofuran (THF) at 80 °C. After 24 h, we successfully obtained a PMMA–PEG amphiphilic block copolymer with \(M_n = 4300\) and PDI = 1.15 (after purification). The block copolymer was purified by reprecipitation in methanol/water (2/1) mixture; Figure 9c shows the NMR spectrum. The connected point (f) and the ethylene oxide units (g and h) of PEG clearly appeared at 4.28 ppm and 3.63-3.68 ppm, respectively. From the peak area for the methoxy units (a (g and h) of PEG, the fraction of PMMA–PEG (over all PMMA chains) was calculated to be 97% (with experimental error range of 87-100%) (Table 4 (entry 1)). The IR absorption of N3 at 2120 cm\(^{-1}\) completely disappeared (Figure 8e), meaning quantitative consumption of N3 through the click reaction. We also synthesized PMMA–PEG with longer PMMA chains (DP = 51 and 80) (Table 4 (entries 2 and 3) and Supporting Information (Figure S11)). The fraction of the PMMA–PEG chains was 94% and 82%, respectively. These results demonstrate successful synthesis of PMMA–PEG block copolymers in high yields.

![Figure 10. GPC chromatograms for the MMA/PMMA-X/ONI system (60 °C) for 0 and 3 h: [MMA]0 = 8 M; [PMMA-X]0 = 80 mM; [ONI]0 = 80 mM. PMMA-X is (a) PMMA-I and (b) PMMA-N3 prepared in Table 3 (entry 1).](image-url)
Table 4. Chain-End Functionality of PMMA–N₃.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Polymera</th>
<th>N(exp) (%)</th>
<th>N(theo) (%)</th>
<th>Fraction of N₃ chain end (%) estimated by EA</th>
<th>Fraction of N₃ chain end (%) estimated from PEG-functionalizationb</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PMMA–N₃ (DP = 32)</td>
<td>1.25</td>
<td>1.40</td>
<td>90%</td>
<td>97%</td>
</tr>
<tr>
<td>2</td>
<td>PMMA–N₃ (DP = 51)</td>
<td>0.94</td>
<td>0.99</td>
<td>93%</td>
<td>94%</td>
</tr>
<tr>
<td>3</td>
<td>PMMA–N₃ (DP = 80)</td>
<td>0.65</td>
<td>0.61</td>
<td>99%</td>
<td>82%</td>
</tr>
</tbody>
</table>

a Synthetic conditions are given in Table 3. b A mixture of PMMA–N₃ (10 wt%) (1 eq), 3-(poly(ethylene)glycol)-prop-1-ynyl (1.5 eq), CuBr (1.5 eq), N,N,N',N''-pentamethyldiethylenetriamine (2 eq), and THF (90 wt%) was stirred at room temperature for 24 h.

Table 5. One-Pot Synthesis of Azide-Chain-End Functionalized Polymer Brushes on Surface.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Target surface coverage of N₃</th>
<th>[MMA]₀/[(CP–I)₀]/[NaN₃]₀</th>
<th>[crown ether]₀ (mM)</th>
<th>t (h)</th>
<th>Conv (%)</th>
<th>M_dot,c (Mₐ, theo, d)</th>
<th>PDI</th>
<th>Thickness (nm)</th>
<th>Graft density (σ) (chain nm⁻²)</th>
<th>Surface coverage of the graft polymer</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>100%</td>
<td>8000/40/40/40</td>
<td>16</td>
<td>81</td>
<td>17400</td>
<td>1.32</td>
<td>7.0</td>
<td>0.29</td>
<td>0.16</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>75%</td>
<td>8000/40/30/30</td>
<td>20</td>
<td>87</td>
<td>18700</td>
<td>1.35</td>
<td>8.0</td>
<td>0.31</td>
<td>0.17</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>50%</td>
<td>8000/40/20/20</td>
<td>24</td>
<td>74</td>
<td>15400</td>
<td>1.35</td>
<td>8.8</td>
<td>0.41</td>
<td>0.23</td>
<td></td>
</tr>
</tbody>
</table>

Polymerization condition. The solvent was toluene (MMA/toluene = 75/25). c Conv. d Theoretical Mₙ calculated with [MMA]₀ [CP–I]₀ and monomer conversion.

Assuming that the click reaction is quantitative, these results in turn indicate high yields of PMMA–N₃ after the above mentioned reaction of PMMA–I with NaN₃ in DMF. The fraction of N₃ at the chain end estimated by EA and PEG-functionalization was 82-99% in the three studied cases (Table 4), again confirming the successful one-pot synthesis of PMMA–N₃ in high yields.

One-Pot Synthesis of Azide-Chain-End Functionalized Polymer Brushes on Surface. The one-pot synthesis was applied to obtain N₃-chain-end functionalized polymer brushes on a surface. A unique aspect studied was the control of the N₃ coverage.

The surface of a material plays crucial roles in many important properties such as thermodynamic, mechanical, chemical, and biological properties as an interface to external phases. Surface-initiated graft polymerization, in which polymerization is conducted from an initiator bound to a surface, is among the most effective surface modification methods. The use of LRP in surface-initiated graft polymerization can afford a polymer brush with a high surface density. Such a so-called concentrated polymer brush takes a highly extended chain conformation so that the chain end tends to be localized at the outermost surface of the brush layer. Thus, the chain-end can effectively interact with external phases. Such localization is not attainable by conventional semi-dilute and dilute brushes.

We conducted a one-pot synthesis of N₃-functionalized polymer brushes on a surface. We used a surface-immobilizing initiator, 6-(2-iodo-2-isobutoxy)hexyltriethoxysilane (IHE) (Figure 11a), consisting of an alkyl iodide (initiating) moiety and a triethoxysilylethoxysilane (TEOS) group. IHE was fixed on a silicon wafer through the TEOS group. The IHE-immobilized wafer was immersed in a mixture of MMA, a non-immobilized free initiator CP–I, NaN₃, crown ether, and toluene (solvent) and heated at 70 °C for the polymerization (Table 5). The free initiator CP–I was added because its addition can improve the control over the Mₙ and PDI of the graft polymer. The Mₙ and PDI of the free polymers generated from the free initiators are usually in good agreement with those of the graft polymers.

Figure 11. Surface-initiated graft polymerization of MMA. The experimental condition is given in Table 5 (entry 2). (a) Schematic illustration and (b) AFM height profile in the scratched and non-scratched areas of obtained brush.
We varied the molar ratio of NaN₃ to CP−I from 0.5, 0.75, to 1.0 for controlling the chain-end functionality of N₃ from 50%, 75%, to 100%. Because the number of brush polymers is much smaller than that of the free polymer, the N₃ functionality of the brush polymer is virtually the same as that of the free polymer and is thus controllable by the molar ratio of NaN₃ to the free initiator CP−I. Precise control of the N₃ functionality of the brush is difficult without the free polymer, because the number of the graft polymer is extremely small. The present method enables precise fractional control of the N₃ functionality of the brush by simply altering the molar ratio of NaN₃ to CP−I.

The N₃-functionalized brushes were reacted with alkynes bearing PEG and a fluorinated alkyl (C₈F₁₇) group for obtaining PEG- and C₈F₁₇-functionalized brushes. Figure 12 shows the contact angle (θ) of a water droplet on the brushes. The θ value was 79 degrees for all of the 50, 75, and 100% N₃-functionalized brushes (circles). After the PEG (hydrophilic) (squares) and C₈F₁₇ (super-hydrophobic) (triangles) functionalization, the θ value clearly decreased and increased, respectively, with an increase of the surface functionality. This result clearly demonstrates the successful fractional control of the N₃, PEG, and C₈F₁₇ functionalities of the polymer brush. This fractional control may also be applied to molecular bottle brushes and hyper-branched polymers, which will be studied in our group.

**Figure 12.** Plot of contact angle vs surface coverage of N₃, PEG, and C₈F₁₇ on PMMA brushes. The symbols are indicated in the figure. The preparation of the samples is given in Table 5.

The C₈F₁₇ functionalization of the brush was also confirmed by X-ray photoelectron spectroscopy (XPS) analysis (Supporting Information (Figure S12)), which clearly exhibited the F 1s signal.

**CONCLUSIONS**

R−I reacted with N₃, SCN, and OCN to reversibly generate R* in non-polar solvents. With this new reaction, these anions were employed as efficient catalysts for LRP. The reaction of R−I with N₃ and SCN was solvent-selective, generating substitution products (R−N₃ and R−SCN) in polar solvents. Exploiting this solvent selectivity, the one-pot synthesis of PMMA−N₃ and PMMA−SCN was achieved with the dual use of N₃ and SCN as polymerization catalysts in a non-polar solvent and substitution agents in a polar solvent. The one-pot synthesis was also applied to surface-initiated polymerization, uniquely attaining the fractional control of the N₃ functionality of the polymer brush in the desired manner. Through the N₃ functionality, the linear and brush polymers can be connected to various molecules such as biological molecules and sensing probes, possibly offering advanced materials. The facile operation, access to unique polymer designs, and no requirement for excess NaN₃ are highly beneficial in various applications.

**ASSOCIATED CONTENT**

**Supporting Information**

Experiments, syntheses of CP−N₃, EMA−N₃, and functional alkynes, polymerizations of MMA with lower concentrations of NaN₃, polymerizations of MMA for higher molecular weights, and spectral (IR, NMR, and XPS) data. This material is available free of charge via the Internet at http://pubs.acs.org.

**AUTHOR INFORMATION**

**Corresponding Author**

*agoto@ntu.edu.sg

**Notes**

The authors declare no competing financial interest.

**ACKNOWLEDGMENTS**

This work was partly supported by Start-Up-Grant of Nanyang Technological University.

**REFERENCES**

Solvent-selective reaction

R-I + N₃⁻ \rightleftharpoons R^{*} \text{ in non-polar solvent}

R-N₃ \text{ in polar solvent}

One-pot synthesis of polymer-N₃

monomer → NaN₃ → non-polar solvent → polymer-N₃ → polar solvent